CHAPTER 1

What Is Evidence-Based Physical Diagnosis?

Clinicians diagnose disease to label the patient's experience by placing it into a specific category, a process implying specific pathogenesis, prognosis, and treatment, thus allowing clinicians to explain to patients what is happening and how best to restore health. A century ago, such categorization of the patient's disease, or diagnosis, rested almost entirely on empiric observation, that is, what clinicians saw, heard, and felt at the patient's bedside. Although some technologic testing was available then (e.g., microscopic examination of sputum and urine), its role in diagnosis was meager, and almost all diagnoses were based on traditional examination (Fig. 1-1). For example, if patients presented a century ago with complaints of fever and cough, the diagnosis of lobar pneumonia rested on the presence of accompanying characteristic findings such as fever, tachycardia, tachypnea, grunting respirations, cyanosis, diminished excursion of the affected side, dullness to percussion, increased tactile fremitus, diminished breath sounds (and, later, bronchial breath sounds), abnormalities of vocal resonance (bronchophony, pectoriloquy, and egophony), and crackles. If these findings were absent, the patient did *not* have pneumonia. Chest radiography played no role in diagnosis because it was not widely available until the early 1900s.

Modern medicine, of course, relies on technology much more than medicine did a century ago (to our patients' advantage), and for many modern categories of disease the diagnostic standard is a technologic test (see Fig. 1-1). For example, if patients present today with fever and cough, the diagnosis of pneumonia is based on the presence of an infiltrate on the chest radiograph. Similarly, the diagnosis of systolic murmurs depends on echocardiography and that of ascites on abdominal ultrasonography. In these disorders, the clinician's principal interest is the result of the technologic test, and decisions about treatment depend much more on that result than on whether the patient has egophony, radiation of the murmur into the neck, or shifting dullness. This reliance on technology creates tension for medical students, who spend hours mastering the traditional examination yet later learn (when first appearing on hospital wards) that the traditional examination pales in importance compared with technologic studies, a realization prompting a fundamental question: What actually is the diagnostic value of the traditional physical examination? Is it outdated and best discarded? Is it completely accurate and underutilized? Is the truth somewhere between these two extremes?

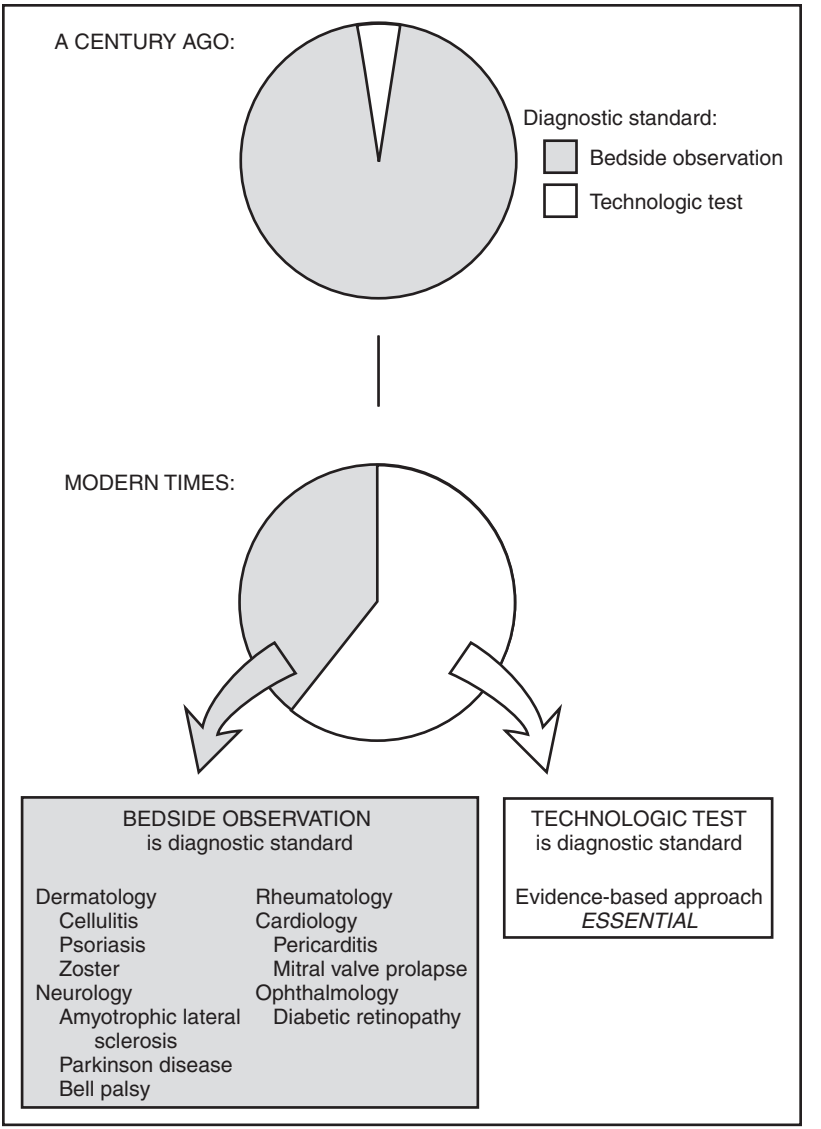


FIGURE 1-1 Evolution of diagnostic standard. The figure compares the diagnostic process one century ago (*top*, before introduction of clinical imaging and modern laboratory testing) to modern times *(bottom)*, illustrating the relative contributions of bedside examination *(grey shade)* and technologic tests *(white shade)* to the diagnostic standard. One century ago, most diagnoses were defined by bedside observation, whereas today, technologic standards have a much greater diagnostic role. Nonetheless, there are many examples today of diagnoses based solely on bedside findings (examples appear in *large grey shaded box*). "Evidence-based" physical diagnosis, on the other hand, principally addresses those diagnoses *defined by technologic standards*, because it identifies those traditional findings that accurately predict the result of the technologic test. See text.

Examination of Figure 1-1 indicates that diagnosis today is split into two halves. For some categories of disease, the diagnostic standard remains empiric observation (e.g., what the clinician sees, hears, and feels), just as it was for all diagnoses a century ago. For example, how does a clinician know that a patient has cellulitis? By going to the bedside and observing a sick patient with fever and localized bright erythema, warmth, swelling, and tenderness on the leg. There is no other way to make this diagnosis, not by technologic studies or by any other means. Similarly, there is no technologic standard for Parkinson disease (during the patient's life), Bell palsy, or pericarditis. All of these diagnoses, and many others in the fields of dermatology, neurology, musculoskeletal medicine, and ophthalmology, are based entirely on empiric observation by experienced clinicians; technology has a subordinate diagnostic role. In fact, this dependence of some diagnoses on bedside findings is one of the principal reasons medical students must still study and master the traditional examination.

The principal role of evidence-based physical examination, in contrast, is in the second category of diseases, that is, those whose categorization today is based on technologic studies. Clinicians want to know the results of the chest radiograph when diagnosing pneumonia, of the echocardiogram when diagnosing systolic murmurs, and of the ultrasound examination when diagnosing ascites. For each of these problems, the evidence-based approach compares traditional findings with the technologic standard and then identifies those findings that increase or decrease the probability of disease (as defined by the technologic standard), distinguishing them from unhelpful findings that fail to change probability. Using this approach, the clinician will calculate the *Heckerling score*[*] to predict the findings of the chest radiograph (see Chapter 30), define the topographic distribution of the murmur on the chest wall to predict the findings of the echocardiogram (see Chapter 41), and look for a fluid wave or edema to predict the findings of the abdominal ultrasound examination (see Chapter 49).

There are thus two distinct ways physical examination is applied at the bedside. For many disorders (i.e., those still lacking a technologic standard), the clinician's observations define the diagnosis. For other disorders (i.e., those based on technologic tests), the clinician's application of an evidence-based approach quickly identifies the relatively few findings that predict the results of the technologic standard. Both approaches to the bedside examination make physical examination more efficient and accurate and, ultimately, more relevant to the care of patients.

[*]The Heckerling score assigns one point to each of five independent predictors of pneumonia that may be present: temperature, >37.8° C; heart rate, >100/min; crackles; diminished breath sounds; and absence of asthma (see Chapter 30).

CHAPTER 2

Diagnostic Accuracy of Physical Findings

I. INTRODUCTION

If a physical sign characteristic of a suspected diagnosis is present (i.e., **positive finding**), that diagnosis becomes more likely; if the characteristic finding is absent (i.e., **negative finding**), the suspected diagnosis becomes less likely. How much these positive and negative results modify probability, however, is distinct for each physical sign. Some findings, when positive, shift probability upward greatly, but they change it little when negative. Other signs are more useful if they are absent, because the negative finding practically excludes disease, although the positive one changes probability very little.

Much of this book consists of tables that specifically describe how positive or negative findings change the probability of disease, a property called **diagnostic accuracy.** Understanding these tables first requires review of four concepts: pretest probability, sensitivity, specificity, and likelihood ratios.

II. PRETEST PROBABILITY

Pretest probability is the probability of disease (i.e., prevalence) before application of the results of a physical finding. Pretest probability is the starting point for all clinical decisions. For example, the clinician may know that a certain physical finding shifts the probability of disease upward 40%, but this information alone is unhelpful unless the clinician also knows the starting point: if the pretest probability for the particular diagnosis was 50%, the finding is diagnostic (i.e., post-test probability 50% + 40% = 90%); if the pretest probability was only 10%, the finding is less helpful, because the probability of disease is still the flip of a coin (i.e., post-test probability 10% + 40% = 50%).

Published estimates of disease prevalence, given a particular clinical setting, are summarized in the Appendix for all the clinical problems discussed in this book (these estimates derive from clinical studies reviewed in all the EBM boxes); Table 2-1 provides a small sample of these pretest probabilities. Even so, clinicians must adjust these estimates with information from their own practice. For example, large studies based in emergency departments show that 15% to 35% of patients presenting with cough and fever have pneumonia (Table 2-1). The probability of pneumonia, however, is certainly lower in patients presenting with cough and fever to an

TABLE 2-1 Pretest Probability

Setting (Reference)	Diagnosis	Probability (%)
Acute abdominal pain[1-3]	Small bowel obstruction	4
Ankle injury[4,5]	Ankle fracture	10-14
Cough and fever[6]	Pneumonia	15-35
Acute calf pain or swelling[7-15]	Proximal deep vein thrombosis	13-43
Pleuritic chest pain, dyspnea, or hemoptysis [16-19]	Pulmonary embolism	9-43
Diabetic foot ulcer[20-22]	Osteomyelitis	52-68

office-based practice in the community, and it may be higher if cough and fever develop in patients with cancer or human immunodeficiency virus (HIV) infection. In fact, because the best estimate of pretest probability incorporates information from the clinician's own practice—how specific underlying diseases, risks, and exposures make disease more or less likely—the practice of evidence-based medicine is never "cookbook" medicine but instead consists of decisions based on the unique characteristics of the patients the clinician sees.

III. SENSITIVITY AND SPECIFICITY

A. DEFINITIONS

Sensitivity and specificity describe the discriminatory power of physical signs. **Sensitivity** is the proportion of patients *with* the diagnosis who *have* the physical sign (i.e., have the *positive* result). **Specificity** is the proportion of patients *without* the diagnosis who *lack* the physical sign (i.e., have the *negative* result).

Calculation of sensitivity and specificity requires construction of a 2×2 table (Fig. 2-1) that has two columns (one for "diagnosis present" and another for "diagnosis absent") and two rows (one for "physical sign present" and another for "physical sign absent"). These rows and columns create four boxes: one for the "true positives" (cell a, sign and diagnosis present), one for the "false positives" (cell b, sign present but disease absent), one for the "false negatives" (cell c, sign absent but disease present), and one for the "true negatives" (cell d, sign and disease absent).

Figure 2-1 presents data from a hypothetical study of 100 patients presenting with pulmonary hypertension. The clinician knows that tricuspid regurgitation is a complication of pulmonary hypertension and wonders how accurately a single physical sign—the presence of a holosystolic murmur at the left lower sternal border—detects this complication.* In this study, 42 patients have significant tricuspid regurgitation (the sum of column 1) and 58 patients do not (the sum of column 2). The **sensitivity** of the holosystolic murmur is the proportion of patients with disease (i.e.,

*The numbers used in this example are very close to those in reference 23. See also Chapter 44.

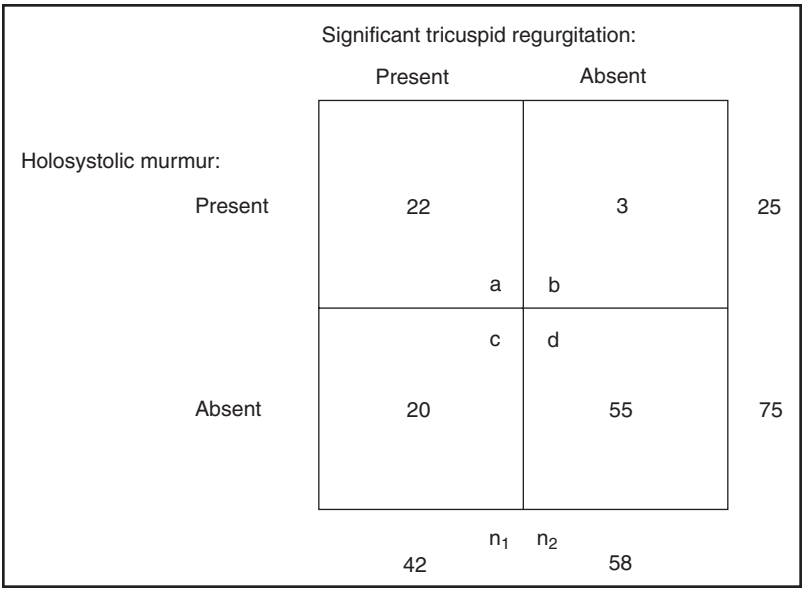


FIGURE 2-1 2×2 table. The total number of patients with disease (tricuspid regurgitation in this example) is the sum of the first column, or $n_1 = a + c$. The total number of patients without disease is the sum of the second column, or $n_2 = b + d$. The **sensitivity** of a physical finding (holosystolic murmur at the left lower sternal edge, in this example) is the proportion of patients with disease who have the finding (i.e., $a/(a+c)$ or a/n_1). The **specificity** of a physical finding is the proportion of patients without disease who lack the finding [i.e., $d/(b+d)$ or d/n_1]. The **positive likelihood ratio (LR)** is the proportion of patients with disease who have a positive finding (a/n_1) divided by the proportion of patients without disease who have a positive finding (b/n_2), or sensitivity/(1 − specificity). The **negative LR** is the proportion of patients with disease who lack the finding (c/n_1) divided by the proportion of patients without disease who lack the finding (d/n_1), or (1 − sensitivity)/specificity. In this example, the sensitivity is 0.52 (22/42), the specificity is 0.95 (55/58), the positive LR is 10.1 [(22/42)/(3/58)], and the negative LR is 0.5 [(20/42)/(55/58)].

tricuspid regurgitation, 42 patients) who have the characteristic murmur (i.e., the *positive* result, 22 patients), which is 22/42 = 0.52 or 52%. The **specificity** of the holosystolic murmur is the proportion of patients *without* disease (i.e., no tricuspid regurgitation, 58 patients) who *lack* the murmur (i.e., the *negative* result, 55 patients), which is 55/58 = 0.95 or 95%.

To recall how to calculate sensitivity and specificity, Sackett and others[24,25] have suggested helpful mnemonics: sensitivity is "pelvic inflammatory disease" (or "PID," meaning "positivity in disease") and specificity is "National Institutes of Health" (or "NIH," meaning "negativity in health").

B. USING SENSITIVITY AND SPECIFICITY TO DETERMINE PROBABILITY OF DISEASE

The completed 2×2 table can be used to determine the accuracy of the holosystolic murmur, which is how well its presence or absence discriminates between those with tricuspid regurgitation and those without it. In Figure 2-1, the first row includes all 25 patients with the murmur (i.e.,

the positive results). Of these 25 patients, 22 have tricuspid regurgitation; therefore, the probability of tricuspid regurgitation, if the murmur is present (*positive* finding), is 22/25 or 88% (i.e., the "post-test probability" if the murmur is present). The second row includes all 75 patients without the murmur. Of these 75 patients, 20 have tricuspid regurgitation; therefore, the post-test probability of tricuspid regurgitation, if the murmur is absent (i.e., *negative* finding) is 20/75 or 27%.

In this example, the pretest probability of tricuspid regurgitation is 42%. The presence of the murmur (positive result) shifts the probability of disease upward considerably more (i.e., 46%, from 42% to 88%) than the absence of the murmur (negative result) shifts it downward (i.e., 15%, from 42% to 27%). This illustrates an important property of physical signs with a high specificity: when present, physical signs with *high specificity* greatly *increase* the probability of disease. A corollary to this applies to findings with high sensitivity: when *absent*, physical signs with a high *sensitivity* greatly *decrease* the probability of disease. The holosystolic murmur has a high specificity (95%) but only a meager sensitivity (52%), meaning that at the bedside, a positive result (the presence of a murmur) has greater diagnostic importance than the negative result (the absence of the murmur). The presence of the characteristic murmur argues compellingly for tricuspid regurgitation, but its absence is less helpful, simply because many patients with significant regurgitation lack the characteristic murmur.

Sackett and others[25] have suggested mnemonics for these characteristics as well: "SpPin" (i.e., a *Sp*ecific test, when *P*ositive, rules *in* disease) and "SnNout" (i.e., a *Sn*sitive test, when *N*egative, rules *out* disease).

IV. LIKELIHOOD RATIOS

Likelihood ratios, like sensitivity and specificity, describe the discriminatory power of physical signs. Although they have many advantages, the most important is how simply and quickly they can be used to estimate post-test probability.

A. DEFINITION

The likelihood ratio (LR) of a physical sign is the proportion of patients *with* disease who have a particular finding divided by the proportion of patients *without* disease who also have the same finding.

$$\text{LR} = \frac{\text{Probability of finding in patients } \textit{with} \text{ disease}}{\text{Probability of same finding in patients } \textit{without} \text{ disease}}$$

The adjective *positive* or *negative* indicates whether the LR refers to the presence of the physical sign (i.e., positive result) or to the absence of the physical sign (i.e., negative result).

A **positive LR,** therefore, is the proportion of patients *with* disease who *have* a physical sign divided by the proportion of patients *without* disease who also *have* the same sign. The numerator of this equation—proportion of patients with disease who have the physical sign—is the sign's sensitivity.

The denominator—proportion of patients without disease who have the sign—is the complement of specificity, or (1 – specificity). Therefore,

$$\text{Positive LR} = \frac{(\text{sens})}{(1 - \text{spec})}$$

In our hypothetical study (Fig. 2-1), the proportion of patients with tricuspid regurgitation who have the murmur is 22/42 or 52.4% (i.e., the finding's sensitivity) and the proportion of patients without tricuspid regurgitation who also have the murmur is 3/58 or 5.2% (i.e., 1 − specificity). The ratio of these proportions [i.e., (sensitivity)/(1 − specificity)] is 10.1, which is the positive LR for a holosystolic murmur at the lower sternal border. This number means that patients *with* tricuspid regurgitation are 10.1 times more likely to have the holosystolic murmur than those *without* tricuspid regurgitation.

Similarly, the **negative LR** is the proportion of patients *with* disease *lacking* a physical sign divided by the proportion of patients *without* disease also *lacking* the sign. The numerator of this equation— proportion of patients with disease *lacking* the finding—is the complement of sensitivity, or (1 − sensitivity). The denominator of the equation— proportion of patients without disease *lacking* the finding—is the specificity. Therefore,

$$\text{Negative LR} = \frac{(1 - \text{sens})}{(\text{spec})}$$

In our hypothetical study, the proportion of patients with tricuspid regurgitation lacking the murmur is 20/42 or 47.6% (i.e., 1 − sensitivity) and the proportion of patients without tricuspid regurgitation lacking the murmur is 55/58 or 94.8% (i.e., the specificity). The ratio of these proportions [i.e. (1 − sensitivity)/(specificity)] is 0.5, which is the negative LR for the holosystolic murmur. This number means that patients *with* tricuspid regurgitation are 0.5 times less likely to lack the murmur than those *without* tricuspid regurgitation. (The inverse statement is less confusing: patients *without* tricuspid regurgitation are two times more likely to lack a murmur than those *with* tricuspid regurgitation.)

Although these formulae are difficult to recall, the interpretation of LRs is straightforward. Findings with LRs greater than 1 increase the probability of disease; the greater the LR, the more compelling the argument *for* disease. Findings whose LRs lie between between zero and 1 decrease the probability of disease; the closer the LR is to zero, the more convincing the finding argues *against* disease. Findings whose LRs equal 1 lack diagnostic value because they do not change probability at all. "Positive LR" describes how probability changes when the finding is *present*. "Negative LR" describes how probability changes when the finding is *absent*.

LRs, therefore, are nothing more than diagnostic weights, whose possible values range from zero (i.e., excluding disease) to infinity (i.e., pathognomonic for disease; Fig. 2-2).

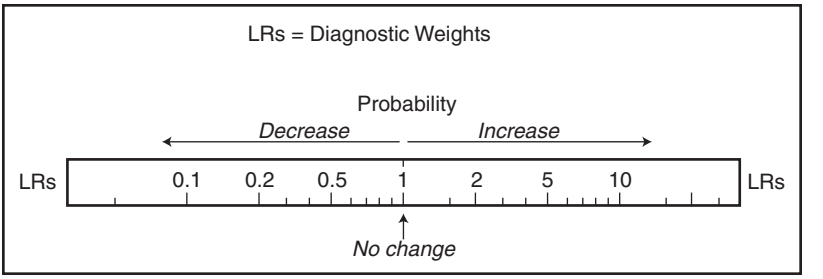


FIGURE 2-2 Likelihood ratios (LRs) as diagnostic weights. The relationship between a specific physical sign and a specific disease is described by a unique number—its likelihood ratio (LR)—which is nothing more than a diagnostic weight describing how much that sign argues for or against that specific disease. The possible values of LRs range from zero to infinity (∞). Findings with LRs greater than 1 argue *for* the specific disease (the greater the value of the LR, the more the probability of disease increases). Findings with LRs less than 1 argue *against* the disease (the closer the number is to zero, the more the probability of disease decreases). LRs that equal 1 do not change probability of disease at all.

B. USING LRS TO DETERMINE PROBABILITY

The clinician can use the LR of a physical finding to estimate probability of disease in three ways: (1) using graphs or other easy-to-use nomograms[26,27]; (2) using bedside approximations, or (3) using formulas.

1. Using Graphs

a. Parts of the Graph

Figure 2-3 is an easy-to-use graph that illustrates the relationship between pretest probability (*x*-axis) and post-test probability (*y*-axis), given the finding's LR. The straight line bisecting the graph into an upper left half and lower right half describes the LR of 1, which has no discriminatory value because, for findings with this LR, post-test probability always equals pretest probability. Physical findings that argue *for* disease (i.e., LRs >1) appear in the upper left half of the graph; the larger the value of the LR, the more the curve approaches the upper left corner. Physical findings that argue *against* disease (i.e., LRs <1) appear in the lower right half of the graph: the closer the LR is to zero, the more the curve approaches the lower right corner.

In Figure 2-3, the three depicted curves with LRs greater than 1 (i.e., LR = 2, 5, and 10) are mirror images of the three curves with LRs less than 1 (i.e., LR = 0.5, 0.2, and 0.1). (This assumes the "mirror" is the line LR = 1.) This symmetry indicates that findings with an LR of 10 argue as much *for* disease as those with an LR of 0.1 argue *against* disease (although this is true only for the intermediate pretest probabilities). Similarly, an LR of 5 argues as much for disease as an LR of 0.2 argues against it, and an LR of 2 mirrors an LR of 0.5. Keeping these companion curves in mind will help the clinician interpret the LRs throughout this book.*

*These companion pairs are easy to recall because they are the inverse of each other: the inverse of 10 is 1/10 = 0.1; the inverse of 5 is 1/5 = 0.2; the inverse of 2 is 1/2 = 0.5.

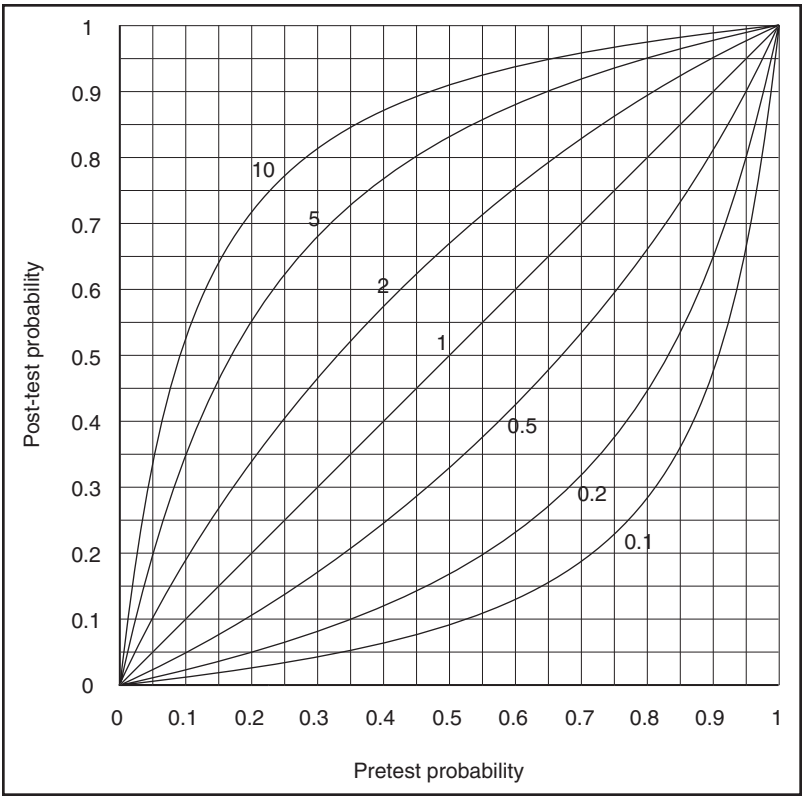


FIGURE 2-3 Probability and likelihood ratios. The curves describe how pretest probability (*x*-axis) relates to post-test probability (*y*-axis), given the likelihood ratio (LR) for the physical finding. Only the curves for seven likelihood ratios are depicted (from LR = 0.1 to LR = 10). See text.

If a finding has an LR other than one of these depicted seven curves, its position can be estimated with little loss in accuracy. For example, the curve for LR = 4 lies between LR = 5 and LR = 2, though closer to LR= 5 than to LR = 2.

b. Using the Graph to Determine Probability

To use this graph, the clinician identifies on the *x*-axis the patient's pretest probability, derived from published estimates and clinical experience, and extends a line upward from that point to meet the LR curve for the physical finding. The clinician then extends a horizontal line from this point to the *y*-axis to identify post-test probability.

Figure 2-4 depicts this process for the lower sternal holosystolic murmur and tricuspid regurgitation. The pretest probability of tricuspid regurgitation is 42%. If the characteristic murmur is present (positive LR = 10), a line is drawn upward from 0.42 on the *x*-axis to the LR = 10 curve; from this point, a horizontal line is drawn to the *y*-axis to find the post-test probability (88%). If the murmur is absent (negative LR = 0.5), the post-test

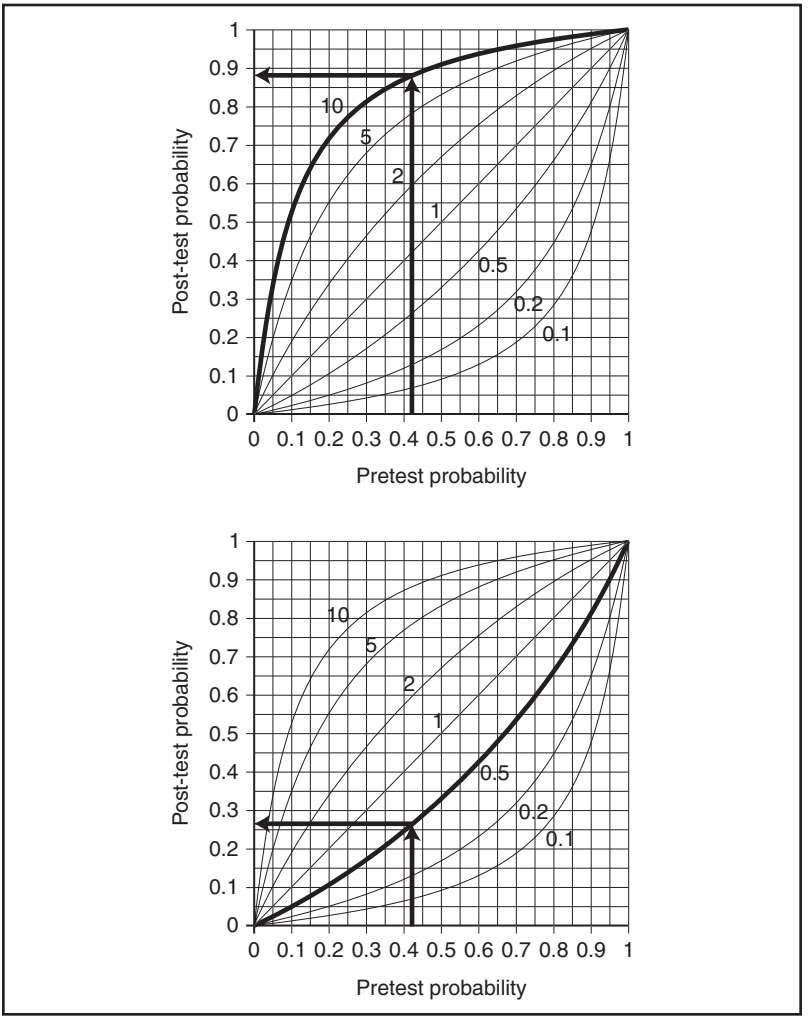


FIGURE 2-4 Probability and likelihood ratios: patients with pulmonary hypertension. In our hypothetical clinician's practice, 42% of patients with pulmonary hypertension have the complication of tricuspid regurgitation (i.e., pretest probability is 42%). To use the curves, the clinician finds 0.42 on the *x*-axis and extends a line upward. The post-test probability of tricuspid regurgitation is read off the *y*-axis where the vertical line intersects the curve of the appropriate LR. The probability of tricuspid regurgitation if a holosystolic murmur is present at the left lower sternal edge (LR = 10.1) is 88%; the probability if the finding is absent (LR = 0.5) is 27%.

probability is the *y*-value where the vertical line intersects the LR = 0.5 curve (i.e., post-test probability of 27%).

These curves illustrate an additional important point: Physical signs are diagnostically most useful when they are applied to patients who have pretest probabilities in the intermediate range (i.e., 20% to 80%) because in this range the different LR curves diverge the most from the LR = 1 curve

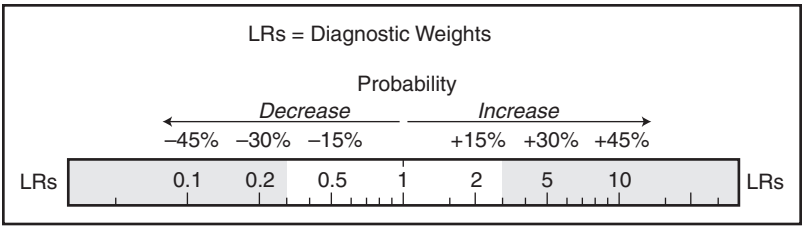


FIGURE 2-5 Approximating probability. Clinicians can estimate changes in probability by recalling the LRs 2, 5, and 10 and the first three multiples of 15 (i.e., 15, 30, and 45). A finding whose LR is 2 increases probability about 15%; one of 5 increases it 30%; and one of 10 increases it 45% (these changes are *absolute* increases in probability). LRs whose values are 0.5, 0.2, and 0.1 (i.e., the reciprocals of 2, 5, and 10) decrease probability 15%, 30%, and 45%, respectively. Throughout this book, LRs with values of ≥3 or ≤0.3 (represented by the shaded part of the diagnostic weight "ruler") are presented in boldface type to indicate those physical findings that change probability sufficiently to be clinically meaningful (i.e., they increase or decrease probability at least 20% to 25%).

(thus, shifting probability up or down by a large amount). If instead the pretest probability is already very low or very high, all the LR curves cluster close to the line LR = 1 curve in either the bottom left or upper right corners, thus changing probability relatively little.

2. Approximating Probability

The clinician can avoid using graphs and instead approximate post-test probability by remembering the following two points: (1) The companion LR curves in Figure 2-3 are LR = 2 and LR = 0.5, LR = 5 and LR = 0.2, and LR = 10 and LR = 0.1. (2) The first three multiples of "15" are 15, 30, and 45. Using this rule, the LRs of 2, 5, and 10 increase probability about 15%, 30%, and 45%, respectively (Fig. 2-5). The LRs of 0.5, 0.2, and 0.1 decrease probability about 15%, 30%, and 45%, respectively.[28] These estimates are accurate to within 5% to 10% of the actual value, as long the clinician rounds estimates over 100 to an even 100% and estimates below zero to an even 0%.

Therefore, in our hypothetical patient with pulmonary hypertension, the finding of a holosystolic murmur (LR = 10) increases the probability of tricuspid regurgitation from 42% to 87% (i.e., 42% + 45% = 87%, which is only 1% lower than the actual value). The absence of the murmur (LR = 0.5) decreases the probability of tricuspid regurgitation from 42% to 27% (i.e., 42% − 15% = 27%, which is identical to the actual value).

Table 2-2 summarizes similar bedside estimates for all LRs between 0.1 and 10.

3. Calculating Probability

The post-test probability also can be calculated by first converting pretest probability (P_{pre}) into pretest odds (O_{pre}):

$$O_{pre} = \frac{P_{pre}}{(1 - P_{pre})}$$

TABLE 2-2 Likelihood Ratios and Bedside Estimates

Likelihood Ratio	Approximate Change in Probability*
0.1	−45%
0.2	−30%
0.3	−25%
0.4	−20%
0.5	−15%
1	No change
2	+15%
3	+20%
4	+25%
5	+30%
6	+35%
7	
8	+40%
9	
10	+45%

*These changes describe *absolute* increases or decreases in probability. For example, a patient with a pretest probability of 20% and a physical finding whose LR is 5 would have a post-test probability of 20% + 30% = 50%. The text describes how to easily recall these estimates. From McGee S. Simplifying likelihood ratios. *J Gen Intern Med*. 2002;17:646-649.

The pretest odds (O_{pre}) are multiplied times the LR of the physical sign to determine the post-test odds (O_{post}):

$$O_{post} = O_{pre} \times LR$$

The post-test odds (O_{post}) convert back to post-test probability (P_{post}), using:

$$P_{post} = \frac{O_{post}}{(1 + O_{post})}$$

Therefore, in our hypothetical example of the patients with pulmonary hypertension, the pretest odds for tricuspid regurgitation are [(0.42)/(1−0.42)] or 0.72. If the murmur is present (LR = 10), the post-test odds are [0.72 × 10] or 7.2, which translates to a post-test probability of [(7.2)/(1 + 7.2)] or 0.88 (i.e., 88%). If the murmur wave is absent (LR = 0.5), the post-test odds are [0.72 × 0.5] or 0.36, which translates to a post-test probability of [(0.36)/(1 + 0.36)] or 0.27 (i.e., 27%).

Clinical medicine, however, is rarely as precise as these calculations suggest, and for most decisions at the bedside, the approximations described in this section on "approximating probability" are more than adequate.

C. ADVANTAGES OF LIKELIHOOD RATIOS

1. Simplicity

In a single number, the LR conveys to clinicians how convincingly a physical sign argues for or against disease. If the LR of a finding is large, disease is likely, and if the LR of a finding is close to zero, disease is doubtful. This advantage allows clinicians to quickly compare different diagnostic strategies and thus refine clinical judgment.[28]

2. Accuracy

Using LRs to describe diagnostic accuracy is superior to using sensitivity and specificity because the earlier described mnemonics, SpPin and SnNout, are sometimes misleading. For example, according to the mnemonic SpPin, a finding with a specificity of 95% should argue conclusively for disease, but it does so only if the positive LR for the finding is a high number. If the finding's sensitivity is 60%, the positive LR is 12 and the finding does argue convincingly for disease (i.e., consistent with the SpPin mnemonic); if the finding's sensitivity is only 10%, however, the positive LR is 2 and post-test probability changes only slightly (i.e., inconsistent with the SpPin mnemonic). Similarly, a highly sensitive finding argues convincingly against disease (i.e., SnNout) only when its calculated negative LR is a number close to zero.

3. Levels of Findings

Another advantage of LRs is that a physical sign measured on an ordinal scale (e.g., 0, 1+, 2+, 3+) or a continuous scale (e.g., blood pressure) can be categorized into different levels to determine the LR for each level, thereby increasing the accuracy of the finding. Other examples include continuous findings such as heart rate, respiratory rate, temperature, and percussed span of the liver, and ordinal findings such as intensity of murmurs and degree of edema.

For example, in patients with chronic obstructive lung disease (i.e., emphysema, chronic bronchitis), breath sounds are typically faint. If the clinician grades the intensity of breath sounds on a scale from 0 (absent) to 24 (very loud), based on the methods discussed in Chapter 28, he or she can classify the patient's breath sounds into one of four groups: scores of 9 or less (very faint), 10 to 12, 13 to 15, or greater than 15 (loud).[29,30] Each category then has its own LR (Table 2-3): scores of 9 or less significantly increase the probability of obstructive disease (LR = 10.2), whereas scores greater than 15 significantly decrease it (LR = 0.1). Scores from 10 to 12 argue somewhat for disease (LR = 3.6), and scores from 13 to 15 provide no diagnostic information (LR not significantly different from 1). If the clinician had instead identified breath sounds as simply "faint" or "normal/increased" (i.e., the traditional positive or negative finding), the finding may still discriminate between patients with and without obstructive disease, but it misses the point that the discriminatory power of the sign resides mostly with scores less than 10 and greater than 15.

TABLE 2-3 Breath Sound Intensity and Chronic Airflow Limitation

Breath Sound Score	Likelihood Ratio
9 or less	10.2
10-12	3.6
13-15	NS
>15	0.1

NS, not significant,

From Bohadana AB, Peslin R, Uffholtz H. Breath sounds in the clinical assessment of airflow obstruction. *Thorax*. 1978;33:345-351; Pardee NE, Martin CJ, Morgan EH. A test of the practical value of estimating breath sound intensity: breath sounds related to measured ventilatory function. *Chest*. 1976;70(3):341-344.

When findings are categorized into levels, the term *specificity* becomes meaningless. For example, the specificity of a breath sound score of 13 to 15 is 80%, which means that 80% of patients without chronic airflow limitation have values other than 13 to 15, though the "80%" does not convey whether most of these other values are greater than 15 or less than 13. Similarly, when findings are put into more than two categories, the LR descriptor *negative* is no longer necessary, because all LRs are positive ones for their respective category.

4. Combining Findings

A final advantage of LRs is that clinicians can use them to combine findings, which is particularly important for those physical signs with LRs between 0.5 and 2, signs that by themselves change probability little but when combined change probability a greater amount. Individual LRs can be combined, however, only if the findings are "independent."

a. Independence of Findings

Independence means that the LR for the second finding does not change once the clinician determines whether the first finding is present or absent. For a few diagnostic problems, investigators have identified which findings are independent of each other. These findings appear as components of "diagnostic scoring schemes" in the tables throughout this book. For most physical findings, however, very little information is available about independence, and the clinician must judge whether combining findings is appropriate.

One important clue is that most independent findings have a unique pathophysiologic basis. For example, when considering pneumonia in patients with cough and fever, the clinician could combine the findings of abnormal mental status and diminished breath sounds, using the individual LRs of each finding, because abnormal mental status and diminished breath sounds probably have separate pathophysiologic bases. Similarly, when considering heart failure in patients with dyspnea, the clinician could combine the findings of elevated neck veins and third heart sound because these findings also have different pathophysiologic bases.

Examples of findings whose individual LRs should *not* be combined (because the findings share the same pathophysiologic basis) are flank dullness and shifting dullness in the diagnosis of ascites (both depend on intra-abdominal contents dampening the vibrations of the abdominal wall during percussion), neck stiffness and Kernig sign in the diagnosis of meningitis (both are caused by meningeal irritation), and edema and elevated neck veins in the diagnosis of heart failure (both depend on elevated right atrial pressure).

Until more information is available, the safest policy for the clinician to follow, when combining LRs of individual findings, is to combine no more than three findings, all of which have a distinct pathophysiologic basis.

b. How to Combine Findings

The clinician can use any of the methods previously described to combine findings, simply by making the post-test probability from the first finding the pretest probability for the second finding. For example, a hypothetical patient with acute fever and cough has two positive findings that we believe have separate pathophysiologic bases and therefore are independent: abnormal mental status (LR = 1.9 for pneumonia) and diminished breath sounds (LR = 2.3 for pneumonia). The pretest probability of pneumonia, derived from published estimates and clinical experience, is estimated to be 20%. Using the graph, the finding of abnormal mental status increases the probability from 20% to 32%; this post-test probability then becomes the pretest probability for the second finding, diminished breath sounds, which increases the probability from 32% to 52%—the overall probability after application of the two findings. Using the approximating rules, both findings (LRs ≈ 2) increase the probability about 15%; the post-test probability is thus 20% + 15% + 15% = 50% (an error of only 2%). Using formulas to calculate probability, the LRs of the separate findings are multiplied together, and the product is used to convert pretest into post-test odds. The product of the two LRs is 4.4 (1.9 × 2.3); the pretest odds are 0.2/0.8 = 0.25; and the post-test odds are 0.25 × 4.4 = 1.1, which equals a probability of 1.1/2.1 = 52%.

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 3

Using the Tables in This Book

I. INTRODUCTION

Information about the diagnostic accuracy of physical findings is presented in two types of displays in this book: (1) "Frequency of Findings" tables, which show only the sensitivity of physical signs, and (2) EBM (evidence-based medicine) boxes titled Diagnostic Accuracy, which present the sensitivity, specificity, and likelihood ratios (LRs) of various physical signs.

II. FREQUENCY OF FINDINGS TABLES

A. DEFINITION

Frequency of findings tables summarize multiple studies of patients with a specific diagnosis and present the sensitivity of physical signs found in that disorder. These tables provide no information about a sign's specificity. An example is Table 3-1, listing the frequency of findings in constrictive pericarditis, a disorder in which a diseased and unyielding pericardium interferes with diastolic filling of the heart.

B. PARTS OF THE TABLE

1. Finding

The first column lists the various physical signs, organized by organ system, with the findings of each organ system listed from most to least frequent.

2. Frequency

The second column lists the sensitivity (or frequency) of the physical signs. If the sensitivity from every study is statistically similar, the overall mean frequency is presented (e.g., in Table 3-1, 98% of patients with constrictive pericarditis have elevated neck veins). If the sensitivities from the different studies are statistically diverse ($p < .05$ by the chi-square test), the range of values is instead presented (e.g., in Table 3-1, 28% to 94% have a pericardial knock, a loud heart sound heard near the apex during early diastole).

3. Footnotes

The footnotes to these tables present the source of the information and the diagnostic standards used. For example, the information in Table 3-1 is based on 331 patients from nine different studies, which based the diagnosis of constrictive pericarditis on surgical, postmortem, or hemodynamic findings.

TABLE 3-1 Constrictive Pericarditis*†

Physical Finding	Frequency (%)‡
NECK VEINS	
Elevated neck veins	98
Prominent *y* descent (Friedreich's sign)	57-100
Kussmaul's sign	50
ARTERIAL PULSE	
Irregularly irregular (atrial fibrillation)	36-70
BLOOD PRESSURE	
Pulsus paradoxus >10 mm Hg	17-43
AUSCULTATION OF HEART	
Pericardial knock	28-94
Pericardial rub	3
OTHER FINDINGS	
Hepatomegaly	87-100
Edema	63
Ascites	53-89

*Data from 331 patients from references 1 to 9.
†Diagnostic standard: For constrictive pericarditis, surgical and postmortem findings[1,2,5,6] are sometimes seen in combination with hemodynamic findings.[3,4,7–9]
‡Results are overall mean frequency or, if statistically heterogeneous, the range of values.

C. INTERPRETATION

Because the frequency of findings tables provide just information about a sign's sensitivity, they can only be used to support a statement that a physical sign, when *absent*, argues *against* disease. The absence of any finding whose sensitivity (or frequency) is greater than 95% is a compelling argument against that diagnosis (i.e., the negative LR is ≤0.1, even if the specificity of the finding, which is unknown, is as low as 50%). In Table 3-1, elevated venous pressure is such a finding (sensitivity, 98%): if the clinician is considering the diagnosis of constrictive pericarditis but the patient's bedside estimate of venous pressure is normal, the diagnosis becomes very unlikely.

Similarly, the absence of two or three independent findings having sensitivities greater than 80% is also a compelling argument against disease.* (See Chapter 2 for a definition of *independent findings*.)

*This statement assumes that the product of the LRs being combined is less than 0.1. Therefore, $LR^n = \left[\frac{(1-\text{sens})}{(\text{spec})}\right]^n \leq 0.1$, where n = number of findings being combined. If the specificity of the findings is as low as 50%, each of two findings being combined must have a sensitivity greater than 84%, and each of three findings being combined must have a sensitivity greater than 77%.

III. DIAGNOSTIC ACCURACY BOXES (EBM BOXES)

A. DEFINITION

Diagnostic accuracy tables summarize information from large numbers of patients who present with similar symptoms but different diagnoses. These EBM boxes present the physical sign's sensitivity, specificity, and positive and negative LRs, which then indicate how well that physical sign discriminates between patients with a particular diagnosis of interest and those without it.

EBM Box 3-1 presents an example summarizing the diagnostic accuracy of physical signs for pneumonia, as applied to a large number of patients with cough and fever. (See Chapter 30 for the complete EBM box.) In these studies, only about 20% of patients had pneumonia; the remainder had other causes of cough and fever such as sinusitis, bronchitis, or rhinitis.

B. PARTS OF THE EBM BOX

1. Finding

The first column presents the physical signs, organized by organ system, and the source of the information. Validated scoring schemes that combine findings appear in the bottom rows of EBM boxes.

2. Sensitivity and Specificity

The second and third columns present the range of a physical sign's sensitivity and specificity observed in these studies.

3. Likelihood Ratios

The third and fourth columns present the physical sign's positive and negative LR. (For clarity, "likelihood ratio if finding *present*" refers to the positive LR, and "likelihood ratio if finding *absent*" refers to the negative LR.) In contrast to sensitivity and specificity, which are presented as a range of values, LRs are described by a single number, derived by using a statistical technique called the random effects model. (See the section on Summarizing Likelihood Ratios in this chapter.[18]) Only statistically significant LRs are presented in the EBM boxes. If the 95% confidence interval (CI) for an LR, positive or negative, includes the value of 1, that result of the physical finding fails to statistically discriminate between patients with disease and those without it, and the notation "NS" (for not significant) is recorded in the EBM box.

4. Footnote

The footnotes to EBM boxes describe the diagnostic standards used in the studies and, if necessary, definitions of findings. The footnote for EBM Box 3-1, for example, indicates that the diagnostic standard for pneumonia was the chest radiograph; it also describes the components of the Heckerling diagnostic scoring scheme presented in the bottom rows of the EBM box.

EBM BOX 3-1
*Pneumonia**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
General Appearance				
Cachexia[10]	10	97	**4**	NS
Abnormal mental status[11–13]	12-14	92-95	1.9	NS
Lung Findings				
Percussion dullness[10–12,14,15]	4-26	82-99	**3**	NS
Diminished breath sounds[11,12,14,15]	15-49	73-95	2.3	0.8
Bronchial breath sounds[11]	14	96	**3.3**	NS
Egophony[10–12]	4-16	96-99	**4.1**	NS
Crackles[10–16]	19-67	36-94	1.8	0.8
Wheezing[11–16]	15-36	50-85	0.8	NS
Diagnostic Score (Heckerling et al[11,17])				
0 or 1 findings	7-29	33-65	**0.3**	—
2 or 3 findings	48-55	—	NS	—
4 or 5 findings	38-41	92-97	**8.2**	—

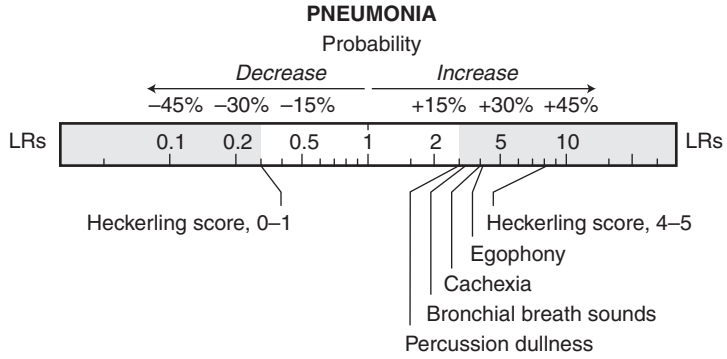
*Diagnostic standard: For pneumonia, infiltrate on chest radiograph.

†Definition of findings: For the Heckerling diagnostic score, the clinician scores 1 point for each of the following five findings that are present: temperature >37.8°C, heart rate >100/min, crackles, diminished breath sounds, and *absence* of asthma.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

NS, not significant.

Click here to access calculator.



C. INTERPRETATION OF EBM BOX

To use these EBM boxes, the clinician need only glance at the LR columns to appreciate the discriminatory power of different findings. LRs with the greatest value increase the probability of disease the most; LRs with the value closest to zero decrease the probability of disease the most. Boldface type highlights all findings with an LR of 3 or more or of 0.3 or less, thus allowing quick identification of the physical signs that increase probability more that 20% to 25% (LR ≥3) and those that decrease it more than 20% to 25% (LR ≤0.3; see also Chapter 2).

In patients with cough and fever (EBM Box 3-1), the individual findings increasing the probability of pneumonia the most are egophony (LR = 4.1), cachexia (LR = 4), bronchial breath sounds (LR = 3.3), and percussion dullness (LR = 3). In contrast, no *individual* finding, when present or absent, significantly *decreases* the probability of pneumonia. (No LR has a value ≤0.3.)

EBM Box 3-1 also shows that a score of 4 or more points using the Heckerling diagnostic scheme significantly *increases* the probability of pneumonia (LR = 8.2), whereas a score of 0 or 1 point significantly *decreases* it (LR = 0.3).

IV. CRITERIA FOR SELECTING STUDIES USED IN DIAGNOSTIC ACCURACY TABLES

All studies of adult patients that meet the following four criteria are included in the EBM boxes of this book.

A. PATIENTS WERE SYMPTOMATIC

The study must have enrolled patients presenting to clinicians with symptoms or other problems. Therefore, studies using asymptomatic controls, which tend to inflate the specificity of physical signs, were excluded. Clinicians do not need a physical sign to help them distinguish patients with pneumonia from healthy persons (who would not be consulting the doctor); instead, they are interested in the physical signs distinguishing pneumonia from other causes of cough and fever.

B. DEFINITION OF PHYSICAL SIGN

The physical sign in the study must be clearly defined.

C. INDEPENDENT COMPARISON TO A DIAGNOSTIC STANDARD

There must be an independent comparison to an acceptable diagnostic standard. *Independent comparison* means that the physical sign was not used to select patients for testing with the diagnostic standard. Acceptable diagnostic standards include laboratory testing, clinical imaging, surgical findings, or postmortem analysis.

D. 2×2 TABLE COULD BE CONSTRUCTED

The studies must provide figures or tables from which numbers could be extracted to construct 2×2 tables and calculate sensitivity, specificity, and LRs. If any cell of the 2×2 table contained the value of

zero, 0.5 was added to all cells, to avoid creating the unlikely LR of 0 or infinity.

V. SUMMARIZING LIKELIHOOD RATIOS

The random effects model by Dersimonian and Laird,[18] which considers both within study and between study variance to calculate a pooled LR, was used to summarize the LRs from the various studies. Table 3-2 illustrates how this model works. In the top rows of this table are the individual data from all studies of egophony that appear in EBM Box 3-1, including the finding's sensitivity and specificity, the positive and negative LRs, and the LR's 95% CIs. The bottom row of Table 3-2 shows how all of this information is summarized throughout the book.

In each of the studies, egophony was specific (96% to 99%) but not sensitive (4% to 16%). The positive LRs are all greater than 1, indicating that the finding of egophony increases the probability of pneumonia. For one of the three studies (i.e., Gennis and others[12]), the positive LR lacked statistical significance because its 95% CI includes the value of 1 (i.e., the LR value of 1 has no discriminatory value). For the other two studies, the 95% CI of the positive LR excluded the value of 1, thus making them statistically significant. The summary measure for the positive LR (fourth row of this table) is both clinically significant (4.08, a large positive number) and statistically significant (its 95% CI excludes 1). All of this information is summarized, in the notation used in this book (last row), by simply presenting the pooled LR of 4.1. (Interested readers may consult the Appendix for the 95% CIs of all LRs in this book.)

In contrast, the negative LRs from each study have both meager clinical significance (i.e., 0.87 to 0.96, values close to 1) and, for two of the three studies, no statistical significance (i.e., the 95% CI includes 1). The pooled negative LR also lacks clinical and statistical significance. Because it is statistically no different from 1 (i.e., the 95% CI of the pooled value, 0.88 to 1.01, includes 1), it is summarized using the notation "NS" for *not significant*.

Presenting the single pooled result for statistically significant LRs and NS for the statistically insignificant ones simplifies the EBM boxes and makes it much simpler to grasp the point that the finding of egophony

TABLE 3-2 Egophony and Pneumonia: Individual Studies

Reference	Sensitivity (%)	Specificity (%)	Positive LR (95% CI)	Negative LR (95% CI)
Diehr[10]	4	99	7.97 (1.77, 35.91)	0.96 (0.91, 1.02)
Heckerling[11]	16	97	4.91 (2.88, 8.37)	0.87 (0.81, 0.94)
Gennis[12]	8	96	2.07 (0.79, 5.41)	0.96 (0.9, 1.02)
Pooled result			4.08 (2.14, 7.79)	0.93 (0.88, 1.01)
Notation used in book	4-16	96-99	4.1	NS

NS, not significant.

in patients with cough and fever increases the probability of pneumonia (LR = 4.1), but the absence of egophony changes probability very little or not at all.

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 4

Reliability of Physical Findings

Reliability refers to how often multiple clinicians, examining the same patients, agree that a particular physical sign is present or absent. As characteristics of a physical sign, reliability and accuracy are distinct qualities, although significant interobserver disagreement tends to undermine the finding's accuracy and prevents clinicians from applying it confidently to their own practice. Disagreement about physical signs also contributes to the growing sense among clinicians, not necessarily justified, that physical examination is less scientific than more technologic tests, such as clinical imaging and laboratory testing, and that physical examination lacks their diagnostic authority.

The most straightforward way to express reliability, or interobserver agreement, is **simple agreement,** which is the proportion of total observations in which clinicians agree about the finding. For example, if two clinicians examining 100 patients with dyspnea agree that a third heart sound is present in 5 patients and is absent in 75 patients, simple agreement would be 80% [i.e., (5 + 75)/100 = 0.8; in the remaining 20 patients, only one of the two clinicians heard a third heart sound]. Simple agreement has advantages, including being easy to calculate and understand, but a significant disadvantage is that agreement may be quite high by chance alone. For example, if one of the clinicians in our hypothetical study heard a third heart sound in 10 of the 100 dyspneic patients and the other heard it in 20 of the patients (even though they agreed about the presence of the heart sound in only 5 patients), simple agreement *by chance alone* would be 74%.* With chance agreement this high, the observed 80% agreement no longer seems so impressive.

To address this problem, most clinical studies now express interobserver agreement using the kappa (κ) statistic, which usually has values between 0 and 1. (The Appendix at the end of this chapter shows how to calculate the κ-statistic.) A κ-value of 0 indicates that observed agreement is the same as that expected by chance, and a κ-value of 1 indicates perfect agreement. According to convention, a κ-value of 0 to 0.2 indicates *slight* agreement; 0.2 to 0.4, *fair* agreement; 0.4 to 0.6, *moderate* agreement; 0.6 to 0.8,

*Agreement by chance approaches 100% as the percentage of positive observations for both clinicians approaches 0% or 100% (i.e., both clinicians agree that a finding is very uncommon or very common). The Appendix at the end of this chapter shows how to calculate chance agreement.

substantial agreement; and 0.8 to 1, almost *perfect* agreement.* Rarely, physical signs have κ-values of less than 0 (theoretically, as low as −1), indicating the observed agreement was worse than chance agreement.

Table 4-1 presents the κ-statistic for most of the physical signs discussed in this book, demonstrating that with rare exceptions, observed agreement is better than chance agreement (i.e., κ-statistic exceeds 0). About 60% of findings have a κ-statistic of 0.4 or more, indicating that observed agreement is moderate or better.

Clinical disagreement occurs for many reasons—some causes clinicians can control, but others are inextricably linked to the very nature of clinical medicine and human observation in general. The most prominent reasons include the following: (1) The physical sign's definition is vague or ambiguous. For example, experts recommend about a dozen different ways to perform auscultatory percussion of the liver, thus making the sign so nebulous that significant interobserver disagreement is guaranteed. Ambiguity also results if signs are defined with terms that are not easily measurable. For example, clinicians assessing whether a peripheral pulse is present or absent demonstrate moderate to almost perfect agreement (κ = 0.52 to 0.92; see Table 4-1), but when the same clinicians are asked to record whether the palpable pulse is normal or diminished, they have great difficulty agreeing about the sign (κ = 0.01 to 0.15) simply because they have no idea what the next clinician means by "diminished." (2) The clinician's technique is flawed. For example, common mistakes are using the diaphragm instead of the bell of the stethoscope to detect the third heart sound, or stating that a muscle stretch reflex is absent without first trying to elicit it using a reinforcing maneuver (e.g., Jendrassik maneuver). (3) There is biologic variation of the physical sign. Many signs, including the pericardial friction rub, pulsus alternans, cannon A waves, and Cheyne-Stokes respirations, are notoriously evanescent, tending to come and go over time. (4) The clinician is careless or inattentive. The bustle of an active practice may lead clinicians to listen to the lungs while conducting the patient interview, or to search for a subtle murmur in a noisy emergency room. Reliable observations require undistracted attention and an alert mind. (5) The clinician's biases influence the observation. When findings are equivocal, expectations influence perceptions. For example, in a patient who just started taking blood pressure medications, borderline hypertension may become normal blood pressure; in a patient with increasing bilateral edema, borderline distended neck veins may become clearly elevated venous pressure; or in a patient with new onset of weakness, the equivocal Babinski sign may become clearly positive. Sometimes, biases actually create the finding: If the clinician holds a flashlight too long over an eye with suspected optic nerve disease, the light may temporarily bleach the retina of the eye and produce the Marcus Gunn pupil, thus confirming the original suspicion.

The lack of perfect reliability with physical diagnosis is sometimes regarded as a significant weakness, a reason that physical diagnosis is less reliable and scientific than clinical imaging and laboratory testing. Nonetheless,

*No measure of reliability is perfect, especially for findings whose prevalence clinicians agree approaches 0% or 100%. For these findings, simple agreement tends to overestimate reliability and the κ-statistic tends to underestimate reliability.

Text continues on pg. 36

TABLE 4-1 Interobserver Agreement and Physical Signs

Finding (Reference)	κ-statistic*
GENERAL APPEARANCE	
Mental Status Examination	
Mini-Mental Status Examination[1]	0.28-0.80
Clock-drawing test (Wolf-Klein method)[2]	0.73
Confusion Assessment Method for delirium[3–6]	0.70-0.91
Altered mental status[7]	0.71
Stance and Gait	
Abnormal gait[8,9]	0.11-0.71
Skin	
Patient appears anemic[10,11]	0.23-0.48
Nailbed pallor[12]	0.19-0.34
Conjunctival pallor (rim method)[13]	0.54-0.75
Ashen or pale skin[7]	0.34
Cyanosis[10,14]	0.36-0.70
Jaundice[15]	0.65
Loss of hair[16]	0.51
Vascular spiders[15–17]	0.64-0.92
Palmar erythema[15–17]	0.37-1
Hydration Status	
Patient appears dehydrated[10]	0.44-0.53
Axillary dryness[18]	0.50
Increased moisture on skin[10]	0.31-0.53
Capillary refill >3 seconds[7]	0.29
Nutritional Assessment	
Abnormal nutritional state[10]	0.27-0.36
Other Findings	
Consciousness impaired[10]	0.65-0.88
Patient appears older than age[10]	0.38-0.42
Patient appears in pain[10]	0.43-0.75
Generally unwell in appearance[10]	0.52-0.64
VITAL SIGNS	
Tachycardia (heart rate >100/min)[19]	0.85
Bradycardia (heart rate <60/min)[19]	0.87
Systolic hypertension (SBP >160 mm Hg)[19]	0.75
Hypotension (SBP <90 mm Hg)[19,20]	0.27-0.90
Osler sign[21–23]	0.26-0.72
Rumpel-Leede (tourniquet) test[24]	0.88
Elevated body temperature, palpating the skin[10]	0.09-0.23
Tachypnea[7,14,19]	0.25-0.60
HEAD AND NECK	
Diabetic Retinopathy	
Microaneurysms[25,26]	0.58-0.66
Intraretinal hemorrhages[25,26]	0.89
Hard exudates[25,26]	0.66-0.74

Continued

TABLE 4-1 Interobserver Agreement and Physical Signs—cont'd

Finding (Reference)	κ-statistic*
Cotton-wool spots[25,26]	0.56-0.67
Intraretinal microvascular abnormalities (IRMA)[25,26]	0.46
Neovascularization near disc[25,26]	0.21-0.48
Macular edema[25,26]	0.21-0.67
Overall grade[25,26]	0.65
Hearing	
Whispered voice test[27]	0.16-1
Finger rub test[28]	0.83
Thyroid	
Thyroid gland diffuse; multinodular or solitary nodule[29]	0.25-0.70
Goiter[30,31]	0.38-0.77
Meninges	
Nuchal rigidity, present or absent[32]	0.76
LUNGS	
Inspection	
Clubbing (method undefined)[14,33]	0.33-0.45
Clubbing (interphalangeal depth ratio)[34]	0.98
Clubbing (Schamroth sign)[34]	0.64
Breathing difficulties[10]	0.54-0.69
Gasping respirations[7]	0.63
Reduced chest movement[14,35,36]	0.14-0.38
Kussmaul respirations[37]	0.70
Pursed lip breathing[36]	0.45
Asymmetrical chest expansion[38]	0.85
Scalene or sternocleidomastoid muscle contraction[7,36,39]	0.52-0.57
Kyphosis[33]	0.37
Barrel chest[36]	0.62
Thoracic ratio ≥0.9[36]	0.32
Displaced trachea[14]	0.01
Palpation	
Tracheal descent during inspiration[39]	0.62
Laryngeal height ≤5.5 cm[36]	0.59
Impalpable apex beat[14,33]	0.33-0.44
Decreased tactile fremitus[14,38]	0.24-0.86
Increased tactile fremitus[14]	0.01
Subxiphoid point of maximal cardiac impulse[40]	0.30
Paradoxic costal margin movement[39]	0.56
Percussion	
Hyperresonant percussion note[14,35,40]	0.26-0.50
Dull percussion note[14,35,38,41]	0.16-0.84
Diaphragm excursion more or less than 2 cm, by percussion[40]	−0.04
Diminished cardiac dullness[40]	0.49
Auscultatory percussion abnormal[38,42]	0.18-0.76

TABLE 4-1 Interobserver Agreement and Physical Signs—cont'd

Finding (Reference)	κ-statistic*
Auscultation	
Reduced breath sound intensity[14,35,36,38,40,41,43,44]	0.16-0.89
Bronchial breathing[14,35]	0.19-0.32
Whispering pectoriloquy[14]	0.11
Reduced vocal resonance[38]	0.78
Crackles[14,41,43,45–47]	0.21-0.65
Wheezes[14,40,41,43,44]	0.43-0.93
Rhonchi[35,44]	0.38-0.55
Pleural rub[14,38]	−0.02-0.51
Special Tests	
Snider's test <10 cm[40]	0.39
Forced expiratory time[36,40,48,49]	0.27-0.70
Hoover sign[44]	0.74
Wells simplified rule for pulmonary embolism[50]	0.54-0.62
HEART	
Neck Veins	
Neck veins, elevated or normal[45–47,51]	0.08-0.71
Abdominojugular test[51]	0.92
Palpation	
Palpable apical impulse present[52–54]	0.68-0.82
Palpable apical impulse measurable[55]	0.56
Palpable apical impulse displaced lateral to midclavicular line[45,52,53,56]	0.43-0.86
Apical beat normal, sustained, double, or absent[56]	0.88
Percussion	
Cardiac dullness >10.5 cm from midsternal line[57,58]	0.57
Auscultation	
S_2 diminished or absent, vs. normal[59]	0.54
Third heart sound[45–47,51,60–62]	−0.17-0.84
Fourth heart sound[61,63]	0.15-0.71
Systolic murmur, present or absent[59]	0.19
Systolic murmur radiates to right carotid[59]	0.33
Systolic murmur, long systolic or early systolic[64]	0.78
Murmur intensity (Levine grading scale)[65]	0.43-0.60
Systolic murmur grade >2/6[66]	0.59
Carotid Pulsation	
Delayed carotid upstroke[59]	0.26
Reduced carotid volume[59]	0.24
ABDOMEN	
Inspection	
Abdominal distention[67,68]	0.35-0.42
Abdominal wall collateral veins, present vs. absent[15]	0.47
Palpation and Percussion	
Ascites[15,17,47]	0.47-0.75
Abdominal tenderness[67–69]	0.31-0.68
Surgical abdomen[68]	0.27

Continued

TABLE 4-1 Interobserver Agreement and Physical Signs—cont'd

Finding (Reference)	κ-statistic*
Abdominal wall tenderness test[70]	0.52
Rebound tenderness[67]	0.25
Guarding[67,68]	0.36-0.49
Rigidity[67]	0.14
Abdominal mass palpated[68]	0.82
Palpable spleen[15,17]	0.33-0.75
Palpable liver edge[71,72]	0.44-0.53
Liver consistency, normal or abnormal[15]	0.4
Liver firm to palpation[73]	0.72
Liver, nodular or not[15]	0.29
Liver, tender or not[17]	0.49
Liver, span >9 cm by percussion[45]	0.11
Spleen palpable or not[74]	0.56-0.70
Spleen percussion sign (Traube sign), positive or not[75]	0.19-0.41
Abdominal aortic aneurysm, present vs. absent[76]	0.53
Auscultation	
Normal bowel sounds[68]	0.36
EXTREMITIES	
Peripheral Vascular Disease	
Peripheral pulse, present vs. absent[77,78]	0.52-0.92
Peripheral pulse, normal or diminished[77]	0.01-0.15
Cool extremities[47]	0.46
Diabetic Foot	
Monofilament sensation, normal or abnormal[79–81]	0.48-0.83
Probe-to-bone test[82]	0.80
Edema and Deep Venous Thrombosis	
Dependent edema[45–47]	0.39-0.73
Wells pretest probability for deep venous thrombosis[83,84]	0.74-0.75
Musculoskeletal System, Shoulder	
Shoulder tenderness[85]	0.32
Painful arc[85–87]	0.45-0.64
External rotation of shoulder <45 degrees[85]	0.68
Supraspinatus test (empty can)[85,88]	0.47-0.94
Infraspinatus test (resisted external rotation)[85,86]	0.49-0.67
Impingement sign (Hawkins-Kennedy sign)[85,86,88]	0.29-1
Drop arm test[85]	0.28
Musculoskeletal System, Hip	
Patrick test[89]	0.47
Passive internal rotation ≤25 degrees[89]	0.51
Musculoskeletal System, Knee	
Ottawa knee rules[90]	0.77
Knee effusion visible[90–92]	0.28-0.59
Knee flexion <90 degrees[90]	0.74
Patellar tenderness[90,91]	0.69-0.76
Head of fibula tenderness[90]	0.64

TABLE 4-1 Interobserver Agreement and Physical Signs—cont'd

Finding (Reference)	κ-statistic*
Inability to bear weight immediately and in emergency room after knee injury[90,91]	0.75-0.81
Bony swelling of knee[93]	0.55
Medial joint line tenderness of knee[92,93]	0.21-0.40
Lateral joint line tenderness of knee[92,93]	0.25-0.43
Patellofemoral crepitus[93]	0.24
Mediolateral instability of knee[93]	0.23
McMurray sign[92,94]	0.16-0.35
Musculoskeletal System, Ankle	
Inability to walk four steps immediately and in emergency room after ankle injury[95,96]	0.71-0.97
Medial malleolar tenderness[96]	0.82
Lateral malleolar tenderness[96]	0.80
Navicular tenderness[96]	0.91
Base of fifth metatarsal tenderness[96]	0.94
Ottawa ankle rule[97]	0.41
Ottawa midfoot rule[97]	0.77
NEUROLOGIC EXAMINATION	
Visual Fields	
Visual fields by confrontation[98]	0.63-0.81
Cranial Nerves	
Pharyngeal sensation, present or absent[99]	1
Facial palsy, present or absent[100,101]	0.57
Dysarthria, present or absent[102]	0.61-0.77
Water swallow test (50 mL)[103]	0.60
Oxygen desaturation test (for aspiration risk)[103]	0.60
Abnormal tongue strength[102]	0.55-0.63
Motor Examination	
Muscle strength, Medical Research Council (MRC) scale[104–106]	0.69-0.93
Foot tapping test[107]	0.73
Muscle atrophy[108]	0.32-0.81
Spasticity, 6-point scale[109]	0.21-0.61
Rigidity, 4-point scale[110]	0.64
Asterixis[15]	0.42
Sensory Examination	
Light touch sensation, normal, diminished, or increased[108]	0.63
Pain sensation, normal, diminished, or increased[105,108]	0.41-0.57
Vibratory sensation, normal or diminished[108]	0.45-0.54
Reflex Examination	
Reflex amplitude, National Institute of Neurological Disorders and Stroke (NINDS) scale[111]	0.51-0.61
Ankle jerk, present or absent[105,112,113]	0.34-0.94
Asymmetrical knee jerk[105]	0.42
Primitive reflexes, amplitude and persistence[114]	0.46-1
Babinski response[100,101,107,115,116]	0.17-0.55

Continued

TABLE 4-1 Interobserver Agreement and Physical Signs—cont'd

Finding (Reference)	κ-statistic*
Coordination	
Finger-to-nose test[100,101]	0.55
Dysmetria, finger-to-nose test, rated 0 to 3[117]	0.36-0.40
Peripheral Nerves	
Spurling test[118]	0.60
Flick sign[119]	0.90
Hypalgesia index finger[119]	0.50
Tinel sign[119]	0.47
Phalen sign[119]	0.79
Straight leg–raising test[105,120–124]	0.21-0.80
Crossed leg–raising test[105]	0.49

*Interpretation of the κ-statistic: 0 to 0.2, slight agreement; 0.2 to 0.4, fair agreement; 0.4 to 0.6, moderate agreement; 0.6 to 0.8, substantial agreement; 0.8 to 1, almost perfect agreement.

Table 4-2 shows that for most of our **diagnostic standards**—chest radiography, computed tomography, screening mammography, angiography, magnetic resonance imaging, ultrasonography, endoscopy, and pathology—interobserver agreement is also less than perfect, with κ-statistics similar to those observed with physical signs. Even with laboratory tests, which present the clinician with a single, indisputable number, interobserver disagreement is still possible and even common, simply because the clinician has to interpret the laboratory test's **significance.** For example, in one study of three endocrinologists reviewing the same thyroid function tests and other clinical data of 55 consecutive outpatients with suspected thyroid disease, the endocrinologists disagreed about the final diagnosis 40% of the time.[29] Computerized interpretation of test results performs no better: In a study of pairs of electrocardiograms taken only 1 minute apart from 92 patients, the computer interpretation was significantly different 40% of the time, even though the tracings showed no change.[143]

By defining abnormal findings precisely, by studying and mastering examination technique, and by observing every detail at the bedside attentively and without bias or distraction, clinicians can minimize interobserver disagreement and make physical diagnosis more precise. It is simply impossible, however, to abstract every detail of clinicians' observations of patients into exact physical signs, and, in this way, physical diagnosis is no different than any of the other tools used to categorize disease. So long as both the material and the observers of clinical medicine are human beings, a certain amount of subjectivity always will be with us.

APPENDIX: CALCULATION OF THE KAPPA-STATISTIC

The observations of two observers who are examining the same number (N) of patients independently are customarily displayed in a 2×2 table, similar to that in Figure 4-1. Observer A finds the sign to be present in w_1

TABLE 4-2 Interobserver Agreement: Diagnostic Standards

Finding (Reference)	κ-statistic*
CHEST RADIOGRAPHY	
Cardiomegaly[51]	0.48
Pulmonary infiltrate[125]	0.38
Interstitial edema[51]	0.83
Pulmonary vascular redistribution[51]	0.50
Grading pulmonary fibrosis, 4-point scale[126]	0.45
CONTRAST VENOGRAPHY	
Deep vein thrombosis in leg[127]	0.53
SCREENING MAMMOGRAPHY	
Suspicious lesion, present vs. absent[128]	0.47
DIGITAL SUBTRACTION ANGIOGRAPHY	
Renal artery stenosis[129]	0.65
CORONARY ARTERIOGRAPHY	
Classification of coronary artery lesions[130]	0.33
ARTHROSCOPY	
Inflamed or torn tear of supraspinatus muscle[131]	0.47
COMPUTED TOMOGRAPHY OF HEAD	
Normal or abnormal, patient with stroke[132]	0.60
Lesion on right or left side, patient with stroke[132]	0.65
Mass effect, present or absent[132]	0.52
COMPUTED TOMOGRAPHY OF THE CHEST	
Lung cancer staging[133]	0.40-0.60
Submassive pulmonary embolism present (angiography)[134]	0.47
MAGNETIC RESONANCE IMAGING OF HEAD	
Compatible with multiple sclerosis[135]	0.57-0.87
MAGNETIC RESONANCE IMAGING OF LUMBAR SPINE	
Intervertebral disc extrusion, protrusion, bulge, or normal[136]	0.59
Lumbar nerve root compression[137]	0.83
ULTRASONOGRAPHY	
Calf deep vein thrombosis, present or absent[138]	0.69
Thyroid nodule, present or absent[139,140]	0.57-0.66
Goiter is present[31]	0.63
ENDOSCOPY	
Grade of reflux esophagitis[141]	0.55
PATHOLOGIC EXAMINATION OF LIVER BIOPSY	
Cholestasis[142]	0.40
Alcoholic liver disease[142]	0.49
Cirrhosis[142]	0.59

*Interpretation of the κ-statistic: 0 to 0.2, slight agreement; 0.2 to 0.4, fair agreement; 0.4 to 0.6, moderate agreement; 0.6 to 0.8, substantial agreement; 0.8 to 1, almost perfect agreement.

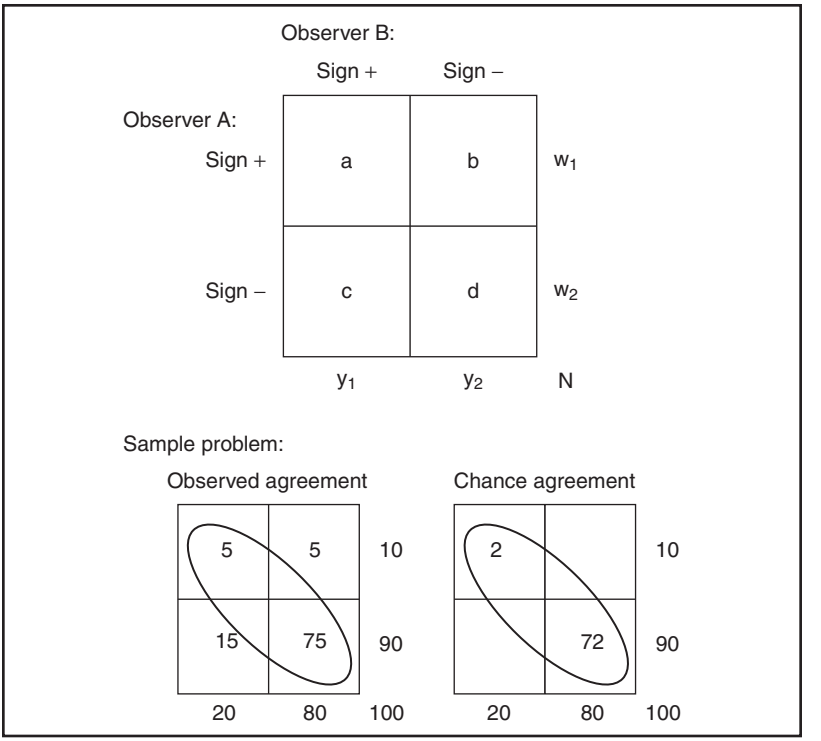


FIGURE 4-1 Interobserver agreement and the κ-statistic. *Top half:* Conventional 2×2 table displaying data for calculation of κ-statistic. *Bottom half:* A sample case, in which observed agreement is 80%, chance agreement is 74%, and the κ-statistic is 0.23. (See Appendix at the end of this chapter for discussion.)

patients and absent in w_2 patients; observer B finds the sign to be present in y_1 patients and absent in y_2 patients. The two observers agree that the sign is present in *a* patients and absent in *d* patients. Therefore, the observed agreement (P_O) is:

$$P_O = (a + d)/N$$

Calculation of the κ-statistic first requires calculation of the agreement that would have occurred by chance alone. Among all the patients, observer A found the fraction w_1/N to have the sign; therefore, by chance alone, among the y_1 patients with the sign according to observer B, observer A would find the sign in (w_1/N) times y_1 or (w_1y_1/N) patients (i.e., this is the *number* of patients in which both observers agree the sign is present, by chance alone). Similarly, both observers would agree that the sign is absent by chance alone in (w_2y_2/N) patients. Therefore, the expected chance agreement (P_E) is their sum, divided by N:

$$P_E = (w_1y_1 + w_2y_2)/N^2$$

This equation shows that agreement by chance alone (P_E) approaches 100% as both w_1 and y_1 approach 0 or N (i.e., both clinicians agree that a finding is rare or that it is very common).

The κ-statistic is the increment in observed agreement beyond that expected by chance ($P_O - P_E$), divided by the maximal increment that could have been observed had the observed agreement been perfect ($1 - P_E$):

$$\kappa = \frac{(P_O - P_E)}{(1 - P_E)}$$

For example, Figure 4-1 depicts the observations of two observers in a study of 100 patients with dyspnea. Both agree that the third heart sound is present in 5 patients and absent in 75 patients; therefore, simple agreement is (5 + 75)/100 or 0.8. By chance alone, they would have agreed about the sound being present in (10 × 20)/100 patients (i.e., 2 patients) and absent in (90 × 80)/100 patients (i.e., 72 patients); therefore, chance agreement is (2 + 72)/100 patients or 0.74. The κ-statistic for this finding becomes (0.80 − 0.74)/(1 − 0.74) = (0.06)/(0.26) = 0.23.

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 5

Mental Status Examination

I. INTRODUCTION

Dementia is a clinical syndrome characterized by deteriorating cognition, behavior, and autonomy that affects 3% to 11% of adults older than 65 years living in the community.[1] Before making the diagnosis of dementia, the clinician must exclude delirium (i.e., acute confusion; see the section on Diagnosis of Delirium).

Of the many simple and rapid bedside tests developed to diagnose dementia, the most extensively investigated ones are the clock-drawing test, Mini-Cog test, and Mini-Mental Status Examination (MMSE).

II. CLOCK-DRAWING TEST

The clock-drawing test was originally developed in the early 1900s to evaluate soldiers who had suffered head wounds to the occipital or parietal lobes, injuries that often led to difficulty composing images correctly with the appropriate number of parts of correct size and orientation (i.e., constructional apraxia).[2] To depict a clock, patients must be able to follow directions, comprehend language, visualize the proper orientation of an object, and execute normal movements, all tasks that may be disturbed in dementia.

A. TECHNIQUE AND SCORING

There are at least a dozen different methods for performing and scoring the clock-drawing test, some with intricate grading systems that defeat the test's simplicity.[3,4] In a simple and well-investigated method,[5] the clinician gives the patient a piece of paper with a preprinted circle 4 inches in diameter and asks the patient to "draw a clock." If the patient has any questions, the clinician repeats the same instructions and gives no other guidance. The patient may take as long as he or she wants to complete the task. Figure 5-1 describes how to score the drawing.

B. CLINICAL SIGNIFICANCE

In patients without other known causes of constructional apraxia (e.g., parietal lobe lesion), a positive clock-drawing test increases the probability of dementia (LR = 5.3; EBM Box 5-1). A normal clock-drawing test is a less useful result, being elicited from many patients with dementia as defined by other measures. In contrast to the MMSE, the clock-drawing test is unaffected by the patient's level of education.[6]

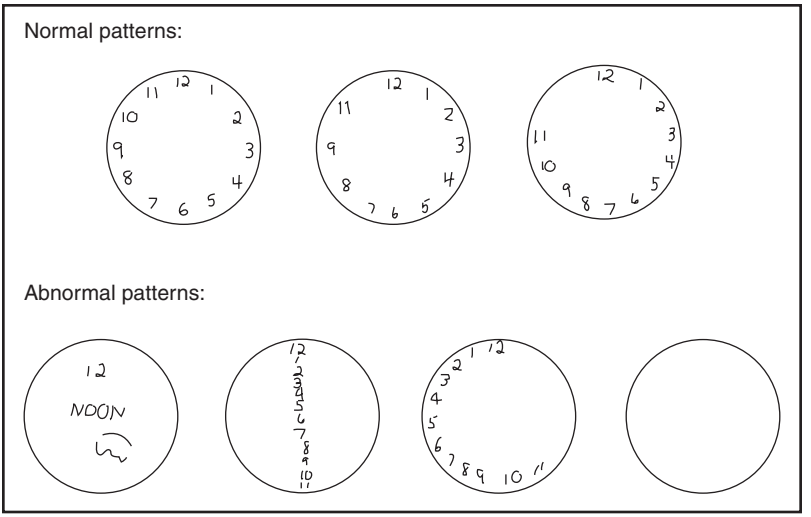


FIGURE 5-1 The clock-drawing test (Wolf-Klein method). The clock-drawing test is normal if the patient has included most of the 12 numbers in the correct clockwise orientation. The patient does not need to draw the hands of the clock, and abnormal spacing of the numbers, however inappropriate, is still regarded as normal as long as the numbers are in the correct order and near the rim. Normal clock-drawing patterns, from left to right, are "normal," "missing one number," and "inappropriate spacing." Abnormal clock-drawing patterns, from left to right, are "irrelevant figures," "unusual arrangement" (i.e., vertical orientation of numbers), "counterclockwise rotation," and "absence of numbers." *(Adapted with permission from Wolf-Klein, Silverstone FA, Levy AP, et al. Screening for Alzheimer's disease by clock drawing. J Am Geriatr Soc. 1989;37:730-734.)*

III. MINI-COG TEST

A. TECHNIQUE AND SCORING

The Mini-Cog test combines a clock-drawing test with tests of recall to provide a brief screening tool suitable for primary care patients, even those who do not speak English as their native language.[10] To perform the test, the clinician asks the patient to register three unrelated words (e.g., *banana*, *sunrise*, and *chair*) and then asks the patient to draw a clock, stating, "Draw a large circle, fill in the numbers on a clock face, and set the hands at 8:20." The patient is allowed 3 minutes to draw the clock, and instructions may be repeated if necessary. After drawing the clock (or after 3 minutes has elapsed), the patient is asked to recall the three words. The Mini-Cog test is scored by assigning one point for each word recalled (score, 0 to 3) and two points for a "normal" clock, which should have the correct orientation and spacing of numbers and hands. An "abnormal" clock receives no points, thus creating possible total scores of 0 to 5.[34]

B. CLINICAL SIGNIFICANCE

As displayed in EBM Box 5-1, a Mini-Cog score of 2 or less increases the probability of dementia (LR = 9.5).

IV. MINI-MENTAL STATUS EXAMINATION (MMSE)

A. INTRODUCTION

The MMSE (Table 5-1) was introduced by Folstein in 1975 as an 11-part bedside test requiring only 5 to 10 minutes to administer, a much briefer time compared with the 1 to 2 hours required by more formal tests of dementia.[35]

B. CLINICAL SIGNIFICANCE

EBM Box 5-1 illustrates that assuming there is no evidence of delirium (see section on Diagnosis of Delirium), a MMSE score of 23 or less increases the probability of dementia greatly (LR = 8.9), whereas a score of 24 to 30 decreases it (LR = 0.2). Nonetheless, because false-positive results become a concern when applying this threshold to large populations with a low incidence of dementia, such as persons living independently in the community, some experts prefer interpreting the MMSE score in three ranges (see EBM Box 5-1): A score of 20 or less rules in dementia (LR = 14.4); one of 26 or more rules out dementia (LR = 0.1); and one of 21 to 25 is regarded as less conclusive (LR = 2.1), thus prompting further investigation.

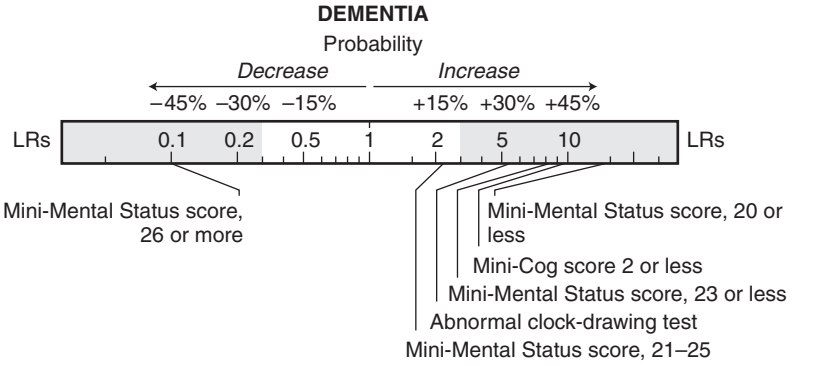
EBM BOX 5-1
*Dementia and Delirium**

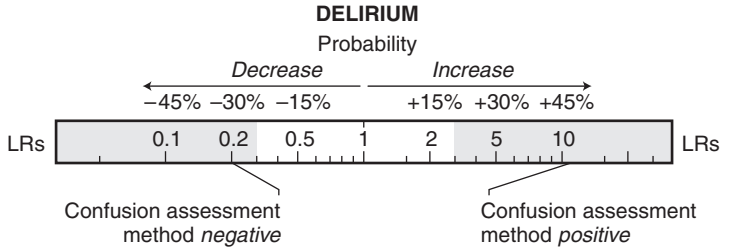
Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Dementia†				
Abnormal clock-drawing test[5–9]	36-75	72-98	**5.3**	0.5
Mini-Cog score 2 or less[10,11]	76-99	89-93	**9.5**	NS
MINI-MENTAL STATUS EXAMINATION: TRADITIONAL THRESHOLD				
23 or less[11–24]	53-100	78-99	**8.9**	**0.2**
MINI-MENTAL STATUS EXAMINATION: THREE LEVELS[14,16–18,23]				
20 or less	29-69	93-99	**14.4**	—
21-25	26-57	—	2.1	—
26 or more	4-14	14-31	**0.1**	—
Delirium				
Positive test using Confusion Assessment Method†[25–31]	46-94	83-98	**10.7**	**0.2**

*Diagnostic standards: For *dementia*, dementia by NINCDS-ADRDA criteria,[5,6,32,33] DMS criteria,[8–13,15,16,18,20,21,23] CAMDEX instrument,[14] AGECAT,[19,22] or neurologist opinion[17,24]; for *delirium*, the DMS criteria.[19,25–31]

†Definition of findings: For abnormal clock-drawing test, see Figure 5-1; for Mini-COG test and Confusion Assessment Method, see text.

‡Likelihood ratio (LR) if finding is present = positive LR; LR if finding is absent = negative LR. *Click here to access calculator.*





The MMSE score may be used to follow patients over time, but only changes of four points or more reliably indicate a change of cognition.[36] The level of the patient's education also affects the MMSE score, whether or not dementia is present,[13,37] and some have suggested adjusting the threshold for a positive test downward slightly in more poorly educated persons.[13]

V. DIAGNOSIS OF DELIRIUM (CONFUSION ASSESSMENT METHOD)

Delirium is an acute and reversible confusional state that affects up to 20% of elderly patients hospitalized with acute medical illnesses.[26] Of the several screening tools available to diagnose delirium,[26] one simple and well-investigated one is the Confusion Assessment Method.[25]

A. SCORING

The clinician looks for the following four clinical features: (1) change in mental status (compared with the patient's baseline status) that is *acute* and *fluctuating*; (2) difficulty in focusing attention or trouble keeping track of what is being said; (3) disorganized thinking (e.g., rambling or irrelevant conversation, unpredictable switching between subjects, illogical flow of ideas); and (4) altered level of consciousness (e.g., lethargic, stuporous, or hyperalert).

A positive test requires both features 1 and 2 *and* either 3 or 4.

TABLE 5-1 Mini-Mental Status Examination

Test	Maximum Score
ORIENTATION	
1. What is the year? Season? Date? Day? Month?*	5
2. Where are we? State? County? City? Hospital? Floor?*	5
REGISTRATION	
3. Name three objects. Ask the patient to name the items.* Repeat the answers until the patient learns all three.	3
ATTENTION AND CALCULATION	
4. Serial sevens (ask the patient to begin with 100 and count backwards by sevens, stopping after five subtractions: 93, 86, 79, 72, 65).* or Spell "world" backwards.*	5
RECALL	
5. Ask the patient to name the three objects learned under "registration," above.*	3
LANGUAGE	
6. Point to a pencil and a watch, asking the patient to name both items.*	2
7. Have the patient repeat "No ifs, ands, or buts."	1
8. Have the patient follow a three-stage command. For example, say "Take a paper in your right hand. Fold the paper in half. Put the paper on the floor."*	3
9. Have the patient read and obey the following sentence, written in large letters: "Close your eyes."	1
10. Have the patient write a sentence.†	1
11. Have the patient copy a picture of two intersecting pentagons.	1
Total	30

*Give one point for each correct answer.

†The sentence should make sense and contain a subject and object to earn the one point; spelling errors are ignored.

Adapted from Anthony JC, LeResche L, Niaz U, et al. Limits of the "Mini-Mental State" as a screening test for dementia and delirium among hospital patients. *Psychol Med*. 1982;12: 397-408; Folstein MF, Folstein SE, McHugh PR. "Mini-Mental State": a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975;12:189-198.

B. CLINICAL SIGNIFICANCE

As illustrated in EBM Box 5-1, a positive test argues strongly *for* delirium (LR = 10.7) and a negative test argues *against* delirium (LR = 0.2). Another version of this test, adapted for use in mechanically ventilated patients who cannot talk, has similar accuracy.[38,39] In any patient with delirium, positive bedside tests for *dementia* are inaccurate because of a high false-positive rate.

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 6

Stance and Gait

I. INTRODUCTION

Observation of gait not only uncovers important neurologic and musculoskeletal problems (e.g., Parkinson disease, hemiparesis, spinal stenosis, hip disease) but also provides clues to a patient's emotions and overall function and can even give clues to the prognosis. For example, the speed of an elderly person's gait accurately predicts falls, future disability, and risk of institutionalization.[1-5] In patients with congestive heart failure, gait speed predicts cardiac index, future hospitalization, and mortality as well as the ejection fraction and better than the treadmill test.[6,7] Even depressed patients have a characteristic gait, marked by an abnormally short stride and weak lift-off of the heel.[8]

The phases of the normal gait are depicted in Figure 6-1.

II. ETIOLOGY OF GAIT DISORDERS

Among patients presenting to neurologists, the most common causes of gait disorder are stroke and Parkinson disease, followed by frontal gait disorder, myelopathy (e.g., cervical spondylosis, B_{12} deficiency), peripheral neuropathy, and cerebellar disease.[11,12] Among patients presenting to general clinicians, most gait abnormalities are caused by arthritis, followed by orthostatic hypotension, stroke, Parkinson disease, and intermittent claudication.[13]

III. TYPES OF GAIT DISORDERS AND THEIR SIGNIFICANCE

Disorders of gait reflect one of four possible problems: pain, immobile joints, muscle weakness, or abnormal limb control. Abnormal limb control, in turn, may result from spasticity, rigidity, diminished proprioception, cerebellar disease, or problems with cerebral control.

When analyzing a patient's gait, the most important initial question to settle is whether the gait is symmetrical or asymmetrical. Pain, immobile joints, and muscle weakness are usually unilateral and thus cause *asymmetrical* abnormalities of gait. Rigidity, proprioceptive disorders, cerebellar diseases, and problems with central control all cause *symmetrical* abnormalities of gait. Spasticity may cause *asymmetrical* gait abnormalities (i.e., hemiplegia) or *symmetrical* ones (i.e., paraplegia).

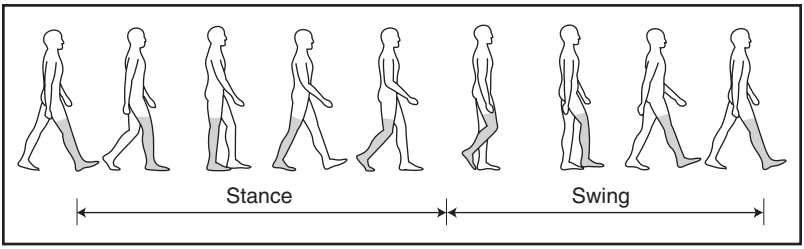


FIGURE 6-1 Normal gait. This figure illustrates the phases of normal gait, focusing on the right leg *(gray)*. Normal gait consists of the stance phase (the period during which the leg bears weight) and swing phase (the period during which the leg advances and does not bear weight). The stance and swing make up the stride, which is the interval from the time one heel strikes the ground to when it again strikes the ground. During the normal stance phase, it is the extensor muscles that contract—the gluteus maximus muscle in early stance, the quadriceps muscle in mid stance, and the plantar flexor muscles (soleus and gastrocnemius muscles) in terminal stance pushing off the heel. The healthy swing, in contrast, requires contraction of the flexor muscles, all of which are activated early in the swing phase—hip flexors (iliopsoas muscles), knee flexors (hamstring muscles), and ankle flexors (tibialis anterior and toe extensor muscles). *(Figure adapted with permission from references 9 [The pathokinesiology service and the physical therapy department of the Rancho Los Amigos Medical Center. Observational Gait Analysis. Downey, Calif: Los Amigos Research and Education Institute, Inc.; 1993] and 10 [Perry J. Gait Analysis: Normal and Pathological Function. Thorofare, NJ: Slack, Inc.; 1992.])*

A. PAINFUL GAIT (ANTALGIC GAIT)

If bearing weight on a limb is painful, patients adopt an antalgic gait to minimize the pain. (*Antalgic* is from the Greek *an* and *algesis*, meaning "against pain.") All antalgic gaits are characterized by a short contralateral step.

1. Short Contralateral Step

After bearing weight on the affected leg, patients with pain quickly step onto the sound leg. The short contralateral step produces an uneven cadence, one identical to that produced in anyone if a rock is in one shoe.

2. Other Characteristic Features

Depending on whether the pain is located in the foot, knee, or hip, each antalgic gait is distinctive, allowing diagnosis from a distance.

a. Foot Pain

In patients with foot pain, the foot contacts the ground abnormally. For example, patients may bear weight during stance on the heel only or forefoot only or along the lateral edge of the foot.

b. Knee Pain

Patients with knee pain display a stiff knee that does not extend or flex fully during stride.[14]

c. Hip Pain (Coxalgic Gait)

Patients with hip pain limit the amount of hip extension during late stance (when the normal hip extends 20 degrees). Even so, the most characteristic feature of the coxalgic gait is the so-called **lateral lurch**: When the patient

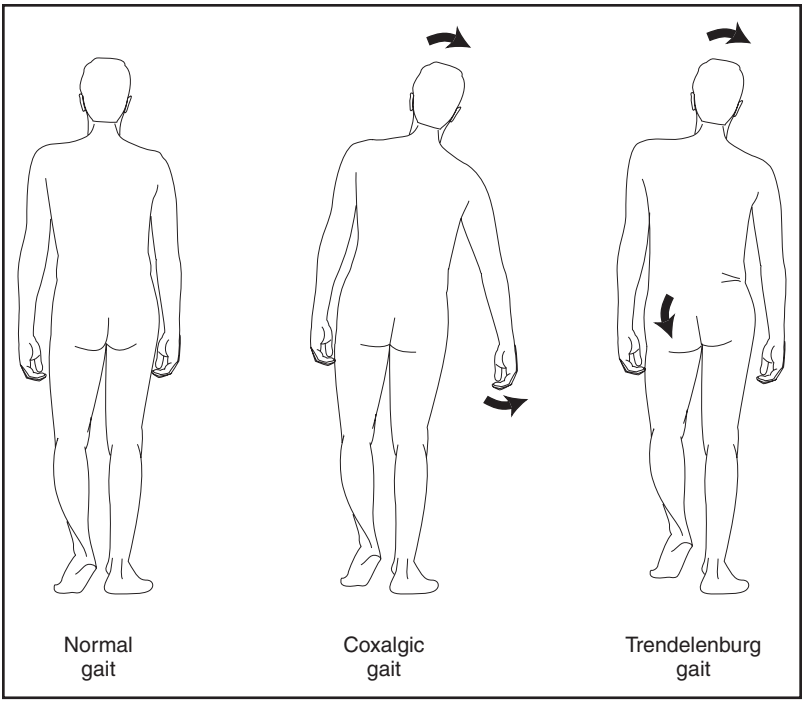


FIGURE 6-2 Comparison of coxalgic and Trendelenburg gait. In both abnormal gaits (middle and right figures), the trunk may lean over the abnormal leg during stance *(arrow),* but in patients with hip pain (coxalgic gait, middle figure), the trunk lean and accompanying ipsilateral arm movement *(arrow)* is more dramatic (lateral lurch) and the opposite pelvis does not fall excessively. In the Trendelenburg gait (from ineffective or weak hip abductors, right figure), the opposite pelvis falls excessively *(arrow),* and the conspicuous but opposing swings of the upper body and pelvis create the impression of a hinge between the sacral and lumbar spine. In these figures, the patient is bearing weight on the affected side, that is, *right* hip pain (coxalgic gait) and ineffective *right* hip abductors (Trendelenburg gait).

is bearing weight on the painful limb, there is an excessive asymmetrical lateral shift of the upper body toward the weight-bearing side, causing the trunk to lean and ipsilateral arm to abduct (Fig. 6-2).[15,16]

Lateral lurch reduces the pain of patients with hip disease because it minimizes the need to activate the ipsilateral hip abductor muscles. These muscles normally support the upper body during swing of the other leg, but, when activated, they can easily put 400 pounds of pressure on the femoral head, an intolerable force if there is hip disease. By leaning over the painful limb during stance, patients effectively balance their center of gravity over the painful limb and thus avoid activation of the hip abductors.

B. IMMOBILE JOINTS

Most clinicians do not consider immobile joints as a cause of abnormal gait, but the condition is well known to physiatrists. A common example is plantar flexion contracture, a complication that may occur after prolonged

periods of plaster immobilization or confinement to bed. Affected patients may place their weight on the forefoot during initial stance (instead of the heel), or during midstance, they may lift the heel too early or lean the trunk forward. During swing phase, the abnormally flexed foot has difficulty clearing the floor, leading the patient to drag the foot or develop an unusual movement to clear it, such as contralateral trunk lean or contralateral vaulting.[9,10]

The clinician can easily identify immobile joints as the cause of abnormal gait by testing the range of motion of hips, knees, and ankles of both legs.

C. WEAKNESS OF SPECIFIC MUSCLES

Three muscle groups, when weak, cause specific gait abnormalities: (1) the hip extensor and abductor muscles (i.e., gluteus maximus and medius/minimus muscles), (2) the knee extensors (i.e., quadriceps muscles), and (3) the foot and toe dorsiflexors (i.e., the tibialis anterior and toe extensor muscles). The gluteus maximus and quadriceps gaits were frequently observed historically as complications of poliomyelitis and diphtheria.

1. Trendelenburg Gait and Sign (Abnormal Gluteus Medius and Minimus Gaits)

a. Definition of Trendelenburg Gait (or Trendelenburg's symptom; Friedrich Trendelenburg, 1844 to 1924)

The Trendelenburg gait occurs when the gluteus medius and minimus muscles do not function properly. These two muscles abduct the hip, an action that supports the opposite pelvis and prevents it from dropping excessively during the normal single-limb stance. During walking, a slight dip of the opposite pelvis is normal during stance phase on one limb. The finding of *excessive drop* of the opposite pelvis, however, is the abnormal Trendelenburg gait. When the abnormality is bilateral, the pelvis waddles like that of a duck.

Like patients with the coxalgic gait (see previous section on Hip Pain/Coxalgic Gait), patients with Trendelenburg gait may lean their trunk over the abnormal leg during stance, but the lean lacks the dramatic lurch seen in coxalgic gait, and the opposing sways of the ipsilateral shoulder and opposite pelvis make it appear as if patients with the Trendelenburg gait have a hinge between the sacral and lumbar spine (see Fig. 6-2).[16,17]

b. Etiology of Trendelenburg Gait

Causes of Trendelenburg gait include the following: **(1) neuromuscular weakness of the hip abductors** (although poliomyelitis and progressive muscular atrophy were important causes historically, this gait now occurs as a complication of hip arthroplasty using a lateral approach, which risks damage to the superior gluteal nerve or gluteus medius muscle[18,19]) and **(2) hip disease,** especially congenital dislocation of the hip and coxa vara (i.e., *bent hip*, a deformity in which the angle between the femoral neck and body is significantly decreased). In both of these disorders, the abnormal upward displacement of the greater trochanter shortens the fibers of the gluteus medius muscle and makes them more horizontal instead of vertical, thus abolishing their role as abductors.

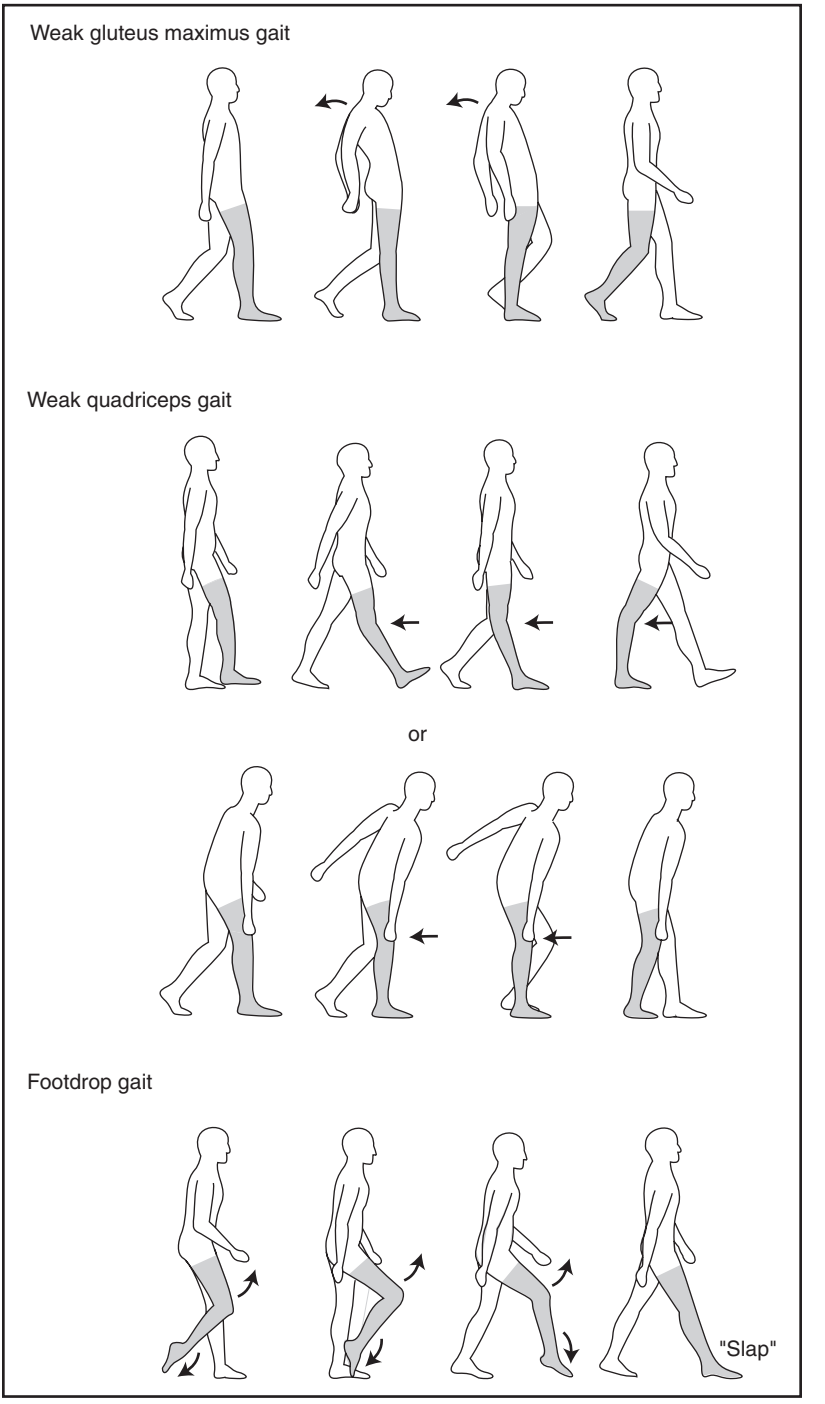

Weak gluteus maximus gait
Weak quadriceps gait
or
Footdrop gait
"Slap"

FIGURE 6-3

FIGURE 6-3 Characteristic gaits of weak muscles. In each figure, the *shading* indicates the limb with the weak muscle, and the *black arrows* indicate the diagnostic movements. Because both the gluteus maximus and quadriceps muscles are *extensor* muscles, abnormalities of these muscles produce characteristic findings during the *stance* phase. Because the foot dorsiflexors (i.e., the weak muscles causing footdrop) are *flexor* muscles, abnormalities produce characteristic findings during the *swing* phase. In the weak gluteus maximus gait *(top row),* there is an abnormal backward lean during stance. In the weak quadriceps gait *(middle rows),* patients may hyperextend their knee during stance (i.e., genu recurvatum, *second row*) or place their ipsilateral arm on the leg to prevent the knee from buckling *(third row).* In the footdrop gait *(bottom row),* the actual foot weakness is conspicuous *(bottom arrows),* and there is excessive flexion of the hip and knee during the swing phase *(upper curved arrows)* and a slapping sound of the foot when it strikes the ground. See text.

c. Trendelenburg Sign

In 1895, before the use of roentgenography, Friedrich Trendelenburg was the first to show that the waddling gait of patients with congenital dislocation of the hip was due to weak abductor function, not the upward movement of the femur during stance (which was what his contemporaries believed). He successfully argued this by inventing a simple test, now known as Trendelenburg sign. In this test, the patient is asked to stand on one leg with the other hip flexed to 90 degrees. (The clinician may help the patient balance by supporting the ipsilateral arm to align the ipsilateral shoulder over the hip being tested.[20]) In patients with normal abductor strength, the contralateral buttock rises, but if the abductor muscles are weak, the contralateral buttock falls. (The buttock falls until the ipsilateral femur and pelvis come into contact.)

It is important to remember that the side being tested is the one bearing the weight. Some deformities of the leg, such as severe genu varum, may cause a false-positive result.[21]

d. Clinical Significance

In one study of patients clinically diagnosed with "trochanteric bursitis" (i.e., lateral hip pain and maximal tenderness over the greater trochanter),[22] the finding of *both* Trendelenburg sign *and* gait on the symptomatic side accurately foretold the magnetic resonance imaging (MRI) finding of a tear in the gluteus medius tendon (sensitivity = 73%, specificity = 77%, positive LR = 3.2, negative LR not significant). This sign was superior to directly testing gluteus medius strength (by resisting the patient's active hip abduction or internal rotation, LRs not significant). The results of this study suggest that some patients with "trochanteric bursitis" actually have tendinitis or tears of the gluteus medius tendon, a discovery analogous to the historic realization that many patients with "subacromial bursitis" (in the shoulder) actually have disorders of the rotator cuff tendons.

2. Gluteus Maximus Gait

If the hip extensors are weak, the patient develops a characteristic abnormal backward trunk lean during early stance, which places the patient's center of gravity behind the hip joint line and removes the need for the gluteus maximus muscle to contract (Fig. 6-3).

3. Weak Quadriceps Gait

If the knee extensors are weak, two different abnormalities of gait may appear. Some patients develop a characteristic hyperextension of the knee during stance (see Fig. 6-3). This at first seems paradoxic because the normal action of the quadriceps muscle is knee extension, which should therefore be weak in these patients. However, the main role of the quadriceps muscle during gait is to support the flexed knee during stance, and patients with a weak quadriceps muscle avoid bearing weight on a flexed knee by hyperextending the joint (i.e., genu recurvatum). They can fully extend the knee because the hip flexes strongly during swing and then decelerates abruptly, which whips the tibia forward.[10] Alternatively, other patients with a weak quadriceps muscle may place the hand just above the knee to support the weak leg and prevent the knee from buckling during stance (see Fig. 6-3).

Most patients with weak quadriceps muscles have great difficulty walking on uneven ground.

4. Footdrop (Weak Tibialis Anterior and Toe Extensor Muscles)

There are two characteristic features: (1) *foot slap*, which is the uncontrolled slap of the forefoot immediately after the heel makes contact, thus producing (in patients with *unilateral* footdrop) a characteristic cadence of two sounds alternating with a single sound (i.e., stance of abnormal foot alternating with that of normal foot): "dada…da….dada…da"; and (2) *steppage gait*, which occurs during the forward swinging phase of the affected foot, when the patient flexes the hip and knee excessively to clear the foot from the ground, thus creating the appearance of the abnormal foot "stepping over" an invisible object (see Fig. 6-3).[9]

D. SPASTICITY

Spasticity is a feature of weakness of the upper motor neuron type (see Chapter 59). Characteristic gaits are the hemiplegic gait and diplegic (paraplegic) gait.

1. Hemiplegic Gait

This gait is the result of poor control of the flexor muscles during swing phase and spasticity of the extensor muscles acting to lengthen the affected leg (compared with the healthy side). The ankle is abnormally flexed downward and inward (equinovarus deformity), and initial contact during stance is abnormal, along the lateral edge of the foot or forefoot. The knee is stiff, hyperextends during stance, and does not flex normally during swing. The contralateral step often advances just to meet the position of the paralyzed limb instead of advancing normally beyond it.

Because the paralyzed leg is hyperextended, and therefore longer than the sound leg, the patient may drag the toe of the affected leg during swing or adopt abnormal movements to clear that limb during the swing phase. These movements include contralateral trunk lean, which raises the ipsilateral pelvis to clear the paralyzed leg, and circumduction, which describes

the toe tracing a semicircle on the floor, first moving outward and then inward as it advances, instead of the normal straight forward movement (Fig. 6-4).

According to classic teachings, the clinician should suspect mild hemiplegia if a patient swings his or her arms asymmetrically while walking, although this finding appears in 11% to 70% of normal persons[23,24] and the sign did not accurately detect focal cerebral disease in one study (sensitivity 22%, specificity 89%, positive and negative LRs not significant).[23]

2. Diplegic Gait

Diplegic gait affects patients with spinal cord disease (e.g., spinal cord trauma, cervical spondylosis, B_{12} deficiency). The combinations of spasticity and abnormal proprioception cause a characteristic slow, laborious, and stiff-legged gait. In some spastic diplegias of childhood, adductor spasm causes the feet to cross in front of each other (scissors gait).

E. RIGIDITY

Chapter 59 describes the characteristic features of rigidity and distinguishes it from spasticity. The most common gait abnormality due to rigidity is the parkinsonian gait.

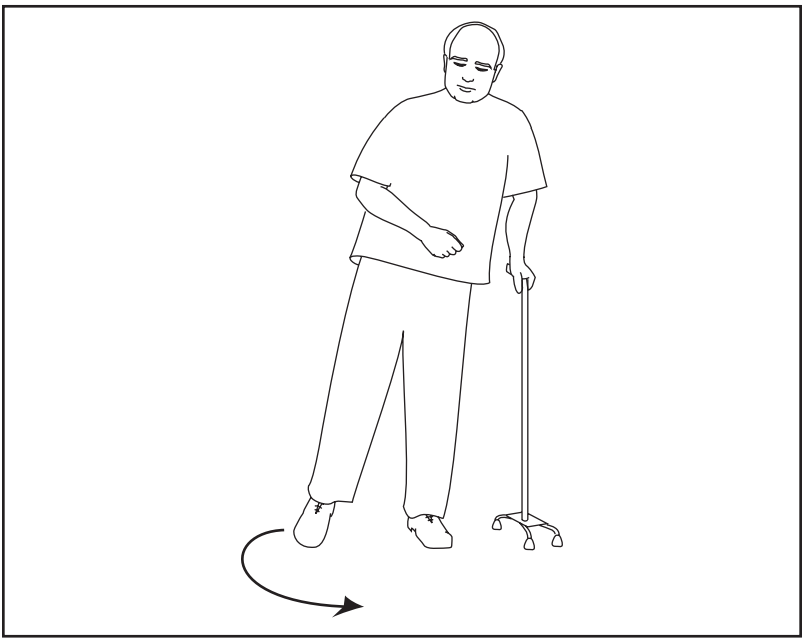


FIGURE 6-4 Hemiplegic gait. In a patient with right hemiparesis, the paretic arm is flexed and paretic leg is hyperextended. To clear the extended right leg from the floor, the patient leans over the healthy left leg and slowly advances the stiffened, paralyzed right leg with a circumducting movement *(arrow)*.

1. Parkinsonian Gait (Fig. 6-5)

The characteristic features are (1) flexed posture of the arms, hips, trunk, and neck; (2) rigidity of movement (en bloc turning, difficulty initiating gait); (3) steps that are flat-footed, small, shuffling, and with a narrow base; (4) diminished arm swing (normal arm excursion, measured at the wrist, averages 16 inches; the average value for patients with Parkinson disease is 5 inches); (5) involuntary hastening of gait (festination); and (6) poor postural control (retropulsion).

2. Differential Diagnosis

Patients with spinal stenosis superficially resemble those with Parkinson disease in that they have a flexed stance (simian stance), which reduces the tension on the lumbosacral nerves.[25] Patients with spinal stenosis, however, complain of pain and otherwise have a normal gait.

The distinguishing features of the frontal gait disorder, which also may superficially resemble the parkinsonian gait, are discussed later in the section on Frontal Gait Disorder.

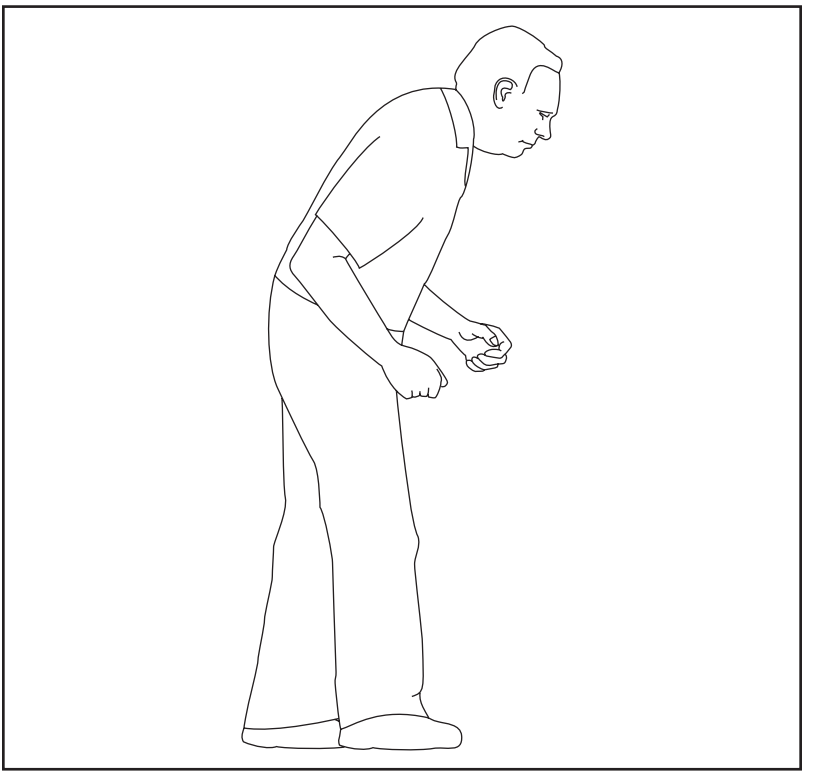


FIGURE 6-5 Parkinsonian gait. The characteristic features are flexed posture (trunk, neck, and arms), diminished arm swing, narrow-based gait, and shuffling steps.

3. Clinical Significance

Patients presenting with **parkinsonism** (i.e., combinations of rigidity, bradykinesia, and tremor) have either **Parkinson disease** (a disorder from pathologic depigmentation of the substantia nigra that responds to levodopa) or a group of mimicking disorders called **Parkinson-plus syndromes** (disorders with distinct pathologic findings that respond less well to levodopa; e.g., progressive supranuclear palsy and multiple system atrophy; see Chapter 64).

The gait of patients with Parkinson disease has a narrower base than the gait of patients with the Parkinson-plus syndromes, suggesting that the latter group (Parkinson-plus patients) may have greater instability during tandem gait. In clinical studies, the inability of a patient *with parkinsonism* to walk 10 tandem steps decreases the probability of Parkinson disease (LR = 0.1, EBM Box 6-1) and increases the probability of a mimicking Parkinson-plus syndrome (see Chapter 64).

F. ATAXIA

The characteristic features of the ataxic gait are its wide base and the irregular, uneven, and sometimes staggering steps. (The normal base, measured when one limb swings past the other at mid-stance, is 2 to 4 inches.) There are two types of ataxia, sensory and cerebellar.

1. Sensory Ataxia

Sensory ataxia affects patients with significant proprioceptive loss (see Chapter 60). Characteristically, the patient looks down and walks as if throwing the feet, which tend to slap on the ground. Smooth, familiar routes cause less trouble than uneven, rough ones.

2. Cerebellar Ataxia

Affected patients place their feet too far apart or too close together irregularly, swaying, staggering, and reeling in all directions as if intoxicated by alcohol. In contrast to sensory ataxia, patients with cerebellar ataxia have other cerebellar signs, including dysmetria, hypotonia, intention tremor, dysarthria, and nystagmus (see Chapter 63).

3. Romberg Sign

a. Introduction

In his famous textbook, written between 1840 and 1846, Moritz Romberg described the sign now bearing his name, as a finding in patients with severe sensory ataxia from syphilitic damage to the dorsal columns of the spinal cord **(tabes dorsalis).** According to Romberg, when a patient with tabes dorsalis stands and closes the eyes, "He immediately begins to moves from side to side, and the oscillations soon attain such a pitch that unless supported, he falls to the ground."[28] Most authors claim that Romberg sign is negative in patients with cerebellar ataxia, although Romberg did not make this claim. (Cerebellar disease was not defined during his time; Duchenne and Babinski later added this diagnostic point.[29])

EBM BOX 6-1

*Gait Abnormalities in Patients with Parkinsonism or Dementia**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Detecting Parkinson Disease in Patients with Parkinsonism				
Unable to perform 10 perfect tandem steps[26]	8	18	**0.1**	**5.0**
Detecting Type of Dementia§				
Any gait or balance disorder (moderate or worse), detecting Alzheimer dementia[27]	16	25	**0.2**	**3.4**
Parkinsonian gait, detecting Lewy body dementia or Parkinson disease with dementia[27]	78	91	**8.8**	**0.2**
Frontal gait, detecting vascular dementia[27]	56	91	**6.1**	0.5

*Diagnostic standard: For *Parkinson-plus disorder*, the conventional diagnostic criteria for multiple system atrophy, progressive supranuclear palsy, Lewy body dementia, corticobasal degeneration, or vascular dementia[26]; for *Alzheimer dementia*, conventional diagnostic criteria.

†Definition of findings: For *unable to perform tandem gait*, the patient was instructed to take 10 consecutive tandem steps along a straight line without walking aids and support, with eyes open, and the clinician observed 1 side step or more during testing.[26]

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

§All patients have dementia.

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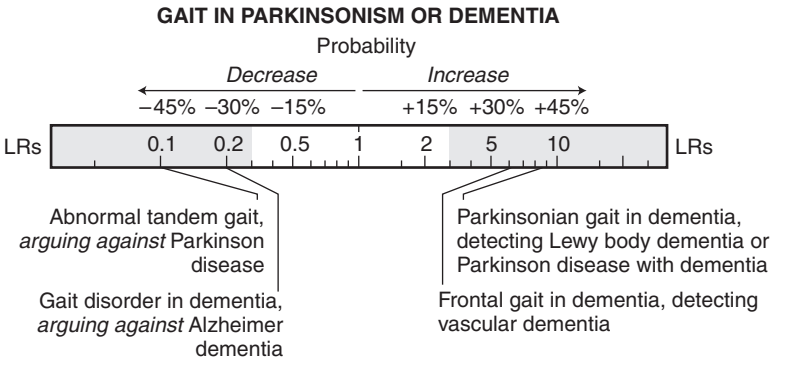

b. Definition of Positive Romberg Sign

One problem with Romberg sign is that various authors define the positive test differently: Some state that it is the increased swaying that occurs when the eyes close, while others require the patient to be on the verge of falling down.[28] Increased swaying alone seems inadequate, because most normal persons sway more when they close their eyes, as do patients with vestibular, cerebellar, and Parkinson disease.[30]

The best definition of a positive Romberg sign is inability to stand for 60 seconds with the feet together and the eyes closed. In one study, every healthy person and over half of the patients with cerebellar ataxia could maintain this position for 60 seconds, whereas half of the patients with sensory ataxia lasted only 10 seconds before beginning to topple over.[31]

A related sign, the sharpened Romberg sign,[32] in which patients must stand with one foot in front of the other with the eyes closed, has little proven diagnostic value. Many normal persons, especially elderly ones, are unable to stand like this for very long.[31]

G. FRONTAL GAIT DISORDER

1. Definition

Frontal gait disorder is an imprecise term describing a combination of findings seen in patients with cerebral tumors, subdural hematomas, dementing illness, normal pressure hydrocephalus, and multiple lacunar infarcts.[33,34] The characteristic findings are (1) slow, shuffling, wide-based gait **(marche a petit pas);** (2) hesitation in starting to walk **(ignition failure);** (3) difficulty picking feet off the floor **(magnetic foot response);** and (4) poor postural control. Motor function of the legs is sometimes much better when these patients are seated or lying, suggesting an element of gait apraxia.

Some of these findings resemble parkinsonism, but the distinguishing features of the frontal gait disorder are its wide base, normal arm swing, absence of other parkinsonian features, more upright posture, and higher incidence of dementia and urinary incontinence.

2. Clinical Significance

In studies of elderly patients undergoing computed tomography (CT) of the head because of neurologic symptoms, the finding of a frontal gait disorder correlates strongly with the CT finding of ventricular enlargement.[12,35,36] Only a minority of these patients, however, met the criteria for normal pressure hydrocephalus, suggesting that the findings of ventricular enlargement and gait disturbance are general ones occurring in many different forebrain disorders.[12,35]

Analysis of gait assists the diagnosis of patients with dementia. The presence of a gait disturbance makes Alzheimer disease less likely (especially if it appears early in the patient's course; LR = 0.2, EBM Box 6-1); a parkinsonian gait in patients with dementia increases the probability of Lewy body dementia or Parkinson disease with dementia (LR = 8.8), and a frontal gait increases probability of vascular dementia (LR = 6.1).

IV. EVALUATION OF GAIT DISORDERS

The methods of evaluating gait range from very simple tests that require minutes to complete (e.g., assessing the fall risk in elderly patients) to comprehensive observational gait analysis, which physiatrists use to break down complicated gait abnormalities into smaller components to direct treatment.[10] Most clinicians adopt an intermediate approach and ask the patient first to walk back and forth several strides at a time, and then again on the toes and heels and using tandem steps, all maneuvers that may bring out weak muscles or difficulties with balance.

Testing gait is essential, whatever the method, because patients often appear normal during conventional tests of motor, sensory, musculoskeletal, and visual function, yet, when asked to stand and walk, demonstrate abnormal balance and gait.[37]

A. OBSERVATIONAL GAIT ANALYSIS[9,10]

Using this method, the clinician focuses on one limb at a time as the patient walks, first observing the ankle, then the knee, hip, pelvis, and trunk. At each joint, the clinician considers each of the four fundamental ingredients of abnormal gait: pain, immobile joints, muscle weakness, and abnormal limb control.

As an example, the differential diagnosis of "abnormal ipsilateral trunk lean during stance" includes ipsilateral hip pain, ipsilateral short limb (>1.5 inches shorter), or intentional attempts to clear the contralateral limb during swing (e.g., drop foot or extended limb). "Dragging of the foot or toe during swing" may occur because of weak ipsilateral ankle dorsiflexor muscles, ipsilateral plantar flexion contractures, inadequate ipsilateral hip or knee flexion, or impaired proprioception.

An excellent manual of observational gait analysis has been published.[9]

B. PREDICTING FALLS

Thirty percent of persons over the age of 65 living in the community fall each year.[4] Of the many brief tests designed to identify patients at higher risk for falls, the best studied are "stops walking when talking," "timed up-and-go," and "timed chair stands." In studies of these tests, the history of a prior fall during the previous year predicts another fall in the next 6 to 12 months, with a sensitivity of 20% to 62%, specificity of 71% to 93%, and positive LR of 2.4.[4,38,39]

1. Findings

a. Stops Walking When Talking

The premise behind this test is that elderly patients at risk for falls have difficulty completing separate tasks simultaneously. To perform the test, the patient is accompanied while walking and then observed to see what happens when the examiner initiates conversation. If the patient stops walking when talking, the test is positive.

b. Timed Up-and-Go Test[3]

The clinician measures the time it takes the patient to rise from a standard chair, walk to a line on the floor 3 meters away, turn, return, and sit down again. The patient is instructed to walk at normal speed and is allowed one trial before timing. The timing starts when the patient's back comes off the chair and ends when the buttocks touch the seat of the chair.

c. Timed Chair Stands

The clinician times how long it requires for the patient to get up from a chair and sit down 3 times in a row.[40]

2. Clinical Significance

According to the LRs presented in EBM Box 6-2, the findings that are most compelling in suggesting an increased risk of falls are failure to stand with the feet together and the eyes open for 10 seconds (LR = 4.5), a positive "stops walking when talking" test (LR = 3.0), a positive

EBM BOX 6-2
*Predicting Falls**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Neurologic Examination				
Palmomental reflex present[4]	31	89	2.8	0.8
Failure to stand with feet together and eyes open for 10 seconds[38]	4	99	**4.5**	NS
Failure to tandem walk (>2 errors)[38]	53	70	1.7	0.7
Special Tests				
Stops walking when talking[2,41–43]	14-53	70-97	**3.0**	NS
Timed up-and-go test[39]				
<15 sec	4	67	**0.1**	—
15-35 sec	60	—	NS	—
≥35 sec	36	86	2.6	—
Timed chair stands (get up and sit down 3 times) >10 sec[40]	32	79	1.5	NS

*Diagnostic standard: For falls, ≥1 fall during 6-month follow-up[2,39,41–43] or 12-month follow-up.[4,38,40,41]

†Definition of findings: For palmomental reflex, see Chapter 61; for all other tests, see text.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. NS, not significant.

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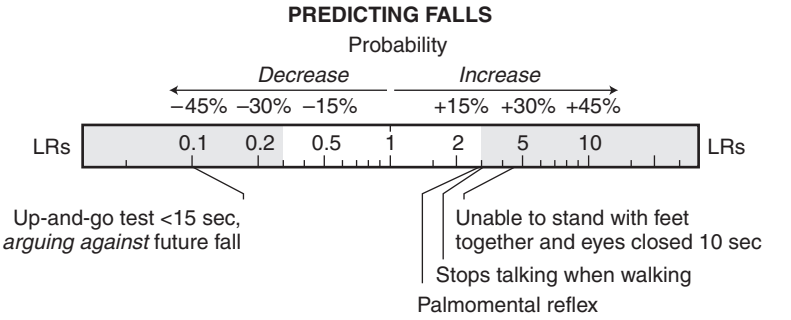

palmomental reflex (LR = 2.8, see Chapter 61), and a timed up-and-go test of 35 seconds or more (LR = 2.6). The clinician's overall global assessment that the patient is a high fall risk is also accurate (LR = 2.8). A timed up-and-go test result of less than 15 seconds identifies patients who are at lower risk of falls (LR = 0.1).

V. CANES

Physical examination of gait is incomplete without considering the length of the patient's cane and which arm the patient uses to hold the cane.

A. LENGTH OF CANE

Twenty-three percent to 42% of the time, the patient's cane is too long or too short by 5 cm or more.[44,45] An appropriately fitted cane should extend the distance from the distal wrist crease to the ground when the patient is wearing everyday shoes and dangling the arms at the side.[46]

B. CONTRALATERAL VERSUS IPSILATERAL USE OF CANE

Patients with hip and knee arthritis are conventionally taught to hold the cane in the contralateral hand, although compelling evidence for contralateral cane use exists only for patients with hip arthritis.[47,48] By placing just 20, 33, or 38 pounds of pressure on a cane contralateral to a diseased hip when standing on that hip, the patient can *reduce* the pressure on the diseased femoral head by 165, 272, or 319 pounds, respectively.[47]

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 7

Jaundice

I. INTRODUCTION

Jaundice is an abnormal yellowish discoloration of the skin and mucous membranes caused by accumulation of bile pigment. There are three forms: (1) **hemolytic jaundice** (due to increased bilirubin production from excessive breakdown of red cells), (2) **hepatocellular jaundice** (due to disease of the liver parenchyma, e.g., alcoholic liver disease, drug-induced liver disease, viral hepatitis, or metastatic carcinoma), and (3) **obstructive jaundice** (due to mechanical obstruction of the biliary ducts outside the liver, e.g., choledocholithiasis or pancreatic carcinoma). In most published series of jaundiced patients, hemolysis is uncommon, and the usual task of the clinician at the bedside is to differentiate hepatocellular disease from obstructed biliary ducts.[1,2]

II. FINDINGS

A. JAUNDICE

Jaundice is usually first noted in the eyes, but the traditional term for this finding **(scleral icterus)** is actually a misnomer because pathologic studies reveal most of the pigment to be deposited in the conjunctiva, not the avascular sclera.[3] As jaundice progresses and the serum bilirubin increases, the face, mucous membranes, and eventually the entire skin acquire a yellow or orange hue.

Prominent yellowish subconjunctival fat may be mistaken for conjunctival jaundice, but fat usually is limited to the conjunctival folds and, unlike jaundice, spares the area near the cornea. Patients with carotenemia (from excess carrot or multivitamin ingestion) also develop a yellowish discoloration of the skin, especially the palms, soles, and nasolabial fold, but, in contrast to jaundice, the conjunctiva are spared.[4]

B. ASSOCIATED FINDINGS

According to classic teachings, several findings distinguish hepatocellular disease from obstructed biliary ducts.

1. Hepatocellular Jaundice

Characteristic findings are spider telangiectasias, palmar erythema, gynecomastia, dilated abdominal wall veins, splenomegaly, asterixis, and fetor hepaticus.

a. Spider Telangiectasias (Spider Angiomas)

Spider telangiectasias are dilated cutaneous blood vessels with three components: (1) a central arteriole (the "body" of the spider) that when compressed slightly with a glass slide, can be seen to pulsate; (2) multiple radiating "legs"; and (3) surrounding erythema, which may encompass the entire lesion or only its central portion.[5] After blanching, the returning blood fills the central arteriole first before traveling to the peripheral tips of each leg. Spiders are most numerous on the face and neck, followed by the shoulders, thorax, arms, and hands. They are rare on the palms and scalp and below the umbilicus.[5] This peculiar distribution may reflect the neurohormonal properties of the microcirculation because it is similar to the distribution of blushing where it is most intense.[5]

Acquired vascular spiders are associated with three clinical conditions: liver disease, pregnancy, and malnutrition.[6] In patients with liver disease, the spiders advance and regress with disease severity,[7] and their appearance correlates somewhat with an abnormally increased ratio of serum estradiol to testosterone levels.[8] In pregnant women, spiders typically appear between the second and fifth months and usually disappear within days after delivery.[6] Vascular spiders also have been described in normal persons, but these lesions, in contrast to those of liver disease, are always few in number (average, three) and size.[5]

Vascular spiders were first described by the English physician Erasmus Wilson in 1867.[5]

b. Palmar Erythema

Palmar erythema is a symmetrical reddening of the surfaces of the palms, most pronounced over the hypothenar and thenar eminences.[6] Palmar erythema occurs in the same clinical conditions as vascular spiders, and the two lesions tend to come and go together.[6]

c. Gynecomastia and Diminished Body Hair

Many patients with liver disease have **gynecomastia** (defined as a palpable, discrete button of firm subareolar breast tissue ≥2 cm in diameter) and diminished pubic and body hair; both findings are attributed to increased circulating estrogen-to-testosterone levels.

d. Dilated Abdominal Veins

In some patients with cirrhosis, elevated portal venous pressures lead to the development of collateral vessels from the portal venous to systemic venous systems. One group of such vessels surrounds the umbilicus, decompressing the left portal vein via the paraumbilical vessels into abdominal wall veins.[9] Sometimes these abdominal wall veins become so conspicuous that they resemble a cluster of serpents, thus earning the name **caput medusae.**[10] Collateral vessels may generate a continuous humming murmur heard during auscultation between the xiphoid and umbilicus.[11]

Collateral abdominal vessels also may appear in patients with superior vena cava syndrome (if the obstruction also involves the azygous system)[12]

or inferior vena cava syndrome.[13] In these disorders, however, the vessels tend to appear on the lateral abdominal wall. A traditional test to distinguish inferior vena cava obstruction from portal hypertension is to strip abdominal wall veins below the umbilicus and see which way blood is flowing. (In portosystemic collaterals, blood should flow away from the umbilicus, whereas in inferior vena cava collaterals, flow is reversed and toward the head.) Even so, this test is unreliable because most dilated abdominal vessels lack competent valves, and the clinician can "demonstrate" that blood flows in either direction in most patients with both conditions.

e. Palpable Spleen

One of the principal causes of splenomegaly is portal hypertension from severe hepatocellular disease.[14] Therefore, a traditional teaching is that the finding of splenomegaly in a jaundiced patient increases the probability of hepatocellular disease.

f. Asterixis

Originally described by Adams and Foley in 1949,[15,16] asterixis is one of the earliest findings of hepatic encephalopathy and is thus a finding typical of hepatocellular jaundice. To elicit the sign, the patient holds both arms outstretched with fingers spread apart. After a short latent period, both fingers and hands commence to "flap," with abrupt movements occurring at irregular intervals of a fraction of a second to seconds (thus earning the name **liver flap**). The fundamental problem in asterixis is the inability to maintain a fixed posture (the word *asterixis* comes from the Greek *sterigma,* meaning "to support"), and, consequently, asterixis can also be demonstrated by having the patient elevate the leg and dorsiflex the foot, close the eyelids forcibly, or protrude the tongue.[15] Because some voluntary contraction of the muscles is necessary to elicit asterixis, the sign disappears once coma ensues (although some comatose patients exhibit the finding during the grasp reflex; see Chapter 61).[15]

Electromyography reveals that asterixis represents the abrupt disappearance of electrical activity in the muscle (i.e., **negative myoclonus**).[17] Asterixis is not specific to liver disease but also appears in encephalopathy from other causes such as hypercapnia or uremia.[18] Unilateral asterixis indicates structural disease in the contralateral brain.[19,20]

g. Fetor Hepaticus

Fetor hepaticus is the characteristic breath of patients with severe parenchymal disease, which has been likened to a mixture of rotten eggs and garlic. Gas chromatography reveals that the principal compound causing the odor is dimethylsulfide.[21] Fetor hepaticus correlates best with severe portosystemic shunting, not encephalopathy per se, because even alert patients with severe portosystemic shunting have the characteristic breath.[22]

2. Obstructive Jaundice: Palpable Gallbladder (Courvoisier Sign)

The presence of a smooth, nontender, distended gallbladder in a patient with jaundice is a traditional sign of obstructive jaundice. Courvoisier

sign refers to the association of the palpable gallbladder and extrahepatic obstruction, a sign discussed fully in Chapter 49.

III. CLINICAL SIGNIFICANCE

A. DETECTION OF JAUNDICE

Although many textbooks claim that jaundice becomes evident once the serum bilirubin exceeds 2.5 to 3 mg/dL, clinical studies reveal that only 70% to 80% of observers detect jaundice at this threshold.[23,24] The sensitivity of examination increases to 83% when bilirubin exceeds 10 mg/dL and 96% when it exceeds 15 mg/dL.

B. HEPATOCELLULAR VERSUS OBSTRUCTIVE JAUNDICE

Studies show that clinicians accurately distinguish hepatocellular jaundice from obstructive jaundice more than 80% of the time by just using bedside and basic laboratory findings (i.e., before clinical imaging).[25,26] In EBM Box 7-1, *disease* is arbitrarily defined as hepatocellular disease: therefore, likelihood ratios (LRs) with large positive values *increase* the probability of hepatocellular disease, whereas those with values close to zero decrease it and thus *increase* probability for obstructive disease.

These studies show that in patients presenting with jaundice, the physical signs of portal hypertension (dilated abdominal veins, LR = 17.5; ascites, LR = 4.4; and palpable spleen, LR = 2.9), palmar erythema (LR = 9.8), and spider angiomas (LR = 4.7) all increase the probability of hepatocellular jaundice. The only finding arguing strongly *against* hepatocellular jaundice is the palpable gallbladder (LR = 0.04; in other words, the finding of a palpable gallbladder argues *for* obstructed bile ducts with an LR of 26, the inverse of 0.04).

Weight loss does not discriminate well between hepatocellular and obstructive causes. Also unhelpful are liver tenderness and a palpable liver. The palpable liver remains unhelpful even when it is defined as a liver edge extending more than four to five fingerbreadths below the right costal margin.[25]

C. DIAGNOSIS OF CIRRHOSIS

The diagnosis of cirrhosis in patients with liver disease has important prognostic and therapeutic implications. EBM Box 7-2 displays the diagnostic accuracy of physical findings in detecting cirrhosis, determined from hundreds of patients presenting with diverse chronic liver diseases. According to this EBM box, the findings increasing the probability of cirrhosis the most are dilated abdominal wall veins (LR = 9.5), encephalopathy (irrational behavior, disordered consciousness, and asterixis; LR = 8.8), reduced body or pubic hair (LR = 8.8), gynecomastia (LR = 7), ascites (LR = 6.6), spider angiomas (LR = 4.5), palmar erythema (LR = 4.3), jaundice (LR = 3.8), and peripheral edema (LR = 3). Other findings (but less compelling ones) are a liver edge that is firm to palpation (LR = 2.7), a palpable left lobe of the liver in the epigastrium (LR = 2.7), and splenomegaly (LR = 2.5). The only findings decreasing the probability of cirrhosis in these patients are *absence* of a palpable liver in the epigastrium (LR = 0.3) and *absence* of a firm liver edge (LR = 0.4).

EBM BOX 7-1
*Findings Predicting Hepatocellular Disease in Patients with Jaundice**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
General Appearance				
Weight loss[25,27]	10-49	21-97	NS	NS
Skin				
Spider angiomas[25,27]	35-47	88-97	**4.7**	0.6
Palmar erythema[25]	49	95	**9.8**	0.5
Dilated abdominal veins[25]	42	98	**17.5**	0.6
Abdomen				
Ascites[25]	44	90	**4.4**	0.6
Palpable spleen[25,27]	29-47	83-90	2.9	0.7
Palpable gallbladder[25]	0†	69	**0.04**	1.4
Palpable liver[25,27]	71-83	15-17	NS	NS
Liver tenderness[25,27]	37-38	70-78	NS	NS

*Diagnostic standard: For *nonobstructive (vs. obstructive) jaundice*, needle biopsy of liver, surgical exploration, or autopsy.

†None of the 41 patients with medical jaundice in this study had a palpable gallbladder; for calculation of the LRs, 0.5 was added to all cells of the 2×2 table.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

NS, not significant.

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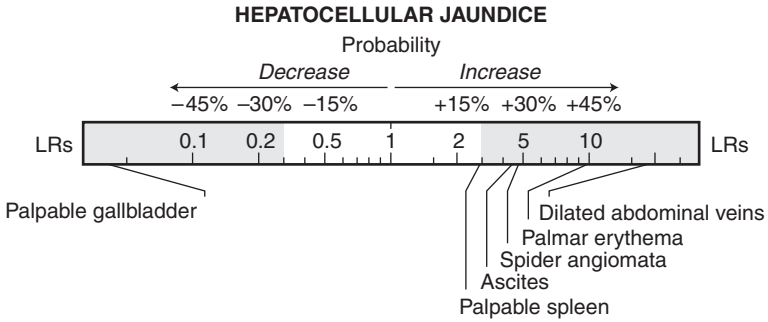

D. DETECTING LARGE GASTROESOPHAGEAL VARICES IN PATIENTS WITH CIRRHOSIS

In studies of more than 700 patients with cirrhosis who have not had prior gastrointestinal bleeding, no physical finding reliably predicts which patients have significant gastroesophageal varices (as detected by endoscopy). For most findings—caput medusae, spider angiomas, jaundice, hepatomegaly, splenomegaly, and hepatic encephalopathy—the LR is not

EBM BOX 7-2

*Findings Predicting Cirrhosis in Patients with Chronic Liver Disease**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Skin				
Spider angiomas[6,28–38]	33-84	48-98	**4.5**	0.5
Palmar erythema[29,31,32,34,37]	12-70	49-98	**4.3**	0.6
Gynecomastia[29,37]	18-58	92-97	**7**	NS
Reduction of body or pubic hair[29,37]	24-51	94-97	**8.8**	NS
Jaundice [29,33,35,37,39]	16-44	83-99	**3.8**	0.8
Dilated abdominal wall veins[29,34,37]	9-51	79-100	**9.5**	NS
Abdomen				
Hepatomegaly[29,32–36,38,40]	31-96	20-96	2.3	0.6
Palpable liver in epigastrium[35,38]	50-86	68-88	2.7	**0.3**
Liver edge firm to palpation[32,40]	71-78	71-74	2.7	0.4
Splenomegaly[28,30–36,38–40]	5-85	35-100	2.5	0.8
Ascites[28,29,31,33–35,39]	14-52	82-99	**6.6**	0.8
Other Findings				
Peripheral edema[29,33,34]	24-56	87-92	**3.0**	0.7
Encephalopathy[28,29,31]	9-29	98-99	**8.8**	NS

*Diagnostic standard: For *cirrhosis*, needle biopsy of liver.

†Definition of findings: For *hepatomegaly* and *splenomegaly*, examining clinician's impression using palpation, percussion, or both; *encephalopathy*, disordered consciousness and asterixis.[15]

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. NS, not significant.

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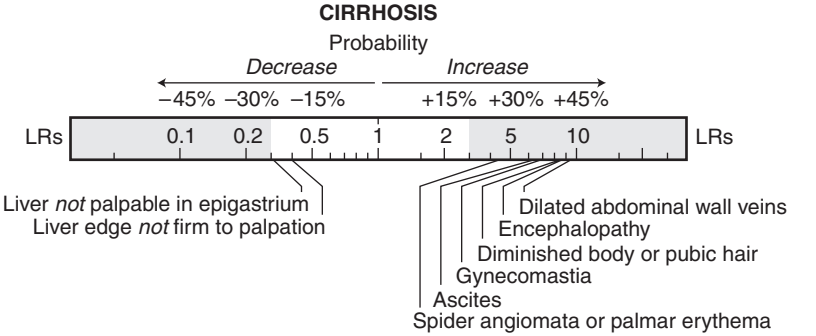

EBM BOX 7-3

*Findings Detecting Hepatopulmonary Syndrome in Patients with Chronic Liver Disease**

Finding (Reference)	Sensitivity (%)	Specificity (%)	Likelihood Ratio† if Finding Is	
			Present	*Absent*
Clubbing[45–48]	22-80	64-95	**4.6**	0.6
Cyanosis[45,46]	8-86	79-99	**4.3**	NS
Palmar erythema[45,49]	57-80	54-70	NS	NS
Spider angiomas[45–49]	39-97	26-70	1.4	NS
Ascites[47,48]	56-79	20-57	NS	NS

*Diagnostic standard: For *hepatopulmonary syndrome*, all three of the following criteria were present: (1) cirrhosis, (2) contrast echocardiography revealing intrapulmonary right→left shunting, and (3) hypoxemia, variably defined as arterial pO_2 <70 mm Hg[49] or <80 mm Hg,[45] alveolar-arterial pO_2 gradient ≥15 mm Hg[48] or >20 mm Hg,[46] or *either* pO_2 <70 mm Hg or $AapO_2$ >20 mm Hg.[47]

†Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. NS, not significant.

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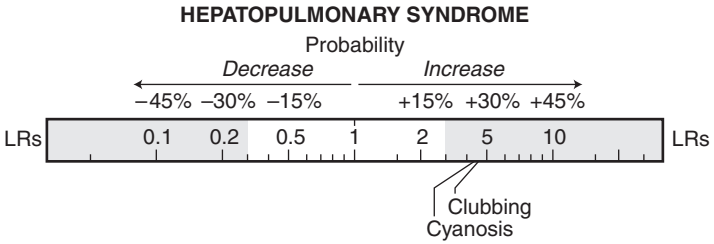

significant; only for ascites is the LR statistically significant (LR = 1.5), although its clinical significance is minimal.[41-44]

E. DETECTING HEPATOPULMONARY SYNDROME

Hepatopulmonary syndrome is a serious complication of cirrhosis causing intrapulmonary vascular shunting and significant hypoxemia. In five studies of over 400 patients with cirrhosis (EBM Box 7-3), most awaiting liver transplantation, the findings of finger clubbing (LR = 4.6) and cyanosis (LR = 4.3) increased the probability of hepatopulmonary syndrome.

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 8

Cyanosis

I. DEFINITIONS

Cyanosis is an abnormal bluish discoloration of the skin and mucous membranes, caused by blue-colored blood circulating in the superficial capillaries and venules. The blue color usually represents excessive amounts of deoxygenated hemoglobin, although in some patients it results from increased amounts of methemoglobin or sulfhemoglobin. Cyanosis may be central or peripheral. In **central cyanosis,** the blood leaving the heart is colored blue; in **peripheral cyanosis,** the blood leaving the heart is red but becomes blue by the time it reaches the fingers and toes. **Pseudocyanosis,** in contrast, refers to a permanent bluish discoloration caused by deposition of blue pigments in the skin.

Cyanosis was first described in 1761 by Morgagni, who attributed it to pulmonic stenosis.[1] In 1869, Claude Bernard described the qualitative difference in blood gases between blue venous blood and red arterial blood. The first person to quantify how much deoxygenated hemoglobin was necessary to produce the blue color was Lundsgaard in 1919.[1]

II. PATHOGENESIS

A. THE BLUE COLOR

Blood becomes blue when an absolute amount of blue pigment (usually, deoxyhemoglobin) accumulates, probably because only then is the blue color deep enough to be seen through the opaque epidermis.[1-4] Once this minimal amount of deoxyhemoglobin accumulates and cyanosis appears, the amount of additional red blood (or oxyhemoglobin) matters little to the overall skin color.

The color of the skin depends on the color of blood flowing through the dermal capillaries and subpapillary venous plexus, not the arteries and veins, which lie too deep to contribute to skin color.[1,5] There has been much confusion over the absolute concentration of deoxyhemoglobin required for cyanosis, primarily because some investigators have mistakenly equated arterial levels of deoxyhemoglobin, which are easy to measure, with capillary levels, which impart the blue color but must be higher than the measured arterial levels. In patients with central cyanosis, the *average* amount of *arterial* deoxyhemoglobin is 3.48 ± 0.55 g/dL (or 5.35 g/dL in the capillaries and small venules). The *minimal* amount of

TABLE 8-1 Cyanosis and Hemoglobin Concentration

Hemoglobin Concentration (g/dL)	Cyanosis Appears at:*	
	Oxygen Saturation (%) Below:	*Arterial pO_2 (mm Hg) Below:*
6	60	31
8	70	36
10	76	40
12	80	45
14	83	47
16	85	50
18	87	54
20	88	56

*These figures assume that central cyanosis begins to appear when 2.38 g/dL of deoxygenated hemoglobin accumulates in arterial blood (see text for calculations). The corresponding pO_2 was obtained from standard hemoglobin dissociation curves for oxygen.

arterial deoxyhemoglobin causing cyanosis is 2.38 g/dL (or 4.25 g/dL in the capillaries and small venules).*[4]

Because cyanosis depends on the absolute quantity of deoxyhemoglobin, not the relative amount, the appearance of cyanosis also depends on the patient's total hemoglobin concentration (i.e., 5 g/dL of capillary deoxyhemoglobin represents a higher percentage of oxygen desaturation for an anemic patient, who has less total hemoglobin, than it does for a polycythemic patient). Table 8-1 displays this relationship: polycythemic patients (hemoglobin = 20 g/dL) may appear cyanotic with only mild hypoxemia (i.e., oxygen saturation [SaO_2] = 88% or pO_2 = 56 mm Hg), yet anemic patients (hemoglobin = 8 g/dL) do not develop the finding until hypoxemia is severe (i.e., SaO_2 = 70% or pO_2 = 36 mm Hg).†

B. PERIPHERAL CYANOSIS

In peripheral cyanosis, blood leaving the heart is red, but because of increased extraction of oxygen by peripheral tissues, enough deoxyhemoglobin accumulates to render it blue in the subepidermal blood vessels of the feet and hands. The clinician can easily demonstrate peripheral cyanosis by wrapping a rubber band around a finger and watching the distal digit turn blue as oxygen continues to be extracted from the stagnant blood.

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*Capillary deoxyhemoglobin is 1.87 g/dL more than arterial levels, based on three assumptions: (1) the difference in oxygen content between the arteries and veins is 5 mL of oxygen per deciliter of blood; (2) the amount of deoxyhemoglobin in the capillaries is midway between that of the arteries and vein; and (3) 1.34 mL of oxygen binds to 1 g of saturated hemoglobin. Therefore, $5/(2 \times 1.34) = 1.87$.

†These figures are calculated as follows: For the polycythemic patient (hemoglobin = 20 g/dL), 2.38 g/dL of arterial deoxyhemoglobin indicates that there is 20 − 2.38 or 17.62 g/dL of arterial oxyhemoglobin. Oxygen saturation, therefore, is (17.62)/(20) = 0.88, or 88%. For the anemic patient, the calculation is (8 − 2.38)/8 = 0.7, or 70% saturation.

III. FINDINGS

Cyanosis is best appreciated in areas where the overlying epidermis is thin and subepidermal vessels are abundant, such as the lips, nose, cheeks, ears, hands, feet, and mucous membranes of the oral cavity.[1,6] Cyanosis is detected more easily with fluorescent lighting than with incandescent lighting or daylight.[4]

A. CENTRAL CYANOSIS

Patients with central cyanosis have blue discoloration of the lips, tongue, and sublingual tissues, as well as the hands and feet. The correlation between severity of oxygen desaturation and depth of cyanotic color is best when one is examining the patient's lips and buccal mucosa.[7,8] Some patients with long-standing central cyanosis have associated clubbing (see Chapter 26).

When central cyanosis is suspected yet administration of oxygen fails to diminish the blue color, the clinician should consider **methemoglobinemia** or **sulfhemoglobinemia.** The color of patients with methemoglobinemia often has a characteristic brownish hue **(chocolate cyanosis).**[9]

Because cyanosis depends on blue blood being present in the underlying blood vessels, maneuvers that express blood out of the vessels (e.g., pressure on the skin) make the blue color disappear temporarily.

B. PERIPHERAL CYANOSIS

Peripheral cyanosis causes blue hands and feet, although the mucous membranes of the mouth are pink. Warming the patient's limb skin often diminishes peripheral cyanosis because blood flow to the involved area improves, whereas central cyanosis stays the same or deepens after warming of the skin.

C. PSEUDOCYANOSIS

In patients with pseudocyanosis, the mucous membranes of the mouth are pink, and pressure on the skin fails to blanch the abnormal color.[6]

D. CYANOSIS AND OXIMETRY

Cyanosis affects CO-oximetry (i.e., blood gas analysis in the laboratory) differently than it affects pulse oximetry (i.e., equipment used at the bedside; see Chapter 19). Because CO-oximetry can distinguish deoxyhemoglobin from other abnormal hemoglobins, it indicates hypoxemia only in patients with central cyanosis (i.e., it samples *arterial* blood and therefore indicates normal oxygen levels in peripheral cyanosis). Pulse oximetry, in contrast, detects the *color* of the pulsatile waveform in the digit. Although it also indicates hypoxemia in patients with central cyanosis, pulse oximetry sometimes falsely indicates arterial hypoxemia in patients with peripheral cyanosis or with abnormal hemoglobins (see Chapter 19). Both CO-oximetry and pulse oximetry indicate normal oxygen levels in pseudocyanosis.

EBM BOX 8-1

Central Cyanosis, Detecting Arterial Deoxyhemoglobin ≥2.38 g/dL[*]

Finding (Reference)[†]	Sensitivity (%)	Specificity (%)	Likelihood Ratio if Finding Is	
			Present	*Absent*
Central cyanosis[2,4]	79-95	72-95	**7.4**	**0.2**

*Corresponding to O_2 saturation of 80% and pO_2 of 45 mm Hg if hemoglobin concentration is 12 g/dL.

[†]See Table 8-1.

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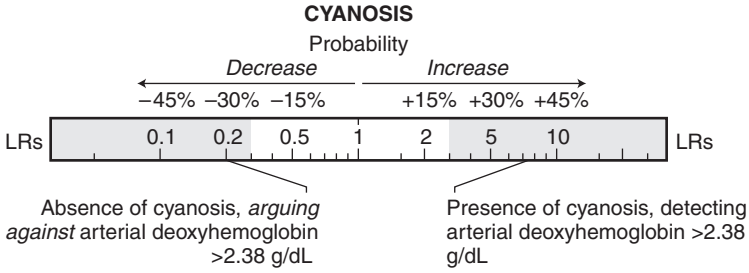

IV. CLINICAL SIGNIFICANCE

A. CENTRAL CYANOSIS

Any disorder causing hypoxemia may generate sufficient deoxyhemoglobin in the blood from the heart to produce central cyanosis. Typical etiologic findings are pulmonary edema, pneumonia, and intracardiac right-to-left shunts. The finding of central cyanosis increases greatly the probability of hypoxemia (LR = 7.4, EBM Box 8-1; **hypoxemia** is defined as an arterial deoxyhemoglobin level ≥2.38 g/dL, corresponding to SaO_2 ≤80% and pO_2 ≤45 mm Hg in patients with normal amounts of hemoglobin; see Table 8-1). The absence of central cyanosis greatly decreases the likelihood of such severe hypoxemia (LR = 0.2, EBM Box 8-1).

In patients with chronic liver disease, the finding of cyanosis increases the probability of hepatopulmonary syndrome (LR = 4.3; see Chapter 7).

B. PERIPHERAL CYANOSIS

In clinical practice, common causes of peripheral cyanosis are low cardiac output, arterial disease or obstruction (e.g., Raynaud disease), and venous disease.

C. PSEUDOCYANOSIS

Pseudocyanosis may occur after exposure to metals (**argyria** from topical silver compounds; **chrysiasis** from gold therapy) or drugs (amiodarone, minocycline, chloroquine, or phenothiazines).[10,11]

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 9

Anemia

I. INTRODUCTION

Anemia refers to an abnormally low number of circulating red cells, caused by blood loss, hemolysis, or underproduction of cells by the bone marrow. In patients with acute blood loss, the abnormal vital signs of hypovolemia are the most prominent physical findings (see Chapter 16), but in chronic anemia (the subject of this chapter), physical findings instead reflect changes in the color of the skin and conjunctiva.

II. FINDINGS

Chronic anemia causes the skin and conjunctiva to appear abnormally pale because of reduced amounts of red-colored oxyhemoglobin circulating in the dermal and subconjunctival capillaries and venules.[1] Nonetheless, pallor does not always indicate anemia, because skin color also depends on the diameter of these minute vessels, the amount of circulating deoxyhemoglobin, and the patient's natural skin pigments.[1] Vasoconstriction from cold exposure or sympathetic stimulation also may cause pallor, and the pallor of anemia may be obscured by the red color of vasodilation (inflammation or permanent vascular injury from ischemia, cold, or radiation), the blue color of cyanosis (see Chapter 8), or the brown pigments of dark-skinned persons. Theoretically, examination of the conjunctiva, nailbeds, and palms avoids the effects of the patient's natural skin pigments.

Most clinicians assess for pallor subjectively, by comparing the patient's skin color with their own color or their recollection of normal skin color. One definition of pallor, however, is more objective: **conjunctival rim pallor** is present if examination of the inferior conjunctiva reveals the color of the anterior rim to have the same pale fleshy color of the deeper posterior aspect of the palpebral conjunctiva.[2] In persons without anemia, the normal bright red color of the anterior rim contrasts markedly with the fleshy color of the posterior portion.

III. CLINICAL SIGNIFICANCE

EBM Box 9-1 presents the diagnostic accuracy of physical signs for chronic anemia as applied to hundreds of patients. These studies excluded patients with acute bleeding or those who had recently received transfusions. As much as possible, the color of the skin and conjunctiva was determined using natural lighting.

EBM BOX 9-1
*Anemia**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Pallor at any site[3–6]	22-77	66-92	**4.0**	0.5
Facial pallor[4]	46	88	**3.8**	0.6
Nailbed pallor[4,5]	59-60	66-93	NS	0.5
Palmar pallor[4,5]	58-64	74-96	**5.6**	0.4
Palmar crease pallor[4]	8	99	**7.9**	NS
Conjunctival pallor[4,5,7,8]	31-62	82-97	**4.7**	0.6
Tongue pallor[9]	48	87	**3.7**	0.6
Conjunctival rim pallor[2]				
Pallor present	10	99	**16.7**	—
Pallor borderline	36	—	2.3	—
Pallor absent	53	16	0.6	—

*Diagnostic standard: For *anemia*, hematocrit <35%,[4] hemoglobin (Hb) <10 g/dL,[6] Hb <9 g/dL,[9] Hb <11 g/dL,[2,5,7,8] or Hb <11 g/dL in women and <13 g/dL in men.[3]

†Definition of findings: For *pallor at any site*, examination of skin, nailbeds, and conjunctiva[3–5]; for *facial pallor*, the study excluded black patients; for *palmar crease pallor*, examination after gentle extension of the patient's fingers; for *conjunctival rim pallor*, see text.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. NS, not significant.

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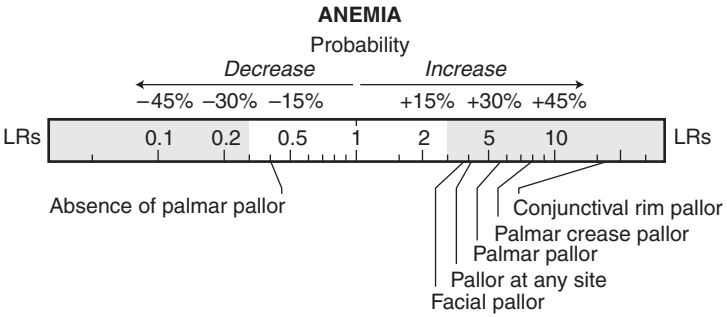

According to EBM Box 9-1, the finding of conjunctival rim pallor (likelihood ratio [LR] = 16.7) increases the probability of anemia the most, followed by palmar crease pallor (LR = 7.9), palmar pallor (LR = 5.6), conjunctival pallor (i.e., not specifically conjunctival rim pallor, LR = 4.7), pallor at any site (LR = 4), facial pallor (light-skinned persons only, LR = 3.8), and tongue pallor (LR = 3.7). Nailbed pallor lacks diagnostic value (LR not significant). Importantly, no physical sign convincingly *decreases* the probability of anemia (i.e., no LR <0.4).

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 10

Hypovolemia

I. INTRODUCTION

The term *hypovolemia* refers collectively to two distinct disorders: (1) **volume depletion,** which describes the loss of sodium from the extracellular space (i.e., intravascular and interstitial fluid) that occurs during gastrointestinal hemorrhage, vomiting, diarrhea, and diuresis, and (2) **dehydration,** which refers to the loss of intracellular water (and total body water) that ultimately causes cellular desiccation and elevates the plasma sodium concentration and osmolality.[1] Chapter 16 discusses the accuracy of abnormal vital signs in patients with volume depletion; this chapter discusses assorted additional findings.

II. FINDINGS AND THEIR PATHOGENESIS

Many of the traditional signs of hypovolemia—dry mucous membranes, sunken eyes, shriveled skin, poor skin turgor, and confusion—were originally described historically in patients with cholera who were near vascular collapse.[2] Presumably, cellular dehydration, interstitial space dehydration, and poor perfusion contribute to these signs.

Poor skin turgor refers to the slow return of skin to its normal position after being pinched between the examiner's thumb and forefinger.[3,4] In one study, persistence of skin tenting for 3 seconds or more after 3 seconds of pinching was defined as abnormal.[5] The protein elastin is responsible for the recoil of skin, and in vitro experiments show that its recoil time increases 40-fold after loss of as little as 3.4% of its wet weight.[3] Elastin also deteriorates with age, however, suggesting that the specificity of poor skin turgor diminishes as patients age.

III. CLINICAL SIGNIFICANCE

EBM Box 10-1 presents clinical studies comparing traditional signs to laboratory tests of hypovolemia (i.e., elevated serum urea-to-creatinine level, serum osmolarity, or serum sodium). These studies enrolled mostly elderly patients presenting to emergency departments with vomiting, decreased oral intake, or diarrhea. Few if any were as desperately hypovolemic as patients with classic cholera.

In these studies, the findings of abnormal skin turgor (tested in the subclavicular area, likelihood ratio [LR] = 3.5, EBM Box 10-1), dry mucous membranes (LR = 3.1), and dry axilla (LR = 2.8) *increase* the probability of hypovolemia. Testing skin turgor over the thighs, sternum, or subclavicular

EBM BOX 10-1
*Hypovolemia**

Finding† (Reference)	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Skin, Eyes, and Mucous Membranes				
Dry axilla[6]	50	82	2.8	NS
Dry mucous membranes of mouth and nose[5,7]	49-85	58-88	**3.1**	0.4
Longitudinal furrows on tongue[7]	85	58	NS	**0.3**
Sunken eyes[7]	62	82	NS	0.5
Abnormal skin turgor (subclavicular area)[5]	73	79	**3.5**	**0.3**
Neurologic Findings				
Confusion[5,7]	49-57	73-99	NS	0.5
Weakness[7]	43	82	NS	NS
Speech unclear or rambling[7]	56	82	NS	0.5

*Diagnostic standard: For *hypovolemia*, serum urea nitrogen to creatinine ratio is >25; osmolarity >300 mOsm/L, or serum sodium >145-150 mEq/L.
†Definition of findings: For *abnormal skin turgor*, see text.
‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. NS, not significant.
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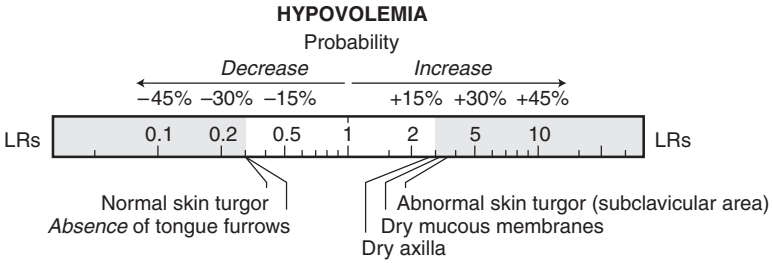

area was more accurate than testing skin over the forearms.[5] Absence of tongue furrows and presence of normal skin turgor *decrease* the probability of hypovolemia (LR = 0.3 for both findings). The presence or absence of sunken eyes, weakness, or abnormal speech had little diagnostic value in these studies. The finding of confusion also lacked diagnostic value, although it is strongly associated with mortality in elderly patients with hypovolemia.[5]

Although poor capillary refill time has been advanced as a reliable sign of hypovolemia, it lacked diagnostic value in one study.[7]

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 11

Protein–Energy Malnutrition and Weight Loss

PROTEIN–ENERGY MALNUTRITION

I. INTRODUCTION

The most common cause of malnutrition worldwide is an inadequate food supply, although in industrialized countries the cause is more frequently increased nutrient loss (e.g., malabsorption, diarrhea, nephrotic syndrome) or increased nutrient requirements (e.g., fever, cancer, infection, or surgery), or both. Among patients admitted to surgical services in industrialized nations, 9% to 27% have signs of severe malnutrition.[1,2]

II. FINDINGS

In children of developing nations, there are two distinct syndromes of protein–energy malnutrition: **marasmus** (profound weight loss, muscle wasting, and fat wasting) and **kwashiorkor** (abdominal distention, edema, and hypopigmented hair). In industrialized countries, however, most malnourished patients have less dramatic findings and present instead with combinations of low body weight, atrophy of muscle and subcutaneous fat, weakness, and various laboratory abnormalities (e.g., low albumin or other serum proteins).

A. ARM MUSCLE CIRCUMFERENCE

Arm muscle circumference is a decades-old anthropometric measurement of the amount of muscle in the arm, which theoretically reflects the total amount of muscle or protein in the body. The clinician measures the upper arm circumference (C_a, using a flexible tape measure) and the triceps skinfold thickness (h, using calipers) and estimates the arm muscle circumference (AMC) with the following formula*:

$$AMC = C_a - \pi h$$

*This formula assumes that the arm is a cylinder of only skin and muscle (i.e., disregards the humerus). To derive this formula: (1) $AMC = \pi d_1$ (d_1 = diameter of muscle component of the arm); (2) $d_1 = d_2 - h$ (d_2 = diameter of arm; h = skinfold thickness, which, since the skin is pinched, actually includes a *double* layer of skin and subcutaneous tissue); (3) therefore, $AMC = \pi d_1 = \pi(d_2 - h) = \pi d_2 - \pi h = C_a - \pi h$. If the clinician desires to directly enter the skinfold thickness in millimeters (mm) (as it is measured), 0.314 is substituted for π in the formula (i.e., AMC and C_a are measured in centimeters [cm]).

Age- and sex-standardized values of the normal AMC have been published.[3] The technique for forearm muscle circumference is similar.

B. GRIP STRENGTH

Based on the hypothesis that malnutrition influences the outcome of surgical patients and that muscle weakness is an important sign of malnutrition, Klidjian in 1980 investigated 102 surgical patients and demonstrated that hand grip strength accurately predicts postoperative complications.[4] In his method, the patient squeezes a simple hand-held spring dynanometer three times, resting 10 seconds between each attempt, and the clinician records the highest value obtained. (Patients with arthritis, stroke, or other obvious causes of weakness are excluded.)

Age- and sex-standardized values of normal grip strength have been published.[5] Clinical studies of grip strength always test the nondominant arm, but this may be unnecessary because studies show that both arms are similar.[5]

III. CLINICAL SIGNIFICANCE

EBM Box 11-1 addresses the accuracy of physical examination in predicting significant postoperative complications among patients undergoing major surgery. In these studies, complications are significant if they prolong hospital stay, threaten the patient's life, or cause death (e.g., sepsis, wound infections, myocardial infarction, or stroke).

In these studies, the findings of reduced arm or forearm muscle circumference (likelihood ratio [LR] = 2.5 to 3.2), reduced grip strength (LR = 2.2), and low body weight (LR = 2) all modestly increase the probability of postoperative complications. Normal grip strength *decreases* the probability of complications (LR = 0.4). Interestingly, the presence of recent weight loss has little diagnostic value in predicting complications, possibly because this finding is seen not only in patients with weight loss from malnutrition (which should increase complications) but also in overweight patients who voluntarily lose weight before surgery (which should decrease complications).

WEIGHT LOSS

I. INTRODUCTION

Involuntary weight loss reflects either diuresis, decreased caloric intake, or the increased caloric requirements of malabsorption, glucosuria, or a hypermetabolic state. In series of patients presenting with involuntary weight loss (exceeding 5% of their usual weight), organic disease is diagnosed in 65% of patients (most commonly, cancer and gastrointestinal disorders, although virtually any chronic disease may cause weight loss) and psychiatric disorders are diagnosed in 10% of patients (depression, anorexia nervosa, schizophrenia). In 25% of patients, the cause remains unknown despite at least 1 year of follow-up.[13-17]

EBM BOX 11-1

*Protein–Energy Malnutrition and Major Surgical Complications**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Body Weight				
Weight loss >10%[4,6–9]	15-75	47-88	1.4	NS
Low body weight[4,7,8,10]	11-35	83-97	2.0	NS
Anthropometry				
Upper arm muscle circumference <85% predicted[4,7,8]	26-38	83-91	2.5	0.8
Forearm muscle circumference <85% predicted[4,7,8]	14-42	85-97	**3.2**	0.8
Muscle Strength				
Reduced grip strength[4,5,7,8,11,12]	33-90	46-93	2.2	0.4

*Diagnostic standard: In each of these studies, *disease* is defined as a major postoperative complication, including those prolonging hospital stay, threatening the patient's life, or causing death.

†Definition of findings (all findings from preoperative physical examination): For *weight loss >10%,* (recalled usual weight − measured weight)/(recalled usual weight) >10%); for *low body weight,* weight-for-height less than normal lower limit,[10] <90% of predicted,[4] or <85% of predicted[7,8]; for *predicted arm muscle circumference*, published standardized values[3]; for *forearm muscle circumference* <85%, <20 cm in men and <16.3 cm in women[4,8]; and for *reduced grip strength*, specific thresholds differ but all correspond closely to published age- and sex-standardized abnormal values from reference.[5]

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. NS, not significant.

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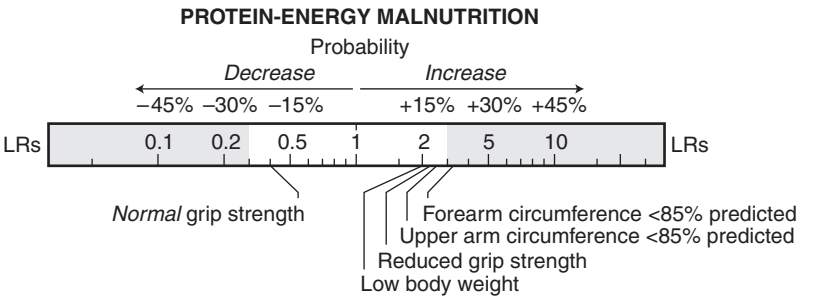

II. CLINICAL SIGNIFICANCE

Weight loss is rarely due to occult disease, and most diagnoses are made during the initial evaluation, including the patient interview, physical examination, and basic laboratory testing.[13,14,16,17]

In patients with involuntary weight loss, the presence of alcoholism (LR = 4.5) and cigarette smoking (LR = 2.2) increases the probability that an organic cause will be discovered during 6 months of follow-up, whereas prior psychiatric disease (LR = 0.2) and a *normal* initial physical examination (LR = 0.4) decrease the probability of discovering organic disease.[18] Also, the patient's perceptions of the weight loss—whether he or she significantly underestimates or overestimates it—help predict the final diagnosis. The patient is asked to estimate his or her weight before the illness (W) and the amount of weight lost (E). The observed weight loss (O) is the former weight (W) minus the current measured weight. Significant *underestimation* of weight loss, defined as (O – E) greater than 0.5 kg, predicts an *organic* cause of weight loss with a sensitivity of 40%, specificity of 92%, positive LR of 5.4, and negative LR of 0.6.[19] Significant *overestimation* of weight loss, defined as (E – O) greater than 0.5 kg, predicts a *nonorganic* cause of weight loss with a sensitivity of 70%, specificity of 81%, positive LR of 3.6, and negative LR of 0.4.[19]

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 12

Obesity

I. INTRODUCTION

Obesity increases the risk of coronary artery disease, diabetes, hypertension, osteoarthritis, cholelithiasis, certain cancers, and overall mortality.[1] Clinicians have recognized the hazards of obesity for thousands of years. (According to one Hippocratic aphorism, "Sudden death is more common in those who are naturally fat than in the lean."[2]) Two thirds of adults in the United States are overweight or obese.[3]

II. FINDINGS AND THEIR SIGNIFICANCE

Several different anthropometric parameters have been used to identify those patients at greatest risk for the medical complications of obesity. The most important ones are body mass index, skinfold thickness, waist-to-hip ratio, waist circumference, and sagittal diameter.

A. BODY MASS INDEX

1. Findings

The body mass index (BMI, or **Quetelet index**) is the patient's weight in kilograms divided by the square of the height in meters (kg/m^2). If pounds and inches are used, the quotient should be multiplied by 703.5 to convert the units to kg/m^2. An individual is overweight if the BMI exceeds 25 kg/m^2, and obese if the BMI exceeds 30 kg/m^2.[4]

The BMI was derived by a 17th century Belgian mathematician and astronomer, Lambert-Adolphe-Jacques Quetelet, who discovered that this ratio best expressed the natural relationship between weight and height.[5]

2. Clinical Significance

The BMI is an easy and reliable measurement that correlates well with precise measures of total body fat ($r = 0.70$ to 0.96), much better than other formulas of weight (W) and height (H) (e.g., W/H, W/H^3, $W/H^{0.3}$).[6] The BMI also correlates significantly with a patient's cholesterol level, blood pressure, incidence of coronary events, and overall mortality.[1,7-10]

The arbitrary cutoff of 25 kg/m^2 was chosen in part because it reflects the level at which there is a significant increase in mortality, although increased rates of some complications such as diabetes appear at lower cutoffs.[7,11] Many studies of BMI and mortality revealed a J-shaped relationship

(i.e., both lean and overweight patients have increased mortality), but the increased risk of lean individuals is related to their age, cigarette use, and illness-related weight loss.[9,10]

B. SKINFOLD THICKNESS

Another measure of obesity is "total skinfold thickness," which is estimated by adding together the skinfold thickness (measured with calipers) of multiple sites (mid-biceps, mid-triceps, subscapular, and suprailiac areas). These sums are then converted by formulas into estimates of total body fat, which correlate well with more precise measures (r = 0.7 to 0.8).[6] Skinfold measurements are rarely used today, partly because they are too complex but mostly because relatively few studies show that the number is clinically significant.

C. WAIST-TO-HIP RATIO

1. Findings

The waist-to-hip ratio (WHR) is the circumference of the waist divided by that of the hips. It is based on the premise that the most important characteristic of obesity is its distribution, not its quantity. **Abdominal obesity** (also called android, upper body, or apple-shaped obesity; Fig. 12-1) has a much worse prognosis than **gluteal-femoral obesity** (also called gynoid, lower body, or pear-shaped obesity).

Most authorities measure the waist circumference at the midpoint between the lower costal margin and the iliac crest and the hip circumference at the widest part of the gluteal region. Adverse health outcomes increase significantly when the WHR exceeds 1 in men and 0.85 in women, values that are close to the top quintiles in epidemiologic studies.[13]

The French diabetologist Jean Vague is usually credited with making the observation in the 1940s that abdominal obesity, common in men, is associated with worse health outcomes than obesity over the hips and thighs, more common in women. (American life insurance companies, however, made the same observation in the late 1800s.[14]) Vague's original "index of masculine differentiation," a complicated index based on skinfold and limb circumferences,[12] is no longer used, having been replaced by the much simpler WHR in the 1980s.

2. Clinical Significance

Even after controlling for the effects of BMI, the WHR correlates significantly with blood pressure, cholesterol level, incidence of diabetes mellitus, stroke, coronary events, and overall mortality.[8,13,15]

3. Pathogenesis

The main contributor to abdominal obesity is visceral fat (i.e., omental, mesenteric, and retroperitoneal fat), not subcutaneous fat. Visceral fat is metabolically active, constantly releasing free fatty acids into the portal circulation, which probably contributes to hyperlipidemia, atherogenesis, and hyperinsulinemia.[16] Gluteal-femoral fat, on the other hand, is metabolically inactive except during pregnancy and the postpartum period,

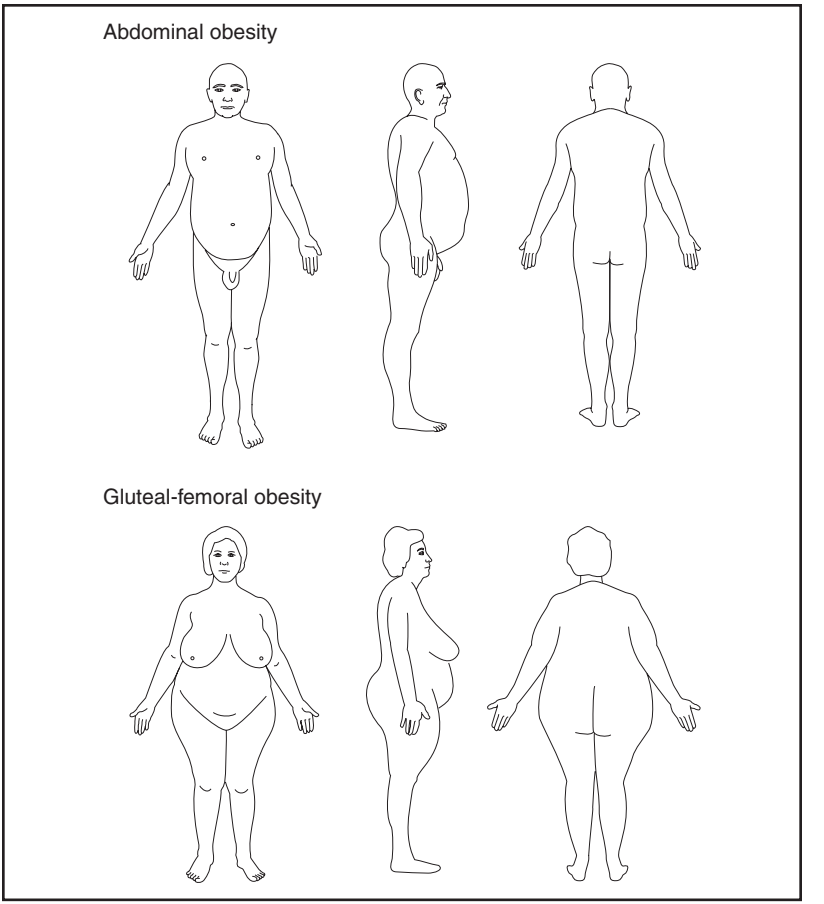

FIGURE 12-1 Comparison of abdominal and gluteal-femoral obesity. Abdominal obesity is depicted in the top row; gluteal-femoral obesity in the bottom row. The drawings in this figure are adapted from photographs published by Jean Vague,[12] who is credited with first associating adverse health outcomes with abdominal obesity.

which has led some to suggest that the role of lower body fat is to help guarantee the survival of the species by providing a constant source of energy to the lactating female even when external nutrients are unavailable.

D. WAIST CIRCUMFERENCE

Waist circumference is simply the numerator of the WHR calculation. It has the advantages of being simpler to measure and of avoiding attention to the hips, which, because they encompass bone and skeletal muscle as well as fat, should have no biologically plausible relationship to diabetes, hypertension, and atherosclerosis. Recommended cutoffs for increased health risk are a waist circumference of more than 102 cm (>40 inches) for men and more than 88 cm (>35 inches) for women.[4]

Waist circumference is strongly associated with risk of death, independent of BMI.[8,17] Waist circumference is also a criterion for the **metabolic syndrome** (defined as the presence of three or more of the following five variables: large waist circumference, hypertension, elevated triglyceride levels, low high-density lipoprotein [HDL] cholesterol levels, and elevated fasting glucose levels).[18]

E. SAGITTAL DIAMETER

Because waist circumference encompasses both subcutaneous and visceral fat, investigators have looked for better anthropometric measures of just visceral fat. One proposed measure is the sagittal diameter, which is the total anteroposterior distance between the anterior abdominal wall of the *supine* patient and the surface of the examining table. Theoretically, visceral fat maintains the abdominal depth in the supine patient, whereas subcutaneous fat allows the abdominal depth to partially collapse from the force of gravity.[19] Even so, there are few studies of this measure, and most correlate it with variables of uncertain clinical significance such as cardiovascular risk factors or the amount of visceral fat visualized on body imaging.[16]

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 13

Cushing Syndrome

I. INTRODUCTION

Cushing syndrome refers to clinical findings—such as hypertension, central obesity, weakness, hirsutism (in women), depression, skin striae, and bruises—induced by excess circulating glucocorticoids. The most common cause is exogenous administration of corticosteroid hormones.[1] **Endogenous Cushing syndrome** results from pituitary tumors producing adrenocorticotropic hormone (ACTH) (i.e., **Cushing disease;** 70% of endogenous cases), ectopic production of ACTH (usually by small cell carcinoma of the lung or carcinoid tumors of the lung or mediastinum; 10% of cases), adrenal adenomas (10% of cases), or adrenal carcinomas (5% of cases).[1] Cushing disease and ectopic ACTH syndrome are referred to as **ACTH-dependent disease** because the elevated cortisol levels are accompanied by inappropriately high ACTH levels. Adrenal tumors are referred to as **ACTH-independent disease.**

The bedside findings of Cushing syndrome were originally described by Harvey Cushing in 1932.[2] Corticosteroid hormones were first used as therapeutic agents to treat patients with rheumatoid arthritis in 1949; within 2 years, clear descriptions of exogenous Cushing syndrome appeared.[3]

II. FINDINGS AND THEIR PATHOGENESIS

Table 13-1 presents the physical signs of more than 1000 patients with Cushing syndrome.

A. BODY HABITUS

Patients with Cushing syndrome develop **central obesity** (also known as truncal obesity or centripetal obesity), a term describing the accumulation of fat centrally on the neck, chest, and abdomen, which contrasts conspicuously with the muscle atrophy affecting the extremities.

There are three definitions of central obesity.

1. Obesity sparing the extremities (a subjective definition and also the most common one)[4,12]
2. Obesity as defined by the **central obesity index,** a complicated ratio of the sum of three truncal circumferences (neck, chest, and abdomen) divided by the sum of six limb circumferences (bilateral arms, thighs, and lower legs); values higher than 1 are abnormal[13]

TABLE 13-1 Frequency of Individual Findings in Cushing Syndrome*

Physical Finding†	Frequency (%)‡
VITAL SIGNS	
Hypertension	64-88
BODY HABITUS	
Moon facies	67-92
Central obesity	44-97
Buffalo hump	34-75
SKIN FINDINGS	
Thin skin	27
Plethora	28-94
Hirsutism, women	48-81
Ecchymoses	23-75
Red or purple striae	46-68
Acne	21-52
EXTREMITY FINDINGS	
Proximal muscle weakness	39-68
Edema	15-66
OTHER FINDINGS	
Significant depression	12-40

*Information is based on 1056 patients from references 4 to 11. Each study enrolled more than 50 patients with disease.
†Diagnostic standard: For *Cushing syndrome,* elevated daily cortisol or corticosteroid metabolites, or both, with loss of circadian rhythm and with abnormal dexamethasone suppression tests.
‡Results are overall mean frequency or, if statistically heterogeneous, the range of values.

3. Obesity as defined by an abnormal waist-to-hip circumference ratio (i.e., >1 in men and >0.85 in women; see Chapter 12)[14]

Defining central obesity based on the abnormal waist-to-hip circumference is not recommended, because there are many false-positive results (i.e., for Cushing syndrome).

Other characteristic features of the body habitus in Cushing syndrome are accumulation of fat in the bitemporal region **(moon facies),**[15] between the scapulae and behind the neck **(buffalo hump),** in the supraclavicular region (producing a "collar" around the base of the neck),[14] and in front of the sternum **(dewlap,** named for its resemblance to the hanging fold of skin at the base of the bovine neck [Fig.13-1]).[16] Many experts state that the buffalo hump is not specific for Cushing syndrome but accompanies weight gain from any cause[17,18]; this hypothesis has not been formally tested. Morbid obesity is rare in Cushing syndrome.[19]

The truncal obesity of Cushing syndrome reflects increased intra-abdominal visceral fat, not subcutaneous fat,[20] probably from glucocorticoid-induced reduction in lipolytic activity and activation of lipoprotein lipase, which allows tissues to accumulate triglyceride.

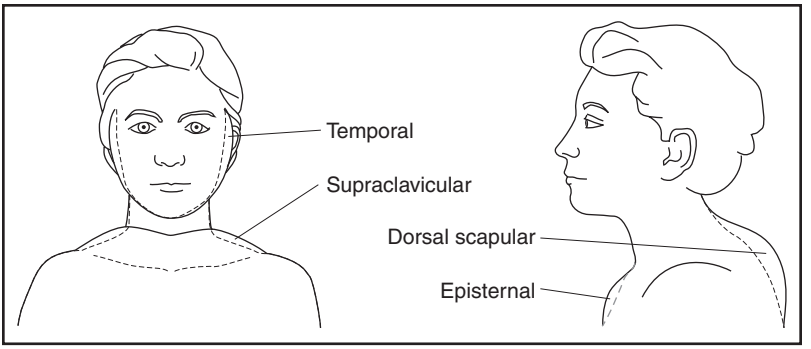

FIGURE 13-1 Distribution of adipose tissue in Cushing syndrome. Rounding of cheeks and prominent bitemporal fat produce the characteristic moon facies. Fat also may accumulate bilaterally above the clavicles (supraclavicular collar), in front of the sternum (episternal area, or dewlap), and over the back of the neck (dorsal cervical fat pad, or buffalo hump). In these drawings, the *dotted line* depicts normal contours of patients without Cushing syndrome.

B. HYPERTENSION

Hypertension affects three of four patients with Cushing syndrome. Proposed mechanisms are suppressed vasodepressor systems (prostaglandins, kallikrein-kinin), exaggerated pressor responses to vasoactive substances, and possible activation of the renin-angiotensin system.[21] Most patients do *not* have a positive salt and water balance.[14]

C. SKIN FINDINGS

The characteristic skin findings are thin skin, striae, plethora, hirsutism (in women), acne, and ecchymoses.

Significant thinning of the skin probably arises from corticosteroid-induced inhibition of epidermal cell division and dermal collagen synthesis.[14] To measure skin thickness, many experts recommend using calipers (either skinfold calipers or electrocardiograph calipers) on the back of the patient's hand, an area lacking significant subcutaneous fat and thus representing just epidermis and dermis.[22,23] In women of reproductive age, this skinfold should be thicker than 1.8 mm.[22] Precise cutoffs have not been established for men, in whom the skin is normally thicker than in women, or for elderly patients, in whom the skin is normally thinner than in younger patients.[23]

The striae of Cushing syndrome are wide (>1 cm) and deep red or purple, in contrast to the thinner, paler pink or white striae that occur normally during rapid weight gain of any cause.[4,24] Striae are usually found on the lower abdomen but may occur on the buttocks, hips, lower back, upper thighs, and arms. In one of the original Cushing syndrome patients, wide striae extended from the lower abdomen to the axillae.[2] Pathologically, striae are dermal scars, with collagen fibers all aligned in the direction of stress, covered by an abnormally thin epidermis.[25] The pathogenesis of striae is not understood, but they may represent actual rupture of the

weakened connective tissue of the skin, under tension from central obesity, which leaves a thin translucent window to the red- and purple-colored dermal blood vessels. Striae are more common in younger patients with Cushing syndrome than in older patients.[24,26]

Plethora is an abnormal diffuse purple or reddish color of the face.[4] Hirsutism and acne occur because of increased adrenal androgens.[14,24] Ecchymoses probably appear because the blood vessels, lacking connective tissue support and protection, are more easily traumatized.

The severity of striae, acne, and hirsutism correlates poorly with cortisol levels, indicating that other factors—temporal, biochemical, or genetic—play a role in these physical signs.[24]

D. PROXIMAL WEAKNESS

Painless proximal weakness of the legs is common and prominent in Cushing syndrome, especially in elderly patients.[26] Because the weakness is a true myopathy, patients lack fasciculations, sensory changes, or reflex abnormalities. Chapter 59 discusses how to assess proximal muscle strength.

E. DEPRESSION

Patients with Cushing syndrome may have crying episodes, insomnia, impaired concentration, difficulty with memory, and suicide attempts.[27,28] The severity of depression correlates with the cortisol level,[27] and, unless the depression antedates the endocrine symptoms by years, it usually improves dramatically after treatment.[28]

F. PSEUDO-CUSHING SYNDROME

Several disorders, including chronic alcoholism, depression, and human immunodeficiency virus (HIV) infection, may mimic the physical findings and biochemical findings of Cushing syndrome and are referred to as pseudo-Cushing syndrome. Patients with chronic alcoholism may develop the physical findings or the biochemical abnormalities, or both, probably because of overproduction of ACTH by the hypothalamic-pituitary axis, an abnormality that resolves after several weeks of abstinence.[29,30] Depressed patients may have the biochemical abnormalities of Cushing syndrome, but they usually lack the physical findings.[31] Patients with HIV infection, particularly if they are receiving protease inhibitors, may develop some of the physical findings (especially the buffalo hump and truncal obesity) but rarely the biochemical abnormalities.[32-34]

III. CLINICAL SIGNIFICANCE

A. DIAGNOSTIC ACCURACY OF FINDING

EBM Box 13-1 presents the diagnostic accuracy of individual physical signs for Cushing syndrome, as applied to 247 patients with suspected disease. The findings that significantly *increase* the probability of Cushing syndrome are thin skinfold (likelihood ratio [LR] = 115.6), ecchymoses (LR = 4.5), central obesity (LR = 3), and plethora (LR = 2.7). (The astronomical LR for thin skinfold thickness [LR = 115.6] derives from young women

EBM BOX 13-1
*Cushing Syndrome**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Vital Signs				
Hypertension[4,12]	25-38	83-94	2.3	0.8
Body Habitus				
Moon facies[12]	98	41	1.6	**0.1**
Central obesity[4,12,13]	72-90	62-97	**3.0**	**0.2**
Generalized obesity[4]	4	38	**0.1**	2.5
Skin Findings				
Thin skinfold[22]	78	99	**115.6**	**0.2**
Plethora[4]	83	69	2.7	**0.3**
Hirsutism, in women[4,12]	50-76	56-71	1.7	0.7
Ecchymoses[4,12]	54-71	69-94	**4.5**	0.5
Red or blue striae[4,12]	46-52	63-78	1.9	0.7
Acne[4]	52	76	2.2	0.6
Extremity Findings				
Proximal muscle weakness[4,12]	62-63	69-93	NS	0.4
Edema[4,12]	38-57	56-83	1.8	0.7

*Diagnostic standard: For *Cushing syndrome,* elevated daily cortisol or corticosteroid metabolites, or both, with loss of circadian rhythm and with abnormal dexamethasone suppression test.

†Definition of findings: For *hypertension*, diastolic blood pressure >105 mm Hg; for *central obesity,* central obesity index exceeds 1[13] or subjective appearance of central obesity sparing the extremities[4,12]; for *thin skinfold,* skinfold thickness on back of hand <1.8 mm (women of reproductive age only).[22]

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. NS, not significant.

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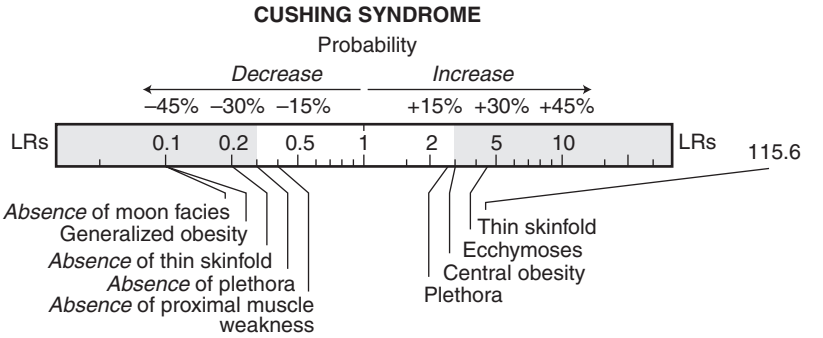


presenting with hirsutism and menstrual irregularity and thus applies only to similar patients.) The findings that *decrease* the probability of Cushing syndrome are generalized obesity (LR = 0.1), absence of moon facies (LR = 0.1), absence of central obesity (LR = 0.2), and normal skinfold thickness (LR = 0.2).

In these same studies, one of the more powerful predictors of Cushing syndrome is osteoporosis (sensitivity of 61% to 63%, specificity of 94% to 97%, positive LR = 17.6, and negative LR = 0.4).[4,12] Osteoporosis was identified radiographically in these studies, but it is often apparent at the bedside from vertebral fractures, kyphosis, and loss of height. Presumably, these bedside findings also accurately identify Cushing syndrome.

B. ETIOLOGY OF CUSHING SYNDROME AND BEDSIDE FINDINGS

Patients who take exogenous corticosteroids have the same frequency of central obesity, moon facies, and bruising as patients with endogenous Cushing syndrome but a significantly lower incidence of hypertension, hirsutism, acne, striae, and buffalo humps.[7]

Patients with the ectopic ACTH syndrome from small cell carcinoma are more often male, have Cushing syndrome of rapid onset (over months instead of years), and present with prominent weight loss, myopathy, hyperpigmentation, and edema.[17,31,35] The irregular hepatomegaly of metastatic disease may suggest this diagnosis.[35] In studies of patients with ACTH-dependent Cushing syndrome, two findings increase the probability of ectopic ACTH syndrome: weight loss (positive LR = 20) and symptom duration of less than 18 months (positive LR = 15).[9,35]

Hirsutism and acne may occur in any woman with endogenous Cushing syndrome, but the presence of virilization (i.e., male pattern baldness, deep voice, male musculature, clitoromegaly) argues strongly for adrenocortical carcinoma.[36-38]

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 14

Pulse Rate and Contour

PULSE RATE

I. INTRODUCTION

Taking the patient's pulse is one of the oldest physical examination techniques, practiced as long ago as 3500 BC by ancient Egyptian physicians, who believed a weakening pulse indicated advancing disease.[1] The pulse was one of Galen's (ca. 129-200 AD) favorite subjects, occupying several treatises that directed clinicians to observe the pulse's speed, force, and duration.[2,3] The first accurate observations of heart rate in disease were by John Foyer (1649-1734), who published his clinical observations in 1707 based on his invention, the pulse-watch.[3] The first clinicians to establish the significance of bradycardia were Adams and Stokes, who, between 1827 and 1846, pointed out that not all seizures and fainting episodes represented disease of the brain but instead could occur because of the slow pulse of heart block.[1]

II. TECHNIQUE

Most clinicians determine the pulse rate by palpating the radial pulse or, less often, by listening to the heart tones with the stethoscope (i.e., apical rate). Counting the pulse for 30 seconds and doubling the result is more accurate than 15 seconds of observation.[4] In a patient with a fast heart rate, especially if the patient has atrial fibrillation, counting the apical rate is more accurate than counting the radial pulse, and 60 seconds of observation is more accurate than shorter periods.[5]

A difference between the radial pulse rate and the apical rate (the apical rate always being greater) is called the **pulse deficit.** A pulse deficit has traditionally been associated with atrial fibrillation, although it is a common finding with extrasystoles and all fast heart rates and by itself has little diagnostic significance.[6]

III. FINDINGS

Many textbooks state that the normal sinus rate ranges from 60 beats/min to 100 beats/min, but more recent information indicates that the heart rate of 95% of healthy persons instead ranges from 50 beats/min to 95 beats/min.[7] **Bradycardia** is a pulse rate less than 50 beats/min; **tachycardia** is a rate greater than 100 beats/min.

IV. CLINICAL SIGNIFICANCE

An important role of any vital sign is to provide the clinician with an early indication that trouble is afoot for the patient. EBM Box 14-1 shows that the finding of tachycardia serves this role well. In a wide variety of clinical disorders, including septic shock, pneumonia, myocardial infarction, gallstone pancreatitis, and pontine hemorrhage, the finding of tachycardia (variably defined as rate >90 beats/min to >110 beats/min) predicts both increased complications and worse survival rates (likelihood ratio [LR] = 1.5 to 25.4). In patients with myocardial infarction, the increased risk of adverse outcome is a continuum, being greater for patients with higher heart rates and persisting whether or not the patient has a low ejection fraction, takes beta-blocker medications, or receives thrombolytic therapy.[12,15-18] In patients with septic shock, the relationship between tachycardia and mortality is independent of whether the patient receives vasopressor medications,[9] and, in patients with pontine hemorrhage, tachycardia is a better predictor of mortality than some other neurologic findings, such as extensor posturing or the absence of withdrawal to pain.[14] The *absence* of tachycardia, on the other hand, decreases the probability of hospital mortality in patients with trauma, septic shock, or pontine hemorrhage (LR = 0.1 to 0.3; see EBM Box 14-1).

Heart rates less than 50 beats/min or greater than 120 beats/min may also indicate heart rhythms other than sinus rhythm (e.g., complete heart block, atrial flutter), a subject discussed fully in Chapter 15.

ABNORMALITIES OF PULSE CONTOUR

I. PULSUS ALTERNANS

A. FINDINGS

Pulsus alternans describes a regular pulse that has alternating strong and weak beats (Fig. 14-1). The pulse must be absolutely regular to diagnose pulsus alternans and distinguish it from the bigeminal pulse, which also has beats of alternating strength although the rhythm is irregular (see Chapter 15).[19] Rarely, in patients with pulsus alternans, the weak pulse is so faint that it is imperceptible, with only half of the beats reaching the radial artery **(total alternans).**[20] Pulsus alternans is often accompanied by alternation of the intensity of heart sounds and murmurs **(auscultatory alternans).**[19,21]

Traube first described pulsus alternans in 1872.[22]

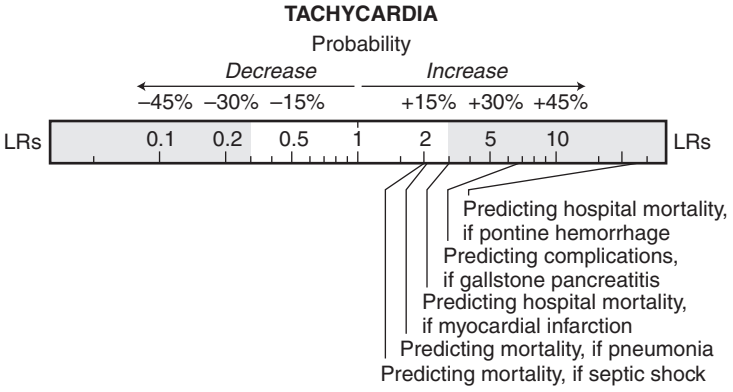
B. TECHNIQUE

Palpating the radial pulse or using the blood pressure cuff is the best way to detect pulsus alternans. When using the blood pressure cuff, the clinician should stop deflating the cuff at the first appearance of Korotkoff sounds and hold the cuff pressure just below systolic level for several beats. In patients with pulsus alternans, only the Korotkoff sounds belonging to the strong beats are heard. After further deflation of the cuff, cuff pressure eventually falls below the systolic pressure of the weaker beats, causing the cadence of

EBM BOX 14-1
Tachycardia

Finding (Reference)	Sensitivity (%)	Specificity (%)	Likelihood Ratio* if Finding Is	
			Present	*Absent*
Heart Rate >90 Beats/Min				
Predicting hospital mortality in trauma patients with hypotension[8]	94	38	1.5	**0.2**
Heart rate >95 Beats/Min				
Predicting hospital mortality in patients with septic shock[9]	97	53	2.0	**0.1**
Heart Rate >100 Beats/Min				
Predicting mortality in patients with pneumonia[10]	45	78	2.1	NS
Predicting hospital mortality in patients with myocardial infarction[11,12]	6-9	97-98	**3.0**	NS
Predicting complications in patients with gallstone pancreatitis[13]	86	87	**6.8**	NS
Heart Rate >110 beats/min				
Predicting hospital mortality in patients with pontine hemorrhage[14]	70	97	**25.4**	**0.3**

*Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.
NS, not significant.
Click here to access calculator.



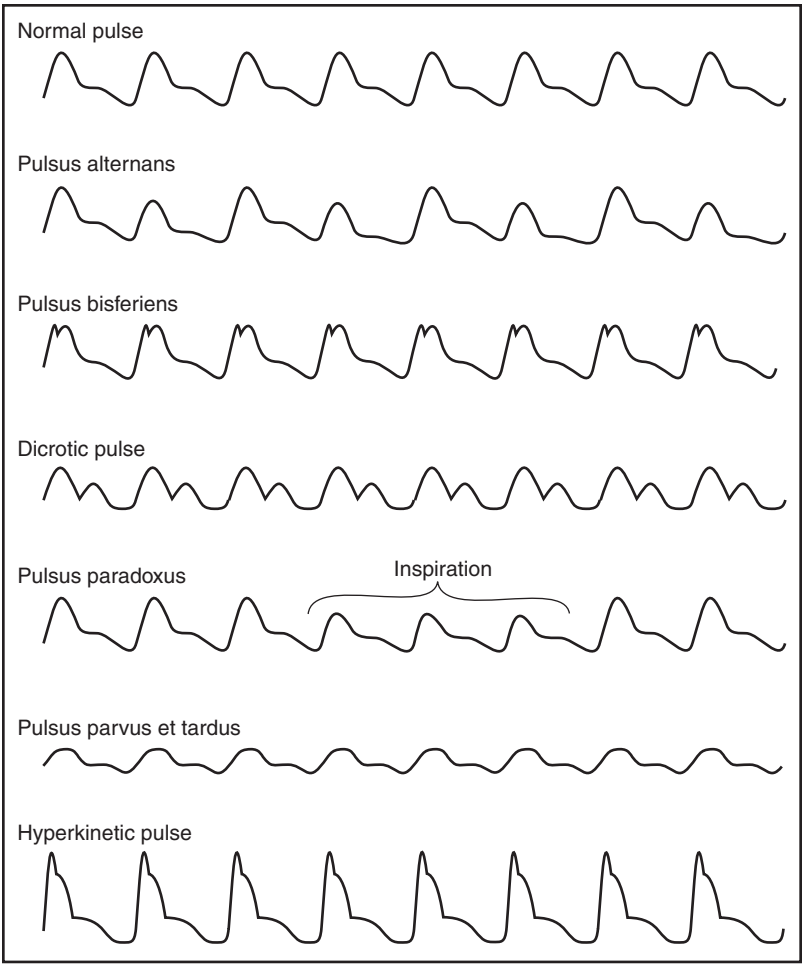


FIGURE 14-1 Abnormalities of pulse contour. The normal pulse tracing *(top row)* is displayed with six tracings of abnormal pulse contours *(bottom rows)*. **Pulsus alternans** *(second row)* is a *regular* pulse that has alternating strong and weak beats. Both **pulsus bisferiens** *(third row)* and the **dicrotic pulse** *(fourth row)* have two beats per cardiac cycle: In pulsus bisferiens, both beats are systolic, whereas in the dicrotic pulse, one is systolic and the other diastolic. **Pulsus paradoxus** *(fifth row)* is a pulse whose systolic blood pressure falls more than 10 to 12 mm Hg during inspiration. **Pulsus parvus et tardus** *(sixth row)* is a pulse that has a small volume and rises slowly. The **hyperkinetic pulse** *(last row)* is a pulse with unusually abrupt and strong force; it may have a normal diastolic blood pressure (e.g., severe mitral insufficiency) or low diastolic blood pressure (e.g., severe aortic regurgitation). These tracings are facsimiles of actual pulse tracings made over 100 years ago. See text for pathogenesis and clinical significance.

Korotkoff sounds to suddenly double. The usual difference in systolic pressure between the strong and weak beats is only 15 to 20 mm Hg.[20]

Pulsus alternans often is most prominent in the several beats immediately after a pause in the heart rhythm. Typically, the pause is caused by a premature beat or the abrupt termination of a paroxysmal tachycardia.[23]

C. CLINICAL SIGNIFICANCE

In patients with normal heart rates, the finding of pulsus alternans indicates severe left ventricular dysfunction, caused by ischemic or valvular heart disease, long-standing hypertension, or idiopathic cardiomyopathy.[24-26] In one series of patients presenting for cardiac catheterization, investigators specifically looked for pulsus alternans after premature beats or 10 seconds of pacemaker-induced atrial tachycardia: Those with pulsus alternans had worse ejection fractions and higher left ventricular filling pressures than those without the finding.[23]

In patients with rapid heart rates, pulsus alternans has less significance because even patients with normal hearts sometimes develop the finding during paroxysmal tachycardia.[27] Also, pulsus alternans rarely may reflect an intermittent left bundle branch block that alternates with ventricular beats having normal conduction.[28]

D. PATHOGENESIS

There has been considerable debate whether the primary cause of pulsus alternans is alternation of intrinsic contractility of the heart (contractility argument) or alternation of filling of the ventricles (hemodynamic argument).

One version of the hemodynamic argument is particularly compelling.[22,29] In patients with a *regular* pulse, the sum of the length of systole and the length of the subsequent diastole must be constant. If systole lengthens for any reason, the subsequent diastole must be shorter; if systole shortens for any reason, the subsequent diastole must be longer. In patients with left ventricular dysfunction, a sudden increase in ventricular filling (such as that induced by a postextrasystolic pause) causes the subsequent systole to produce a strong beat, although it takes longer than normal for the weakened heart to eject this blood (i.e., thus lengthening systole). By prolonging systole, the strong beat thus shortens the next diastole, which reduces filling of the heart and causes the next beat to be weaker. The weaker beat is ejected more quickly, shortening systole and causing the next diastole to be longer, thus perpetuating the alternating pulse.

Nonetheless, the hemodynamic argument does not explain how pulsus alternans ever gets started when there is no pause in the rhythm from an extrasystole or termination of a tachycardia. Most experts now believe that alternation of intrinsic contractility is the fundamental problem in pulsus alternans, because alternation can even be demonstrated in vitro in isolated muscles at constant length and resting tension.[25,26] Once alternans begins, however, the hemodynamic effects probably contribute to the alternating amplitude of the pulse.

II. PULSUS BISFERIENS

A. FINDINGS

Pulsus bisferiens (Latin *bis*, meaning "twice," and Latin *ferire*, meaning "to beat") has two beats per cardiac cycle, both of which occur in systole. (The first beat is called the **percussion wave,** the second, the **tidal wave;** see Fig. 14-1.[19]) Descriptions of pulsus bisferiens appear in the writings of Galen.[30]

B. TECHNIQUE

Pulsus bisferiens is detected by palpating the brachial or carotid pulse with moderate compression of the vessel, or by using the blood pressure cuff.[31] When using the blood pressure cuff, the clinician hears a quick double tapping sound instead of the typical single sound. (The clinician can mimic the double sound by saying "pa-da…pa-da" as fast as possible.[32])

C. CLINICAL SIGNIFICANCE

Pulsus bisferiens is a finding in patients with moderate-to-severe aortic regurgitation.[30,32,33] Pulsus bisferiens also occurs in patients with combined aortic stenosis and regurgitation, though the principal lesion is usually the regurgitation and the stenosis is mild.[30,33,34] There are exceptional cases of the finding in severe aortic stenosis.[31]

Pulsus bisferiens is sometimes described in patients with hypertrophic cardiomyopathy,[35] although almost always as a finding seen on direct intra-arterial pressure tracings, not as one palpated at the bedside.[36]

D. PATHOGENESIS

The bisferiens pulse probably results from rapid ejection of blood into a flexible aorta. Because of the **Venturi effect,** the rapidly moving bloodstream temporarily draws the walls of the aorta together, reducing flow momentarily and producing a notch with two systolic peaks in the waveform. (In hypertrophic cardiomyopathy, the Venturi effect draws the anterior leaflet of the mitral valve and the interventricular septum together.[31,37]) Although this hypothesis was proposed over 40 years ago, direct evidence supporting it is difficult to find.

III. PULSUS PARADOXUS

A. FINDINGS

Pulsus paradoxus is an exaggerated decrease of systolic blood pressure during inspiration (see Fig. 14-1).[19,38] Although the usual definition is an inspiratory fall in systolic blood pressure exceeding 10 mm Hg, a better threshold may be 12 mm Hg, which is the upper 95% confidence interval for inspiratory decline in normal persons (i.e., the average inspiratory decrease in systolic pressure of normal persons is 6 ± 3 mm Hg).[39] In patients with pulsus paradoxus, the systolic blood pressure and pulse pressure fall dramatically during inspiration, though the diastolic blood pressure changes little.[38,39]

In 1873, Kussmaul first described pulsus paradoxus in three patients with pericardial disease.[40,41] Kussmaul called the finding "paradoxical" because the pulse of his patients disappeared during inspiration even though the apical beat persisted throughout the respiratory cycle. The term is unfortunate because the finding is nothing more than an exaggeration of normal physiologic change.

B. TECHNIQUE

When checking for pulsus paradoxus, the clinician should have the patient breathe quietly and regularly because even normal persons can induce pulsus paradoxus with vigorous respirations. Pulsus paradoxus is detected by palpating the pulse or using the blood pressure cuff, although only paradoxic

pulses exceeding 15 to 20 mm Hg are palpable.[42,43] For this reason, most clinicians use the blood pressure cuff, which has the added advantage of quantifying the finding (Fig. 14-2).

Pulsus paradoxus also has been noted in pulse oximetry tracings, appearing as respiratory movement of the tracing's baseline.[44] The amplitude of this oscillation correlates with the severity of pulsus paradoxus.[44] When

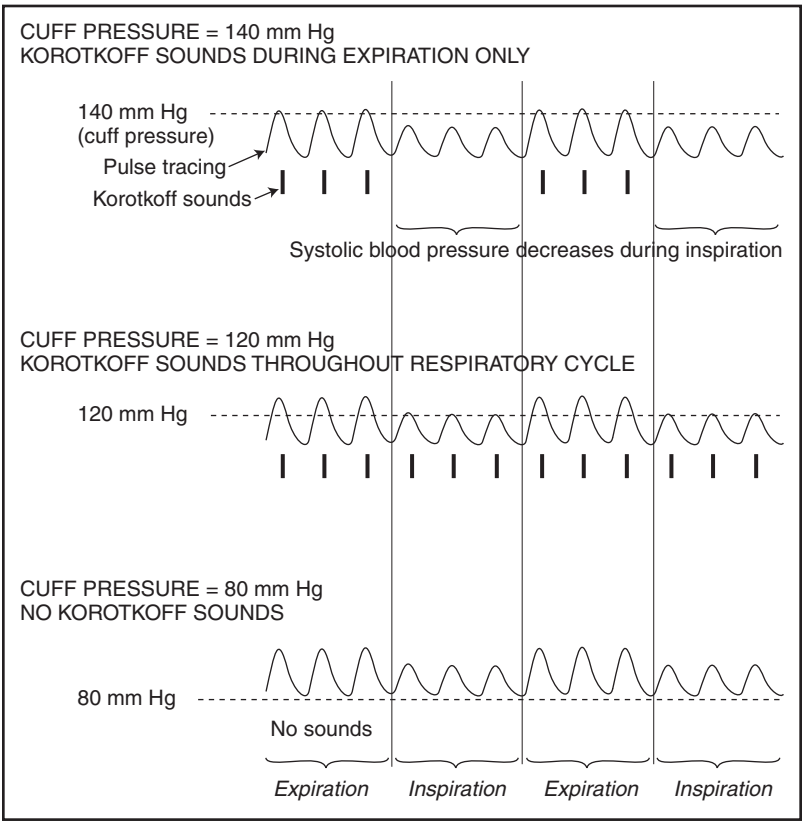


FIGURE 14-2 Technique for measuring pulsus paradoxus. The figure simultaneously depicts the pressure in the blood pressure cuff *(dashed horizontal line),* the patient's pulse tracing *(solid line),* and Korotkoff sounds (*solid vertical bars* under pulse tracing) during two breaths. (Expiration and inspiration are separated by *vertical lines.*) The pulse tracing shows the fall in systolic pressure during inspiration, which is characteristic of pulsus paradoxus. To detect and measure the paradoxic pulse, the clinician begins by checking the blood pressure in the usual way, but slowly deflates the cuff to precisely identify the *cuff pressure* at three points: (1) The moment Korotkoff sounds first appear *(top tracing).* In patients with pulsus paradoxus, cuff pressure will fall below the systolic pressure of just the expiratory beats, and the Korotkoff sounds will repeatedly come and go during quiet respiration, disappearing with inspiration and reappearing with expiration. (2) The moment when Korotkoff sounds persist throughout the respiratory cycle *(middle tracing);* at this point, cuff pressure has fallen below systolic blood pressure of all beats. (3) The moment when Korotkoff sounds disappear (i.e., the diastolic pressure, *bottom tracing*).

In this patient, only expiratory Korotkoff sounds are heard between cuff pressures of 140 mm Hg and 120 mm Hg, but Korotkoff sounds are heard throughout the respiratory cycle between pressures of 120 mm Hg and 80 mm Hg. The patient's blood pressure is therefore "140/80 mm Hg with a paradox of 20 mm Hg" (i.e., 20 = 140 − 120).

using the blood pressure cuff to quantify pulsus paradoxus, clinicians may actually look at the visual display of the pulse oximeter instead of listening to the Korotkoff sounds.[45]

C. CLINICAL SIGNIFICANCE

Pulsus paradoxus is a common finding in two conditions, cardiac tamponade and acute asthma.

1. Cardiac Tamponade

Pulsus paradoxus of more than 10 mm Hg occurs in 98% of patients with cardiac tamponade (i.e., a pericardial effusion under high pressure compressing the heart and compromising cardiac output; see Chapter 45). Because it is one of three key findings of tamponade—the others being elevated neck veins (sensitivity = 100%) and tachycardia (sensitivity = 81% to 100%)—the clinician should consider tamponade and check for pulsus paradoxus in any patient suspected of having pericardial disease, such as those with elevated neck vein pressure, unexplained dyspnea, pericardial rub, or known pericardial effusion.[43]

In patients with pericardial effusions, the finding of pulsus paradoxus of more than 12 mm Hg discriminates patients with tamponade from those without tamponade with a sensitivity of 98%, specificity of 83%, positive LR of 5.9, and negative LR of 0.03.*[39]

2. Cardiac Tamponade without Pulsus Paradoxus

In only 2% of patients with tamponade, pulsus paradoxus is absent. These patients usually have one of five disorders: (1) atrial septal defect, (2) severe left ventricular dysfunction (especially those with uremic pericarditis),[46] (3) regional tamponade (tamponade affecting only one or two heart chambers, a complication of cardiac surgery),[47] (4) severe hypotension,[48-50] or (5) aortic regurgitation. Knowing that aortic regurgitation may eliminate pulsus paradoxus is especially significant because patients with proximal (type A) aortic dissection and hemopericardium usually lack the paradoxic pulse despite significant tamponade, and the unaware clinician may exclude the possibility of tamponade to the harm of the patient.

The section on pathogenesis explains why pulsus paradoxus is absent in these clinical disorders.

3. Asthma

EBM Box 14-2 shows that in patients with acute asthma, pulsus paradoxus exceeding 20 mm Hg almost certainly indicates severe bronchospasm (LR = 8.2). Nonetheless, pulsus paradoxus has limited clinical utility in patients with acute asthma, for two reasons.

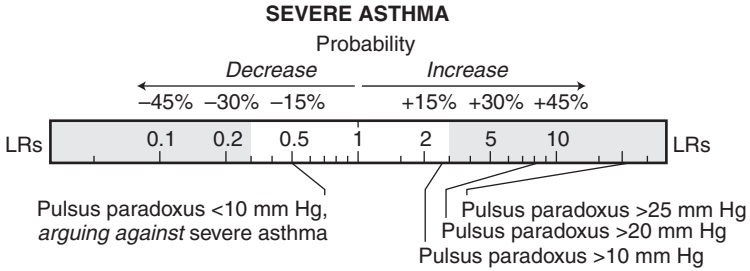
1. Up to half of patients with severe bronchospasm lack a pulsus paradoxus of more than 10 mm Hg (see EBM Box 14-2). The sensitivity

*Tamponade was defined in this study as improvement in cardiac output of 20% or more following pericardiocentesis. See Chapter 45.

EBM BOX 14-2
*Pulsus Paradoxus Predicting Severe Asthma**

Finding (Reference)	Sensitivity (%)	Specificity (%)	Likelihood Ratio† if Finding Is	
			Present	*Absent*
Pulsus paradoxus >10 mm Hg[42,51-53]	52-68	69-92	2.7	0.5
Pulsus paradoxus >20 mm Hg[42,51,52]	19-39	91-100	**8.2**	0.8
Pulsus paradoxus >25 mm Hg[53]	16	99	**22.6**	0.8

*Diagnostic standard: For *severe asthma,* an FEV_1/FVC <50%,[42] FEV_1 <1 L,[51] peak flow <200 L/min,[53] and peak flow <30% predicted.[52] All patients in these studies had acute asthma.
†Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.
FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity.
Click here to access calculator.



is low because in asthma, pulsus paradoxus is notably dependent on respiratory rate and effort, even when the degree of airway obstruction remains constant.[52,54]

2. The best measure of bronchospasm (and the criterion standard in EBM Box 14-2) is peak expiratory flow rate. In a busy emergency department with an anxious and dyspneic patient, it is much more convenient to measure peak flow rates using handheld flowmeters than to try to interpret the coming and going of Korotkoff sounds.

In patients being mechanically ventilated, the amount of pulsus paradoxus, as reflected in the changing baseline of the pulse oximeter tracing, correlates with the degree of the patient's auto–positive end expiratory pressure (PEEP) (a measure of expiratory difficulty in ventilated patients).[44]

4. Pulsus Paradoxus in Other Conditions

Pulsus paradoxus has been described as an uncommon finding in constrictive pericarditis, right ventricular infarction, pulmonary embolism, and severe pectus excavatum (see Chapter 45).[38,55]

5. Reversed Pulsus Paradoxus

Reversed pulsus paradoxus,[56] which is systolic blood pressure that falls more than 10 mm Hg *during expiration*, occurs in three clinical disorders.

1. Hypertrophic cardiomyopathy
2. Isorhythmic dissociation (i.e., inspiration accelerates the sinus rate, which temporarily positions the P waves before the QRS complex, thus coordinating the atrial and ventricular contractions and raising blood pressure; expiration slows the sinus rate, removes atrioventricular coordination, and lowers blood pressure)
3. Intermittent inspiratory positive-pressure breathing in the presence of left ventricular failure (This is a variation of the Valsalva square wave response in heart failure; see Chapter 46.)

D. PATHOGENESIS

1. Cardiac Tamponade

Tamponade develops when the pressure of fluid inside the pericardial space exceeds the diastolic filling pressure of the heart chambers. Once this occurs, the diastolic pressure in the heart chambers, reflected in the neck veins, becomes a measurement of the force acting to compress the heart. The four chambers, now smaller in size, begin to compete for space, and an increase in the size of one comes at the expense of the size of another. Inspiration increases filling to the right side of the heart and shifts the interventricular septum to the left and posteriorly, thus obliterating the left ventricular chamber and causing the cardiac output to fall. During expiration, filling of the right side of the heart is less, which increases left ventricular size, and both cardiac output and blood pressure increase.[38,47,57-60]

This explains why pulsus paradoxus is absent in regional tamponade and tamponade associated with atrial septal defect, severe left ventricular dysfunction, and aortic insufficiency. (See the section on Cardiac Tamponade without Pulsus Paradoxus.) Inspiratory movement of the interventricular septum is prevented when the right ventricle does not fill more during inspiration (atrial septal defect, see Chapter 38), when the left ventricular pressures are very high (severe left ventricular dysfunction), or when the left ventricle fills from some source other than the left atrium (aortic insufficiency). Regional tamponade, by definition, compresses only one or two chambers, enough to impair cardiac output but too confined to cause the heart chambers to compete for space.

2. Asthma

The mechanism of pulsus paradoxus in asthma is complex and not fully understood. Difficulty breathing causes wide swings of intrapleural pressure, which then are transmitted directly to the aorta, contributing to the paradoxic pulse. This is not a complete explanation, however, because the amount of pulsus paradoxus in asthma often exceeds the pressure shifts of these respiratory excursions.[54] Furthermore, the pulse pressure also declines during inspiration of some asthma patients, which would not happen if transmission of pressures were the only cause. Other proposed mechanisms are an inspiratory reduction in pulmonary venous return to the left

heart[38,54,61,62] and the compressive action of the hyperinflated chest, which, like tamponade, may reduce the size of the heart chambers and cause them to compete for space.[52,63]

IV. PULSUS PARVUS ET TARDUS

A. FINDINGS AND TECHNIQUE

Pulsus parvus et tardus describes a carotid pulse with a small volume (pulsus parvus) that rises slowly and has a delayed systolic peak (pulsus tardus; see Fig. 14-1).[19] It is routinely detected by palpation.

B. CLINICAL SIGNIFICANCE

Pulsus parvus et tardus is a finding of aortic stenosis. Of its two components, pulsus tardus is the better discriminator, detecting severe aortic stenosis with a sensitivity of 31% to 90%, specificity of 68% to 93%, positive LR of 3.3, and negative LR of 0.4 (see Chapter 42).

C. PATHOGENESIS

Pulsus tardus depends on both obstruction to flow and the compliance of the vessel distal to the obstruction. The pulse waveform rises rapidly in stiff vessels but slowly in more compliant vessels, which act like low-pass filters and remove the high-frequency components of the waveform.[64] That the delay in the pulse reflects the severity of obstruction is a principle also used by Doppler sonography to gauge the severity of renal artery stenosis.[64]

V. DICROTIC PULSE

A. FINDINGS AND TECHNIQUE

The **dicrotic pulse** has two beats per cardiac cycle, but, unlike pulsus bisferiens, one peak is systolic and the other is diastolic (see Fig. 14-1).[19] It is usually detected by palpation of the carotid artery.[65]

The second wave of the dicrotic pulse is identical in timing to the small dicrotic wave of normal persons, obvious on arterial pressure tracings but never palpable. The dicrotic wave is felt to represent rebound of blood against the closed aortic valve.

B. CLINICAL SIGNIFICANCE

The dicrotic pulse occurs in younger patients with severe myocardial dysfunction, low stroke volumes, and high systemic resistance.[65,66] In patients who have had valvular replacement surgery, the finding of a persistent dicrotic pulse is associated with a poor prognosis.[66]

C. PATHOGENESIS

A dicrotic pulse relies on the simultaneous presence of two conditions: (1) low stroke volume, which significantly lowers the height of the pulse's initial systolic wave, thus increasing the chances that the dicrotic wave will be palpable;[67] and (2) a resilient arterial system, which amplifies the rebound of the pulse waveform during diastole. The importance of a

resilient arterial system may explain why the dicrotic pulse usually occurs in young patients with cardiomyopathy, who have more compliant vessels than older patients.[65,66]

The importance of low stroke volume to the dicrotic pulse is illustrated by the observation that the dicrotic pulse sometimes disappears with beats that have larger stroke volumes, such as the beat after a premature beat, the stronger beats of pulsus alternans, and the expiratory beats of pulsus paradoxus.[65,67] Vasodilators often cause the dicrotic pulse to disappear, perhaps because of better forward flow and a greater stroke volume.[65]

VI. HYPERKINETIC PULSE

A. FINDINGS

The hyperkinetic pulse strikes the examiner's fingers with unusually abrupt and strong force (see Fig. 14-1). Hyperkinetic pulses may have either a normal pulse pressure (e.g., severe mitral regurgitation, hypertrophic obstructive cardiomyopathy) or increased pulse pressure (e.g., aortic insufficiency and other disorders with abnormal aortic runoff).[19] In both severe mitral regurgitation and hypertrophic obstructive cardiomyopathy, the blood is ejected rapidly from the left ventricle but the integrity of the aortic valve preserves a normal arterial diastolic and pulse pressure.[68] In aortic regurgitation, the rapid ejection of blood is accompanied by an incompetent aortic valve, which causes a very low diastolic pressure in the aortic root, thus increasing the pulse pressure and causing the **Corrigan pulse** or **water-hammer pulse** characteristic of this disorder (see Chapter 43).

B. CLINICAL SIGNIFICANCE

Chapter 43 discusses the significance of the water-hammer pulse and large pulse pressure of aortic regurgitation.

In patients with mitral stenosis, the pulse is characteristically normal or diminished. If the clinician instead finds a hyperkinetic pulse in these patients, the probability is high that additional valvular disease is present, such as significant mitral regurgitation (sensitivity 71%, specificity 95%, positive LR = 14.2, negative LR = 0.3; see Chapter 44).[69]

VII. PULSES AND HYPOVOLEMIC SHOCK

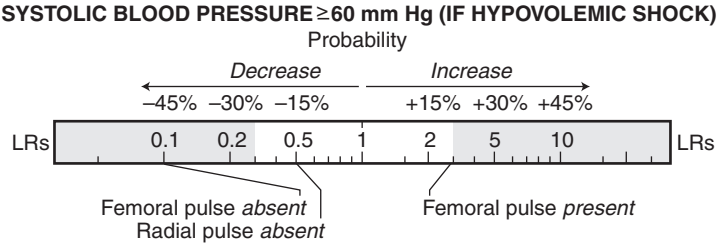
In patients with hypovolemic shock, the peripheral pulses provide a rough guide to the patient's systolic blood pressure.[70] As blood pressure progressively diminishes, the radial pulse generally disappears first, then the femoral pulse, and finally the carotid pulse. In one study of 20 patients with hypovolemic shock, summarized in EBM Box 14-3, the femoral pulse had the greatest diagnostic accuracy in determining severity of shock: the presence of a palpable femoral pulse increased probability of a systolic blood pressure higher than 60 mm Hg (LR = 2.9), whereas its absence decreased the probability of a blood pressure this high (LR = 0.1).

EBM BOX 14-3
Pulses and Hypovolemic Shock[*70]

Finding	Sensitivity (%)	Specificity (%)	Likelihood Ratio† if Finding Is	
			Present	*Absent*
Detecting Systolic Blood Pressure ≥60 mm Hg				
Carotid pulse present	95	22	NS	NS
Femoral pulse present	95	67	2.9	**0.1**
Radial pulse present	52	89	NS	0.5

*Diagnostic standard: For *systolic blood pressure*, invasive arterial blood pressure measurements.

†Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.
NS, not significant.
Click here to access calculator.



The references for this chapter can be found on www.expertconsult.com.

CHAPTER 15

Abnormalities of Pulse Rhythm

I. INTRODUCTION

In the late 19th and early 20th centuries, before the introduction of electrocardiography, clinicians could examine the patient's arterial pulse, heart tones, and jugular venous waveforms and, from these observations alone, diagnose atrial and ventricular premature contractions, atrial flutter, atrial fibrillation, complete heart block, Mobitz type 1 and 2 atrioventricular blocks, and sinoatrial block.[1–3] In fact, clinicians were familiar enough with the bedside findings of these arrhythmias that early textbooks of electrocardiography included tracings of the arterial and venous pulses to help explain the electrocardiogram (ECG) (Fig. 15-1).[4]

The bedside diagnosis of arrhythmias today is probably little more than an intellectual game because all significant arrhythmias require electrocardiography for confirmation and monitoring. Nonetheless, bedside diagnosis of arrhythmias is still possible, using the principles discovered 100 years ago by Mackenzie, Wenckebach, and Lewis. These principles, based on extensive investigation and many polygraph recordings of the arterial and venous pulses,[1–4] allow diagnosis of simple arrhythmias when the electrocardiograph is not immediately nearby.

II. TECHNIQUE

The first step in diagnosing arrhythmias is to determine the basic rhythm of the patient's radial pulse. Most arrhythmias can be classified as one of five basic abnormalities: (1) the pause, (2) regular bradycardia, (3) regular tachycardia, (4) irregular rhythm that varies with respiration, and (5) irregularly irregular (or chaotic) rhythm (Fig. 15-2).

The radial pulse may not correspond to the ventricular pulse (or apical pulse), as determined by auscultation of the heart tones or palpation of the cardiac impulse, because some ventricular contractions are too weak to propel blood to the radial artery. Although the clinician must compare the radial pulse with the ventricular pulse to diagnose arrhythmias, the difference in *rate* between the two by itself indicates no particular diagnosis.

After the basic rhythm of the radial pulse is identified, analysis of the jugular venous waveforms, heart tones, and response of the heart rhythm to vagal maneuvers may further distinguish the various causes.

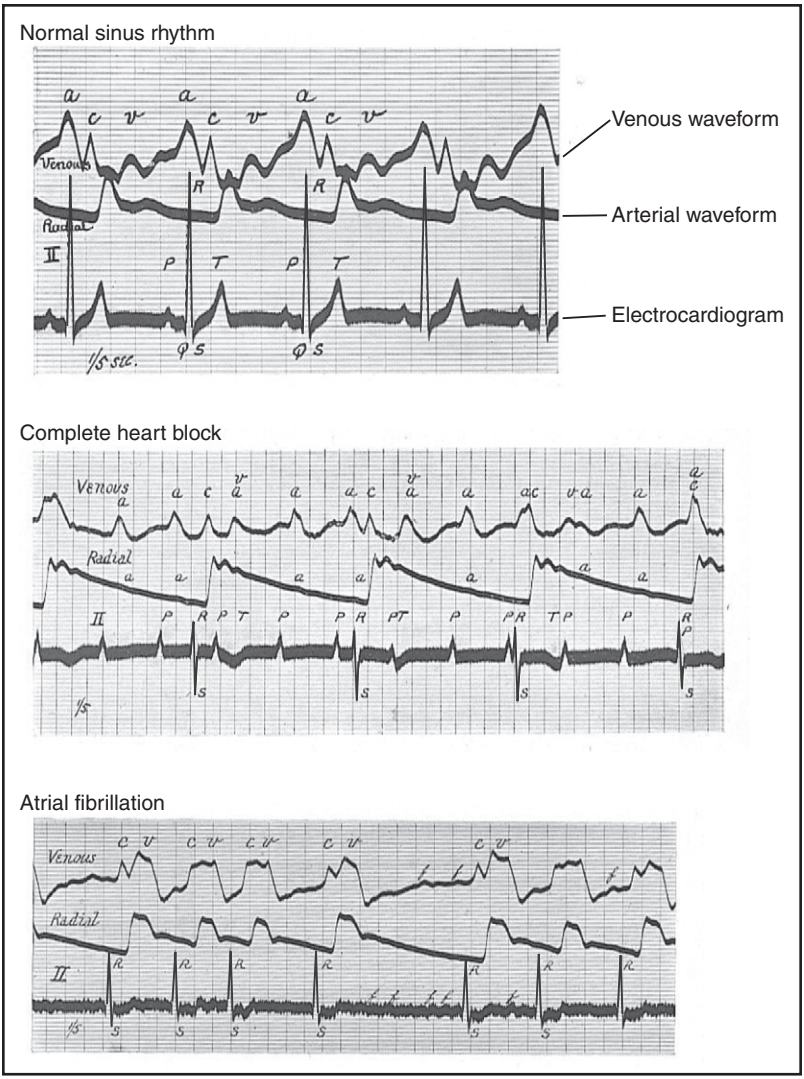


FIGURE 15-1 Simultaneous venous, arterial, and electrocardiographic curves. To help clinicians understand the P, QRS, and T waves of the newly introduced electrocardiogram, early textbooks displayed simultaneous venous and arterial waveforms with the electrocardiogram. These examples, reproduced from Sir Thomas Lewis's 1925 work *Mechanism and Graphic Registration of the Heart Beat*, 3rd ed. (London: Shaw and Sons Ltd.), depict normal sinus rhythm *(top)*, complete heart block *(middle)*, and atrial fibrillation *(bottom)*. See text.

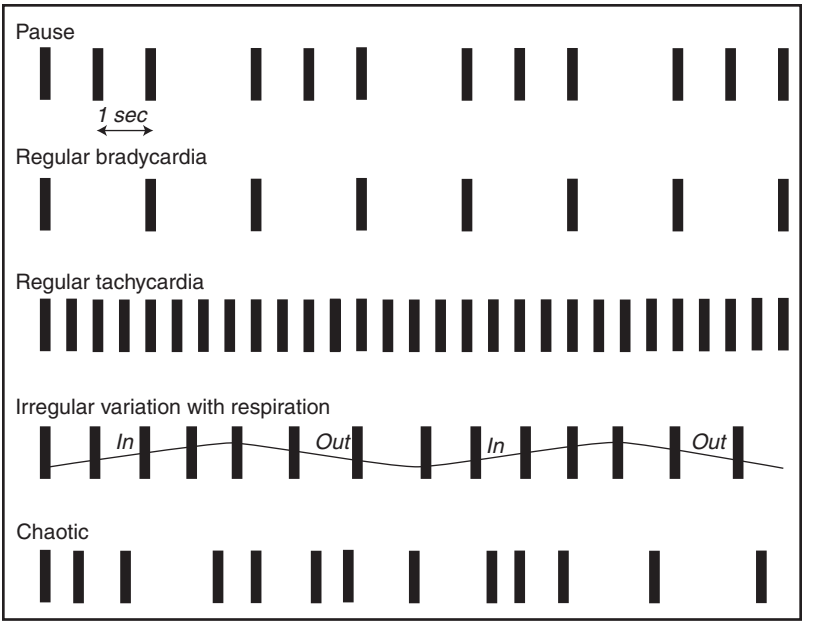


FIGURE 15-2 Basic abnormalities of pulse rhythm are (1) the pause, (2) regular bradycardia, (3) regular tachycardia, (4) irregular rhythm that varies with respiration ("in" depicts inspiration and "out" depicts expiration), and (5) irregularly irregular (or chaotic) rhythm. See text.

III. FINDINGS AND THEIR CLINICAL SIGNIFICANCE

A. THE PAUSE

The pause has two important causes: premature contractions (common) and heart block (uncommon).

1. Terminology

When the radial pulse consists of the regular repetition of two beats followed by a pause, the term **bigeminal pulse** or **bigeminal rhythm** is used. When there are three radial pulse beats between each pause, the appropriate term is **trigeminal pulse** or **trigeminal rhythm.** The finding of several beats between each pause is usually called **group beating,** and much longer periods of regular rhythm interrupted by the rare pause is sometimes referred to as **pulse intermissions.** The basic mechanism for all of these rhythm disturbances is the same; only the frequency of premature beats or heart block differs among them.

Because the cadence of these rhythms becomes predictable after short periods of observation, the term *regularly irregular* is sometimes used. This term, however, inaccurately conveys to others what actually is going on and is best discarded.

2. Basic Mechanism of the Pause

The pause has three basic mechanisms, illustrated in Figure 15-3. The two most important questions that distinguish these mechanisms are the following: (1) Is there a premature radial pulse immediately preceding the pause? (2) Do additional ventricular beats (identified by listening to the heart tones or palpating the apical pulse) occur during the pause?

a. Premature Beat

Patients with premature contractions (the first two examples in Fig. 15-3) have evidence of a premature ventricular beat during or immediately preceding the pause in the radial pulse. This early beat is always evident in the

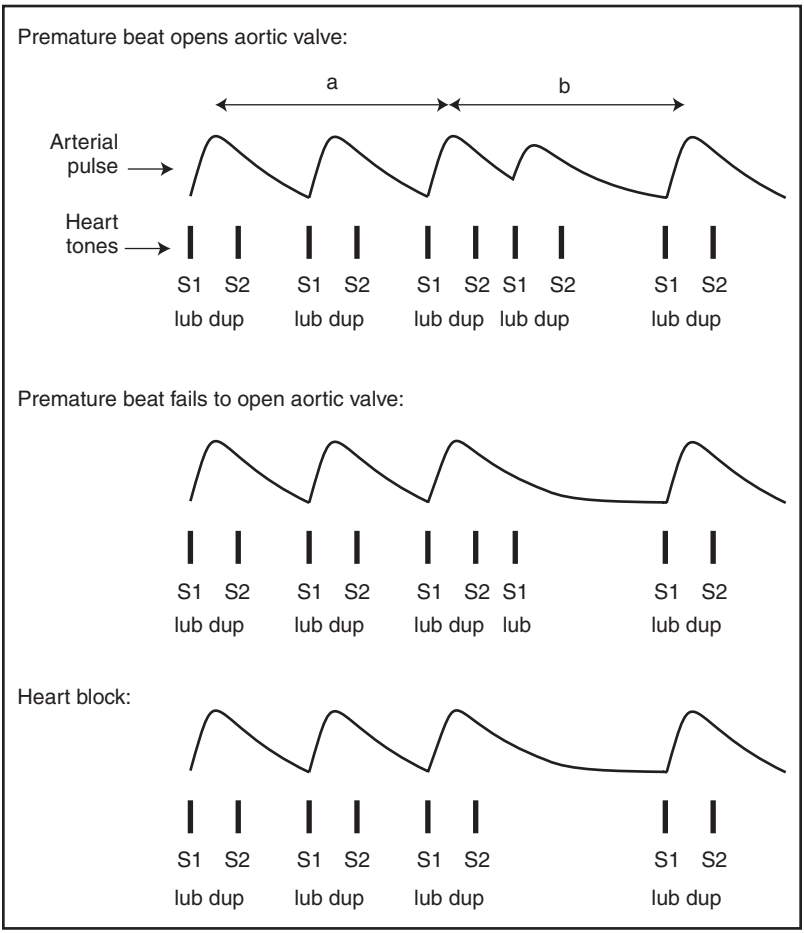


FIGURE 15-3 Mechanism of the pause. The radial pulse tracing and heart tones are presented, illustrating the three mechanisms for the pause: (1) premature contraction that opens the aortic valve, (2) premature contraction that fails to open the aortic valve, and (3) heart block. Onomatopoeia of the heart tones appears below each tracing. (*Lub* is the first heart sound, *dup* is the second heart sound.) See text.

form of a palpable apical impulse or additional heart tones, although it may not be felt in the radial artery.

Some premature contractions are strong enough to open the aortic valve (first example in Fig. 15-3). If so, the clinician will feel a quick beat in the radial pulse just preceding the pause, although the quick beat is usually not as strong as a normal sinus beat. When listening to the heart tones, the clinician will hear both the first and second heart sounds of the early beat, which produces the following characteristic cadence:

lub dup lub dup lub dup lub dup lub dup

(In this and the following two examples, *lub* is the first heart sound and *dup* is the second sound; each rhythm begins with three normal beats, i.e., three *lub dups*.)

If the premature contraction is too weak to open the aortic valve (second example in Fig. 15-3), the clinician palpating the pulse will not detect the quick beat but will only feel the pause. Listening to the heart, he or she will hear only the first sound of the premature beat (S_2 is absent because the aortic valve does not open):

lub dup lub dup lub dup lub lub dup

b. Heart Block

Patients with heart block (third example in Fig. 15-3), whether sinoatrial or atrioventricular, have no palpable apical impulse or extra heart tones during the pause. The cadence of heart tones contrasts with those of the premature beat:

lub dup lub dup lub dup lub dup

3. Bigeminal and Trigeminal Rhythms, and Grouped Beating

Based on the mechanisms previously discussed, there are three causes of the bigeminal pulse rhythm: (1) alternating normal and premature contractions; (2) premature contractions occurring every third beat, although the premature contraction is too weak to open the aortic valve; and (3) 3:2 heart block (atrioventricular or sinoatrial). In causes 2 and 3, both beats of the couplet are strong, but cause 2 has evidence of a ventricular contraction during the pause whereas cause 3 does not.

The same analysis is used for trigeminal rhythms (i.e., possible causes are premature contractions after every two or three normal beats or 4:3 heart block) and for grouped beating.

4. Atrial Versus Ventricular Premature Contractions

Two helpful bedside findings distinguish atrial premature contractions from ventricular ones.

a. Compensatory Pause

Beats that originate in the ventricle usually do not upset the underlying sinus rhythm, causing the beat immediately following the pause to fall

exactly where the clinician anticipates it would. Tapping the foot during the normal regular rhythm helps determine this. In Figure 15-3, the distance "b" equals "a," meaning there is a "complete compensatory pause."

Beats that originate in the atria, in contrast, often reset the sinus node, causing the next beat to appear early. In Figure 15-3, "b" would be less than "a," and the clinician tapping the foot would find that the basic meter of rhythm changes.

This rule is much more helpful when the pause is not compensatory (i.e., b < a, indicating that the beat is atrial), because many atrial premature contractions also seem to have a complete compensatory pause at the bedside.

b. Cannon A Waves

The appearance of a sudden prominent venous wave in the neck (cannon A wave) *during the pause* indicates that the premature beat was ventricular (see also Chapter 34). This occurs because the right atrium, still beating under the direction of the uninterrupted sinus impulses, contracts after the ventricular premature contraction has closed the tricuspid valve. Rarely, a very early atrial premature beat may also produce a cannon A wave, but this wave precedes the first heart sound of the premature contraction, whereas cannon A waves from ventricular premature contractions always follow the first heart sound of the premature beat.

B. REGULAR BRADYCARDIA

Regular bradycardia is a heart rate of less than 50 beats/min. There are three causes of regular bradycardia that are recognizable at the bedside: sinus bradycardia, complete heart block, and halved pulse.

1. Sinus Bradycardia

This arrhythmia resembles the normal rhythm in every way except for the abnormally slow rate: The venous waveforms in the neck are normal, the intensity of the first heart sound is the same with each beat, and there is no evidence of ventricular contractions between radial pulsations (as determined by palpation of apical impulse or auscultation of the heart tones).

2. Complete Heart Block

In complete heart block, the atria and ventricles beat independently of each other (i.e., atrioventricular dissociation). Sometimes the atrial and ventricular contractions are contiguous, and sometimes they are far apart. Atrioventricular dissociation causes two important bedside findings: changing intensity of the first heart sound and intermittent cannon A waves in the venous pulse.

a. Changing Intensity of the First Heart Sound

In complete heart block, the first heart sound of most beats is faint. Intermittently, however, the atrium contracts just before the ventricle contracts, which results in a first heart sound of booming intensity (named **bruit de canon** for its explosive quality; see Chapter 38 for the pathophysiology of S_1 intensity).[5]

The finding of a changing first heart sound is significant only when the pulse is regular because in irregular rhythms its intensity varies with the length of the previous diastole (i.e., long diastoles cause the next first heart sound to be loud; short ones cause it to be soft). If the ventricular pulse is regular, however, a changing first heart sound (or intermittent "booming" of the first heart sound) indicates only one diagnosis, atrioventricular dissociation.

b. Intermittent Appearance of Cannon A Waves in the Venous Pulse

When the atrial contraction falls intermittently just after a ventricular contraction in complete heart block, the right atrium is contracting against a closed tricuspid valve, causing an abrupt systolic outward wave in the jugular venous pulse (i.e., cannon A wave; see also Chapter 34).

In many different arrhythmias, cannon A waves appear with *every* arterial pulse. If cannon A waves appear *intermittently*, however, in a patient whose ventricular pulse is *regular*, the only diagnosis is atrioventricular dissociation.

c. Other Evidence of Atrioventricular Dissociation

Other uncommon signs of atrioventricular dissociation are regular small A waves in the venous pulse; regular muffled fourth heart sounds at the apex; or, in patients with mitral stenosis, regular short murmurs from the atrium pushing blood across the stenotic valve. All of these findings represent regular atrial contractions that continue during the long ventricular diastoles.

A rare sign of complete heart block is an intermittently audible summation gallop (or third heart sound; see Chapter 39).[6]

3. Halved Pulse

Halved pulse refers to the finding of twice as many ventricular beats as radial pulse beats. This is almost always due to premature contractions, which appear every other beat but are too weak to open the aortic valve and reach the radial pulse. Rarely, pulsus alternans may be the cause (total alternans),[7] although in these patients the heart tones at the apex are regular, whereas in premature contractions they are bigeminal.

C. REGULAR TACHYCARDIA

The regular tachycardias that *sometimes* are recognizable at the bedside include sinus tachycardia, atrial flutter, paroxysmal supraventricular tachycardia, and ventricular tachycardia. The bedside observations that distinguish these arrhythmias are response to vagal maneuvers, signs of atrioventricular dissociation, and abnormalities of the neck veins. Even so, bedside examination is diagnostic in only a minority of patients with rapid rates, and the careful clinician always relies on electrocardiography for diagnosis.

1. Vagal Maneuvers

The usual maneuvers are the Valsalva maneuver and carotid artery massage.

a. Technique

Both maneuvers are performed when the patient is supine. To perform the Valsalva maneuver, the clinician asks the patient to bear down and strain

against a closed glottis as if "having a bowel movement." Patients who have difficulty following this instruction sometimes respond better when asked to put the tip of their own thumb in their mouth and pretend it is a balloon to blow up. In patients with supraventricular tachycardia, 15 seconds of straining is as effective as 30 seconds.[8] The maneuver increases vagal tone and has its maximal effect on tachycardias *after* the release of the Valsalva, not while the patient is straining.[8]

In carotid artery massage, the clinician finds the bifurcation of one carotid artery, located just below the angle of the jaw, and massages or presses on it for 5 seconds.[8,9]

The Valsalva maneuver is preferred for two reasons: (1) It tends to be more efficacious, terminating supraventricular tachycardia 20% to 50% of the time, compared with only a 10% efficacy with carotid massage[8,10]; (2) in elderly patients with carotid artery disease, carotid artery massage risks causing strokes.[9,11–13]

b. Response of Regular Tachycardias to Vagal Maneuvers[9]

Transient slowing of the pulse during a vagal maneuver indicates sinus tachycardia. **Abrupt termination** of the tachycardia indicates paroxysmal supraventricular tachycardia. (This occurs with both nodal re-entry tachycardias and reciprocating tachycardias dependent on accessory pathways.) **Abrupt halving** of the rate may occur in atrial flutter. **No response** is unhelpful, being characteristic of ventricular tachycardia[14] but also occurring with every other regular tachycardia.[8,10]

2. Atrioventricular Dissociation

Any finding of atrioventricular dissociation in patients with regular tachycardia indicates that the rhythm is ventricular tachycardia. These findings include the *intermittent* appearance of cannon A waves in the neck veins, changing intensity of the first heart sound, and changing systolic blood pressure (usually detected with the blood pressure cuff).[15] In one study of patients with ventricular tachycardia, in which atrioventricular association or dissociation was determined by pacing, the finding of a changing S_1 increased the probability of atrioventricular dissociation (likelihood ratio [LR] = 24.4, EBM Box 15-1) and the *absence* of intermittent cannon A waves decreased the probability of atrioventricular dissociation (LR = 0.1).

Even so, these LRs are misleading because some patients with ventricular tachycardia lack atrioventricular dissociation and instead have 1:1 retrograde conduction or atrial fibrillation.[14] Given the serious consequences of misdiagnosing this arrhythmia, an ECG should always be obtained.

3. Flutter Waves in the Venous Pulse

In elderly patients with a ventricular pulse of 130 to 160 beats/min, the clinician should suspect atrial flutter with 2:1 conduction. In addition to performing vagal maneuvers, the clinician may see rapid, small undulations (with a rate of ~300/min) in the venous pulse, which are called flutter waves (or f waves) and which correspond to the wave of the same name on the ECG.[17]

EBM BOX 15-1
*Atrioventricular Dissociation and Ventricular Tachycardia**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Varying arterial pulse[16]	63	70	NS	NS
Intermittent cannon A waves, neck veins[16]	96	75	**3.8**	**0.1**
Changing intensity S_1[16]	58	98	**24.4**	0.4

*Diagnostic standards: For *atrioventricular dissociation*, ventricular-paced rhythm at a rate independent of the atrial rate.

†Definition of findings: For *varying arterial pulse*, varying amplitude of radial pulse or carotid pulse by palpation.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. NS, not significant.

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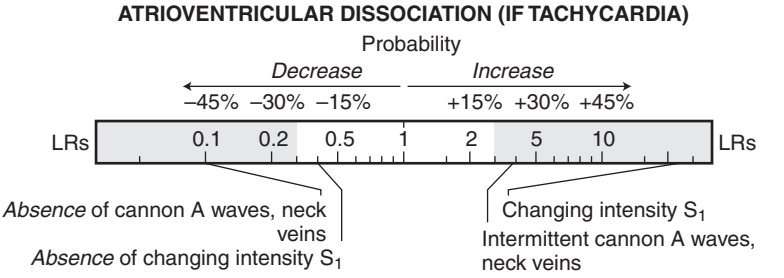


4. Sensation of Pounding in the Neck

In one study of 244 consecutive patients referred for electrophysiologic testing, all of whom had intermittent rapid palpitations, the history of feeling *rapid, regular* pounding in the neck during the palpitations discriminated atrioventricular nodal re-entrant tachycardia from other causes of tachycardia, with a sensitivity of 92%, specificity of 100%, positive LR of 350.7, and negative LR of 0.1.[18] The pounding occurs because both the carotid pulsation and cannon A waves arrive in the neck simultaneously. (Atrial and ventricular pulsations practically coincide in these patients.) Patients with reciprocating tachycardias using an accessory pathway, another common supraventricular tachycardia, lack these pounding sensations, because the atrial contraction is delayed until well after the ventricular contraction.

D. IRREGULAR RHYTHM THAT VARIES WITH RESPIRATION

This rhythm is **sinus arrhythmia,** an especially common and prominent arrhythmia of younger patients. The pulse characteristically quickens during inspiration and slows during exhalation (see Fig. 15-2).[19] The slowing during expiration is sometimes so conspicuous that it mimics the finding of a pause.

E. IRREGULARLY IRREGULAR RHYTHM

Irregularly irregular rhythm (chaotic rhythm) describes a cadence of ventricular and radial beats that is completely irregular and unpredictable. The diagnosis is usually atrial fibrillation. In studies of over 2000 patients, the finding of an *irregular* radial pulse increases the probability of atrial fibrillation (LR = 3.3, EBM Box 15-2), whereas the absence of this finding (i.e., the pulse is *regular*) decreases the probability of atrial fibrillation (LR = 0.1). In one of these studies, the finding of a "chaotic" pulse during only 20 seconds of observation markedly increased the probability of atrial fibrillation (LR = 24.1).

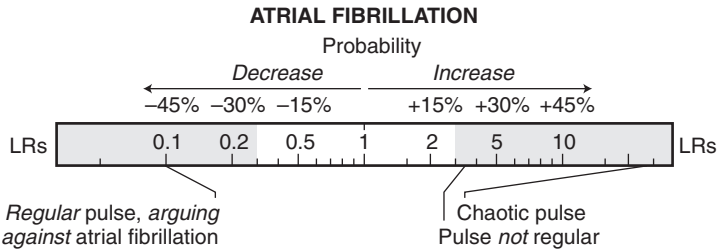
Frequent multifocal premature contractions may sometimes seem chaotic at the bedside, but two findings distinguish this rhythm from atrial fibrillation.

1. **Venous pulse.** In atrial fibrillation, the venous pulse is simple and consists of only one wave per cardiac cycle (i.e., there is no A wave and the x′ descent is diminished, revealing a sole y descent; see Chapter 34). In frequent premature contractions, in contrast, the venous pulse is complex and consists of intermittent cannon A waves superimposed on two venous movements per cardiac cycle.

EBM BOX 15-2
*Atrial Fibrillation**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Pulse not regular[20–22]	90-98	70-76	**3.3**	**0.1**
Chaotic pulse[22]	54	98	**24.1**	0.5

*Diagnostic standards: For *atrial fibrillation*, electrocardiogram.
†Definition of findings: For *chaotic pulse*, "frequent or continuous irregularity" during 20-second examination of the radial pulse.
‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.
Click here to access calculator.



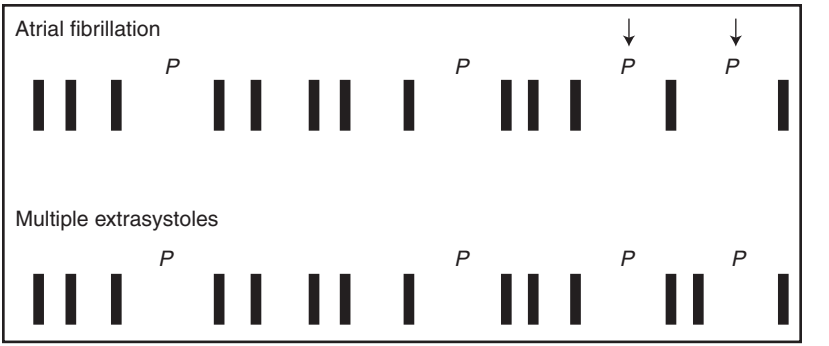


FIGURE 15-4 The chaotic rhythm. The irregularly irregular, or chaotic, rhythm may represent atrial fibrillation *(top)* or sinus rhythm with multiple extrasystoles *(bottom)*. "P" marks conspicuous pauses that appear in the cadence of *apical* heart tones. (Each bar depicts one cardiac cycle, or one *lub dup*.) In this example, the cadence of the two arrhythmias is identical until the end of the tracing: in atrial fibrillation, two pauses occur sequentially *(arrows)*, thus distinguishing it from the pauses of multiple extrasystoles, which are flanked by quick beats or beats of normal cadence. See text.

2. **Rhythm of ventricular pulse** (Fig. 15-4). In atrial fibrillation, the interval between ventricular beats is random, and it is quite common to have one pause followed by an even longer pause. In frequent premature contractions, this is impossible because the pause must be followed by another quick beat or the normal sinus interval. This difference in rhythm, which again focuses on the ventricular rhythm at the apex, not the radial pulse, is quite conspicuous once the clinician is aware of it.

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 16

Blood Pressure

I. INTRODUCTION

Systolic blood pressure is the maximal pressure within the artery during ventricular systole, **diastolic blood pressure** is the lowest pressure in the vessel just before the next systole, and **pulse pressure** is the difference between them. Pulse pressure may be normal, abnormally small (narrow), or abnormally large (wide; see the section on Abnormal Pulse Pressure). The mean arterial pressure can be estimated by (S + 2D)/3, where S is systolic blood pressure and D is diastolic blood pressure.[1]

The first person to measure blood pressure was Stephen Hales, an English clergyman of creative genius, who in 1708 directly connected the left crural artery of a horse to a 9-foot–tall glass manometer using brass tubes and a trachea of goose.[2,3] Vierordt of Germany introduced the indirect method of measuring blood pressure in 1855, based on the principle that blood pressure is equal to the amount of external pressure necessary to obliterate the distal pulse. Indirect measurements required cumbersome mechanical devices and were not widely accepted until 1896, when the Italian Riva-Rocci invented the blood pressure cuff.[2,3]

Blood pressure was the last of the four traditional vital signs to be routinely monitored in hospitalized patients. In 1901, after Harvey Cushing first brought the blood pressure cuff to America and encouraged its use in neurosurgical patients, most clinicians resisted using it because they believed palpation of the pulse revealed much more information, including its "fullness," "tension," "rate," "rhythm," "size," "force," and "duration."[4,5] Two events were responsible for clinicians eventually accepting the blood pressure cuff: (1) Korotkoff described his sounds in 1905, which allowed clinicians to easily measure systolic and diastolic blood pressure, and (2) Janeway published his book *Clinical Study of Blood Pressure* in 1907, which proved that monitoring blood pressure was clinically useful. (Janeway showed, for example, that the first sign of intestinal perforation or hemorrhage in typhoid fever was a falling blood pressure.[6]) By the time of the First World War, blood pressure was routinely recorded by most clinicians, along with the patient's pulse, respirations, and temperature.[5,7,8]

II. TECHNIQUE

A. RECOMMENDED METHOD OF MEASURING BLOOD PRESSURE

Published recommendations for measuring blood pressure[9,10] are based on the consensus opinion of expert committees who have reviewed all available scientific evidence. These recommendations, however, are designed to avoid misdiagnosis of *hyper*tension and may not be as relevant to clinicians using the blood pressure cuff to diagnose other abnormalities, such as hypotension or abnormalities of pulse contour (see later and Chapter 14).

The important elements of the correct technique are as follows:

1. The patient should sit in a chair with his or her back supported and should rest for at least 5 minutes before the blood pressure is measured.
2. The patient's arm should be at the level of the heart.
3. The length of the blood pressure cuff's bladder should encircle at least 80% of the arm's circumference.
4. The clinician should inflate the cuff to a pressure 20 to 30 mm Hg above systolic pressure, as first identified by palpation of the distal pulse (i.e., the pulse disappears when cuff pressure exceeds systolic pressure).
5. The pressure in the cuff should be released at a rate of 2 mm Hg per second.
6. The clinician should obtain at least two readings separated by at least 30 seconds and average them; if these differ by more than 5 mm Hg, additional readings are necessary.
7. The readings should be rounded off to the nearest 2 mm Hg.

These recommendations sometimes state that the bell of the stethoscope should be used, because Korotkoff sounds contain primarily low-frequency sound, although this technique is often inconvenient, and two studies have demonstrated that measurements with the bell and the diaphragm are the same.[11,12]

In some clinical scenarios, described in the section on Findings and Their Clinical Significance, additional measurements are necessary, including those of the legs or opposite arm, or measurements taken with the patient in different positions.

B. KOROTKOFF SOUNDS

1. Definition of Systolic and Diastolic Blood Pressure

As the cuff is slowly deflated from a point above systolic pressure, the first appearance of sound (Korotkoff phase 1) indicates systolic blood pressure.* Clinicians have debated for decades whether the muffling of sound

*There are five Korotkoff phases, numbered in order as they appear during deflation of the cuff. The initial tapping sound at systolic blood pressure is phase 1; a swishing murmur is phase 2; the reappearance of a softer tapping sound is phase 3; the disappearance of the tapping and appearance of a much softer murmur (muffling) is phase 4, and: the disappearance of all sound is phase 5.[2] Korotkoff described only four of these sounds (phases 1, 2, 3, and 5). Ettinger added the muffling point (phase 4) in 1907.[7,13,14] All five phases are audible with electronic stethoscopes in 40% of adults.[15]

(Korotkoff phase 4) or disappearance of sound (Korotkoff phase 5) better indicates diastolic blood pressure, although now all experts favor using phase 5 for the following reasons:

1. In most studies, phase 5 sounds correlate better with intra-arterial measurements of diastolic blood pressure.[16,17]
2. Many persons lack phase 4 sounds.[16,18]
3. Interobserver agreement is better for phase 5 sounds than phase 4 sounds.[16,18]
4. Most important, long-term studies showing that hypertension increases the risk of cardiovascular events and that treatment reduces this risk have used phase 5 sounds as the definition of diastolic blood pressure.[19–21]

2. Pathogenesis

Korotkoff sounds are produced underneath the *distal* half of the blood pressure cuff.[22] The sounds occur with cuff pressures between the systolic and diastolic blood pressure, because the underlying artery is collapsing completely and then reopening with each heartbeat. The artery collapses because cuff pressure exceeds diastolic pressure; it opens again with each beat because cuff pressure is less than systolic pressure. The sound represents the sudden deceleration of the rapidly opening arterial walls, which causes a snapping or tapping sound, just like the sail of a boat as it snaps when it suddenly tenses after tacking in the wind or like a handkerchief as it snaps when its ends are suddenly drawn taut.[22–26] Once cuff pressure falls below the diastolic blood pressure, the sound disappears because the vessel wall no longer collapses but instead gently ebbs and expands with each beat, being held open by diastolic pressure.

The genesis of the Korotkoff sounds, therefore, is similar to the genesis of other snapping or tapping sounds produced by the sudden deceleration of other biologic membranes, such as the normal first and second heart sounds or the femoral pistol shot sounds of aortic regurgitation (see Chapters 38 and 43).

C. MEASUREMENT USING PALPATION

Even before the discovery of Korotkoff sounds, clinicians used the blood pressure cuff to measure both systolic and diastolic blood pressure.[6] Systolic blood pressure was simply the amount of cuff pressure necessary to obliterate the pulse. Clinicians still use this technique to measure the pressure of patients with hypotension, when Korotkoff sounds are faint, or to determine whether the patient has an auscultatory gap (see later section).

To identify diastolic pressure, clinicians can use one of two methods. In the first method, the clinician applies light pressure to palpate the brachial artery just below the blood pressure cuff. As the cuff is deflated, the first appearance of a pulse indicates systolic blood pressure. As the cuff pressure falls more and approaches diastolic pressure, the pulsatile forces distending the artery distal to the cuff progressively grow, eventually causing a sudden shock to strike the clinician's fingers as the artery abruptly opens and then completely collapses with each beat. (This abrupt tapping sensation

is similar to the "water-hammer pulse" of aortic regurgitation.[23]) At the moment the cuff pressure falls below diastolic blood pressure, the shocking sensations disappear, being replaced by a much gentler pulse, because the underlying artery no longer collapses completely between beats. The cuff pressure at this "lower limit of maximal pulsation" indicates the diastolic blood pressure.[6]

A second method requires a rigid and tightly applied cuff, so that the arterial pulsations under the cuff are actually transmitted to the manometer. As the cuff pressure decreases, the mercury column of a mercury manometer or the indicator needle of an aneuroid manometer starts to bob with increasing amplitude, until the bobbing suddenly disappears at the moment that cuff pressure falls below diastolic pressure.[6] Many patients with tightly applied cuffs also experience a similar pounding sensation in the arm near the diastolic pressure, which abruptly disappears the moment that cuff pressure falls below diastolic blood pressure.

Measurements of systolic and diastolic blood pressure by palpation differ from readings by auscultation by only 6 to 8 mm Hg or less.[27,28]

D. POSTURAL VITAL SIGNS

When obtaining postural vital signs (i.e., comparison of measurements when the patient is supine with those when the patient is upright),[29] clinicians should wait 2 minutes before measuring the supine vital signs and 1 minute after standing before measuring the upright vital signs. These recommendations are based on the following observations:

1. Shorter periods of supine rest significantly reduce the sensitivity of postural vital signs in detecting blood loss.
2. After normal persons stand, the pulse change stabilizes after 45 to 60 seconds, and the blood pressure stabilizes after 1 to 2 minutes. Counting the heart rate first, beginning at 1 minute, allows more time for the blood pressure to stabilize.

Supine vital signs should always be compared with standing vital signs, because sitting instead of standing significantly reduces the clinician's ability to detect postural changes after blood loss.[30,31]

E. COMMON ERRORS

Biologic variation of blood pressure is common, and many studies show that blood pressure measurements vary with physical activity, smoking, caffeine ingestion, emotional state, temperature of the room, and season.[21,32,33] In addition, the blood pressure measurement may be inaccurate because of inappropriate technique, improper equipment, or other biases related to the observer.[14,33]

1. Wrong Cuff Size

In 1901, von Recklinghausen discovered that Riva-Rocci's original blood pressure cuff, whose bladder was about the size of a bicycle tire, was too narrow and often overestimated the true blood pressure, especially in larger arms.[7,34,35] Subsequent investigations have shown that both the bladder width and length affect the measurement, although if the bladder

TABLE 16-1 Blood Pressure Cuff Size and Error in Measurement*

	Arm Circumference		
Cuff Bladder Size	**28 cm or less**	**29-42 cm**	**43 cm or more**
Regular (12 × 23 cm)	Accurate	Overestimates SBP by 4-8 mm Hg DBP by 3-6 mm Hg	Overestimates SBP by 16-17 mm Hg DBP by 10-11 mm Hg
Large (15 × 33 cm)	Underestimates SBP by 2-3 mm Hg DBP by 1-2 mm Hg	Accurate	Overestimates SBP by 5-7 mm Hg DBP by 2-4 mm Hg
Thigh (18 × 36 cm)	Underestimates SBP by 5-7 mm Hg DBP by 1-3 mm Hg	Underestimates SBP by 5-7 mm Hg DBP by 2-4 mm Hg	Accurate

**Overestimation* means that hypertension may be diagnosed in someone with normal blood pressure; *underestimation* means that the blood pressure reading may be normal in someone who actually has high blood pressure. See text for further discussion.

DBP, diastolic blood pressure reading; SBP, systolic blood pressure reading.

Data from Maxwell MH, Waks AU, Schroth PC, et al. Error in blood-pressure measurement due to incorrect cuff size in obese patients. *Lancet*. 1982;2:33-35.[37]

encircles at least 80% of the arm's circumference, the effect of width is minimized.[17,34,36] The bladder of the standard cuff measures 12 × 23 cm and thus is appropriate only for arm circumferences up to 28 cm, which includes only 60% to 70% of the European adult population.[34]

Cuffs that are too short overestimate blood pressure because they transmit cuff pressure inefficiently to the underlying soft tissues. Much higher cuff pressures are then necessary to cause collapse of the artery, leading the clinician to misdiagnose hypertension when it is not present.[36] This error is greater the farther the *center* of the bladder is positioned from the brachial artery.[17]

The significance of the opposite error—underestimation of true blood pressure by using too large a cuff—is controversial, although most studies show that such an error is small. Table 16-1 presents the mean errors resulting from using cuffs too small or too large. These data are based on measurements of blood pressure in the same individual with three cuffs of different sizes, assuming that the most accurate measurement is the one made with the smallest cuff that can encircle 80% of the arm. The greatest errors, according to these data, occur from using too small a cuff; the risk of underestimating true pressure with too large a cuff is relatively small.

2. Auscultatory Gap

Up to 20% of elderly patients with hypertension have an **auscultatory gap,** which means that the phase 1 Korotkoff sounds normally appear at systolic pressure but then disappear for varying lengths of time before they reappear

above the diastolic pressure.[38] This auscultatory gap is important because inflation of the cuff only to the initial disappearance of sounds (i.e., the auscultatory gap) significantly underestimates the true systolic blood pressure. Because the distal pulse persists during the auscultatory gap, however, clinicians can avoid this mistake by palpating the systolic pressure before using the stethoscope.

The cause of the auscultatory gap remains a mystery. Patients with auscultatory gaps have twice as much arterial atherosclerotic plaque as those without a gap, suggesting perhaps that the gap is somehow related to arterial stiffness.[38] Venous congestion also seems to promote auscultatory gaps because slow cuff inflation (which increases venous congestion) sometimes makes auscultatory gaps appear and elevation of the arm before inflating the cuff makes them disappear.[35]

The auscultatory gap was discovered by Krylov in 1906, 1 year after Korotkoff's discovery.[13] In part, the discovery of the auscultatory gap was responsible for the initial reluctance of clinicians to adopt Korotkoff's method of indirect blood pressure measurement.[7]

3. Stethoscope Pressure Too Firm

Excessive pressure with the stethoscope artificially lowers the diastolic reading, sometimes by 10 mm Hg or more, although the systolic reading is usually unaffected.[39] This error occurs because the stethoscope pressure then contributes to the collapse of the underlying artery (i.e., the total tissue pressure around the artery represents the sum of both cuff and stethoscope pressure). If the clinician applies 10 mm Hg of stethoscope pressure to the arm of a patient whose intra-arterial diastolic pressure is 80 mm Hg, the diastolic reading will be 70 mm Hg (i.e., Korotkoff sounds disappear at a tissue pressure of 80 mm Hg = 70 mm Hg cuff pressure—the basis for the reading—and 10 mm Hg of stethoscope pressure).

4. Inappropriate Level of the Arm

The recommended position of the patient's elbow is the "level of the heart," which is usually regarded to be the fourth intercostal space at the sternum. If the patient's arm is instead 6 to 7 cm higher (e.g., at the level of the sternomanubrial junction), both the systolic and diastolic readings will be about 5 mm Hg lower. If the arm is 7 to 8 cm lower (e.g., at the level of the xiphosternal junction), the pressures will be about 6 mm Hg higher.[40]

These errors are completely explained by the hydrostatic effect. When the arm is at the lower position, for example, the measured pressure is the sum of the blood pressure in the artery plus the weight of a column of blood 8 cm high: i.e., 8 cm blood = (8 ÷ 13.6) × 1.06 = 0.6 cm or 6 mm Hg; 13.6 = density of mercury; 1.06 = density of blood.

5. Terminal Digit Preference

Clinicians often tend to round off blood pressure readings to the nearest 0, 5, or other preferred number, a bias called **terminal digit preference.**[32,33] Clinical studies minimize this and other observer biases by using

oscillometric devices, which measure oscillations of pressure instead of Korotkoff sounds and use computer programs to digitally display the blood pressure reading,[10] or by using a random zero sphygmomanometer, which blinds the clinician to the true reading.[21,41]

III. FINDINGS AND THEIR CLINICAL SIGNIFICANCE

A. HYPERTENSION

1. Essential Hypertension

Essential hypertension is defined as three or more blood pressure readings taken over three visits separated by weeks whose average exceeds 140/90 mm Hg (i.e., systolic blood pressure of 140 mm Hg and diastolic blood pressure of 90 mm Hg).[9] The threshold is lower for patients with diabetes or chronic kidney disease (i.e., hypertension = readings >130/80 mm Hg). Detecting essential hypertension is the reason that blood pressure should be measured in every person, even when asymptomatic, because the disorder is common and treatable and because treatment reduces cardiovascular morbidity and overall mortality rates.

2. Pseudohypertension and Osler Sign

Pseudohypertension describes the finding of elevated indirect measurements in persons who have normal intra-arterial pressure. The traditional explanation for pseudohypertension is that the artery under the cuff is so stiff and calcified it remains open long after the cuff pressure exceeds systolic blood pressure, continuing to produce Korotkoff sounds.

The diagnosis of pseudohypertension requires direct cannulation of the patient's artery, which is of course inappropriate and impractical during daily routine care. A single study from 1985 proposed that a simple physical finding, **Osler sign,** accurately identifies patients with pseudohypertension.[42] This sign is positive if the patient's radial or brachial artery distal to the cuff remains palpable after inflation of the cuff above systolic blood pressure.

Osler sign, however, has limited clinical value. It occurs commonly in elderly individuals, whether or not they have hypertension (11% over the age of 75 years and 44% over 85 years have a positive Osler sign).[43] Other investigators have shown that almost all patients with Osler sign do not have pseudohypertension but instead have direct measurements that exceed the indirect ones.[44,45]

Although pseudohypertension remains an important problem in blood pressure measurement of the legs, especially in diabetic patients with intermittent claudication (see Chapter 52), undue emphasis on pseudohypertension in the brachial artery misses the point that all clinical studies demonstrating the benefits of treating essential hypertension used the blood pressure cuff and indirect measurements, not intra-arterial measurements.

B. HYPOTENSION

In patients with acute illness, **hypotension** is ominous. It predicts death in patients hospitalized in the intensive care unit (ICU) (LR = 3.1; EBM Box 16-1) and in patients with bacteremia (LR = 4.9), pneumonia (LR = 7.6), and myocardial infarction (LR = 15.5). Presumably, it predicts mortality in many other acute disorders as well. The APACHE (Acute Physiology and Chronic Health Evaluation) scoring system, which predicts the risk of hospital mortality among patients in the ICU, assigns more points (and thus a higher risk) to severe hypotension than to any other vital sign or laboratory variable.[56]

Hypotension also predicts adverse outcomes besides death. In patients with myocardial infarction, a systolic blood pressure less than 80 mm Hg predicts a much higher incidence of congestive heart failure, ventricular tachycardia and fibrillation, and complete heart block.[54] In hospitalized patients, low blood pressure readings increase greatly the risk of serious

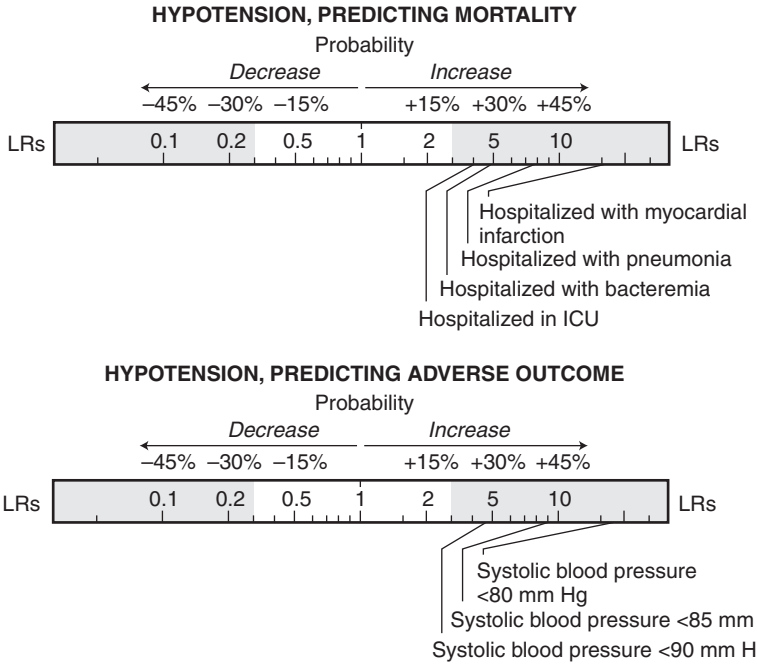
EBM BOX 16-1
*Hypotension and Prognosis**

Finding (Reference)	Sensitivity (%)	Specificity (%)	Likelihood Ratio† if Finding Is	
			Present	*Absent*
Predicting Hospital Mortality				
SYSTOLIC BLOOD PRESSURE <90 MM HG				
Patients in intensive care unit[46,47]	21-78	67-95	**3.1**	NS
Patients with bacteremia[48,49]	13-71	85-98	**4.9**	NS
Patients with pneumonia[50–53]	11-41	90-99	**7.6**	0.8
SYSTOLIC BLOOD PRESSURE ≤80 MM HG				
Patients with acute myocardial infarction[54]	32	98	**15.5**	0.7
Predicting Adverse Outcome in Hospitalized Patients[55]				
Systolic blood pressure ≤90 mm Hg	34	93	**4.7**	0.7
Systolic blood pressure ≤85 mm Hg	25	97	**9.0**	0.8
Systolic blood pressure ≤80 mm Hg	21	99	**16.7**	0.8

*Diagnostic standard: For *adverse outcome*, unexpected cardiac arrest, unplanned ICU admission, or unexpected death.

†Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. NS, not significant.

Click here to access calculator.



adverse outcomes in the next 24 hours (≤90 mm Hg, LR = 4.7; ≤85 mm Hg, LR = 9; ≤80 mm Hg, LR = 16.7; see EBM Box 16-1).*

C. DIFFERENCES IN PRESSURE BETWEEN THE ARMS

The average difference in systolic blood pressure between the two arms is 6 to 10 mm Hg.[57,58] Differences of 20 mm Hg or more are uncommon and usually indicate obstructed flow in the subclavian artery leading to the arm with the lower pressure. This is a significant finding in the following two clinical settings.

1. Subclavian Steal Syndrome

The finding of one weak radial pulse in a patient with symptoms of vertebrobasilar ischemia (episodic vertigo, visual complaints, hemiparesis, ataxia, or diplopia) suggests **subclavian steal syndrome.** In this syndrome, stenosis or occlusion of one subclavian artery proximal to the origin of the vertebral artery reduces the pressure distal to the obstruction, which causes the flow in the vertebral artery to reverse directions: Instead of traveling

*Although two thirds of these patients with adverse outcomes were transferred to ICU care (which is circular reasoning because hypotension is likely the principal reason for transfer), the other one third were patients who suffered *unexpected cardiac arrest* or *unexpected death* in the general medicine ward.

normally up the vertebral artery to perfuse the brain, blood flow courses downward to perfuse the arm (i.e., the arm "steals" blood from the posterior circulation).*[59] Ninety-four percent of patients with subclavian steal syndrome have a systolic blood pressure that is 20 mm Hg or more lower on the affected side compared with the opposite arm. (The mean difference between the arms is 45 mm Hg in affected patients.[61]) Most patients have an ipsilateral radial pulse that is diminished or absent and a systolic bruit over the ipsilateral subclavian artery.[61] The left side is affected in 70% and the right side in 30% of patients.[61]

2. Aortic Dissection

The finding of a difference in blood pressure between the two arms in a patient with acute chest pain suggests aortic dissection. EBM Box 16-2 presents the accuracy of physical examination in over 400 patients presenting to emergency departments with acute chest or upper back pain suspicious for aortic dissection. In these studies, two findings increased the probability of aortic dissection: focal neurologic signs (from obstruction of cranial or spinal arteries, LR = 33.4) and the presence of a pulse deficit (i.e., absent extremity or carotid pulse, LR = 6). Mediastinal or aortic widening on chest radiography also increased the probability of dissection, although only modestly (LR = 2); the *absence* of mediastinal widening *decreased* the probability (LR = 0.3).[62,64,65]

In these studies, the murmur of aortic regurgitation was diagnostically unhelpful, possibly because of the highly selected nature of enrolled patients: these patients represented only 0.3% of patients with chest or back pain evaluated in these centers[64]; one third had the murmur of aortic regurgitation, and one half had the diagnosis of dissection eventually confirmed.

Von Kodolitsch and others[64] have identified three independent predictors of aortic dissection in patients with acute chest pain:

1. Pain that is tearing or ripping.
2. Pulse deficits or blood pressure differentials (>20 mm Hg), or both (see footnote to EBM Box 16-2 for definition).
3. Mediastinal or aortic widening on chest radiography.

The absence of all three predictors *decreases* the probability of dissection (LR = 0.1; see EBM Box 16-2); the presence of two predictors increases the probability of dissection (LR = 5.3), and the presence of all three predictors is pathognomonic for dissection (LR = 65.8).

Rare patients with aortic dissection present with the physical findings of pulsatile sternoclavicular joints[66] or unilateral femoral pistol shot sounds (see Chapter 43).[67]

In patients with established aortic dissection, three findings increase the probability that the dissection involves the proximal aorta (i.e., that it is a type A dissection, not a type B dissection): systolic blood pressure less than 100 mm Hg (LR = 5), murmur of aortic regurgitation (LR = 5), and a pulse

*An excellent online video of vertebral retrograde flow in a patient with subclavian stenosis is available in the supplementary material to Aithal and Ulrich.[60]

EBM BOX 16-2
*Aortic Dissection**

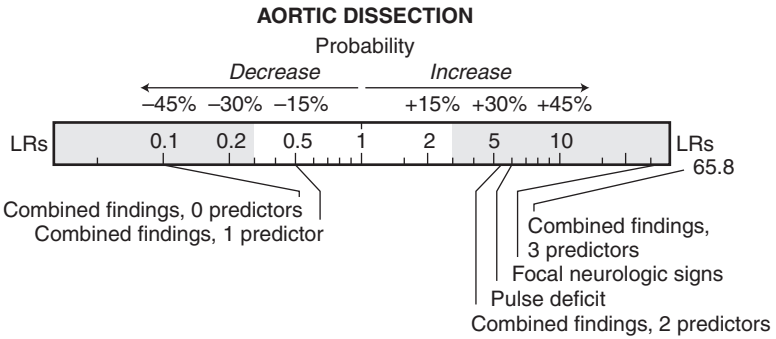
Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Individual Findings				
Pulse deficit[62–64]	12-49	82-99	**6.0**	NS
Aortic regurgitation murmur[62–65]	15-49	45-95	NS	NS
Focal neurologic signs[64]	14	100	**33.4**	NS
Combined Findings[64]				
0 predictors	4	47	**0.1**	—
1 predictor	20	—	0.5	—
2 predictors	49	—	**5.3**	—
3 predictors	27	100	**65.8**	—

*Diagnostic standard: For *aortic dissection*, transesophageal echocardiography,[62,65] aortography,[63] or any of a variety of tests (i.e., computed tomography, magnetic resonance imaging, transesophageal echocardiography, or digital angiography).[64]

†Definition of findings: For *pulse deficit*, absent extremity or carotid pulse[62,63] or difference in blood pressure in the arms of 20 mm Hg or absent extremity or carotid pulse, or both[64]; for *combined findings*, see text.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. NS, not significant.

Click here to access calculator.



deficit (LR = 2.3).[62,63,66,68,69] In patients with acute type A dissection, pulse deficits are associated with increased hospital mortality rates.[70]

D. DIFFERENCES IN PRESSURE BETWEEN ARMS AND LEGS

This finding is valuable in two clinical settings.

1. Chronic Ischemia of the Lower Extremities

Chapter 52 describes calculation of the ankle–arm index, which is the principal bedside tool used in patients with intermittent claudication.

2. Coarctation of the Aorta

In young patients with hypertension, the finding of an unobtainable blood pressure in the legs or a blood pressure that is much lower in the legs than the arms suggests the diagnosis of coarctation of the aorta.[71,72] These patients also have hypertension of the arms (96% have a blood pressure >140/90 mm Hg), femoral pulses that are absent or diminished and delayed (100%), augmented carotid pulsations, various murmurs (usually a systolic murmur at the sternal border and a continuous murmur posteriorly over the upper spine), and visible collateral arteries (usually around the scapula, intercostal spaces, or axilla).[71,72]

During simultaneous palpation of the femoral and radial arteries of healthy persons, it is impossible to tell which comes first. In patients with coarctation, however, the femoral pulse is delayed, owing both to delay in arrival at the legs and to more rapid than normal conduction of the wave to the arms.[73]

In one study of 1206 children with unexplained heart murmurs, clinicians correctly diagnosed coarctation of the aorta in 18 of 22 affected patients. (In this study, the overall accuracy for detecting coarctation by bedside examination—presumably using arm-to-leg blood pressure or pulse discrepancies—was sensitivity of 82%, specificity of 100%, positive LR = 242, and negative LR = 0.2.[74])

E. ABNORMAL PULSE CONTOUR

The three abnormalities of pulse contour—pulsus paradoxus, pulsus alternans, and pulsus bisferiens—are easily detectable using the blood pressure cuff (see Chapter 14).

F. ABNORMAL PULSE PRESSURE

1. Abnormally Small Pulse Pressure

Because the pulse pressure depends on the stroke volume, clinicians have tried for decades to use it as a way to quantify cardiac output. This relationship has been validated in one setting, in patients with known left ventricular dysfunction: In these patients, the finding of a proportional pulse pressure (i.e., the pulse pressure divided by the systolic pressure) of less than 0.25 detects a cardiac index of less than 2.2 L/min/m^2 with a sensitivity of 70% to 91%, specificity of 83% to 93%, positive LR = 6.9, and negative LR = 0.2.[75,76]

In contrast to conventional teachings, many patients with significant aortic stenosis have a normal pulse pressure (see Chapter 42).[77] Chapter 68 discusses how to use changes in pulse pressure after passive leg elevation to predict volume responsiveness in critically ill patients.

2. Abnormally Large Pulse Pressure

In patients with the murmur of aortic insufficiency, a pulse pressure of 80 mm Hg or higher increases the probability that the regurgitation is moderate or severe, with a sensitivity of 57%, specificity of 95%, and positive LR = 10.9.[78]

G. ORTHOSTATIC HYPOTENSION

When a person stands, 350 to 600 mL of blood shifts to the lower body. Normally, the blood pressure remains relatively stable during this shift because of compensatory increases in cardiac output, heart rate, and systemic vascular resistance, and transfer of blood from the pulmonary circulation to the systemic side.[29] Orthostatic hypotension, usually defined as a fall in systolic blood pressure of 20 mm Hg or more when the patient stands from the supine position, may occur if (1) compensatory mechanisms fail (i.e., autonomic insufficiency) or (2) the patient has lost excessive amounts of fluid from the vascular space (e.g., acute blood loss).

1. Postural Vital Signs in Healthy Persons

As normovolemic persons stand up from the supine position, the pulse increases on average by 10.9 beats/min, systolic blood pressure decreases by 3.5 mm Hg, and diastolic blood pressure increases by 5.2 mm Hg.[29] Postural hypotension, defined as a decrement in systolic blood pressure of 20 mm Hg or more, occurs in 10% of normovolemic individuals younger than 65 years and in 11% to 30% older than 65 years.[29] As persons age, the postural pulse increment diminishes ($r = -0.50$; $p < .02$); this phenomenon and the observation that older persons have more postural hypotension suggest that autonomic reflexes decline as persons age.

2. Vital Signs and Hypovolemia

Table 16-2 presents the vital signs from normal persons before and after phlebotomy of 450 to 630 mL (moderate blood loss) or 630 to 1150 mL (large blood loss).* Chapter 10 reviews the other physical findings of hypovolemia.

a. Postural Change in Pulse

Table 16-2 shows that the most valuable observation is *either* a postural pulse increment of 30/min or more *or* the inability of the patient to stand long enough for vital signs because of severe dizziness. Most persons have one or both of these findings after large amounts of blood loss (sensitivity = 98%), but only one of five persons develops either of them after moderate blood loss (sensitivity ranges from 7% to 57%; see Table 16-2).[29] These findings are durable after hemorrhage, lasting at least 12 to 72 hours if intravenous fluids are withheld.[31,87,88]

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*Calculating likelihood ratios (LRs) for these data is not appropriate, because "acute blood loss" has endless gradations of severity, many of which are important to the clinician. For example, the LR of physical signs for moderate blood loss are of little use to the clinician who, when taking care of the patient with melena, regards blood loss of 400 mL ("disease-negative" according to the LR) to be as significant as a loss of 500 mL ("disease-positive"). Table 16-2 instead just illustrates the general trends of vital signs with increasing amounts of blood loss.

TABLE 16-2 Vital Signs and Acute Blood Loss*

Physical Finding (Reference)†	Moderate Blood Loss, Sensitivity (%)	Large Blood Loss, Sensitivity (%)	Specificity (%)
Postural pulse increment ≥30/min or severe postural dizziness[30,79–81]	7-57	98	99
Postural hypotension (≥20 mm Hg decrease in SBP)[79,80]	9	—	90-98
Supine tachycardia (pulse >100/min)[31,81–84]	1	10	99
Supine hypotension (SBP <95 mm Hg)[31,82,83,85,86]	13	31	98

*Data obtained from 568 normal persons, mostly young and healthy, after "moderate" blood loss (phlebotomy of 450 to 630 mL) or "large" blood loss (phlebotomy of 630 to 1150 mL). "Specificity" from same patients when euvolemic, before blood loss. Results are overall mean frequency or, if statistically heterogeneous, the range of values.

†Definition of finding: For *postural,* the difference between supine and standing measurements; for *postural hypotension (≥20 mm Hg decrease in SBP)*, the finding applies only to patients able to stand without severe dizziness.

SBP, systolic blood pressure.

Adapted from McGee S, Abernethy WB, Simel DL. Is this patient hypovolemic? *JAMA.* 1999;281:1022-1029.[29]

b. Postural Change in Blood Pressure

After excluding those patients unable to stand for vital signs (which includes almost all patients after large amounts of blood loss), the finding of postural hypotension (≥20 mm Hg postural decrement in systolic blood pressure) has no proven value, being found just as often in patients before blood loss as after it. For example, in persons younger than 65 years, postural hypotension is found in 8% before moderate blood loss and 9% after blood loss. For those 65 years or older, postural hypotension is detected in 11% to 30% before blood loss and about 25% after blood loss.[29,80]

Obviously, because severe dizziness with standing is a valuable finding, but postural hypotension of 20 mm Hg is not, there must be an intermediate level of postural fall in pressure (e.g., 30 mm Hg, 40 mm Hg, or another value), not yet identified, that better discriminates between patients with and without blood loss.

c. Supine Pulse and Supine Blood Pressure

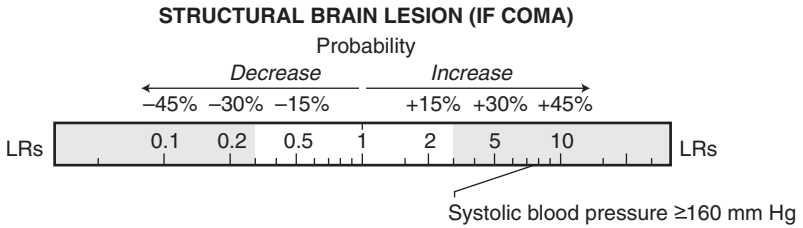
In patients with suspected blood loss, both supine tachycardia and supine hypotension are specific indicators of significant blood loss, although both are infrequent. After moderate blood loss, 1% have tachycardia in the supine position and only 13% have supine hypotension; after a large blood loss, only 10% have tachycardia and 31% have hypotension.

Sinus bradycardia, in contrast, is a common arrhythmia after blood loss and frequently precedes the drop in blood pressure that causes patients to faint.[29]

EBM BOX 16-3
Systolic Blood Pressure and Impaired Consciousness

Finding (Reference)	Sensitivity (%)	Specificity (%)	Likelihood Ratio* if Finding Is	
			Present	*Absent*
Detecting Structural Brain Lesion				
Systolic blood pressure ≥160 mm Hg[89,90]	37-58	93-94	**7.3**	0.6

*Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.
Click here to access calculator.



H. BLOOD PRESSURE AND IMPAIRED CONSCIOUSNESS

Patients with impaired consciousness may have either a structural intracranial lesion (e.g., stroke or brain tumors) or metabolic encephalopathy (e.g., hepatic encephalopathy, diabetic coma, drug intoxication, or sepsis). Patients with structural lesions tend to have higher blood pressures (from reflex responses to increases in intracranial pressure—the Cushing reflex—or from the etiologic association of hypertension and stroke) than patients with metabolic encephalopathy (whose severe comorbidities often are associated with lower blood pressure). In two studies of consecutive patients with impaired consciousness (i.e., Glasgow coma scale score <15) but no history of head trauma, a systolic blood pressure of 160 mm Hg or higher significantly increased the probability of a structural lesion (LR = 7.3; EBM Box 16-3).

I. CAPILLARY FRAGILITY TEST (RUMPEL-LEEDE TEST)

Traditionally, the blood pressure cuff also was used to test capillary fragility, although measurements of blood pressure were not part of the test. Capillary fragility tests were designed to detect abnormally weakened capillary walls in the skin that would burst more easily when distended, resulting in the appearance of high numbers of petechiae. The diseases associated with capillary fragility were legion, ranging from coagulopathies, vitamin deficiencies (e.g., scurvy), infectious diseases (e.g., scarlet fever), and endocrine disorders (e.g., hyperthyroidism) to dermatologic disorders (e.g., Osler-Weber-Rendu syndrome).[91] Both negative and positive pressure methods were used. The negative pressure technique applied suction

to a defined area of the skin, a technique whose undoing was the eventual demonstration that the number of resulting petechiae depended not only on the age of patient but also on the time of day, season, and psychic influences.[92] Positive pressure methods, introduced at the turn of the century by Drs. Rumpel and Leede, consisted of raising the venous pressure by placing a tourniquet or blood pressure cuff around the arm and counting petechiae that subsequently developed in a defined area distally. This test was eventually standardized,[92] but interest fell after the introduction of better diagnostic tests for coagulation and the other associated disorders. More recently, increased capillary fragility was believed to represent a sign of diabetic retinopathy,[93] but this was soon disproven.[94]

Nonetheless, a variation of the Rumpel-Leede test (called the **tourniquet test***) remains important in the developing world as a diagnostic test for dengue fever and its complications. In one study of 905 Vietnamese patients presenting with presumed dengue infection, a positive tourniquet test detected serologically confirmed dengue infection with a sensitivity of 42%, specificity of 94%, and positive LR of 7.4.[95]

The references for this chapter can be found on www.expertconsult.com.

*In this study, the blood pressure cuff was held midway between systolic and diastolic blood pressure for 5 minutes, and the clinician counted the number of petechiae that formed in a 2.5-cm^2 circle just distal to the antecubital fossa. A test is positive when 20 petechiae or more are present.

CHAPTER 17

Temperature

I. INTRODUCTION

Fever is a fundamental sign of almost all infectious diseases and many noninfectious disorders. Clinicians began to monitor the temperature of febrile patients in the 1850s and 1860s, after Traube introduced the thermometer to hospital wards and Wunderlich published an analysis based on observation of an estimated 20,000 subjects that convinced clinicians of the value of graphing temperature over time.[1–3] These temperature charts, showing the first vital sign to be routinely recorded in hospitalized patients, were originally named **Wunderlich curves.**[4]

II. TECHNIQUE

A. SITE OF MEASUREMENT

Thermometers are used to measure the temperature of the patient's oral cavity, rectum, axilla, tympanic membrane, or forehead (i.e., temporal artery). The time-honored mercury thermometer is being phased out (because of environmental concerns), replaced by electronic thermometers with thermistors (oral, rectal, and axillary measurements) and infrared thermometers (tympanic or forehead measurements). These instruments provide more rapid results than the traditional mercury thermometer.[5]

Normal body temperature varies widely, depending in part on the site measured. Rectal readings on average are the highest and axillary ones the lowest (Fig. 17-1). Tympanic measurements are potentially ideal because they are rapid, convenient, and theoretically best reflect core temperature (i.e., the core temperature is the temperature of the hypothalamus, which is supplied by the same artery as the tympanic membrane),[7] but some studies question their precision, demonstrating poor correlation between the right and left tympanic temperatures in the same person, measured only minutes apart ($r = 0.57$).[8] There is very little information on normal forehead measurements in adults.

B. VARIABLES AFFECTING THE TEMPERATURE MEASUREMENT

1. Eating and Smoking[9–12]

The *oral* temperature measurement increases about 0.3° C after sustained chewing and stays elevated for up to 20 minutes, probably because of increased blood flow to the muscles of mastication. Drinking hot liquids

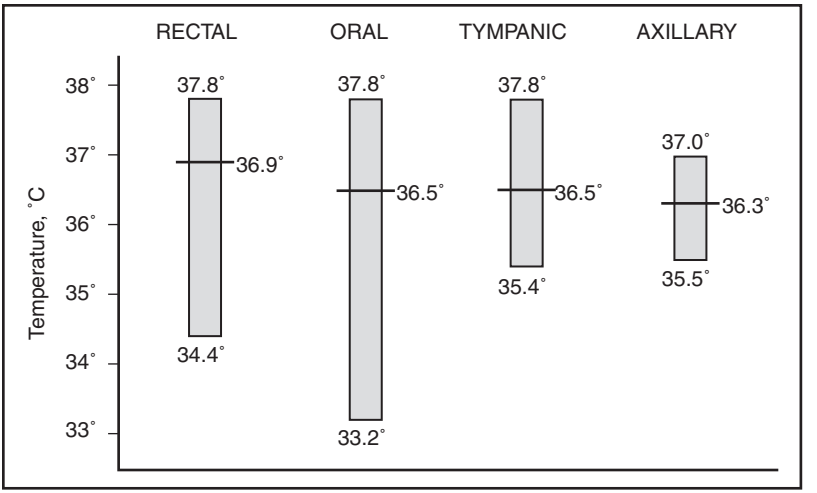


FIGURE 17-1 Normal body temperature. The figure illustrates the average value *(black horizontal line)* and range of values *(gray bar)* from over 2500 normal adults, as measured at different sites.[6]

also increases oral readings about 0.6° to 0.9° C, for up to 15 to 25 minutes, and smoking a cigarette increases oral readings about 0.2° C for 30 minutes. Drinking ice water causes the oral reading to fall 0.2° to 1.2° C, a reduction lasting about 10 to 15 minutes.

2. Tachypnea

Tachypnea reduces the *oral* temperature reading about 0.5° C for every 10 breaths/min increase in the respiratory rate.[13,14] This phenomenon probably explains why marathon runners, at the end of their race, often have a large discrepancy between normal oral temperatures and high rectal temperatures.[15]

In contrast, administration of oxygen by nasal cannula does not affect oral temperature.[16]

3. Cerumen

Cerumen lowers *tympanic* temperature readings, simply because it obstructs radiation of heat from the tympanic membrane.[10]

4. Hemiparesis

In patients with hemiparesis, *axillary* temperature readings are about 0.5° C lower on the weak side compared with the healthy side. The discrepancy between the two sides correlates poorly with the severity of the patient's weakness, suggesting that it is not due to difficulty in holding the thermometer under the arm but instead to other factors, such as differences in cutaneous blood flow between the two sides.[17]

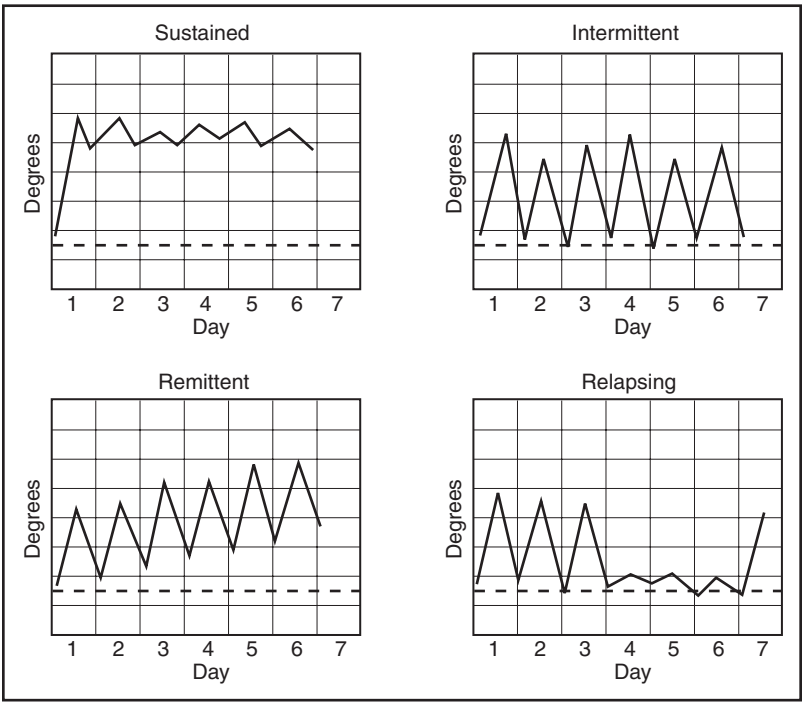


FIGURE 17-2 Fever patterns. The four basic fever patterns are sustained, intermittent, remittent, and relapsing. The *dashed line* in each chart depicts normal temperature. See text for definitions and clinical significance.

III. FINDINGS

A. NORMAL TEMPERATURE AND FEVER

In healthy persons, the mean oral temperature is 36.5° C (97.7° F) (see Fig. 17-1), a value slightly lower than Wunderlich's original estimate of 37° C (98.6° F), which in turn had been established using foot-long axillary thermometers that may have been calibrated higher than the thermometers used today.[1] The temperature is usually lowest at 6 AM and highest at 4 PM to 6 PM (a variation called diurnal variation).[18] One investigator has defined fever as the 99th percentile of maximum temperatures in healthy persons, or an *oral* temperature greater than 37.7° C (99.9° F).[18] Inspection of Figure 17-1 demonstrates that measurement of a temperature of more than 37.8° C (>100° F) *at any site* is abnormally high and indicative of fever.

B. FEVER PATTERNS

In the early days of clinical thermometry, clinicians observed that prolonged fevers could be categorized into one of four fever patterns—sustained, intermittent, remittent, or relapsing (Fig. 17-2).[19–21]

1. **Sustained fever.** In this pattern, the fever varies little from day to day. (The modern definition is variation ≤0.3° C [≤0.5° F] each day.)
2. **Intermittent fever.** In this pattern, the temperature returns to normal between exacerbations. If the exacerbations occur daily, the fever is quotidian; if they occur every 48 hours, it is tertian (i.e., they appear again on the third day); and if they occur every 72 hours, it is quartan (i.e., they appear again on the fourth day).
3. **Remittent fevers.** Remittent fevers vary at least 0.3° C (0.5° F) each day but do not return to normal. **Hectic fevers** are intermittent or remittent fevers with wide swings in temperature, usually greater than 1.4° C (2.5° F) each day.
4. **Relapsing fevers.** These fevers are characterized by periods of fever lasting days interspersed by equally long afebrile periods.

Each of these patterns was associated with prototypic diseases: for sustained fever—lobar pneumonia (lasting 7 days until it disappeared abruptly by "crisis" or gradually by "lysis"); for intermittent fever—malarial infection; for remittent fever—typhoid fever (causing several days of ascending remittent fever, whose curve resembles climbing steps, before becoming sustained); for hectic fever—chronic tuberculosis or pyogenic abscesses; and for relapsing fever—relapse of a previous infection (e.g., typhoid fever). Other causes of relapsing fever are the Pel-Ebstein fever of Hodgkin disease,[22] rat-bite fever (*Spirillum minus* or *Streptobacillus moniliformis*),[23] and *Borrelia* infections.[24]

Despite these etiologic associations, early clinicians recognized that the diagnostic significance of fever patterns was limited.[25] Instead, they used these labels more often to communicate a specific observation at the bedside rather than imply a specific diagnosis, much like we use the words "systolic murmur" or "lung crackle" today.

C. ASSOCIATED FINDINGS

1. Focal Findings

Over 80% of patients with bacterial infections have specific focal signs or symptoms that point the clinician to the correct diagnosis.[26] There are countless focal signs associated with febrile illness (e.g., the tender swelling of an abscess or the diastolic murmur of endocarditis), which are reviewed in detail in infectious diseases textbooks. One potentially misleading focal sign, however, is jaundice. Although fever and jaundice are often due to hepatitis or cholangitis, jaundice is also a nonspecific complication of bacterial infection distant to the liver, occurring in 1% of all bacteremias.[27,28] This "reactive hepatopathy of bacteremia" was recognized over a century ago by Osler, who wrote that jaundice appeared in pneumococcal pneumonia with curious irregularity in different outbreaks.[25]

2. Relative Bradycardia

Relative bradycardia, a traditional sign of intracellular bacterial infections (e.g., typhoid fever), refers to a pulse rate that is inappropriately slow for the patient's temperature. One definition is a pulse rate that is lower than the 95% confidence limit for the patient's temperature, which can be

estimated by multiplying the patient temperature in degrees Celsius times 10 and then subtracting 323.[29] For example, if the patient's temperature is 39° C, relative bradycardia would refer to pulse rates below 67/min (i.e., 390 − 323).*

3. Anhidrosis

Classically, patients with heat stroke have "bone-dry skin," but most modern studies show that anhidrosis appears very late in the course and has a sensitivity of only 3% to 60%.[30–32] In contrast, 91% of patients with heat stroke have significant pyrexia (exceeding 40° C), and 100% have abnormal mental status.

4. Muscle Rigidity

Muscle rigidity suggests the diagnosis of neuroleptic malignant syndrome (a febrile complication from dopamine antagonists) or serotonin syndrome (from proserotonergic drugs).[33,34]

IV. CLINICAL SIGNIFICANCE

A. DETECTION OF FEVER

Two findings modestly increase the probability of fever: the patient's subjective report of fever and the clinician's perception that the patient's skin is abnormally warm (likelihood ratios [LRs] = 2.8 to 2.9; EBM Box 17-1). When either of these findings is absent, the probability of fever decreases (LR = 0.3).

B. PREDICTORS OF BACTEREMIA IN FEBRILE PATIENTS

In patients hospitalized with fever, 8% to 21% will have documented bacteremia,[39–47] a finding associated with an increased hospital mortality rate.[48] Of all the bedside findings that help diagnose bacteremia, the most important are the patient's underlying disorders, in particular the presence of renal failure (LR = 4.6; EBM Box 17-2), hospitalization for trauma (LR = 3), and poor functional status (i.e., bedridden or requiring attendance, LR = 3.6).† A few physical findings also modestly increase the probability of bacteremia: presence of an indwelling urinary catheter (LR = 2.4), hypotension (LR = 2.2), or presence of a central venous catheter (LR = 1.9). The only finding significantly decreasing the probability of bacteremia is age under 50 years (LR = 0.3).

In nine studies of over 5500 patients with fever, the presence of "chills" modestly increased the probability of bacteremia (sensitivity

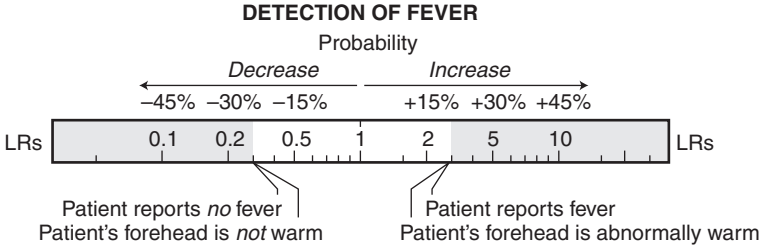
*This formula combines separate formulas for women (<11 × T° C − 359) and men (<10.2 × T° C − 333) provided in reference 29, which in turn were based on observations of 700 febrile patients.

†For comparison, the LRs of these findings are superior to those for traditional laboratory signs of bacteremia, such as leukocytosis and bandemia. In detecting bacteremia, a white blood cell (WBC) count of more than 15,000/μL has an LR of only 1.6,[26,40,47,53] whereas a band count of more than 1500/μL has an LR of 2.6.[26,40,43]

EBM BOX 17-1
*Detection of Fever**

Finding (Reference)	Sensitivity (%)	Specificity (%)	Likelihood Ratio† if Finding Is	
			Present	*Absent*
Patient's report of fever[35,36]	80-83	55-83	2.9	**0.3**
Patient's forehead abnormally warm[36–38]	67-85	72-74	2.8	**0.3**

*Diagnostic standard: For *fever*, measured axillary temperature >37.5° C,[72,38] oral temperature >38° C,[35] or rectal temperature >38.1° C.[37]
†Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. *Click here to access calculator.*



EBM BOX 17-2
*Detection of Bacteremia in Febrile Patients**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Risk Factors				
Age 50 years or more[26,40]	89-95	32-33	1.4	**0.3**
Renal failure[41]	19-28	95	**4.6**	0.8
Hospitalization for trauma[39,49]	12-63	79-98	**3.0**	NS
Intravenous drug use[44]	7	98	2.9	NS
Previous stroke[41]	17	94	2.8	NS
Diabetes mellitus[26,40,41,43,47,50]	17-38	82-90	1.6	NS
Poor functional performance[41]	48-61	83-87	**3.6**	0.6
Rapidly fatal disease (<1 mo)[44,46]	2-30	88-99	2.7	NS

EBM BOX 17-2
Detection of Bacteremia in Febrile Patients—cont'd

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Physical Examination				
INDWELLING LINES AND CATHETERS				
Indwelling urinary catheter present[40,41,43,47]	22-38	83-95	2.4	NS
Central intravenous line present[39,51,52]	8-24	90-96	1.9	NS
VITAL SIGNS				
Temperature ≥38.5° C[43,52]	62-87	27-53	1.2	0.7
Tachycardia[39,47,52]	61-73	42-56	1.3	0.7
Respiratory rate >20/min[47]	65	30	NS	NS
Hypotension[43,44,47,52]	7-38	82-99	2.2	NS
OTHER FINDINGS				
Acute abdomen[44,46,51]	2-20	90-100	1.7	NS
Confusion or depressed sensorium[39,43,47,50,51]	5-52	68-96	1.5	NS

*Diagnostic standard: For *bacteremia*, true bacteremia (not contamination), as determined by number of positive cultures, organism type, and results of other cultures.

†Definition of findings: For *renal failure*, serum creatinine >2 mg/dL; for *rapidly fatal disease*, >50% probability of fatality within 1 month (e.g., relapsed leukemia without treatment, hepatorenal syndrome); for *poor functional status*, see text; for *tachycardia*, pulse rate >90 beats/min[39] or >100 beats/min[47]; for *hypotension*, systolic blood pressure <100 mm Hg,[47] <90 mm Hg,[44,52] or "shock."[43]

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

NS, not significant.

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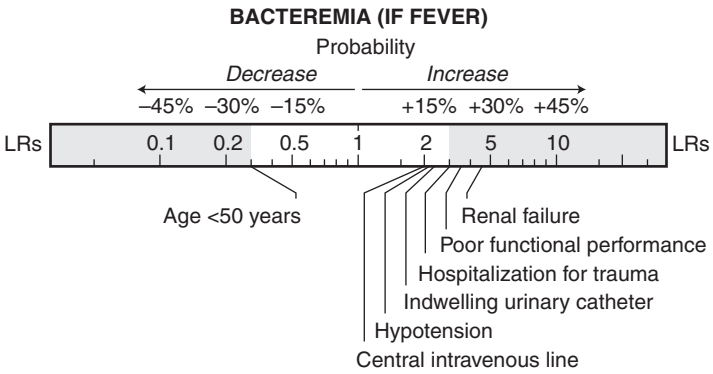


24% to 75%; specificity 64% to 88%; positive LR = 2, negative LR = 0.7).[41,43,44,46,47,50,51,54,55] If chills are instead prospectively defined as mild, moderate, or shaking, the finding of shaking chills is an accurate sign of bacteremia (sensitivity 45%, specificity 90%, positive LR = 4.7).[56] The "toxic appearance" fails to discriminate serious infection from trivial illness.[26,57]

C. EXTREME PYREXIA AND HYPOTHERMIA

Extreme pyrexia (i.e., temperature exceeding 41.1° C [106° F]) has diagnostic significance because the cause is usually gram-negative bacteremia or problems with temperature regulation (i.e., heat stroke, intracranial hemorrhage, severe burns).[32]

In a wide variety of disorders, the finding of a very high or low temperature indicates a worse prognosis.[58,59] For example, temperatures over 39° C are associated with an increased risk of death in patients with pontine hemorrhage (LR = 23.7; EBM Box 17-3). Very low temperatures are associated with an increased risk of death in patients hospitalized with congestive heart failure (LR = 6.7), pneumonia (LR = 3.5), or bacteremia (LR = 3.3).

D. FEVER PATTERNS

Most fevers today, whether infectious or noninfectious in origin, are intermittent or remittent and lack any other characteristic feature.[65,66] Antibiotic medications have changed many traditional fever patterns. For example, the fever of lobar pneumonia, which in the preantibiotic era was sustained and lasted 7 days, now lasts only 2 to 3 days.[67,68] The double quotidian fever pattern (i.e., two daily fever spikes), a feature of gonococcal endocarditis present in 50% of cases during the preantibiotic era, is consistently absent in reported cases from the modern era.[69] The characteristic tertian or quartan intermittent fever of malaria infection also is uncommon today because most patients are treated before the characteristic synchronization of the malaria cycle.[70]

Nonetheless, although traditional fever patterns may be less common, they still have significance. In tropical countries, the presence of the "stepladder" remittent pattern of fever is highly specific for the diagnosis of typhoid fever (LR = 177.4).[71] In addition, among travelers with malarial infection who reported a tertian pattern, most were infected with *Plasmodium vivax* (traditionally the most common cause of this pattern).[72]

Moreover, the antibiotic era has given fever patterns a new significance, because once antibiotics have been started, the finding of an unusually prolonged fever is an important sign indicating either that the diagnosis of infection was incorrect (e.g., the patient instead has a connective tissue disorder or neoplasm) or that the patient has one of several complications, such as resistant organisms, superinfection, drug fever, or an abscess requiring surgical drainage.

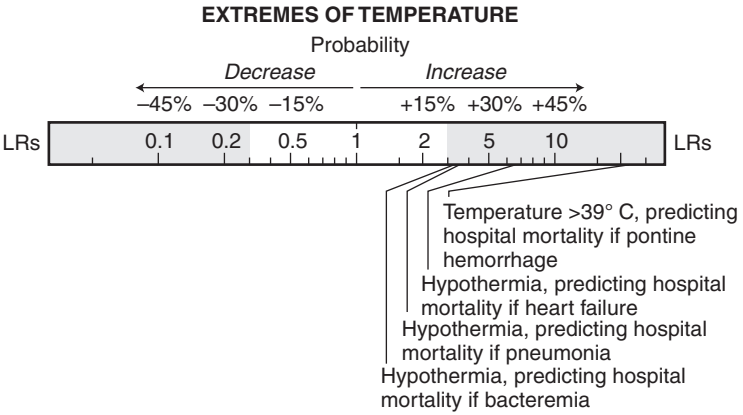
E. RELATIVE BRADYCARDIA

Clinical studies demonstrate that some infections, such as intracellular bacterial infections (e.g., typhoid fever or legionnaires' disease) and arboviral infections (e.g., sandfly fever or dengue fever), do produce less tachycardia

EBM BOX 17-3
Extremes of Temperature and Prognosis

Finding (Reference)	Sensitivity (%)	Specificity (%)	Likelihood Ratio* if Finding Is	
			Present	*Absent*
Temperature >39° C				
Predicting hospital mortality in patients with pontine hemorrhage[60]	66	97	**23.7**	0.4
Hypothermia†				
Predicting hospital mortality from pump failure in patients with congestive heart failure[61]	29	96	**6.7**	NS
Predicting hospital mortality in patients with pneumonia[62,63]	14-43	93	**3.5**	NS
Predicting hospital mortality in patients with bacteremia[64]	13	96	**3.3**	NS

*Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.
†Definition of findings: For *hypothermia*, temperature <35.2° C,[61] <36.1° C,[63] <36.5° C,[64] or <37.0° C.[62]
NS, not significant.
Click here to access calculator.



than other infections, but few patients with these infections actually have relative bradycardia, as defined earlier in the Findings section. Nonetheless, in one study of 100 febrile patients admitted to a Singapore hospital, a pulse rate of 90/min or less increased the probability of dengue infection (LR = 3.3), and a pulse rate of 80/min or less increased the probability even more (LR = 5.3).[73]

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 18

Respiratory Rate and Abnormal Breathing Patterns

RESPIRATORY RATE

I. INTRODUCTION

The respiratory rate (i.e., number of breaths per minute) is one of the four traditional vital signs, the others being heart rate, blood pressure, and temperature.

One of the first clinicians to recommend routine measurement of the respiratory rate was Stokes in 1825,[1] although routine charting of this vital sign was infrequent until the late 19th century.[2,3]

II. TECHNIQUE

The respiratory rate is usually measured while the clinician is holding the patient's wrist and ostensibly measuring the pulse, primarily because the respiratory rate may change if attention is drawn to it. This practice seems reasonable because the respiratory rate is the only vital sign under voluntary control.

As routinely recorded in the patient's hospital record, the respiratory rate is often inaccurate.[4,5] In one study of patients whose actual respiratory rates ranged from 11 to 33 breaths/min, the recorded rate 98% of the time was 18 to 22 breaths/min.[5] Some of these errors represent too short a period of observation (i.e., the clinician counting the number of breaths in 10 seconds multiplying the result times 6). Consequently, it is probably good practice to observe respirations for at least 30 to 60 seconds, a time span that may not only make the measured rate more accurate but also allow detection of unusual breathing patterns, such as Cheyne-Stokes respirations (see later).

III. FINDING

A. NORMAL RESPIRATORY RATE

The normal respiratory rate averages 20 breaths/min (range, 16 to 25 breaths/min), based on careful measurement in persons without fever, heart disease, or lung disease.[6,7] This estimate is identical to that made

over 150 years ago by Lambert Quetelet, who was the first to compile and analyze vital and social statistics.*[8] For unclear reasons, many textbooks, citing no data, mistakenly record the normal rate as 12 to 18 breaths/min.[6]

B. TACHYPNEA

Definitions of **tachypnea** vary, but the most reasonable one, based on the normal range and clinical studies, is respirations of 25 breaths/min or more.

C. BRADYPNEA

Bradypnea is defined as a respiratory rate of less than 8 breaths/min, a threshold derived from studies of patients taking opioid medications, because this rate best predicts respiratory depression and correlates well with level of sedation.[9]

IV. CLINICAL SIGNIFICANCE

A. TACHYPNEA

The finding of tachypnea has both diagnostic and prognostic value. As a diagnostic sign, it argues modestly for the diagnosis of pneumonia in outpatients with cough and fever (LR = 2.7; EBM Box 18-1). Tachypnea also increases the probability of pneumonia in hospitalized patients, the abnormal sign sometimes appearing as early as 1 to 2 days before the diagnosis is apparent by other means.[7,10]

One characteristic of a vital sign is that it accurately predicts the patient's prognosis, and EBM Box 18-1 shows that tachypnea predicts subsequent cardiopulmonary arrest in hospitalized patients (LR = 3.1) much better than does tachycardia or abnormal blood pressure.[12] During trials of weaning from a ventilator, tachypnea also is a significant although modest predictor of weaning failure (LR = 2.9).[11,22] In patients hospitalized with pneumonia, severe tachypnea (i.e., rate >30 breaths/min) predicts subsequent hospital death (LR = 2.1).

B. TACHYPNEA AND OXYGEN SATURATION

The respiratory rate correlates poorly with the patient's level of oxygen desaturation (r = 0.16).[23] Although this at first seems surprising (i.e., the lower the oxygen level, the more rapid a patient should breathe), this actually is expected because some hypoxemic patients, by breathing rapidly, are able to bring their oxygen level back up to normal (i.e., hyperventilation raises arterial oxygen levels), and other patients are hypoxemic simply because they have a primary hypoventilatory disorder. Consequently, the respiratory rate and oxygen saturation level are both valuable to the clinician, each providing information independent from the other.

*Quetelet's 1835 monumental treatise also provided our current formula for body mass index, known as the Quetelet index (see Chapter 12).

EBM BOX 18-1
*Tachypnea**

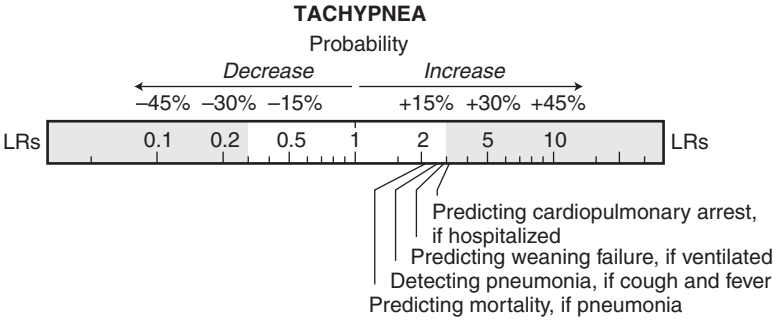
Finding (Reference)	Sensitivity (%)	Specificity (%)	Likelihood Ratio† if Finding Is	
			Present	*Absent*
Rate >24/min				
Predicting failure of weaning from the ventilator, in intubated patients[11]	94	68	2.9	NS
Rate >27/min				
Predicting cardiopulmonary arrest, in medical inpatients[12]	54	82	**3.1**	0.6
Rate >28/min				
Detecting pneumonia, in patients with cough and fever[13–16]	7-36	80-99	2.7	0.9
Rate >30/min				
Predicting hospital mortality, in patients with pneumonia[17–21]	41-85	63-87	2.1	0.6

*Diagnostic standard: For *failure of weaning*, progressive hypoxemia or respiratory acidosis; for *pneumonia*, infiltrate on chest radiograph.

†Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

NS, not significant.

Click here to access calculator.



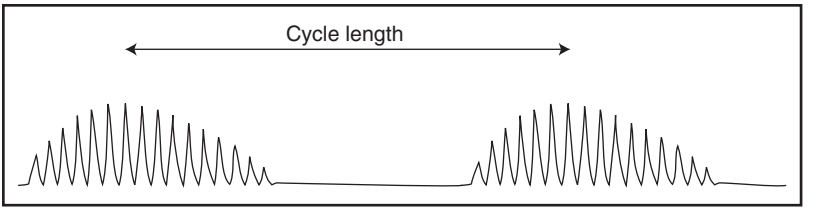


FIGURE 18-1 Cheyne-Stokes respirations. There are alternating cycles of hyperpnea and apnea. During the hyperpnea phase, only the tidal volume oscillates; the respiratory frequency is constant.

ABNORMAL BREATHING PATTERNS

I. CHEYNE-STOKES BREATHING (PERIODIC BREATHING)

A. INTRODUCTION

Cheyne-Stokes breathing consists of alternating periods of apnea and hyperpnea (Fig.18-1). Some authors equate the term **periodic breathing** with Cheyne-Stokes breathing,[24,25] whereas others reserve periodic breathing for oscillations of tidal volume that lack intervening periods of apnea.[26]

Cheyne-Stokes breathing was described by John Cheyne in 1818 and William Stokes in 1854.[27]

B. FINDINGS

1. The Breathing Pattern

At the end of each apneic period, breathing commences with excursions of the chest that initially are small but gradually increase for several breaths and then diminish until apnea returns. The respiratory rate is constant during the hyperpnea phase and does not gradually increase and then decrease, as has often been surmised.[28] Cheyne-Stokes breathing often first appears when the patient lies down, probably because this position reduces the patient's functional residual capacity, thus diminishing the lung's ability to buffer changes in carbon dioxide (see the section on Pathogenesis).[25,29]

The time between two consecutive peaks of hyperpnea is called the **cycle length** or **period.** Each cycle length is divided into a hyperpnea phase (lasting about 30 seconds on average in patients with congestive heart failure) and an apnea phase (lasting about 25 seconds on average).[30]

2. Associated Bedside Observations

Several additional findings appear in patients with Cheyne-Stokes breathing. During the hyperpnea phase, the patient is alert and sometimes agitated, with dilated pupils, hyperactive muscle stretch reflexes, and increased muscle tone. During the apnea phase, the patient appears motionless and asleep, with constricted pupils, hypoactive reflexes, and reduced muscle tone.[31,32] The agitation of the hyperpnea phase can easily startle a patient out of sleep, a nocturnal symptom that clinicians can mistake for the

paroxysmal nocturnal dyspnea of heart failure caused by transient pulmonary edema.[33,34]

C. CLINICAL SIGNIFICANCE

1. Associated Conditions

Cheyne-Stokes breathing affects 30% of patients with stable congestive heart failure.[26] The breathing pattern also appears in many neurologic disorders, including hemorrhage, infarction, tumors, meningitis, and head trauma involving the brainstem or higher levels of the central nervous system.[31,32,35,36] Normal persons often develop Cheyne-Stokes breathing during sleep[24] or at high altitudes.[31]

2. Prognostic Importance

Modern studies confirm Dr. Stokes' original impression that in patients with heart disease, this breathing pattern carries a poor prognosis. Compared with heart failure patients with normal breathing, patients with Cheyne-Stokes breathing have lower cardiac outputs, higher pulmonary capillary wedge pressures, and shorter survival times.[26,37–41]

D. PATHOGENESIS

The fundamental problem causing Cheyne-Stokes breathing is enhanced sensitivity to carbon dioxide. The circulatory delay between the lungs and systemic arteries, caused by poor cardiac output, also contributes to the waxing and waning of breaths. Cerebral blood flow increases during hyperpnea and decreases during apnea, perhaps explaining the fluctuations of mental status.[30,42]

1. Enhanced Sensitivity to Carbon Dioxide

Whether because of congestive heart failure or neurologic disease, patients with Cheyne-Stokes breathing have two to three times the normal sensitivity to carbon dioxide.[31,42–44] This causes patients to hyperventilate excessively, eventually driving the carbon dioxide level so low that central apnea results. After patients stop breathing, carbon dioxide levels again rise, eliciting another hyperventilatory response and thus perpetuating the alternating cycles of apnea and hyperpnea.

Mountain climbers develop Cheyne-Stokes breathing because hypoxia induces hypersensitivity to carbon dioxide. In contrast, their native Sherpa guides, who are acclimated to hypoxia, lack an exaggerated ventilatory response and do not develop Cheyne-Stokes breathing.[31]

2. Circulatory Delay between Lungs and Arteries

Ventilation is normally controlled by the medullary respiratory center, which monitors arterial carbon dioxide levels and directs the lungs to ventilate more if carbon dioxide levels are too high and less if levels are too low. The medulla signals the lungs almost immediately, the message traveling via the nervous system. The feedback to the medulla, however, is much slower because it requires circulation of blood from lungs back to systemic arteries.

In Cheyne-Stokes breathing, the carbon dioxide levels in the alveoli and those of the systemic arteries are precisely out of sync. During peak hyperpnea, carbon dioxide levels in the alveoli are very low, yet the medulla is just beginning to sample blood containing high carbon dioxide levels from the previous apnea phase and thus still directs the lungs to continue breathing deeply.[31] The delay in feedback to the medulla contributes to the gradual waxing and waning of tidal volume.

The length of circulatory delay also governs the cycle length of Cheyne-Stokes breathing, the two correlating closely ($r = 0.8$ between cycle length and circulation time from lung to arteries; $p < .05$).[30,42] The cycle length is about two times the circulation time, just as would be expected from the observation that carbon dioxide levels in the lungs and arteries are precisely out of sync. This suggests that the clinician should be able to take a stopwatch to the bedside and time the patient's cycle length, using this number as a rough guide to the patient's cardiac output. This idea, however, has never been formally tested.

II. KUSSMAUL RESPIRATIONS

Kussmaul respirations are rapid and deep and appear in patients with metabolic acidosis.[45] The unusually deep respirations are distinctive because other causes of tachypnea, such as heart and lung disease, reduce vital capacity and thus cause rapid, *shallow* respirations.

In children with severe malaria, the finding of Kussmaul respirations detects a severe metabolic acidosis with a sensitivity of 91%, specificity of 81%, positive LR of 4.8, and negative LR of 0.1.[46]

III. GRUNTING RESPIRATIONS

A. DEFINITION

Grunting respirations are short, explosive sounds of low-to-medium pitch produced by vocal cord closure during expiration. The actual sound is the rush of air that occurs when the glottis opens and suddenly allows air to escape. Grunting respirations are more common in children,[47] although the finding also has been described in adults as a sign of respiratory muscle fatigue[48] and, in the preantibiotic era, as a cardinal sign of lobar pneumonia, usually appearing after 4 to 6 days of illness.[3,49]

B. PATHOGENESIS

Grunting respirations slow down expiration and allow more time for maximal gas exchange.[48] In animal experiments, artificial mimicking of grunting respirations causes the pO_2 to increase by 10% and the pCO_2 to fall by 11%, whether or not the animal has pneumonia.[50] Grunting respirations also produce positive pressure exhalation that may reduce exudation of fluid into the alveoli, based on an old observation that administration of morphine to patients with pneumonia often reduced the grunting respirations but was sometimes followed immediately by fatal pulmonary edema.[49]

IV. ABNORMAL ABDOMINAL MOVEMENTS

A. NORMAL ABDOMINAL MOVEMENTS

In the absence of massive gaseous distention, the abdominal viscera are noncompressible and act like hydraulic coupling fluid that directly transmits movements of the diaphragm to the anterior abdominal wall.[51] Abdominal respiratory movements, therefore, indicate indirectly how the diaphragm is moving. During normal respiration, the chest and abdomen move synchronously: both out during inspiration and both in during expiration (Fig. 18-2). The chest wall moves more when the person is upright, and the abdomen moves more when the person is supine.[52,53]

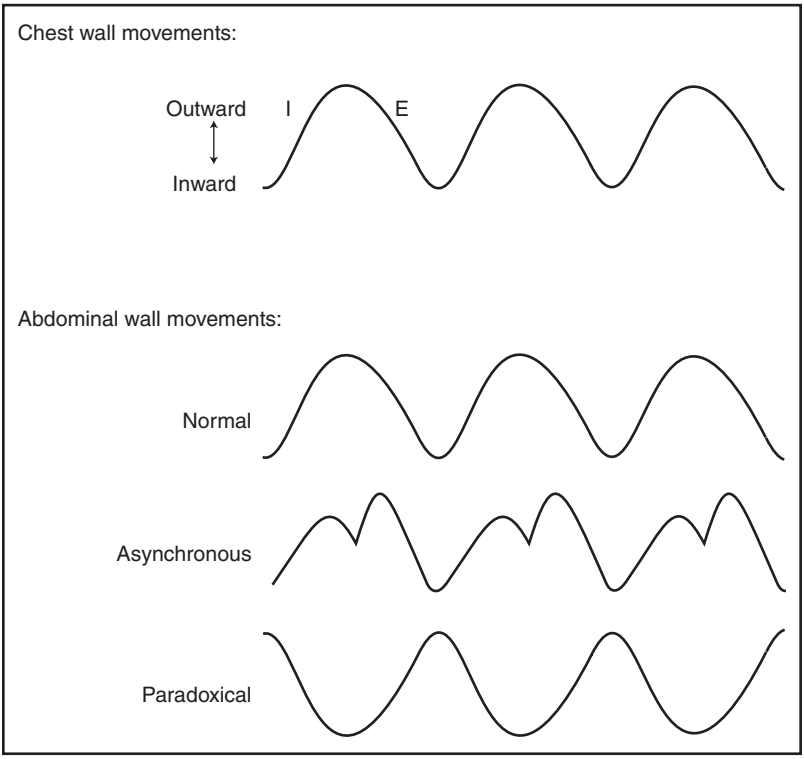


FIGURE 18-2 Respiratory abdominal movements. Chest movements are depicted in the first row. "I" denotes inspiration and "E" denotes expiration. Upward-sloping lines on the drawing indicate outward body wall movements; downward-sloping lines, inward movements. In normal persons, the abdominal and chest wall movements are completely in sync. In asynchronous breathing, only expiratory abdominal movements are abnormal. In paradoxical abdominal movements, both inspiratory and expiratory abdominal movements are abnormal. *See text.*

B. ABNORMAL ABDOMINAL MOVEMENTS

Three abnormal abdominal movements are signs of chronic airflow obstruction or respiratory muscle weakness: asynchronous breathing, respiratory alternans, and paradoxical abdominal movements.

1. Asynchronous Breathing

a. Findings

Asynchronous breathing is an abnormal *expiratory* movement that sometimes develops in patients with chronic airflow obstruction. In these patients, the normal smooth inward abdominal movement during expiration is replaced by an abrupt inward and then outward movement (see Fig. 18-2).[54,55]

b. Clinical Significance

In patients with chronic airflow obstruction, asynchronous breathing correlates with lower forced expiratory volumes and a much poorer prognosis.[55] Among patients with chronic airflow obstruction who develop acute respiratory symptoms, the presence of an asynchronous breathing pattern predicts subsequent hospital death or the need for artificial ventilation with a sensitivity of 64%, specificity of 80%, and positive LR of 3.2. (negative LR not significant).[54]

c. Pathogenesis

The outward abdominal movement during expiration probably reflects the strong action of chest wall accessory muscles during expiration, which push the flattened diaphragm temporarily downward, and thus the abdomen abruptly outward.[52,54]

2. Respiratory Alternans

Respiratory alternans describes a breathing pattern that alternates between inspiratory movements that are mostly abdominal and inspiratory movements that are mostly thoracic.[22]

3. Paradoxical Abdominal Movements

a. Finding

Paradoxical abdominal movements are completely out of sync with those of the chest wall. During inspiration, the abdomen moves in as the chest wall moves out; during expiration, the abdomen moves out as the chest wall moves in.[51,56–58]

b. Clinical Significance

The finding of paradoxical abdominal movements is a sign of bilateral diaphragm weakness. Most of these patients also complain of severe orthopnea. In one study of patients with dyspnea and neuromuscular disease, the finding of paradoxical abdominal movements detected diaphragm weakness with a sensitivity of 95%, specificity of 70%, and positive LR of 3.2. (In this study, the definition of paradoxical movements was any inspiratory

inward abdominal movement, and the definition of diaphragm weakness was a maximal transdiaphragmatic pressure ≤30 cm H_2O; the normal sniff transdiaphragmatic pressure is >98 cm H_2O.[56])

c. Pathogenesis

If the diaphragm is totally paralyzed, the inspiratory outward movement of the chest wall will draw the diaphragm upward, and thus the abdomen inward. The weight of the abdominal viscera probably also plays a role, because paradoxical movements are most obvious in affected patients who are positioned supine and are often absent when the patient is upright.[56]

A mimic of paradoxical abdominal movements is seen in patients with tetraplegia. In these patients, respiratory motion relies entirely on the diaphragm: as it descends during inspiration, pushing the abdominal wall out, the paralyzed chest wall may be drawn inward. The chest and abdomen are completely out of sync in these patients, but, in contrast to the paradoxical abdominal movements of diaphragm weakness, the abdominal wall of tetraplegia patients moves *outward* during inspiration, not *inward*.

V. ORTHOPNEA, TREPOPNEA, AND PLATYPNEA

These terms describe tachypnea (and dyspnea) that appears abruptly in particular positions: when the patient is supine (orthopnea), lying on a side (trepopnea), or upright (platypnea). These findings are often first detected during observation of the patient.

A. ORTHOPNEA

1. Finding

Orthopnea describes dyspnea that appears when the patient lies down but is relieved when the patient sits up (from the Greek words *ortho,* meaning straight or vertical, and *pnea,* meaning to breathe).

2. Clinical Significance

Orthopnea occurs in a variety of disorders, including massive ascites, bilateral diaphragm paralysis, pleural effusion, morbid obesity, and severe pneumonia, although its most important clinical association is congestive heart failure.[56,57,59] In one study of patients with known chronic obstructive pulmonary disease, the finding of orthopnea distinguished between those patients with an abnormally low ejection fraction (<0.50) and those with a normal ejection fraction with a sensitivity of 97%, specificity of 64%, positive LR of 2.7, and negative LR of 0.04.[60] This suggests that in patients with lung disease, the *presence* of orthopnea has limited value (i.e., occurs in both lung and heart disease), but the *absence* of orthopnea is more compelling, *decreasing* the probability of associated left ventricular dysfunction (LR = 0.04).

3. Pathogenesis

In patients with orthopnea, lung compliance and vital capacity decrease significantly after the patient moves from the upright to the supine position. This explains in part why dyspnea worsens in the supine position and

why orthopnea is a finding common to so many different clinical conditions.[59,61,62] Nonetheless, orthopnea cannot be entirely caused by postural changes in lung mechanics, for several reasons. First, orthopnea is uncommon in other disorders with similar reductions of vital capacity and compliance (e.g., interstitial fibrosis). Second, in patients with congestive heart failure, orthopnea correlates poorly with the pulmonary artery wedge pressure, which should have some relation to interstitial edema and pulmonary mechanics.[63] Finally, elevation of the head alone brings prompt relief to some orthopneic patients. It was once believed that elevation of the head relieved dyspnea because it reduced intracranial venous pressure and thus improved cerebral perfusion, although this hypothesis has been experimentally disproved.[59]

B. TREPOPNEA

1. Finding

Trepopnea* (from the Greek *trepo*, meaning twist or turn) describes dyspnea that is worse in one lateral decubitus position and relieved in the other.

2. Clinical Significance

There are three primary causes of trepopnea.

a. Unilateral Lung Disease[66,67]

Affected patients usually prefer to position their healthy lung down, which improves oxygenation because blood preferentially flows to the lower lung.

b. Congestive Heart Failure from Dilated Cardiomyopathy[64,65,68]

Patients usually prefer to have their right side down. Whether this is due to positional changes in lung mechanics (e.g., left lung atelectasis from cardiomegaly), right ventricular preload, or airway compression is unclear.

c. Mediastinal or Endobronchial Tumor

Tumors may compress the airways or central blood vessels in one position but not the other.[69–71] A clue to this diagnosis is a localized wheeze that appears in the position causing symptoms.[69]

C. PLATYPNEA

1. Finding

Platypnea (from the Greek *platus*, meaning "flat") is the opposite of orthopnea: Patients experience worse dyspnea when upright (sitting or standing) and relief after lying down. (A related term, *orthodeoxia*, described a similar deterioration of oxygen saturation in the upright position.) This

*In 1937, Drs. Wood and Wolferth first described trepopnea in patients with congestive heart failure.[64] In searching for a name for the finding, a patent lawyer suggested to them *rolling relief*, which they translated into *rotopnea*, until a Dr. Kern pointed out that *roto* was a Latin root and the pure Greek term *trepopnea* would be better.[65]

rare syndrome was first described in 1949, and the term *platypnea* was first coined in 1969.[72,73]

2. Clinical Significance

Platypnea occurs in patients with right-to-left shunting of blood through intracardiac or intrapulmonary shunts.

a. Right-to-Left Shunting of Blood through a Patent Foramen Ovale or Atrial Septal Defect

These patients often first develop the finding after undergoing pneumonectomy or developing a pulmonary embolus or pericardial effusion, which for unclear reasons promotes right-to-left shunting in the upright position.[74–79]

b. Right-to-Left Shunting of Blood through Intrapulmonary Shunts

Right-to-left shunting of blood through intrapulmonary shunts located in the bases of the lungs occurs in the hepatopulmonary syndrome, a complication of chronic liver disease (see Chapter 7).[80] In these patients, the upright position causes more blood to flow to the bases, thus aggravating the right-to-left shunting of blood and the patient's hypoxemia.

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 19

Pulse Oximetry

I. INTRODUCTION

Pulse oximetry measures the arterial oxygen saturation rapidly and conveniently. It is regarded as the fifth vital sign,[1,2] although some clinicians argue that pulse oximetry is a diagnostic test, not a physical sign, because it requires special equipment. Measurement of oxygen saturation, however, is no different from the other vital signs whose measurement requires a thermometer, sphygmomanometer, or stopwatch.

Takuo Aoyagi of Japan discovered the basic principle of pulse oximetry—pulsatile transmission of light through tissue depends on the patient's arterial saturation—in the mid-1970s.[3] The first pulse oximeters were successfully marketed in the 1980s.[4]

II. THE FINDING

Measurements are obtained by using a self-adhesive or clip-type probe attached to the patient's finger or ear. The oximeter makes several hundred measurements each second and then displays an average value based on the previous 3 to 6 seconds, which is updated about every second.[5] Although the digital display of pulse oximeters creates a sense of precision, studies show that between oxygen saturation levels of 70% and 100%, pulse oximeters are only accurate within 5% (i.e., ± 2 standard deviations) of measurements made by in vitro arterial blood gas analysis using CO-oximetry.[4,6,7]

The most common causes of inadequate oximeter signals are poor perfusion (due to cold or hypotension), excessive ambient light, and motion artifact. The clinician can sometimes correct these problems and thus improve the signal by warming or rubbing the patient's hand, repositioning the probe, or resting the patient's hand on a soft surface.[5] If inadequate signals persist, the clinician should try obtaining measurements with the clip probe attached to the lobe or pinna of the patient's ear.

In patients with hemiparesis, the results of pulse oximetry on the right and left sides of the body are the same.[8]

III. CLINICAL SIGNIFICANCE

A. ADVANTAGES OF PULSE OXIMETRY

As a sign of low oxygen levels, pulse oximetry is superior to the physical sign of cyanosis, because oximetry is more sensitive and because readings do not depend on the patient's hemoglobin level (see Chapter 8).

Consequently, pulse oximetry has become indispensable in the monitoring of patients in emergency departments, recovery and operating rooms, pulmonary clinics, and intensive care units, where measurements often reveal unsuspected oxygen desaturation, leading to changes in diagnosis and treatment.[9] Oxygen therapy prolongs survival times of some hypoxemic patients, such as patients chronically hypoxemic from lung disease.[10,11] Presumably, oxygen therapy benefits patients with acute hypoxemia as well.

In hospitalized patients, an O_2 saturation of less than 90% predicts hospital mortality (LR = 4.5; EBM Box 19-1). As a diagnostic sign, an O_2 saturation of less than 96% increases the probability of hepatopulmonary

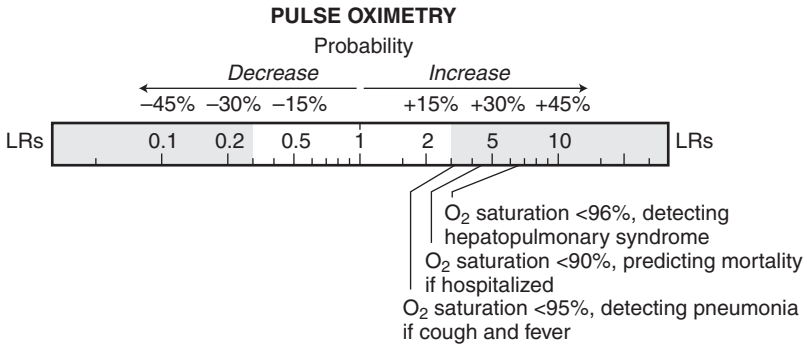
EBM BOX 19-1
*Oxygen Saturation by Pulse Oximetry**

Finding (Reference)	Sensitivity (%)	Specificity (%)	Likelihood Ratio† if Finding Is	
			Present	*Absent*
Predicting Hospital Mortality in Hospitalized Patients				
Oxygen saturation <90%[12,13]	21-39	87-97	**4.5**	0.8
Detecting Hepatopulmonary Syndrome in Patients with Chronic Liver Disease				
Oxygen saturation <96%[14]	39	94	**6.7**	0.6
Detecting Pneumonia in Outpatients with Cough and Fever				
Oxygen saturation <95%[15–18]	33-52	80-86	**3.1**	0.7

*Diagnostic standard: For *hepatopulmonary syndrome*, triad of cirrhosis, intrapulmonary shunting by contrast echocardiography, and alveolar to arterial oxygen gradient >20 mm Hg; for *pneumonia*, chest radiography.

†Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

Click here to access calculator.



syndrome in patients with chronic liver disease (LR = 6.7), and an O_2 saturation of less than 95% increases the probability of pneumonia in patients with cough and fever (LR = 3.1). The use of pulse oximetry to diagnose aspiration in patients with stroke (during swallowing) is discussed in Chapter 58.

B. LIMITATIONS OF PULSE OXIMETRY[4,6,19,20]

Because pulse oximetry readings indicate only the degree of oxygen saturation of hemoglobin, they fail to detect problems of poor oxygen delivery (e.g., anemia, poor cardiac output), hyperoxia, and hypercapnia. Other limitations of pulse oximetry measurements are discussed in the following sections.

1. Dyshemoglobinemias

The pulse oximeter interprets carboxyhemoglobin to be oxyhemoglobin and therefore seriously underestimates the degree of oxygen desaturation in patients with carbon monoxide poisoning. In patients with methemoglobinemia, the pulse oximetry readings decrease initially but eventually plateau at around 85%, despite true oxyhemoglobin levels that continue to decrease to much lower levels.

2. Dyes

Methylene blue causes a spurious decrease in oxygen saturation readings. Some colors of nail polish and finger pigments also interfere with oximetry and should be removed before pulse oximetry monitoring.[21–23] Hyperbilirubinemia and jaundice, however, do not affect the pulse oximeter's accuracy.

3. Low Perfusion Pressure

In patients with hypotension or peripheral vascular disease, the arterial pulse may be so weak that the pulse oximeter is unable to pick up the arterial signal, thus making measurements difficult or impossible.

4. Exaggerated Venous Pulsations

In patients with right-sided heart failure or tricuspid regurgitation, the oximeter may mistake the venous waveform for the arterial one, leading to spuriously low oxygen saturation readings.

5. Excessive Ambient Light

Excessive ambient light (or malposition of the probe allowing ambient light to reach the sensor) also may interfere with the oximeter's accuracy, falsely lowering the value in patients with normal oxygen saturation and, more important, overestimating it in patients with significant hypoxemia.

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 20

The Pupils

NORMAL PUPILS

I. INTRODUCTION

The integrity of the pupil depends on the iris, cranial nerves II and III, and the sympathetic nerves innervating the eye.

II. SIZE

The size of the normal pupil decreases as persons grow older ($r = -0.75$, $p < .001$): At 10 years of age, the mean diameter is 7 mm, at 30 years it is 6 mm, and at 80 years it is 4 mm.[1,2] Throughout human history, large pupils have been associated with youth, beauty, and vigor, explaining why the plant yielding the pupillary dilator atropine was named *belladonna*, which literally means "beautiful lady."

III. HIPPUS

Under steady illumination, the normal pupil is in continual motion, repeatedly dilating and contracting by small amounts. This restless undulation, called **hippus,** or **pupillary unrest,** is more prominent in younger patients and during exposure to bright light. Clinicians of the 19th century associated hippus with diverse disorders, ranging from myasthenia gravis to brain tumors, but hippus is now known to be a normal phenomenon.[3] The oscillations of the right and left pupil are synchronous, which suggests hippus is under central control.

IV. SIMPLE ANISOCORIA

Simple anisocoria, a normal finding, is defined as a difference in pupil diameter of 0.4 mm or more that cannot be attributed to any of the pathologic pupils discussed later, intraocular drugs, ocular injury, or ocular inflammation.[2] Simple anisocoria affects up to 38% of healthy persons (only half of whom have anisocoria at any given moment) and is a constant finding in 3% of persons. When simple anisocoria waxes and wanes, the same eye usually displays the larger pupil.[2]

The difference in pupil size in simple anisocoria rarely exceeds 1 mm.[2] Other features distinguishing it from pathologic anisocoria are described later, under the section on Abnormal Pupils.

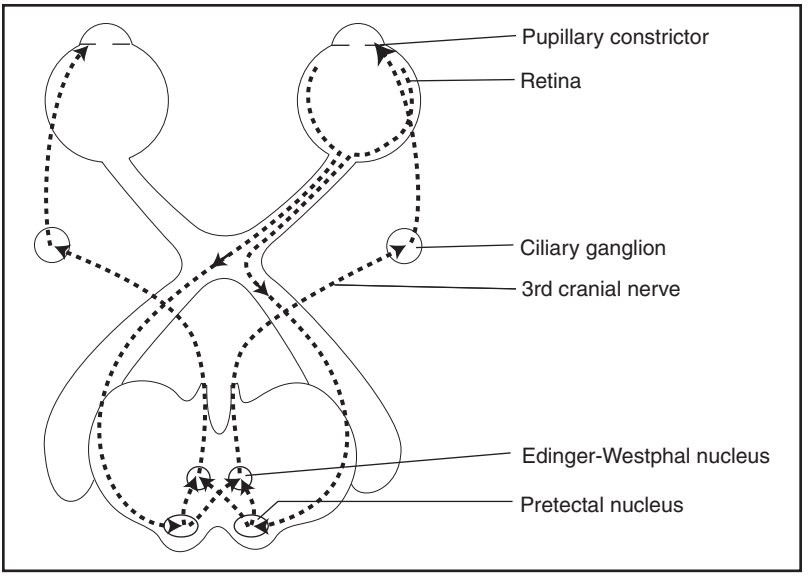


FIGURE 20-1 Anatomy of the pupillary light reflex. The *dotted lines* show how nerve impulses from the retina and optic nerve on one side (right eye in this example) contribute to the nerve impulses of both third nerves, via the crossing of the nerve impulses from the nasal retina in the optic chiasm and the abundant interconnections between both pretectal nuclei and both Edinger-Westphal nuclei. Unless there is asymmetrical disease of the efferent pathway (i.e., third nerve, ciliary ganglion and postganglionic fibers, iris), the pupils are thus symmetrical.

V. NORMAL LIGHT REFLEX

A. ANATOMY

Figure 20-1 illustrates the nerves responsible for the normal light reflex. Because both pupillary constrictor muscles normally receive identical signals from the midbrain, they constrict the same amount, which may be small or large depending on the *summation* of light intensity coming into *both* eyes. For example, both pupils dilate the same amount in darkness, constrict an identical small amount when a dim light is held in front of one eye, and constrict an identical larger amount when a bright light is held in front of one eye.

With a light held in front of one eye, ipsilateral pupillary constriction is called **direct reaction** to light, and contralateral constriction is called **consensual reaction.**

B. CLINICAL SIGNIFICANCE

The anatomy of the normal light reflex has two important clinical implications.

1. Anisocoria Is Absent in Disorders of the Optic Nerve or Retina (i.e., Afferent Connections)

Because the signal in both outgoing third nerves is identical in these disorders, representing the summation of light intensity from both eyes, the pupils are the same size. Unilateral afferent disease is similar to the experiment of holding a bright light in front of one eye (i.e., the opposite eye, thus mimicking one with an afferent defect): Despite the asymmetry of light signals in the two optic nerves, both pupils have an identical diameter.

2. Anisocoria Indicates Asymmetrical Disease of the Iris, Cranial Nerve III, or Sympathetic Nerves (i.e., Efferent Connections and Iris)

Asymmetrical disease of the efferent connections guarantees that the signals arriving at the pupil are different and that the pupil size, therefore, will be different.

VI. NEAR SYNKINESIS REACTION

The near synkinesis reaction occurs when a person focuses on a near object. The reaction has three parts.

1. Constriction of the pupils (pupilloconstrictor muscle)
2. Convergence of eyes (medial rectus muscles)
3. Accommodation of the lenses (ciliary body)

ABNORMAL PUPILS

I. RELATIVE AFFERENT PUPILLARY DEFECT (MARCUS GUNN PUPIL)

A. INTRODUCTION

The relative afferent pupillary defect is the most common abnormal pupillary finding, more common than all other pupillary defects combined.[4]

Although the relative afferent pupillary defect was described by R. Marcus Gunn in 1904, it is clear from his report that the sign was generally known to clinicians of his time. Kestenbaum named the finding in 1946 after Marcus Gunn,[4] and, in 1959, Levatin introduced the swinging flashlight test, which is how most clinicians now elicit the finding.[5]

B. THE FINDING

Because the pupils are equal in patients with disorders of the retina and optic nerves (see the section on Normal Pupils, earlier, and Fig. 20-1), the **swinging flashlight test** is necessary to uncover disorders of the afferent half of the light reflex. This test compares the amount of pupilloconstriction produced by illuminating one eye with that produced by illuminating the other.

To perform the test, the clinician swings the flashlight back and forth from eye to eye, holding it over one pupil for 1 to 2 seconds at a time before immediately shifting it to the other pupil (Fig. 20-2). Both pupils constrict strongly when the light is shining into the normal eye, but as the light swings over to illuminate the abnormal eye, both pupils dilate. (Dilation occurs because the pupils respond as if the light were much dimmer, producing *less* bilateral constriction—or net dilation—compared to when the light is shining in the normal eye.[4,6]) As long as the clinician swings the light back and forth, the reaction persists—pupils constrict when the normal eye is being illuminated and dilate when the abnormal eye is being illuminated. Because clinicians usually focus on the illuminated pupil, the one that dilates is labeled as having a "relative afferent pupillary defect," or the Marcus Gunn pupil.

There has been some debate whether eyes with afferent defects also display an abnormal pupillary release (i.e., **pupillary release** is the small amount of pupillary dilation immediately following initial constriction during steady illumination).[7] Nonetheless, two studies demonstrated that only the swinging flashlight test reliably uncovers the afferent defect.[8,9]

Light reflecting off the cornea may sometimes obscure the movements of the pupils. To overcome this, the clinician should angle the light by holding the light source slightly below the horizontal axis.

Interpreting the swinging flashlight test has three caveats.[6]

1. **Correct interpretation of the test ignores hippus,** which otherwise can make interpretation difficult.
2. **The clinician should avoid the tendency to linger with the flashlight on the eye suspected to have disease.** Uneven swinging of the light may temporarily bleach the retina being illuminated more, thus eventually producing a relative pupillary defect and erroneously confirming the initial suspicion. To avoid this and to ensure equal illumination of both retinas, the clinician should silently count: "one, two, switch, one two, switch," and so on.
3. **Only one working iris is required to interpret this pupillary sign.** If the patient has only one pupil that reacts to light (see the section on Anisocoria), the test is performed in the same way, although the clinician focuses only on the normal iris to interpret the results.

C. CLINICAL SIGNIFICANCE

A relative afferent defect implies ipsilateral optic nerve disease or severe retinal disease.

1. Optic Nerve Disease

Patients with optic nerve disease (e.g., optic neuritis, ischemic optic neuropathy) have the most prominent relative afferent pupillary defects. If the disease is asymmetrical, the sensitivity of the finding is 92% to 98%, much higher than that for any other test of afferent function, including visual acuity, pupil cycle times, appearance of optic disc during funduscopy, and visual evoked potentials.[10,11] The finding depends, however, on *asymmetrical* optic nerve function (hence, the word *relative* in its

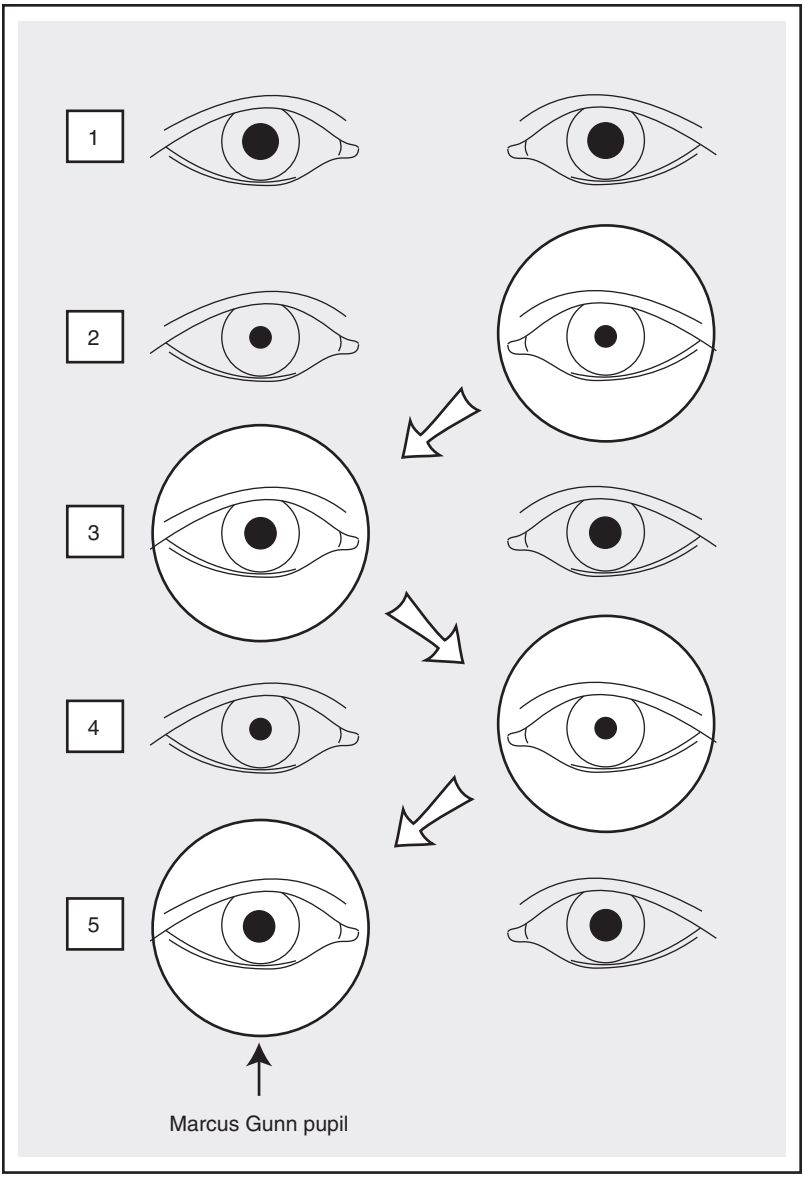


FIGURE 20-2 The relative afferent pupillary defect (Marcus Gunn pupil). The figure depicts a patient with an abnormal *right* optic nerve. Under normal room light illumination *(row 1)*, the pupils are symmetrical. During the swinging flashlight test, the pupils constrict when the normal eye is illuminated *(rows 2 and 4)* but dilate when the abnormal eye is illuminated *(rows 3 and 5)*. Although both pupils constrict or dilate simultaneously, the clinician is usually focused on just the illuminated pupil. The pupil that dilates during the swinging flashlight test has the "relative afferent pupillary defect" and is labeled the Marcus Gunn pupil. See text.

label); consequently, if patients with suspected unilateral disease lack the afferent pupillary finding, bilateral optic nerve disease is eventually found in 65%.[11]

2. Retinal Disease

Severe retinal disease may cause a relative afferent pupillary defect, although the retinal disease must be markedly asymmetrical to produce the finding, and, once the finding appears, it is subtle compared with that seen in optic nerve disease.[12]

3. Cataracts Do Not Cause the Relative Afferent Pupillary Defect[13]

Although this seems surprising, it is because the retina, if healthy, compensates over minutes for any diminished brightness, just as it does after a person walks into a dark movie theater. In fact, during the time of Galen, the Roman physician, clinicians tested the pupillary light reaction of patients with cataracts to determine whether vision could be restored after couching (an ancient treatment for cataracts that used a needle to displace the cataract posteriorly; a preserved light reaction indicated that the retina and optic nerve behind the cataract were intact).[14]

II. ARGYLL ROBERTSON PUPILS

A. THE FINDING[15,16]

Argyll Roberton pupils have four characteristic findings.

1. Bilateral involvement
2. Small pupils that fail to dilate fully in dim light
3. No light reaction
4. Brisk constriction to near vision and brisk redilation to far vision

Originally described by Douglas Moray Cooper Lamb Argyll Robertson in 1868, this finding had great significance a century ago because it settled a long-standing debate whether general paresis and tabes dorsalis were the same disease. The pupillary abnormality was found in a high proportion of patients with both diseases and was limited to these diseases, arguing for a common syphilitic origin of both. The introduction of Wasserman's serologic test for syphilis in 1906 confirmed that the two diseases had the same cause.

B. CLINICAL SIGNIFICANCE

1. Associated Disorders

In addition to neurosyphilis, there are rare, scattered reports of Argyll Robertson pupils in patients with various other disorders, including diabetes mellitus, neurosarcoidosis, and Lyme disease (see the section on Diabetic Pupil).[15] The responsible lesion is probably located in the dorsal midbrain, where damage would interrupt the light reflex fibers but spare the more ventrally located fibers innervating the Edinger-Westphal nuclei that control the near reaction.[17,18]

2. Differential Diagnosis of Light-Near Dissociation

Argyll Robertson pupils display light-near dissociation, that is, they fail to react to light but constrict during near vision. Other causes of light-near dissociation include the following.

a. Adie Tonic Pupil (see later)

b. Optic Nerve or Severe Retinal Disease

Either of these disorders may eliminate the light reaction when light is directed into the abnormal eye, although the pupils still constrict with the near synkinesis. In contrast to other causes of light-near dissociation, however, optic nerve and retinal disease severely impair vision.

c. Dorsal Midbrain Syndrome (Parinaud Syndrome, Sylvian Aqueduct Syndrome, Pretectal Syndrome)[19]

Characteristic findings of the dorsal midbrain syndrome are light-near dissociation, vertical gaze palsy, lid retraction, and convergence-retraction nystagmus (a rhythmic inward movement of both eyes from co-contraction of the extraocular muscles, usually elicited during convergence on upward gaze; most neuro-ophthalmologists use an optokinetic drum rotating downward to elicit the finding). Common causes of the dorsal midbrain syndrome are pinealoma in younger patients and multiple sclerosis and basilar artery strokes in older patients.

d. Aberrant Regeneration of the Third Nerve

After damage to the third nerve (from trauma, aneurysms, or tumors, but *not* ischemia), regenerating fibers originally destined for the medial rectus muscle may instead reinnervate the pupillary constrictor muscle, thus causing pupillary constriction during convergence but no reaction to light. Unlike Argyll Robertson pupils, however, this finding is unilateral, and most patients also have anisocoria, ptosis, and diplopia.[20]

3. Near-Light Dissociation

The phenomenon opposite to light-near dissociation, **near-light dissociation,** describes pupils that react to light but not during the near synkinesis. Near-light dissociation was historically associated with von Economo encephalitis lethargica, although experts now believe it only indicates that the patient is not trying hard enough to focus on the near object.[15] For this reason, many neuro-ophthalmologists save time during their examination and skip testing the near response unless the patient demonstrates no pupillary light reaction.

III. OVAL PUPIL

There are three causes of the oval pupil.

A. EVOLVING THIRD NERVE PALSY FROM BRAIN HERNIATION

These patients are invariably comatose from cerebral catastrophes causing elevated intracranial pressure.[21,22] As the pupil enlarges, it may appear oval for a short time before it becomes fully round, dilated, and fixed.

B. ADIE TONIC PUPIL (SEE LATER)

Adie tonic pupil may sometimes appear oval from segmental iris palsy.[23] These patients are alert and, if complaining of anything, describe only blurring of vision in the involved eye (from paralysis of accommodation).

C. PREVIOUS SURGERY OR TRAUMA TO THE IRIS

IV. ANISOCORIA

A. DEFINITION

Anisocoria is defined as a difference of 0.4 mm or more in the diameter of the pupils. It represents a problem with either the pupillary constrictor muscle (parasympathetic denervation, iris disorder, pharmacologic pupil) or the pupillary dilator muscle (sympathetic denervation, simple anisocoria).

B. TECHNIQUE

Figures 20-3 and 20-4 summarize the initial approach to anisocoria. The most important initial questions follow.

1. Is Anisocoria Old or New?

Examination of a driver's license photograph or other facial photograph, magnified with the direct ophthalmoscope (using the +10 lens), may reveal a preexisting pupillary inequality.[26]

2. Do Both Pupils Constrict Normally during the Light Reflex?

If there is a poor light reaction in the eye with the larger pupil, the pupillary constrictor of that eye is abnormal. If there is a good light reaction in both eyes, the pupillary dilator of the eye with the smaller pupil is abnormal.

3. Is Anisocoria Worse in Bright Light or Dim Light/Darkness?

If anisocoria is worse in light than darkness, the pupillary constrictor of the eye with the larger pupil is abnormal. If anisocoria is worse in darkness than light, the pupillary dilator of the eye with the smaller pupil is abnormal (see Fig. 20-4).*[27]

*To determine the amount of anisocoria in darkness, neuro-ophthalmologists often take flash photographs of patients in darkness. Because there is a delay of about 1.5 seconds between the flash of light and subsequent pupillary constriction, a photograph that is synchronous with the initial flash will actually reflect pupil size *in darkness*.[4] (This delay explains why modern cameras reduce "red eye" by flashing repeatedly *before* the photograph is taken.)

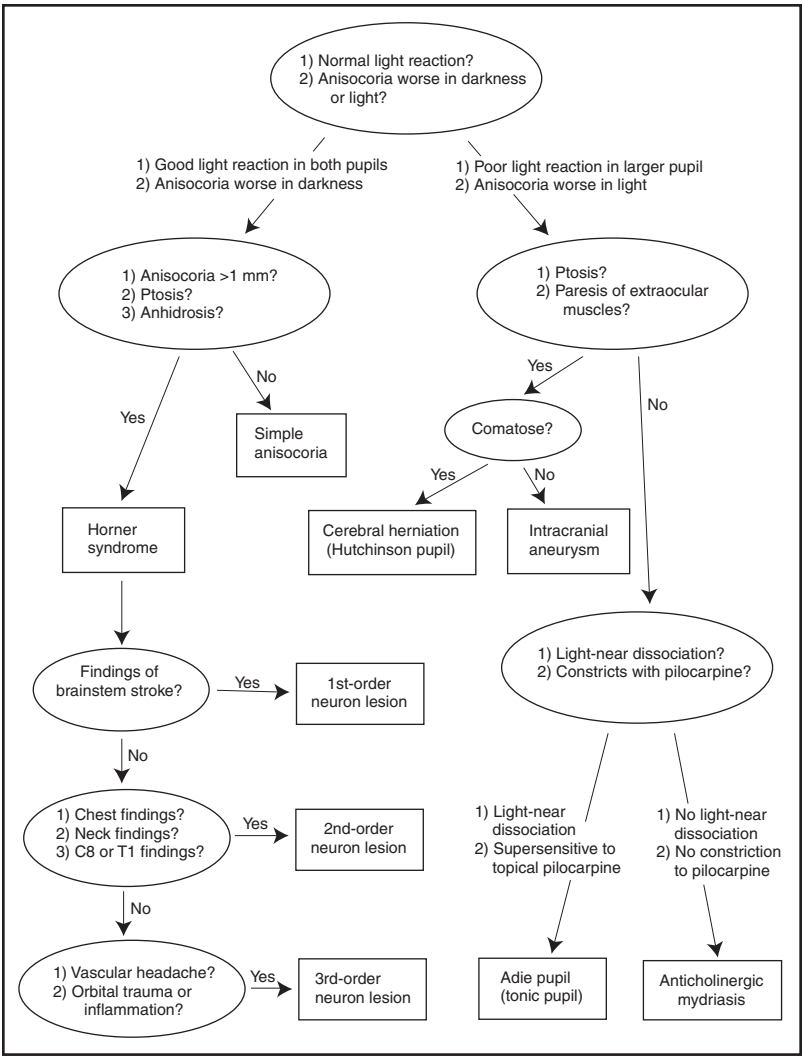


FIGURE 20-3 **Summary of approach to anisocoria.** The first two questions (Is there a normal light reaction? and Is anisocoria worse in darkness or light?) (see also Fig. 20-4) distinguish problems with the pupillary dilator muscle (i.e., Horner syndrome, simple anisocoria; *left side* of figure) from problems with the pupillary constrictor muscle (i.e., third cranial nerve, iris; *right side* of Fig. 20-3). Two other tests distinguish Horner syndrome from simple anisocoria: the cocaine test (see text) and pupillary dilator lag (i.e., the pupil dilates slowly in darkness, as documented by photographs, see text). Figure 20-3 is based on references 24 and 25.

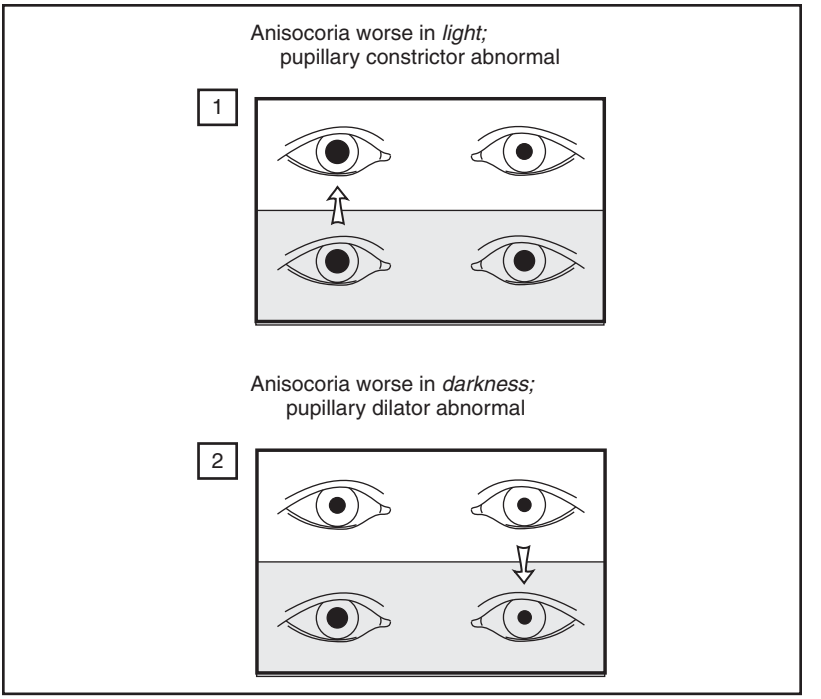


FIGURE 20-4 Comparing anisocoria in light and darkness. Patient 1 *(top)* has more prominent anisocoria in light than darkness, indicating that the pupillary *constrictor* of the *larger* pupil is abnormal (i.e., it fails to constrict in light, *arrow*). Patient 2 has more prominent anisocoria in darkness than light, indicating that the pupillary *dilator* of the *smaller* pupil is abnormal (i.e., it fails to dilate in darkness, *arrow*). The diagnosis in patient 1 (abnormal pupillary constrictor) could be a third nerve palsy, tonic pupil, pharmacologic mydriasis, or a disorder of the iris (right side of Fig. 20-3). The diagnosis in patient 2 (abnormal pupillary dilator, left side of Fig. 20-3) could be Horner syndrome or simple anisocoria. In patient 2, both pupils will react to light, whereas the larger pupil of patient 1 does not react well to light.

C. ABNORMAL PUPILLARY CONSTRICTOR MUSCLE

If an abnormal papillary constrictor muscle is present, the "fixed, dilated pupil" is due to a parasympathetic defect, iris disorder, or pharmacologic blockade. The most important questions in these patients are the following:

1. Is there a full third nerve palsy or are the findings confined to the pupillary constrictor (Fig. 20-5)?
2. Is there altered mental status or other neurologic findings?

1. Full Third Nerve Palsy: Associated Ptosis and Paralysis of Ocular Movements

Because the third cranial nerve controls the levator muscle of the upper eyelid (which lifts the eyelid) and four of the six eye muscles (medial, inferior, and superior rectus muscles and inferior oblique muscle), a full third nerve palsy causes a dilated pupil, ptosis, and ophthalmoplegia with an

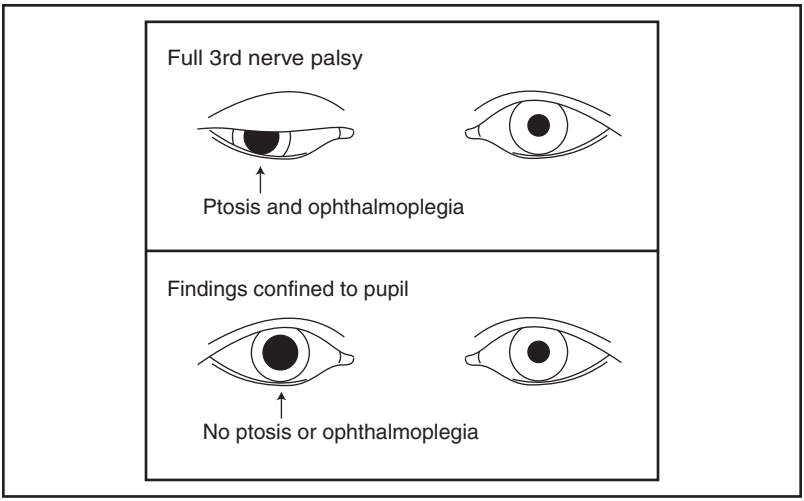


FIGURE 20-5 Types of abnormal pupillary constrictor. Both patients in this figure have a paralyzed right pupillary constrictor (i.e., a dilated pupil that fails to react well to light; see Fig. 20-4). The patient in the *top row* also has ptosis and ophthalmoplegia (i.e., eyes not aligned), indicating a full third nerve palsy: Possible diagnoses are transtentorial herniation (if comatose) or intracranial aneurysm (if mentally alert). The patient in the *bottom row* lacks ptosis and ophthalmoplegia, indicating that the findings are confined to the pupil itself: Possible diagnoses are the tonic pupil, pharmacologic mydriasis, or a disorder of the iris. See text.

eye deviated outward and downward (see Fig. 20-5, *top row*). In patients with anisocoria, this has two important causes: ipsilateral brain herniation (Hutchinson pupil) and posterior communicating artery aneurysm.

a. Ipsilateral Brain Herniation (Hutchinson Pupil)[28,29]

These patients are in the midst of a neurologic catastrophe from an expanding unilateral cerebral mass that causes coma, damage to the ipsilateral third nerve (dilated pupil, ptosis, and ophthalmoplegia), and, eventually, damage to the contralateral cerebral peduncle (which may lead to the false localizing sign of hemiplegia on the *same* side as the lesion). Although the involvement of the ocular muscles may be difficult to recognize, most patients have narrowing of the ipsilateral palpebral fissure and an eye that (if not dysconjugate) moves poorly during the vestibulo-ocular reflex.

Examination of the pupils is essential in patients with acute neurologic catastrophes.

1. In patients with **head trauma** and acute **subdural hematomas,** about 40% have anisocoria, and the dilated pupil is *ipsilateral* to the expanding mass about 90% of the time, just as Hutchinson suggested.[30–33] In addition, the presence of anisocoria or absent light reaction in patients with subdural hematomas predicts a worse outcome after craniotomy (i.e., dependence on others, persistent vegetative state, or death; sensitivity 63% to 69%, specificity 70% to 88%, positive LR = 3.4).[34,35]

2. In patients with **coma** (i.e., Glasgow coma scale score, ≤7),[36] anisocoria of more than 1 mm increases the probability of an intracranial structural disorder (e.g., expanding hemispheric or posterior fossa mass; LR = 9; EBM Box 20-1), whereas preservation of light reactions in both pupils decreases the probability of a structural disorder (LR = 0.2) and thus makes metabolic encephalopathy more likely

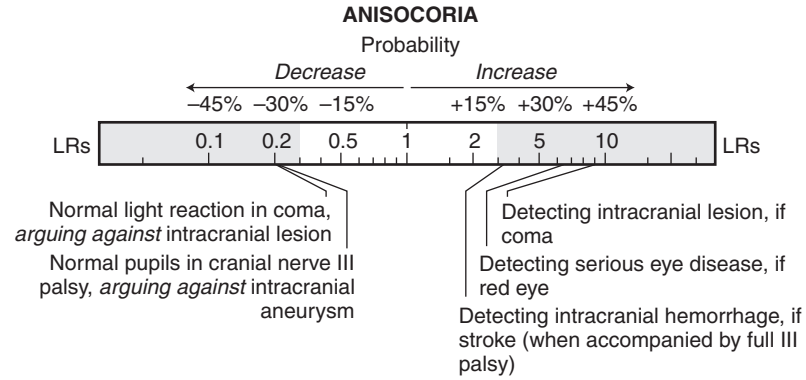
EBM BOX 20-1
*Pupils**

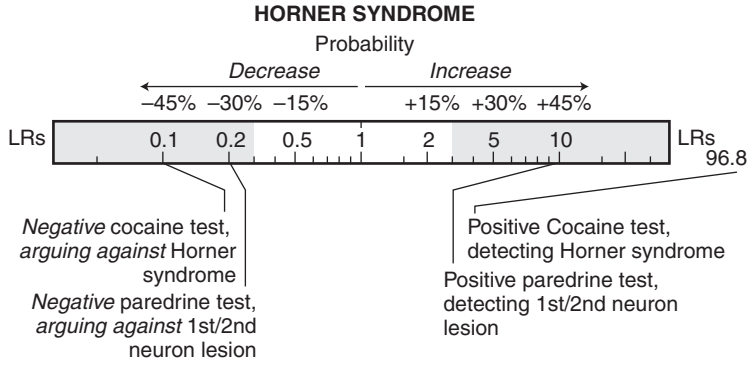
Finding (Reference)	Sensitivity (%)	Specificity (%)	Likelihood Ratio† if Finding Is	
			Present	*Absent*
Detecting Intracranial Structural Lesion in Patients with Coma[36]				
Anisocoria >1 mm	39	96	**9.0**	0.6
Absent light reflex in at least one eye	83	77	**3.6**	**0.2**
Detecting Intracranial Hemorrhage in Patients with Stroke[37]				
Anisocoria and full third nerve palsy	34	90	**3.2**	0.7
Detecting Intracranial Aneurysm in Patients with Third Nerve Palsy[38–40]				
Anisocoria or abnormal light reaction	80-93	62-75	2.4	**0.2**
Detecting Horner Syndrome[41,42]				
Post-topical cocaine anisocoria ≥1 mm	95	99	**96.8**	**0.1**
Detecting First or Second Nerve Lesions in Horner Syndrome (vs. Third Nerve Lesions)				
Small pupil dilates with topical hydroxyamphetamine (Paredrine)[43,44]	83-92	79-96	**9.2**	**0.2**
Small pupil fails to dilate with dilute phenylephrine[45]	88	79	**4.2**	NS
Asymmetrical facial sweating[46]	53	78	NS	0.6
Detecting Serious Eye Disease in Patients with Unilaterally Red Eye[47]				
Anisocoria ≥1 mm	19	97	**6.5**	0.8

*Diagnostic standard: For *structural lesion*, supratentorial and subtentorial lesions with gross anatomic abnormality, including cerebrovascular disease, intracranial hematoma, tumor, and contusion; for *intracranial hemorrhage*, computed tomography (CT); for *intracranial aneurysm*, contrast arteriography or rupture[40] or CT/MRI (magnetic resonance imaging) angiography[38,39]; for *serious eye disease*, corneal foreign body or abrasion, keratitis, or uveitis.

†Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

Click here to access calculator.





(e.g., drug overdose, hypoglycemia, sepsis, uremia, or other metabolic disorder).

3. In patients with **stroke**, anisocoria with full third nerve palsy increases the probability of intracranial hemorrhage (LR = 3.2; see EBM Box 20-1), thus decreasing the probability of ischemic infarction.

b. Posterior Communicating Artery Aneurysm

The most common of all intracranial aneurysms, posterior communicating artery aneurysms, present with ipsilateral third nerve palsy (thus dilating the pupil) up to 60% of the time.[48] It is essential to recognize this disorder promptly because of the risk of subsequent, devastating subarachnoid hemorrhage. Importantly, the abnormal pupil is almost always accompanied by at least some degree of ptosis and ophthalmoplegia (i.e., features of a full third nerve palsy; see Fig. 20-5); isolated anisocoria is rare.

In alert patients with new-onset third nerve palsy (i.e., at least some degree of ptosis and ophthalmoplegia), the presence of a *normal* pupil *decreases* the probability of an intracranial aneurysm or other compressive lesion (LR = 0.2; see EBM Box 20-1; see also Pupil-Sparing Rules in Chapter 57), although the pupil-sparing rule is less relevant today because

most patients undergo modern noninvasive neurovascular imaging to exclude intracranial aneurysms.[49]

2. The Tonic Pupil

a. The Finding

The tonic pupil has five important features (Fig. 20-6).

1. Unilateral dilation of a pupil
2. Poor or absent response to light
3. Extensive, slow (over seconds), and long-lasting constriction during near vision (this is why the pupil is tonic; i.e., it is analogous to myotonia)
4. Disturbances of accommodation (which cause the main concern for many patients, i.e., inability of the involved eye to focus)
5. Supersensitivity of pupillary constriction to pilocarpine[23,50,51]

Although both the Argyll Robertson pupil and the tonic pupil display light-near dissociation, they are easily distinguished by the characteristics in Table 20-1.

b. Pathogenesis

The tonic pupil occurs because of injury to the ciliary ganglion and postganglionic fibers (see Fig. 20-1) and subsequent misdirection of nerve fibers as they regenerate from the ciliary ganglion to the eye. In the normal eye, the ciliary ganglion sends 30 times the number of nerve fibers to the ciliary body (the muscle that focuses the lens during the near synkinesis) as to the iris (i.e., the pupillary constrictor).[52] Once these fibers are disrupted, odds are 30 to 1 that the iris will receive regenerating fibers that were originally intended for the ciliary body instead of the normal ones that participate in the light reaction. The pupil of these patients thus fails to respond to light, although during near vision, which normally activates the ciliary body, the misdirected fibers to the iris cause the pupil to constrict (i.e., light-near dissociation).

c. Clinical Significance

Because the ciliary ganglion and postganglionic fibers are contiguous to the eyeball, a variety of local disorders cause the tonic pupil, including orbital trauma, orbital tumors, or varicella-zoster infections of the ophthalmic division of the trigeminal nerve. Most cases, however, are idiopathic, which has been dubbed **Adie pupil** (named after William John Adie, although the syndrome was more thoroughly and accurately described by others before his 1931 paper).[50]

3. Disorders of the Iris

a. Pharmacologic Blockade of the Pupil with Topical Anticholinergic Drugs

Pharmacologic blockade causes an isolated fixed, dilated pupil without paralysis of eye movements. Not all patients with this problem are surreptitiously instilling mydriatic drops. Causes include unintended exposure of the eye to anticholinergic nebulizer treatments,[53] scopolamine patches,[54] and plants containing anticholinergic substances (blue nightshade, angel's

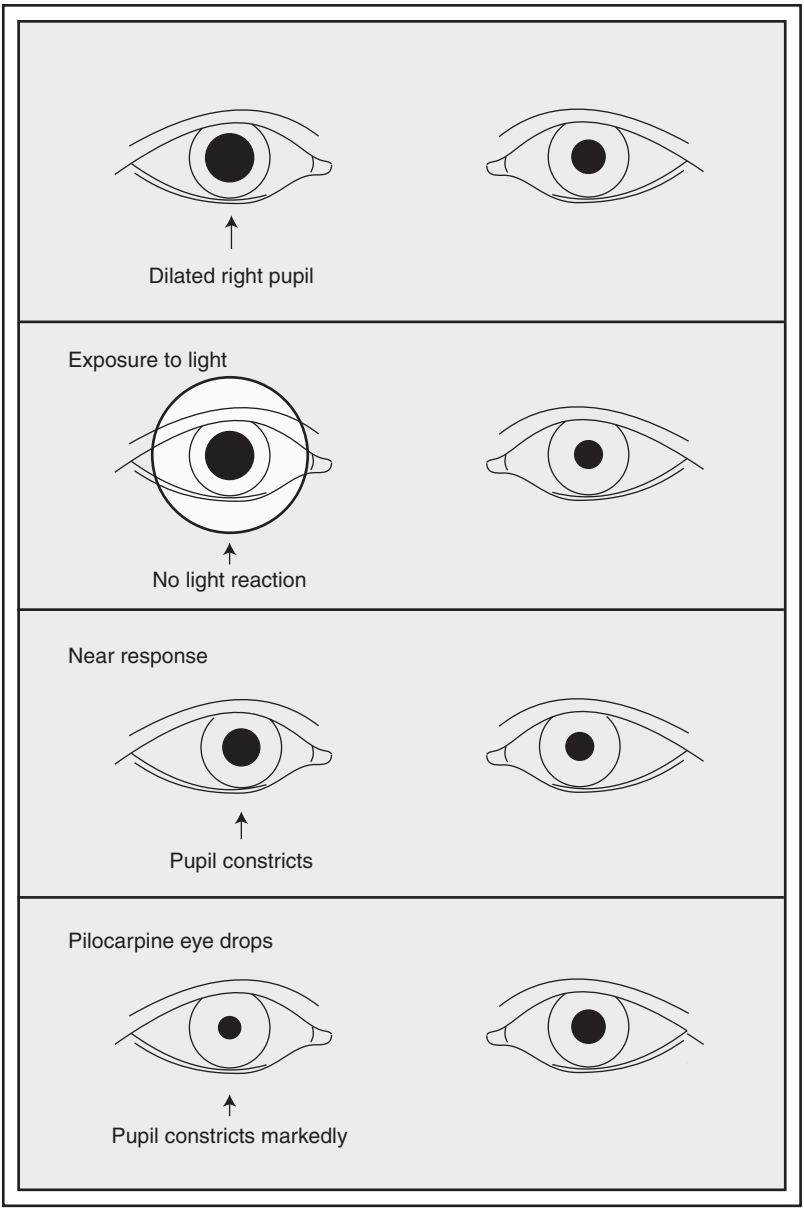


FIGURE 20-6 **Tonic pupil (Adie pupil).** The patient in this figure has a *right* tonic pupil. At baseline, there is anisocoria, with the right pupil larger than the left *(first row)*. The dilated pupil fails to react to light *(second row)* but constricts slowly (i.e., tonic contraction) when the patient focuses on a near object *(third row)*. After instillation of dilute pilocarpine eyedrops *(fourth row)*, the pupil constricts markedly.

TABLE 20-1 Comparison of Tonic Pupil and Argyll Robertson Pupil*

Finding	Tonic Pupil	Argyll Robertson Pupil
Pupil size	Large	Small
Laterality	Mostly unilateral	Mostly bilateral
Reaction to near vision	Extremely slow and prolonged with slow redilation	Normal with brisk redilation

*Based on reference 50.

trumpet, jimsonweed, moonflower).[55] Nebulizer treatments are an important cause to recognize in the intensive care unit, where metabolic encephalopathy is also common, leading clinicians to misdiagnose the Hutchinson pupil in patients with pharmacologic anisocoria and unresponsiveness.

The pharmacologic pupil characteristically fails to constrict with topical pilocarpine.

4. The Poorly Reactive Pupil—Response to Pilocarpine

In difficult diagnostic problems, especially when pharmacologic blockade is a consideration, the pupil's response to topical pilocarpine solution is helpful. Pilocarpine constricts Adie pupil and the dilated pupil from parasympathetic denervation (Hutchinson pupil or intracranial aneurysm) but not the dilated pupil from pharmacologic blockade.[56]

D. ABNORMAL PUPILLARY DILATOR

1. Definition

The most important cause of an abnormal pupillary dilator muscle is sympathetic denervation of the pupil, or **Horner syndrome,** which has three characteristics.

1. Ipsilateral miosis (paralyzed pupillodilator muscle)
2. Ipsilateral ptosis (paralyzed superior tarsal muscle)
3. Ipsilateral anhidrosis of the face (from damage to sudomotor fibers)

Sometimes, an elevated lower lid creates the appearance of enophthalmos, although the eye is not actually retracted. Figure 20-7 describes the neuroanatomy of the sympathetic pathways innervating the eye.

Horner syndrome is named after the Swiss ophthalmologist Johann Horner, who described the syndrome in 1869, but, like other eponymous pupillary findings (Adie pupil and Marcus Gunn pupil), earlier published descriptions of the finding exist.[57]

2. Horner Syndrome Versus Simple Anisocoria

When evaluating a pupil that dilates abnormally (left half of Fig. 20-3; patient 2 in Fig. 20-4), the findings of anisocoria of more than 1 mm, associated ptosis, or asymmetrical facial sweating indicate Horner syndrome.

In difficult cases, the definitive test of sympathetic denervation is the **cocaine test.** (Cocaine drops diminish the anisocoria of simple anisocoria but aggravate that of Horner syndrome; see Fig. 20-8.[58]) In one study of 169 persons, the presence of post–cocaine test anisocoria of 1 mm or more was

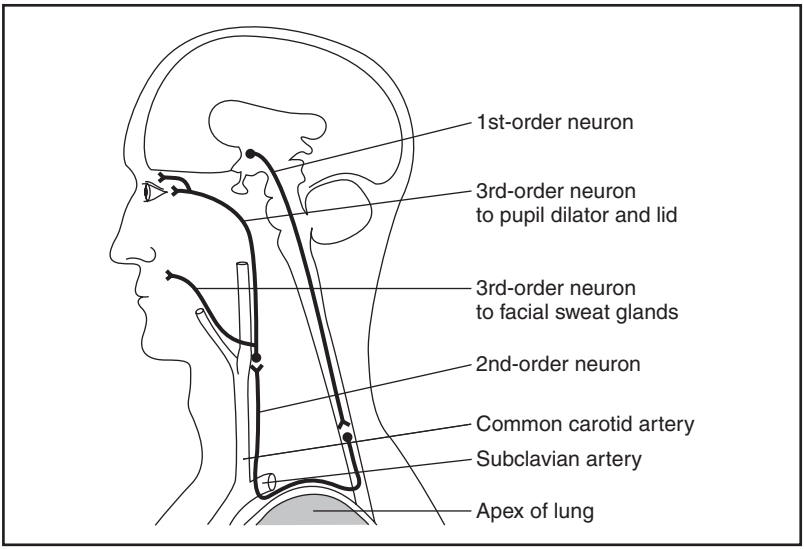


FIGURE 20-7 Anatomy of sympathetic pathways to the eye. The sympathetic innervation of the eye consists of three neurons connected in series: first-order neurons, second-order neurons, and third-order neurons. The first-order neurons (central neurons) extend from the posterior hypothalamus to the C8 to T2 level of the spinal cord. The second-order neurons (preganglionic neurons) leave the spinal cord and travel over the lung apex, around the subclavian artery, and along the carotid artery to the superior cervical ganglion. The third-order neurons (postganglionic neurons) diverge and take two paths: Those to the pupil and lid muscles travel along the internal carotid artery through the cavernous sinus to reach the orbit; those to the facial sweat glands travel with the external carotid artery to the face. Lesions in any of these neurons cause Horner syndrome and distinct associated physical signs (see Fig. 20-3 and text).

pathognomonic for Horner syndrome (LR = 96.8; see EBM Box 20-1), and its absence made Horner syndrome unlikely (LR = 0.1).

Nonetheless, cocaine eyedrops are difficult to obtain and store, and they render urine drug tests positive for up to 48 hours.[59] A proposed alternative agent is apraclonidine, a topical glaucoma eyedrop, which dilates the Horner pupil but not normal ones.[60] False-negative test results with apraclonidine have already been described, however, and thus far this eyedrop has not been widely tested in large numbers of patients with anisocoria of diverse causes.[61]

3. Clinical Significance of Horner Syndrome

a. Etiology

The etiologies of Horner syndrome that a clinician is likely to see depend on the clinician's specialty. In a neurologic service, 70% of patients with Horner syndrome have lesions in the first-order neuron, usually strokes in the brainstem (see Table 60-2 in Chapter 60).[62] In a medical service, 70% of afflicted patients have lesions in the second-order neuron, usually from tumors (e.g., lung and thyroid tumors) or trauma (e.g., to the neck, chest, spinal nerves, or subclavian or carotid arteries).[63] Causes of third-order

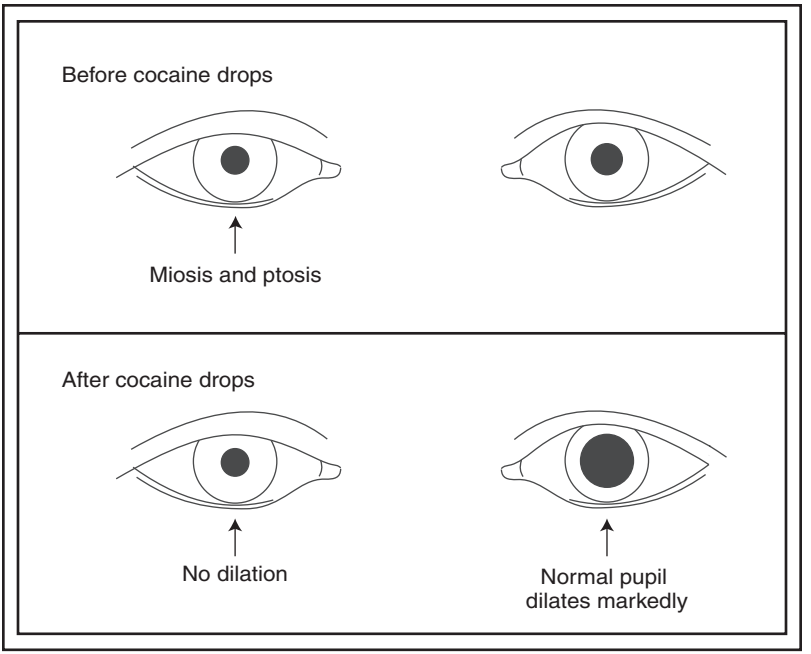


FIGURE 20-8 **Horner syndrome and the cocaine test.** Both pictures are of the same patient, before *(top)* and 45 minutes after *(bottom)* instillation of cocaine drops into each eye. At baseline, there is a mild right ptosis and miosis, which suggests the diagnosis of Horner syndrome of the right pupil. After instillation of the cocaine eyedrops into both eyes, the patient's right pupil fails to dilate, markedly aggravating the anisocoria and confirming the diagnosis of Horner syndrome. Cocaine eyedrops block the reuptake of norepinephrine at the myoneural junction of the iris dilator, causing the pupil to dilate unless norepinephrine is absent because of sympathetic denervation.

neuron lesions are vascular headache, skull fracture, and cavernous sinus syndrome.

b. Localizing the Lesion

(1) Associated Findings. Helpful features include the following:

1. Findings from the ipsilateral brainstem (e.g., lateral medullary syndrome), pointing to a first-order neuron lesion (see Table 60-2 in Chapter 60)
2. Abnormal chest or neck findings, a supraclavicular mass, or motor, reflex, or sensory findings of the ipsilateral C8 to T1 spinal roots, all pointing to the second-order neuron lesion
3. Orbital trauma, orbital inflammation, or migraine or neck pain, pointing to a third-order neuron lesion

Acute *pain* in Horner syndrome suggests dissection of the carotid artery.

(2) Facial Sweating. The sudomotor sympathetic fibers to the face diverge from the sympathetic pathway at the bifurcation of the carotid artery and therefore do not accompany the sympathetic nerves to the

pupil and lid. Theoretically, therefore, Horner syndrome from a third-order neuron lesion would preserve facial sweating, whereas Horner syndrome from first- and second-order neurons would cause asymmetrical facial sweating. In one study, however, this finding lacked diagnostic value (see EBM Box 20-1).

(3) Distinguishing Third-Order Nerve Lesions from First- or Second-Order Nerve Lesions: The Paredrine Test. When the cause of Horner syndrome remains unexplained despite careful bedside examination, many clinicians now routinely order magnetic resonance imaging to investigate the entire sympathetic pathway to the eye. An alternative and older method uses eyedrop tests to distinguish first-order or second-order nerve lesions from third-order nerve lesions. The most studied is the **Paredrine test** (i.e., topical hydroxyamphetamine). Dilation of the Horner miotic pupil after instillation of topical Paredrine indicates a first- or second-order neuron lesion (LR = 9.2; see EBM Box 20-1). Because Paredrine is now difficult to obtain, some investigators have recommended substituting dilute phenylephrine eyedrops. (In this test, the *absence of dilation* of the Horner miotic pupil after topical phenylephrine indicates a first- or second-order neuron lesion; LR = 4.2; see EBM Box 20-1.)

E. INTRAOCULAR INFLAMMATION

As part of the eye's response to intraocular inflammation, the ipsilateral pupil often constricts. In one study of 317 patients with the unilaterally red eye, anisocoria of 1 mm or more with the smaller pupil in the red eye significantly increased the probability of serious eye disease (i.e., corneal foreign body or abrasion, keratitis, and uveitis; LR = 6.5; see EBM Box 20-1) and thus decreased the probability of more benign problems (i.e., subconjunctival hemorrhage, conjunctivitis). The absence of anisocoria was unhelpful in this study (LR = 0.8).

V. DIABETES AND THE PUPIL

The pupils of patients with long-standing diabetes show signs of sympathetic denervation (small size and poor dilation in darkness), parasympathetic denervation (sluggish light reaction), and decreased amplitude of hippus.[64] Denervation alone, however, does not explain all of the diabetic pupillary abnormalities, because the pupils of many patients also respond poorly to dilating and constricting eyedrops, a finding suggesting additional problems in the iris itself (i.e., denervated pupils are classically supersensitive to eyedrops).[65] Some reviews state that diabetes causes the Argyll Robertson pupil, but the data for this are meager and the few studies that exist suggest that the finding is very rare.[15]

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 21

Diabetic Retinopathy

I. INTRODUCTION

Diabetic retinopathy is the leading cause of blindness in adults between the ages of 25 and 74 years.[1] Whether a patient develops retinopathy depends on the type and duration of diabetes: Those with type 1 diabetes have a 0% risk of proliferative retinopathy at 5 years after diagnosis, 4% at 10 years, and 50% at 20 years, whereas those with type 2 diabetes, especially if taking insulin, have a risk of 3% to 4% at the time of diagnosis, 10% at 10 years, and 20% at 15 years.[2] Once retinopathy develops, however, one of the best predictors of progression to sight-threatening retinopathy is the extent of retinopathy during the baseline examination: The higher the grade of retinopathy during the initial examination, the greater the risk of progression (Table 21-1). In type 1 diabetics, pregnancy increases the risk of progression 2.3-fold.[2]

In large cross-sectional surveys of diabetic patients seen by general practitioners, sight-threatening retinopathy (i.e., proliferative retinopathy and more severe forms of nonproliferative retinopathy) is found in 5% to 15% of patients.[6,7]

II. FINDINGS

The findings of diabetic retinopathy are divided into nonproliferative changes, which occur *within* the retina, and proliferative changes, which are located on the inner surface of the retina or in the vitreous.[8] The terms *background retinopathy* and *preproliferative retinopathy* are outdated and no longer recommended, having been replaced by the grades of retinopathy shown in Table 21-1. Diabetic retinopathy progresses in an orderly fashion through these grades.

A. NONPROLIFERATIVE CHANGES (Fig. 21-1)[3]

The earliest changes to appear in diabetic retinopathy are **microaneurysms,** which are distinct red, round spots less than one twelfth the diameter of an average optic disc, or 125 μm in longest dimension. (The average optic disc is about 1500 μm in diameter; 125 μm is approximately the width of an average major vein at the disc margin.) **Dot hemorrhages** are larger red dots with sharp borders; red spots with indistinct borders are **blot hemorrhages.** Both dot and blot hemorrhages are located in the

TABLE 21-1 Progression to High-Risk Proliferative Diabetic Retinopathy*

Grade of Baseline Retinopathy	Principal Clinical Findings	Cumulative Risk (%) of High-Risk Proliferative Retinopathy at:	
		1 Year	*5 Years*
NONPROLIFERATIVE RETINOPATHY			
Mild	Microaneurysms Dot and blot hemorrhages Soft exudates	1	16
Moderate	Extensive microaneurysms and hemorrhages IRMA Venous beading	3-8	27-39
Severe	Same as moderate†	15	56
Very severe	Same as moderate†	45	71
PROLIFERATIVE RETINOPATHY‡			
	Neovascularization Preretinal/vitreous hemorrhages Fibrovascular proliferation	22-46	64-75

*High-risk proliferative retinopathy is NVD > ¼ disc area in size, NVD < ¼ disc area *and* vitreous or preretinal hemorrhage, OR NVE > ½ disc area *and* vitreous or preretinal hemorrhage. These figures assume that the patient is untreated.

†Moderate, severe, and very severe nonproliferative retinopathy share the same funduscopic findings, although they differ in severity (based on standardized photographs) and the number of retinal quadrants involved.[3–5]

‡Percentages are for patients whose baseline evaluation reveals proliferative retinopathy with characteristics that are less than high-risk characteristics.

IRMA, intraretinal microvascular abnormalities; NVD, neovascularization within one disc diameter of the optic disc; NVE, neovascularization elsewhere (i.e., beyond one disc diameter of the optic disc) (see text).

inner retinal layers. **Hard exudates** (deposition of lipid in the inner retina) are small, white or yellowish-white deposits with sharp margins that often have a waxy or glistening appearance. **Soft exudates** (or **cotton-wool exudates**) are ischemic swellings of the superficial nerve fiber layer, which appear as white, round, or oval patches with ill-defined, feathery edges. As retinal ischemia progresses, two other abnormalities appear: venous beading (veins resembling a string of beads) and intraretinal microvascular abnormalities (IRMA), which are extratortuous vessels *within* the retina that may be either new vessels or dilated preexisting capillaries.

B. PROLIFERATIVE RETINOPATHY

Proliferative retinopathy is new vessel formation (i.e., neovascularization) on the inner surface of the retina or vitreous, which threatens vision by increasing the risk of retinal detachment or vitreous hemorrhage. These new vessels often resemble a small wagon wheel, with individual vessels

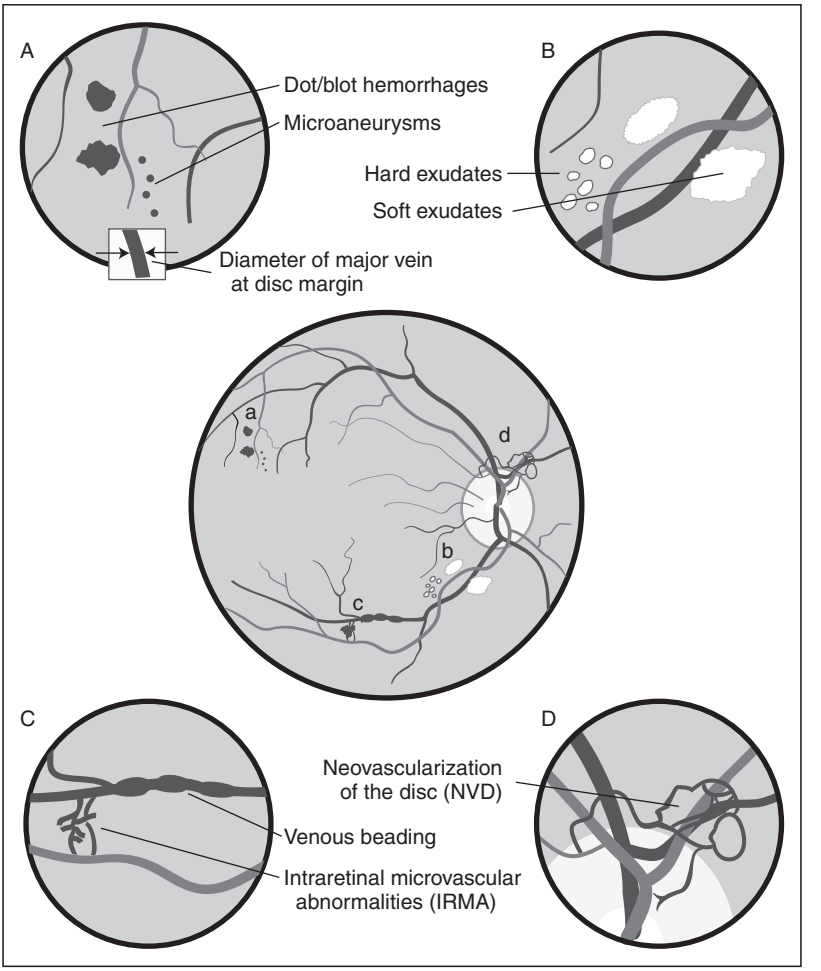


FIGURE 21-1 Types of diabetic retinopathy. The center figure depicting the fundus of a patient with diabetic retinopathy is surrounded by four enlarged views, each labeled with a letter (A to D) corresponding to specific locations on the center figure. *A*, Microaneurysms and dot/blot hemorrhages. The diameter of microaneurysms is less than the width of a major vein at the disc margin (reproduced in square inset). *B*, Hard and soft exudates. *C*, Venous beading and intraretinal microvascular abnormalities (IRMA). *D*, Neovascularization, which may be located within one disc diameter of the optic disc (NVD) or elsewhere (NVE). Although both IRMA and neovascularization represent the formation of new blood vessels, IRMA is confined to the layers of the retina, whereas neovascularization is on the inner surface of the retina or vitreous. See text.

radiating like spokes to a circumferential vessel forming the rim.[9] New vessel formation is subdivided into neovascularization of the disc (within one disc diameter of the optic disc, abbreviated NVD) and neovascularization elsewhere (NVE). Of the two, NVD has a much worse visual prognosis.[5]

C. MACULAR EDEMA

Macular edema, which may accompany any stage of nonproliferative or proliferative retinopathy, is very difficult to visualize using the direct ophthalmoscope, although important clues are rings of hard exudates (often surrounding the edematous area) and diminished visual acuity.[8]

III. CLINICAL SIGNIFICANCE

In patients with high-risk proliferative retinopathy or those with clinically significant macular edema, laser photocoagulation reduces the risk of subsequent visual loss by at least 50%.[1] (The footnote of Table 21-1 defines high-risk proliferative retinopathy.) Retinal examination is the only way to detect these lesions, thereby making diabetic retinopathy one of the best examples of a disorder benefiting from careful, attentive physical examination.

The findings that best predict subsequent proliferative retinopathy are venous beading, intraretinal microvascular abnormalities, and the extent of microaneurysms and hemorrhages. Soft exudates are less predictive, and the extent of hard exudates correlates poorly with subsequent proliferative retinopathy.[5]

A. VISUAL ACUITY AND DIABETIC RETINOPATHY

Diminished visual acuity per se is a poor screening test for diabetic retinopathy (EBM Box 21-1: positive LR = 1.5, negative LR = NS). In fact, the most common causes of diminished visual acuity in diabetics are cataracts (49% of diabetics with diminished acuity) and macular degeneration (29%), not diabetic retinopathy (15%).[10]

B. DIAGNOSTIC ACCURACY OF OPHTHALMOSCOPY

EBM Box 21-1 displays the accuracy of various methods in detecting sight-threatening retinopathy (i.e., proliferative changes and macular edema), using multiview dilated pupil retinal photographs or slit lamp biomicroscopy as the diagnostic standard. Not surprisingly, specialists using direct ophthalmoscopy perform better than general clinicians, and dilated examinations are superior to nondilated ones. Many diabetic centers now routinely screen their patients for retinopathy using three-view nonmydriatic photographs, which have excellent diagnostic accuracy (see EBM Box 21-1).

Macular edema is rarely detected by general providers using direct ophthalmoscopy. (Sensitivity is close to 0%.[11]) Because many patients with macular edema have normal visual acuity (i.e., the sensitivity of "visual acuity worse than 20/30" for macular edema is only 38%),[11] clinicians who screen for macular edema using just visual acuity are missing many patients who would benefit from laser photocoagulation.

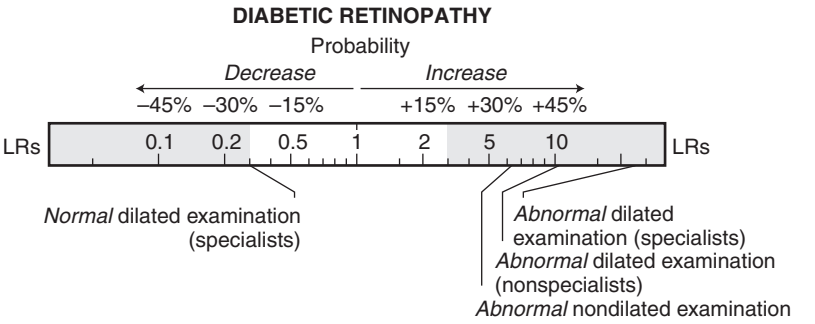
C. SCREENING RECOMMENDATIONS

Diabetic retinopathy is common, treatable, and detectable using simple tools: consequently, it is the prototype of a disease that would benefit from organized screening. Table 21-2 reviews the screening schedule recommended by the American Diabetes Association.[1] Given the stakes of missing serious

EBM BOX 21-1
*Diabetic Retinopathy**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Detecting Any Diabetic Retinopathy				
Visual acuity 20/40 or worse[10,12]	21-28	82-86	1.5	NS
Detecting Sight-Threatening Retinopathy Using the Following Technique				
Direct ophthalmoscopy, nondilated pupils[13]	50	92	**6.2**	0.5
Direct ophthalmoscopy, dilated pupils, general providers[6,7,14–16]	53-69	91-96	**10.2**	0.4
Direct ophthalmoscopy, dilated pupils, specialists[14,15,17,18]	48-82	90-100	**25.5**	**0.3**
Nonmydriatic three-view digital photographs[19,20]	73-89	97-98	**31.5**	**0.2**

*Diagnostic standard: For *sight-threatening retinopathy,* retinal photographs through dilated pupils or slit lamp biomicroscopy reveal proliferative retinopathy, macular edema, or both.
†Definition of findings: For *sight-threatening retinopathy,* proliferative retinopathy or macular edema, or both.
‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. *Click here to access calculator.*



retinopathy and the less than optimal performance of general clinicians using just direct ophthalmoscopy, only clinicians with training and experience—in most cases, optometrists and ophthalmologists—should screen patients. Any patient with macular edema, more than moderate nonproliferative retinopathy, or proliferative retinopathy should be seen by eye care providers with experience in the management of diabetic retinopathy.

TABLE 21-2 Recommended Ophthalmologic Examination Schedule for Patients with Diabetes Mellitus

Time of Onset of Diabetes	Recommended First Examination	Minimal Routine Follow-up
Less than 30 years of age*	Within 5 years after diagnosis of diabetes	Yearly†
30 years of age or older*	At time of diagnosis of diabetes	Yearly†
Pregnancy in preexisting diabetes	Prior to conception and during first trimester	Physician discretion pending results of first-trimester examination

*Less than 30 years and greater than 30 years are operational definitions of type 1 and type 2 diabetes used in the Wisconsin Epidemiologic Study of Diabetic Retinopathy.
†In some patients with normal eye examinations, eye specialists may advise less frequent examinations (every 2 to 3 years).[1]

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 22

Hearing

I. INTRODUCTION

Hearing loss, which affects 25% to 40% of individuals over the age of 65 years, is associated with depression, difficulty communicating, and reduced mobility.[1] Clinicians using casual assessment in the office overlook significant hearing loss about half the time.[2] The causes of hearing loss are either neurosensory (i.e., damage to the auditory nerve or cochlear hair cells) or conductive (i.e., damage to the parts of the ear that conduct sound from air to the cochlea). Most neurosensory hearing loss is due to presbycusis (the degenerative hearing loss of aging). Less common causes are Ménière disease and acoustic neuroma. The most common causes of conductive loss are impacted cerumen, otitis media, perforated eardrum, and otosclerosis.[1]

II. TECHNIQUE

A. WHISPERED VOICE TEST

Many tests of hearing are available to general clinicians, some more formal (handheld audiometer) than others (listening to whisper, watch, finger rub, or tuning fork). One validated test not requiring special tools is the whispered voice test. In this test, the clinician whispers a combination of three letters or numbers (e.g., "5, B, 6") while standing at arm's length (i.e., about 2 feet) behind the patient, and then asks the patient to repeat the sequence. If the patient answers correctly, hearing is considered normal and testing is stopped. If the patient misidentifies any of the three items, the clinician repeats different triplets of numbers or letters one or two more times. If 50% or more of the items in the two or three triplets are incorrect, the test is abnormal.

The clinician stands behind the patient to prevent lip reading. Only one ear is tested at a time, the other being masked by the examiner's finger, which occludes the external auditory canal and makes continuous circular rubbing motions (occlusion without rubbing is insufficient masking). The clinician should quietly exhale before whispering to produce the quietest whisper possible.[3]

B. FINGER RUB TEST

The clinician stands directly in front of the patient with outstretched arms and tests one ear at a time by rubbing the thumbs against the distal fingers (Fig. 22-1).[4] During testing, the patient has the eyes closed and is

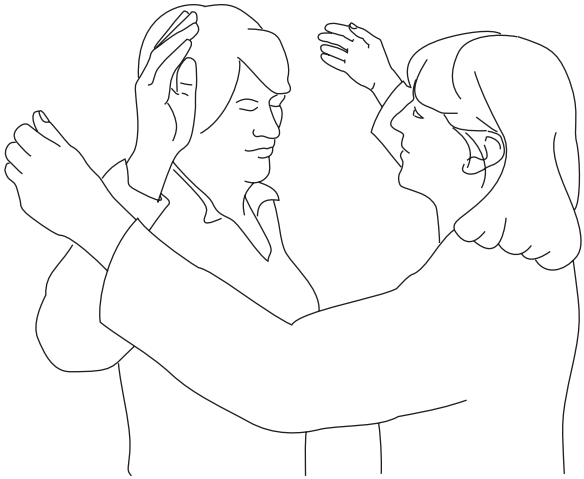


FIGURE 22-1 Finger rub test. In this illustration, the clinician is testing the patient's right ear, and the patient indicates by raising the right arm that the sound of the finger rub is perceived (i.e., "test negative" defined as the patient *can* hear the finger rub). In the original study of this finding,[4] each ear was tested three times (with both faint and strong stimuli), and "cannot hear finger rub" was defined as failure to hear any of the three stimuli. Because the patient must raise the arm to indicate the side on which the stimulus is heard, masking the untested ear is unnecessary (i.e., if the right ear is being tested in a patient with severe unilateral right hearing loss, the clinician would be able to detect that the unmasked left ear is detecting the sound because the left arm is raised).

encouraged to listen very carefully to indicate on which side the rubbing is heard by raising the ipsilateral arm. A *strong* finger rub is as loud as the clinician can muster without snapping the fingers; a *faint* rub is the softest the clinician can still hear. *Inability* to hear the finger rub is rated as "test positive."

C. TUNING FORK TESTS

1. Introduction

Once hearing loss is identified, tuning fork tests distinguish neurosensory from conductive loss. All tuning fork tests are based on the same fundamental principle, discovered almost 500 years ago*: Sound conducts preferentially through bone to ears with disease causing conductive hearing loss. Tuning fork tests were introduced into clinical otology in the early 1800s, and at one time there were over 15 distinct tuning fork tests.[6] After introduction of audiometry, however, enthusiasm for tuning fork tests waned, and now only two are commonly used, the Weber test and the Rinne test.

2. The Frequency of the Tuning Fork

Most authorities recommend using the 512-Hz tuning fork for tuning fork tests[7] because frequencies above 512 Hz detect conductive hearing loss less well and because frequencies of 128 Hz or lower generate so many

*The Italian physician Capivacci made this discovery after connecting his subject's teeth to a zither and then plucking the zither's strings.[5]

vibrations that even patients without hearing can sense them.[8–10] The 512-Hz fork is preferred to the 256-Hz fork because the 256-Hz fork produced more false-positive results in some studies.[11,12]

3. Method of Striking the Fork

Most authorities recommend striking the fork against a soft surface, such as a rubber pad or the muscles of the forearm.[7] The principal tone produced is the same whether the tines are struck on a soft or harder surface, but the harder surface generates multiple overtones that may confound interpretation by the patient.[6] Weights, sometimes added to the tines to minimize overtones, also shorten the time of vibration and are not recommended.

4. Weber Test

In this test, the clinician strikes the fork, places it in the middle of the patient's vertex, forehead, or bridge of nose, and asks, "Where do you hear the sound?" (Fig. 22-2). In patients *with unilateral hearing loss*, the sound is

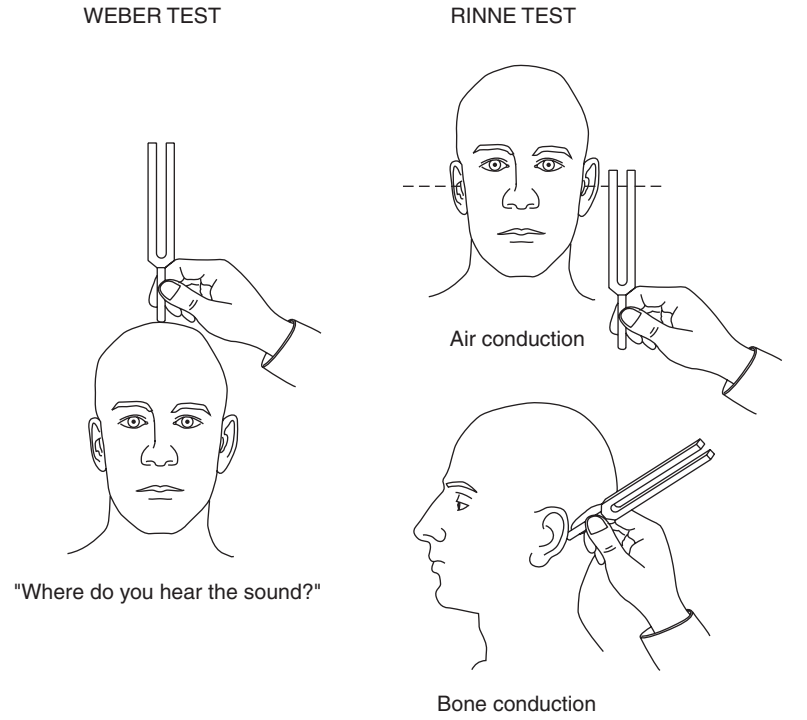


FIGURE 22-2 Weber and Rinne tuning fork tests. In the Weber test *(left),* the clinician holds the vibrating tuning fork in the midline against the patient's vertex, forehead, or bridge of nose and asks, "Where do you hear the sound?" In the Rinne test *(right),* the clinician tests one ear at a time, comparing perception of sound conducted through air *(top right)* to perception of sound conducted through bone *(bottom right).* When testing air conduction, the tuning fork is held so that an axis through both external auditory canals *(dashed line)* passes through both tines of the fork. When testing bone conduction, the stem of the vibrating fork is held against the mastoid.

preferentially heard in the *good* ear if the loss is neurosensory and in the *bad* ear if the loss is conductive.[7,13] Weber himself recommended placing the vibrating fork on the incisors,[14] and subsequent studies do show that this is the most sensitive technique,[15] although concerns about transmitting infectious diseases now prohibit this method.

According to traditional teachings, persons with normal hearing perceive the sound in the midline or inside the head, but studies show that up to 40% of normal-hearing persons also lateralize the Weber test.[10] The Weber test should therefore be interpreted only in patients with hearing loss.

5. Rinne Test

In the Rinne (pronounced "RIN-neh") test, the clinician tests each ear individually to determine whether that ear detects sound better through air or bone (see Fig. 22-2). Air conduction (AC) is tested by holding the vibrating fork about 2.5 cm away from the ear, with the axis joining the tips of the tines in line with the axis through both external auditory canals.* Bone conduction (BC) is tested by holding the stem of the vibrating fork against the mastoid.[16] (Excessive force should be avoided because it diminishes the test's specificity.) There are two methods for comparing air and bone conduction.

1. Loudness comparison technique, in which the fork is held for about 2 seconds in each position and the patient indicates which position is louder
2. Threshold technique, in which the clinician uses a stopwatch to time how long the patient hears the sound, from the moment the fork is struck to when the sound disappears, first for air conduction and then for bone conduction[7]

Patients with normal hearing or neurosensory hearing loss perceive sound better (i.e., louder or longer) through air conduction than through bone conduction, whereas those with conductive hearing loss perceive it better through bone conduction. According to a confusing tradition, this result is recorded "Rinne negative," although it is more explicit to record "BC > AC" for the abnormal result.

Table 22-1 presents examples of different Weber test and Rinne test results and possible interpretations.

III. CLINICAL SIGNIFICANCE

A. WHISPERED VOICE TEST

EBM Box 22-1 reveals that the abnormal whispered voice test accurately increases the probability of significant hearing loss (i.e., >30 dB; LR = 6) and the normal test practically excludes significant hearing (LR = 0.03).

*During air conduction, the orientation of the tines of the fork is important because sound waves emanate in two directions from the fork: one direction parallel to the axis of the tines and the other perpendicular to it. If the tines are held at an oblique angle, these sound waves may actually cancel each other out and diminish the sound.[6] Clinicians can easily convince themselves of this by rotating the stem of a vibrating fork near their own ear, noting that the sound intermittently disappears.

TABLE 22-1 Traditional Interpretation of Tuning Fork Tests*

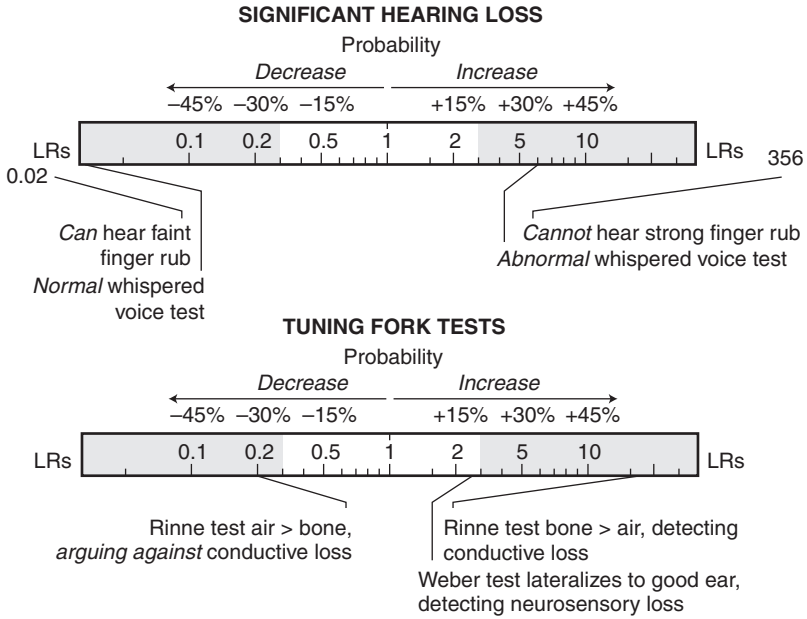
Weber Test	Rinne Test	Possible Interpretations
Midline	AC > BC, bilateral	1. Normal hearing, bilateral 2. Neurosensory loss, bilateral
Louder in left	BC > AC, left AC > BC, right	1. Conductive loss, left
Louder in left	AC > BC, bilateral	1. Normal hearing, bilateral 2. Neurosensory loss, worse on right
Louder in right	BC > AC, bilateral	1. Conductive loss, bilateral but worse on right 2. Conductive loss on right and severe neurosensory loss on left†

*From reference 7.
†Some patients with severe neurosensory loss have the finding BC > AC because the BC stimulus is cross-heard by the better cochlea on the side not being tested.
AC, air conduction; BC, bone conduction.

EBM BOX 22-1
*Hearing Tests**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Hearing Tests				
Abnormal whispered voice test[2,3,17]	90-99	80-87	**6.0**	**0.03**
Cannot hear *strong* finger rub[4]	61	100	**355.4**	0.4
Cannot hear *faint* finger rub[4]	98	75	**3.9**	**0.02**
Tuning Fork Tests (Patients with Unilateral Hearing Loss)				
Rinne test, detecting conductive hearing loss[12,18]	60-90	95-98	16.8	0.2
Weber test lateralizes to good ear, detecting neurosensory loss[10]	58	79	2.7	NS
Weber test lateralizes to bad ear, detecting conductive loss[10]	54	92	NS	0.5

*Diagnostic standard: For *hearing loss*, mean pure tone threshold >25 dB (finger rub test) or >30 dB (whispered voice test) on audiometry; for *conductive hearing loss (Rinne test)*, air–bone gap on audiometry ≥20 dB.
†Definition of findings: For *abnormal whispered voice test* and *finger rub test*, see text; for *Rinne test*, bone conduction (BC) greater than air conduction (AC), using the loudness comparison technique; all tuning fork tests used 512-Hz tuning fork.
‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. NS, not significant.
Click here to access calculator.



B. FINGER RUB TEST

In a study of 221 outpatients to a neurology clinic, the *inability* to hear the *strong* finger rub is pathognomonic for hearing loss (LR = 355.4), whereas the *ability* to hear the *faint* finger rub indicates that the patient's hearing was normal on that side (LR = 0.02).

C. TUNING FORK TESTS

Using the loudness comparison technique, the Rinne test accurately detects conductive hearing loss. The finding of "BC > AC" increases the probability of an audiometric air–bone gap of more than 20 dB (LR = 16.8; see EBM Box 22-1); the finding of "AC > BC" decreases the probability of an air–bone gap this large (LR = 0.2). The larger the patient's air–bone gap on audiometry, the more likely that the Rinne test will reveal "BC > AC." (For comparison, the mean air–bone gap in otosclerosis and otitis media is 21 to 27 dB.[12,18,19])

The Weber test, on the other hand, is less accurate. When the sound lateralizes to the good ear in patients with unilateral hearing loss, the probability of neurosensory hearing loss increases only by a small amount (LR = 2.7). The Weber test performs poorly because many patients with unilateral hearing loss, whether neurosensory or conductive, localize the tuning fork sound in the midline.[10]

Tuning fork tests cannot distinguish normal hearing from bilateral neurosensory losses (see Table 22-1) and thus should always follow hearing tests. Moreover, tuning fork tests cannot distinguish a pure conductive loss from a mixed conductive and neurosensory defect (see Table 22-1).

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 23

Thyroid and Its Disorders

GOITER

I. INTRODUCTION

In industrialized areas of the world, goiter (i.e., enlarged thyroid) occurs in up to 10% of women and 2% of men, the usual causes being multiple nodules, Hashimoto thyroiditis, or Graves disease.[1] (The most common cause worldwide is endemic goiter, largely from inadequate iodine intake.) About 80% of patients with goiter are clinically euthyroid; 10% are hypothyroid, and 10% are hyperthyroid. Most patients are asymptomatic or present for evaluation of a neck mass. A few patients, especially those with substernal goiters, present with dyspnea, stridor, hoarseness, or dysphagia (see the section on Substernal Goiters).

Endemic goiter has been described for millennia, although it is unclear whether early clinicians distinguished goiter from other causes of neck swelling such as tuberculous lymphadenitis. The first person to clearly differentiate cystic goiter from cervical lymphadenopathy was Celsus, the Roman physician writing in AD 30.[2]

II. TECHNIQUE

A. NORMAL THYROID[3]

The important landmarks for locating the thyroid gland are the V at the top of the thyroid cartilage (the *laryngeal prominence* of the thyroid cartilage) and the cricoid cartilage (Fig. 23-1). These two structures, which are usually 3 cm apart, are the most conspicuous structures in the midline of the neck. The isthmus of the normal thyroid lies just below the cricoid cartilage and is usually 1.5 cm wide, covering the second through fourth tracheal rings. Each lateral lobe of the thyroid is 4 to 5 cm long and hugs the trachea tightly, extending from the middle of the thyroid cartilage down to the fifth or sixth tracheal ring. A pyramidal lobe is found in up to 50% of anatomic dissections, usually on the left side, and is palpable in 10% of nontoxic goiters but seldom palpable in normal-sized glands.

The thyroid has a constant relationship with the laryngeal prominence (which is about 4 cm above the thyroid isthmus) and the cricoid cartilage (which is just above the isthmus), but the position of these structures in the neck (and thus of the thyroid in the neck) varies considerably among patients (see Fig. 23-1).[4] If the laryngeal prominence and suprasternal

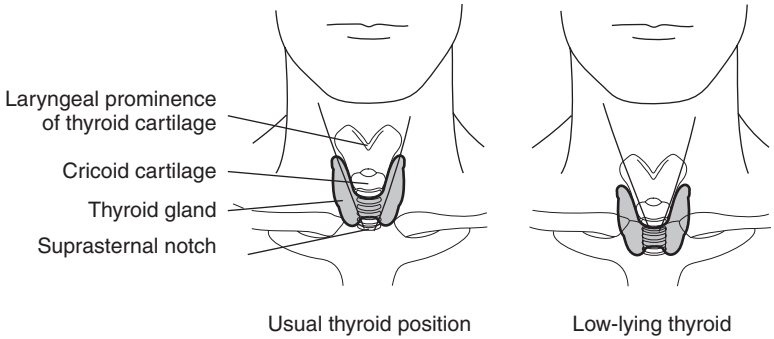


FIGURE 23-1 The normal thyroid. The thyroid gland has a constant relationship with the two most prominent landmarks of the middle of the neck—the laryngeal prominence of the thyroid cartilage and the cricoid cartilage. On the left is the usual position of the thyroid gland. On the right is a "low-lying" thyroid, most of which is hidden behind the clavicles and sternum, inaccessible to palpation.

notch of the manubrium are far apart (separated by >10 cm), the patient may have a conspicuous "high-lying" thyroid, which resembles a goiter even though it is normal sized. (See the section on Pseudogoiter.) If the laryngeal prominence is close to the suprasternal notch (separated by <5 cm), the patient has a "low-lying" thyroid, which often is concealed behind the sternocleidomastoid muscles and clavicles, making complete palpation of the gland impossible.[4,5] Low-lying thyroids are more common in elderly patients.

In areas of the world with iodine-replete diets, the normal thyroid is less than 20 mL in volume.[6]

B. EXAMINATION FOR GOITER

1. Inspection

Two maneuvers make the thyroid more conspicuous.

1. Extending the patient's neck, which lifts the trachea (and thyroid) about 3 cm away from the suprasternal notch and stretches the skin against the thyroid
2. Inspecting the patient's neck from the side

In patients with normal- or high-lying thyroids, the line between the cricoid prominence and suprasternal notch, when viewed from the side, should be straight. Anterior bowing of this line suggests a goiter (Fig. 23-2).[7]

2. Palpation

Palpation of the thyroid may proceed from the patient's front or back, whichever is most comfortable and effective for the clinician, because studies fail to show either method to be superior.[8] The patient's neck should be slightly flexed (to relax the sternocleidomastoid and sternohyoid muscles), and a firm technique should be used. The following features should be noted: thyroid size, consistency (i.e., soft, firm, or hard; a "soft" thyroid has the consistency of the surrounding tissue in the neck), texture (diffuse

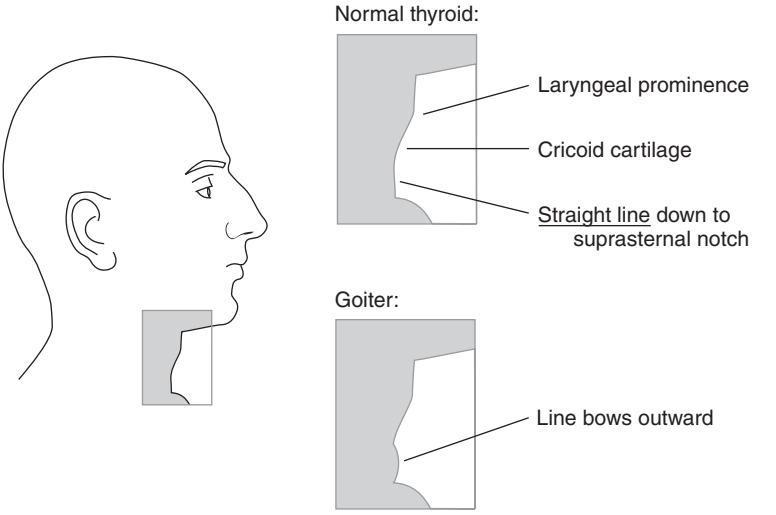


FIGURE 23-2 Neck contour and goiter. The shaded profile of the neck *(left)* is enlarged on the right, to contrast the normal thyroid contour with that of a goiter. Below the cricoid cartilage, the contour of the normal neck in the midline *(top right)* is a straight line downward to the suprasternal notch. In patients with goiter, this line bows outward *(bottom right)* because of enlargement of the thyroid isthmus. This line is visible only in patients with normal-lying and high-lying thyroids, not low-lying thyroids (see Fig. 23-1).

or nodular), tenderness, tracheal deviation (a clue to asymmetrical goiter), and lymphadenopathy.

3. Observing the Patient Swallow[9]

Because the thyroid and trachea are firmly attached by ligaments and must move together, observation during a patient swallow helps distinguish thyroid tissue from other neck structures. During a normal swallow, both the thyroid and trachea make an initial upward movement of 1.5 to 3.5 cm; the larger the oral bolus, the greater the movement. The thyroid and trachea then hesitate for 0.2 to 0.7 seconds before returning to their original position.

A neck mass is probably *not* in the thyroid, therefore, if one of the following is detected.

1. The mass is immobile during a swallow or it moves less than the thyroid cartilage.
2. The mass does not hesitate before descending to its original position.
3. The mass returns to its original position before complete descent of the thyroid cartilage.

III. THE FINDINGS

A. CERVICAL GOITER

Common definitions of goiter include the following.

1. **Rule of thumb.** This states that a lateral lobe is enlarged if it is larger than the distal phalanx of the patient's thumb.

2. **Estimates of thyroid volume by palpation**. For example, a thyroid whose lateral lobes each measure 3 cm wide, 2 cm deep, and 5 cm long would have an estimated volume of 60 mL (i.e., $2 \times 3 \times 2 \times 5 = 60$). Any estimate more than 20 mL is classified as a goiter (i.e., each lateral lobe is normally <10 mL).
3. **Epidemiologic definitions of goiter.** These definitions are designed for clinicians who survey large numbers of persons rapidly in areas of endemic goiter. (Some clinicians examine 150 to 200 patients per hour.) The revised World Health Organization definition has three grades:
   Grade 0—no palpable or visible goiter
   Grade 1—goiter that is palpable *but not visible* with the head in the normal position
   Grade 2—a goiter that is clearly visible when the neck is in a normal position[10]

B. SUBSTERNAL AND RETROCLAVICULAR GOITERS

Large goiters may extend from the neck to the superior mediastinum, passing through the inflexible thoracic inlet (i.e., the bony ring formed by the upper sternum, first ribs, and first thoracic vertebral body). At the thoracic inlet, such goiters may compress the trachea, esophagus, or neck veins and thus produce dyspnea, dysphagia, facial plethora, cough, and hoarseness. Sometimes, when these patients flex or elevate the arms, the thoracic inlet is pulled up into the cervical goiter, just as if the thyroid were a cork and the thoracic inlet were the neck of a bottle. This causes the characteristic **Pemberton sign,** which is congestion of the face, cyanosis, and eventual distress induced by arm elevation (Fig. 23-3).[11–13] The exact frequency of Pemberton sign is unknown. In two small series of patients with substernal goiter, it was present in every patient,[14,15] whereas two other larger series did not mention the sign at all.[16,17]

In patients with substernal goiters, associated findings include cervical goiter (i.e., palpable goiter above the thoracic inlet, 86% of patients), tracheal deviation (33% by palpation, 75% by chest radiograph), distention of neck veins (22%), and stridor (10%).

C. THYROGLOSSAL CYST[18]

Thyroglossal cysts are cystic swellings of the thyroglossal duct, an epithelium-lined remnant marking the embryologic descent of thyroid tissue from the base of the tongue to its final location anterior to the larynx. Thyroglossal cysts present at any age, appearing as tense, nontender, mobile, nonlobulated round tumors, usually at the level of the hyoid bone or just below it. (The hyoid bone is *above* the thyroid cartilage.) Pain and tenderness may follow infection or acute hemorrhage into the capsule. The cysts are in the midline of the neck, unless they are so low that they lie to one side of the thyroid cartilage. Despite their cystic structure, they do not usually transilluminate. If the cyst remains attached to the base of the tongue or hyoid bone, a characteristic physical sign of thyroglossal cysts is upward movement when the patient protrudes the tongue, just as if the two

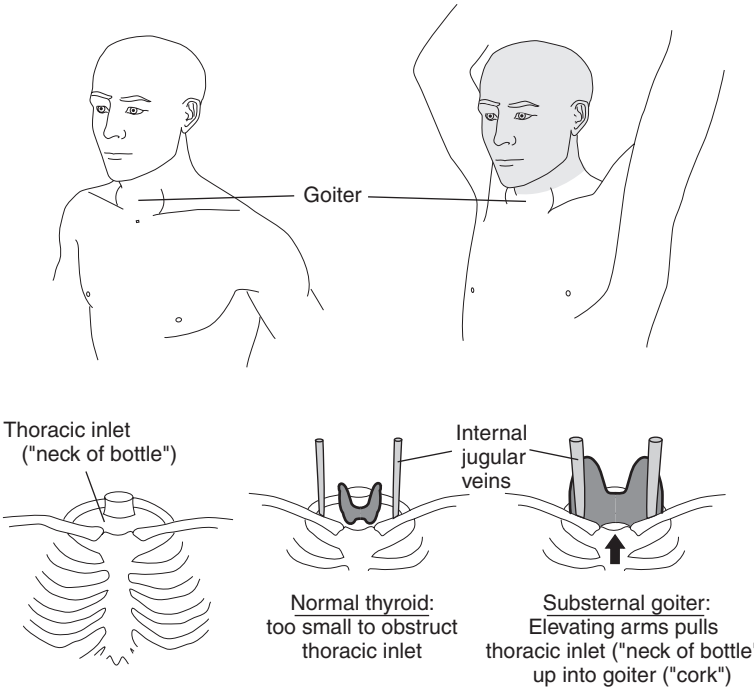


FIGURE 23-3 Pemberton sign. If a patient with retrosternal goiter elevates the arms *(top row),* dramatic facial congestion may occur (i.e., positive Pemberton sign). This occurs because the thoracic inlet ("neck of the bottle," *bottom left*) is an inflexible bony ring formed by the first thoracic vertebra, first ribs, and upper sternum. (Its outline is about the same size and shape as the patient's kidney.) A normal-sized thyroid *(bottom middle)* is too small to obstruct the thoracic inlet. In contrast, a goiter of sufficient size *(bottom right)* may obstruct the thoracic inlet, especially if the goiter extends below the sternum and the patient elevates the arms (which pulls the thoracic inlet, or "neck of the bottle," up into the goiter, or "cork," *arrow*).

structures were connected by a string. Thyroglossal cysts account for three quarters of congenital neck masses, the other one quarter being branchial cleft cysts, which are located more laterally, usually anterior to the sternocleidomastoid muscle at the level of the hyoid bone.[19,20]

D. PSEUDOGOITER

Pseudogoiter refers to a thyroid gland that appears enlarged even though it is normal sized. There are three causes.

1. **High-lying thyroid gland,** which, although normal sized, lies so high in the neck it is unusually conspicuous after neck extension. In these patients, the laryngeal prominence is 10 cm or more above the suprasternal notch, and both thyroid lobes are smaller than the distal phalanx of the patient's thumb. In one study, high-lying but normal-sized thyroids accounted for 8% of suspected goiters referred to an endocrinology service.[4]

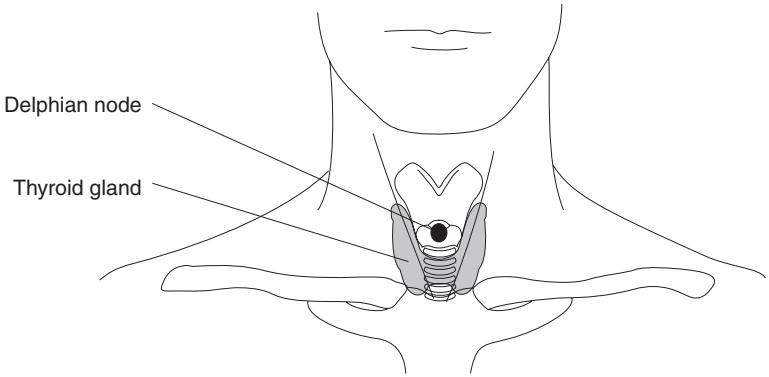


FIGURE 23-4 The Delphian node. The Delphian node lies in the midline of the neck, just above the thyroid isthmus and in front of the cricothyroid ligament, where it can easily be palpated against the unyielding cricoid cartilage.

2. **Other cervical masses,** such as adipose tissue, cervical lymphadenopathy, branchial cleft cysts, and pharyngeal diverticula (see Chapter 25). Observation during swallowing helps identify these lesions.
3. **Modigliani syndrome,** which describes a normal-sized thyroid lying in front of an exaggerated cervical spine lordosis,[21] named after the painter Amedeo Modigliani, whose portraits had subjects with long, curved necks.

E. THE DELPHIAN NODE

The Delphian node, a lymph node that drains the thyroid gland and larynx, lies directly anterior to the cricothyroid ligament (just cephalad to the thyroid isthmus; Fig. 23-4). When enlarged, the node is readily palpable because of its superficial location in front of the unyielding trachea. The node is called *Delphian* because it is the first one exposed during surgery, and its appearance often foretells what the surgeon will find in the thyroid (e.g., carcinoma), just as the oracle at Delphi foretold the future.* The Delphian node enlarges in some patients with thyroid cancer, Hashimoto thyroiditis, and laryngeal cancer. Its involvement in both laryngeal and thyroid cancer is associated with a worse prognosis.[23,24]

IV. CLINICAL SIGNIFICANCE

A. DETECTING GOITER

The findings listed in EBM Box 23-1 are categorized into three levels.

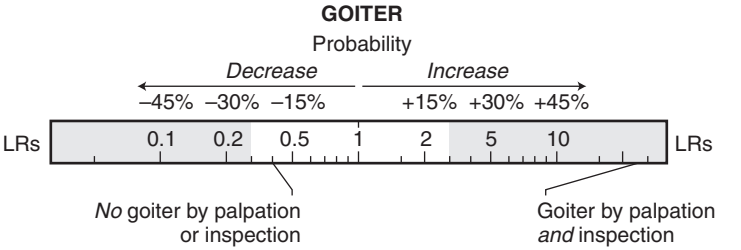
1. No goiter by palpation or inspection (including inspection of the extended neck)
2. Goiter by palpation, but the gland is not conspicuous until the patient's neck is extended

*The word *Delphian* was originally suggested by Raymond Randall, a fourth-year medical student attending the thyroid clinic at The Massachusetts General Hospital.[22]

EBM BOX 23-1
*Goiter**

Finding (Reference)	Sensitivity (%)	Specificity (%)	Likelihood Ratio† if Finding Is Present
No goiter by palpation or inspection[7,25–29]	5-57	0-26	0.4
Goiter by palpation, visible only after neck extension[25]	13	—	NS
Goiter by palpation and inspection with neck in normal position[25–27,29]	43-82	88-100	**26.3**

*Diagnostic standard: For *goiter,* ultrasound volume >20 mL,[25–27,29] ultrasound volume >18 mL (women) or >25 mL (men),[28] or surgical weight >23 g.[7]
†Likelihood ratio (LR) if finding present = positive LR.
NS, not significant.
Click here to access calculator.



3. Goiter by palpation and inspection with the neck in the normal position

The first finding, absence of goiter by inspection and palpation, decreases the probability of an enlarged thyroid modestly (likelihood ratio [LR] = 0.4; see EBM Box 23-1). Although up to half of patients with enlarged glands by ultrasonography have this finding, these goiters are presumably small. The intermediate finding (i.e., goiter by palpation but visible only after neck extension) fails to distinguish goiter from normal-sized glands (LR not significant), suggesting that subtle enlargement by palpation, not confirmed by inspection of the neck in the normal position, is an unreliable sign of goiter. A gland that is both enlarged by palpation and visible when the neck is in the normal position greatly increases the probability of an enlarged thyroid (LR = 26.3).

B. ETIOLOGY OF GOITER

In clinically euthyroid patients with goiter, the most common causes are multinodular goiter or Hashimoto thyroiditis. In hypothyroid patients, it is Hashimoto thyroiditis, and in hyperthyroid patients, it is Graves disease

or multinodular goiter. The associated finding of ophthalmopathy (tearing, diplopia, proptosis) or dermopathy (pretibial myxedema) indicates Graves disease. (See the section on Graves Ophthalmopathy.)

Although thyroid cancer can also cause a goiter, cancer usually presents instead as a thyroid nodule. (See the section on Thyroid Nodule.) Three findings increase the probability that a goiter contains carcinoma: vocal cord paralysis (LR = 45.2; EBM Box 23-2), cervical adenopathy (LR = 15.4), and fixation of the goiter to surrounding tissues (LR = 10.5).

Silent and postpartum lymphocytic thyroiditis may also produce a goiter, but it is rarely prominent and the clinician's attention is instead directed toward the findings of hyperthyroidism or hypothyroidism.[34] The finding of a painful or tender thyroid gland, sometimes mimicking pharyngitis, suggests subacute thyroiditis[35] or hemorrhage into a cyst or nodule (although most thyroid hemorrhage is painless).[36] In subacute thyroiditis, the thyroid is modestly enlarged, usually 1.5 to 3 times the normal size.

THYROID NODULES

I. INTRODUCTION[37]

Palpable thyroid nodules occur in about 5% of women and 1% of men, most of whom are clinically euthyroid. Although thyroid nodules raise concerns about thyroid cancer, over 95% of nodules reflect benign disorders, such as colloid cysts, adenomas, or dominant nodules of a multinodular gland.

II. OCCULT NODULES

Because thyroid nodules are palpable in only 1% to 5% of persons yet are discovered in up to 50% of patients during ultrasound or autopsy surveys,[38] it is obvious that most thyroid nodules are "occult" (i.e., detectable by clinical imaging but not by palpation). Furthermore, when the clinician feels a single *palpable* nodule in the patient's thyroid gland, ultrasonography reveals multiple nodules half the time.[39] Occult nodules are not palpable, because either the patient's neck is too short or too thick,[40] the nodules are buried in the posterior parts of the gland,[41] or the nodules are too small (i.e., the mean diameter of a *palpable* nodule is 3 cm; palpation fails to detect 50% of nodules <2 cm in diameter and over 90% of nodules <1 cm in diameter).[40]

III. CLINICAL SIGNIFICANCE

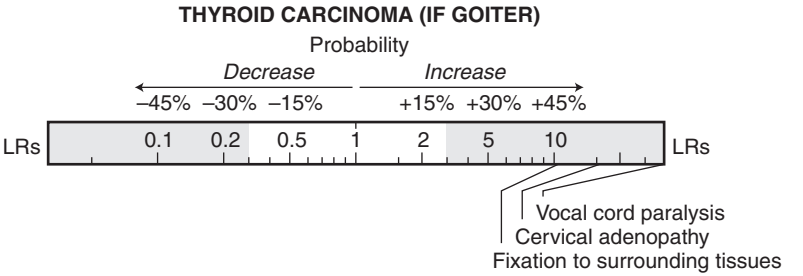
The most important diagnostic test for thyroid nodules is fine-needle aspiration. Nonetheless, a few signs, if present, increase the probability of carcinoma in thyroid nodules (see EBM Box 23-2): vocal cord paralysis (LR = 17.9), fixation of the nodule to surrounding tissues (LR = 7.8), and cervical adenopathy (LR = 7.2). All of these findings, however, are insensitive: Only one of three patients with thyroid carcinoma (at most) have any of these findings.

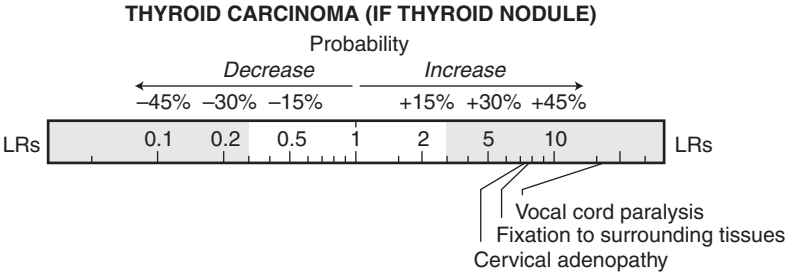
EBM BOX 23-2

*Goiter and Thyroid Nodule Findings That Predict Carcinoma**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Goiter				
Vocal cord paralysis[30]	24	99	**45.2**	0.8
Cervical adenopathy[30]	45	97	**15.4**	0.6
Fixation to surrounding tissues[30]	60	94	**10.5**	0.4
Goiter nodular (vs. diffuse)[30]	78	49	1.5	0.4
Pyramidal lobe present[30]	3	90	NS	NS
Thyroid Nodule				
Vocal cord paralysis[31,32]	5-14	99-100	**17.9**	NS
Fixation to surrounding tissues[31,33]	13-37	95-98	**7.8**	NS
Cervical adenopathy[31,32]	24-31	96-97	**7.2**	0.8
Diameter ≥4 cm[33]	66	66	1.9	0.5
Very firm nodule[31]	3	99	NS	NS

*Diagnostic standard: For *carcinoma*, pathologic examination of tissue.[30–33]
†Definition of findings: For *vocal cord paralysis*, direct visualization of vocal cords.
‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.
NS, not significant.
Click here to access calculator.





HYPOTHYROIDISM (MYXEDEMA)

I. INTRODUCTION

Hypothyroidism is a clinical syndrome that results from diminished levels of thyroid hormone, which reduces the patient's metabolic rate, slows neuromuscular reactions, and causes accumulation of mucopolysaccharides in skin and other tissues throughout the body. In areas of the industrialized world with iodine-replete diets, hypothyroidism affects 9% of women and 1% of men.[1] The usual cause is disease in the thyroid gland itself (primary hypothyroidism), most often from Hashimoto thyroiditis (60% to 70% of cases) or previous radioiodine treatment for Graves disease (20% to 30% of cases).[1]

The diagnosis of hypothyroidism relies on laboratory tests, which have been available for over 100 years.* Nonetheless, bedside diagnosis is still essential for two reasons.

1. Examination estimates the likelihood of thyroid disease, which then can be used to identify subgroups of patients with high or low probability of abnormal thyroid function, thus increasing the yield of laboratory testing.
2. Examination is essential when diagnosing subclinical hypothyroidism or sick euthyroid syndrome, conditions that by definition describe patients with abnormal laboratory tests but without bedside findings of thyroid disease.

All of the classic bedside findings of hypothyroidism—puffy skin, slow reflexes, thick speech, and sluggish thinking—were first described by William Gull and William Ord in the 1870s.[43,44]

II. FINDINGS AND THEIR PATHOGENESIS

A. SKIN AND SOFT TISSUE[45,46]

The nonpitting puffiness of hypothyroidism results from dermal accumulation of mucopolysaccharides (mostly hyaluronic acid and chondroitin sulfate), which freely bind water. These changes cause a "jelly-like swelling (and) overgrowth of mucus-yielding cement," which led Ord to coin the term **myxedema** in 1877.[44] Even after effective thyroid replacement, these changes may persist for months.

Some myxedematous patients also have a yellow tint to their skin, which occurs because of hypercarotinemia from diminished conversion of carotenoids to retinol. The apparent coolness of the skin is attributed to diminished dermal blood flow, and dryness results in part from decreased sebum production. The loss of hair from the lateral eyebrows occurs in some hypothyroid patients but is one of the least specific signs (see later).

*The first thyroid test was the basal metabolic rate (BMR) (i.e., oxygen consumption), introduced in the 1890s; radioactive iodine uptake testing appeared in the 1940s; serum protein-bound iodide (PBI) testing in the 1950s; serum total thyroxine (T_4) testing in the 1960s; and sensitive assays for thyroid-stimulating hormone in the 1980s.[42]

B. THE ACHILLES REFLEX

The ankle jerk has been investigated more extensively than any other physical finding of thyroid disease. By the 1970s, at least nine different instruments had been designed to precisely measure the duration of reflex to the nearest millisecond (ms). Both the contraction and relaxation phases of the ankle jerk are prolonged in hypothyroidism, although prolonged relaxation seems most prominent to the human eye (and on many of the tracings of the reflex). In one study, the mean half-relaxation time (i.e., the time from the hammer tap to the moment the Achilles tendon has returned halfway to its original position) for hypothyroid patients was 460 ms (standard deviation [SD], 40 ms), compared with 310 ms (SD, 30 ms) for euthyroid patients.[47] Experiments in hypothyroid rats suggest that the prolongation results from diminished calcium transport by the sarcoplasmic reticulum and subsequent slowing of the interaction between actin and myosin.[48]

When testing for hypothyroidism, clinicians usually elicit the ankle jerk by tapping on the Achilles tendon with the patient kneeling on a chair.* The force of the tap does not affect the duration of the reflex, although slightly more force is necessary in hypothyroid patients to generate a reflex than in hyperthyroid patients.

C. HYPOTHYROID SPEECH

Hypothyroid speech, seen in about one third of patients with hypothyroidism, has a slow rate and rhythm and is characteristically deep, low-pitched, and hyponasal (i.e., as if the patient has a cold).[50] Some patients even slur their words slightly, leading one clinician to describe the hypothyroid voice as "a bad gramophone record of a drowsy, slightly intoxicated person with a bad cold and a plum in the mouth."[51] Biopsies of vocal cords have revealed deposition of mucinous material.

D. OBESITY

Obesity is no more common in hypothyroid patients than in euthyroid patients.[52]

III. CLINICAL SIGNIFICANCE

EBM Box 23-3 summarizes the diagnostic accuracy of physical signs associated with hypothyroidism, as applied to over 1500 patients with suspected thyroid disease. The **Billewicz scoring scheme,** which combines symptoms and signs, is fully described in Table 23-1.

In patients with suspected thyroid disease, the findings increasing the probability of hypothyroidism the most are hypothyroid speech (LR = 5.4; see EBM Box 23-3), cool *and* dry skin (LR = 4.7), slow pulse rate (LR = 4.2),

*Other muscle stretch reflexes may also be delayed in hypothyroidism, as illustrated in an online video of a delayed biceps reflex.[49]

EBM BOX 23-3
*Hypothyroidism**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Skin				
Cool and dry skin[53]	16	97	**4.7**	0.9
Coarse skin[54,55]	29-61	74-95	**3.4**	0.7
Cold palms[54]	37	77	NS	NS
Dry palms[54]	42	73	NS	NS
Periorbital puffiness[54,55]	53-91	21-81	NS	0.6
Puffiness of wrists[54]	39	86	2.9	0.7
Hair loss of eyebrows[54]	29	85	1.9	NS
Pretibial edema[55]	78	31	NS	NS
Speech				
Hypothyroid speech[54]	37	93	**5.4**	0.7
Pulse				
Slow pulse rate[53,55,56]	29-43	89-98	**4.2**	0.7
Thyroid				
Enlarged thyroid[53]	46	84	2.8	0.6
Neurologic Findings				
Delayed ankle reflexes[55]	48	86	**3.4**	0.6
Slow movements[55]	87	13	NS	NS
Billewicz Score[57,58]				
Less than −15 points	3-4	28-68	**0.1**	—
−15 to +29 points	35-39	—	NS	—
+30 points or more	57-61	90-99	**18.8**	—

*Diagnostic standard: For *hypothyroidism*, low free T_4 level and high thyroid-stimulating hormone (TSH) level,[55,56,58] or low protein-bound iodide (PBI) level.[53,54,57] The PBI level and total T_4 level correlate closely, except in patients with thyroiditis and those who ingest exogenous iodides (e.g., radiocontrast dye, cough suppressants), diagnoses in which the PBI level may be falsely high. These diagnoses, however, were largely excluded from the studies reviewed here.

†Definition of findings: For *slow pulse rate*, <60 beats/min[55,56] or <70 beats/min[53]; for *delayed ankle reflexes*, assessment of contraction and relaxation of calf muscle by naked eye[55]; for *slow movements*, patients required more than 1 minute to fold a 2-meter-long bed sheet.[55]

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

NS, not significant.

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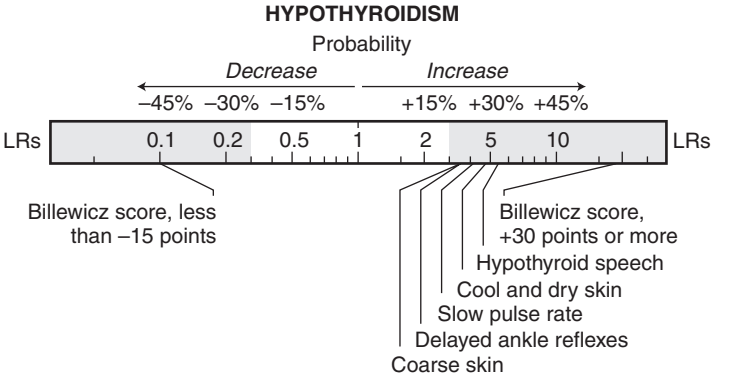

coarse skin (LR = 3.4), and delayed ankle reflexes (LR = 3.4).* Hair loss of the eyebrows was one of the least compelling diagnostic signs (LR = 1.9), and the finding of *isolated* coolness or dryness of the palms is unhelpful (LR not significant). No individual finding, when present or absent, significantly decreases the probability of hypothyroidism (i.e., no LR has a value <0.6).

A Billewicz score of +30 points or higher greatly increases the probability of hypothyroidism (LR = 18.8), whereas a score of −15 points or lower decreases the probability of hypothyroidism (LR = 0.1). The Billewicz score may perform less well in elderly patients, who, as a rule, have fewer findings than younger patients.[60]

HYPERTHYROIDISM

I. INTRODUCTION

Hyperthyroidism is a clinical syndrome due to increased production or release of thyroid hormone, which elevates the metabolic rate and causes characteristic findings of the skin, thyroid, eyes, and neuromuscular system. The most common causes of hyperthyroidism are Graves disease (60% to 90% of cases), toxic nodular goiter, thyroiditis (subacute, silent, or postpartum), and iatrogenic overtreatment with thyroid replacement.[61] Hyperthyroidism affects women (4% prevalence) more than men (0.2% prevalence).

Three clinicians—Caleb Parry, Robert Graves, and Adolf von Basedow—all writing between 1825 and 1840, independently described the classic physical signs associated with thyrotoxicosis. All three were

*Precise measurements of the ankle jerk using special instruments discriminate well between patients with and without hypothyroidism: The finding of a half-relaxation time of more than 370 to 380 ms detects hypothyroidism with a sensitivity of 91% to 99%, specificity of 94% to 97%, positive LR = 18.7, and negative LR = 0.1.[47,53,59]

TABLE 23-1 Billewicz Diagnostic Index for Hypothyroidism*

Finding†	Points Scored if Finding Is	
	Present	*Absent*
SYMPTOMS		
Diminished sweating	+6	−2
Dry skin	+3	−6
Cold intolerance	+4	−5
Weight increase	+1	−1
Constipation	+2	−1
Hoarseness	+5	−6
Paresthesias	+5	−4
Deafness	+2	0
PHYSICAL SIGNS		
Slow movements	+11	−3
Coarse skin	+7	−7
Cold skin	+3	−2
Periorbital puffiness	+4	−6
Pulse rate <75/min	+4	−4
Slow ankle jerk	+15	−6

*Source: Reference 57.

†Definition of findings: For *weight increase,* recorded increase in weight or tightness of clothing; for *slow movements*, observations while patient is removing and replacing a buttoned garment; for *coarse skin,* roughness and thickening of skin of hands, forearms, and elbows; for *slow ankle jerk*, reflex appears slow with patient kneeling on a chair, grasping its back.

especially impressed with the triad of goiter, prominent eyes, and forceful tachycardia.[62]

II. FINDINGS AND THEIR PATHOGENESIS

A. THE THYROID

A goiter is present in 70% to 93% of patients with hyperthyroidism.[63–65] The goiter is diffuse and symmetrical in patients with Graves disease and thyroiditis but nodular in those with toxic nodular goiter.[65]

A thyroid bruit is a common feature of Graves disease (73% of patients in one study).[66] Nonetheless, the finding also was noted in 30% of elderly patients with toxic nodular goiter,[67] suggesting that the finding is not as specific for Graves disease as is classically taught. Bruits often radiate far from their source, and perhaps the "thyroid bruit" in the elderly person with toxic nodular goiter is actually a carotid bruit made prominent by the increased cardiac output of hyperthyroidism.*

*The opposite phenomenon—a "carotid bruit" emanating from the superior thyroid artery—has also been described.[68]

B. EYE FINDINGS

Three distinct eye findings are associated with hyperthyroidism: lid lag (von Graefe sign, 1864), lid retraction (Dalrymple sign, 1849),* and Graves ophthalmopathy. Graves ophthalmopathy afflicts exclusively patients with Graves disease, whereas lid lag and lid retraction may occur in hyperthyroidism from any etiology.

1. Lid Lag

This sign describes the appearance of white sclera between the margin of the upper eyelid and the corneal limbus as the patient looks downward. In von Graefe's words, "…as the cornea looks down, the upper eyelid does not follow."[62]

2. Lid Retraction

This sign describes a peculiar staring appearance of the eyes, caused by a widened palpebral fissure. As the patient looks straight ahead, the upper eyelid is positioned abnormally high, revealing white sclera between the lid margin and the superior limbus. Normally, the margin of the upper eyelid rests just below the edge of the corneal limbus and covers about 1 mm of the iris.[71]

Both lid lag and lid retraction are attributed to the sympathetic hyperactivity of hyperthyroidism, which causes excess contraction of Müller muscle (the involuntary lid elevator whose paralysis causes the ptosis of Horner syndrome). Although the findings improve after treatment with β-blocking medications,[72] mechanisms other than sympathetic hyperactivity must contribute to the lid findings of patients with Graves disease (even those without exophthalmos or obvious ophthalmopathy; see later), because the lid findings of Graves disease may be unilateral and often persist after the patient becomes euthyroid, and because the pupils of patients with lid findings are usually normal sized (instead of the dilated pupils of sympathetic hyperactivity).[73,74]

Other common causes of lid retraction are unilateral ptosis, facial muscle weakness, previous eyelid surgery, or the irritation of wearing contact lenses.[75] Ptosis causes contralateral lid retraction because attempts to elevate the weakened lid generate excessive neural signals to the motor neuron of the healthy lid, thus elevating it.[76] A simple test confirming ptosis as the cause is to occlude the eye that has ptosis, which then causes the lid retraction in the opposite eye to resolve. Facial weakness causes retraction of the ipsilateral eyelid because the lid elevators are no longer opposed by the orbicularis oculi muscle.[77]

3. Graves Ophthalmopathy

Graves ophthalmopathy is a constellation of findings, apparent in 25% to 50% of patients with Graves disease, that results from edema and lymphocytic infiltration of orbital fat, connective tissue, and eye muscles.[78,79]

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*The British eye surgeon John Dalrymple (1803-1852) apparently thought so little of his sign that he never published a description of it. Writing in 1849, W. White Cooper attributed the sign to his friend Dalrymple.[69] Albrecht von Graefe (1828-1870) described his sign in 1864.[62] Ruedemann coined the term *lid lag* in 1932.[70]

Characteristic physical findings are lid edema, limitation of eye movements, conjunctival chemosis and injection, and exophthalmos (as measured with an exophthalmometer). Clinicians should suspect Graves ophthalmopathy when patients complain of a gritty sensation in the eyes, tearing, eye discomfort, or diplopia. The orbital swelling of Graves ophthalmopathy may threaten the optic nerve and vision. The bedside findings best predicting incipient optic neuropathy are lid edema and limitation of eye movements—not, surprisingly, the degree of proptosis.[74,80] (Proptosis does not predict incipient optic neuropathy, perhaps because intraocular pressure is relieved by the outward protrusion.)

C. CARDIOVASCULAR FINDINGS

Hyperthyroidism may cause a fast heart rate, loud snapping first heart sounds, midsystolic flow murmurs, and supraventricular arrhythmias.[81] Rare patients with severe hyperthyroidism may develop the **Means-Lerman scratch,**[82] a systolic rub or murmur with a prominent rough or grating character that appears near the left second intercostal space. Its pathogenesis is unknown.

D. SKIN FINDINGS[45,46]

The skin of hyperthyroid patients is warm, moist, and smooth, probably because of increased sympathetic tone to sweat glands and increased dermal blood flow. These skin findings often resolve after treatment with β-blocker medications.

Up to 4% of patients with Graves disease develop a skin lesion with the confusing name of **pretibial myxedema,** characterized by bilateral, asymmetrical raised firm plaques or nodules, which are pink to purple-brown in color and usually distributed over the anterior shins.[45,83]

E. NEUROMUSCULAR FINDINGS

The neuromuscular findings of hyperthyroidism are weakness and diminished exercise tolerance, tremor, and brisk ankle jerks. The diminished exercise tolerance (affecting 67% of patients) is due to an inability to increase cardiac output appropriately with exercise and to proximal muscle wasting and weakness from accelerated protein catabolism.[65,81,84] The fine tremor of hyperthyroidism occurs because of increased sympathetic tone and resolves with β-blocking medications. Brisk reflexes are noted at the bedside in only 25% of patients or less,[85] and even precise measurements of the half-relaxation time (see the section on Hypothyroidism for definition) reveal considerable overlap between normal values (range, 230 to 420 ms) and hyperthyroid values (range, 200 to 300 ms).[47]

III. CLINICAL SIGNIFICANCE

EBM Box 23-4 presents the diagnostic accuracy of physical signs for hyperthyroidism, as applied to over 1700 patients with suspected thyroid disease. The **Wayne index,** which combines symptoms and signs, is described fully in Table 23-2.

EBM BOX 23-4
*Hyperthyroidism**

Finding (Reference)	Sensitivity (%)	Specificity (%)	Likelihood Ratio† if Finding Is	
			Present	*Absent*
Pulse				
Pulse ≥90 beats/min[65]	80	82	**4.5**	**0.2**
Skin				
Skin moist and warm[65]	34	95	**6.8**	0.7
Thyroid				
Enlarged thyroid[65]	93	59	2.3	**0.1**
Eyes				
Eyelid retraction[65]	34	99	**33.2**	0.7
Eyelid lag[65]	19	99	**18.6**	0.8
Neurologic Findings				
Fine finger tremor[65]	69	94	**11.5**	**0.3**
Wayne Index[86,87]				
<11 points	1-6	13-32	**0.04**	—
11-19 points	12-30	—	NS	—
≥20 points	66-88	92-99	**18.2**	—

*Diagnostic standards: For *hyperthyroidism*, high levels of PBI for patients evaluated in the 1960s, total T_4 for those in the 1970s, and total T_4 and TSH for those in the 1980s and 1990s. (See footnote to EBM Box 23-3 for discussion of PBI.)

†Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

NS, not significant.

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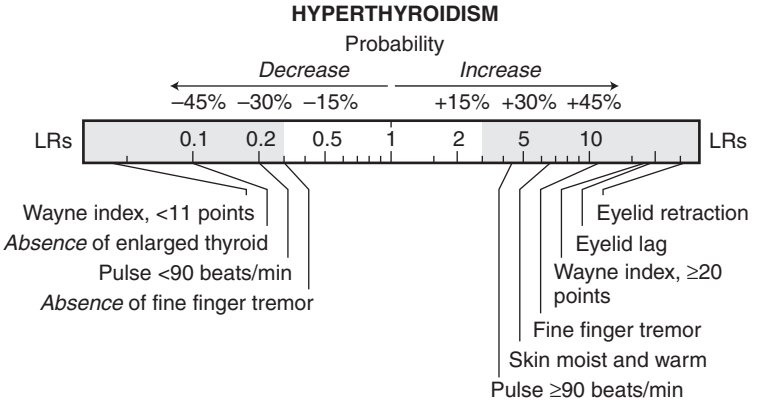


TABLE 23-2 Wayne Diagnostic Index for Hyperthyroidism*

Symptoms of Recent Onset or Increased Severity	Present	Signs	Present	Absent
Dyspnea on effort	+1	Palpable thyroid	+3	−3
Palpitations	+2	Bruit over thyroid	+2	−2
Tiredness	+2	Exophthalmos	+2	
Preference for heat (irrespective of duration)	−5	Lid retraction	+2	
Preference for cold	+5	Lid lag	+1	
Excessive sweating	+3	Hyperkinetic movements	+4	−2
Nervousness	+2	Fine finger tremor	+1	
Appetite increased	+3	Hands		
Appetite decreased	−3	Hot	+2	−2
Weight increased	−3	Moist	+1	−1
Weight decreased	+3	Casual pulse rate		
		Atrial fibrillation	+4	
		<80 beats/min, regular	−3	
		80-90 beats/min, regular	0	
		>90 beats/min, regular	+3	

*Source: Reference 86.

The findings that increase the probability of hyperthyroidism the most are lid retraction (LR = 33.2; see EBM Box 23-4), lid lag (LR = 18.6), fine finger tremor (LR = 11.5), moist and warm skin (LR = 6.8), and pulse of 90 beats/min or more (LR = 4.5). The findings that decrease the probability of hyperthyroidism the most are normal thyroid size (LR = 0.1), pulse less than 90 beats/min (LR = 0.2), and absence of finger tremor (LR = 0.3).

A Wayne index score of 20 or higher increases the probability of hyperthyroidism (LR = 18.2), and one of less than 11 decreases the probability of hyperthyroidism (LR = 0.04). This index, however, may be less useful in elderly patients,[88] who, as a rule, have less goiter and tachycardia than younger patients.[89–91] In one study, 36% of elderly hyperthyroid patients had scores of less than 11.[67] Elderly patients also have more weight loss and atrial fibrillation than younger patients,[65,67,92,93] but the frequency of lid retraction and lid lag is the same.[65,67]

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 24

Meninges

I. FINDINGS

The terms *meningeal signs* and *meningismus* refer to the physical findings that develop after meningeal irritation from inflammation, tumor, or hemorrhage. Those most widely known are neck stiffness (or *nuchal rigidity*), Kernig sign, and Brudzinski sign.

A. NECK STIFFNESS

Neck stiffness denotes involuntary resistance to neck flexion, which the clinician perceives when trying to bend the patient's neck, bringing the chin down to the chest. Occasionally, the aggravated extensor tone of the neck and spine is so severe that the patient's entire spine is hyperextended, leaving the torso of the supine patient supported only by the occiput and the heels, an extreme posture called **opisthotonus.**

B. KERNIG SIGN

The Kernig sign was first described by Vladimir Kernig in 1882. With the patient's hip and knee flexed, the Kernig sign is positive when the patient resists extension of the knee. Kernig called this a "contracture" of the hamstrings because the knee would not extend beyond 135 degrees (with the hip flexed), even though the knee extended fully if the hip was first positioned in the fully extended position (Fig. 24-1).[1] Most clinicians perform this test in the supine patient, although Kernig described the test being performed in the seated patient.

C. BRUDZINSKI SIGN

Jozef Brudzinski described several meningeal signs between 1909 and 1916. In his most popular sign, flexion of the supine patient's neck causes the patient to flex both the hips and the knees, thus retracting the legs toward the chest (see Fig. 24-1).[1]

II. PATHOGENESIS OF MENINGEAL SIGNS

The basis for all meningeal signs is the patient's natural rejection of any movement that stretches the spinal nerves, all of which pass through the irritated subarachnoid space. Experiments with cadavers show that flexion of the neck pulls the spinal cord toward the head, thus stretching the spinal nerves, whereas flexion of the hips with the knees extended pulls on the sciatic nerve, thus

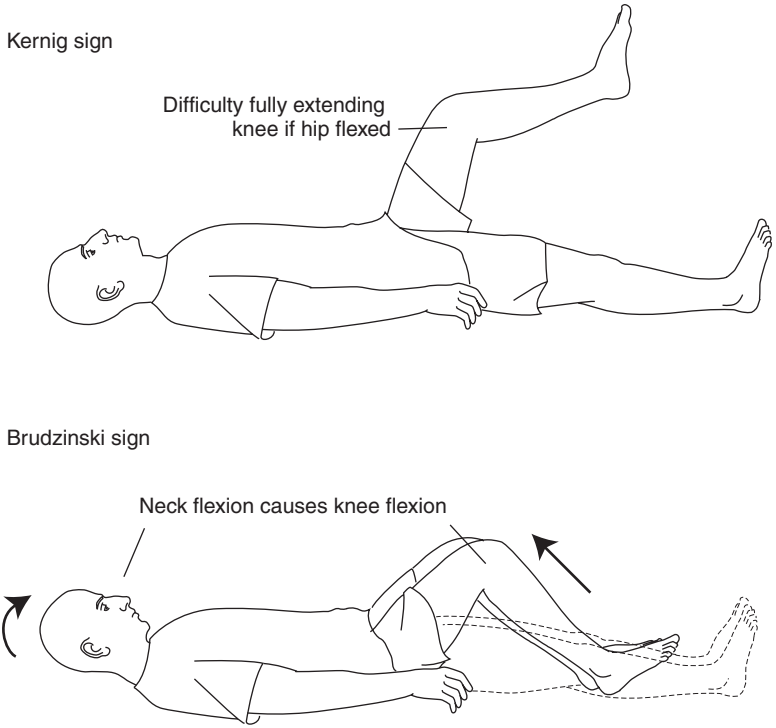


FIGURE 24-1 Kernig sign and Brudzinski sign. In the Kernig sign *(top),* the patient resists full extension of the knee when the knee and hip are first flexed (patient's left leg), although the knee extends normally if the hip is extended (patient's right leg). In the Brudzinski sign *(bottom),* flexion of the patient's neck causes the hips and knees to flex, pulling both legs up toward the chest. See text.

displacing the conus of the spinal cord downward toward the sacrum.[2] Flexion of the hips with the knees flexed, in contrast, does not stretch the sciatic nerve.

These experiments explain why patients with meningeal irritation have neck stiffness and a positive Kernig sign, and they also show that the Kernig sign does not differ from the straight leg–raising test for sciatica (see Chapter 62). The Brudzinski sign, however, is more difficult to understand. At first, it seems logical that patients with meningeal irritation would want to extend their hips and flex their knees when their neck is flexed. Although this position removes tension from the sciatic nerve, it stretches the femoral nerve,[2] explaining why the Brudzinski test causes the patient to flex both the hips and the knees, relieving tension on both nerves.

III. CLINICAL SIGNIFICANCE

A. ACUTE BACTERIAL MENINGITIS

Table 24-1 summarizes the frequency of individual findings in almost 1500 adults with acute bacterial meningitis (principally from *Streptococcus pneumoniae*, *Neisseria meningiditis*, and *Listeria monocytogenes;* cases of

TABLE 24-1 Acute Bacterial Meningitis and Subarachnoid Hemorrhage*

Finding	Frequency (%)†‡
ACUTE BACTERIAL MENINGITIS	
Neck stiffness	84
Fever	66-97
Altered mental status	53-95
Kernig or Brudzinski sign	61
Focal neurologic signs	9-37
Seizures	5-28
Petechial rash	3-52
SUBARACHNOID HEMORRHAGE	
Neck stiffness	21-86
Seizures	32
Altered mental status	29
Focal neurologic findings	13-36
Fever	8
Preretinal hemorrhages	2

*Data obtained from almost 1500 patients with meningitis from references 3 to 12 and 583 patients with subarachnoid hemorrhage from references 13 to 15.
†Diagnostic standard: For *meningitis*, cerebrospinal fluid pleocytosis and microbiologic or postmortem data supporting bacterial meningitis; for *subarachnoid hemorrhage*, computed tomography or lumbar puncture.
‡Results are overall mean frequency or, if statistically heterogeneous, the range of values.

tuberculosis were excluded). This table reveals that the most frequent findings in bacterial meningitis are neck stiffness, fever, and altered mental status. Neck stiffness is a more frequent sign than the Kernig or Brudzinski sign (sensitivity is 84% for neck stiffness vs. 61% for the Kernig or Brudzinski sign), although this difference is not significant and may reflect in part the clinician's diligence in looking for these findings. Of patients with petechial rash, 72% to 92% have infection with *Neisseria meningiditis*.[6,12]

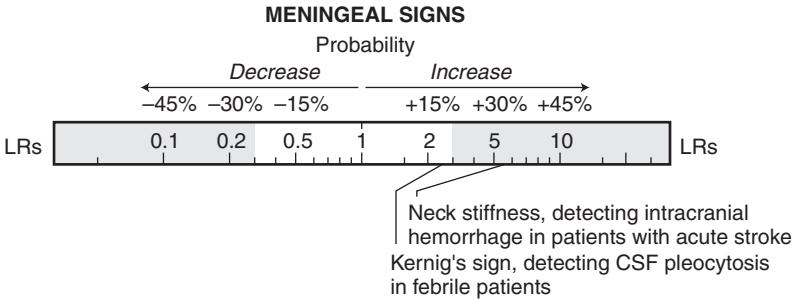
Some of the heterogeneity in these studies (see Table 24-1) is due to the ages of the patients. Compared with younger patients, elderly patients (defined as >65 years old in three of four studies and >50 years old in one study) have a higher frequency of mental status changes (90% vs. 72%), focal neurologic signs (30% vs. 17%), and fever (94% vs. 84%), but no difference in the frequency of neck stiffness.[5,8,16,17]

Few studies have addressed the overall accuracy of meningeal signs. In two studies of over 400 patients undergoing lumbar puncture because of suspected meningitis, both the Kernig sign (likelihood ratio [LR] = 2.4; EBM Box 24-1) and neck stiffness (LR = 1.5) slightly increased the probability of meningitis (i.e., cerebrospinal fluid white blood cell count ≥100/mL). Surprisingly, the sensitivity of findings in these studies (e.g., only 41% to 52% for neck stiffness) is much lower than that seen in observational studies of meningitis (84%; see Table 24-1), probably because few patients with meningitis in the studies reviewed in EBM Box 24-1 actually had acute bacterial meningitis.[18,19] (Most had aseptic meningitis.) Other studies have addressed just the specificity of meningeal signs: In one such study,

EBM BOX 24-1
Meningeal Signs

Finding (Reference)*	Sensitivity (%)	Specificity (%)	Likelihood Ratio† if Finding Is	
			Present	*Absent*
Detecting Meningitis[18,19]				
Neck stiffness	41-52	69-71	1.5	NS
Kernig sign	9-18	93-96	2.4	NS
Brudzinski sign	9-14	94-96	NS	NS
Detecting Intracranial Hemorrhage				
Neck stiffness[20-25]	16-48	81-98	**5.4**	0.7
Kernig or Brudzinski sign[20,22]	3-15	98	NS	NS

*Diagnostic standard: for *meningitis*, cerebrospinal fluid pleocytosis ≥100 white blood cells per microliter[18,19]; for *intracranial hemorrhage*, neuroimaging.
†Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.
NS, not significant.
Click here to access calculator.



nuchal rigidity was found in 35% of hospitalized elderly patients (mean age, 79 years), none of whom had meningitis (i.e., specificity, 65%).[26] In addition, the Kernig sign may appear in patients with sciatica and those with subarachnoid or epidural hemorrhage or tumor of the cauda equina.[27]

When present, the Kernig sign should be symmetrical. In one study of 51 consecutive comatose patients with the Kernig sign, asymmetry of the sign was a reliable indicator that the patient would have hemiparesis after awakening, the side with the less prominent Kernig sign indicating the side with paresis.[28]

B. SUBARACHNOID HEMORRHAGE AND INTRACEREBRAL HEMORRHAGE

Table 24-1 summarizes the findings of over 500 patients with subarachnoid hemorrhage, 80% of whom presented with a severe precipitous headache. The most common physical finding in these patients was neck stiffness (sensitivity, 21% to 86%). Only 29% had altered mental status.

Any large intracerebral hemorrhage may also lead to subarachnoid blood and neck stiffness. (Intraventricular blood may pass through the

median and lateral apertures of the fourth ventricle into the subarachnoid space at the base of the brain.) In studies of almost 1000 patients presenting to emergency departments with "stroke" (i.e., acute neurologic deficits believed to be vascular in origin), the finding of neck stiffness increased the probability of intracranial blood, either subarachnoid or intracerebral hemorrhage (LR = 5.4). Subarachnoid hemorrhage is more likely in these patients if there are no focal findings (sensitivity, 64%; specificity, 89%; positive LR = 5.9).[15]

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 25

Peripheral Lymphadenopathy

I. INTRODUCTION

Lymphatic vessels are located in all tissues and organs of the body except the central nervous system. These vessels collect extracellular tissue fluid (or lymph) and carry it to the systemic venous system, traversing along the way regional collections of bean-shaped structures called **lymph nodes.** As these lymph nodes slowly filter the lymph fluid, they may encounter microbes, malignant cells, particulate debris, or other substances to which they react, enlarge, and harden. Should such nodes enlarge or harden enough, they may become palpable, a problem called **peripheral lymphadenopathy.**

Ancient Greek and Roman physicians recognized peripheral lymphadenopathy as an important sign of tuberculosis (scrofula),[1,2] and for more than a century clinicians have known that lymphadenopathy may signify serious disorders such as carcinoma, lymphoma, leukemia, and certain infectious diseases (tuberculosis, syphilis, and plague, among others).[3] How often adenopathy reflects one of these serious disorders in current practice depends on the clinical setting. In family practice clinics, peripheral lymphadenopathy is benign 99% of the time, sometimes reflecting known disorders (such as pharyngitis, dermatitis, or insect bites) but more often appearing and resolving without explanation.[4,5] In specialized lymph node clinics, however, 18% to 24% of referred patients are eventually diagnosed with malignant disease (i.e., lymphoma or metastatic cancer), and up to 5% have a treatable infectious or granulomatous disorder (e.g., tuberculosis, HIV infection, or sarcoidosis).[6–8] This chapter focuses on those physical findings that help discriminate serious causes of lymphadenopathy from more benign causes.

II. ANATOMY AND PATHOGENESIS

A. INTRODUCTION

The lymphatic drainage of the body is subdivided into seven distinct regions, all of which converge and drain into the great veins near the base of the neck (Fig. 25-1). A normal adult has approximately 400 to 450 lymph nodes, although only about a quarter are in locations that could ever become palpable: 30 in the arm and axilla, 20 in the leg, and 60 to 70 in the head and neck.[9] (The remaining lymph nodes reside deep in the thorax and abdomen and are detectable only by clinical imaging.) Anatomists divide lymph nodes into **superficial nodes** and **deep nodes,** based on whether they accompany superficial or deep blood vessels. Superficial nodes lie just under the surface

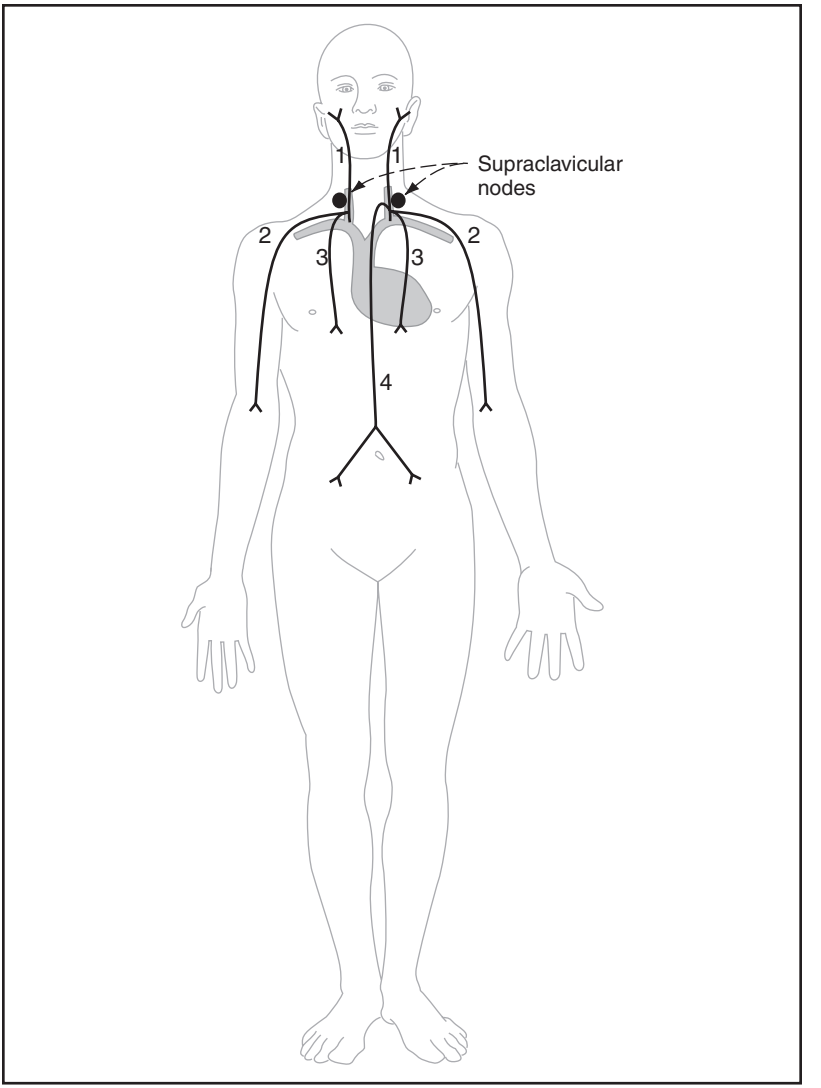


FIGURE 25-1 The seven regions of lymphatic drainage. All lymphatic drainage of the body converges on the right and left junctions of the internal jugular and subclavian veins (*shaded gray,* along with the superior vena cava and heart). The great veins on the right side of the neck receive drainage from: the right head and neck (region 1, traversing cervical nodes); the right arm, chest wall, and breast (region 2, traversing axillary nodes); and the right lung and mediastinal structures (region 3, via mediastinal and tracheobronchial nodes but no peripheral nodes). The left great veins receive drainage from similar regions of the left upper body (regions 1 to 3) and, via the thoracic duct, drainage from all tissues below the diaphragm (region 4). Only the supraclavicular nodes are depicted, illustrating their strategic proximity to the confluence of these seven major lymph channels.

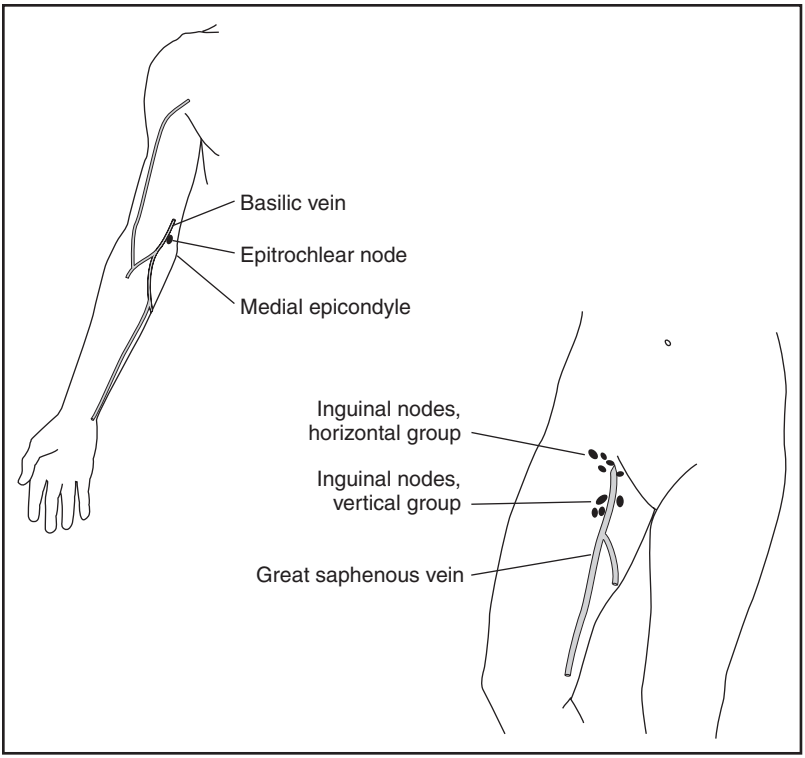


FIGURE 25-2 Epitrochlear and inguinal nodes. The epitrochlear nodes *(left side of figure)* are located 2 to 3 cm above the medial epicondyle of the humerus, just medial to the basilic vein, which lies along the groove medial to the biceps muscle. The inguinal nodes *(right side of figure)* consist of a horizontal group and vertical group; the vertical group lies along the termination of the greater saphenous vein.

of the skin, accompany superficial veins, and often are visible when enlarged. Most palpable nodes are superficial nodes. The only deep nodes detectable by bedside examination are the deep cervical nodes (which accompany the carotid artery and internal jugular vein under the sternocleidomastoid muscle) and the axillary nodes (which surround the axillary vessels).

The fact that lymph nodes accompany blood vessels is helpful when searching for two nodal groups.

1. The epitrochlear nodes, which lie near the basilic vein
2. The vertical group of inguinal nodes, which surround the proximal saphenous vein (Fig. 25-2)

B. REGIONAL LYMPH NODE GROUPS

Maps of regional lymphatic drainage are based on older experiments in living humans and cadavers, in which injections of mercury, Prussian blue stain, radiocontrast materials, or other dyes were used to highlight normal lymph channels and regional nodes.[9–12] (Lymph vessels are otherwise difficult to distinguish from small veins during dissection.) These maps of lymph drainage

are helpful because they allow clinicians to predict the spread of local infections or neoplasms and, when faced with isolated adenopathy, to focus the diagnostic search to a particular region. Nonetheless, clinical experience demonstrates that disease does not always spread in an orderly way through these channels and nodes. For example, infections and malignant diseases may occasionally skip one regional node group to travel to another (e.g., an infection of the ring finger may involve the axillary nodes and skip the epitrochlear nodes), and malignant diseases may sometimes travel in a retrograde direction between nodal groups (e.g., supraclavicular adenopathy; see the section on Supraclavicular Nodes).[11] Also, despite the implication of these maps, isolated adenopathy does not necessarily reflect focal disease but instead may represent the sole sign of a generalized disorder (e.g., tuberculosis or lymphoma).

1. Cervical Nodes

All structures of the head and neck drain into the deep cervical nodes, either directly or via intermediary superficial nodes (Fig. 25-3). The skin of the face and neck drains into the superficial nodes in a predictable fashion (see Fig. 25-3). The pharynx, nasal cavity, and sinuses usually drain to the upper deep cervical nodes; the mouth and teeth to the submandibular nodes and, eventually, the upper cervical nodes; and the larynx to both the

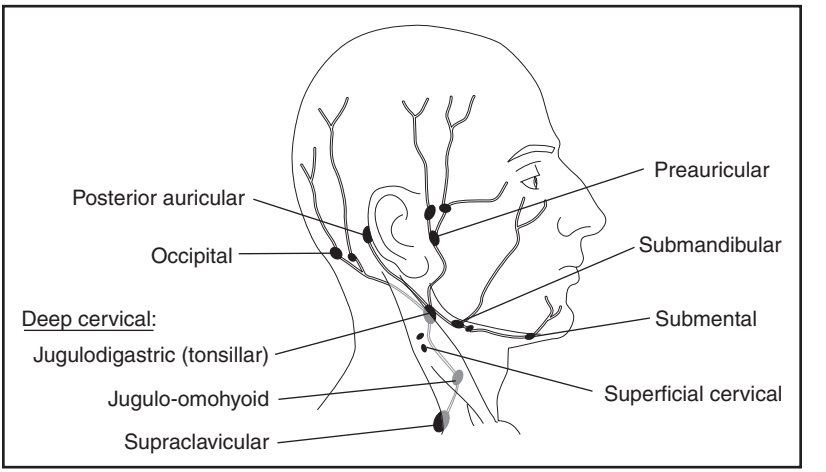


FIGURE 25-3 Cervical lymph nodes. Superficial cervical nodes are named according to their regional anatomy: occipital nodes, posterior auricular (or mastoid) nodes, preauricular (or parotid nodes), submandibular nodes, submental nodes, and superficial cervical nodes. Deep cervical nodes lie along the carotid sheath and are mostly buried under the sternocleidomastoid muscle, although the uppermost nodes appear in front of this muscle and the lowermost posterior to it. Three deep cervical nodes have specific names because of their size and clinical importance: (1) the jugulodigastric node, an upper deep cervical node at the level of the hyoid bone that becomes tender and prominent in patients with pharyngitis (i.e., the tonsillar node); (2) the jugulo-omohyoid node, a lower deep cervical node located where the omohyoid muscle crosses the jugular vein (this node drains the tongue and may become enlarged in patients with tongue carcinoma); and (3) the supraclavicular nodes, which are the lowermost deep cervical nodes and are considered separately in the section on Supraclavicular Nodes.

upper and lower cervical nodes. The tongue has the most diverse drainage: Efferents travel to the submental, submandibular, upper deep cervical, and lower deep cervical nodes, and disease near the midline may travel to either side.[9,11,13,14]

2. Supraclavicular Nodes

Although supraclavicular nodes actually belong to the deep cervical node group, they are considered separately because of their strategic location in the base of the neck, close to where all lymph drainage returns to the systemic venous system (see Fig. 25-1). Because of this location, supraclavicular adenopathy may signify serious disease located in the thoracic or abdominal cavities, regions where nodes are otherwise hidden from the examiner. The anatomy depicted in Figure 25-1 predicts that right supraclavicular adenopathy would be associated with disorders of the right thorax, arm, and neck and that left supraclavicular adenopathy would be associated with disorders of the left thorax, arm, neck, and abdomen and pelvis.

Normally, lymph flows from supraclavicular nodes downward toward the confluence of the lymph channels and great veins (see Fig. 25-1). For intra-abdominal or intrathoracic disorders to involve the supraclavicular nodes, therefore, disease must spread in a *retrograde* direction from the thoracic duct or bronchomediastinal lymphatic vessels through the cervical efferents leaving the supraclavicular nodes. Such retrograde spread easily occurs and does not imply obstruction of lymphatic channels. In one investigation of 92 patients undergoing lymphangiography of the lower limbs, radiopaque material appeared in the supraclavicular nodes within 48 hours in 55% of patients.[15] As expected, the dye opacified exclusively the left supraclavicular nodes in 48 of 51 patients, but it opacified both right and left supraclavicular nodes in 2 patients and exclusively the right supraclavicular nodes in 1 patient, indicating normal anatomic variation in the connections between the thoracic duct and supraclavicular nodes.[15]

Supraclavicular adenopathy appears just behind the clavicle, underneath or posterior to the sternocleidomastoid muscle. A Valsalva maneuver may make these nodes more prominent, by pushing the apical pleural surface upward against the nodes and bringing them into view.[16] In 1848, Virchow first observed the association between abdominal malignant diseases and metastases to the supraclavicular nodes.[15,17,18] Unaware of Virchow's description, the French clinician and pathologist Trosier described the same association in 1886, emphasizing the predisposition to the left side.[15,17,18] Left supraclavicular adenopathy has been therefore called **Virchow nodes, Trosier nodes, Virchow-Trosier nodes, sentinel nodes,** or **signal nodes.**[19]

3. Epitrochlear Nodes

Epitrochlear nodes (supratrochlear or cubital nodes; see Fig. 25-2) are superficial nodes, located on the anteromedial arm 2 to 3 cm above the medial epicondyle of the humerus. They drain the ulnar side of the forearm and hand (i.e., little and ring fingers) and send efferents to the axillary nodes. A common method for palpating these nodes is for the clinician to face the patient and reach across to shake the patient's hand on the side

to be examined. The examiner then places his or her free hand behind the patient's arm, just proximal to the elbow, and uses his fingertips to palpate these nodes above and anterior to the medial epicondyle.

Although epitrochlear adenopathy may indicate infection or malignant disease on the ulnar side of the forearm or hand, these nodes have historically been associated with conditions causing generalized lymphadenopathy, especially when they are enlarged bilaterally. (See the sections on Epitrochlear Adenopathy and Identifying HIV Infection in Developing Nations.) One hundred years ago, epitrochlear adenopathy was felt to be a compelling sign of secondary syphilis, occurring in 25% to 93% of cases.[20–22] Modern examples of this specific association, however, are scarce.

4. Axillary Nodes

Axillary nodes drain the ipsilateral arm, breast, and chest wall (Fig. 25-4). To examine these nodes, the clinician should ensure that the patient's axillary skin is relaxed, by first supporting and adducting the patient's arm. Nodes are located in the posterior, anterior, or medial walls of the axillary fossa or in its apex. Efferent lymph vessels travel directly to the systemic veins at the root of the neck, although a few efferents pass first through the ipsilateral supraclavicular nodes (see Fig. 25-4).[9,11]

5. Inguinal Nodes

Inguinal nodes are superficial nodes that are organized into two groups: a proximal or "horizontal" group located just below the inguinal ligament, which drains the external genitalia, perineum, and lower anterior abdominal, and a distal or "vertical" group located at the termination of the great saphenous vein, which drains the leg (see Fig. 25-2).[9]

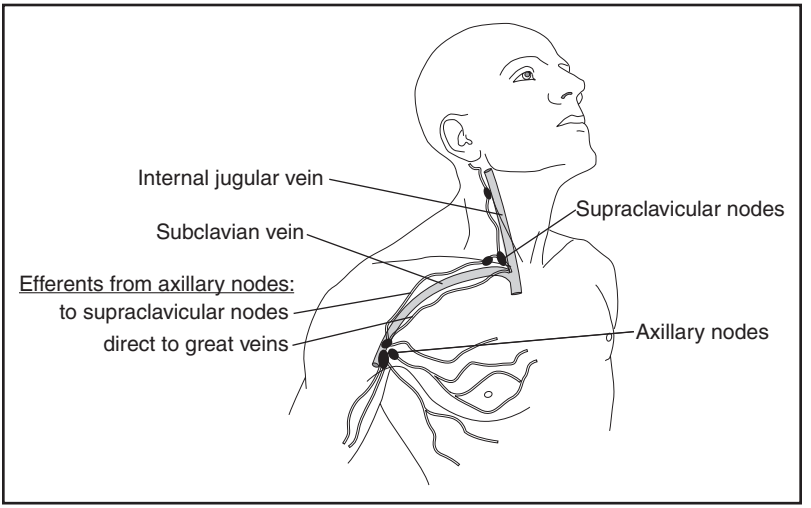


FIGURE 25-4 Axillary nodes. The axillary nodes receive lymphatic drainage from the ipsilateral arm, breast, and chest wall. Efferent vessels travel to the great veins at the root of the neck, although a few vessels travel first through the supraclavicular nodal group.

III. THE FINDING

A. DESCRIBING ADENOPATHY

Important features to observe when describing adenopathy are the location, size, number, hardness, and tenderness of the affected nodes. *Fixed nodes* are immobile from attachments to adjacent structures, implying malignant invasion of these tissues. A *hard node* has the consistency of a rock, again implying malignant disease. (The hardness presumably reflects the accompanying fibrosis induced by the tumor.) *Shotty adenopathy* indicates multiple tiny superficial nodes, mimicking the sensation of buckshot under the skin, a finding sometimes observed in the inguinal region but without particular diagnostic significance.[23] The size of a particular node can be indicated by recording its maximal length and width or, as some investigators suggest, by recording the product of these two numbers (e.g., a node measuring 2.5 cm × 3 cm is "7.5 cm^2").

B. GENERALIZED LYMPHADENOPATHY

Generalized adenopathy is defined as simultaneous enlargement of two or more regional lymph node groups.[24] Most affected patients have either combined cervical and inguinal adenopathy or combined cervical and axillary adenopathy.[25] Generalized lymphadenopathy implies a systemic disorder affecting lymph nodes, such as lymphoma or leukemia, specific infectious diseases (e.g., infectious mononucleosis, HIV infection, or syphilis), anticonvulsant hypersensitivity syndrome, sarcoidosis, or connective tissue disorders.[24]

C. "GLANDULAR" SYNDROMES

The term *glandular* refers to lymph nodes (e.g., *glandular fever* was the original name for infectious mononucleosis). The **ulceroglandular syndrome** is the triad of fever, ulceration on the distal arm or leg (indicating the portal of entry of infectious agent), and regional adenopathy. The **oculoglandular syndrome (Parinaud syndrome*)** describes the association of conjunctivitis with ipsilateral preauricular and submandibular adenopathy. Both ulceroglandular and oculoglandular syndromes have been associated with specific microbial agents. (See the section on Ulceroglandular and Oculoglandular Syndromes.)

Chapter 23 reviews the Delphian node and Chapter 48 discusses the Sister Mary Joseph nodule.

IV. CLINICAL SIGNIFICANCE

A. DEFINITION OF DISEASE

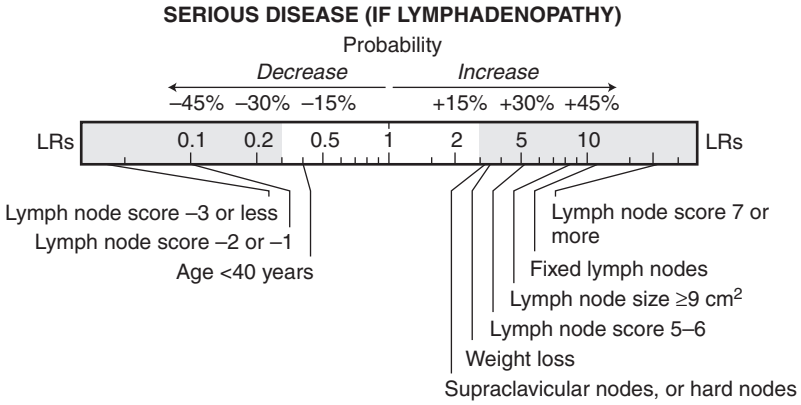
EBM Box 25-1 reviews the diagnostic accuracy of physical examination in distinguishing serious causes of adenopathy from more benign disorders. All of the patients in these studies were referred to specialists

*Henri Parinaud, one of the world's first neuro-ophthalmologists, was recruited to Paris by Charcot in the late 1800s. He also described the pupillary and eye movement abnormalities of the pretectal syndrome (see Chapter 20).[26]

EBM BOX 25-1
*Lymphadenopathy**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
General and Skin Findings				
Male sex[6,7,27–29]	44-59	49-72	1.3	0.8
Age ≥40 years[6,7,27,28,30,31]	48-91	53-87	2.4	0.4
Weight loss[6,7,28,32]	19-28	90-95	**3.4**	0.8
Fever[6,7,29,32]	1-31	60-80	NS	NS
Distribution of Adenopathy				
Head and neck nodes (excluding supraclavicular nodes)[6–8,27–29,31–33]	21-79	15-69	NS	NS
Supraclavicular nodes[6–8,28,31–33]	8-61	84-98	**3.2**	0.8
Axillary nodes[6–8,27–29,31–33]	8-52	30-91	0.8	NS
Inguinal nodes[6–8,27–29,31–33]	3-22	61-96	0.6	NS
Epitrochlear nodes[29]	2	97	NS	NS
Generalized lymphadenopathy[8,27,34]	32-48	31-87	NS	NS
Characteristics of Adenopathy				
Lymph node size[6,7]				
<4 cm^2	33-36	9-37	0.4	—
4-8.99 cm^2	26-30	—	NS	—
≥9 cm^2	37-38	91-98	**8.4**	—
Hard texture[6,7]	48-62	83-84	**3.2**	0.6
Lymph node tenderness[6,7,29,32]	3-18	50-86	0.4	1.3
Fixed lymph nodes[6,32]	12-52	97	**10.9**	NS
Other Findings				
Rash[7,29]	4-8	85-95	NS	NS
Palpable spleen[6,7,29]	5-10	92-96	NS	NS
Palpable liver[7,29]	14-16	86-89	NS	NS
Lymph Node Score[6,7]				
−3 or less	1-3	42-72	**0.04**	—
−2 or −1	1-3	—	**0.1**	—
0 to 4	23	—	NS	—
5 or 6	17-26	—	**5.1**	—
7 or more	49-56	94-99	**21.9**	—

*Diagnostic standard: For *diagnosis*, see text.
†Definition of findings: For *finding*, see text.
‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.
NS, not significant.
Click here to access calculator.



because of persistent unexplained peripheral lymphadenopathy. Most patients (35% to 83%) presented with cervical adenopathy, 1% to 29% with supraclavicular adenopathy, 4% to 24% with axillary adenopathy, 3% to 16% with inguinal adenopathy, and 16% to 32% with generalized adenopathy.[4,6,8,25,27,31,32]

The etiology of lymphadenopathy in these studies was determined by either fine-needle or excisional biopsy or, in a few low-risk patients who did not undergo biopsy, prolonged periods of observation.[7,8] Some of these studies defined a "serious disorder" (or "disease") as any disorder in which the biopsy results would imply a specific treatment or prognosis. These studies therefore included both malignant disease and granulomatous disease (e.g., tuberculosis or sarcoidosis) as "disease."[6,7,29–31,34,35] Other studies confined "disease" to the diagnosis of malignancy alone.[8,27,28,32,33] Both definitions of disease are combined in EBM Box 25-1 because analyzing the definitions separately revealed the same diagnostic accuracy and because the overwhelming majority of patients in all studies had a malignant cause for their disease.

B. EXTRANODAL MIMICS OF LYMPH NODES

Up to 15% of patients referred for unexplained "lymphadenopathy" instead have extranodal explanations for their subcutaneous lumps.[8] Common mimics of lymphadenopathy at all locations are skin nodules such as lipomas or epidermoid cysts. In the cervical region, thyroglossal cysts, branchial cleft cysts, and prominent carotid sinuses may be mistaken for nodes (see Chapter 23). In the supraclavicular region, synovial cysts from rheumatoid arthritis of the shoulder,[36] cervical ribs, and abnormal articulations of the first rib[37,38] have all been mistaken for nodes.

C. INDIVIDUAL FINDINGS

In these studies, the symptom of generalized pruritus argued for a serious cause, probably because of its association with lymphoma (sensitivity 6% to 10%, specificity 98% to 100%, likelihood ratio [LR] = 4.9).[6,7] According

to the LRs in EBM Box 25-1, several physical findings also argue for serious disease: fixed lymph nodes (LR = 10.9), size of 9 cm^2 or more (i.e., the equivalent of 3 × 3 cm or larger, LR = 8.4), weight loss (LR = 3.4), hard texture (LR = 3.2), supraclavicular adenopathy (LR = 3.2), and age of 40 years or more (LR = 2.4).

Only three findings argue against serious disease, all of them reducing the probability only modestly: age less than 40 years (LR = 0.4), lymph node size less than 4 cm^2 (i.e., 2 × 2 cm or smaller, LR = 0.4), and lymph node tenderness (LR = 0.4). Tenderness may be less specific for benign disorders than expected because hemorrhage or necrosis into neoplastic nodes also causes discomfort mimicking acute inflammatory changes. The symptom of throat soreness also argues against serious disease (sensitivity 3% to 14%, specificity 23% to 89%, LR = 0.2).[6,7,35]

Findings that are unhelpful in distinguishing serious from benign disease include rash, regional distribution of nodes (other than supraclavicular location), fever, a palpable spleen, and a palpable liver (all LRs either not significant or very close to the value of 1).

The finding of generalized adenopathy, defined as involvement of two or more regional node groups, also lacks diagnostic value (LR not significant). Even when generalized lymphadenopathy is defined as involvement of four or more regional lymph node groups, it fails to discriminate serious from benign causes (LR not significant),[34] probably because this finding appears just as often in benign disorders (e.g., infectious mononucleosis) as in serious disorders (e.g., lymphoma).

D. COMBINED FINDINGS

Based on evaluation of more than 300 patients, Vassilakopoulos and others[7] have identified six independent predictors of serious disease, creating a "lymph node score" that can easily be calculated at the bedside (Table 25-1).[7] According to this scheme, a score of −3 or less

Table 25-1 Lymph Node Score*

Finding	Points
Age >40 years	+5
Lymph node tenderness	−5
Lymph node size	
<1 cm^2	0
1-3.99 cm^2	+4
4-8.99 cm^2	+8
≥9 cm^2	+12
Generalized pruritus	+4
Supraclavicular nodes present	+3
Lymph node is hard	+2
Correction factor	−6†

*Based on reference 7.

†Included in every patient's score. For example, a 55-year-old asymptomatic patient with nontender but hard supraclavicular adenopathy measuring 6 cm^2 has a score of 12 (i.e., 5 + 8 + 3 + 2 – 6).

virtually excludes serious disease (LR = 0.04; see EBM Box 25-1), one of −2 or −1 argues *against* a serious cause (LR = 0.1), one of 5 or 6 argues *for* a serious disorder (LR = 5.1), and one of 7 or more is practically diagnostic *for* serious disease (LR = 21.9). Scores of 0 to 4 lack diagnostic significance.

E. LYMPH NODE SYNDROMES

1. Supraclavicular Adenopathy

In studies confined to patients undergoing biopsy of supraclavicular adenopathy, 54% to 87% of patients are discovered to have malignant disease, mostly metastatic carcinomas (46% to 69% of all patients).[38–44] As expected, supradiaphragmatic carcinomas (e.g., lung or breast carcinoma) are equally distributed between the right and left sides. Most lung and breast cancers spread to the ipsilateral supraclavicular nodes, although examples of contralateral spread occur.[11,18,39–44]

Surprisingly, infradiaphragmatic carcinomas do not always spread to the left supraclavicular nodes, as would be predicted by normal anatomy (see Fig. 25-1) and implied by Virchow's and Trosier's eponym. On average, only three quarters of infradiaphragmatic carcinomas metastatic to supraclavicular nodes go to the left side; one quarter appear on the *right* side (range, 0% to 38%). Two proposed mechanisms for involvement of the right side by these tumors include the following:

1. Some patients normally have anatomic connections between the thoracic duct and the right supraclavicular nodes (see the section on Supraclavicular Nodes).
2. Metastatic tumor first involves the mediastinal nodes, which via the right bronchomediastinal lymphatic vessels provide passage to the right neck.

In support of the second explanation, one autopsy study of patients with infradiaphragmatic malignant disease metastatic to the supraclavicular nodes documented that most patients also had mediastinal metastases.[18]

About 50% of patients whose supraclavicular node biopsies revealed malignancy were unaware of the diagnosis before biopsy,[18,41] illustrating the diagnostic importance of this node. In patients with metastases to the *right* supraclavicular node, the most common primary tumors by far are lung and breast cancers, followed by esophageal cancer and a medley of other tumors located above and below the diaphragm.[18,39–44] In those with metastases to the *left* side, lung, breast, gastric, and gynecologic primary tumors figure prominently in reported series of cases, although carcinoma of virtually any organ located in the thorax, abdomen, or pelvis has been associated with metastases to these nodes.[18,39–47]

2. Epitrochlear Adenopathy

Epitrochlear nodes are a rare finding in normal individuals but are commonly observed in patients with disorders causing generalized lymphadenopathy. They are palpable in 25% to 30% of patients with sarcoidosis, lymphoma, or chronic lymphocytic leukemia and in up to 55% of patients with infectious mononucleosis.[20]

3. Identifying HIV Infection in Developing Nations

Adenopathy provides an important clue to HIV infection in patients from developing nations. In one study of hospitalized patients in Zimbabwe, where HIV infection is prevalent, the finding of epitrochlear adenopathy (i.e., epitrochlear nodes >0.5 cm in diameter) distinguished patients with HIV seropositivity from those without it (sensitivity 84%, specificity 81%, positive LR = 4.5, negative LR = 0.2).[48] In studies from both Zimbabwe and India, the finding of axillary adenopathy in patients being treated for active tuberculosis detects HIV coinfection (sensitivity 24% to 43%, specificity 93% to 95%, positive LR = 4.9).[48,49]

4. Staging Patients with Known Cancer

The absence of regional adenopathy is unhelpful when staging patients with known malignant diseases. For example, up to 50% of patients with head and neck tumors and negative nodes by examination have nodal metastases discovered during surgical neck exploration.[50–52] Similarly, up to one third of women with breast carcinoma and a negative axillary examination have axillary nodal metastases discovered at surgery,[53] and up to one quarter of patients with lung carcinoma and negative supraclavicular nodes have involvement of these nodes histologically.[54,55] Bedside examination is inaccurate because malignant disease may involve regional nodes without changing their appearance. Even surgeons directly inspecting the physical characteristics of dissected nodes during staging operations often cannot distinguish metastatic nodes from normal ones.[50,52]

5. Ulceroglandular and Oculoglandular Syndromes

Common reported causes of the ulceroglandular syndrome are tularemia, rickettsial infections, and *Herpes simplex* infections.[56] Important etiologies of the oculoglandular syndrome are cat-scratch disease, tularemia, and viral infections (especially, enterovirus and adenovirus infections).[57]

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 26

Inspection of the Chest

This chapter discusses the findings of clubbing, barrel chest, pursed-lips breathing, accessory muscle use, and inspiratory white noise. Other relevant findings from inspection of the respiratory system include cyanosis (Chapter 8), abnormal respiratory rate, and abnormal breathing patterns (Chapter 18).

I. CLUBBING (ACROPACHY, HIPPOCRATIC FINGERS)

A. INTRODUCTION

Clubbing is a painless focal enlargement of the connective tissue in the terminal phalanges of the digits.[1,2] Clubbing is usually symmetrical, affecting fingers more prominently than toes. Although some persons have hereditary clubbing, the finding usually indicates serious underlying disease. (See the section on Clinical Significance.)

Hippocrates first described clubbing in the 3rd century BC. He noted it in patients with empyema, commenting that "the fingernails become curved and the fingers become warm, especially at their tips."[3]

B. THE FINDING

Precise definitions of clubbing were developed in the 1960s and 1970s, prompted by reports that clinicians of that time were using at least a dozen different definitions[4] and by the observation that clubbing regresses after effective treatment of the underlying disorder, making accurate measures of this physical finding an important end point to follow. There are three substantiated definitions of clubbing (Fig. 26-1).

1. Interphalangeal depth ratio greater than 1
2. Hyponychial angle greater than 190 degrees
3. Positive Schamroth sign

1. Interphalangeal Depth Ratio

Measurement of the interphalangeal depth ratio is described in Figure 26-1. If this ratio exceeds 1, clubbing is present, a conclusion supported by two observations.

1. The interphalangeal depth ratio of normal persons is 0.895 ± 0.041, making the threshold of 1 more than 2.5 standard deviations (SDs) above normal.[5,6]

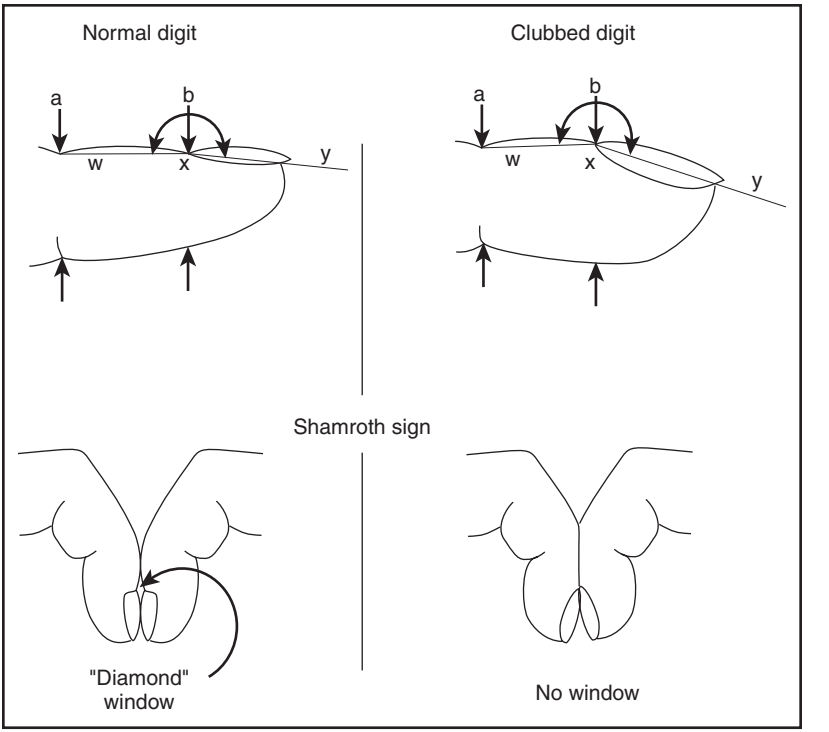


FIGURE 26-1 Clubbing. The normal digit is on the *left*: the clubbed one, on the *right*. The distal interphalangeal joint is denoted by *a;* the junction of the nail and skin at the midline is denoted by *b*. The interphalangeal depth ratio is the ratio of the digit's depth measured at *b* divided by that at *a*. The hyponychial angle is the angle *wxy*. In the figure, the depth ratio is 0.9 for the normal digit and 1.2 for the clubbed digit (a ratio >1 indicates clubbing), and the hyponychial angle is 185 degrees for the normal digit and 200 degrees for the clubbed digit (a hyponychial angle >190 degrees indicates clubbing). The Schamroth sign refers to the absence of the normal diamond-shaped window that appears when the terminal phalanges of similar digits are opposed to each other.

2. A ratio of 1 distinguishes digits of healthy persons from those of patients with disorders traditionally associated with clubbing (such as cyanotic heart disease and cystic fibrosis).

For example, studies demonstrate that 75% to 91% of patients with cystic fibrosis have an interphalangeal depth ratio exceeding 1, but only 0% to 1.5% of normal persons do.[5,6]

2. Hyponychial Angle

Measurement of the hyponychial angle is described in Figure 26-1. If this angle exceeds 190 degrees, clubbing is present, a conclusion supported by three observations.

1. The normal hyponychial angle is 180 ± 4.2 degrees, and the 190-degree threshold is therefore almost 2.5 SDs above normal.[5,7,8]

2. The hyponychial angle is the best parameter distinguishing plaster casts of digits labeled "definitely clubbed" by experienced clinicians from those labeled "definitely normal."[9]
3. Studies show that 69% to 80% of patients with cystic fibrosis have hyponychial angles exceeding 190 degrees, whereas only 0% to 1.6% of normal persons have angles this large.[7,8]

A disadvantage of the hyponychial angle is the special equipment required for precise measurements. Historically, clinicians used an apparatus called the shadowgraph, an instrument projecting the silhouette of the finger against a screen fitted with a movable protractor.[10] Modern investigators use computerized analysis of digital photographs.[8]

3. Schamroth Sign

After watching his own clubbing come and go during an episode of endocarditis, the renowned electrocardiographer Leo Schamroth[11] suggested in 1976 that clinicians place the terminal phalanges of similar fingers back to back (especially, ring fingers) and look for a small diamond-shaped window outlined by the bases of the nail beds and nails. Clubbing is absent when this window appears; clubbing is present when this window is absent (see Fig. 26-1). Schamroth suggested further study of his sign. In 2010, investigators, using the interphalangeal depth ratio as the diagnostic standard, demonstrated that the Schamroth sign had a sensitivity of 77% to 87%, specificity of 90%, positive LR of 8, and negative LR of 0.2.[12]

4. Other Definitions

Parameters found to be less accurate definitions of clubbing (compared with the hyponychial angle and the interphalangeal depth ratio) are the distal interphalangeal *width* ratio, the longitudinal curvature of the nail, the transverse curvature of the nail, and the profile angle (i.e., the angle between line *wx* in Figure 26-1 and a second line extending from *x* to a point on the top of the nail about a third of the distance from the nail fold to the nail tip).[9,13]

C. CLINICAL SIGNIFICANCE

1. Etiology

In a study of 350 patients with clubbing, 80% had underlying respiratory disorders (e.g., lung tumor, bronchiectasis, lung abscess, empyema, or interstitial fibrosis), 10% to 15% had miscellaneous disorders (congenital cyanotic heart disease, liver cirrhosis, chronic diarrhea, or subacute endocarditis), and 5% to 10% had hereditary or idiopathic clubbing.[14]

2. Relationship of Clubbing to Hypertrophic Osteoarthropathy

Clubbing may be associated with hypertrophic osteoarthropathy, a painful condition causing swelling and arthritis of the distal arms and legs. Radiographs reveal periosteal elevation of the diaphysis of long bones.[15] The usual cause is intrathoracic neoplasm (e.g., lung cancer or mesothelioma).

3. Clubbing and Cystic Fibrosis

In patients with cystic fibrosis, clubbing (i.e., interphalangeal depth ratio >1) predicts significant hypoxemia (i.e., PaO_2 ≤88 mm Hg on room air) with a positive LR of 3.2 and a negative LR of 0.1 (EBM Box 26-1). After lung transplantation, the clubbing of cystic fibrosis regresses slowly over months.[21]

4. Clubbing and Endocarditis

In a study of almost 2000 patients undergoing evaluation for endocarditis,[16] the finding of clubbing increased the probability of a final diagnosis of definite endocarditis (LR = 5.1; see EBM Box 26-1).

EBM BOX 26-1
*Clubbing**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Detecting hypoxemia (pO_2 ≤88 mm Hg) in patients with cystic fibrosis[6]	91	72	**3.2**	**0.1**
Detecting "definite" endocarditis[16]	6	99	**5.1**	NS
Detecting hepatopulmonary syndrome in patients with cirrhosis[17–20]	22-80	64-95	**4.6**	0.6

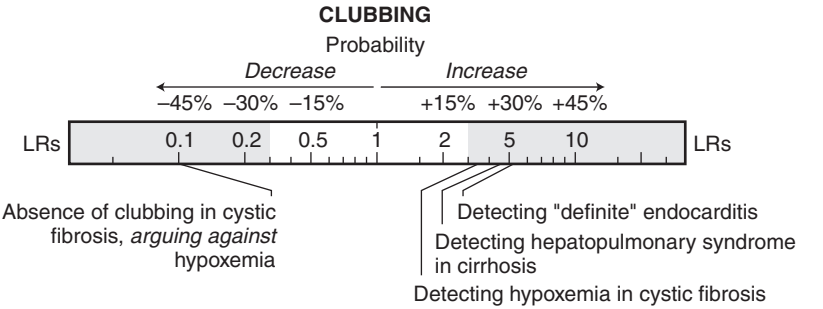
*Diagnostic standard: For *endocarditis*, "definite endocarditis" by modified Duke criteria; for *hepatopulmonary syndrome*, triad of cirrhosis, intrapulmonary shunting by contrast echocardiography, and arterial pO_2 ≤70 mm Hg,[18] ≤80 mm Hg,[17] or alveolar to arterial oxygen gradient ≥15 mm Hg[19] or >20 mm Hg.[20]

†Definition of findings: For *clubbing*, interphalangeal depth ratio >1[6] or undefined.[16–19]

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

NS, not significant; pO_2, pressure of oxygen.

Click here to access calculator.



5. Clubbing and Hepatopulmonary Syndrome

In patients with liver cirrhosis, the finding of clubbing increases the probability of hepatopulmonary syndrome (LR = 4.6; see EBM Box 26-1 and Chapter 7).

D. PATHOGENESIS

The increased volume of the clubbed digit is primarily because of increased amounts of vascular connective tissue,[22] although the cause of this fibrovascular proliferation is still debated. According to one hypothesis, clubbing results from large megakaryocytes and clumps of platelets that become trapped in the distal digits and then release growth factors, causing soft tissue growth.[23,24] Normally, megakaryocytes do not appear in arterial blood: They leave the bone marrow and travel in the systemic veins to the pulmonary capillaries, where they become trapped because of their large size (20 to 50 μ in diameter) and fragment into smaller platelets. In most patients with clubbing, either the pulmonary capillaries are damaged (e.g., as in many inflammatory and neoplastic pulmonary disorders) or a right-to-left shunt exists (e.g., as in congenital heart disease or the hepatopulmonary syndrome of cirrhosis). These abnormalities allow the large megakaryocytes to travel freely through the lung into arterial blood and the distal digits, where they become wedged in the digital capillaries and release growth factors, causing fibrovascular proliferation and clubbing.

This hypothesis explains why clubbing accompanies endocarditis and why it is sometimes found unilaterally in the digits distal to an infected dialysis shunt. In both examples, platelet clumps are presumably released from the infected surface to travel to the digits, where they become embedded within capillaries and release growth factors.[23]

An alternative (though not necessarily contradictory) hypothesis proposes that clubbing stems from elevated levels of prostaglandin E_2 (PGE_2). In families of patients with hereditary clubbing and osteoarthropathy, defective catabolism of PGE_2 causes high levels of it to accumulate.[25]

II. BARREL CHEST

A. THE FINDING

The normal chest is shaped like an oval cylinder, its anteroposterior diameter being less than its lateral diameter. The ratio of the anteroposterior diameter to the lateral diameter (called the thoracic ratio, thoracic index, or chest index) is normally about 0.70 to 0.75 in adults, and it increases as persons grow older. The upper normal limit is about 0.9.[26]

Barrel chest deformity refers to a chest with a transverse section that is more round than oval. It is traditionally a finding of chronic obstructive lung disease (i.e., chronic bronchitis or emphysema). Most patients also have dorsal kyphosis, a prominent sternum, widened intercostal spaces, elevated clavicles, and a shortened neck.[26] According to traditional teachings, the thoracic ratio of these patients exceeds 0.9, presumably because overactivity of the scalene and sternocleidomastoid muscles lifts the upper ribs and sternum. (See the section on Accessory Muscle Use.)

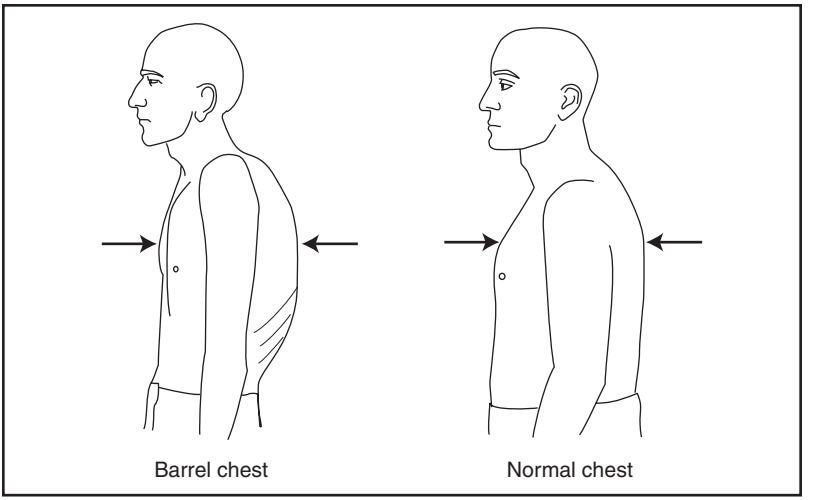


FIGURE 26-2 Barrel chest deformity. In some patients, the "large" anteroposterior dimension of the barrel chest *(left)* is an illusion because it is no bigger than the anteroposterior dimension of the normal chest *(right)*. Instead, what strikes the clinician's eyes is the barrel chest's prominent dorsal kyphosis and the marked contrast between the preserved anteroposterior chest dimension and the thin abdomen.

B. CLINICAL SIGNIFICANCE

Evidence linking the barrel chest deformity with chronic obstructive lung disease is conflicting. Two studies did find a significant correlation between barrel chest deformity and more severe airflow obstruction,[27,28] although another two studies found no relationship between the two conditions.[26,29] Additional problems with this physical sign are that the barrel chest is not specific for obstruction but also occurs in elderly persons without lung disease.[26] In some patients, the large anteroposterior dimension of the barrel chest is an illusion; the actual anteroposterior dimension is normal, but it appears to be abnormally large because it contrasts with an abnormally thin abdominal dimension caused by weight loss (Fig. 26-2).[30]

In a single study, the presence of barrel chest—defined either as the clinician's global impression of barrel chest or, more precisely, as a thoracic ratio ≥0.9—modestly increased the probability of obstructive disease (LR = 1.5 to 2; EBM Box 26-2).

III. PURSED-LIPS BREATHING

A. THE FINDING

Many patients with chronic obstructive lung disease instinctively learn that pursing the lips during expiration reduces dyspnea. The exact cause of the relief of dyspnea is still debated. Pursed-lips breathing significantly reduces the respiratory rate (from about 20 breaths/min to 12 to 15 breaths/min), increases tidal volume (by about 250 to 800 mL), decreases the $PaCO_2$ (by 5%), and increases oxygen saturation (by 3%).[34–37] Dyspnea may diminish

because there is less work of breathing (from a slower rate), less expiratory airway collapse (the pressure drop across the lips, 2 to 4 cm of water, provides continuous expiratory positive pressure), or recruitment of respiratory muscles in a way that is less fatiguing to the diaphragm.[34,35,38]

EBM BOX 26-2
*Inspection of the Chest**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Chest Wall Appearance				
Barrel chest, detecting chronic obstructive lung disease[31]	65	58	1.5	0.6
AP/L chest diameter ratio ≥0.9, detecting chronic obstructive lung disease[31]	31	84	2.0	NS
Pursed-Lips Breathing				
Pursed-lips breathing, detecting chronic obstructive lung disease[31]	58	78	2.7	0.5
Accessory Muscle Use				
Scalene/sternocleidomastoid muscle use, detecting chronic obstructive lung disease[31]	39	88	**3.3**	0.7
Scalene/sternocleidomastoid muscle use in patients with amyotrophic lateral sclerosis, detecting respiratory neuromuscular weakness[32]	81	83	NS	**0.2**
Accessory muscle use, detecting pulmonary embolism[33]	17	89	NS	NS

*Diagnostic standard: for *chronic obstructive lung disease*, $FEV_1/FVC < 0.7$; for *respiratory neuromuscular weakness*, transdiaphragmatic sniff pressure <70 cm water; and for *pulmonary embolism*, pulmonary angiogram.

†Definition of findings: for *accessory muscle use* in amyotrophic lateral sclerosis, the patients were examined in the supine position.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

AP/L, ratio of anteroposterior chest dimension to lateral dimension; FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 second; NS, not significant.

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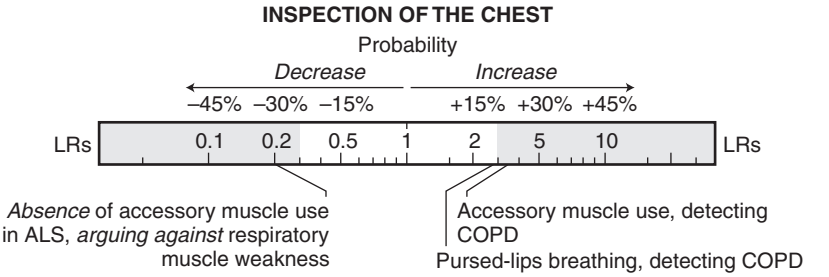


B. CLINICAL SIGNIFICANCE

In a study of 200 patients presenting for pulmonary function testing, the finding of pursed-lips breathing increased the probability of chronic obstructive disease (LR = 2.7).

IV. ACCESSORY MUSCLE USE

A. THE FINDING

The only muscle used in normal breathing is the diaphragm, which contracts during inspiration. Normal expiration is a passive process that relies on the elastic recoil of the lungs.[39] The term **accessory muscle use,** therefore, refers to the contraction of muscles other than the diaphragm during inspiration (usually, the sternocleidomastoid and scalene muscles) or to the contraction of any muscle during expiration (primarily, the abdominal oblique muscles). Accessory muscle use is a common finding in patients with chronic obstructive lung disease or respiratory muscle fatigue.

B. PATHOGENESIS

Contraction of the sternocleidomastoid and scalene muscles lifts the clavicles and first ribs, which helps expand the thorax of distressed patients, especially those with chronic obstructive lung disease whose flattened diaphragm generates only meager inspiratory movements. Contraction of the abdominal oblique muscles assists ventilation in two ways.

1. In patients with obstructed airways, the abdominal muscles help expel air across the obstructed airways.
2. In patients with respiratory muscle fatigue (e.g., amyotrophic lateral sclerosis), the abdominal muscles characteristically contract right at the moment that expiration ends, to compress the respiratory system so that the early part of the subsequent inspiration can occur passively.[40]

C. CLINICAL SIGNIFICANCE

Accessory muscle use—defined as inspiratory contraction of the sternocleidomastoid and scalene muscles—is associated with severe obstructive disease.[27,29,41–43] Over 90% of patients hospitalized with acute exacerbations of chronic obstructive lung disease use accessory muscles, but by

hospital day 5, less than half do.[44] In one study, lifting the clavicle more than 5 mm during inspiration identified patients with more severe obstructive disease (mean FEV_1* 0.6 L vs. 1.5 L, $p < .001$).[41] In patients referred for pulmonary function testing, accessory muscle use increases the probability of chronic obstructive disease (LR = 3.3; see EBM Box 26-2).

Inspection of accessory muscles also provides useful information in patients with amyotrophic lateral sclerosis. When these patients are supine, the *absence* of sternocleidomastoid and scalene contractions decreases the probability of respiratory neuromuscular weakness (LR = 0.2).

Accessory muscle use is less specific in the evaluation of acute dyspnea. In one study of patients with suspected pulmonary embolism, the finding had no diagnostic value. (See EBM Box 27-2.)

V. INTENSITY OF BREATHING SOUNDS (INSPIRATORY WHITE NOISE, NOISY BREATHING)

A. THE FINDING

The breathing of normal persons is inaudible more than a few centimeters from the mouth, unless the person is sighing, panting, or gasping.[46] In three clinical settings, breathing sometimes becomes very noisy and is easily heard a distance from the bedside.

1. Patients with lower airway obstruction, who may have audible *expiratory* wheezing (see Chapter 28)
2. Patients with upper airway obstruction, who may have *inspiratory* stridor (see Chapter 28)
3. Patients with chronic bronchitis or asthma, who may have *inspiratory* white noise[46]

White noise is an acoustical term meaning that unlike wheezing and stridor, the sound lacks a musical pitch and therefore resembles more the static of a radio tuned between stations. In patients with chronic bronchitis and asthma, the loud inspiratory white noise heard at the bedside without the stethoscope often contrasts sharply with the quiet inspiratory sounds heard through the stethoscope during auscultation (see Chapter 28).

B. PATHOGENESIS

Inspiratory white noise results from air turbulence caused by narrowed central airways,[47] a conclusion based on the observation that the sounds diminish after the patient receives effective bronchodilator treatment (which increases the patient's FEV_1) or breathes a mixture of oxygen and helium (a gas mixture that reduces turbulence).[47] Inspiratory white noise is

*FEV_1 is forced expiratory volume in 1 second, a measure of ventilatory capacity. Normal values are 3 to 3.8 L.[45] The FEV_1 is abnormally low in obstructive lung disease and restrictive lung disease, dyspnea first appearing in these conditions when the FEV_1 falls below 2.5 L. An FEV_1 of less than 1 L in chronic obstructive lung disease indicates severe disease.

not a feature of emphysema, presumably because the inspiratory caliber of the central airways in these patients is normal.[47]

C. CLINICAL SIGNIFICANCE

Inspiratory white noise is a feature of chronic bronchitis and asthma, not emphysema. The intensity of white noise in patients with asthma and chronic bronchitis correlates inversely with the patient's FEV_1 ($r = -0.60$ to -0.64).[47]

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 27

Palpation and Percussion of the Chest

PALPATION

I. INTRODUCTION

Palpation of the chest is limited because the bony rib cage conceals many abnormalities of the underlying lungs. The traditional reasons to palpate the chest are to detect the following signs:

1. Chest wall tenderness or masses
2. Pleural friction rubs
3. Bronchial fremitus
4. Abnormal respiratory excursion
5. Asymmetrical tactile fremitus

Bronchial fremitus is an inspiratory vibratory sensation felt in some patients with airway secretions. Respiratory excursion is assessed while the patient breathes in and out, either by simultaneously palpating symmetrical areas of the chest or by measuring the changing circumference with a tape measure. According to traditional teachings, chest excursion is reduced bilaterally in chronic airflow obstruction and neuromuscular disease (see Chapter 31) and unilaterally in pleural effusion and consolidation.

II. TACTILE FREMITUS

A. THE FINDING

Tactile fremitus (vocal fremitus) is the vibration felt by the clinician's hand resting on the chest wall of a patient who is speaking or singing.

B. TECHNIQUE

To elicit the sign, the patient usually says "one-two-three" or "ninety-nine" repeatedly and evenly while the clinician compares symmetrical areas of the chest. Some early German physical diagnosticians used the word *neun-und-neunzig* (German for "ninety-nine") to elicit vocal fremitus, prompting modern English-speaking authors to suggest that the "oy" sound is necessary to elicit the finding (e.g., "toy boat" or "Toyota," to mimic the vowel sound in the German word *neun-und-neunzig*). This is incorrect, however, and the early German diagnosticians just as often used other words, such as

"one, one, one" (*eins, eins, eins*) and "one, two, three" (*eins, zwei, drei*)[1–3] or had their patients sing or scream to elicit the finding.[3]

C. FINDINGS

Vocal fremitus is more prominent in men than women because men have lower-pitched voices, which conduct more easily though lung tissue than do higher-pitched voices. (See the section on Pathogenesis of Vocal Resonance in Chapter 28.) Tactile fremitus, therefore, may be absent in some healthy persons, especially those with high-pitched or soft voices or those with thick chest walls (which insulate the hand from the vibrating lung). Consequently, only *asymmetrical* tactile fremitus is an abnormal finding: According to traditional teachings, fremitus is asymmetrically diminished whenever air, fluid, or tumor tissue pushes the lung away from the chest wall (*unilateral* pneumothorax, pleural effusion, or neoplasm) and is asymmetrically increased when there is consolidation of the underlying lung (i.e., *unilateral* pneumonia).

The pathogenesis of tactile fremitus is discussed in Chapter 28 (section on Vocal Resonance).

III. CLINICAL SIGNIFICANCE

A. CHEST EXPANSION

Just as is traditionally taught, the finding of asymmetrical chest wall expansion increases the probability of unilateral pneumonia in patients with cough and fever (the side with pneumonia moves less; likelihood ratio [LR] = 44.1; EBM Box 27-1), and it increases the probability of underlying pleural effusion in hospitalized patients with respiratory complaints (LR = 8.1). After intubation of a patient, asymmetrical chest wall expansion increases greatly the probability of right mainstem bronchus intubation (LR = 15.7).

Nonetheless, the opposite finding—*symmetrical* chest expansion—does *not* change the probability of either pneumonia or right endobronchial intubation, although it does decrease the probability of underlying pleural effusion (LR = 0.3). Physical examination should never be used as the sole tool in confirming the placement of an endotracheal tube after intubation.

B. TACTILE FREMITUS

In a study of 278 patients hospitalized with respiratory complaints, the finding of asymmetrical diminished tactile fremitus significantly increased the probability of an underlying pleural effusion (LR = 5.7; see EBM Box 27-1); symmetrical fremitus decreased the probability of effusion (LR = 0.2).

C. CHEST WALL TENDERNESS

According to traditional teachings, the finding of chest wall tenderness in a patient with chest complaints suggests benign disease, commonly referred to as **costochondritis.** Even so, this conclusion is accurate only in patients with acute atraumatic chest pain, in whom chest wall tenderness decreases

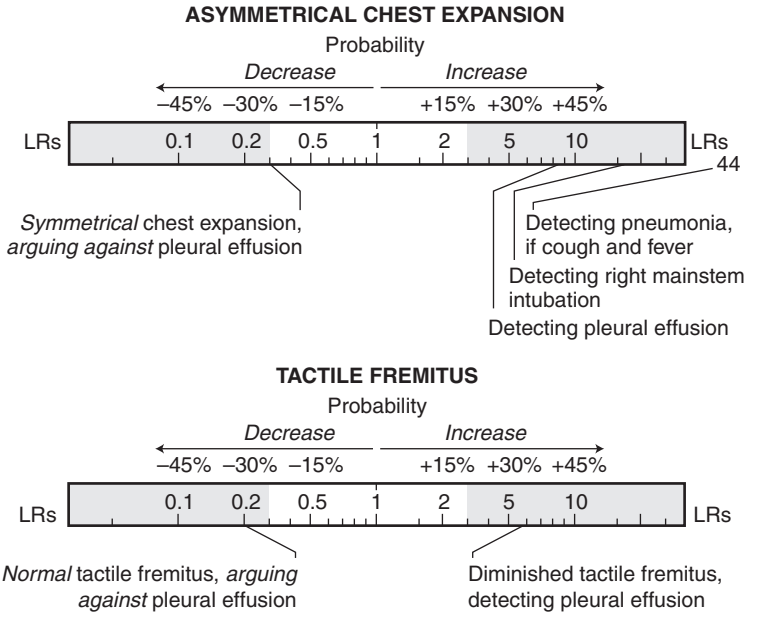
the probability of myocardial infarction (LR = 0.3; see EBM Box 27-1). In contrast, in studies of pneumonia, chronic coronary artery disease, and pulmonary embolism, the finding has little diagnostic value, occurring just as often in serious disease as in benign disorders (LRs not significant; see EBM Box 27-1).

EBM BOX 27-1
*Diagnostic Accuracy of Palpation of the Chest**

Finding (Reference)	Sensitivity (%)	Specificity (%)	Likelihood Ratio† if Finding Is	
			Present	*Absent*
Asymmetrical Chest Expansion				
Detecting pneumonia in patients with acute cough[4]	5	100	**44.1**	NS
Detecting pleural effusion in hospitalized patients with respiratory complaints[5]	74	91	**8.1**	**0.3**
Asymmetrical chest wall movements after intubation, detecting right main-stem bronchus intubation[6]	30	98	**15.7**	NS
Diminished Tactile Fremitus				
Detecting pleural effusion[5]	82	86	**5.7**	**0.2**
Chest Wall Tenderness				
Detecting pneumonia in patients with acute cough[7]	5	96	NS	NS
Detecting pulmonary embolism in patients with pleuritic chest pain[8,9]	11-17	79-80	NS	NS
Detecting coronary artery disease in outpatients with chronic chest pain[10–13]	1-69	16-97	0.8	NS
Detecting myocardial infarction in patients with acute nontraumatic chest pain[14–16]	3-15	64-83	**0.3**	1.3

*Diagnostic standard: For pleural effusion, chest radiograph; for pulmonary embolism, coronary artery disease, and myocardial infarction, see Chapters 32 and 47.

†Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. *Click here to access calculator.*



PERCUSSION

I. INTRODUCTION

In 1761, after studying patients and cadavers at the Spanish Hospital in Vienna for 7 years, Leopold Auenbrugger published a 95-page booklet containing the first detailed description of chest percussion.[17] His work was largely ignored for half a century, until Corvisart (physician to Napoleon) translated it into French and taught the technique to his students, including Laennec, the subsequent inventor of the stethoscope.[18] The discovery of percussion was a major diagnostic advance because for the first time, clinicians could reliably distinguish empyema from tuberculosis and other pneumonias.[18] Until the discovery of roentgen rays in 1895, percussion and auscultation were the only methods for investigating and defining diseases of the lungs during the patient's life.

II. TECHNIQUE

A. DIRECT VERSUS INDIRECT METHOD

In the direct method, the percussion blow lands directly on the body wall (the method of Auenbrugger and Laennec). In the indirect method, the blow falls instead on an intervening substance, called a pleximeter, placed against the body wall. Historically, pleximeters were made of ivory or wood, or a coin was used, although today most clinicians use the middle finger of their left hand.

B. TYPES OF PERCUSSION

There are three ways to percuss the patient.

1. Comparative percussion (the original method of Auenbrugger and Laennec)
2. Topographic percussion (invented by Piorry of France in 1828)[19,20]
3. Auscultatory percussion (introduced by the Americans Camman and Clark in 1840)[18,21]

Today, most clinicians use the indirect method with comparative and topographic percussion and the direct method with auscultatory percussion.

1. Comparative Percussion

Comparative percussion identifies disease by comparing the right and left sides of the chest. Prominent dullness or unusual hyperresonance over one side indicates disease in that part. Bilateral disease, by definition, is more difficult to identify using comparative percussion.

2. Topographic Percussion

Topographic percussion attributes any dullness in the chest or abdomen to airless intrathoracic tissue lying directly beneath the percussion blow. Topographic percussion differs from comparative percussion in implying that the clinician can precisely outline the borders of underlying organs and then measure their span. The technique is still used today to measure excursion of the diaphragm (and to identify an enlarged heart or liver; see Chapters 35 and 49).

When using topographic percussion to determine diaphragm excursion, the clinician locates the point of transition between dullness and resonance on the lower posterior chest, first during full inspiration and then during full expiration. The diaphragm excursion is the vertical distance between these two points. The reported normal excursion of healthy persons ranges from 3 to 6 cm. (For comparison, the corresponding excursion on the chest radiograph is about 5 to 7 cm in normal persons and 2 to 3 cm in patients with lung disease.[18,22,23])

3. Auscultatory Percussion

Auscultatory percussion was introduced to further refine the goals of topographic percussion.[21] Instead of listening to sounds as they resonate off the chest into the surrounding room, the clinician using auscultatory percussion places the stethoscope on the body wall and listens through it to the sounds transmitted by nearby percussive blows.

Over the past 150 years, auscultatory percussion of the chest has repeatedly fallen out of favor and then resurfaced as a "new sign."[18] In the most recent version of auscultatory percussion of the chest, introduced in 1974, the clinician taps lightly over the manubrium and listens over the posterior part of the chest with the stethoscope.[24,25] Using this technique, the clinician should find identical sounds at corresponding locations of the two sides of the chest; a note of decreased intensity on one side supposedly indicates ipsilateral disease between the tapping finger and the stethoscope.

The technique of using auscultatory percussion to detect pleural fluid, first developed in 1927,[26] is slightly different. The clinician places the stethoscope on the posterior chest of the seated patient, 3 cm below the twelfth rib, and percusses the posterior chest from apex to base. At some point, the normal dull note changes to an unusually loud note: if this occurs with strokes above the 12th rib, the test is abnormal, indicating pleural fluid.[27]

C. THE PERCUSSION BLOW

1. Force

Each percussion blow should strike the same part of the pleximeter with identical force, and the pleximeter finger should be applied with the same force and orientation when comparing right and left sides. Consistent technique is important because both the percussion force and the pleximeter govern the percussion sound produced. Lighter strokes produce sounds that are duller than those produced by stronger strokes. Lifting the pleximeter finger, even slightly, can transform a resonant note into a dull one.

Even though a consistent technique is important, the force and speed of percussion blows vary threefold among different clinicians,[28] which probably explains why interobserver agreement for topographic percussion is poor compared with that for other physical findings (see Chapter 4).

2. Rapid Withdrawal of Plexor

The traditional teaching is that the plexor finger should be promptly withdrawn after a blow, mimicking the action of a piano key striking a string. The only study of this found that clinicians could not distinguish the note created by a rapid withdrawal from one in which the plexor finger lightly rested on the pleximeter after the blow.[29]

III. THE FINDING

A. PERCUSSION SOUNDS

There are three percussion sounds—**tympany** (normally heard over the abdomen), **resonance** (heard over a normal lung), and **dullness** (heard over the liver or thigh) (Fig. 27-1). Tympany differs from resonance and dullness because it contains vibrations of a dominant frequency that allow the clinician to actually identify its musical pitch. Resonance and dullness, in contrast, are "noise" in an acoustic sense, consisting of a jumble of frequencies that prevent identification of a specific musical pitch. The three sound characteristics distinguishing resonance and dullness are intensity, duration, and frequency content: Resonance is louder and longer and contains more low-frequency energy.[18,30] Of these three sound characteristics, clinicians appreciate most easily that resonance is louder than dullness.

Some clinicians take advantage of resonance being louder than dullness and apply a technique called threshold percussion, in which percussion blows are so light that dull areas produce no sound. As the blows move along the body wall with precisely the same amount of force, a note abruptly appears the moment the blow encounters a resonant area. An old

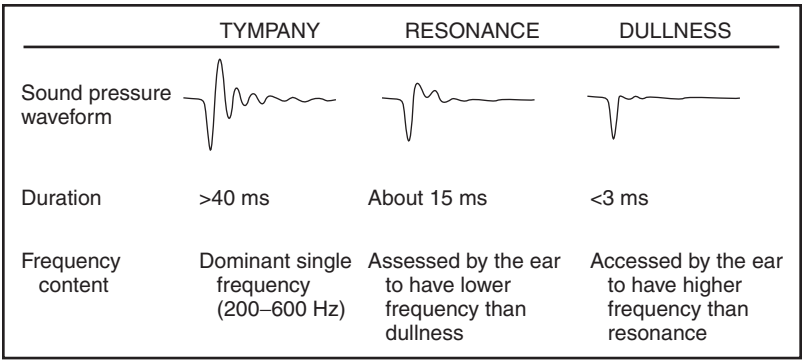


FIGURE 27-1 The percussion sounds. The figure is adapted from references 18 and 30. In the older literature, synonyms for resonance were "full," "clear," and "distinct"; synonyms for dullness were "empty," "not distinct," and "thigh" sound.

adage in percussion, attributed to Weil, is that it is much easier to distinguish "something from nothing" than to distinguish "more from less."[18]

B. SENSE OF RESISTANCE

All great teachers of percussion have emphasized that the tactile sense in the pleximeter finger provides as much information as the audible notes. Dull areas, according to these teachers, move less or offer more resistance than resonant areas (thus earning pleural effusion the descriptor "stony dullness"). Experiments using lightweight accelerometers taped to the pleximeter finger confirm that dull areas do move less than resonant areas.[31]

C. GLOSSARY OF ADDITIONAL PERCUSSION TERMS

Historically, the vocabulary of clinical percussion was diverse. Some of the more commonly used terms appear below.

1. Skodaic Resonance

Skodaic resonance is a hyperresonant note produced by percussion of the chest above a pleural effusion. The cause of this finding is unknown. Skodaic resonance was originally described by Josef Skoda,[32] a champion of topographic percussion and the first to apply the principles of physics to percussion.

2. Grocco Triangle

The **Grocco triangle** is a right-angled triangle of dullness found over the posterior region of the chest *opposite* a large pleural effusion. The horizontal side of the triangle follows the diaphragm for several centimeters; the vertical side lies over the spinous processes but usually ends below the top level of the effusion.[18] This finding was originally described by Koranyi (Hungary, 1897) and later by Grocco (Italy, 1902) and Rauchfuss (Germany, 1903).

3. Metallic Resonance (Amphoric Resonance; Coin Test)

Metallic resonance is a pure tympanitic sound containing very high frequencies, found over large superficial pulmonary cavities or pneumothoraces.[32,33] Flicking the tense cheek while holding the mouth open mimics the sound. The sound was best elicited with a hard plexor and pleximeter (e.g., two coins) and is best perceived through the stethoscope or with the examiner's ear near the patient's chest.[18]

4. Krönig Isthmus

Krönig isthmus is a narrow band of resonance over each lung apex that lies between the dullness from the neck and the dullness from the shoulder muscles. Diseases of the lung apex, such as tuberculosis, supposedly reduced the width of the band.[18] Georg Krönig (Germany) described the finding in 1889.[34]

5. Cracked-Pot Resonance

Cracked-pot resonance is a percussion sound over superficial tubercular cavities, mimicked by pressing the palms together and hitting the back of one hand against the knee.[32,35] To detect the sound in patients, the clinician delivers a strong percussion blow and listens near the patient's open mouth.[2,36] Although the sound was traditionally attributed to the sudden efflux of air through bronchi communicating with a tubercular cavity, the only published pathologic study found no bronchial communication in 11 patients with this sound.[37]

IV. PATHOGENESIS

A. TOPOGRAPHIC PERCUSSION VERSUS CAGE RESONANCE THEORY

From the earliest days of percussion, two opposing theories have explained the genesis of percussion sounds: the **topographic percussion theory** and the **cage resonance theory.** The topographic percussion theory argued that only the physical characteristics of the soft tissues directly beneath the percussion blow controlled whether resonance or dullness was produced. This theory emphasized that the body wall itself contributed little to the resulting sound but acted merely to convey the vibrations from the underlying tissues (much like a diaphragm in a microphone transmits the sound vibrations imparted to it). A fundamental tenet of the topographic percussion theory was the **several centimeter rule,** advanced by Weil in 1880,[38] which stated that the percussion stroke penetrated only the most superficial 4 to 6 cm of tissue, and only anatomic abnormalities in this layer influenced the sound produced.

In contrast, the cage resonance theory argued that the percussion sound reflected the ease with which the body wall vibrates, which in turn was influenced by many variables, including the strength of the stroke, the condition and state of the body wall, and the underlying organs. Advocates of the cage resonance theory argued that precise topographic percussion was impossible because underlying organs or disease could cause dullness to occur at distant sites.

The topographic percussion theory became very popular—largely through the persuasive efforts of renowned clinical teachers, including Piorry, Skoda, Mueller, and Mueller's pupil, Ralph Major, who wrote one of the most popular American physical diagnosis textbooks.[1] Nonetheless, the evidence cited to support this theory and the several centimeter rule was meager and of uncertain relevance:[18] It included only a few experiments with cadavers[38] and some sound recordings of exenterated lung slices as they were being percussed.[39]

In contrast, considerable evidence supports the cage resonance theory.

1. Analysis of Sound Recordings

The percussion sound contains more frequencies than can be explained by vibrations of just the area of the body wall percussed.[31,40–42] Areas of the body wall distant to the blow must also vibrate and contribute to the sound.

2. Condition and State of the Body Wall

External pressure on the chest—from a pillow, a stretcher, or an extra hand placed near the point of percussion—impedes chest wall motion and dampens the percussion note.[33,43]

Pressure against the inner wall of the chest of cadavers also causes dullness, even in areas of the body wall distant from where the pressure is applied.[33] The best clinical example of the distant effects of internal pressure is the Grocco triangle, a right-angled triangle of dullness found over the posterior region of the chest *opposite* a large pleural effusion (see earlier discussion). The Grocco triangle proves that pressure on the chest wall at one point (e.g., from pleural fluid) may cause dullness at sites distant to that pressure (i.e., over the opposite chest). Even in patients without pleural fluid, external pressure on one side of the posterior chest from a hand or water bottle will produce the Grocco triangle on the opposite chest.[44,45]

Heavier patients have larger liver spans than patients who weigh less,[46] not because the livers of heavier patients are larger but because the excess subcutaneous fat influences the cage resonance and dampens the vibrations, resulting in more dullness and larger spans.

3. The Strength of the Percussion Blow

The strength of the blow influences whether resonance or dullness is produced, especially near areas of the body wall marking the transition between resonance and dullness. For example, in percussion of the liver, the span of the liver is about 3 cm smaller when using strong strokes than it is when using light strokes (see Chapter 49).[46–48] This occurs because the heavy stroke, when located near where the liver touches the body wall, more easily generates the vibrations necessary for the resonant note, whereas the light stroke is insufficient until further removed. These findings contradict the assertion of topographic percussionists, who taught that stronger blows penetrated tissues more deeply than softer ones; if this were true, percussion of the liver with heavy strokes should produce a larger span than with light strokes (because heavier strokes would detect the dome of the liver, which is removed from the body wall).

B. AUSCULTATORY PERCUSSION

The advocates of auscultatory percussion believe that sound waves travel directly from the tapping finger through the lung to the stethoscope and are altered along the way by diseased tissue. It is much more likely, however, that these sounds are conducted circumferentially in the chest wall, for several reasons.

1. The technique fails to detect the heart, which should render some notes of the left chest more dull if sound waves traveled directly to the stethoscope.
2. Sound recordings during auscultatory percussion are the same whether the patient breathes room air or a mixture of helium and oxygen.[49] Because sound characteristics depend on the gas density of the conducting medium, which is different for the two gas mixtures, it is unlikely that sound travels through the lung.
3. The characteristics of the sound change during the Valsalva and Mueller maneuvers, which increase tension in the chest wall but do not alter the underlying lung.[49]
4. Contour maps reveal that the loudest sounds during auscultatory percussion appear over bony prominences, such as the scapula, indicating that the sound produced depends on the contour of the chest wall. The intervening lung contributes less to the sound heard because these sound maps do not change even when there is a large underlying tumor.[50]

V. CLINICAL SIGNIFICANCE

A. COMPARATIVE PERCUSSION

EBM Box 27-2 shows that asymmetrical dullness is a helpful though infrequent finding that increases the probability of pneumonia in patients with fever and cough (LR = 3), of underlying abnormalities on the chest radiograph of unselected patients (LR = 3), and of pleural effusion in hospitalized patients with respiratory complaints (LR = 4.8). In these studies, percussion detected all large pleural effusions (sensitivity 100%) but very few consolidations (sensitivity 0% to 15%) and no intraparenchymal nodules or granulomas. The presence of normal resonance decreases significantly the probability of underlying pleural effusion (LR = 0.1) but does not change the probability of other significant pathologic lung characteristics.

In chronic smokers, hyperresonance of the upper right anterior chest is a valuable finding increasing the probability of chronic airflow obstruction (LR = 5.1; see EBM Box 27-2).[58]

B. TOPOGRAPHIC PERCUSSION OF THE DIAPHRAGM

In patients with lung disease, clinicians usually overestimate the actual movements of the diaphragm and differ from the chest film by 1 to 3 cm.[22,59] The correlation between actual and percussed movements is poor in the only study of this finding ($r = 0.14$ to 0.42, not significant half the time).[22] Another study showed that a percussed diaphragm excursion of less than 2 cm is an infrequent and unreliable diagnostic sign of chronic obstructive lung disease (both LRs not significant; see EBM Box 27-2).[58]

C. AUSCULTATORY PERCUSSION

Studies of auscultatory percussion have widely varying results, usually showing that the technique has greater sensitivity than comparative percussion but also lower specificity. Overall, the pooled results show that this

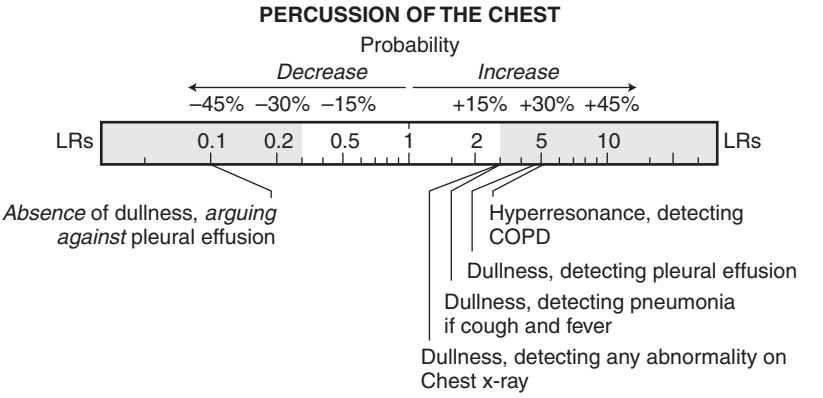
EBM BOX 27-2
*Diagnostic Accuracy of Percussion of the Chest**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Comparative Percussion				
PERCUSSION DULLNESS				
Detecting pneumonia in patients with fever and cough[4,51–54]	4-26	82-99	**3.0**	NS
Detecting any abnormality on chest radiograph[55–57]	8-15	94-98	**3.0**	NS
Detecting pleural effusion in patients with respiratory complaints[5]	89	81	**4.8**	**0.1**
HYPERRESONANCE				
Detecting chronic airflow obstruction[58]	33	94	**5.1**	NS
Topographic Percussion				
DIAPHRAGM EXCURSION <2 CM				
Detecting chronic airflow obstruction[58]	13	98	NS	NS
Auscultatory Percussion				
ABNORMAL DULLNESS				
Detecting any abnormality on chest radiograph[55–57]	16-69	74-88	NS	NS
Detecting pleural fluid[5,27]	58-96	85-95	**8.3**	NS

*Diagnostic standard: For *pneumonia* or *pleural effusion*, infiltrate or effusion on chest radiograph; for *chronic airflow obstruction*, FEV_1 <60% predicted or the FEV_1/FVC ratio <0.6.

†Definition of findings: For *hyperresonance*, hyperresonance of the upper right anterior chest[58]; for *abnormal dullness during auscultatory percussion for chest radiograph abnormalities*, asymmetrical dullness, with stethoscope on posterior chest and while directly percussing sternum anteriorly; for *abnormal dullness during auscultatory percussion for pleural fluid*, transition to unusually loud note above 12th rib posteriorly in midclavicular line, with stethoscope 3 cm below 12th rib and while directly percussing posterior chest from apex to base.[27]

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; NS, not significant. *Click here to access calculator.*



technique is an unreliable diagnostic sign. (Both positive and negative LRs are not significant; see EBM Box 27-2.)

Like conventional percussion, auscultatory percussion identifies most pleural effusions (sensitivity 58% to 96%; see EBM Box 27-2). A positive result (see the section on Auscultatory Percussion for a definition of the technique) significantly increases the probability of pleural effusion (LR = 8.3).

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 28

Auscultation of the Lungs

The three categories of auscultatory findings of the lungs are breath sounds, vocal resonance (i.e., the sound of the patient's voice through the stethoscope), and adventitious sounds (i.e., sounds other than breath sounds or vocal resonance). Almost all of the findings discussed in this chapter were originally described in 1819 by Laennec in his masterpiece *A Treatise on the Diseases of the Chest*.[1]

I. BREATH SOUNDS

A. FINDING

1. Vesicular Versus Bronchial Breath Sounds

There are two types of breath sounds.

1. Vesicular breath sounds, which are normally heard over the posterior chest
2. Bronchial breath sounds, which are normally heard over the trachea and right apex

These sounds are distinguished by their timing, intensity, and pitch (Fig. 28-1). Vesicular sounds are mostly inspiratory sounds that have a soft, breathy quality, which Laennec likened to the sound of leaves rustling in a gentle breeze. Bronchial sounds have a prominent expiratory component and much harsher quality, sounding like air being blown forcibly through a tube. (Hence, they are sometimes called tubular breath sounds.)

Bronchial breath sounds are abnormal when they occur over the posterior or lateral chest (especially the lower parts). According to traditional teachings, which in turn are based on postmortem examinations, bronchial breath sounds occur in these locations only if solid, collapsed, or consolidated lung is contiguous with the chest wall and extends some distance toward the hilum.[7–9] The usual causes are pneumonia and pleural effusion. (Large pleural effusions presumably compress the underlying lung just enough to alter its acoustic properties.[10])

2. Breath Sound Score

One important feature of vesicular breath sounds is their intensity, which can be graded using a scoring system developed by Pardee.[11] According to this system, the clinician listens sequentially over six locations on the patient's chest: bilaterally over the upper anterior portion of the chest, in

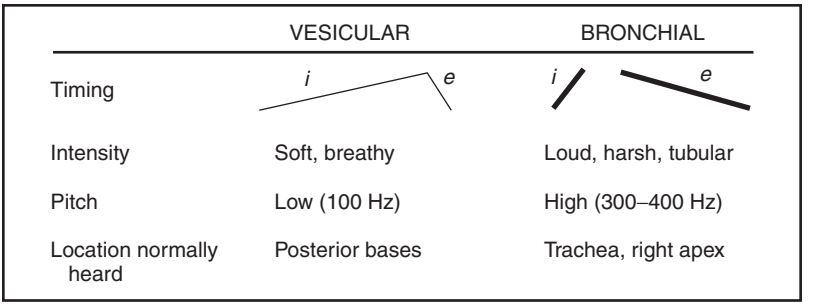


FIGURE 28-1 Comparison of vesicular and bronchial breath sounds. In vesicular sounds *(left),* inspiration *(i)* is longer than expiration *(e),* and there is no gap between inspiration and expiration. In bronchial sounds *(right),* expiration is longer than inspiration, and there is a conspicuous gap between inspiration and expiration. This figure is based on information from references 2 to 6.

the midaxillas, and at the posterior bases. At each site, the clinician grades the *inspiratory* sound as absent (0 points), barely audible (1 point), faint but definitely heard (2 points), normal (3 points), or louder than normal (4 points). The patient's total score may range from 0 (absent breath sounds) to 24 (very loud breath sounds).

B. PATHOGENESIS

1. Vesicular Sounds

a. Origin

The *inspiratory* component of vesicular breath sounds originates in the peripheral portions of the lung near where the stethoscope is placed. It does not represent simple filtration of tracheal sounds by the intervening inflated lung. The *expiratory* component of vesicular sounds probably originates in more proximal, larger airways. Several lines of evidence support these statements.

1. In experiments performed with sheep's and calf's lungs over a century ago, Bullar kept the airways of both lungs patent but rhythmically inflated only one of the two lungs using negative pressure.[12] He showed that vesicular sounds occurred only if the lung contiguous to the stethoscope filled with air; if it remained airless, it simply transmitted the upper airway bronchial sounds.
2. The intensity of the inspiratory component of breath sounds, corrected for flow rate at the mouth, is roughly proportional to regional ventilation.[13]
3. The inspiratory component of vesicular sounds remains the same as the stethoscope is moved progressively from the upper to lower posterior chest, although the expiratory component becomes softer.[14]
4. Vesicular sounds contain low-frequency components lacking in tracheal sounds that cannot be reproduced in experiments interposing inflated lung between the trachea and the stethoscope.[2–4]

b. Intensity

The intensity of vesicular sounds is proportional to the flow rate of air at the mouth, which in turn depends on the patient's effort and ventilatory capacity.[11,15,16] Breath sounds are thus louder if a normal person breathes hard after exercise, and they are faint if obstructive lung disease diminishes flow rates.[17] Breath sounds are also reduced when air or fluid is interposed between the chest wall and the lung, as in patients with pneumothorax or pleural effusion.

2. Bronchial Sounds

Bronchial breath sounds originate in larger proximal airways. They are normally heard over the right upper chest posteriorly but not over the left upper chest, because the trachea is contiguous with the right lung near the first thoracic vertebra but separated from the left lung by most of the mediastinum.[18] The glottis is not necessary to the sound, because bronchial sounds may occur in patients after laryngectomy or after intubation.[19] The pathogenesis of bronchial breath sounds in pneumonia and pleural effusion is discussed later in the section on Pathogenesis of Vocal Resonance.

C. CLINICAL SIGNIFICANCE

1. Breath Sound Intensity

A breath sound score of 9 or less greatly increases the probability of chronic airflow obstruction (likelihood ratio [LR] = 10.2; EBM Box 28-1), and a score of 16 or more greatly decreases the probability (LR = 0.1). The breath sound score is superior to the clinician's "overall impression" of breath sound intensity in diagnosing chronic airflow obstruction (LR = 3.2 for overall impression of "diminished" breath sounds and LR = 0.5 for "normal or increased" breath sounds; see EBM Box 28-1).

The presence of unilaterally diminished breath sounds increases the probability of pleural effusion in hospitalized patients with respiratory complaints (LR = 5.2); in patients with acute respiratory distress syndrome receiving mechanical ventilation, the absence of breath sounds over a specific region of the chest also increases the probability of underlying pleural fluid (LR = 4.3). Also, the appearance of reduced breath sounds during methacholine challenge increases the probability of asthma (LR = 4.2), and in patients with fever and cough, the appearance of diminished breath sounds modestly increases the probability of pneumonia (LR = 2.3).

The presence of normal breath sound intensity greatly decreases the probability of underlying pleural effusion (LR = 0.1).

2. Asymmetrical Breath Sounds after Intubation

If the endotracheal tube is placed too low during intubation of a patient, it risks intubating the right mainstem bronchus and leaving the left lung unventilated, a complication that logically would produce asymmetrical breath sounds. In studies of patients after intubation, asymmetrical breath sounds indeed are pathognomonic for endobronchial intubation (LR = 24.4; see EBM Box 28-1), but the converse is not true: The presence of symmetrical breath sounds does *not* significantly decrease the probability

EBM BOX 28-1
*Breath Sounds and Vocal Resonance**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Breath Sound Score				
Detecting chronic airflow obstruction[11,15]				
≤9	23-46	96-97	**10.2**	—
10-12	34-63	—	**3.6**	—
13-15	11-16	—	NS	—
≥16	3-10	33-34	**0.1**	—
Diminished Breath Sounds				
Detecting pleural effusion in hospitalized patients[20]	88	83	**5.2**	**0.1**
Detecting chronic airflow obstruction[21–24]	29-82	63-96	**3.2**	0.5
Detecting underlying pleural effusion in mechanically ventilated patient[25]	42	90	**4.3**	0.6
Detecting asthma during methacholine challenge testing[26]	78	81	**4.2**	**0.3**
Detecting pneumonia in patients with cough and fever[27–30]	15-49	73-95	2.3	0.8
Asymmetrical Breath Sounds After Intubation				
Detecting right main-stem bronchus intubation[31,32]	28-41	98-99	**24.4**	0.7
Bronchial Breath Sounds				
Detecting pneumonia in patients with cough and fever[27]	14	96	**3.3**	NS
Egophony				
Detecting pneumonia in patients with cough and fever[27,29,33]	4-16	96-99	**4.1**	NS

EBM BOX 28-1
Breath Sounds and Vocal Resonance—cont'd

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Diminished Vocal Resonance				
Detecting pleural effusion in hospitalized patients[20]	78	88	**6.5**	**0.3**

*Diagnostic standard: For *chronic airflow obstruction*, FEV_1 <40% predicted (breath sound score) or FEV_1/FVC (%) ratio <0.6 to 0.7 (diminished breath sounds); for *underlying pleural effusion*, chest radiography or (if mechanically ventilated) computed tomography; for *asthma*, FEV_1 decreases ≥20% during methacholine challenge; for *pneumonia*, infiltrate on chest radiograph; for *right mainstem intubation*, chest radiograph[31] or direct endoscopic visualization.[32]

†Definition of findings: For *breath sound score*, see text; for *diminished vocal resonance intensity*, the transmitted sounds from the patient's voice when reciting numbers, as detected by a stethoscope on the patient's posterior chest, are reduced or absent.[20]

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. NS, not significant.

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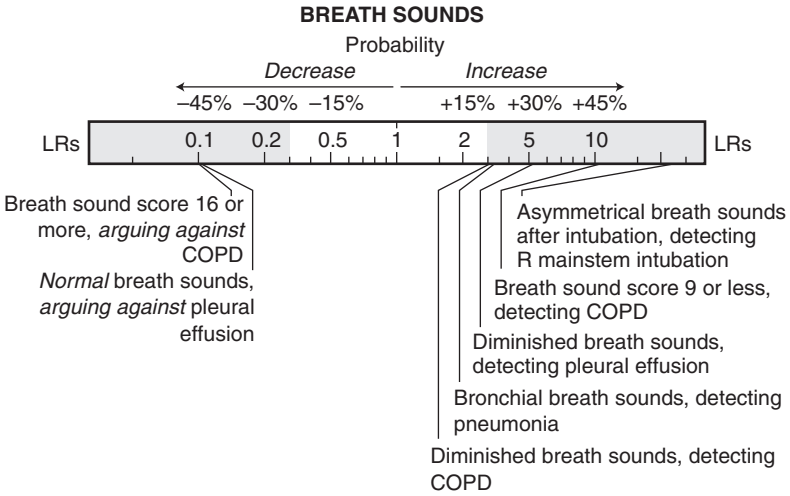
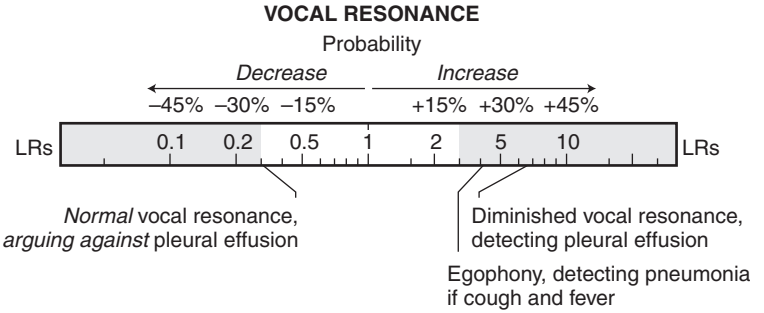




of endobronchial intubation (LR = 0.7). Confirmation of appropriate tube placement by means other than physical examination is always indicated.

3. Bronchial Breath Sounds

In patients with cough and fever, bronchial breath sounds increase the probability of pneumonia (LR = 3.3), although the sign is infrequent (sensitivity is 14%).

II. VOCAL RESONANCE

A. THE FINDING

Vocal resonance refers to the sound of the patient's voice as detected through a stethoscope placed on the patient's chest. Normally, the voice sounds muffled, weak, and indistinct over most of the inferior and posterior chest, and words are unintelligible. Abnormal vocal resonance is classified as either bronchophony, pectoriloquy, or egophony, all terms originally introduced by Laennec.[1] Although these abnormalities have distinct definitions, the pathogenesis for all three is similar, and all may appear simultaneously in the same patient, frequently accompanied by bronchial breath sounds.

1. Bronchophony

Bronchophony describes a voice that is much louder than normal, as if the sounds were emitted directly into the stethoscope. The patient's words are not necessarily intelligible.

2. Pectoriloquy

Pectoriloquy implies that the patient's words are intelligible. Most clinicians test this by having the patient whisper words like "one-two-three"; intelligible whispered speech is called **whispered pectoriloquy.**

3. Egophony

Egophony is a peculiar nasal quality to the sound of the patient's voice, which Laennec likened to the "bleating of a goat."[1] Clinicians usually elicit the finding by having the patient vocalize the long vowel "EE" and then listening for the abnormal transformation of the sound into a loud nasal "AH." (The "AH" sound ranges from the "a" of the word *hat* to the "a" of the word *cart;* this finding is sometimes called **E-to-A change**.*) Although all vowel sounds are altered by the lung (even healthy lung), what makes egophony distinctive is the intensity of the change and the suddenness with which it appears over a small area on *one* side of the chest.[36] Before concluding that a patient has egophony, therefore, the clinician should confirm that a similar change of sound is absent over the identical location of the opposite chest.

*The E-to-A change was simultaneously discovered in 1922 by Shibley[34] and Fröschel.[35] Shipley discovered it while testing for pectoriloquy in Chinese patients. He asked the patients to say "one-two-three" in the local dialect *(ee-er-san)*, and he noted that the long "EE" of "one" acquired a loud nasal "AH" quality over areas of pneumonia or effusion.[34]

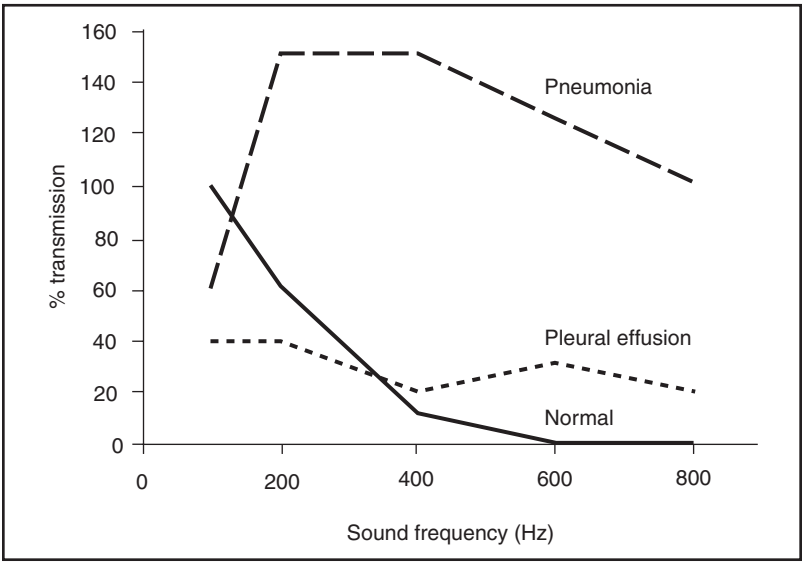


FIGURE 28-2 Transmission of sound to the chest wall. In this experiment, a speaker emitting pure musical tones of different frequencies was placed in the mouth of patients with normal lungs *(solid line)*, pneumonia *(long dashes)*, or pleural effusion *(short dashes)*. Microphones on the chest wall recorded the transmission of each frequency. (For purposes of comparison, 100% transmission is the transmission of 100 Hz in normal persons.) Adapted from reference 37.

B. PATHOGENESIS

Figure 28-2 depicts the transmission of sound from the larynx to the chest wall in normal persons and in those with pneumonia or pleural effusion. Normal lung behaves like a low-pass filter, which means it easily transmits low-frequency sounds (100 to 200 Hz) but filters out high-frequency sounds (>300 Hz).[6,37–39] Because tactile fremitus (the palpable vibrations on the chest wall from the patient's voice) consists of low-frequency vibrations (100 to 200 Hz), it is a normal finding when symmetrical, although tactile fremitus is naturally more prominent in healthy men than healthy women (i.e., men's voices are lower pitched and therefore more likely to generate low-frequency vibrations than women's voices). Tactile fremitus also diminishes as a healthy person sings an ascending scale because the underlying lung resonates less well with higher pitches.

Abnormal vocal resonance (i.e., bronchophony, whispered pectoriloquy, and egophony) requires transmission of higher frequencies (>300 Hz) to the chest wall; understanding whispered speech requires the transmission of frequencies of more than 400 Hz (i.e., whispered pectoriloquy). The sound "AH" contains more high-frequency energy than the sound "EE." If the underlying lung preferentially amplifies the high-frequency energy of a vocalized "EE," it may render it into a nasal "AH" (i.e., egophony).[6,38] Because the normal lung does not transmit high-frequency (>300 Hz) sounds well, especially to the lower posterior and lateral chest, the presence

of egophony and bronchial breath sounds at these locations always indicates the presence of *abnormal* lung between the patient's vocal cords and the clinician's stethoscope.

According to Figure 28-2, consolidated lung transmits both high and low frequencies well; this explains why patients with pneumonia may simultaneously exhibit both increased tactile fremitus and abnormal vocal resonance (i.e., egophony). A moderate or large pleural effusion, in contrast, may *decrease* transmission of frequencies below 200 to 300 Hz but *augment* those greater than 400 Hz, compared with normal lung (see Fig. 28-2).[6,10,37–39] This explains why some patients with pleural effusion exhibit both *decreased* tactile fremitus yet *abnormal* vocal resonance (i.e., egophony).

Nonetheless, egophony (abnormal vocal resonance) in patients with pleural effusion is an inconstant finding, and many patients instead demonstrate *reduced* or *absent* vocal resonance over the affected side (i.e., the patient's spoken voice is inaudible or markedly diminished and the nasal "AH" is absent). Laennec himself taught that egophony is not always present in pleural effusion but first appears when effusions are moderate in size, then *disappears* as effusions continue to grow larger, and finally *reappears* as effusions began to resolve.[1] The conventional explanation for these findings is that atelectatic lung, resting on top of an effusion, remains close enough to the chest wall to preferentially conduct enough high-frequency sounds to produce abnormal vocal resonance (loudest near the angle of the scapula); as effusions continue to grow larger, the distance between the compressed lung and the chest wall increases and egophony thus disappears.

This explanation has never been verified, and it remains a mystery why some patients with effusion have prominent egophony over large areas of the posterior chest wall yet others have diminished vocal resonance. The only study of this finding shows that pleural effusions producing abnormal vocal resonance (e.g., egophony) have higher positive intrapleural pressures than effusions without the finding.[10] From an acoustic standpoint, the variables responsible for abnormal vocal resonance might include not only the size of effusion and condition of the underlying compressed lung but also the distance between the lung and the chest wall, the viscosity of the pleural fluid, and the condition of the underlying inflamed pleural surface and chest wall.

C. CLINICAL SIGNIFICANCE

Abnormal vocal resonance has the same significance (and pathogenesis) as bronchial breath sounds. In patients with cough and fever, the finding of egophony increases the probability of pneumonia (LR = 4.1; see EBM Box 28-1), and in hospitalized patients with a variety of respiratory complaints, the finding of diminished vocal resonance (i.e., diminished intensity of the voice when the patient is reciting numbers) increases the probability of an underlying pleural effusion (LR = 6.5).

According to traditional teachings, an obstructed bronchus should diminish vocal resonance. This teaching is probably incorrect, however, based on both the observation that some patients with egophony and

pneumonia have obstructed bronchi from tumors[38] and experiments showing that sound conducts down the substance of the porous lung itself to the chest wall, not down the airway ducts.*[40]

III. ADVENTITIOUS SOUNDS

A. INTRODUCTION

Adventitious sounds are all sounds heard during auscultation other than breath sounds or vocal resonance. The common adventitious sounds are crackles, rubs, wheezes, rhonchi, and stridor.

Adventitious sounds have the most ambiguous and confusing nomenclature in all of physical diagnosis, and studies show clinicians use up to 16 different terms in scientific publications to describe similar sounds.[41] This confusion stems from the earliest days of auscultation and the writings of Laennec, who, in the first edition of his treatise, identified five adventitious sounds but called them all *rales*, distinguishing them further only by adding adjectives (e.g., "moist crepitus rale" for a crackling sound, or "dry sibilus rale" for a whistling sound).[1,42] In later editions, Laennec substituted *rhonchus* for *rale* because he became worried that patients hearing *rale* would mistake it for the death rattle. (*Rale* means rattle.) In 1831, a British editor introduced the Anglo-Saxon term *wheeze*, again to refer to all lung sounds.[42] Finally, Robertson in 1957 proposed using *crackling sounds* for discontinuous sounds and *wheezes* for continuous, musical sounds, and suggested eliminating *rale* and *rhonchus* altogether.[43]

According to the American Thoracic Society, the recommended terms for lung sounds, based on their acoustic characteristics,[44] are **crackle** for discontinuous sounds and **wheeze** or **rhonchus** for continuous sounds (Table 28-1).

B. THE FINDING

1. Crackles

Crackles are discontinuous sounds, resembling the sound produced by rubbing strands of hair together in front of the ear or by pulling apart strips of Velcro. There are **coarse crackles,** which are loud, low-pitched, and fewer in number per breath, and **fine crackles,** which are soft, higher-pitched, and greater in number per breath. Crackles that appear early during inspiration and do not continue beyond midinspiration are called **early inspiratory** crackles; those that continue into the second half of inspiration are called **late inspiratory** crackles.[47] Many American clinicians still use the word *rale* as a synonym for crackle, although British clinicians more often use crackle.[48,49]

The term **posturally induced crackles,** which may have significance after myocardial infarction (see the section on Clinical Significance, later), describes crackles that appear when the patient is in the supine position but

*The acoustic characteristics of the transmitted sound are the same whether the patient breathes air or a mixture of oxygen and helium. If sound were conducted down the airways, its characteristics would change with different gas mixtures.[40]

TABLE 28-1 Terminology for Lung Sounds*

Recommended ATS Term	Acoustic Characteristics	Terms in Some Textbooks	British Usage
Coarse crackle	Discontinuous sound: loud, low in pitch	Coarse rale	Crackle
Fine crackle	Discontinuous sound: soft, higher pitch, shorter duration	Fine rale	Crackle
Wheeze	Continuous sound: high-pitched, dominant frequency ≥400 Hz	Sibilant rhonchus	High-pitched wheeze
Rhonchus	Continuous sound: low-pitched, dominant frequency ≤200 Hz	Sonorous rhonchus	Low-pitched wheeze

*Adapted from references 44 to 46.
ATS, American Thoracic Society.

disappear when the patient is in the sitting position. To elicit the finding, the clinician listens to the lower chest wall near the posterior axillary line with the patient in three sequential positions: sitting, supine, and supine with legs elevated 30 degrees.[50] The clinician listens only after the patient has been in each position for 3 minutes. If crackles are absent when the patient is upright but appear when the patient either is supine or has the legs elevated, the test is positive (i.e., the patient has posturally induced crackles).

2. Wheezes and Rhonchi

According to the American Thoracic Society, a **wheeze** is a high-pitched, continuous musical sound and a **rhonchus** is a low-pitched one (see Table 28-1). This distinction may be superfluous because both sounds have the same pathophysiologic characteristics, and there is no proven clinical importance to separating them. The term *rhonchus* is probably best avoided, not only for these reasons but also because many use the term to refer to the coarse discontinuous sounds heard in patients with excess airway secretions.[48]

3. Stridor

Stridor is a loud, musical sound of definite and constant pitch (usually about 400 Hz) that indicates upper airway obstruction.[39,46] It is identical acoustically to wheezing in every way except for two characteristics.

1. Stridor is confined to inspiration, whereas wheezing either is confined entirely to expiration (30% to 60% of patients) or occurs during both expiration and inspiration (40% to 70% of patients)[51,52]
2. Stridor is always louder over the neck, whereas wheezing is always louder over the chest[52]

In some patients with upper airway obstruction, stridor does not appear until the patient breathes rapidly through an open mouth.[53]

4. Pleural Rubs

Pleural rubs are loud grating or rubbing sounds associated with breathing that occur in patients with pleural disease. Sometimes, a pleural rub has a crackling character **(pleural crackling rub)** and acoustically resembles the crackles heard in patients with parenchymal disease.[54,55] The timing of the crackling sound best distinguishes the pleural crackling rub from parenchymal crackles: The pleural crackling rub is predominantly *expiratory* (i.e., 65% of the crackling sound occurs during expiration), but parenchymal crackles are predominantly *inspiratory* (i.e., only 10% of the crackling sound occurs during expiration).[56]

5. Inspiratory Squawk

The **squawk** is a short, late inspiratory musical sound associated with parenchymal crackles in patients with interstitial lung disease,[57] although the sound has also been described in pneumonia.[58] It is best heard over the upper anterior chest when the patient is semirecumbent and breathing deeply. Because the sound is sometimes found in patients with bird fancier's lung (a cause of hypersensitivity pneumonitis), the synonym **chirping rale** has been proposed.[59]

In patients with hypersensitivity pneumonitis, the squawk tends to be shorter, higher pitched, and later in inspiration than the squawk of patients with diffuse pulmonary fibrosis.[57]

C. PATHOGENESIS

1. Crackles

Crackles[39,47,54,60–62] were initially attributed by Laennec and early auscultators to air bubbling through airway secretions. Although some crackles result from secretions, these promptly clear after the patient coughs. All remaining crackling sounds are felt to represent the sounds of distal airways, collapsed from the previous exhalation, as they abruptly open during inspiration. Several lines of evidence support this conclusion.

1. Crackles are predominantly heard during inspiration, whereas air bubbling through secretions would cause both inspiratory and expiratory sounds.
2. The number of crackles has no relationship to the amount of sputum the patient produces. (The disease with the most crackles, interstitial fibrosis, produces scant sputum or no sputum at all.[63])
3. Crackles have a stereotypic pattern with each respiratory cycle (i.e., in a single patient at a single location on the chest, they are always early inspiratory, late inspiratory, or paninspiratory), and individual crackles occur at the same esophageal (transpulmonary) pressure in consecutive respiratory cycles.[64]
4. Crackles are loudest in the lower portions of the chest, even when the lung disease is distributed diffusely.

Course crackles are felt to originate in larger, more proximal airways than fine crackles, based on the observations that distinct patterns of coarse crackles (identified by their fingerprint of identical timing and number)

radiate to a larger area of the chest wall than do distinct patterns of fine crackles.[65,66]

2. Wheezes

Wheezes are caused by vibrations of the opposing walls of narrowed airways.[54,60,67] They are not due to resonance of air in the airways (i.e., like the sound of a flute or pipe organ) for the following reasons:

1. If they were due to resonance of air in a hollow pipe, the length of pipe for some low-pitched wheezes would be several feet, far exceeding the length of human airways.
2. The pitch of a wheeze may change between inspiration and expiration.
3. The pitch of the wheeze remains the same when inspired air is replaced with a gas mixture of oxygen and helium. (If caused by resonance of air, the pitch should change.)

D. CLINICAL SIGNIFICANCE

1. Crackles

The crackles discussed next refer only to crackling sounds that persist after the patient coughs.

a. Normal Persons

Crackles are rare in healthy persons during normal tidal breathing.[68,69] Fine crackling sounds, however, may appear in up to 60% of healthy persons, especially over the anterior chest, if the person first exhales as much as possible and breathes in from residual volume instead of functional residual capacity.[68,69]

b. Crackles and Disease

(1) Presence of Crackles. EBM Box 28-2 indicates that the finding of crackles increases the probability of pulmonary fibrosis in asbestos workers (LR = 5.9), of elevated left atrial pressure in patients with known heart disease (LR = 3.4), of myocardial infarction in patients with chest pain (LR = 2.1), and (modestly) of pneumonia in patients with cough and fever (LR = 1.8). In the evaluation of patients for either pulmonary embolism or pleural effusion, the finding of crackles is unhelpful (LRs not significant; see Chapters 32 and 33).

Some interstitial lung diseases produce more crackles than others. For example, crackles are found in 100% of patients with idiopathic pulmonary fibrosis but in only 5% to 20% of patients with fibrosis from sarcoidosis.[63,87] This suggests that the *absence* of crackles *decreases* the probability of idiopathic pulmonary fibrosis. The only finding from computed tomography that seems to predict crackles in interstitial fibrosis is the degree of subpleural fibrosis.[87]

Although the finding of posturally induced crackles after myocardial infarction has been associated with higher pulmonary capillary wedge pressures and worse survival rates,[50] it is clear that any crackles in patients with acute coronary syndromes portend a worse prognosis. In one study

of patients with acute sustained ischemic chest pain, crackles predicted 30-day mortality with a sensitivity of 36%, specificity of 92%, and positive LR of 4.5.[88] The extent of crackles in patients with newly diagnosed congestive heart failure also predicts future cardiovascular mortality.[89]

(2) Characteristics of Crackles.[56,78,90–92] Table 28-2 describes the characteristic number, timing, and type of crackles in common crackling disorders, such as pulmonary fibrosis, congestive heart failure, pneumonia, and chronic obstructive lung disease. In interstitial fibrosis, the crackles are characteristically fine, have a large number of individual crackling sounds during each inspiration,[6–14] and persist to the end of inspiration (i.e., they are late inspiratory crackles). Crackles of chronic airflow obstruction are coarse or fine, have the smallest number of crackling sounds,[1–4] and are confined to the first half of inspiration (early inspiratory crackles). The crackles of heart failure and pneumonia lie between these extremes; with treatment, the crackles of pneumonia become finer and move toward the end of inspiration.[91,92]

EBM Box 28-2 indicates that the finding of early inspiratory crackles greatly increases the probability of chronic obstructive lung disease (LR = 14.6). Most patients with these crackles have severe obstruction (LR = 20.8).

2. Wheezes

a. Presence of Wheezes

EBM Box 28-2 indicates that the finding of unforced wheezing increases the probability of chronic obstructive lung disease by a small amount (LR = 2.8) and decreases the probability of pulmonary embolism (LR = 0.4). If wheezing appears during methacholine challenge testing, asthma is likely (LR = 6). The absence of wheezing in any of these settings is unhelpful.

In contrast, the finding of *forced* wheezing lacks diagnostic value because it can be produced by most healthy persons if they exhale forcibly enough.[79,93]

b. Characteristics of Wheezing

The characteristics of wheezes are their length, pitch, and amplitude. Of these, only length and pitch vary with severity of obstruction. The longer the wheeze, the more severe the obstruction ($r = -0.89$ between the proportion of the respiratory cycle occupied by wheezing and the patient's forced expiratory volume in 1 second (FEV_1),* $p < .001$).[51,94,95] Higher-pitched wheezes indicate worse obstruction than lower-pitched ones, and effective bronchodilator therapy reduces the pitch of the patient's wheeze.[51,94]

The amplitude of the wheeze, however, does not reflect the severity of obstruction, principally because many patients with severe obstruction have faint or no wheezes.[51,79,94,95] This finding supports the old adage that in a patient with asthma, the quiet chest is not necessarily a favorable sign

*See Chapter 26 for the definition of FEV_1.

EBM BOX 28-2
*Crackles and Wheezes**

Finding (Reference)	Sensitivity (%)	Specificity (%)	Likelihood Ratio† if Finding Is	
			Present	*Absent*
Crackles				
Detecting pulmonary fibrosis in asbestos workers[70]	81	86	**5.9**	**0.2**
Detecting elevated left atrial pressure in patients with cardiomyopathy[71–73]	19-64	82-94	**3.4**	NS
Detecting myocardial infarction in patients with chest pain[74,75]	20-38	82-91	2.1	NS
Detecting pneumonia in patients with cough and fever[27–30,33,76,77]	19-67	36-94	1.8	0.8
Early Inspiratory Crackles				
Detecting chronic airflow obstruction in patients with crackles[47,78]	25-77	97-98	**14.6**	NS
Detecting severe disease in patients with chronic airflow obstruction[47]	90	96	**20.8**	**0.1**
Unforced Wheezing				
Detecting chronic airflow obstruction[21,23,79–82]	13-56	86-99	2.8	0.8
Detecting pneumonia in patients with cough and fever[27–30,76,77]	15-36	50-85	0.8	NS
Detecting pulmonary embolism[83–85]	3-31	68-91	0.4	NS
Wheezing during Methacholine Challenge Testing				
Detecting asthma[26]	44	93	**6.0**	0.6
Pleural Rub				
Detecting pulmonary embolism[85,86]	1-14	91-99	NS	NS
Detecting pleural effusion[20]	5	99	NS	NS

*Diagnostic standard: For *pulmonary fibrosis*, fibrosis on high-resolution computed tomography; for *elevated left atrial pressure*, pulmonary capillary wedge pressure >20 mm Hg[72] or >22 mm Hg[71]; for *myocardial infarction*, development of new electrocardiographic Q waves or elevations of cardiac biomarkers (CK-MB or troponin), or both; for *pneumonia*, infiltrate on chest radiograph; for *chronic airflow obstruction*, $FEV_1/FVC < 0.6$,[21] <0.7,[23,79] <0.75,[47] or less than lower 95% confidence interval for age, gender, and height[78,80–82]; for *severe obstruction*, $FEV_1/FVC < 0.44$[47]; for *asthma*, FEV_1 decrease ≥20% during methacholine challenge[26]; for *pulmonary embolism*, see Chapter 32; and for *pleural effusion*, chest radiograph.

†Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.
NS, not significant.
Click here to access calculator.

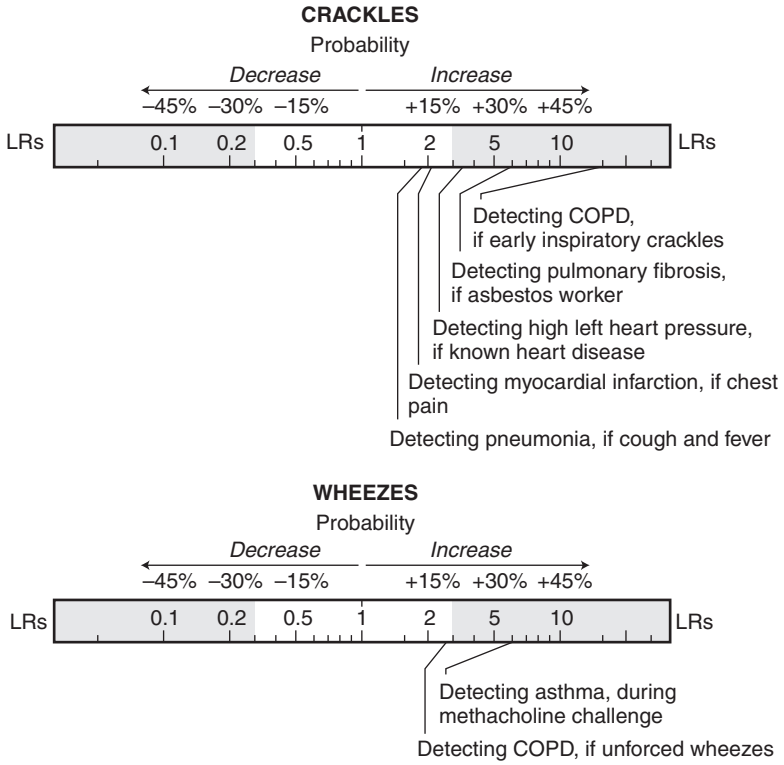


TABLE 28-2 Characteristics of Crackles in Various Disorders*

Diagnosis	Number of Crackles per Inspiration	Timing of Crackle	Type of Crackle
Pulmonary fibrosis	6-14	Late inspiratory (0.5 → 0.9)	Fine
Congestive heart failure	4-9	Late inspiratory or paninspiratory (0.4 → 0.8)	Coarse or fine
Pneumonia	3-7	Paninspiratory (0.3 → 0.7)	Coarse
Chronic airflow obstruction	1-4	Early inspiratory (0.3 → 0.5)	Coarse or fine

**Number of crackles* is mean number of crackles ± 1 standard deviation, after the patient first coughs to clear airway secretions. The descriptors *early inspiratory, late inspiratory, paninspiratory, coarse,* and *fine* are observations made by clinicians listening with the stethoscope; the numbers under *timing* refer to when crackles begin and end during a full inspiration (e.g., 0.5 → 0.9 means that crackles first appear at midinspiration [0.5] and end when the patient has reached 90% of full inspiration [0.9]). Based on references 56, 78, and 90.

but may instead indicate a tiring patient who is unable to push air across the obstructed airways.

The **slide whistle sound,** a unique wheezing sound in which the pitch rises during inspiration and falls during expiration, has been described in a patient with a spherical tumor arising from the carina that nearly completely obstructed the trachea.[96]

3. Stridor

In patients with tracheal stenosis after tracheostomy, stridor is a late finding, usually appearing after symptoms such as dyspnea, irritative cough, or difficulty in clearing the throat.[53] Stridor indicates that the airway diameter is less than 5 mm.[53]

4. Pleural Rub

EBM Box 28-2 indicates that the presence or absence of a pleural rub does not change the probability of pulmonary embolism or pleural effusion.

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 29

Ancillary Tests

I. FORCED EXPIRATORY TIME

A. TECHNIQUE

To measure the forced expiratory time, the clinician places the stethoscope bell over the trachea of the patient in the suprasternal notch and asks the patient to take a deep breath and blow it all out as fast as possible.[1] Using a stopwatch, the duration of the audible expiratory sound is determined to the nearest half second.

Rosenblatt introduced this test in 1962 as a test of obstructive lung disease.[2]

B. PATHOGENESIS

The forced expiratory time should be prolonged in obstructive disease simply because, by definition, the ratio of FEV_1 to FVC (i.e., forced expiratory volume in 1 second divided by forced vital capacity) is reduced in this disorder. Slower flow rates prolong expiratory times.

C. CLINICAL SIGNIFICANCE

EBM Box 29-1 summarizes the accuracy of this finding, showing that a forced expiratory time of 9 seconds or more increases the probability of obstructive disease (likelihood ratio [LR] = 4.1) and a time of less than 3 seconds decreases the probability (LR = 0.2).

The forced expiratory time is a specific test for obstruction. Patients with restrictive lung disease, despite having reductions in the FEV_1 similar to those seen in obstructive lung disease, usually have forced expiratory times of 4 seconds or less.[1,2]

II. BLOW-OUT-THE-MATCH TEST

A. TECHNIQUE

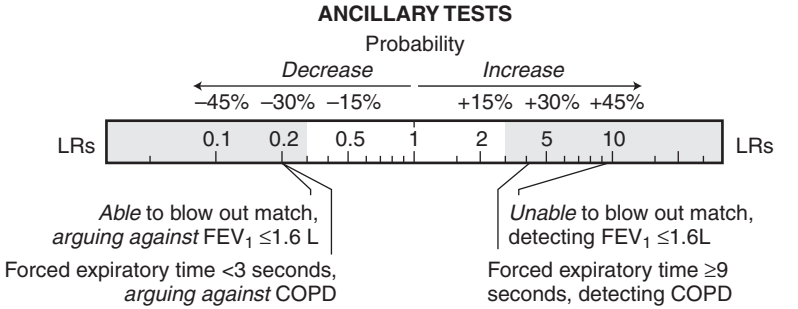
The clinician lights a match and holds it 10 to 15 cm in front of the seated patient, who then attempts to extinguish it by blowing as forcibly as possible. It is important that the patient hold the mouth open and not purse the lips. Inability to extinguish the burning match is the positive finding.

The match test was introduced by Snider in 1959, who reasoned that the ability to extinguish a match was related to the velocity of exhaled air.[5] The test is now often called the **Snider test.**

EBM BOX 29-1
Ancillary Tests

Finding (Reference)*	Sensitivity (%)	Specificity (%)	Likelihood Ratio† if Finding Is	
			Present	*Absent*
Forced Expiratory Time				
Detecting chronic airflow obstruction[1,3,4]				
<3 seconds	8-10	26-62	**0.2**	—
3-9 seconds	42-54	—	NS	—
≥9 seconds	29-50	86-98	**4.1**	—
Blow-out-the-Match Test (Snider Test)				
Detecting FEV_1 of ≤1.6L[5,6]	62-90	91-93	**9.6**	**0.2**

*Diagnostic standard: For *chronic airflow obstruction*, $FEV_1/FVC < 0.7$.
†Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.
FEV_1, forced expiratory volume in 1 second; NS, not significant.
Click here to access calculator.



B. CLINICAL SIGNIFICANCE

EBM Box 29-1 indicates that a positive Snider test (i.e., inability to extinguish the match) greatly increases the probability that the patient's FEV_1 is at least moderately reduced to 1.6 L or less (LR = 9.6). Being able to extinguish the match argues against an FEV_1 this low (LR = 0.2). Unlike the forced expiratory time, the Snider test is abnormal in both obstructive and restrictive lung disease; this probably explains why the Snider test performs less well in studies using it as a specific sign of obstructive disease.[7]

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 30

Pneumonia

I. INTRODUCTION

Like most of the pulmonary examination, the traditional findings of lobar pneumonia were described in 1819 by Laennec, who wrote that clinicians using his newly invented stethoscope could detect acute pneumonia "in every possible case."[1] According to traditional teachings, the earliest findings of pneumonia are crackles and diminished breath sounds, followed by dullness to percussion, increased tactile fremitus and vocal resonance, and bronchial breath sounds.[2]

II. CLINICAL SIGNIFICANCE

A. INDIVIDUAL FINDINGS

EBM Box 30-1 reviews the findings from over 6000 patients presenting with acute fever, cough, sputum production, or dyspnea, all of whom underwent chest radiography (the diagnostic standard for pneumonia). The findings increasing the probability of pneumonia, in descending order of their likelihood ratios (LRs), are asymmetrical chest expansion (LR = 44.1), egophony (LR = 4.1), cachexia (LR = 4), bronchial breath sounds (LR = 3.3), oxygen saturation of less than 95% (LR = 3.1), percussion dullness (LR = 3), respiratory rate higher than 28 breaths/min (LR = 2.7), diminished breath sounds (LR = 2.3), temperature higher than 37.8° C (LR = 2.2), abnormal mental status (LR = 1.9), and crackles (LR = 1.8). The *absence* of sore throat (LR = 1.8) or the *absence* of rhinorrhea (LR = 2.2) each slightly increases the probability of pneumonia among patients with acute cough.[3,14]

The only finding decreasing the probability of pneumonia was the finding that all vital signs were normal (LR = 0.3). In many studies, wheezing was found more often in patients *without* pneumonia, primarily because in these patients the cause of the acute respiratory complaints was more often asthma.[4,5,14,15]

B. LAENNEC VERSUS MODERN STUDIES

There are three reasons why the studies in EBM Box 30-1 contradict Laennec's assertion that physical diagnosis is the perfect diagnostic tool.

1. Patients diagnosed with pneumonia today include those with milder disease than patients diagnosed in Laennec's time, when the only available diagnostic standard was postmortem examination

EBM BOX 30-1
*Pneumonia**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
General Appearance				
Cachexia[3]	10	97	**4.0**	NS
Abnormal mental status[4–6]	12-14	92-95	1.9	NS
Vital Signs				
Heart rate >100 beats/min[3–8]	17-65	60-92	1.7	0.8
Temperature >37.8° C[3–11]	27-69	49-94	2.2	0.7
Respiratory rate >28 breaths/min[5–7,10]	7-36	80-99	2.7	0.9
Oxygen saturation <95%[5,7,8,11]	33-52	80-86	**3.1**	0.7
All vital signs normal[5,8,12,13]	3-38	24-81	**0.3**	2.2
Lung Findings				
Asymmetrical chest expansion[3]	5	100	**44.1**	NS
Chest wall tenderness[9]	5	96	NS	NS
Percussion dullness[3–5,14,15]	4-26	82-99	**3.0**	NS
Diminished breath sounds[4,5,14,15]	15-49	73-95	2.3	0.8
Bronchial breath sounds[4]	14	96	**3.3**	NS
Egophony[3–5]	4-16	96-99	**4.1**	NS
Crackles[3–6,9,14,15]	19-67	36-94	1.8	0.8
Wheezing[4–6,9,14,15]	15-36	50-85	0.8	NS
Diagnostic Score (Heckerling et al)[4,12]				
0 or 1 findings	7-29	33-65	**0.3**	—
2 or 3 findings	48-55	—	NS	—
4 or 5 findings	38-41	92-97	**8.2**	—

*Diagnostic standard: For *pneumonia*, infiltrate on chest radiograph.

†Definition of findings: For *all vital signs* normal, temperature <37.8° C, pulse ≤100 beats/min, respirations ≤20,[5,8,12,13] and oxygen saturations >95%[13]; for *Heckerling diagnostic score*, the clinician scores one point for each of the following five findings that are present: temperature >37.8° C, heart rate >100 beats/min, crackles, diminished breath sounds, and *absence* of asthma.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

NS, not significant.

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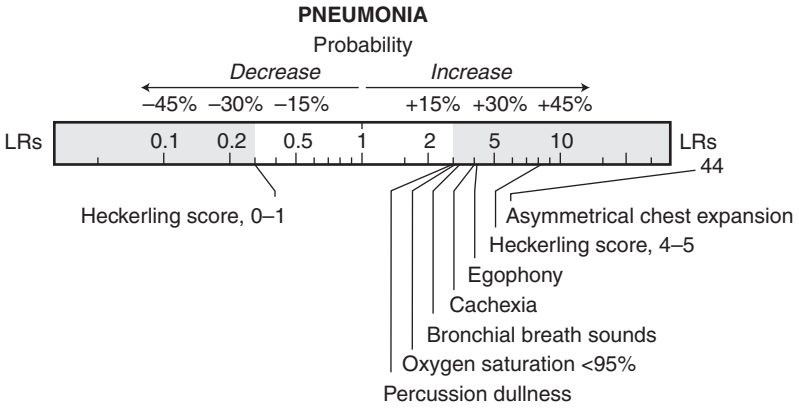


(i.e., his conclusions were drawn from patients with only the most severe disease).

2. Many traditional findings appear only after several days of illness, when the modern clinician, already familiar with the chest radiograph, often examines patients in a more cursory fashion. In contrast, Laennec examined each of his patients diligently day after day, concluding that bronchial breath sounds and bronchophony usually appeared only after 1 to 3 days of hospitalization and dullness to percussion appeared only after day 4.[1,16]
3. Antimicrobial medications probably alter the course of the physical findings. For example, in the preantibiotic era, fever usually lasted 7 days in patients with lobar pneumonia,[17] whereas it now usually lasts only 3 or 4 days.[18,19]

Even so, many great clinicians of the past tempered Laennec's enthusiasm and taught that auscultation was an imperfect diagnostic tool. Writing just 20 years after Laennec's treatise, Thomas Addison* stated it was high time "to strip the stethoscope of the extravagant and meretricious pretensions thrust upon it…and to state fairly what it will not, as well as what it will do…."[20]

C. COMBINED FINDINGS

Combining findings improves the accuracy of bedside examination. One of the best models, validated in four different populations,[4,12] scores one point for each of the following five findings:

1. Temperature higher than 37.8° C
2. Heart rate more than 100 beats/min
3. Crackles

*Thomas Addison, the discoverer of adrenal insufficiency, was also a recognized master of percussion and auscultation.

4. Diminished breath sounds
5. *Absence* of asthma

EBM Box 30-1 shows that a score of 4 or 5 argues compellingly *for* pneumonia (LR = 8.2), whereas a score of 0 or 1 argues *against* pneumonia (LR = 0.3), which in some groups of patients may reduce the probability of pneumonia enough that a chest radiograph becomes unnecessary (e.g., in patients presenting to a community office with cough, in whom the probability of pneumonia is 10% or less, a score of 0 or 1 reduces the probability of pneumonia to 3% or less).

D. PNEUMONIA AND PROGNOSIS

In studies of immunocompetent adults hospitalized with community-acquired pneumonia, the 30-day mortality rate is 4% to 15%. Of the individual findings that predict an increased risk of death (EBM Box 30-2), the most compelling ones are hypotension (LR = 7.6) and hypothermia (LR = 3.5).

Several different scoring schemes combine bedside findings to predict mortality in patients with pneumonia. One of the best validated is the **Pneumonia Severity Index,**[41] which unfortunately has the disadvantage of requiring knowledge of 20 different clinical variables, making it difficult to recall and apply at the bedside. A much simpler rule is the **CURB-65 score,** based on five prognostic variables* identified decades ago by the British Thoracic Society.[29]

1. Confusion
2. Blood urea nitrogen (BUN) levels over 19 mg/dL (>7 mmol/L)
3. Respiratory rate of 30 breaths/min or higher
4. Hypotension (i.e., diastolic blood pressure ≤60 mm Hg or systolic blood pressure ≤90 mm Hg)
5. Age 65 years or older

The presence of three or more of these CURB-65 variables is associated with increased hospital deaths (LR= 2.5 for three findings, LR = 5.4 for four findings, and LR = 11.2 for five findings; see EBM Box 30-2), whereas the absence of all CURB-65 variables is associated with decreased hospital mortality (LR = 0.2 for no findings).

The CURB-65 score requires knowledge of the patient's blood urea nitrogen level, which may not be immediately available to office-based clinicians. Related scores that omit laboratory values have also been studied, although less extensively so: A CRB-65 score of 0 (i.e., a score of 0 indicates that the patient is younger than 65 years and lacks confusion, tachypnea, and hypotension) decreases the probability of mortality (LR = 0.1), and a CRB score of 2 or higher (i.e., two or more of the three findings of confusion, tachypnea, and hypotension) increases the probability of death (LR = 5).[23,24,29,30,33,42–44]

*CURB-65 is an acronym for Confusion, *U*rea, *R*espiratory rate, *B*lood pressure, and age of 65 years or older.

EBM BOX 30-2
Pneumonia: Predictors of Hospital Mortality

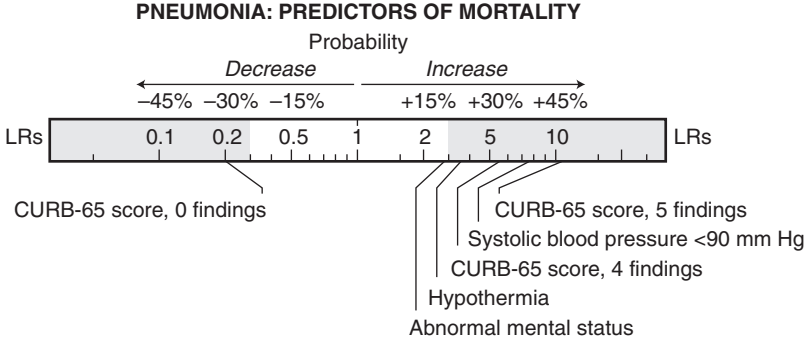
Finding (Reference)*	Sensitivity (%)	Specificity (%)	Likelihood Ratio† if Finding Is	
			Present	*Absent*
General Appearance				
Abnormal mental status[21–25]	48-65	70-87	2.7	0.6
Vital Signs				
Heart rate >100 beats/min[21]	45	78	2.1	NS
Systolic blood pressure <90 mm Hg[22,26–28]	11-41	90-99	**7.6**	0.8
Hypothermia[22,27]	14-43	93	**3.5**	NS
Respiratory rate >30 breaths/min[22,23,29–31]	41-85	63-87	2.1	0.6
CURB-65 Prognostic Score[32–40]				
0 findings	0-8	62-92	**0.2**	—
1 finding	3-20	—	0.4	—
2 findings	19-51	—	NS	—
3 findings	20-61	—	2.5	—
4 findings	8-35	—	**5.4**	—
5 findings	2-12	99-100	**11.2**	—

*Definition of findings: For *hypothermia*, body temperature <36.1° C[22] or <37° C[27]; for CURB-65 prognostic score, the clinician scores one point for each of the following findings that are present: confusion, BUN >19 mg/dL, respiratory rate ≥30 breaths/min, low blood pressure (either systolic blood pressure ≤90 mm Hg or diastolic blood pressure ≤60 mm Hg), and age ≥65 years.

†Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

BUN, blood urea nitrogen; NS, not significant.

Click here to access calculator.



E. HOSPITAL COURSE

Among survivors of pneumonia, abnormalities of the vital signs—fever, tachycardia, tachypnea, and hypotension—usually become normal within 2 to 4 days.[18,19] Once this occurs, subsequent clinical deterioration is rare, and fewer than 1% of patients will require subsequent intensive care, coronary care, or telemetry monitoring.[18] If patients are discharged from the hospital before normalization of vital signs, there is an increased risk of readmission and death.[45–47]

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 31

Chronic Obstructive Lung Disease

I. INTRODUCTION

Although descriptions of emphysema date to autopsy reports from the 1600s, it was Laennec who in 1819 recorded the clinical features associated with the disease, including dyspnea, hyperresonance, faint breath sounds, and wheezes.[1] Over the last 200 years, others have embellished Laennec's description, but the principal bedside findings are the same. Writing in 1892, Osler stated that emphysema could be recognized "at a glance" from its characteristic features, including rounded shoulders; barrel chest; prominent epigastric cardiac impulse; hyperresonant chest; loss of cardiac, liver, and splenic dullness; enfeebled breath sounds; and prolonged expiration.[2]

In the 1920s, clinicians began to recognize that these traditional physical signs had shortcomings.[3] In 1927, Cabot wrote that only about 5% of patients with emphysema at autopsy were recognized during life and that, of patients diagnosed with emphysema during life, only 25% actually had it at autopsy.[4] Spirometry, invented in 1846 and used in many forms (stethometers, pneumatometers, doppelstethograms) to supplement bedside diagnosis, gained favor because of these deficiencies and eventually became the favored diagnostic tool.[1]

This chapter compares the traditional physical signs with spirometric findings. As a general rule, the most accurate physical signs are also infrequent, occurring in fewer than 50% of affected patients, usually only those with the most severe disease.[5,6] For decades or longer, patients may harbor mild and moderate disease that is hidden from the eyes of the bedside examiner but is detectable by spirometry.

II. THE FINDINGS

Most of the traditional findings of chronic obstructive pulmonary disease (COPD) result from a hyperinflated chest and the great effort necessary to move air across obstructed airways. Some of these physical signs are discussed in other chapters: asynchronous breathing (Chapter 18); barrel chest, pursed-lips breathing, and accessory muscle use (Chapter 26); hyperresonance to percussion (Chapter 27); pulsus paradoxus (Chapter 14); diminished breath sounds and wheezing (Chapter 28); and prolonged forced expiratory times (Chapter 29).

Additional findings are discussed below.

A. INSPECTION

1. Inspiratory Recession of Supraclavicular Fossa and Intercostal Spaces

Some patients with respiratory distress from obstructive lung disease have recession or indrawing of the soft tissues of the intercostal spaces and supraclavicular fossa. This finding is attributed to excess inspiratory resistance, which introduces a delay between the generation of large negative pleural pressures and the subsequent increase in lung volume.[7]

2. Costal Paradox (Hoover sign; Costal Margin Paradox)

The costal paradox is an abnormal movement of the costal angle, which is the angle formed by both costal margins as they approach the xiphoid process on the anterior body wall. The clinician assesses costal movements by placing his or her hands on each costal margin and observing how the hands move with respect to each other as the patient breathes. In a normal person, inspiration causes the lateral aspects of the lower ribs to move outward, like the handle of a bucket, and the clinician's hands separate as the costal angle widens. In patients with the costal paradox, in contrast, the hyperinflated chest can expand no further and the flattened diaphragm instead pulls the costal margins and the clinician's hands together.

3. Leaning Forward on Arms Propped up on Knees[8,9]

Many patients with obstructive disease experience prompt relief of their dyspnea if they lean forward, which allows them to generate greater inspiratory force with fewer accessory muscles. This position probably diminishes dyspnea because it compresses the abdominal contents and pushes the diaphragm upward, helping to restore the normal domed appearance necessary for efficient and strong inspiratory movements.

B. PALPATION: LARYNGEAL HEIGHT AND DESCENT

According to traditional teachings, the distance between the thyroid cartilage and suprasternal notch (laryngeal height or tracheal length) is shorter than normal in obstructive lung disease because the clavicles and sternum are positioned abnormally high. (See the section on Barrel Chest in Chapter 26.) Patients with severe obstruction also have more forceful diaphragmatic contractions that, although ineffective in moving large amounts of air, may pull the trachea abnormally downward during inspiration (laryngeal descent, tracheal descent, or tracheal tug).

III. CLINICAL SIGNIFICANCE

A. INDIVIDUAL FINDINGS

EBM Box 31-1 shows that several findings increase the probability of obstructive lung disease: early inspiratory crackles (likelihood ratio [LR] = 14.6), absence of cardiac dullness (LR = 11.8), breath sound score of 9 or less (LR = 10.2), subxiphoid cardiac impulse (LR = 7.4), hyperresonance of the chest (LR = 5.1), forced expiratory time of 9 seconds or more

EBM BOX 31-1
*Chronic Obstructive Pulmonary Disease**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Inspection				
Barrel chest[10]	65	58	1.5	0.6
AP/L chest diameter ratio ≥0.9[10]	31	84	2.0	NS
Pursed-lips breathing[10]	58	78	2.7	0.5
Scalene/sternocleidomastoid muscle use[10]	39	88	**3.3**	0.7
Maximum laryngeal height ≤4 cm[11]	36	90	**3.6**	0.7
Laryngeal descent >3 cm[11]	17	80	NS	NS
Hoover sign[12]	58	86	**4.2**	0.5
Palpation				
Subxiphoid cardiac impulse[5,6]	4-27	97-99	**7.4**	NS
Percussion				
Absent cardiac dullness, left lower sternal border[5]	15	99	**11.8**	NS
Hyperresonance, upper right anterior chest[5]	33	94	**5.1**	NS
Diaphragm excursion percussed <2 cm[5]	13	98	NS	NS
Auscultation				
Reduced breath sounds[5,10,12,13]	29-82	63-96	**3.2**	0.5
Breath sound score[14,15]				
≤9	23-46	96-97	**10.2**	—
10 to 12	34-63	—	**3.6**	—
13 to 15	11-16	—	NS	—
≥16	3-10	33-34	**0.1**	—
Early inspiratory crackles[16,17]	25-77	97-98	**14.6**	NS
Any unforced wheeze[5,6,11,12,18,19]	13-56	86-99	2.8	0.8
Ancillary Tests				
Forced expiratory time[19–21]				
≥9 seconds	29-50	86-98	**4.1**	—
3-9 seconds	42-54	—	NS	—
<3 seconds	8-10	26-62	**0.2**	—

Continued

EBM BOX 31-1
*Chronic Obstructive Pulmonary Disease**—cont'd

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Combined Findings				
Two out of the following three present: (1) smoked 70 pack-years or more; (2) self-reported history of chronic bronchitis or emphysema; (3) diminished breath sounds[5]	67	97	**25.7**	**0.3**

*Diagnostic standards: For *chronic obstructive lung disease*, FEV_1/FVC ratio <0.6 to 0.7 (palpation, percussion, diminished breath sounds, and combined findings), FEV_1/FVC <0.7 to 0.75 (inspection, crackles, wheezes, and forced expiratory time), or FEV_1 <40% predicted (breath sound score).

†Definition of finding: For *maximal laryngeal height*, distance between the top of the thyroid cartilage and suprasternal notch at the end of expiration; for *laryngeal descent*, difference in laryngeal height between end inspiration and end expiration; for *Hoover sign*, paradoxic indrawing of the lateral rib margin during inspiration, noted when the patient is standing; for *breath sound score*, see Chapter 28; for *forced expiratory time*, see Chapter 29.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

AP/L, anteroposterior/lateral; cm, centimeters; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; NS, not significant.

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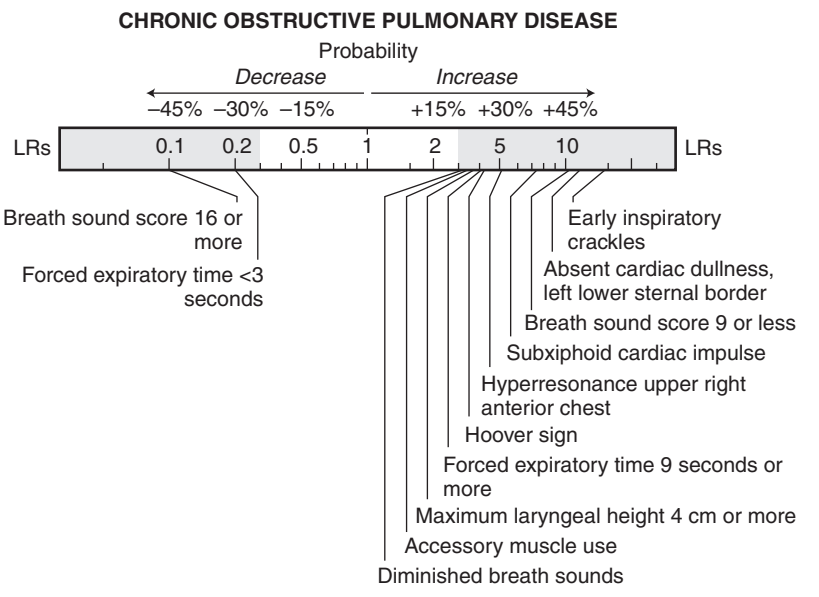

(LR = 4.1), use of the scalene or sternocleidomastoid muscles during inspiration (LR = 3.3), reduced breath sounds (i.e., overall impression without use of the breath sound score, LR = 3.2), and pursed-lips breathing (LR = 2.7). Among patients with known obstructive lung disease, early inspiratory crackles imply that the disease is severe (i.e., $FEV_1/FVC < 0.44$; LR = 20.8).[17]

Only two findings significantly decrease the probability of obstructive disease: a breath sound score greater than or equal to 16 (LR = 0.1) and a forced expiratory time of less than 3 seconds (LR = 0.2).

The evidence supporting the chest wall signs of obstructive lung disease is meager and conflicting. (See also the section on Barrel Chest in Chapter 26.) One study showed that indrawing of the soft tissues correlated with the severity of obstruction,[22] while another did not.[23] In single studies, Hoover sign (LR = 4.2; see EBM Box 31-1) and a maximum laryngeal height of 4 cm or less (LR = 3.6) increased the probability of obstructive lung disease, but in two other studies, these signs correlated poorly with measures of obstruction.[22,24] A thoracic ratio of 0.9 or more increases the probability of obstructive disease slightly (LR = 2). The degree of laryngeal descent is unhelpful (LR not significant).

The chest excursion of patients with obstructive disease (mean, 3 to 4 cm, measured as the change in circumference between maximum inspiration and maximum expiration, using a tape measure at the level of the fourth intercostal space) is less than that of normal persons (mean, 6 to 7 cm), but the lower limit observed in normal persons (2 to 3 cm) makes it impossible to draw significant conclusions in a single person.[24,25]

B. COMBINED FINDINGS

Of the many successful diagnostic schemes that combine findings,[13,19] one of the simplest asks just three questions:

1. Has the patient smoked for more than 70 pack-years?
2. Has the patient been previously diagnosed with chronic bronchitis or emphysema?
3. Are breath sounds diminished in intensity?

Answering "yes" to two or three of these questions is a compelling argument for obstructive disease (LR = 25.7; see EBM Box 31-1).

Although using the self-reported history of emphysema as a diagnostic indicator seems to be a circular argument, the specificity of this question is only 74%, which means that 26% of patients *without* obstructive lung disease actually remembered such a history. This question is more discriminatory than other symptoms (i.e., dyspnea, sputum production, age, or use of theophylline, steroids, inhalers, or home oxygen) and many other findings (i.e., hyperresonant chest, absence of cardiac dullness, and wheezes).[5]

C. PROGNOSIS IN COPD EXACERBATION (BAP-65 SCORE)

In a study of more than 80,000 patients hospitalized with COPD exacerbation, three clinical findings accurately predicted the risk of mechanical ventilation or hospital mortality (overall risk for these complications was 3%):

1. Blood urea nitrogen level of more than 25 mg/dL
2. Altered mental status

EBM BOX 31-2

*Predicting Mechanical Ventilation or Hospital Mortality in Chronic Obstructive Pulmonary Disease: BAP-65 Score**

		Mechanical Ventilation or Hospital Mortality:	
BAP-65 Score	**Definition**	%	*Likelihood Ratio*
1	0 BAP present, age ≤65 years	1.1	0.3
2	0 BAP present, age >65 years	1.5	0.4
3	1 BAP present	4.1	1.2
4	2 BAP present	11.8	3.8
5	3 BAP present	23.8	8.9

*From reference 26. BAP predictors refers to the total number of the following predictors that are present: (1) Blood urea nitrogen >25 mg/dL, (2) Altered mental status (disoriented or Glasgow coma scale score <14), and (3) Pulse ≥110 beats/min.

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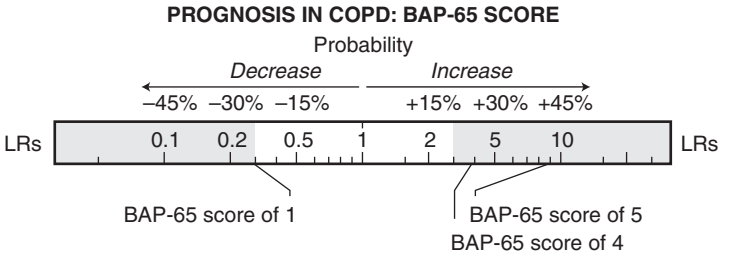


3. Pulse of 110 beats/min or higher (the mnemonic "BAP"* helps clinicians recall these findings)[26]

Based on the number of these findings and the patient's age, the patient can be classified into one of five prognostic groups, as defined in EBM Box 31-2. This classification, in turn, stratifies the patient's risk of death or mechanical ventilation from 1.1% to 23.8% (see EBM Box 31-2).

The references for this chapter can be found on www.expertconsult.com.

*BAP is an acronym for Blood urea nitrogen, Altered mental status, and Pulse.

CHAPTER 32

Pulmonary Embolism

I. INTRODUCTION

The diagnosis of pulmonary embolism is a difficult one that has frustrated clinicians for over a century. In up to half of hospitalized patients who die of pulmonary embolism, for example, the diagnosis is not even considered.[1,2] Today, when pulmonary embolism is suspected, the principal role of bedside examination is to determine the patient's overall probability of disease (i.e., low, intermediate, or high probability). This information, in turn, often combined with quantitative D-dimer levels, is used to select which patients should undergo definitive diagnostic testing for thromboembolism by computed tomography (CT) angiography, compression venous ultrasonography, or ventilation-perfusion lung scanning.

II. FINDINGS

Patients with pulmonary embolism present with dyspnea (61% to 83% of patients), pleuritic chest pain (40% to 48% of patients), hemoptysis (5% to 22% of patients), or syncope (4% to 26% of patients).[3–9] Syncope is more common (affecting 20% to 80% of patients) when pulmonary embolism is "massive," meaning that it obstructs more than half of the pulmonary circulation.[10–12] Ten percent to 35% of patients report a prior history of thromboembolism, and 33% to 42% report calf or thigh pain.[3,5–9]

In recent years, several investigators using multivariate analysis have identified combinations of bedside findings that best identify a patient's overall probability of pulmonary embolism. Two widely studied scores are the **Wells Score** (Table 32-1)[13] and the **revised Geneva score** (Table 32-2).*[14] For each of these scores, the clinician simply adds the points corresponding to each of the independent predictors that are present and uses the total score to determine the overall probability, as defined in the footnotes to Tables 32-1 and 32-2. Both scores combine similar risk factors (prior thromboembolism, immobilization, surgery, and cancer) and clinical findings (hemoptysis, tachycardia, and signs of deep venous thrombosis) to arrive at the overall clinical probability, although the Wells score also considers whether or not an alternative diagnosis is less likely than pulmonary embolism.

*The original Geneva score[8] was later revised to remove the patient's arterial blood gas measurement, which is often unavailable.

TABLE 32-1 Wells Score for Pulmonary Embolism*

Characteristic	Points
RISK FACTORS	
Previous pulmonary embolism or deep venous thrombosis	1.5
Immobilization or surgery in the previous 4 weeks	1.5
Cancer	1
CLINICAL FINDINGS	
Hemoptysis	1
Heart rate >100 beats/min	1.5
Clinical signs of deep venous thrombosis	3
OTHER FINDINGS	
Alternative diagnosis is less likely than pulmonary embolism	3

*From reference 13. Interpretation of total score: 0-1 point, low probability; 2-6 points, moderate probability; 7 or more points, high probability.

TABLE 32-2 Revised Geneva Score for Pulmonary Embolism*

Characteristic	Points
RISK FACTORS	
Age >65 years	1
Previous pulmonary embolism or deep venous thrombosis	3
Surgery (under general anesthesia) or fracture (of lower limbs) within 1 month	2
Cancer (active or considered cured <1 year)	2
CLINICAL FINDINGS	
Unilateral leg pain	3
Hemoptysis	2
Heart rate	
75-94 beats/min	3
≥95 beats/min	5
Pain on leg deep venous palpation and unilateral edema	4

*From reference 14. Interpretation of total score: 0-3 points, low probability; 4-10 points, moderate probability; ≥11 points, high probability.

III. CLINICAL SIGNIFICANCE

A. INDIVIDUAL FINDINGS

The studies included in EBM Box 32-1 enrolled over 4000 patients with suspected pulmonary embolism referred to centers having considerable experience with venous thromboembolism. In these studies, only one of five patients suspected of pulmonary embolism actually had the disorder.

EBM BOX 32-1
*Pulmonary Embolism**

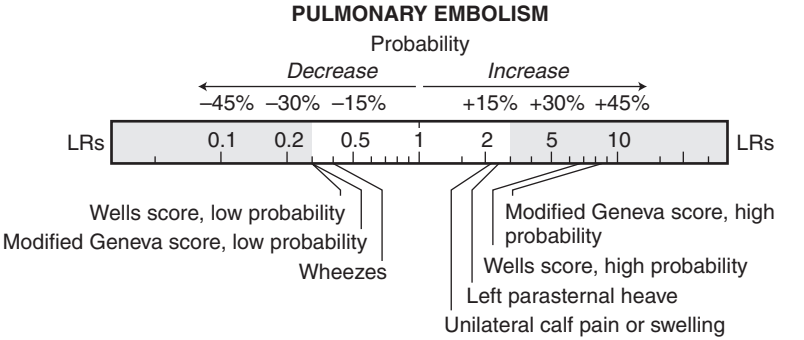
Finding (Reference)	Sensitivity (%)	Specificity (%)	Likelihood Ratio† if Finding Is	
			Present	*Absent*
Individual Findings				
GENERAL DESCRIPTION				
Diaphoresis[9]	4	94	NS	NS
Cyanosis[4,9]	1-3	97-100	NS	NS
VITAL SIGNS				
Pulse >100 beats/min[6–9]	25-43	69-84	NS	NS
Systolic blood pressure ≤100 mm Hg[8]	8	95	1.9	NS
Temperature >38° C[4,6–9]	1-9	78-98	0.5	NS
Respiratory rate >30 breaths/min[8]	21	90	2.0	0.9
LUNGS				
Accessory muscle use[4]	17	89	NS	NS
Crackles[3,9,15]	21-59	45-82	NS	NS
Wheezes[6,9,15]	3-31	68-91	0.4	NS
Pleural friction rub[4,9]	1-14	91-99	NS	NS
HEART				
Elevated neck veins[4,9,15]	3-14	92-96	1.7	NS
Left parasternal heave[4,9]	1-5	98-99	2.4	NS
Loud P_2[3,9]	15-19	84-95	NS	NS
New gallop (S_3 or S_4)[3]	30	89	NS	NS
OTHER FINDINGS				
Chest wall tenderness[4,16]	11-17	79-80	NS	NS
Unilateral calf pain or swelling[5–7,9,15,17]	9-47	77-99	2.2	0.8
Combined Findings				
WELLS SCORE[7,18–24]				
Low probability, 0-1 points	6-53	31-54	**0.3**	—
Moderate probability, 2-6 points	38-71	—	1.5	—
High probability, 7 or more points	7-54	90-100	**6.7**	—
REVISED GENEVA SCORE[14,22–24]	1-27	43-85	**0.3**	—
Low probability, 0-3 points	58-69	—	NS	—
Moderate probability, 4-10 points	10-42	96-99	**8.5**	—
High probability, ≥11 points				

Continued

*Diagnostic standard: For *pulmonary embolism*, pulmonary angiography,[3,6,7,17] ventilation-perfusion scanning (± compression venous ultrasonography or pulmonary angiography),[4,8,15,19,25] ventilation-perfusion scanning or CT angiography,[5,24] or CT angiography (± compression venous ultrasonography).[9,14,16,18,21–23,26] In only six studies[3,4,6,9,15,22] did all patients undergo testing with the diagnostic standard; in the remaining studies, some low-risk patients (i.e., those with a negative quantitative D-dimer and low clinical risk) were not tested but were followed for at least 3 months without anticoagulation; all lacked clinical evidence of thromboembolism.

†Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. NS, not significant.

Click here to access calculator.



Very few individual findings help the clinician distinguish patients with pulmonary embolism from those without it. The only individual symptoms *increasing* the probability of pulmonary embolism are *sudden* dyspnea (likelihood ratio [LR] = 2.4),[6,7] syncope (LR = 2),[4–6] and hemoptysis (LR = 1.9).*[3–9]

The individual physical findings that increase the probability of pulmonary embolism are left parasternal heave (LR = 2.4; see EBM Box 32-1), unilateral calf pain or swelling (LR = 2.2), respiratory rate of more than 30 breaths/min (LR = 2), and systolic blood pressure of 100 mm Hg or less (LR = 1.9). The presence of wheezes (LR = 0.4) and fever higher than 38° C (LR = 0.5) modestly decreases the probability of pulmonary embolism. The presence or absence of a pulse rate of more than 100 beats/min as an isolated finding is unhelpful overall (LR not significant), although in one study, the finding of a pulse rate of less than 90 beats/min decreased the probability of pulmonary embolism (LR = 0.3).[3]

Other individual findings are unhelpful. Chest wall tenderness is found in 11% to 17% of patients in pulmonary embolism and has an LR that is not significant, emphasizing that this sign is not diagnostic of costochondritis. The presence of hypoxemia, defined either as room air pO_2 of less than 80 mm Hg or as an increased alveolar-arterial gradient, is also diagnostically unhelpful (both LRs not significant).[3,8,9,27]

*In these studies, the following risk factors and symptoms were found just as frequently in patients with embolism as in those without it: female sex, older age, previous heart disease, previous lung disease, estrogen use, dyspnea, chest pain (pleuritic or nonpleuritic), and cough. A few individual risk factors have LRs of between 1.3 and 1.7 and thus increase the probability by a small amount: cancer, recent immobilization, recent surgery, recent trauma, and prior venous thromboembolism.

B. COMBINING FINDINGS TO DETERMINE CLINICAL PROBABILITY OF EMBOLISM

In contrast to the modest accuracy of individual findings, EBM Box 32-1 indicates that a determination of "high probability" by either the Wells score (LR = 6.7) or revised Geneva score (LR = 8.5) markedly increases the probability of pulmonary embolism, whereas a determination of "low probability" by either score decreases it (LR = 0.3).

Both scores emphasize that accurate assessment of a patient's probability combines both risk factors and clinical findings. The probability of embolism is high if the patient has typical signs (tachycardia, leg swelling) and risk factors (e.g., cancer, immobilization) and lacks an alternative diagnosis. The probability is low if the presentation is atypical, there are no risk factors, and there *is* a likely alternative diagnosis (e.g., angina, congestive heart failure). Many studies have shown that the probability of pulmonary embolism in patients presenting with both a low clinical probability (using either score) and normal D-dimer levels is so low that further imaging is unnecessary and anticoagulation can be safely withheld.[14,19,21,23,25,28]

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 33

Pleural Effusion

I. INTRODUCTION

Although ancient Greek physicians routinely recognized and treated empyema, the modern diagnostic signs of pleural effusion date to two physicians: Auenbrugger, who described the pathologic dullness and diminished chest expansion of effusions[1]; and Laennec, who described the uniform absence of breath sounds and, in some patients, the appearance of bronchial breath sounds and abnormal vocal resonance.[2] The introduction of percussion into 19th century medicine allowed clinicians to routinely distinguish empyema from tuberculosis in patients with chronic respiratory complaints.[3]

The most common causes of pleural effusions today in adults are heart failure, malignancy, pneumonia, and tuberculosis.[4,5]

II. FINDINGS

Accumulation of a significant amount of pleural fluid expands the hemithorax (and collapses the underlying lung), which may create the appearance of an asymmetrically enlarged hemithorax with flattening or even bulging of the normally concave intercostal spaces. Because pleural fluid reduces the transmission of low-frequency vibrations (see Fig. 28-2), tactile fremitus is diminished on the involved side. All patients have diminished breath sounds, especially in the lower chest, from the combined effects of reduced flow rates (the underlying lung is collapsed) and diminished transmission of the low-frequency vesicular breath sounds through the fluid.

Testing of vocal resonance (i.e., the sound of the patient's voice through the clinician's stethoscope), however, may produce either of two distinct findings:

1. Vocal resonance may be diminished or absent (the patient's voice is muted compared with the uninvolved side)
2. Vocal resonance may be "abnormal," causing egophony, bronchophony, whispered pectoriloquy, and, often, bronchial breath sounds. Chapter 28 discusses further these paradoxic findings (in the section on Vocal Resonance).

III. CLINICAL SIGNIFICANCE

Several findings increase the probability of pleural effusion: abnormal auscultatory percussion (LR = 8.3; EBM Box 33-1), asymmetrical chest expansion (LR = 8.1), diminished vocal resonance (LR = 6.5), reduced tactile

EBM BOX 33-1
*Pleural Effusion**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Inspection				
Asymmetrical chest expansion[6]	74	91	**8.1**	**0.3**
Palpation				
Reduced tactile fremitus[6]	82	86	**5.7**	**0.2**
Percussion				
Dullness by conventional percussion[6]	89	81	**4.8**	**0.1**
Abnormal auscultatory percussion (method of Guarino)[6,7]	58-96	85-95	**8.3**	NS
Auscultation				
Diminished or absent breath sounds[6]	88	83	**5.2**	**0.1**
Diminished vocal resonance[6]	76	88	**6.5**	**0.3**
Crackles[6]	44	38	NS	1.5
Pleural rub[6]	5	99	NS	NS

*Diagnostic standards: For *pleural effusion*, chest radiograph.

†Definition of finding: For *abnormal auscultatory percussion*, the method of Guarino[7] (see the section on Auscultatory Percussion in Chapter 27); for *diminished vocal resonance intensity*, the transmitted sounds from the patient's voice when reciting numbers, as detected by a stethoscope on the patient's posterior chest, are reduced or absent[6]; for all other findings, see Chapters 26 to 28.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. NS, not significant.

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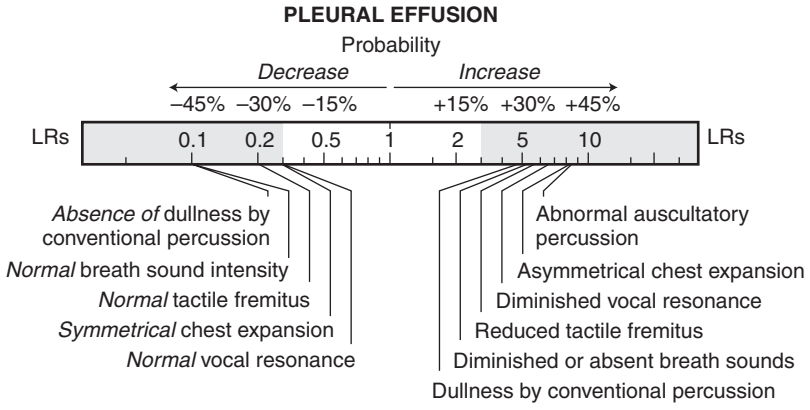

fremitus (LR = 5.7), diminished or absent breath sounds (LR = 5.2), and dullness during comparative percussion (LR = 4.8). Findings that *decrease* the probability of pleural effusion include normal breath sound intensity (LR = 0.1), resonance during percussion (LR = 0.1), normal tactile fremitus (LR = 0.2), symmetrical chest expansion (LR = 0.3), and normal vocal resonance (LR = 0.3).

In one study of patients with acute respiratory distress syndrome requiring mechanical ventilation, the absence of breath sounds over a region of the chest increased the probability of underlying pleural fluid at that location (LR = 4.3).[8]

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 34

Inspection of the Neck Veins

I. INTRODUCTION

Clinicians should inspect the neck veins for the following reasons:

1. To detect elevated central venous pressure
2. To detect specific abnormalities of venous waveforms, which are characteristic of certain arrhythmias and some valvular, pericardial, and myocardial disorders

Clinicians first associated conspicuous neck veins with heart disease about three centuries ago.[1,2] In the late 1800s, Sir James Mackenzie described venous waveforms of arrhythmias and various heart disorders, using a mechanical polygraph applied over the patient's neck or liver. His labels for the venous waveforms—A, C, and V waves—are still used today.[3,4] Clinicians began to estimate venous pressure at the bedside routinely in the 1920s, after the introduction of the glass manometer and after Starling's experiments linking venous pressure to cardiac output.[5]

II. VENOUS PRESSURE

A. DEFINITIONS

1. Central Venous Pressure

Central venous pressure (CVP) is the mean vena caval or right atrial pressure, which, in the absence of tricuspid stenosis, equals right ventricular end-diastolic pressure. Disorders that increase diastolic pressures of the right side of the heart—left heart disease, lung disease, primary pulmonary hypertension, and pulmonic stenosis—all increase the CVP and make the neck veins abnormally conspicuous. CVP is expressed in millimeters of mercury (mm Hg) or centimeters (cm) of water above atmospheric pressure (1.36 cm water = 1 mm Hg).

Estimations of CVP are most helpful in patients with ascites or edema, in whom an elevated CVP indicates heart or lung disease and a normal CVP suggests alternative diagnoses, such as chronic liver disease. Despite the prevailing opinion, the CVP is normal in patients with liver disease; the edema in these patients results from hypoalbuminemia and the weight of ascites compressing veins to the legs.[6–9]

2. Physiologic Zero Point

Physiologists have long assumed that a location in the cardiovascular system (presumed to be the right atrium in humans) tightly regulates venous pressure so that it remains the same even when the person changes

position.[5,10–12] All measurements of CVP—whether by clinicians inspecting neck veins or by catheters in intensive care units—attempt to identify the pressure at this zero point (e.g., if a manometer connected to a systemic vein supports a column of saline 8 cm above the zero point, with the top of the manometer open to atmosphere, the recorded pressure in that vein is 8 cm water). Estimates of CVP are related to the zero point because interpretation of this value does not need to consider the hydrostatic effects of different patient positions, and any abnormal value thus indicates disease.

3. External Reference Point

Clinicians require some external reference point to reliably locate the level of the zero point. Of the many such reference points that have been proposed over the last century,[5] only two are commonly used today: the sternal angle and the phlebostatic axis.

a. Sternal Angle

In 1930, Sir Thomas Lewis, a pupil of Mackenzie, proposed a simple bedside method for measuring venous pressure designed to replace the manometer, which he found too burdensome for general use.[13] He observed that the top of the jugular veins of normal persons (and the top of the fluid in the manometer) always came to lie within 1 to 2 cm of the vertical distance from the sternal angle, whether the person was supine, semiupright, or upright (an observation since confirmed by others).[14] If the top level of the neck veins was more than 3 cm above the sternal angle, Lewis concluded the venous pressure was elevated.

Others have modified this method, stating that the CVP equals the vertical distance between the top of the neck veins and a point 5 cm below the sternal angle (Fig. 34-1).[15] This variation is commonly called the **method of Lewis,** although Lewis never made such a claim.

b. Phlebostatic Axis

The **phlebostatic axis** is the midpoint between the anterior and posterior surfaces of the chest at the level of the fourth intercostal space. This reference point, the most common landmark used in intensive care units and cardiac catheterization laboratories, was originally proposed in the 1940s, when studies showed that using it as the zero point minimized variation in venous pressure of normal persons as they changed position between 0 and 90 degrees.[11]

c. Relative Merits of Sternal Angle and Phlebostatic Axis

Obviously, the measurement of venous pressure is only as good as the reference point used. The phlebostatic axis locates a point in the right atrium several centimeters posterior to the point identified by the method of Lewis (i.e., the zero point using the phlebostatic axis is 9 to 10 cm posterior to the sternal angle; that using the method of Lewis is 5 cm below the sternal angle).[16,17] This means that clinicians using the phlebostatic axis will estimate the CVP to be several centimeters of water higher than those using the method of Lewis, even if these clinicians completely agree on the location of the neck veins.

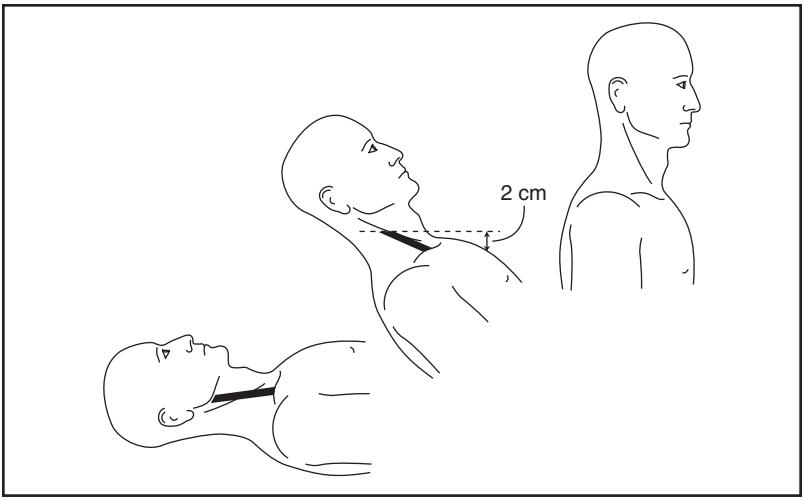

FIGURE 34-1 Measurement of venous pressure. The clinician should vary the patient's position until the top of the neck veins become visible. In this patient, who has normal CVP, the neck veins are fully distended when the patient is supine and completely collapsed when the patient is upright. A semiupright position, therefore, is used to estimate pressure. In this position, the top of the neck veins is 2 cm above the sternal angle, and according to the method of Lewis, the patient's CVP is 2 + 5 = 7 cm water.

The sternal angle is a better reference point for bedside examination, simply because clinicians can reproducibly locate it more easily than the phlebostatic axis. Even using standard patient positions and flexible right-angle triangles or laser levels, experienced observers trying to locate a point similar to the phlebostatic axis disagreed by several centimeters in both horizontal and vertical directions.[18,19]

B. ELEVATED VENOUS PRESSURE

1. Technique

To measure the patient's venous pressure, the clinician should examine the veins on the right side of the patient's neck because these veins have a direct route to the heart. Veins in the left side of the neck reach the heart by crossing the mediastinum, where the normal aorta may compress them, causing left jugular venous pressure to be sometimes elevated even when the CVP and the right venous pressure are normal.[20,21]

The patient should be positioned at whichever angle between the supine and upright positions best reveals the top of the neck veins (see Fig. 34-1). The top of the neck veins is indicated by the point above which the subcutaneous conduit of the external jugular vein disappears or above which the pulsating waveforms of the internal jugular wave become imperceptible.

2. External versus Internal Jugular Veins

Either the external or internal jugular veins may be used to estimate pressure because measurements in both are similar.[22] Traditionally, clinicians have been taught to use only the internal jugular vein because the external

jugular vein contains valves that purportedly interfere with the development of a hydrostatic column necessary to measure pressure. This teaching is erroneous for two reasons:

1. The internal jugular vein also contains valves, a fact known to anatomists for centuries.[23–25] These valves are essential during cardiopulmonary resuscitation, preventing blood from flowing backward during chest compression.[26]
2. Valves in the jugular veins do not interfere with pressure measurements, because flow is normally toward the heart. In fact, they probably act like a transducer membrane (e.g., the diaphragm of a speaker) because they amplify right atrial pressure pulsations and make the venous waveforms easier to see.[23]

3. Definition of Elevated CVP

After locating the top of the external or internal jugular veins, the clinician should measure the vertical distance between the top of the veins and one of the external reference points discussed above (see Fig. 34-1). The venous pressure is abnormally elevated if

1. The top of the neck veins are more than 3 cm above the sternal angle
2. The CVP exceeds 8 cm water using the method of Lewis (i.e., >3 cm above the sternal angle + 5 cm)
3. The CVP is >12 cm water using the phlebostatic axis

C. BEDSIDE ESTIMATES OF VENOUS PRESSURE VERSUS CATHETER MEASUREMENTS

1. Diagnostic Accuracy*

In studies employing a standardized reference point, bedside estimates of CVP are within 4 cm water of catheter measurements 85% of the time.[22,30] According to these studies, the finding of an elevated CVP (i.e., top of neck veins >3 cm water above the sternal angle or >8 cm water using the method of Lewis) greatly increases the probability that catheter measurements are elevated (LR = 9.7; EBM Box 34-1). If the clinician believes the CVP is normal, it almost certainly is less than 12 cm water by catheter measurement (LR = 0.1; see EBM Box 34-1), although some of these patients have catheter measurements that are mildly elevated, between 8 and 12 cm water.†

This tendency to slightly underestimate the measured values, which is elucidated further in the following section, explains why estimates made during expiration are slightly more accurate than those made during inspiration: During expiration, the neck veins move upward in the neck, increasing the bedside estimate and minimizing the error.[22]

*Studies that test the diagnostic accuracy of bedside estimates of CVP are difficult to summarize because they often fail to standardize which external reference point was used.[27–29]

†For purposes of comparison, *measured pressure* here is in centimeters of water using the method of Lewis. Most catheterization laboratories measure pressure in millimeters of mercury (mm Hg) using the phlebostatic axis as the reference point.

EBM BOX 34-1
*Inspection of the Neck Veins**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Estimated Venous Pressure Elevated				
Detecting measured CVP >8 cm water[22,30–32]	47-92	93-96	**9.7**	**0.3**
Detecting measured CVP >12 cm water[22,30]	78-95	89-93	**10.4**	**0.1**
Detecting elevated left heart diastolic pressures[33–35]	10-58	96-97	**3.9**	NS
Detecting low LV ejection fraction[36–38]	7-25	96-98	**6.3**	NS
Detecting myocardial infarction (if chest pain)[39]	10	96	2.4	NS
Predicting postoperative pulmonary edema[40,41]	19	98	**11.3**	NS
Predicting postoperative MI or cardiac death[40,41]	17	98	**9.4**	NS
Estimated Venous Pressure Low				
Detecting measured CVP ≤5 cm water[32]	90	89	**8.4**	**0.1**
Positive Abdominojugular Test				
Detecting elevated left heart diastolic pressures[33,42,43]	55-84	83-98	**8.0**	**0.3**
Early Systolic Outward Movement (CV Wave)				
Detecting moderate-to-severe tricuspid regurgitation[44]	37	97	**10.9**	0.7

*Diagnostic standards: for *measured CVP*, measurement by catheter in supine patient using method of Lewis[22,30–32]; for *elevated left heart diastolic pressures* or *low ejection fraction*, see Chapter 46; for *myocardial infarction*, see Chapter 47.

†Definition of findings: for *elevated venous pressure*, bedside estimate >8 cm water using method of Lewis,[22,30] >12 cm water using phlebostatic axis,[40,41] or unknown method[33–36]; for *low venous pressure*, estimate CVP ≤5 cm water using method of Lewis[32]; and for *positive abdominojugular test*, see text.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.CVP, central venous pressure; LV, left ventricular; MI, myocardial infarction; NS, not significant.

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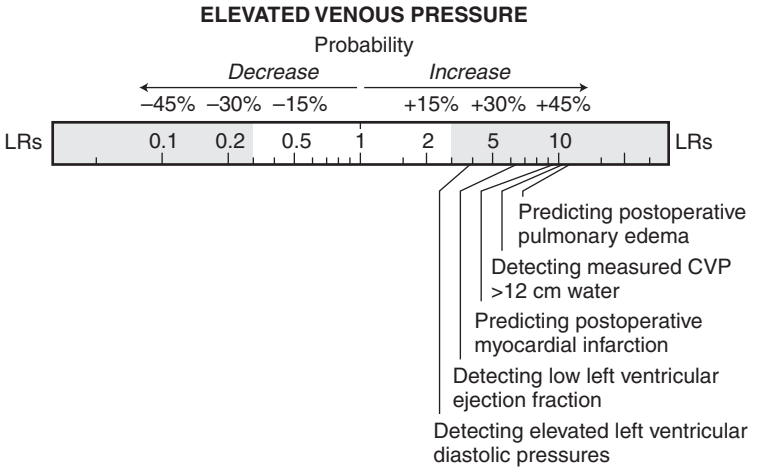


2. Why Clinicians Underestimate Measured Values

Of the many reasons why clinicians tend to underestimate measured values of CVP, the most important one is that the vertical distance between the sternal angle and the physiologic zero point varies as the patient shifts position (Fig. 34-2).[5,45] Catheter measurements of venous pressure are always made while the patient is lying supine, whether the venous pressure is high or low. Bedside estimates of venous pressure, however, must be made in the semiupright or upright position if the venous pressure is high because only these positions reveal the top of distended neck veins. Figure 34-2 shows that the semiupright position increases the vertical distance between the right atrium and the sternal angle by about 3 cm, compared with the supine position, which effectively lowers the bedside estimate by the same amount. The significance of this is that patients with mildly elevated CVP by catheter measurements (i.e., 8 to 12 cm), whose neck veins are interpretable only in more upright positions, may have bedside estimates that are normal (i.e., <8 cm water).

In support of this, even catheter measurements using the sternal angle as a reference point are about 3 cm lower when the patient is in the semiupright position than when the patient is supine.[46–48]

D. CLINICAL SIGNIFICANCE OF ELEVATED VENOUS PRESSURE

1. Differential Diagnosis of Ascites and Edema

In patients with ascites and edema, an elevated venous pressure implies that the heart or pulmonary circulation is the problem; a normal venous pressure indicates that another diagnosis is the cause.

2. Elevated Venous Pressure and Left Heart Disease

EBM Box 34-1 shows that, in patients with symptoms of angina or dyspnea, the finding of elevated venous pressure increases the probability of an elevated

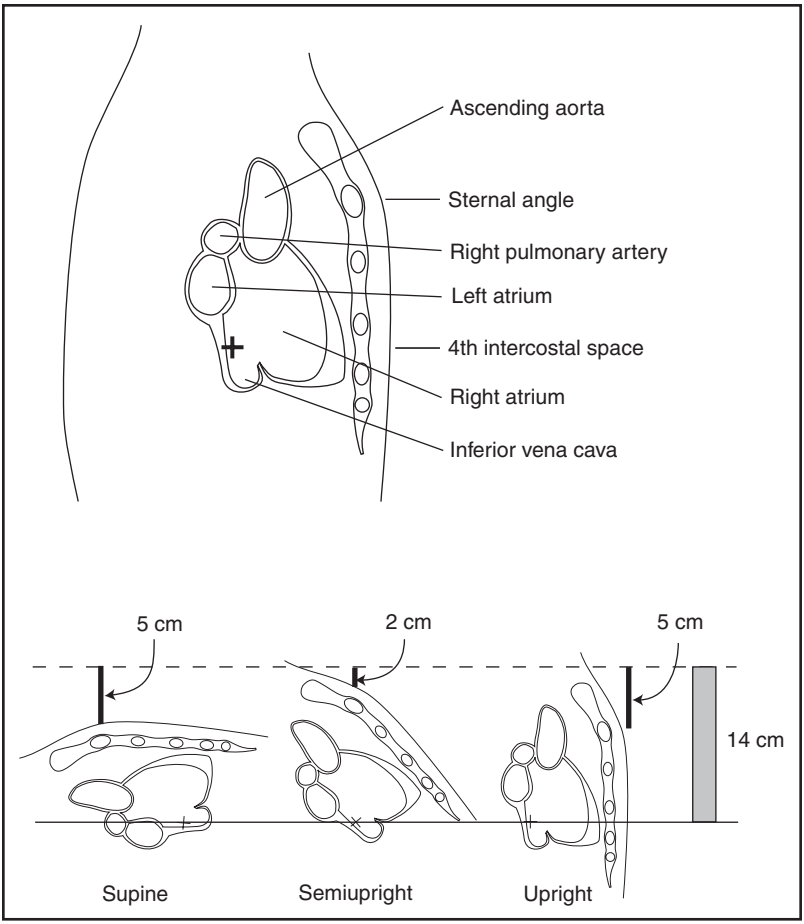


FIGURE 34-2 Central venous pressure and position of patient. The top half of the figure shows the sagittal section of a 43-year-old man, just to the right of the midsternal line, demonstrating the relationship between the sternal angle, right atrium, and phlebostatic axis (indicated by the black cross in the posterior right atrium). The bottom half of the figure illustrates the changing vertical distance between the phlebostatic axis *(solid horizontal line)* and sternal angle in the supine (0 degrees), semiupright (45 degrees), and upright (90 degrees) positions. The venous pressure is the same in each position (14 cm above the phlebostatic axis, *gray bar on right*), but the vertical distance between the sternal angle and the tops of the neck veins changes in the different positions: the vertical distance is 5 cm in the supine and upright positions but only 2 cm in the semiupright position. Using the method of Lewis (see text), therefore, the estimate of venous pressure from the semiupright position (7 cm = 2 + 5) is 3 cm *lower* than estimates from the supine or upright positions (10 cm = 5 + 5 cm). Adapted from reference 5.

left atrial pressure (LR = 3.9; see EBM Box 34-1)* and a depressed ejection fraction (LR = 6.3). The opposite finding (normal neck veins) provides no diagnostic information about left heart pressure or function (negative LRs not significant; see EBM Box 34-1). In patients presenting to emergency departments with sustained chest pain, the finding of elevated venous pressure increases the probability of myocardial infarction (LR = 2.4).

3. Elevated Venous Pressure during Preoperative Consultation

The finding of elevated venous pressure during preoperative consultation is a compelling finding predicting that the patient, without any intervening diuresis or other treatment, will develop postoperative pulmonary edema (LR = 11.3; see EBM Box 34-1) or myocardial infarction (LR = 9.4).

4. Elevated Venous Pressure and Pericardial Disease

Elevated venous pressure is a cardinal finding of cardiac tamponade (100% of cases) and constrictive pericarditis (98% of cases). Therefore, the absence of elevated neck veins is a conclusive argument against these diagnoses. In every patient with elevated neck veins, the clinician should search for other findings of tamponade (i.e., pulsus paradoxus; prominent x′ descent but absent y descent in venous waveforms), and constrictive pericarditis (pericardial knock, prominent x′ and y descents in venous waveforms) (see Chapter 45).

5. Unilateral Elevation of Venous Pressure

Distention of the left jugular veins with normal right jugular veins sometimes occurs because of kinking of the left innominate vein by a tortuous aorta.[20,21] In these patients, the elevation often disappears after a deep inspiration.

Persistent unilateral elevation of the neck veins usually indicates local obstruction by a mediastinal lesion, such as an aortic aneurysm or intrathoracic goiter.[50]

E. CLINICAL SIGNIFICANCE OF LOW ESTIMATED VENOUS PRESSURE

Few studies have addressed whether clinicians can accurately detect *low* venous pressure, a potentially difficult issue because *normal* venous pressure is often defined as less than 8 cm water (i.e., *low* and *normal* measurements overlap). Nonetheless, in one study of 38 patients in the intensive care unit (about half receiving mechanical ventilation), the clinician's estimate of a CVP of 5 cm water or less accurately detected a measured value of 5 cm water or less (positive LR = 8.4), an important finding if the clinician is contemplating whether or not fluid challenge is indicated.

*During cardiac catheterization, a measured right atrial pressure of 10 mm Hg or more detects a measured pulmonary capillary wedge pressure of 22 mm Hg or more with an LR of 4.5, which is similar to that derived from bedside examination (LR = 3.9).[49]

III. ABDOMINOJUGULAR TEST

A. THE FINDING

During the abdominojugular test, the clinician observes the neck veins while pressing firmly over the patient's midabdomen for 10 seconds, a maneuver that probably increases the venous return by displacing splanchnic venous blood toward the heart.[43] The CVP of normal persons usually remains unchanged during this maneuver or rises for a beat or two before returning to normal or below normal.[30,42,43,51,52] If the CVP rises more than 4 cm water and remains elevated for the entire 10 seconds, the abdominojugular test is positive.[33,43] Most clinicians recognize the positive response by observing the neck veins at the moment the abdominal pressure is released, regarding a *fall* of more than 4 cm as positive.

The earliest version of the abdominojugular test was the **hepatojugular reflux,** introduced by Pasteur in 1885 as a pathognomonic sign of tricuspid regurgitation.[53] In 1898, Rondot discovered that patients with normal tricuspid valves could develop the sign, and by 1925, clinicians realized that pressure anywhere over the abdomen, not just over the liver, would elicit the sign.[51] Several investigators have contributed to the current definition of the abdominojugular test.[30,43,54]

B. CLINICAL SIGNIFICANCE

In patients presenting for cardiac catheterization (presumably because of chest pain or dyspnea), a positive abdominojugular test is an accurate sign of elevated left atrial pressure (i.e., ≥15 mm Hg, LR = 8; see EBM Box 34-1). Therefore, a positive abdominojugular test is an important finding in patients with dyspnea, indicating that at least some of the dyspnea is due to disease in the left side of the heart. A negative abdominojugular test decreases the probability of left atrial hypertension (LR = 0.3; see EBM Box 34-1).

IV. KUSSMAUL SIGN

The **Kussmaul sign** is the paradoxic elevation of CVP during inspiration. In healthy persons, venous pressure falls during inspiration because pressures in the right heart decrease as intrathoracic pressures fall. The Kussmaul sign is classically associated with constrictive pericarditis, but it occurs in only a minority of patients with constriction[55,56] and is found in other disorders such as severe heart failure,[56,57] pulmonary embolus,[58] and right ventricular infarction.[59–62]

V. PATHOGENESIS OF ELEVATED VENOUS PRESSURE, ABDOMINOJUGULAR TEST, AND KUSSMAUL SIGN

The peripheral veins of normal persons are distensible vessels that contain about two-thirds of the total blood volume and can accept or donate blood with relatively little change in pressure. In contrast, the peripheral

veins of patients with heart failure are abnormally constricted from tissue edema and intense sympathetic stimulation, a change that reduces extremity blood volume and increases central blood volume. Because constricted veins are less compliant, the added central blood volume causes the CVP to be abnormally increased.[5]

In addition to causing an elevated CVP, venoconstriction probably also contributes to the positive abdominojugular test and the Kussmaul sign, two signs that often occur together. Most patients with constrictive pericarditis and the Kussmaul sign also have a markedly positive abdominojugular test; many patients with severe heart failure and a markedly positive abdominojugular test also have the Kussmaul sign.[56] The venous pressure of these patients, unlike that of healthy persons, is very susceptible to changes in venous return. Maneuvers that increase venous return—exercise, leg elevation, or abdominal pressure—increase the venous pressure of patients with the abdominojugular test and the Kussmaul sign but not that of healthy persons.[5] The Kussmaul sign may be nothing more than an inspiratory abdominojugular test, the downward movement of the diaphragm compressing the abdomen and increasing venous return.[63]

Even so, an abnormal right ventricle probably also contributes to the Kussmaul sign because all of the disorders associated with the sign are characterized by a right ventricle that is unable to accommodate more blood during inspiration (i.e., in constrictive pericarditis, the normal ventricle is constrained by the diseased pericardium, and in severe heart failure, acute cor pulmonale, or right ventricular infarction, the dilated right ventricle is constrained by the normal pericardium). A right side of the heart thus constrained only exaggerates inspiratory increments of CVP, making the Kussmaul sign more prominent.[5]

VI. VENOUS WAVEFORMS

A. IDENTIFYING THE INTERNAL JUGULAR VEIN

Venous waveforms are usually only conspicuous in the internal jugular vein, which lies under the sternocleidomastoid muscle and therefore becomes evident by causing pulsating movements of the soft tissues of the neck (i.e., it does not resemble a subcutaneous vein). Because the carotid artery also pulsates in the neck, the clinician must learn to distinguish the carotid artery from the internal jugular vein, using the principles outlined in Table 34-1.

Of the distinguishing features listed in Table 34-1, the most conspicuous one is the character of the movement. Venous pulsations have a prominent *inward* or *descending* movement, the outward one being slower and more diffuse. Arterial pulsations, in contrast, have a prominent *ascending* or *outward* movement, the inward one being slow and diffuse.

B. COMPONENTS OF VENOUS WAVEFORMS

Although venous pressure tracings reveal three positive and negative waves (Fig. 34-3), the clinician at the bedside usually sees only two descents, a more prominent x′ descent and a less prominent y descent (Fig. 34-4). Figure 34-3 discusses the physiology of these waveforms.

TABLE 34-1 Distinguishing Internal Jugular Waveforms from Carotid Pulses*

Characteristic	Internal Jugular Vein	Carotid Artery
Character of movement	Descending movement most prominent	Ascending movement most prominent
Number of pulsations per ventricular systole	Two, usually	One
Palpability of pulsations	Not palpable or only slight undulation	Easily palpable
Change with respiration	During inspiration, pulsations become more prominent and drop lower in neck	No change
Change with position	Pulsations appear lower in neck as patient sits up	No change
Change with abdominal pressure	Pulsations may temporarily become more prominent and move higher in neck	No change
Change with pressure applied to the neck just below pulsations	Pulsations become less prominent	No change

*Based on references 64 to 67.

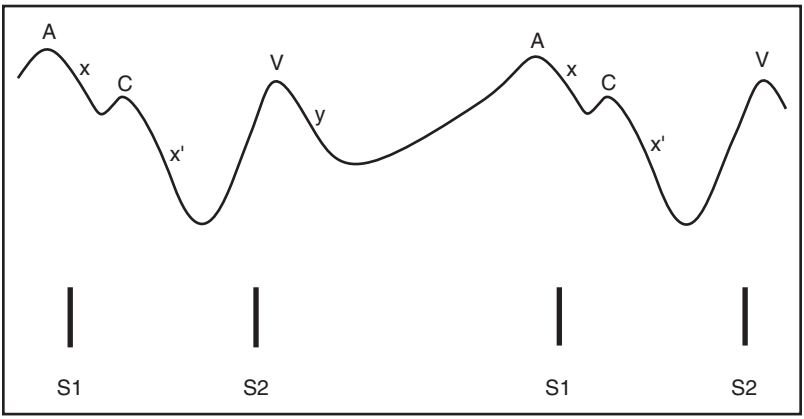


FIGURE 34-3 Venous waveforms on pressure tracings. There are three positive waves (A, C, and V) and three negative waves (x, x′, and y descents). The A wave represents right atrial contraction; the x descent, right atrial relaxation. The C wave—named "C" because Mackenzie originally thought it was a carotid artifact—probably instead represents right ventricular contraction and closure of the tricuspid valve, which then bulges upward toward the neck veins.[68,69] The x′ descent occurs because the floor of the right atrium (i.e., the A-V valve ring) moves downward, pulling away from the jugular veins, as the right ventricle contracts (physiologists call this movement the descent of the base).[70] The V wave represents right atrial filling, which eventually overcomes the descent of the base and causes venous pressure to rise (most atrial filling normally occurs during ventricular systole, not diastole). The y descent begins the moment the tricuspid valve opens at the beginning of diastole, causing the atrium to empty into the ventricle and venous pressure to abruptly fall.

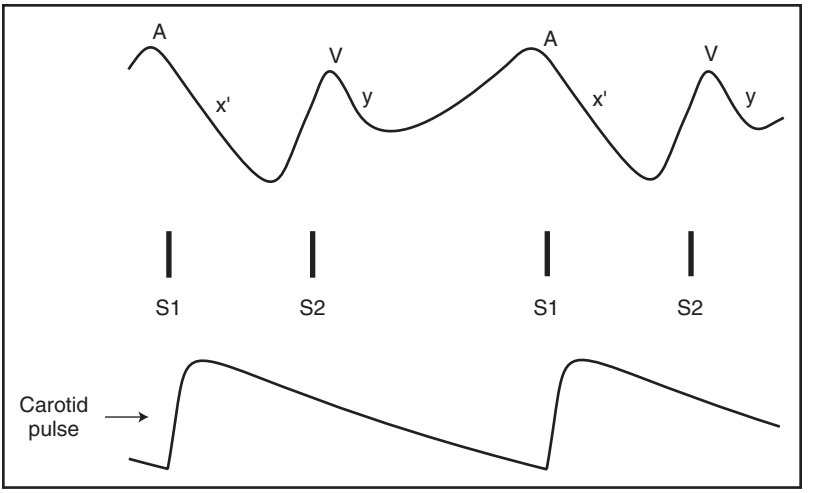


FIGURE 34-4 Venous waveform: What the clinician sees. Although tracings of venous waveforms display three positive and three negative waves (see Fig. 34-3), the C wave is too small to see. Instead, the clinician sees two descents per cardiac cycle: The first represents merging of the x and x′ descents and is usually referred to as the x′ descent (i.e., x-prime descent). The second is the y descent, which is smaller than the x′ descent in normal persons. The clinician identifies the descents by timing them with the heart tones or carotid pulsation (see text).

C. TIMING THE X′ AND Y DESCENTS

The best way to identify the individual venous waveforms is to time their *descents*, by simultaneously listening to the heart tones or palpating the carotid pulsation (see Fig. 34-4).

1. Using Heart Tones

The x′ descent ends just *before* S_2, as if it were a collapsing hill that was sliding into S_2 lying at the bottom. In contrast, the y descent begins just *after* S_2.

2. Using the Carotid Artery

The x′ descent is a systolic movement that coincides with the tap from the carotid pulsation. The y descent is a diastolic movement beginning after the carotid tap, with a delay roughly equivalent to the interval between the patient's S_1 and S_2 sounds.[66,71]

D. CLINICAL SIGNIFICANCE

The normal venous waveform has a prominent x′ descent and a small or absent y descent; there are no abrupt outward movements.[71]

Abnormalities of the venous waveforms become conspicuous at the bedside for one of two reasons:

1. The descents are abnormal.
2. There is a sudden outward movement in the neck veins.

1. Abnormal Descents

There are three abnormal patterns:

1. **The W or M pattern** (x′ = y pattern). The y descent becomes unusually prominent, which, along with the normal x′ descent, creates two prominent descents per systole and traces a W or M pattern in the soft tissues of the neck.
2. **The diminished X′ descent pattern** (x′ < y pattern). The x′ descent diminishes or disappears, making the y descent most prominent. This is the most common abnormal pattern, occurring both in atrial fibrillation (loss of A wave) and many different cardiomyopathies (more sluggish descent of the base).
3. **The absent y descent pattern.** This pattern is only relevant in patients with elevated venous pressure because healthy persons with normal CVP also have a diminutive y descent.

The etiologies of each of these patterns are presented in Table 34-2.

2. Abnormally Prominent Outward Waves

If the clinician detects an abnormally abrupt and conspicuous outward movement in the neck veins, the clinician should determine if the outward movement begins just before S_1 (presystolic giant A waves) or after S_1 (tricuspid regurgitation and cannon A waves).

TABLE 34-2 Venous Waveforms

Finding	Etiology (Reference)
ABNORMAL DESCENTS	
W or M pattern (x′ = y)	Constrictive pericarditis*[65,72]
	Atrial septal defect[73–75]
Diminished x′ descent (x′ < y)	Atrial fibrillation
	Cardiomyopathy[71]
	Mild tricuspid regurgitation
Absent y descent†	Cardiac tamponade[65]
	Tricuspid stenosis[76]
ABNORMALLY PROMINENT OUTWARD WAVES	
Giant A wave (presystolic wave)	Pulmonary hypertension[65]
	Pulmonic stenosis[65]
	Tricuspid stenosis[76,77]
Systolic wave	Tricuspid regurgitation[78–80]
	Cannon A waves[65]

*The prominent y descent of constrictive pericarditis is sometimes called *Friedrich's diastolic collapse of the cervical veins* (after Nikolaus Friedrich, 1825-1882).

†If venous pressure is normal, the absence of a y descent is a normal finding; if venous pressure is elevated, however, the absence of the y descent is abnormal and suggests impaired early diastolic filling.

a. Giant A Waves (Abrupt Presystolic Outward Waves)

Giant A waves have two requirements:

1. Sinus rhythm
2. Some obstruction to right atrial or ventricular emptying, usually from pulmonary hypertension, pulmonic stenosis, or tricuspid stenosis.[64,65,77] Nonetheless, many patients with severe pulmonary hypertension lack this finding, because their atria contract too feebly or at a time in the cardiac cycle when venous pressures are falling.[75,81]

Some patients with giant A waves have an accompanying abrupt presystolic sound that is heard with the stethoscope over the jugular veins.[82]

b. Systolic Waves

(1) Tricuspid Regurgitation. In patients with tricuspid regurgitation and pulmonary hypertension, the neck veins are elevated (>90% of patients) and consist of a single outward systolic movement that coincides with the carotid pulsation and collapses after S_2 (i.e., prominent y descent).[78–80] Some patients have an accompanying midsystolic clicking sound over the jugular veins.[83] Because the jugular valves often become incompetent in chronic tricuspid regurgitation, the arm and leg veins also may pulsate with each systolic regurgitant wave (see Chapter 44).

In one study, the finding of early systolic outward venous waveforms (CV wave) increased greatly the probability of moderate-to-severe tricuspid regurgitation (LR = 10.9; see EBM Box 34-1).

(2) Cannon A Waves. Cannon A waves represent an atrial contraction that occurs just after ventricular contraction, when the tricuspid valve is closed.* Instead of ejecting blood into the right ventricle, the contraction forces blood upward into the jugular veins. Cannon A waves may be regular (i.e., with every arterial pulse) or intermittent.

(a) Regular Cannon A Waves. The finding of regular cannon A waves occurs in many paroxysmal supraventricular tachycardias (fast heart rates) and junctional rhythms (normal heart rates), both of which have retrograde P waves buried within or just after the QRS complex.[65]

(b) Intermittent Cannon A Waves. If the arterial pulse is regular but cannon A waves are intermittent, only one mechanism is possible: atrioventricular dissociation (see Chapter 15). In patients with ventricular tachycardia, the finding of intermittently appearing cannon A waves detects atrioventricular dissociation with a sensitivity of 96%, specificity of 75%, positive LR of 3.8, and negative LR of 0.1 (see Chapter 15).[84]

If the arterial pulse is irregular, intermittent cannon A waves have less importance because they commonly accompany ventricular premature contractions and, less commonly, atrial premature contractions (see Chapter 15).

The references for this chapter can be found on www.expertconsult.com.

*The electrocardiographic correlate of the cannon A wave is a P wave (atrial contraction) falling between the QRS and T waves (ventricular systole).

CHAPTER 35

Percussion of the Heart

I. INTRODUCTION

Percussion of the heart has its roots in the 1820s, when a student of Laennec, Pierre Piorry, enthusiastically introduced topographic percussion, a technique purportedly allowing clinicians to precisely outline the borders of the underlying organs, including those of the heart.[1–3] Although many of Piorry's claims seem extraordinary today—he declared, for example, that he could outline pulmonary cavities, the spleen, hydatid cysts, and even individual heart chambers—many of his innovations persist, including indirect percussion, the pleximeter (Piorry used an ivory plate, but most clinicians now use the left middle finger), and the current practice of using percussion to locate the border of the diaphragm on the posterior chest or the span of the liver on the anterior body wall.[4]

In 1899, only 4 years after the discovery of roentgen rays, Williams challenged the accuracy of cardiac percussion, showing that many patients with moderately large hearts (autopsy weight of 350 to 500 g) had normal findings during cardiac percussion.[5] Cardiac percussion suffered another setback in 1907, when Moritz published the composite outlines of cardiac dullness according to various authorities, showing that these authorities disagreed not only with each other but also with the true roentgenographic outline.[4,6] By the 1930s, many leading clinicians began to regard percussion of the heart as unreliable and often inaccurate.[4,7]

II. CLINICAL SIGNIFICANCE

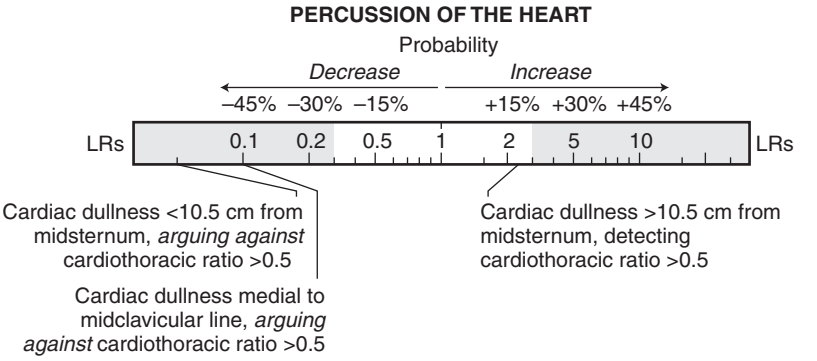
Studies of cardiac percussion have several limitations, the most important of which is selectively enrolling only healthy patients lacking chest deformities or emphysema. Even these studies, however, show that the percussed outline of the heart correlates only moderately with the true cardiac border. Whether the patient is supine or upright, the average error in locating the cardiac border is 1 to 2 cm. (The standard deviation of this error is about 1 cm.) The clinician usually overestimates the left border by placing it too far laterally and underestimates the right border by placing it too near the sternum. (These errors tend to cancel each other if the study's end point is the total transverse diameter of the heart.[8–11]) In patients with emphysema, the errors are even greater.[12]

The traditional sign of an enlarged heart by percussion is cardiac dullness that extends too far laterally. The finding of cardiac dullness extending either beyond the midclavicular line or more than 10.5 cm from the

EBM BOX 35-1
*Percussion of the Heart**

Finding (Reference)	Sensitivity (%)	Specificity (%)	Likelihood Ratio† if Finding Is	
			Present	*Absent*
Dullness Extends More Than 10.5 cm from Midsternal Line, Patient Supine				
Detecting cardiothoracic ratio >0.5[13]	97	61	2.5	**0.05**
Detecting increased left ventricular end-diastolic volume[14]	94	32	1.4	NS
Dullness Extends beyond Midclavicular Line, Patient Upright				
Detecting cardiothoracic ratio >0.5[8]	97	60	2.4	**0.1**

*Diagnostic standards: *Cardiothoracic ratio*, maximal transverse diameter of heart on chest radiography divided by maximal transverse diameter of thoracic cage; *increased left ventricular end-diastolic volume*, volume >186 mL by ultrafast computed tomography.[14]
†Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.
NS, not significant.
Click here to access calculator.



midsternal line argues modestly for an increased probability of an enlarged cardiothoracic ratio (likelihood ratio [LR] = 2.4 to 2.5; EBM Box 35-1). If cardiac dullness does *not* extend beyond these points, the patient probably does *not* have an enlarged cardiothoracic ratio (LR = 0.05 to 0.1; see EBM Box 35-1). It is unlikely that this information is clinically useful, however, because the cardiothoracic ratio has uncertain clinical significance.

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 36

Palpation of the Heart

I. INTRODUCTION

Much of the science of heart palpation is based on impulse cardiography and kinetocardiography, research tools from the 1960s that precisely timed normal and abnormal precordial movements and compared them with hemodynamic data and angiograms of the right and left ventricles. These precise and sensitive instruments could detect very small movements of the body wall, many of which are inconspicuous to the clinician's hand. Although this chapter refers to these studies to make certain points, only those movements easily palpable at the bedside are discussed.

Palpation of the heart is among the oldest physical examination techniques, having been recorded as early as 1550 BC by ancient Egyptian physicians (along with palpation of the peripheral pulses).[1] In the early 19th century, Jean-Nicolas Corvisart, personal physician to Napoleon and teacher of Laennec, was the first to correlate cardiac palpation with postmortem findings and distinguish right ventricular enlargement from left ventricular enlargement.[2–4] During animal experiments performed in 1830, James Hope proved that the cause of the apical impulse was ventricular contraction, which threw the heart up against the chest wall.[5]

II. TECHNIQUE

When palpating the chest, the clinician should describe the location, size, timing, and type of precordial movements.[6]

A. PATIENT POSITION

The clinician should first palpate the heart when the patient is lying supine and again with the patient lying on his or her left side. The supine position is used to locate all precordial movements and to identify whether these movements are abnormally hyperkinetic, sustained, or retracting (see later). The left lateral decubitus position is used to measure the diameter of the apical impulse and to detect additional abnormal diastolic filling movements (i.e., palpable third or fourth heart sounds).[7]

Because the left lateral decubitus position distorts the systolic apical movement, including that of healthy subjects (i.e., up to half of healthy patients have "abnormal" sustained movements in the lateral decubitus position), only the supine position should be used to characterize the patient's outward systolic movement.[8]

B. LOCATION OF ABNORMAL MOVEMENTS

Complete palpation of the heart includes four areas on the chest wall (Fig. 36-1).[1,6,9–12]

1. Apex Beat

The **apex beat,** or **apical impulse,** is the palpable cardiac impulse farthest away from the sternum and farthest down on the chest wall, usually caused by the left ventricle and located near the midclavicular line in the fifth intercostal space.

The clinician should also palpate the areas above and medial to the apex beat, where ventricular aneurysms sometimes become palpable.

2. Left Lower Sternal Area (Fourth Intercostal Space Near Left Edge of Sternum)

Abnormal right ventricular and left atrial movements appear at this location.

3. Left Base (Second Intercostal Space Near Left Sternum)

Abnormal pulmonary artery movements or a palpable P_2 appear at this location.

4. Right Base (Second Intercostal Space Near Right Edge of Sternum) and Sternoclavicular Joint

Movements from an ascending aortic aneurysm may become palpable here.

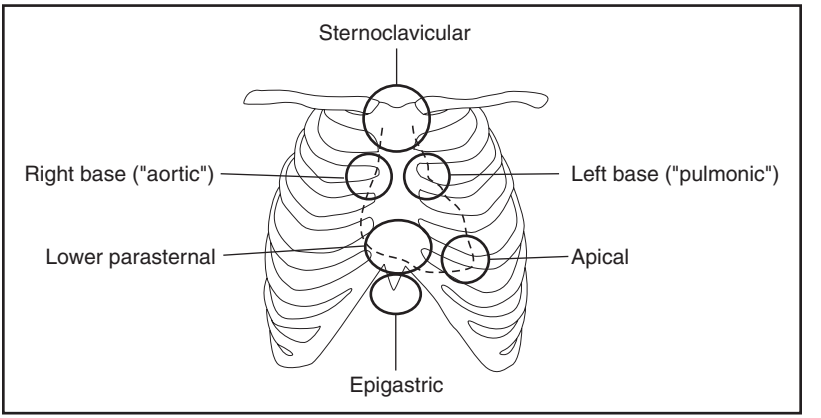


FIGURE 36-1 Locations of precordial movements. The principal areas of precordial pulsations are the apical area, lower parasternal area, left base (i.e., second left intercostal parasternal space, "pulmonic area"), right base (i.e., second right intercostal parasternal space, "aortic area"), and sternoclavicular areas. In some patients, especially those with chronic lung disease, right ventricular movements may appear in the epigastric area. The best external landmark is the sternal angle, which is where the second rib joins the sternum.

C. MAKING PRECORDIAL MOVEMENTS MORE CONSPICUOUS

Two teaching techniques are often used to bring out precordial movements and make them easier to time and characterize. In the first technique, the clinician puts a dot of ink on the area of interest, whose direction and timing then become easy to see. In the second technique, the clinician holds a cotton-tipped applicator stick against the chest wall, with the wooden end of the stick just off the center of the area of interest. (The stick should be several inches long.) The stick becomes a lever and the pulsating chest wall a fulcrum, causing the free end of the stick to trace in the air a magnified replica of the precordial movement. A folded paper stick-on note may be substituted for the applicator stick.[13]

III. THE FINDINGS

Precordial movements are timed by simultaneously listening to the heart tones and noting the relationship between outward movements on the chest wall and the first and second heart sounds. There are four types of systolic movements: normal, hyperkinetic, sustained, and retracting.[1,6,9–11]

A. NORMAL SYSTOLIC MOVEMENT

The normal systolic movement is a small outward movement that begins with S_1, ends by mid-systole, and then retracts inward, returning to its original position long before S_2.

The normal apical impulse is caused by a brisk early systolic anterior motion of the anteroseptal wall of the left ventricle against the ribs.[14] Despite its name, the apex beat bears no consistent relationship to the anatomic apex of the left ventricle.[14] In the supine position, the apex beat is palpable in only 25% to 40% of adults.[15–18] In the lateral decubitus position, it is palpable in 50% to 73% of adults.[15,19,20] The apex beat is more likely to be palpable in patients who have less body fat and who weigh less.[21] Some studies show that the apical impulse is more likely to be present in women than men, but this difference disappears after controlling for the participant's weight.[17]

B. HYPERKINETIC SYSTOLIC MOVEMENT

The hyperkinetic (or overacting) systolic movement is a movement identical in timing to the normal movement, although its amplitude is exaggerated. Distinguishing normal from hyperkinetic amplitude is a subjective process, even on precise tracings from impulse cardiography. This probably explains why the finding has minimal diagnostic value, appearing both in patients with volume overload of the left ventricle (e.g., aortic regurgitation, ventricular septal defect) and in some normal persons who have thin chests or increased cardiac output.

C. SUSTAINED SYSTOLIC MOVEMENT

The sustained movement is an abnormal outward movement that begins at S_1 but, unlike normal and hyperkinetic movements, extends to S_2 or even past it before beginning to descend to its original position. The amplitude

of the sustained movement may be normal or increased. Sustained apical movements are always abnormal, indicating either pressure overload of the left ventricle (e.g., aortic stenosis), volume overload (e.g., aortic regurgitation, ventricular septal defect), a combination of pressure and volume overload (combined aortic stenosis and regurgitation), severe cardiomyopathy, or ventricular aneurysm.

D. RETRACTING SYSTOLIC MOVEMENT

In the retracting movement, inward motion begins at S_1 and outward motion does not start until early diastole. Because retracting movements are sometimes identical to normal movements in every characteristic except for timing, they are easily overlooked unless the clinician listens to the heart tones when palpating the chest. Only two diagnoses cause the retracting impulse, constrictive pericarditis and severe tricuspid regurgitation.[1,8,11]

E. HEAVES, LIFTS, AND THRUSTS

The words *heave* and *lift* sometimes refer to sustained movements, and *thrust* to hyperkinetic ones, but these terms, often used imprecisely, are best avoided.[1,9–11]

IV. CLINICAL SIGNIFICANCE

A. APEX BEAT

1. Location

A traditional sign of an enlarged heart is an abnormally displaced apical impulse, which means it is located lateral to some external reference point. The three traditional reference points are

1. The midclavicular line
2. A set distance from the midsternal line (the traditional upper limit of normal is 10 cm)
3. The nipple line

Of these three landmarks, the midclavicular line is the best, as long as the clinician locates it carefully by palpating the acromioclavicular and sternoclavicular joints and marking the midpoint between them with a ruler.[22,23] In the supine patient, an apical impulse located outside the midclavicular line increases the probability that the heart is enlarged on the chest radiograph (likelihood ratio [LR] = 3.4; EBM Box 36-1), the ejection fraction is depressed (LR = 10.3), the left ventricular end-diastolic volume is increased (LR = 5.1), and the pulmonary capillary wedge pressure is increased (LR = 5.8). Other studies confirm the relationship between a displaced apical impulse and a depressed ejection fraction.[31]

Using a point 10 cm from the midsternal line to define the displaced impulse is not a useful predictor of the enlarged heart (positive LR not significant, negative LR = 0.5; see EBM Box 36-1), probably because the 10-cm threshold is set too low. (The midclavicular line usually lies 10.5 to 11.5 cm from the midsternal line.[22]) Finally, the nipple line is the least reliable of the three landmarks, bearing no consistent relationship to the apical impulse or to the size of the chest, even in men. The distance of the nipple line from the midsternum or midclavicular line varies greatly.[32]

2. Diameter of the Apical Impulse

As measured in the left lateral decubitus position at 45 degrees, an apical impulse with a diameter of 4 cm or more increases the probability that the patient has a dilated heart (LR = 4.7 for increased left ventricular end-diastolic volume; see EBM Box 36-1). Smaller thresholds (e.g., 3 cm) discriminate between dilated and normal hearts in some studies, but not others.[19,30]

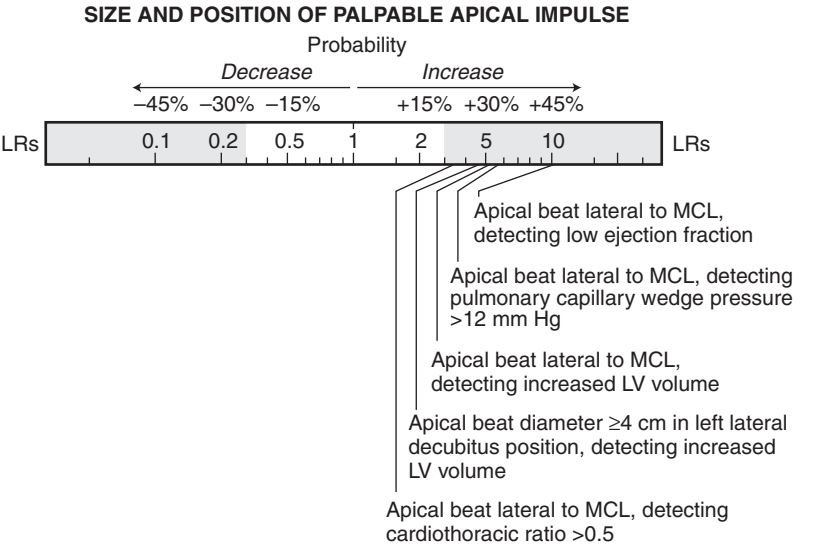
EBM BOX 36-1
*Size and Position of Palpable Apical Impulse**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Position of Apical Beat				
SUPINE APICAL IMPULSE LATERAL TO MCL				
Detecting cardiothoracic ratio >0.5[18,21,24]	39-60	76-93	**3.4**	0.6
Detecting low ejection fraction[25–28]	5-66	93-99	**10.3**	0.7
Detecting increased left ventricular end-diastolic volume[20,29]	33-34	92-96	**5.1**	0.7
Detecting pulmonary capillary wedge pressure >12 mm Hg[29]	42	93	**5.8**	NS
SUPINE APICAL IMPULSE >10 cm FROM MIDSTERNAL LINE				
Detecting cardiothoracic ratio >0.5[16,21,24]	61-80	28-97	NS	0.5
Size of Apical Beat				
APICAL BEAT DIAMETER ≥4 cm IN LEFT LATERAL DECUBITUS POSITION AT 45 DEGREES				
Detecting increased left ventricular end-diastolic volume[19,30]	48-85	79-96	**4.7**	NS

*Diagnostic standards: *Cardiothoracic ratio* is maximal transverse diameter of heart on chest radiography divided by maximal transverse diameter of thoracic cage; *low ejection fraction*, LV ejection fraction <0.50[26] or <0.53[25] by scintigraphy, <0.5 by echocardiography,[28] or LV fractional shortening <25% by echocardiography[27]; *increased LV end-diastolic volume*: >90 mL/M[2][29] or >138 mL (echocardiography[30]), >109.2 mL/M[2] (computed tomography),[20] or upper fifth percentile of normal (echocardiography)[19]; *increased LV mass* is LV mass by ultrafast computed tomography >191 g.[15]

†Definition of findings: Except for apical beat diameter, these data apply to all patients, whether or not an apical beat is palpable (i.e., nonpalpable apical beat = test negative). The only exception is the data for apical beat diameter, which apply only to patients who have a measurable apical beat in the left lateral decubitus position (i.e., apical beat diameter ≥4 cm = test positive; <4 cm = test negative; unable to measure diameter = unable to evaluate using these data).

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.
LV, left ventricle; MCL, midclavicular line; NS, not significant.
Click here to access calculator.



3. Abnormal Movements

a. Hyperkinetic Apical Movements

The hyperkinetic apical movement is an important finding in one setting. In patients with mitral stenosis, left ventricular filling is impaired, causing the apical impulse to be normal or even reduced.[33] If patients with the murmur of mitral stenosis also have a hyperkinetic apical impulse, an abnormality other than mitral stenosis also must therefore be present, such as mitral regurgitation or aortic regurgitation (LR = 11.2; EBM Box 36-2).

b. Sustained Apical Movements

A sustained or double apical movement (*double* refers to the combination of palpable S_4 and apical movement; see Chapter 39) increases the probability of left ventricular hypertrophy (LR = 5.6). In patients with aortic flow murmurs, the finding of a sustained apical impulse increases the probability of severe aortic stenosis (LR = 4.1; see EBM Box 36-2). In patients with the early diastolic murmur of aortic regurgitation, the sustained impulse is less helpful (LR = 2.4 for significant regurgitation), although the finding of a normal or absent apical impulse (i.e., not sustained or hyperkinetic) in these patients *decreases* significantly the probability of moderate-to-severe aortic regurgitation (LR = 0.1; see EBM Box 36-2).

c. Retracting Apical Impulse

(1) Constrictive Pericarditis. In up to 90% of patients with constrictive pericarditis, the apical impulse retracts during systole (sometimes accompanied by systolic retraction of the left parasternal area).[8,40] In these patients, the diseased pericardium prevents the normal outward systolic movement of the ventricles but allows rapid and prominent early diastolic filling of

EBM BOX 36-2
*Abnormal Palpable Movements**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Positive LR‡	Negative LR‡
Hyperkinetic Apical Movement				
Detecting associated mitral regurgitation or aortic valve disease in patients with mitral stenosis[33]	74	93	**11.2**	**0.3**
Sustained or Double Apical Movement				
Detecting left ventricular hypertrophy[20]	57	90	**5.6**	0.5
Sustained Apical Movement				
Detecting severe aortic stenosis in patients with aortic flow murmurs[34]	78	81	**4.1**	**0.3**
Detecting moderate-to-severe aortic regurgitation in patients with basal early diastolic murmurs[35]	97	60	2.4	**0.1**
Lower Sternal Pulsations				
Detecting moderate to severe tricuspid regurgitation[36]	17	99	**12.5**	0.8
Sustained Left Lower Parasternal Movement				
Detecting right ventricular peak pressure ≥50 mm Hg[37]	71	80	**3.6**	0.4
Right Ventricular Rock				
Detecting moderate to severe tricuspid regurgitation[36]	5	100	**31.4**	NS
Pulsatile Liver				
Detecting moderate to severe tricuspid regurgitation[36,38]	12-30	92-99	**6.5**	NS
Palpable P_2				
Detecting pulmonary hypertension in patients with mitral stenosis[39]	96	73	**3.6**	**0.05**

Continued

*Diagnostic standards: for *LV hypertrophy,* computed tomographic LV mass index >104 g/M^2 [20]; for *severe aortic stenosis* and *moderate-to-severe aortic regurgitation*, see EBM boxes in Chapters 42 and 43; for *moderate-to-severe tricuspid regurgitation*, 3+ or 4+ by angiography[38] or as assessed visually from echocardiography[36]; and for *pulmonary hypertension*, mean pulmonary artery pressure ≥50 mm Hg.[39]

†Definition of findings: For *abnormal apical movement*, "apical impulse heave or enlarged,"[35] "sustained,"[34] or "thrust"[33]; for *sustained or double apical movement*, apical movement extending beyond S_2 or combination of palpable S_4 + LV apical movement[20]; for *abnormal parasternal movement*, "movement extending to or past S_2"[37]; for *right ventricular rock*, see text; for *palpable* P_2 "palpable late systolic tap in second left intercostal space next to sternum, which frequently followed parasternal lift."[39]

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

LV, left ventricle; NS, not significant.

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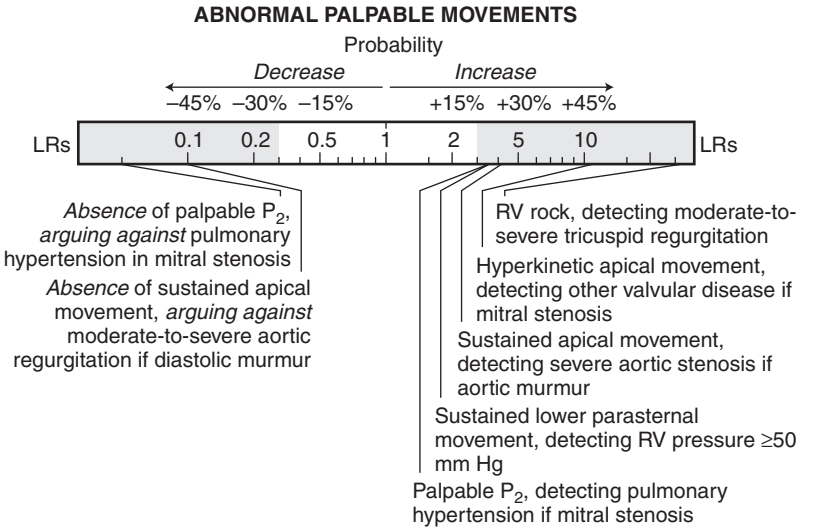


the ventricle. The prominent diastolic filling causes a palpable diastolic outward movement, which contributes to the overall impression that the apical impulse retracts during systole (see Chapter 45).

The first clinician to recognize the retracting apical impulse as a sign of "adhesive" pericarditis was Skoda in 1852.[41]

(2) Tricuspid Regurgitation. In severe tricuspid regurgitation, a dilated right ventricle, occupying the apex, ejects blood into a dilated right atrium and liver, located nearer the sternum.[8] This causes a characteristic rocking motion (or **right ventricular rock**), the apical area retracting inward during systole and the lower left or right parasternal area moving outward during systole,[42] often accompanied by a pulsatile liver. All three findings increase the probability of moderate-to-severe tricuspid regurgitation (LR = 31.4 for right ventricular rock, LR = 12.5 for lower sternal pulsations, and LR = 6.5 for pulsatile liver; see EBM Box 36-2).

B. LEFT LOWER PARASTERNAL MOVEMENTS

In normal persons, the clinician palpates either no movement or only a tiny inward one during systole at this location. Abnormal movements at this location are classified as hyperkinetic or sustained, depending on their relationship to S_2.

1. Hyperkinetic Movements

Hyperkinetic movements of the left lower parasternal area occur in up to 50% of patients with atrial septal defect, which causes volume overload of the right ventricle.[43] This finding nonetheless has limited diagnostic value without other findings of atrial septal defect—exaggerated y descent in the neck veins, wide and fixed S_2 splitting, and midsystolic murmur at the left second intercostal space (usually of grade 2/6)—because it is also sometimes found in patients without heart disease, such as those with thin chests, pectus excavatum, fever, or other high output states.[37,43]

2. Sustained Movements

Sustained movements of the left lower sternal area may represent either an abnormal right ventricle (e.g., pressure overload from pulmonary hypertension or pulmonic stenosis or volume overload from atrial septal defect) or an enlarged left atrium (e.g., severe mitral regurgitation). Both right ventricular and left atrial parasternal movements are outward movements that begin to move inward only at S_2 or just after it and therefore are classified as "sustained"; they are distinguished by when the outward movement *begins*.

a. Right Ventricular Movements

Outward right ventricular movements begin at the first heart sound. If the clinician can exclude volume overload of the right ventricle and mitral regurgitation (both of which also cause parasternal movements), the finding of a sustained left parasternal movement is a modest sign of pulmonary hypertension (often accompanied by tricuspid regurgitation; see earlier). In patients with mitral stenosis, the duration of the sustained lower parasternal movement correlates well with pulmonary pressures.[33] In patients with a wide variety of valvular and congenital heart lesions (excluding mitral regurgitation), the sustained lower left parasternal movement is a modest discriminator between those with peak right ventricular pressures of more than 50 mm Hg and those with lower pressures (positive LR = 3.6, negative LR 0.4; see EBM Box 36-2). Up to 30% of patients with atrial septal defect, whether or not there is associated pulmonary hypertension, also have sustained lower left parasternal movements.[43]

b. Left Atrium and Mitral Regurgitation

In patients with severe mitral regurgitation, ventricular contraction forces blood backward into a dilated left atrium, which lies on the posterior surface of the heart and acts like an expanding cushion to lift up the heart, including the left parasternal area. This sustained movement, most easily palpated in the fourth or fifth intercostal space near the sternum,[44,45] differs from those caused by the right ventricle because outward movement begins

in the second half of systole. (It parallels the V wave on the left atrial pressure tracing.)

In patients with isolated mitral regurgitation, the degree of the late systolic outward movement at the lower sternal edge correlates well with the severity of mitral regurgitation ($r = 0.93$, $p < .01$; the correlation is much worse if there is associated mitral stenosis, which may cause parasternal movements from pulmonary hypertension).[44,45] In pure mitral regurgitation, as in atrial septal defect, the parasternal movement has no relationship to right ventricular pressures.[46]

C. ANEURYSMS

In one study of consecutive patients with ventricular aneurysms identified by angiography, 33% had abnormal precordial movements.[47] Typical findings were

1. A double cardiac impulse, the first component representing the normal apical outward movement and the second component the bulging of the aneurysm during peak ventricular pressures later in systole[48,49]
2. A sustained impulse that extended superiorly or medially from the usual location of the apical impulse[47]

If detectable by palpation, the aneurysm originates in the anterior wall or apex of the left ventricle; aneurysms originating from the inferior or lateral wall are too distant from the anterior chest wall to be detectable by palpation.[47]

D. DIFFUSE PRECORDIAL MOVEMENTS

Diffuse outward movements of the entire precordium, from the apex to lower parasternal area, may result from

1. Right ventricular enlargement (which dilates to occupy the apical area)
2. Left ventricular enlargement (which rotates to occupy the lower parasternal area)
3. Biventricular enlargement[11]

Palpation alone cannot distinguish these different etiologies—even sensitive recordings from impulse cardiography or kinetocardiography cannot do this—and the clinician must rely on other findings to determine which chamber is most likely causing the diffuse movement.

E. RIGHT LOWER PARASTERNAL MOVEMENTS

Abnormal systolic outward movements appear in the right lower parasternal area from tricuspid regurgitation (ejection of blood into the right atrium and liver, which lies under the right side of the sternum) or from mitral regurgitation (ejection of blood in a dilated left atrium).[11,42,50]

F. PALPABLE P_2

A palpable P_2 (i.e., the pulmonic component of the second heart sound) is a sharp, brief, snapping sensation felt over the left base, coincident with S_2. It is much briefer than other precordial movements. In patients with mitral

stenosis, a palpable P_2 increases the probability of pulmonary hypertension (LR = 3.6 for mean pulmonary pressure >50 mm Hg). More importantly, the absence of a palpable P_2 in these patients *decreases* the probability of a pulmonary pressure this high (LR = 0.05; see EBM Box 36-2).

G. PALPABLE THIRD AND FOURTH HEART SOUNDS

Some patients with rapid early ventricular filling (e.g., mitral regurgitation) have a palpable early diastolic movement at the apex. Other patients with strong atrial contractions into stiff ventricles (e.g., hypertensive or ischemic heart disease) have palpable presystolic apical movements. These movements have the same significance as their audible counterparts, the third and fourth heart sounds (i.e., S_3 and S_4; see Chapter 39). They are usually called "palpable S_3" and "palpable S_4.

The S_4 is much more likely to be palpable than the S_3, and both are more likely to be felt when the patient is in the lateral decubitus position.[7,9,10] The palpable S_4 causes either a double outward impulse near S_1 (a common analogy is the grace note in music; see double movement in EBM Box 36-2) or single outward movement, consisting of the palpable S_4 and apical beat together, which is distinguished from the apical beat alone because the outward movement begins slightly before S_1.[10,11]

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 37

Auscultation of the Heart: General Principles

I. CHARACTERISTICS OF HEART SOUNDS AND MURMURS

Different heart sounds and murmurs are distinguished by four characteristics:

1. Timing (i.e., systolic or diastolic)
2. Intensity (i.e., loud or soft)
3. Duration (i.e., long or short)
4. Pitch (i.e., low or high frequency)

A fifth characteristic, the sound's quality, is also sometimes included in the descriptions of sounds (e.g., it is described as "musical," a "whoop," or a "honk"). Almost all heart sounds contain a mixture of frequencies (i.e., they are not musical in the acoustic sense but instead are "noise," like the static of a radio). Therefore, the descriptors *low-frequency* and *high-frequency* do not indicate that a sound has a pure musical tone of a certain low or high pitch but instead that the bulk of the sound's energy is within the low or high range.

Although the human ear can hear sounds with frequencies from 20 to 20,000 cycles per second (Hz), the principal frequencies of heart sounds and murmurs are at the lower end of this range, from 20 to 500 Hz.[1,2] **Low-frequency sounds,** therefore, are those whose dominant frequencies are less than 100 Hz, such as third and fourth heart sounds and the diastolic murmur of mitral stenosis. These sounds are usually difficult to hear because the human ear perceives lower frequencies relatively less well than higher frequencies. The murmur containing the highest-frequency sound is aortic regurgitation, whose dominant frequencies are about 400 Hz. The principal frequencies of other sounds and murmurs are between 100 and 400 Hz.

II. THE STETHOSCOPE

A. BELL AND DIAPHRAGM

The stethoscope has two different heads to receive sound, the bell and the diaphragm. The bell is used to detect low-frequency sounds and the diaphragm to detect high-frequency sounds.

The traditional explanation that the bell selectively transmits low-frequency sounds and the diaphragm selectively filters out low-frequency

sounds is probably incorrect. Actually, the bell transmits all frequencies well, but in some patients with high-frequency murmurs (e.g., aortic regurgitation), any additional low-frequency sound masks the high-frequency sound and makes the murmur difficult to detect.[3] The diaphragm does not selectively filter out low-frequency sounds but instead attenuates all frequencies equally, thus dropping the barely audible low-frequency ones below the threshold of human hearing.[3]

B. PERFORMANCE OF DIFFERENT STETHOSCOPE MODELS

Many studies have examined the acoustics of stethoscopes, but the clinical relevance of this research has never been formally tested. In general, these studies show that shallow bells transmit sound as well as deeper bells and that double-tube stethoscopes are equivalent to single-tube models.[3] The optimal internal bore of a stethoscope is somewhere between one-eighth and three-sixteenths of an inch because smaller bores diminish transmission of the higher-frequency sounds.[1,4,5] Compared with shorter lengths of stethoscope tubing, longer tubes also impair the conduction of high-frequency sounds.[1]

Most modern stethoscopes, however, transmit sound equally well, the differences among various models for single frequencies being very small.[3] The most important source of poor acoustic performance is an air leak, which typically results from poorly fitting earpieces. Even a tiny air leak with a diameter of only 0.015 inch will diminish transmission of sound by as much as 20 dB,* particularly for those sounds of less than 100 Hz.[6]

III. USE OF THE STETHOSCOPE

Between the 1950s and late 1970s, cardiac auscultation was at its peak.† During this time, cardiologists perfected their skills by routinely comparing the bedside findings to the patient's phonocardiogram, angiogram, and surgical findings, which allowed clinicians to make precise and accurate diagnoses from bedside findings alone. The principles of bedside diagnosis used by these clinicians are included elsewhere in this book. How these clinicians specifically used the stethoscope to examine the patient is presented below.

A. EXAMINATION ROOM

Many faint heart sounds and murmurs are inaudible unless there is complete silence in the room. The clinician should close the door to the examination room, turn off the television and radio, and ask that all conversation stop.

B. BELL PRESSURE

To detect low-frequency sounds, the stethoscope bell should be applied to the body wall with only enough pressure to create an air seal and exclude ambient noise. Excessive pressure with the bell stretches the skin, which

*_Decibels_ describe relative intensity (or loudness) on a logarithmic scale.

†In the late 1970s, two events initiated the decline of cardiac auscultation: the widespread introduction of echocardiography and the decision by insurance companies to no longer make reimbursements for phonocardiography.

then acts like a diaphragm and makes low-frequency sounds more difficult to hear. By selectively varying the pressure on the stethoscope bell, the clinician can easily distinguish low-frequency from high-frequency sounds: If a sound is audible with the bell using light pressure but disappears with firm pressure, it is a low-frequency sound. This technique is frequently used to confirm that an early diastolic sound is indeed a third heart sound (i.e., third heart sounds are low-frequency sounds, whereas other early diastolic sounds such as the pericardial knock are high-frequency sounds) and to distinguish the combined fourth and first heart sounds (S_4 plus S_1) from the split S_1. (The S_4 is a low-frequency sound, but the S_1 is not; firm pressure renders the S_4 plus S_1 sounds into a single sound but does not affect the double sound of the split S_1.)

C. PATIENT POSITION

The clinician should listen to the patient's heart with the patient in three positions: supine, left lateral decubitus, and seated upright. The lateral decubitus position is best for detection of the third and fourth heart sounds and the diastolic murmur of mitral stenosis. (To detect these sounds, the clinician places the bell lightly over the apical impulse or just medial to the apical impulse.[7]) The seated upright position is necessary to further evaluate audible expiratory splitting of S_2 (see Chapter 38) and to detect some pericardial rubs and murmurs of aortic regurgitation (see Chapters 43 and 45).

D. ORDER OF EXAMINATION

Routine auscultation of the heart should include the right upper sternal area, the entire left sternal border, and the apex. Some cardiologists recommend proceeding from base to apex[2]; others from apex to base.[8] The diaphragm of the stethoscope should be applied to all areas, especially at the upper left sternal area to detect S_2 splitting and at all areas to detect other murmurs and sounds. After using the diaphragm to listen to the lower left sternal area and apex, the bell should also be applied to these areas to detect diastolic filling sounds (S_3 and S_4) and diastolic rumbling murmurs (e.g., mitral stenosis).

In selected patients, the clinician also should listen over the carotid arteries and axilla (in patients with systolic murmurs, to clarify radiation of the murmur), the lower right sternal area (in patients with the diastolic murmur of aortic regurgitation, to detect aortic root disease), the back (in young patients with hypertension, to detect the continuous murmur of coarctation), or other thoracic sites (in patients with central cyanosis, to detect the continuous murmur of pulmonary arteriovenous fistulas).

E. DESCRIBING THE LOCATION OF SOUNDS

When describing heart sounds and murmurs, the clinician should identify where on the chest wall the sound is loudest. Traditionally, the second right intercostal space next to the sternum is called the aortic area or right base; the second left intercostal space next to the sternum, the pulmonary area or left base; the fourth or fifth left parasternal space, the tricuspid area or left lower sternal border; and the most lateral point of the palpable cardiac impulse, the mitral area or apex (see Fig. 36-1 in Chapter 36).

The terms *aortic area, pulmonary area, tricuspid area,* and *mitral area* are ambiguous, however, and are best avoided. Many patients with aortic stenosis have murmurs loudest in the mitral area, and some with mitral regurgitation have murmurs in the pulmonary or aortic area. A more precise way to describe the location of sounds is to use the apex and the parasternal areas as reference points, the parasternal location being further specified by the intercostal space (first, second, third, or lower sternal border) and whether it is the right or left edge of the sternum. For example, a sound might be loudest at the "apex," the "second left intercostal space" (i.e., next to the left sternal edge in the second intercostal space), or "between the apex and left lower sternal border."

F. TECHNIQUE OF FOCUSING

The human brain has an uncanny ability to isolate and focus on one type of sensory information, by repressing awareness of all other sensations. A common example of this phenomenon is the person reading a book in a room in which a clock is ticking: The person may read long passages of the book without even hearing the clock but hears the ticking clock immediately after putting the book down. When listening to the heart, the clinician's attention is quickly drawn to the most prominent sounds, but this occurs at the expense of detecting the fainter sounds. To avoid missing these fainter sounds or subtle splitting, therefore, the clinician should concentrate sequentially on each part of the cardiac cycle, asking the following questions at each location:

1. Is S_1 soft or loud?
2. Is S_2 split and, if so, how is it split?
3. Are there are any extra sounds or murmurs during systole?
4. Are there are any extra sounds or murmurs during diastole?

G. IDENTIFYING SYSTOLE AND DIASTOLE

Because all auscultatory findings are characterized by their timing, distinguishing systole from diastole accurately is essential. Three principles help the clinician distinguish these events.

1. Systole Is Shorter Than Diastole

If the heart rate is normal or slow, systole can be easily distinguished from diastole because systole is much shorter. The normal cadence of the heart tones, therefore, is

lub dup lub dup lub dup lub dup

(*lub* is S_1 and *dup* is S_2). When the heart rate accelerates, however, diastole shortens, and at a rate of 100 beats/min or more, the cadence of S_1 and S_2 resembles a tic-toc rhythm:

lub dup lub dup lub dup lub dup lub dup lub dup

In these patients, other techniques are necessary to distinguish systole from diastole.

2. Characteristics of the First and Second Heart Sounds

At the second left intercostal space, S_2 is generally louder, shorter, and sharper than S_1. (S_2 has more high-frequency energy than S_1, which is why *dup*, a snappier sound than *lub*, is used to characterize S_2.) If the timing of extra heart sounds and murmurs is confusing at the lower sternal edge or apex (as it often is in patients with fast heart rhythms), the clinician can return the stethoscope to the second left intercostal space, identify S_2 by its louder and sharper sound, and then inch slowly back to the area of interest, keeping track of S_2 along the way.

3. Carotid Impulse

The palpable impulse from the carotid usually occurs just after S_1, which the clinician detects by simultaneously listening to the heart tones and palpating the carotid artery. In elderly patients with tachycardia, however, this rule is sometimes misleading because the carotid impulse seems to fall closer to S_2, although even in these patients the carotid impulse still falls between S_1 and S_2.

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 38

The First and Second Heart Sounds

The first and second heart sounds (S_1 and S_2) define systole and diastole and therefore form the framework for analyzing all other auscultatory physical signs, including the third and fourth heart sounds, clicks and ejection sound, knocks and opening snaps, and systolic and diastolic murmurs. In his classic treatise describing the discovery of the circulatory system, written in 1628, Harvey described both S_1 and S_2, comparing them to the gulping sound made by a horse drinking water.[1] The first person to state that S_1 and S_2 were the sounds of closing heart valves was Rouanet of France, who wrote in his 1832 MD thesis that S_1 occurred when the atrioventricular (i.e., mitral and tricuspid) valves closed and S_2 occurred when the semilunar (i.e., aortic and pulmonic) valves closed.[2]

THE FIRST HEART SOUND (S_1)

I. THE FINDING

S_1 is heard well across the entire precordium, both with the bell and diaphragm of the stethoscope. It is usually loudest at or near the apex and contains more low-frequency energy than does S_2, which explains why, when mimicking the sound, the term *lub* is used for S_1 and the sharper term *dup* for S_2.*

II. PATHOGENESIS

A. CAUSE OF S_1

The precise cause of S_1 has been debated for decades. Although its two recordable components coincide with closure of the mitral and tricuspid valves, the force of valve closure itself is insufficient to generate sound.[4] Instead, their closure probably causes moving columns of blood to abruptly decelerate, which sets up vibrations in the chordae tendineae, ventricles, and blood as a unit (i.e., **cardiohemic system**).[4,5]

*It was Williams in 1840 who invented the *lub dup* onomatopoeia.[3]

B. INTENSITY OF S_1

The most important abnormalities of S_1 relate to its intensity: The sound can be abnormally loud or abnormally faint or can vary in intensity abnormally from beat to beat. The primary variables governing intensity of S_1 are the strength of ventricular contraction and the position of the atrioventricular leaflets at the onset of ventricular systole.

1. Ventricular Contractility

The stronger the ventricular contraction, the louder the S_1. Strong contractions, which have a high dP/dT (i.e., large increase in pressure with respect to time), intensify S_1 because the valves close with more force and generate more vibrations in the cardiohemic system.[6,7]

2. Position of the Valve Leaflets at Onset of Ventricular Systole

If the mitral valve is wide open at the onset of ventricular systole, it will take longer to close completely than if it had been barely open. Even this small delay in closure intensifies S_1 because closure occurs on a later and steeper portion of the left ventricular pressure curve (i.e., dP/dT is greater).[8]

The PR interval is the main variable determining the position of the valves at the beginning of ventricular systole. If the PR interval is short, ventricular systole immediately follows atrial systole (i.e., the R wave immediately follows the P wave). Because atrial systole kicks the valve open, a short PR guarantees that the valve will be wide open at the onset of ventricular systole. In contrast, a long PR interval allows time for the cusps of the atrioventricular valves to float back together before ventricular systole occurs. Studies show that, with PR intervals less than 0.20 seconds, the intensity of S_1 varies inversely with the PR interval (the shorter the PR interval, the louder the sound). With PR intervals greater than 0.20 seconds, S_1 is faint or absent.[8,9]

III. CLINICAL SIGNIFICANCE

A. LOUD S_1

S_1 may be abnormally loud because of unusually vigorous ventricular contractions or because of delayed closure of the mitral valve.

1. Vigorous Ventricular Contractions

Vigorous contractions, such as those occurring from fever and sympathetic stimulation (e.g., beta-adrenergic inhalers, thyrotoxicosis), increase dP/dT and intensify S_1.[6]

2. Delayed Closure of the Mitral Valve

a. Prolapsed Mitral Valve

In patients with the murmur of mitral regurgitation, a loud S_1 is a clue to the diagnosis of early prolapse of the mitral valve. (Many patients with mitral regurgitation have a normal or soft S_1.[10,11]) S_1 is loud in these patients because the prolapsing leaflets stop moving and tense later than normal, when dP/dT in the ventricle is greater.[10]

b. Mitral Stenosis

Ninety percent of patients with pure uncomplicated mitral stenosis have a loud S_1.[12] Because the murmur of mitral stenosis is often difficult to hear, a traditional teaching is that clinicians should suspect mitral stenosis in any patient with a loud, unexplained S_1 and listen carefully for the murmur with the patient lying on the left side.

Mitral stenosis delays closure of the mitral valve because the pressure gradient between the left atrium and left ventricle keeps the leaflets open until the moment of ventricular systole. After successful valvuloplasty, the loud S_1 becomes softer.[12]

c. Left Atrial Myxoma

Many patients with left atrial myxoma (seven of nine in one series) also have a loud S_1 because the tumor falling into the mitral orifice during diastole delays closure of the valve.[13]

B. FAINT OR ABSENT S_1

S_1 is unusually faint if ventricular contractions are weak or if the mitral valve is already closed when ventricular systole occurs.

1. Weak Ventricular Contractions (Low dP/dT)

Common examples of weak contractions causing a faint S_1 are myocardial infarction and left bundle branch block.[14]

2. Early Closure of the Mitral Valve

Common causes of early mitral closure causing the faint S_1 include the following:

a. Long PR Interval (>0.20 Seconds)

See the section on Intensity of S_1.

b. Acute Aortic Regurgitation

In patients with the murmur of aortic regurgitation, the faint or absent S_1 is an important clue that the regurgitation is acute (e.g., endocarditis) and not chronic. Patients with acute aortic regurgitation have much higher left ventricular end-diastolic pressures than those with chronic regurgitation because the acutely failing valve has not allowed time for the ventricle to enlarge, as it does to compensate for chronic regurgitation. The high pressures in the ventricle eventually exceed diastolic left atrial pressures, closing the mitral valve before ventricular systole and thus making S_1 faint or absent.[15]

C. VARYING INTENSITY OF S_1

If the arterial pulse rhythm is *regular* but S_1 varies in intensity, the only possible explanation is that the PR interval is changing from beat to beat, which means the patient has atrioventricular dissociation. In contrast, in patients with *irregular* rhythms, a changing intensity of S_1 has no diagnostic significance, because ventricular filling and dP/dT—and, therefore, S_1 intensity—depend completely on cycle length.

In patients with pacer-induced regular rhythms, an S_1 that varies in intensity is compelling evidence for atrioventricular dissociation (likelihood ratio [LR] = 24.4; EBM Box 38-1). Presumably, the finding is also as accurate in patients with native rhythms. In patients with complete heart block, S_1 intensity is predictable, varying inversely with the PR interval for intervals of less than 0.2 seconds, becoming inaudible for intervals of 0.2

EBM BOX 38-1
*The First and Second Heart Sounds**

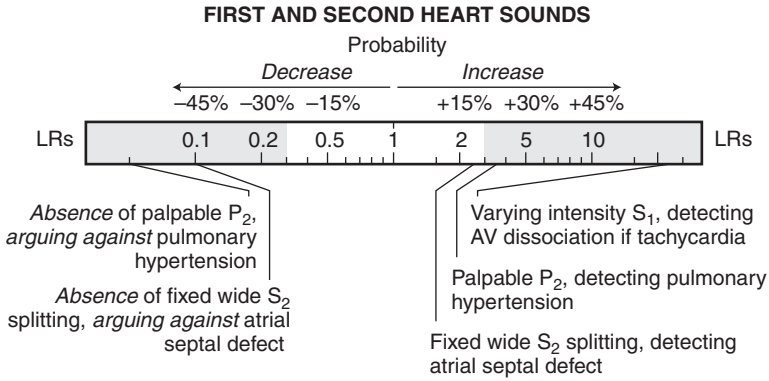
Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
First Heart Sound				
VARYING INTENSITY S_1				
Detecting atrioventricular dissociation[16]	58	98	**24.4**	0.4
Second Heart Sound				
FIXED WIDE SPLITTING				
Detecting atrial septal defect[17]	92	65	2.6	**0.1**
PARADOXIC SPLITTING				
Detecting significant aortic stenosis[18]	50	79	NS	NS
LOUD P_2				
Detecting pulmonary hypertension[19,20]	58-96	19-46	NS	NS
PALPABLE P_2				
Detecting pulmonary hypertension[19]	96	73	**3.6**	**0.05**
ABSENT OR DIMINISHED S2				
Detecting significant aortic stenosis in patients with aortic flow murmurs[18,21–24]	44-90	63-98	**3.1**	0.4

*Diagnostic standard: For *atrioventricular dissociation*, ventricles were paced independently of atria; for *atrial septal defect*, right heart catheterization; for *severe aortic stenosis*, aortic valve area <0.75 cm^2,[21] <0.8 cm^2,[23] peak gradient >50 mm Hg,[18,23] or peak velocity of aortic flow >3.6 m/sec[22] or ≥4 m/sec[24]; for *pulmonary hypertension*, mean pulmonary arterial pressure ≥50 mm Hg.

†Definition of findings: For *loud P_2*, splitting heard with loud second component[19] or S_2 louder at left second interspace than right second interspace[20]; the figures for fixed splitting of S_2 apply only to patients having audible expiratory splitting.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. NS, not significant.

Click here to access calculator.



to 0.5 seconds, and becoming louder again with intervals of more than 0.5 seconds (because the mitral valve reopens).[9]

D. PROMINENT SPLITTING OF S_1

Any delay in the closure of the tricuspid valve, the second component of S_1, accentuates splitting of S_1. This finding therefore occurs in patients with right bundle branch block or in left ventricular ectopic or paced beats, all of which delay the onset of right ventricular systole and also cause wide physiologic splitting of S_2 (see later).[5,25]

How to distinguish the split S_1 from other double sounds occurring around S_1, such as S4 plus S1 and S_1 plus ejection sound, is discussed in Chapter 39.

THE SECOND HEART SOUND (S_2)

The most important diagnostic feature of S_2 is its "splitting," which refers to how the aortic and pulmonic components of S_2 vary in timing during the respiratory cycle. The intensity of S_2 has less diagnostic importance. (This contrasts with S_1, in which intensity is more important than splitting.) Splitting of S_2 was first recognized by Potain in 1865, and its importance to cardiac auscultation was described by Leatham in the 1950s, who called S_2 the "key to auscultation of the heart."[26,27] The correct explanation for normal splitting—increased "hangout" in the pulmonary circulation—was discovered in the 1970s.[28,29]

I. NORMAL SPLITTING OF S_2

A. THE FINDING

In normal persons, the first component of S_2 is caused by closure of the aortic valve (A_2); the second, by closure of the pulmonic valve (P_2). During inspiration, the interval separating A_2 and P_2 increases by about 20 to 30 ms (Fig. 38-1).[17,27,29]

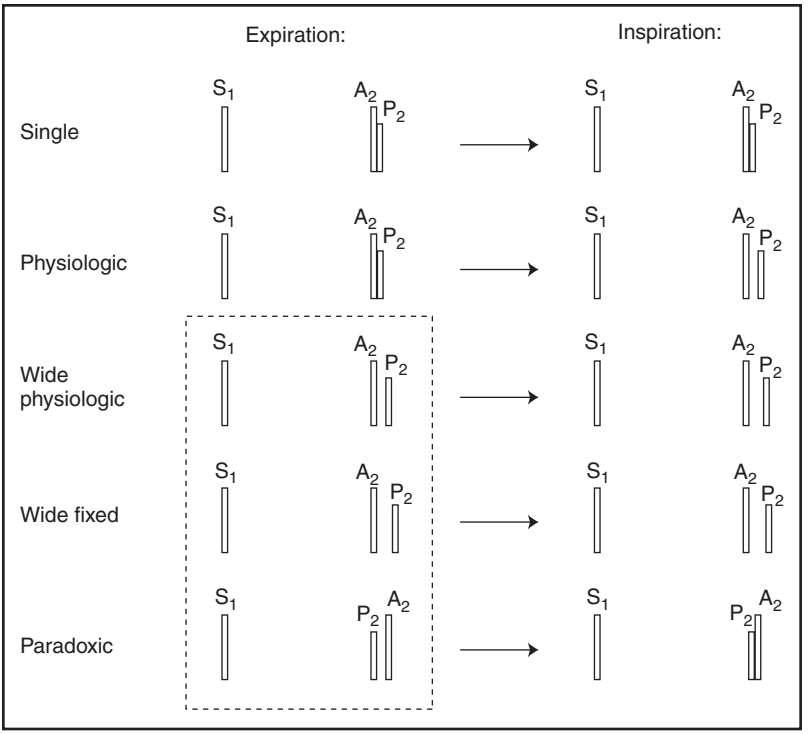


FIGURE 38-1 **S_2 splitting.** Splitting refers to the separation of the aortic component (A_2) and the pulmonic component (P_2) during expiration *(left column)* and inspiration *(right column)*. There are two normal patterns (single and physiologic) and three abnormal patterns (wide physiologic, wide fixed, and paradoxic). The *dotted lines* indicate that all three abnormal forms of splitting are distinguished by audible expiratory splitting. See text.

Although the phonocardiogram almost always records both components of S_2, the human ear perceives them as a single sound *during expiration* in over 90% of normal persons.[30] In normal persons *during inspiration*, the human ear either perceives two components (physiologic splitting, heard in 65% to 75% of normal adults; see Fig. 38-1)* or still perceives a single component (single S_2, heard in 25% to 35% of normal adults). The older the person, the more likely S_2 will be single instead of physiologic.[30,33]

In a minority of normal persons, expiratory splitting is heard in the supine position, although S_2 becomes single during expiration in these patients when they sit up.[34]

*These two components are very close together, bordering the threshold of being perceived as a single sound. Harvey suggests mimicking the normal expiratory sound by striking a single knuckle against a tabletop and mimicking inspiratory physiologic splitting by striking two knuckles almost simultaneously.[31] Constant suggests mimicking inspiratory splitting by rolling the tongue as in a Spanish *dr* or *tr*, or saying *pa-da* as quickly and sharply as possible.[32]

B. LOCATION OF SOUND

S_2 splitting is usually heard only in the second or third intercostal space, next to the left sternum.[33] It is sometimes heard at a slightly lower location, especially in patients with chronic pulmonary disease, and at a slightly higher location in those who are obese.[33] Splitting is not heard at other locations normally because P_2 is too faint.

C. TECHNIQUE

It is important that the patient breathe regularly in and out when evaluating S_2 splitting because held inspiration or held expiration tends to make the two components drift apart, thus making it impossible to interpret the sound.[17]

D. PHYSIOLOGY OF SPLITTING

The normal delay in P_2 results from a long "hangout" interval in the normal pulmonary circulation. (It is not because right ventricular systole ends later than left ventricular systole; they actually end at the same moment; Fig. 38-2.) *Hangout* means that the pulmonary circulation offers so little resistance to blood flow that flow continues for a short period even after completion of right ventricular mechanical systole.[28,29] At the aortic valve, there is little hangout, causing flow to cease and the valve to close immediately after completion of left ventricular contraction.

A_2 and P_2 move apart during inspiration, primarily because inspiration delays P_2 even more. About half of the inspiratory augmentation of the A_2-P_2 interval is due to a further increase in the hangout interval in the pulmonary circulation. About 25% of inspiratory augmentation is due to lengthening of right ventricular systole (from increased filling of the right side of the heart during inspiration), and the remaining 25% is due to shortening of left ventricular systole (from a reduction of filling of the left side of the heart during inspiration).[29]

II. ABNORMAL SPLITTING OF S_2

A. THE FINDING

There are three abnormalities of S_2 splitting (see Fig. 38-1):

1. Wide Physiologic Splitting

Wide physiologic splitting means that splitting occurs during inspiration and expiration, though the A_2-P_2 interval widens further during inspiration.

2. Wide Fixed Splitting

Wide fixed splitting means that splitting occurs during inspiration and expiration, but the A_2-P_2 interval remains constant.

3. Paradoxic Splitting (Reversed Splitting)

Paradoxic splitting means that audible expiratory splitting narrows or melds into a single sound during inspiration. Paradoxic splitting occurs because the order of the S_2 components has reversed: A_2 now follows P_2, and as P_2 is delayed during inspiration, the sounds move together.

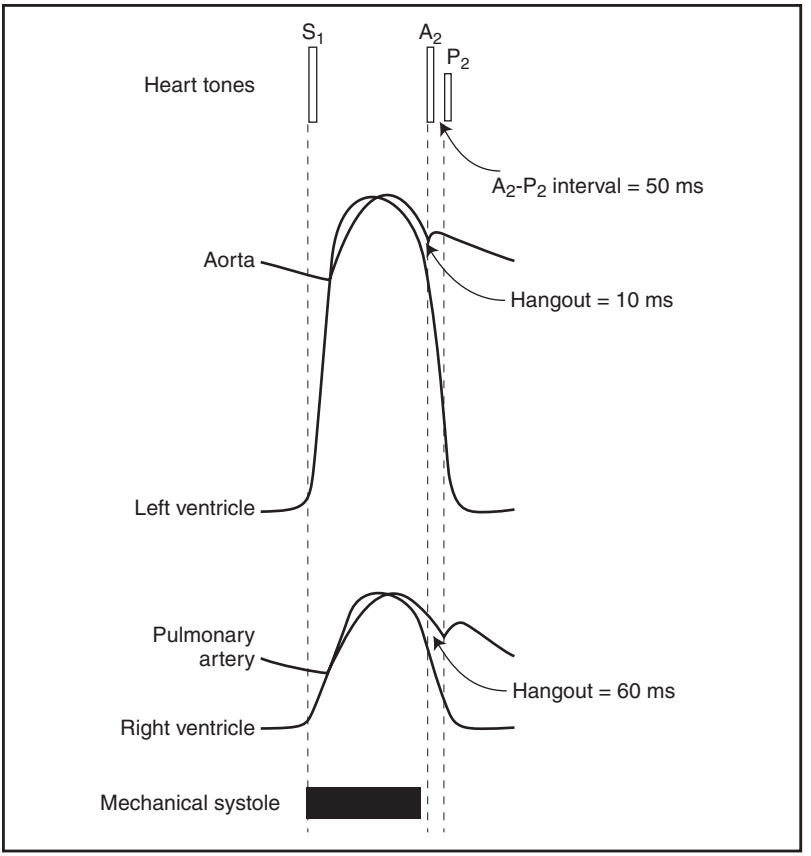


FIGURE 38-2 **Mechanism of S2 splitting.** The timing of heart tones *(top)* is correlated with pressure tracings from the left side of the heart (i.e., aorta and left ventricle, *top pressure tracings*) and right side of the heart (i.e., pulmonary artery and right ventricle, *bottom pressure tracings*). The solid rectangle at the bottom of the figure depicts the duration of mechanical systole, which is the same for the right and left ventricles. A_2 coincides with the incisura (i.e., notch) on the aorta tracing, P_2 coincides with the incisura on the pulmonary artery tracing, and both sounds occur a short interval after completion of mechanical systole (the interval between the end of mechanical systole and valve closure is called hangout). On the left side of the heart, hangout is very short (10 ms; i.e., the aortic valve closes almost immediately after completion of mechanical systole). On the right side of the heart, however, hangout is longer (60 ms) because the compliant pulmonary circulation offers so little resistance to continued forward flow. The difference between these numbers explains why P_2 normally occurs after A_2 (i.e., A_2-P_2 interval in this patient = 60 − 10 = 50 ms). Changes in hangout also explain in part why splitting normally increases during inspiration and why most patients with pulmonary hypertension have a single S_2. See text.

B. SCREENING FOR ABNORMAL SPLITTING OF S_2

Figure 38-1 reveals that all three abnormal second heart sounds—wide physiologic, fixed, and paradoxic sounds—have audible splitting *during expiration* (see dotted lines in Fig. 38-1). Therefore, the best screening tool for the abnormal S_2 is audible expiratory splitting that persists when the patient sits up.[34–37]

TABLE 38-1 Abnormal S_2 Splitting

Splitting and Pathogenesis	Etiology
WIDE PHYSIOLOGIC	
P_2 Late	
Electrical delay of RV systole	RBBB LV paced or ectopic beats
Prolongation of RV systole	Pulmonic stenosis Acute cor pulmonale
Increased hangout interval	Dilation of pulmonary artery
A_2 Early	
Shortening of LV systole	Mitral regurgitation
WIDE AND FIXED	
Increased hangout interval or prolongation of RV systole	Atrial septal defect
Prolongation of RV systole	Right ventricular failure
PARADOXIC	
A_2 Late	
Electrical delay of LV systole	LBBB RV paced or ectopic beats
Prolongation of LV systole	Aortic stenosis Ischemic heart disease

LBBB, left bundle branch block; LV, left ventricular; RBBB, right bundle branch block; RV, right ventricular; RV systole and LV systole, duration of right and left ventricular contraction.

C. CLINICAL SIGNIFICANCE AND PATHOGENESIS

Table 38-1 lists the common causes of abnormal S_2 splitting.

1. Wide Physiologic Splitting

Wide physiologic splitting may result from P_2 appearing too late or A_2 too early (see Table 38-1).[17,35] The most common cause is right bundle branch block.

In pulmonic stenosis, the A_2-P_2 interval correlates well with severity of stenosis (gauged by the right ventricular systolic pressure, $r = 0.87$, $p < .001$),[38] although in many patients the clinician must listen at the third interspace to hear splitting because the murmur is too loud at the second interspace.

In most patients with pulmonary hypertension, the normal hangout interval disappears and S_2 is single. S_2 becomes wide in these patients only if there is associated severe right ventricular dysfunction and prolonged right ventricular systole.[28,29,39] Most patients with pulmonary hypertension and a wide S_2 have either long-standing severe pulmonary hypertension[28,29,39] or massive pulmonary embolism. (The wide S_2 of pulmonary embolism is temporary, usually lasting hours to days.[40])

2. Wide and Fixed Splitting

Patients with atrial septal defect have wide fixed splitting of S_2, although this is true only when their pulse is regular. (If the patient has atrial fibrillation or frequent extrasystoles, the degree of splitting varies directly with the preceding cycle length.[27,41]) The reason S_2 is wide is not the same in every

patient: In some patients, hangout is increased; in others, right ventricular mechanical systole is prolonged.[41] S_2 is fixed because hangout remains constant during respiration[41] and because the presence of a common left and right atrial chamber interrupts the normal respiratory variation of right ventricular filling.[27]

In patients with audible expiratory splitting (and regular rhythm), the *absence* of fixed splitting significantly *decreases* the probability of atrial septal defect (LR = 0.1; see EBM Box 38-1), whereas the presence of fixed splitting increases the probability of atrial septal defect only modestly (LR = 2.6; see EBM Box 38-1). Patients with false-positive results (i.e., fixed splitting without atrial septal defect) commonly have the combination of right ventricular failure and audible expiratory splitting from bundle branch block or some other cause.[17]

3. Paradoxic Splitting

In elderly adults with aortic flow murmurs, the finding of paradoxic splitting does not distinguish significant aortic stenosis from less severe disease (see EBM Box 38-1).

D. S_2 SPLITTING VERSUS OTHER DOUBLE SOUNDS[37]

Other double sounds that mimic S_2 splitting include the following (see also Chapter 40):

1. S_2-Opening Snap

In contrast to the split S_2, the S_2-opening snap interval is slightly wider, the opening snap is loudest at the apex, and the opening snap ushers in the diastolic rumble of mitral stenosis at the apex. Patients with S_2-opening snap sometimes have a triple sound (split S_2 plus opening snap) during inspiration at the upper sternal border.

2. S_2-Pericardial Knock

In contrast to the split S_2, the S_2-knock interval is slightly wider, the pericardial knock is loudest at or near the apex, and the knock is always accompanied by elevated neck veins.

3. S_2-Third Heart Sound

In contrast to the split S_2, the S_2-S_3 interval is two to three times wider, and S_3 is a low-frequency sound heard best with the bell.

4. Late Systolic Click-S_2

Clicks are loudest at or near the apex and are often multiple. Their timing changes with maneuvers (see Chapter 44).

III. INTENSITY OF S_2

Despite traditional teachings, no evidence supports a loud P_2 as a sign of pulmonary hypertension. Whether defined as an S_2 that is louder at the left side of the upper sternum compared with the right side[20] or as a split

S_2 with a louder second component,[19] the finding does not accurately discriminate patients with pulmonary hypertension from those without it (see EBM Box 38-1). Even when A_2 and P_2 are precisely identified by phonocardiography (e.g., A_2 corresponds to aortic incisura on simultaneous aortic pressure tracing), the relative intensities of the two components do not correlate well with pulmonary pressure.[42] Another suggested sign of pulmonary hypertension is audible splitting at the apex, which is based on the observation that P_2 normally is not heard at the apex[30] and the assumption that splitting at this location therefore indicates that P_2 is abnormally loud. But even this finding correlates better with the etiology of heart disease—it is common in atrial septal defect and primary pulmonary hypertension—than it does with measurements of pulmonary pressure.[39,42]

Nonetheless, the *palpable* S_2 does accurately detect pulmonary arterial pressures of 50 mm Hg or more in patients with mitral stenosis (positive LR = 3.6, negative LR = 0.05; see EBM Box 38-1). In this study, the palpable P_2 was defined as an abrupt tapping sensation coincident with S_2 at the second left intercostal space.

In patients with aortic flow murmurs, an absent or diminished S_2 increases the probability of significant aortic stenosis (LR = 3.1; see Chapter 42).

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 39

The Third and Fourth Heart Sounds

I. INTRODUCTION

Although the third and fourth heart sounds (S_3 and S_4) are both sounds that originate in the ventricle from rapid diastolic filling, they differ in timing and clinical significance. S_3 appears in early diastole, and if the patient is older than 40 years of age, the sound indicates severe systolic dysfunction or valvular regurgitation. In persons younger than 40 years of age, S_3 may be a normal finding (i.e., the "physiologic S_3").[1] S_4 appears in late diastole, immediately before S_1, indicating that the patient's ventricle is abnormally stiff from hypertrophy or fibrosis. If discovered in persons of any age, the S_4 is an abnormal finding.

In the late 19th century, the great French clinician Potain accurately described most features of S_3 and S_4, their pathogenesis, and their distinction from other double sounds such as the split S_1 or split S_2.[2] In his writings he called them *gallops*, a term he attributed to his teacher Bouillard.[2,3]

II. DEFINITIONS

Several different terms have been used to describe these diastolic sounds.

A. GALLOP

A **gallop** is a triple rhythm with an extra sound in diastole (either S_3 or S_4, or their summation). The term refers only to pathologic sounds (i.e., it excludes physiologic S_3), and despite its connotation, a patient may have a gallop whether the heart rate is fast or slow.[2,4]

B. THIRD HEART SOUND (S_3)

The third heart sound is sometimes called the **ventricular gallop** or **protodiastolic gallop.**[2] It appears in early diastole, 120 to 180 ms after S_2.[5] To mimic the sound, the clinician should first establish the cadence of the normal S_1 (*lub*) and S_2 (*dup*):

lub *dup* *lub* *dup* *lub* *dup*

and then add an early diastolic sound (*bub*)*:

lub du bub lub du bub lub du bub

The overall cadence of the S_3 gallop (*lub du bub*) is similar to the cadence of the word *Kentucky*.

C. FOURTH HEART SOUND (S_4)

The fourth heart sound is sometimes called the **atrial gallop** or **presystolic gallop**.[2] To mimic the sound, the clinician establishes the cadence of S_1 and S_2 (*lub dup*) and then adds a presystolic sound (*be*):

be lub dup be lub dup be lub dup

The cadence of S_4 gallop (*be lub dup*) is similar to the cadence of *Tennessee*.†

D. SUMMATION GALLOP

The **summation gallop** is a loud gallop that occurs in patients with tachycardia. In fast heart rhythms, diastole shortens, causing the events that produce S_3 (rapid early diastolic filling) to coincide with those producing S_4 (atrial systole). The resulting sound sometimes is louder than the patient's S_1 or S_2.

Not all gallop rhythms in patients with tachycardia are summation gallops. The only way to confirm the finding is to observe the patient after the heart rate slows. (In the past, slowing was often induced by carotid artery massage, although in elderly patients this is no longer recommended; see Chapter 15.) If slowing causes the gallop to disappear or evolve into two distinct but fainter sounds (i.e., S_3 and S_4), it was a genuine summation gallop. If the sound evolves instead into a single S_3 or single S_4, it was not a summation gallop.[4,7]

E. QUADRUPLE RHYTHM

The **quadruple rhythm** consists of S_1 and S_2 and both S_3 and S_4.[4] It is an uncommon finding, usually only evident in patients with slow heart rates. It is sometimes called the **train wheel rhythm** because the sound resembles that produced by the two pairs of wheels from adjacent train cars as they cross the coupling of a railroad track.[3,7]

be lub du bub be lub du bub be lub du bub

III. TECHNIQUE

A. LOCATION OF SOUND AND USE OF STETHOSCOPE

S_3 and S_4 are both low-frequency sounds (20 to 70 Hz), bordering on the threshold of hearing.[8] Therefore, they are best heard with the bell of the stethoscope, applied lightly to the body wall with only enough force to

*To pronounce the S_3 gallop with correct timing, the *p* of *dup* (S_2) must be dropped. In most patients, the accent is on S_2 (*lub* **du** *bub*), although in others, it falls on S_1 or S_3. The clinician can practice all three versions, always maintaining the same cadence, to become familiar with the varying sounds of S_3.

†Canadian teachers have suggested different mnemonics for the timing of S_3 and S_4: *Montreal* (pronounced MON TRE al) for S_3 and *Toronto* (tor ON to) for S4.[6]

create an air seal.[2,5] Gallops that originate in the left ventricle are best heard with the bell over the apical impulse or just medial to it. They are sometimes only audible with the patient lying in the left lateral decubitus position.[9] Gallops from the right ventricle are best heard with the bell over the left lower sternal border or, in patients with chronic lung disease, the subxiphoid area.[2,5]

B. RIGHT VS. LEFT VENTRICULAR GALLOPS

Aside from their different locations, other distinguishing features of right and left ventricular gallops are their response to respirations and association with other findings in the neck veins and precordium. Right ventricular gallops become louder during inspiration; left ventricular gallops become softer during inspiration.[10] The right ventricular S_4 may be associated with giant A waves in the neck veins and sometimes a loud presystolic jugular sound (see Chapter 34).[11] The left ventricular S_4 may be associated with a palpable presystolic movement of the apical impulse (see Chapter 36).

C. DISTINGUISHING THE S_4-S_1 SOUND FROM OTHER SOUNDS

Three combinations of heart sounds produce a double sound around S_1:

1. The S_4-S_1 sound
2. The split S_1
3. The S_1-ejection sound

The following characteristics distinguish these sounds:[10]

1. Use of the Bell

The S_4 is a low-frequency sound, best heard with the bell. Firm pressure with the bell on the skin—which tends to remove low-frequency sounds—will cause the S_4-S_1 combination to evolve into a single sound, in contrast to the split S_1 and the S_1-ejection sounds, which remain double.

2. Location

The S_4-S_1 sound is heard best at the apex, left lower sternal border, or subxiphoid area. (See the section on Location of Sound and Use of Stethoscope.) The split S_1 is loudest from the apex to the lower sternal border but sometimes is also heard well over the upper left sternal area. The aortic ejection sound is heard from the apex to the upper right sternal border. The pulmonary ejection sound is restricted to the upper left sternal area.[12]

3. Effect of Respiration

Although the S_4 may become louder (right ventricular S_4) or softer (left ventricular S_4) during inspiration, respiration does not affect the interval between S_4 and S_1. In contrast, the split S_1 interval varies with respiration in up to one-third of patients.

Expiration makes the pulmonary ejection sound louder.[12] The aortic ejection sound does not vary with respiration.[13]

4. Palpation

Only the S_4-S_1 sound is accompanied by a presystolic apical impulse (see Chapter 36). The intensity of the S_4 (i.e., by auscultation) correlates moderately with the amplitude of the presystolic impulse on apexcardiography ($r = 0.46$, $p < .01$); similarly, the palpability of the presystolic impulse correlates roughly with the amplitude of S_4 on phonocardiography ($r = 0.52$, $p < .01$).[14]

IV. PATHOGENESIS

A. NORMAL VENTRICULAR FILLING CURVES

Filling of the right and left ventricles during diastole is divided into three distinct phases (Fig. 39-1). The first phase, the rapid filling phase, begins immediately after opening of the atrioventricular valves. During this phase, blood stored in the atria rapidly empties into the ventricles. The second phase, the plateau phase (diastasis), begins at the moment the ventricles are unable to relax passively any further. Very little filling occurs during this phase. The third phase, atrial systole, begins with the atrial contraction, which expands the ventricle further just before the next S_1.

B. VENTRICULAR FILLING AND SOUND

Both S_3 and S_4 occur at those times during diastole when blood flow entering the ventricles temporarily stops, that is, the S_3 appears at the end of the rapid filling phase and the S_4 toward the peak of atrial systole (see Fig. 39-1). Sounds become audible if the blood *decelerates abruptly* enough, which transmits sufficient energy to the ventricular walls and causes them to vibrate. (An analogy is the tensing of a handkerchief between two hands: abrupt tensing produces sound, whereas slow tensing is silent.[15–21]) Two variables govern the suddenness of this deceleration and, therefore, whether or not the gallops become audible:

1. The flow rate during entry
2. The stiffness of the ventricle

The greater the flow rate, the *louder* the sound. The stiffer the ventricle, the *higher the frequency* of the sound.[22] Because gallops consist of low frequencies that are difficult to hear (about 20 to 50 Hz), anything increasing its frequency content (i.e., stiff ventricles) makes the sound more likely to be heard.

Even though S_3 and S_4 both result from rapid flow rates into stiff ventricles, the diseases causing them differ completely.

C. THIRD HEART SOUND (S_3)

The S_3 gallop appears when early diastolic filling is exaggerated, which occurs in two types of cardiac disorders: congestive heart failure and regurgitation and shunts.

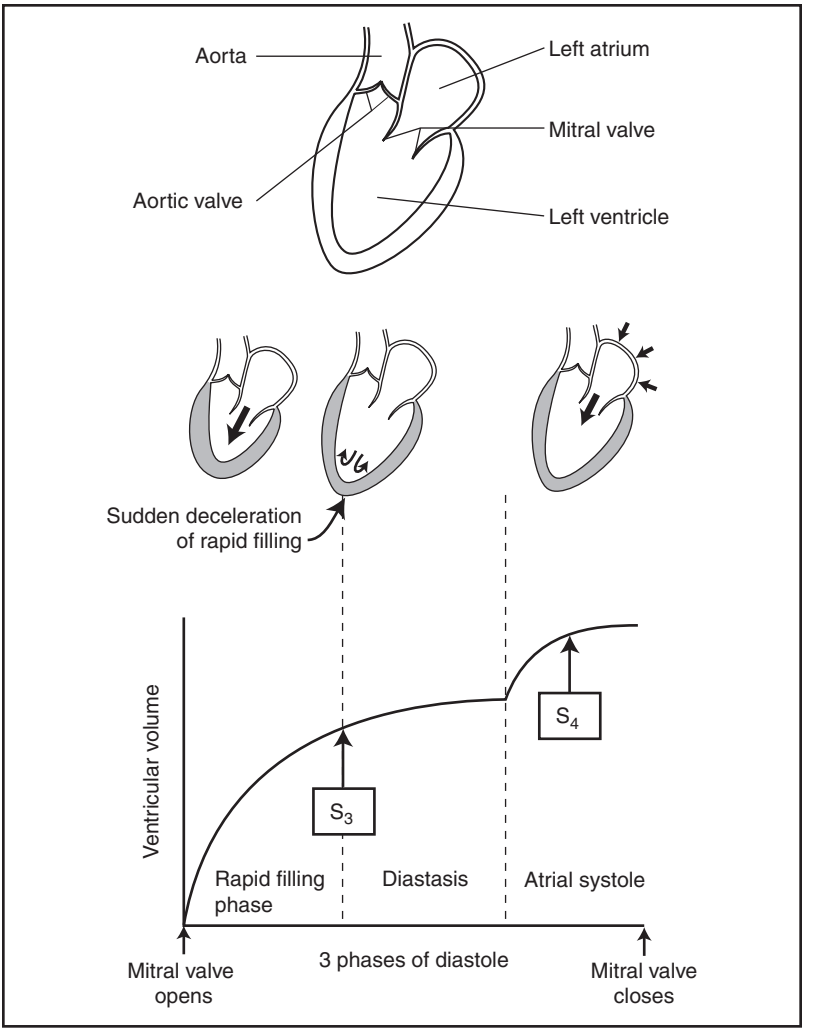


FIGURE 39-1 Timing of third and fourth heart sounds. The figure depicts the three phases of diastolic filling of the left ventricle (*y*-axis on graph, ventricular volume; *x*-axis, time). The S_3 occurs at the end of the rapid filling phase, when passive filling suddenly decelerates. The S_4 occurs during atrial systole. Similar events on the right side of the heart may produce a right ventricular S_3 or S_4. See text.

1. Congestive Heart Failure

The most common cause of the S_3 gallop is congestive heart failure from systolic dysfunction. In these patients, the S_3 indicates that atrial pressure is abnormally high, an especially important finding in patients with dyspnea, implying that heart disease is the principal cause of the shortness of breath. In addition to high atrial pressure, these patients typically have a

dilated cardiomyopathy and low cardiac output.[23,24] Although both high atrial pressure (causing rapid flow rates) and cardiomyopathy (causing stiff ventricles) contribute to the sound, atrial pressure is the more important clinical variable because the sound disappears as soon as pressure falls after diuresis.

2. Regurgitation and Shunts

Patients with valvular regurgitation or left-to-right cardiac shunts also may develop an S_3 gallop, whether or not atrial pressure is high because these disorders all cause excess flow over the atrioventricular valves. Patients with mitral regurgitation, ventricular septal defect, or patent ductus arteriosus may develop a left ventricular S_3 from excess diastolic flow over the mitral valve into the left ventricle. (In mitral regurgitation, the excess diastolic flow simply represents the diastolic return of the regurgitant flow.) Patients with atrial septal defect may develop a right ventricular S_3 from excess flow over the tricuspid valve into the right ventricle.

D. FOURTH HEART SOUND (S_4)

The S_4 gallop occurs in patients with hypertension, ischemic cardiomyopathy, hypertrophic cardiomyopathy, or aortic stenosis—all disorders characterized by ventricles stiffened from hypertrophy or fibrosis.[2,23–25] Patients with the sound must be in sinus rhythm and have strong atrial contractions, and most have normal atrial pressures, normal cardiac output, and normal ventricular chamber size. Unlike the S_3, the S_4 is a durable finding that does not wax and wane unless the patient develops atrial fibrillation (and thus loses the atrial contraction).

E. SUMMATION GALLOP AND QUADRUPLE RHYTHM

The **summation gallop** occurs because fast heart rates shorten diastole, primarily by eliminating the plateau phase (see Fig. 39-1), which brings the events causing S_3 close to those causing S_4. Diastolic filling is concentrated into a single moment, thus causing a very loud sound.

The **quadruple rhythm** typically occurs in patients who have had a long-standing S_4 gallop from ischemic or hypertensive heart disease but who then develop cardiac decompensation, high filling pressures, and an S_3.[7]

Rarely, an intermittent summation gallop may appear in patients with slow heart rates due to complete heart block (or VVI pacing).[26] The gallop appears only during those moments of atrioventricular dissociation when atrial systole and early diastole coincide (i.e., the P wave on the electrocardiogram falls just after the QRS). Although the sound is technically a summation gallop, the clinician perceives what sounds like an intermittent S_3.

F. PHYSIOLOGIC S_3

Persons younger than 40 years of age with normal hearts may also have an S_3 sound (i.e., physiologic S_3) because normal early filling can sometimes be so rapid that it ends abruptly and causes the ventricular walls to vibrate and produce sound. Compared with healthy persons lacking the sound, those

with the physiologic S_3 are leaner and have more rapid early diastolic filling.[1] The physiologic S_3 disappears by age 40 years because normal aging slows ventricular relaxation and shifts filling to later in diastole, thus diminishing the rate of early diastolic filling and making the sound disappear.[27]

V. CLINICAL SIGNIFICANCE

A. THIRD HEART SOUND

1. Congestive Heart Failure

EBM Box 39-1 shows that the presence of the S_3 gallop is a significant finding indicating depressed ejection fraction (LR = 3.4 to 4.1), elevated left atrial pressures (LR = 3.9), and elevated B-type natriuretic peptide (BNP) levels (LR = 10.1). Other studies confirm its value as a predictor of poor systolic function.[35,44] The *absence* of the S_3 gallop argues that the patient's ejection fraction is greater than 30% (i.e., negative LR for ejection fraction <30% is 0.3; see EBM Box 39-1).

In patients with a history of congestive heart failure, the S_3 predicts responsiveness to digoxin[45] and overall mortality.[46]

2. Valvular Heart Disease

In patients with mitral regurgitation, the S_3 is a poor predictor of elevated filling pressure (LR not significant) and depressed ejection fraction (LR = 1.9).[47] Some studies correlate the sound with severity of mitral regurgitation,[20] whereas others do not.[47]

In contrast, the S_3 is a helpful finding in patients with aortic valve disease. In patients with aortic stenosis, the S_3 detects both elevated filling pressures (LR = 2.3 for pulmonary capillary wedge pressures ≥12 mm Hg) and depressed ejection fraction (LR = 5.7 for ejection fraction <50%).[47] In patients with aortic regurgitation, the S_3 detects both severity of regurgitation (LR = 5.9 for regurgitant fraction ≥40%; see Chapter 43) and ejection fraction of less than 50% (LR = 8.3).[20]

3. Patients with Acute Chest Pain

In patients with acute chest pain presenting to emergency departments, the finding of an S_3 increases the probability of myocardial infarction (LR = 3.2).

4. Preoperative Consultation

During preoperative consultation, the finding of S_3 is ominous, indicating that the patient, without any other intervention, has an increased risk of perioperative pulmonary edema (LR = 14.6) and myocardial infarction or cardiac death (LR = 8).[38]

B. FOURTH HEART SOUND

The finding of the S_4 gallop has less diagnostic value, simply because the disorders causing stiff ventricles are so diverse and because the S_4 does not predict the patient's hemodynamic findings. The finding does not predict

EBM BOX 39-1
*Third and Fourth Heart Sounds**

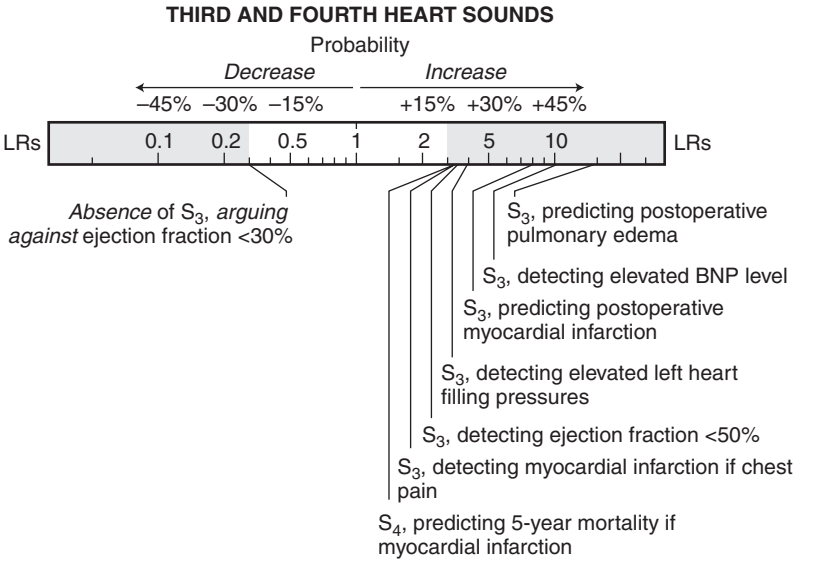
Finding (Reference)	Sensitivity (%)	Specificity (%)	Likelihood Ratio† if Finding Is	
			Present	*Absent*
Third Heart Sound				
Detecting ejection fraction <0.5[20,28–31]	11-51	85-98	**3.4**	0.7
Detecting ejection fraction <0.3[29,30]	68-78	80-88	**4.1**	**0.3**
Detecting elevated left heart filling pressures[31–34]	12-37	85-96	**3.9**	0.8
Detecting elevated BNP level[35,36]	41-65	93-97	**10.1**	0.5
Detecting myocardial infarction in patients with acute chest pain[37]	16	95	**3.2**	NS
Predicting postoperative pulmonary edema[38,39]	17	99	**14.6**	NS
Predicting postoperative myocardial infarction or cardiac death[38,39]	11	99	**8.0**	NS
Fourth Heart Sound				
Predicting 5-year mortality rate in patients after myocardial infarction[40]	29	91	**3.2**	NS
Detecting elevated left heart filling pressures[33,41]	35-71	50-70	NS	NS
Detecting severe aortic stenosis[42,43]	29-50	57-63	NS	NS

*Diagnostic standards: For *ejection fraction*, left ventricular ejection fraction <0.5 or <0.3 (as indicated above) by scintigraphy or echocardiogram (see Chapter 46); for *elevated left heart filling pressures*, pulmonary capillary wedge pressure >12 mm Hg[32] or left ventricular end-diastolic pressure >15 mm Hg[31,33,34,41]; for *elevated BNP level*, ≥100 pg/mL[35] or >1525 pg/mL[36]; for *myocardial infarction*, development of new electrocardiographic Q waves or elevations of CK-MB, or both; for *severe aortic stenosis*, peak gradient >50 mm Hg[42] or valve area <0.75 cm^2.[43]

†Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

BNP, B-type natriuretic peptide; NS, not significant.

Click here to access calculator.



the ejection fraction, left heart filling pressures, or postoperative cardiac complications.[23,24,33,38,39] It also does not predict significant aortic stenosis in elderly patients with aortic flow murmurs, presumably because many patients with mild stenosis have the finding for other reasons, such as ischemic heart disease.[42,43]

When S_4 is detected 1 month after myocardial infarction, it is, nonetheless, a modest predictor of the 5-year cardiac mortality rate (LR = 3.2; see EBM Box 39-1). Experienced auscultators in the past did show that clinical deterioration in patients with ischemic disease caused the S_4-S_1 interval to widen, which could be recognized at the bedside, but proper interpretation of this finding required knowledge of the patient's PR interval, thus limiting its utility.[48] In patients with chaotic heart rhythms, the finding of an S_4 excludes atrial fibrillation and suggests other diagnoses such as multifocal atrial tachycardia.

The S_4 is rare in patients with chronic mitral regurgitation because the dilated atrium of these patients cannot contract strongly. Finding an S_4 gallop in a patient with mitral regurgitation is therefore an important clue to the diagnosis of *acute* mitral regurgitation (e.g., ruptured chorda tendinea; see Chapter 44).[49–51]

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 40

Miscellaneous Heart Sounds

In addition to the first, second, third, and fourth heart sounds, several other discrete, short sounds may occur (Fig. 40-1). These sounds include early systolic sounds (e.g., the aortic or pulmonary ejection sound), midsystolic or late systolic sounds (e.g., the systolic click of mitral valve prolapse), early diastolic sounds (e.g., the opening snap of mitral stenosis, pericardial knock of constrictive pericarditis, and tumor plop of atrial myxoma), and prosthetic valve sounds. All are high-frequency sounds best heard with the diaphragm of the stethoscope.

EJECTION SOUNDS

I. THE FINDING AND PATHOGENESIS

The ejection sound is the most common early systolic sound. It results from abnormal sudden halting of the semilunar cusps as they open during early systole.[2,3] Patients with aortic ejection sounds typically have aortic stenosis, bicuspid aortic valves, or a dilated aortic root.[2,3] Those with pulmonary ejection sounds have pulmonary stenosis, pulmonary hypertension, or a dilated pulmonary trunk.[3,4]

Aortic and pulmonary ejection sounds are distinguished by their location, associated murmurs, and ways in which they vary during respiration. An aortic ejection sound is a loud high-frequency sound (often louder than S_1) best heard at the apex, although commonly also audible at the upper right sternal border.[5] It does not vary with respiration. Pulmonary ejection sounds are confined to the sternal edge at the second or third intercostal space; they often diminish in intensity during inspiration. Ejection sounds associated with aortic or pulmonic stenosis occur immediately before the onset of the systolic murmur.[5,6]

Chapter 39 describes how to distinguish ejection sounds from other double sounds around S_1, including the combination of S_4-S_1 and the split S_1.

II. CLINICAL SIGNIFICANCE

The primary importance of these sounds is their etiologic associations. In patients with aortic stenosis, the ejection sound implies that the stenosis is at the valvular level and that there is some mobility to the valve. Elderly patients with calcific aortic stenosis usually do not have ejection sounds, because the calcific degeneration makes the valve leaflets inflexible. Children with noncalcific aortic stenosis, in contrast, usually have the

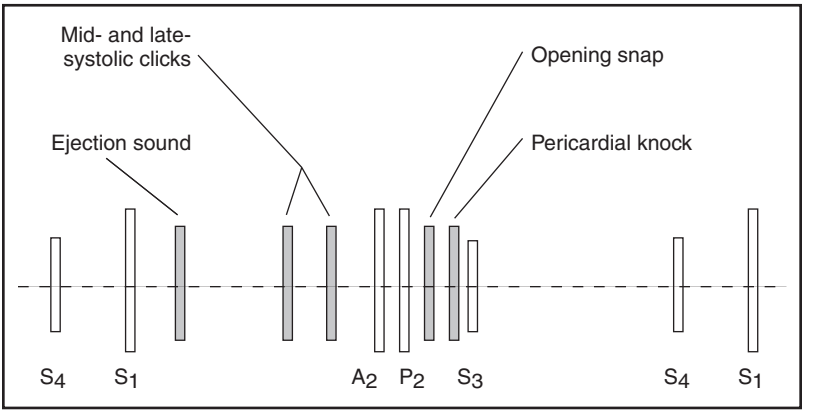


FIGURE 40-1 Miscellaneous heart sounds. The figure shows the timing of the miscellaneous systolic sounds (ejection sounds and midsystolic to late systolic clicks) and diastolic sounds (opening snap and pericardial knock), in relation to the principal heart sounds (first, second, third, and fourth heart sounds). The tumor plop of atrial myxoma, not depicted in the figure, has variable timing, ranging from 80 ms after A_2 (i.e., timing of the opening snap) to 150 ms after A_2 (i.e., timing of the third heart sound).[1]

ejection sound. In one consecutive series of 118 patients with aortic stenosis, the ejection sound was audible in 100% of patients with noncalcific valvular stenosis, in 32% with calcific valvular stenosis, and in none with subvalvular or supravalvular stenosis.[5]

MIDSYSTOLIC TO LATE SYSTOLIC CLICKS

I. THE FINDING AND PATHOGENESIS

Midsystolic to late systolic clicks occur in patients with mitral valve prolapse. These sounds, which are sometimes multiple, are caused by sudden deceleration of the billowing mitral leaflet as it prolapses backward into the left atrium during systole.[7] The click is loudest at the apex or left lower sternal border and is frequently associated with a late systolic murmur.[8]

The hallmark of the click of mitral valve prolapse (and also of the associated murmur) is that its timing shifts during maneuvers that change venous return. For example, the straining phase of the Valsalva maneuver or the squat-to-stand maneuver, both of which decrease venous return, cause the mitral leaflets to prolapse earlier in systole, thus shifting the click (and murmur) closer to S_1 (see Fig. 44-1 in Chapter 44).[8,9]

Clicks have been heard by clinicians for over a century, although they were ascribed to pleuropericardial adhesions or other extracardiac causes[10] until the 1960s, when Barlow demonstrated that the sound coincided with systolic prolapse of the posterior mitral leaflet.[11]

II. CLINICAL SIGNIFICANCE

The presence of the characteristic click or murmur alone is sufficient grounds for the diagnosis of mitral valve prolapse.[12,13] Chapter 44 discusses these findings further.

OPENING SNAP

I. THE FINDING AND PATHOGENESIS

The opening snap is an early diastolic sound heard in patients with mitral stenosis.* The sound occurs because the stenotic mitral leaflets (although fused, they are mobile) billow like a large sail into the ventricle during early diastole but then abruptly decelerate as they meet the limits of movement.[2,7] The abrupt deceleration causes a loud, medium-frequency to high-frequency sound, which is then followed by the mid-diastolic rumbling murmur of mitral stenosis. The opening snap is best heard between the apex and left lower sternal border.

The clinician can mimic the sound of snap and murmur together by first setting up the cadence of S_1, S_2, and opening snap (RUP = S_1; bu = S_2; DUP = opening snap):

RU**P** bu **DUP** R**U**P bu **DUP** R**U**P bu **DUP**

and then adding the murmur:

RU**P** bu **DUP**RRRRRRRR**U**P bu **DUP**RRRRRRRR**U**P bu **DUP**

In some patients, the opening snap is so loud it is easily heard at the second left intercostal space, where it then mimics a widely split S_2. Careful attention to inspiration in these patients, however, may reveal a *triple* sound (split S_2 and opening snap) at this location, confirming the last sound to be the opening snap.

The opening snap of mitral stenosis was first described by Bouillard in 1835.[2]

II. CLINICAL SIGNIFICANCE

According to traditional teachings, the opening snap is inaudible in patients with mitral stenosis whose valve leaflets have become so thickened and inflexible they cannot create sound.[7,14] There is an inverse correlation between the opening snap amplitude and degree of calcification of the mitral valve ($r = -0.675$, $p < .01$).[15]

The interval between the A_2 component of S_2 and the opening snap (A_2-OS interval) has been used to gauge the severity of mitral stenosis. Patients with more severe obstruction tend to have a narrower A_2-OS interval than

*Patients with tricuspid stenosis also may have an opening snap, but all of these patients also have mitral stenosis and the mitral opening snap. Differentiating tricuspid and mitral opening snaps by auscultation alone is difficult.

those with milder disease. This occurs because the mitral valve opens when the pressure in the relaxing ventricle falls below the atrial pressure; the more severe the obstruction, the higher the atrial pressure and the sooner this crossover occurs. Nonetheless, determining the A_2-OS interval is primarily a phonocardiographic exercise, not an auscultatory one.[16] Furthermore, the A_2-OS interval also depends on variables other than severity of stenosis, such as ventricular relaxation time and heart rate, further complicating the accurate interpretation of the interval at the bedside.[16]

The opening snap does indicate that the accompanying diastolic murmur represents mitral stenosis and not a flow rumble from increased flow over a nonstenotic valve. (See Chapter 44 for discussion of flow rumbles.)

PERICARDIAL KNOCK

The pericardial knock is a loud early diastolic sound heard in 28% to 94% of patients with constrictive pericarditis (see Chapter 45).[17–19] It is heard over a wide area between the apex and the left lower sternal border. Compared with the third heart sound, the pericardial knock is a higher-frequency sound (easily detected with the diaphragm of the stethoscope), appears over a wider area of the precordium, and occurs slightly earlier (although still later than the opening snap or widely split second heart sound).[18]

The pericardial knock results from the sudden deceleration of the filling ventricle as it meets the borders of the rigid pericardial sac.[18,19] In this way, it is similar to the third heart sound, although the more abrupt deceleration of constriction is what probably makes the pericardial knock higher-pitched and louder than the third heart sound (see Chapter 39).

TUMOR PLOP

The tumor plop is an early diastolic sound representing prolapse of the pedunculated tumor from the atrium over the mitral (or tricuspid) valve into the ventricle. In two large series of patients with myxoma (283 patients), it was detected in 15% to 50% of patients.[20,21] Characteristically, the intensity and timing of the tumor plop vary between examinations: The plop may occur as early as the timing of an opening snap or as late as that of the third heart sound. It is often associated with a diastolic murmur that mimics the rumbling murmur of mitral stenosis.[20]

PROSTHETIC HEART SOUNDS

I. INTRODUCTION

Abnormal prosthetic heart sounds may be the only clue explaining the patient's dyspnea, syncope, or chest pain. To recognize these abnormal sounds simply and quickly, the clinician must first understand the normal prosthetic heart sounds. This section focuses on rigid mechanical valves, such as caged-ball (Starr-Edwards) valves, single tilting-disc (Bjork-Shiley, Medtronic-Hall) valves, and bileaflet tilting-disc (St. Jude Medical) valves.[22–24]

II. PRINCIPLES

The important observations are

1. Timing and intensity of opening and closing sounds, which typically have a clicking or metallic quality and are often audible without a stethoscope
2. Associated murmurs

Any new or changing sound or murmur requires investigation.

A. OPENING AND CLOSING SOUNDS

In patients with caged-ball valves, the opening sound is louder than the closing sound. In patients with tilting-disc valves (both single-disc and bileaflet valves), the closing sounds are loud and the opening sounds are only faint or inaudible (Fig. 40-2).

1. Caged-Ball Valves

In the aortic position, the caged-ball valve produces a loud opening sound, which is an extra systolic sound occurring just after S_1 with timing identical to the aortic ejection sound (i.e., instead of just S_1 and S_2, *lub dup…lub dup*, the clinician hears *le**dup** dup…le**dup** dup*). Caged-ball valves in the mitral position produce an extra diastolic sound when they open, with timing identical to that of the opening snap (i.e., instead of S_1 and S_2, *lub bup… lub bup*, it is *lub bu**dup**…lub bu**dup***). These opening sounds should always

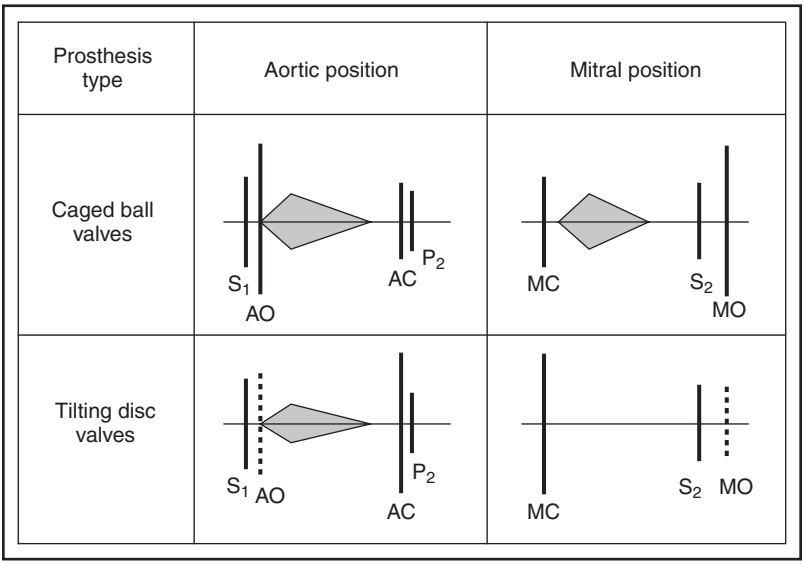


FIGURE 40-2 Prosthetic valve sounds. The normal findings of prosthetic valves, based on references 22 to 24. *AC*, Closure sound of aortic prosthesis; *AO*, opening sound of aortic prosthesis; *MC*, closure sound of mitral prosthesis; *MO*, opening sound of mitral prosthesis; P_2, pulmonary component of second heart sound; S_1, first heart sound; S_2, second heart sound. See text.

be louder than the corresponding closing sound (i.e., closing sounds are coincident with S_2 in aortic prostheses and with S_1 in mitral prostheses). The finding of an inaudible or abnormally soft opening sound indicates something is interfering with excursion of the ball, such as a thrombus.

2. Tilting-Disc Valves

These valves produce distinct, metallic closing sounds coincident with S_1 (mitral position) or S_2 (aortic position). Patients whose closing sounds are abnormally quiet may have significant valve dysfunction.

B. MURMURS

In the aortic position, all rigid valves (caged-ball and tilting-disc) typically produce short midsystolic murmurs that are best heard at the base and sometimes radiate to the neck. Diastolic murmurs in these patients suggest perivalvular regurgitation and require investigation.[22–24]

In patients with rigid valves in the mitral position, any holosystolic murmur suggests perivalvular regurgitation and requires investigation. A normal finding in patients with a caged-ball valve in the mitral position (but not a tilting-disc valve) is an early systolic to midsystolic murmur at the left sternal border. This murmur does not indicate regurgitation but instead represents turbulence caused by the cage of the valve projecting into the left ventricular outflow tract.[22,24]

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 41

Heart Murmurs: General Principles

I. INTRODUCTION

Over the last 180 years, the understanding of heart murmurs has evolved in three distinct stages.[1] In the first stage, brilliant clinicians—James Hope (1801-1841), Austin Flint (1812-1886), and Graham Steell (1851-1942)—attentively observed patients at the bedside and correlated the timing and quality of murmurs to the patients' clinical course and postmortem findings.[2] In the second stage, during the 1950s and 1960s, cardiac catheterization and phonocardiography helped clinicians understand the hemodynamics responsible for heart murmurs,[3–5] and the introduction of cardiac surgery increased the stakes of cardiac auscultation, stimulating clinicians to be as precise and accurate as possible. Finally, in the 1970s and 1980s, the introduction of echocardiography solved many of the remaining mysteries about murmurs, including the cause of ejection sounds in aortic stenosis and late systolic murmurs and clicks in mitral valve prolapse.

This chapter discusses the principles of describing and diagnosing murmurs. Specific cardiac disorders and their associated murmurs are further discussed in Chapters 42 to 44.

II. THE FINDINGS

The important characteristics of heart murmurs are location (both the location at which they are loudest and the direction in which their sound travels, or *radiates*), timing, intensity, and frequency (or *pitch*, which is high-frequency, low-frequency, or a mixture of high and low frequencies).[6] The terms *rough*, *rumbling*, *blowing*, *coarse*, and *musical* are also sometimes used to describe the specific tonal quality of murmurs.

Murmurs frequently vary in intensity during the respiratory cycle, but loud "murmurs" that completely disappear during one phase of the respiratory cycle (inspiration or expiration) are likely pericardial rubs, not murmurs.[7]

A. BASIC CLASSIFICATION OF MURMURS

Murmurs are broadly classified as systolic, diastolic, and continuous (Table 41-1).[6] **Systolic murmurs** occur during the time between S_1 and S_2; **diastolic murmurs** occur at any time from S_2 to the next S_1. **Continuous**

TABLE 41-1 Classification of Murmurs by Timing and Location

Type of Murmur	Location Where Loudest
SYSTOLIC MURMURS	
Abnormal Flow Over Outflow Tract or Semilunar Valve	
Aortic stenosis	R base, LLSB, and apex
Pulmonic stenosis	L base
Atrial septal defect*	L base
Hypertrophic cardiomyopathy with obstruction	LLSB
Regurgitation from High-Pressure Chamber into Low-Pressure Chamber	
Mitral regurgitation	Apex
Tricuspid regurgitation	LLSB
Ventricular septal defect	LLSB
DIASTOLIC MURMURS	
Backward Flow across Leaking Semilunar Valve	
Aortic regurgitation	LLSB
Pulmonary regurgitation	L base
Abnormal Forward Flow over an Atrioventricular Valve	
Mitral stenosis	Apex
Tricuspid stenosis	LLSB
CONTINUOUS MURMURS	
Abnormal Connections between Artery and Vein	
Patent ductus arteriosus	L base
Arteriovenous fistula	Over fistula
Abnormal Flow in Veins	
Venous hum	Above head of clavicle
Mammary soufflé†	Between breast and sternum
Stenosis in Peripheral Artery	
Coarctation of the aorta	Over back

*The murmur of atrial septal defect is due to excess flow of blood over the pulmonary valve (from left-to-right shunting), not from flow through the defect itself.
†*Souffle* (Fr. sound or murmur) is pronounced *SOO-ful*.
Apex, point of apical impulse; L base, second left intercostal space next to sternum; LLSB, fourth and fifth left intercostal spaces next to sternum; R base, second right intercostal space next to sternum.

murmurs begin in systole but extend beyond S_2 into diastole, indicating they do not respect the confines of systole and diastole and thus arise *outside* the four heart chambers. Despite the name, continuous murmurs do not necessarily occupy all of systole and diastole.

1. Systolic Murmurs

a. Etiology

There are two causes of systolic murmurs.

(1) Abnormal Flow over an Outflow Tract or Semilunar Valve. One cause is abnormal flow over an outflow tract or semilunar valve (i.e., aortic or pulmonary valve), such as

1. Forward flow across an obstruction (e.g., aortic stenosis, pulmonic stenosis, or hypertrophic cardiomyopathy)
2. Increased flow across a normal semilunar valve (e.g., atrial septal defect or the flow murmurs of anemia, fever, pregnancy, or thyrotoxicosis)

(2) Regurgitation from a Ventricle into a Low Pressure Chamber. Examples are mitral regurgitation (leak between left ventricle and left atrium), tricuspid regurgitation (leak between right ventricle and right atrium), and ventricular septal defect (leak between left and right ventricles).

b. Older Classifications of Systolic Murmurs: "Ejection" and "Regurgitation" Murmurs

In 1958, Leatham divided all systolic murmurs into "ejection murmurs" and "regurgitant murmurs," based entirely on their relationship to S_2.[3,4] According to his classification, ejection murmurs begin after S_1, have a crescendo-decrescendo shape, and always end before S_2.* Ejection murmurs represent abnormal flow across the aortic or pulmonic valve. In contrast, regurgitant murmurs (e.g., mitral and tricuspid regurgitation) begin with S_1, have a plateau shape, and extend up to S_2 or even slightly past it (thus obliterating S_2).

Leatham's classification is no longer widely used for several reasons:

1. It relies entirely on phonocardiography and does not always correspond to what clinicians hear at the bedside.[8]
2. It depends entirely on the audibility of the aortic and pulmonary components of S_2, sounds that sometimes are inaudible.
3. It assumes that all ejection murmurs result from ejection over a semilunar valve, although experience has shown that many are due to regurgitant lesions.
4. Its fundamental premise, that the intensity of a murmur depends on pressure gradients, is not always true (e.g., the murmur of mitral valve prolapse is loudest during late systole, when gradients are decreasing).

Instead, systolic murmurs are more easily classified using onomatopoeia as midsystolic, early systolic, long systolic, holosystolic, and late systolic, based on whether the murmur obscures S_1 or S_2 or both sounds. (See the section on Timing and Quality of Murmurs Using Onomatopoeia.[1])

2. Diastolic Murmurs

There are two causes of diastolic murmurs.

1. Abnormal backward flow across a leaking semilunar valve (e.g., aortic or pulmonic regurgitation)

*More precisely, ejection murmurs end before the S_2 component belonging to the side of the heart generating the murmur. For example, the murmur of aortic stenosis ends before A_2; the murmur of pulmonic stenosis ends before P_2.

2. Abnormal forward flow across an atrioventricular valve (e.g., mitral stenosis, tricuspid stenosis, and flow rumbles*)

3. Continuous Murmurs

Continuous murmurs result from the following:

1. Abnormal connections between the aorta and pulmonary trunk (e.g., patent ductus arteriosus)
2. Abnormal connections between arteries and veins (e.g., arteriovenous fistulas) (see Chapter 52)
3. Abnormal flow in veins (e.g., venous hum and mammary souffle)
4. Abnormal flow in arteries (e.g., coarctation of the aorta, renal artery stenosis)

B. LOCATION ON THE CHEST WALL

The usual locations of conventional murmurs are described in Table 41-1. Nonetheless, in patients with systolic murmurs, one of the most helpful diagnostic signs is the distribution of the sound on the chest wall with reference to the third left parasternal space, a landmark that lies directly over both the aortic and mitral valves and distinguishes systolic murmurs into one of six possible patterns:

1. Broad apical-base pattern
2. Small apical-base pattern
3. Left lower sternal pattern
4. Broad apical pattern
5. Isolated apical pattern
6. Isolated base pattern (definitions of these patterns appear in Fig. 41-1)[7]

Inspection of the boundary surrounding all six patterns suggests that the primary determinant of a murmur's radiation is not necessarily the direction of blood flow but instead the orientation of the bony thorax, specifically the left lower ribs, sternum, and clavicles (Fig. 41-2). Increased flow across a semilunar valve or through a regurgitant leak generates vibrations in the ventricles or great arteries, or both, which—depending on their location, amplitude, and ease of conduction to the bones of the body wall—produce one of the six different murmur patterns. In fact, one of the best arguments that bone conduction—and not direction of blood flow—governs distribution of sound is the murmur of mitral regurgitation: In this lesion, blood flows from the left ventricle *rightward* and *upward* to the left atrium, yet the murmur radiates almost perpendicular to this, along the left lower ribs to the axilla.[7]

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*__Flow rumbles__ are short, low-frequency diastolic murmurs that result from increased flow over a nonobstructed atrioventricular valve. Atrial septal defects and tricuspid regurgitation increase diastolic flow over the tricuspid valve and may cause tricuspid flow rumbles (which resemble the murmur of tricuspid stenosis). Mitral regurgitation and ventricular septal defect increase diastolic flow over the mitral valve and may produce mitral flow rumbles (which resemble the murmur of mitral stenosis).

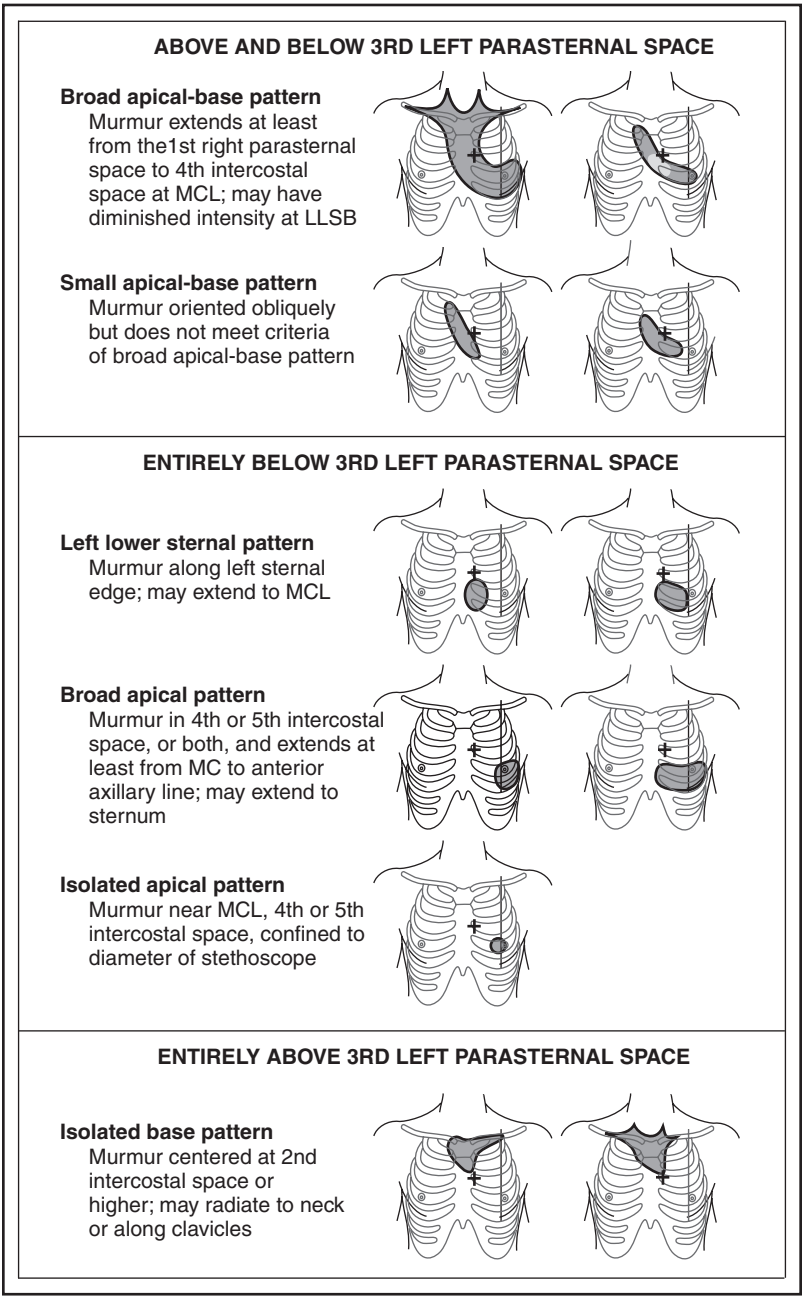

FIGURE 41-1 Six systolic murmur patterns. Each of the six topographic patterns is distinguished by its distribution with reference to the third left parasternal space (indicated by a + symbol in each drawing). This landmark is easily identified by first identifying the sternal angle, where the second rib articulates, and then counting down to the second intercostal space, third rib, and then the third parasternal space. Two of the patterns lie above *and* below this landmark (broad apical-base and small apical-base patterns); three are confined below this landmark (left lower sternal, broad apical, and isolated apical patterns); and one is confined entirely above the landmark (isolated base pattern). ICS, intercostal space; LLSB, left lower sternal border; MCL, midclavicular line. *(Adapted from McGee.[7])*

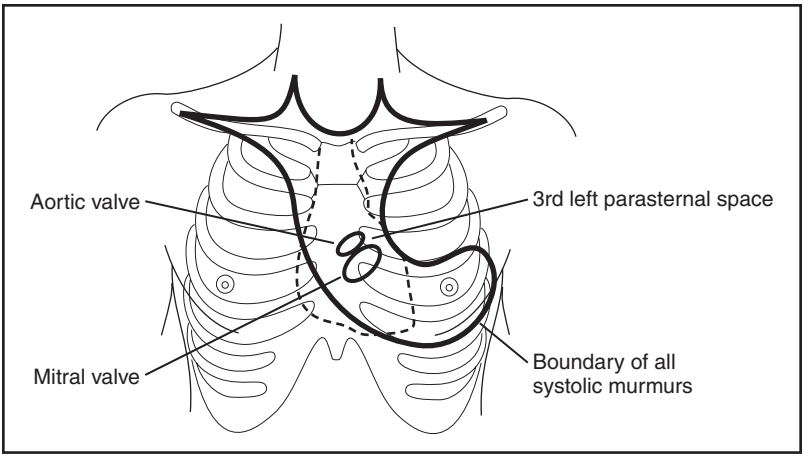

FIGURE 41-2 Boundary of systolic murmur patterns. The third left parasternal space overlies both the aortic and mitral valves. If the ventricles vibrate sufficiently to produce sound, murmurs are generated below this landmark. Vibrations of the right ventricle produce the left lower sternal pattern, whereas those of the left ventricle produce the isolated apical pattern or broad apical pattern. Should the great arteries vibrate sufficiently to make sound, the bones above this landmark vibrate and murmurs radiate from the upper sternum to the clavicles and neck (isolated base pattern). With increased velocity across the aortic valve, both the left ventricle (lower ribs) and great arteries (upper sternum and clavicles) vibrate, causing the apical-base pattern and its variations. *(Adapted from McGee.[7])*

The diagnostic significance of these six systolic murmur patterns is discussed in the section on Differential Diagnosis of Systolic Murmurs.

C. SPECIFIC TIMING AND QUALITY OF MURMURS USING ONOMATOPOEIA

Figure 41-3 presents traditional diagrams of various heart murmurs, which in turn are based on phonocardiographic tracings. Because murmurs are sounds, however, diagrams such as these often fail to convey the precise cadences and tonal qualities that distinguish murmurs. Throughout the history of cardiac auscultation, clinicians have used onomatopoeia to mimic heart sounds and murmurs, finding this to be an effective teaching tool allowing clinicians to rapidly recognize the patterns of different sounds.[2,9,10]

The system described here is based on the published work of Feinstein[11] and Adolph.[12–15] High-frequency murmurs are mimicked by sounds from the front of the mouth; low-frequency murmurs are mimicked by sounds from the back of the throat. The high-frequency murmur of mitral and tricuspid regurgitation is mimicked by saying *SHSHSHSH*. The high-frequency murmur of aortic regurgitation is mimicked by blowing air out through slightly pursed lips or by whispering *PHEWEWEWEWEW* or *AHAHAHAHAH* (hence, the "blowing" descriptor). The low-frequency murmurs of tricuspid or mitral stenosis are mimicked by the *RRRRR* portion of a growl (hence, the "rumbling" descriptor). Murmurs containing a mixture of low and high frequencies, such as aortic stenosis, are mimicked

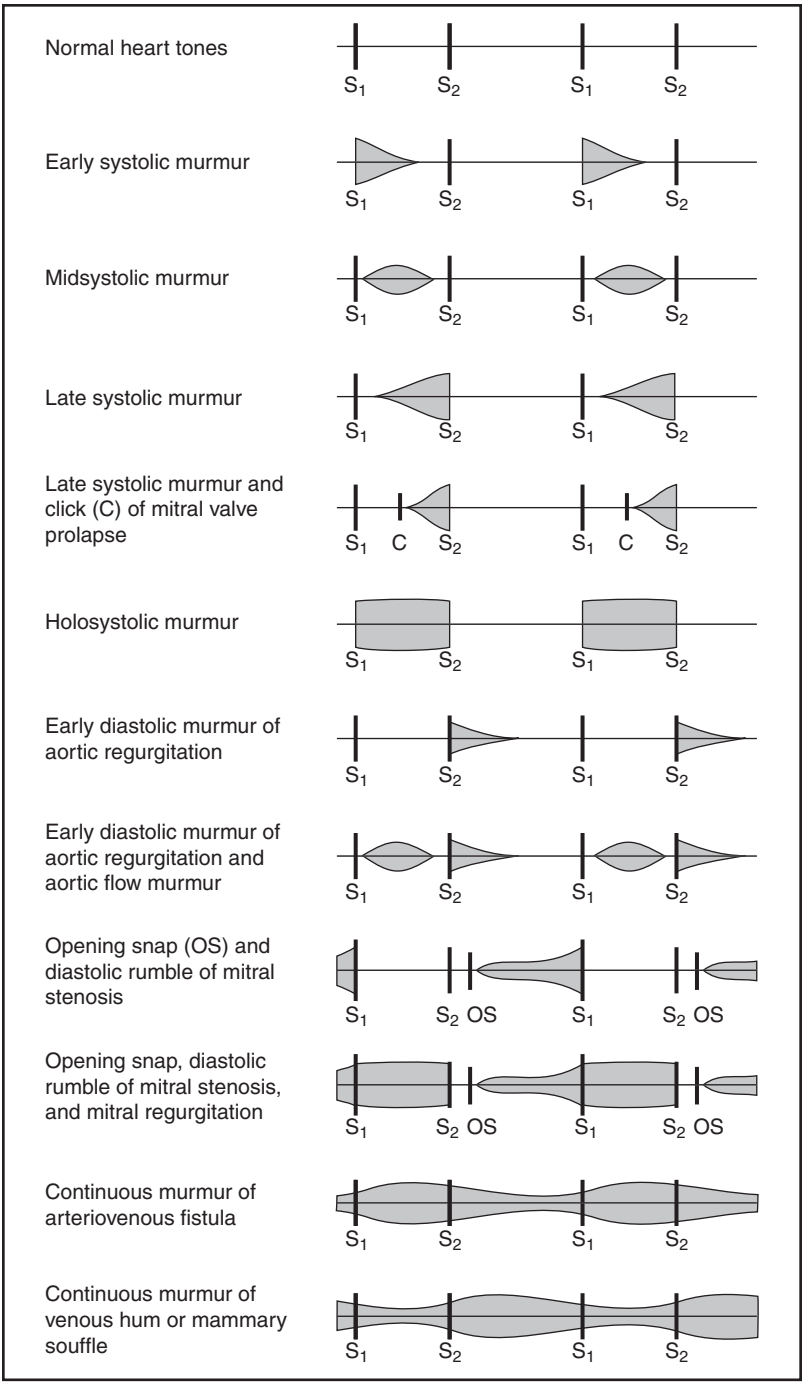

FIGURE 41-3 **Diagrams of various murmurs.**

TABLE 41-2 Using Onomatopoeia to Identify Systolic Murmur Timing

Onomatopoeia	Definition	Timing of Murmur
Lub shsh dup	Both S_1 (lub) and S_2 (dup) distinct	Midsystolic
Shshsh dup *Pushsh dup*	S_1 indistinct, S_2 distinct; gap before S_2	Early systolic
Shshshshdup *Pushshshdup*	S_1 indistinct, S_2 distinct; no gap before S_2	Long systolic
Shshshshshsh *ShshshshshshP* *Pushshshshsh* *PushshshshshP*	S_1 and S_2 indistinct	Holosystolic
Lub shshshP	S_1 distinct, S_2 indistinct	Late systolic

Adapted from reference 7.

by the sound made when clearing the throat. (Common descriptors are "coarse" and "harsh.")

The clinician should first establish the normal cadence of S_1 and S_2 (*lub* is S_1 and *dup* is S_2):

lub dup lub dup lub dup

The clinician should then add the murmur at the appropriate time. For example, the high-frequency late systolic murmur of mitral valve prolapse preserves S_1 but obscures S_2 (i.e., *dup* is replaced by *SHSHP*):

lub SHSHP lub SHSHP lub SHSHP

Table 41-2 describes how to label the timing of systolic murmurs, and Figure 41-4 shows how onomatopoeia can mimic many common murmurs.

By using onomatopoeia, clinicians can quickly learn the cadences of murmurs, and this knowledge sometimes leads to rapid recognition of complicated sounds without first having to sort out the locations of S_1 and S_2. For example, if auscultation reveals a cadence consisting of a single murmur and no heart sounds

SHSHSHSH SHSHSHSH SHSHSHSH

the only possible diagnosis is a holosystolic murmur.

If auscultation reveals murmurs in both systole and diastole, there are three possible causes:

1. A true continuous murmur
2. A to-fro murmur
3. Combined mitral stenosis and regurgitation

In **true continuous murmurs,** the cadence is uninterrupted by the cardiac cycles *(SHSHSHSHSHSHSHSH)*. **To-fro murmurs** consist of two high-frequency murmurs, one in systole and another in diastole *(SHSHSHP PHEWEWEWEWEW)*. To-fro murmurs result from isolated severe aortic regurgitation (the diastolic component representing aortic regurgitation and the systolic one representing increased systolic flow over the aortic valve) or aortic regurgitation combined with another

Normal heart tones	**Lub** **Dup** S_1 S_2	**Lub** **Dup** S_1 S_2
Early systolic murmur	**L**SHSHSH **Dup** S_1 S_2	**L**SHSHSH **Dup** S_1 S_2
Midsystolic murmur	**Lub** SHSH **Dup** S_1 S_2	**Lub** SHSH **Dup** S_1 S_2
Late systolic murmur	**Lub** SHSH**P** S_1 S_2	**Lub** SHSH**P** S_1 S_2
Late systolic murmur and click (C) of mitral valve prolapse	**Lub** **K**SHSH**P** S_1 C S_2	**Lub** **K**SHSH**P** S_1 C S_2
Holosystolic murmur	SHSHSHSHSH S_1 S_2	SHSHSHSHSH S_1 S_2
Early diastolic murmur of aortic regurgitation	**Lub** **P**EWWWww S_1 S_2	**Lub** **P**EWWWww S_1 S_2
Early diastolic murmur of aortic regurgitation and aortic flow murmur	**Lub** SHSH **P**EWWWww S_1 S_2	**Lub** SHSH **P**EWWWww S_1 S_2
Opening snap (OS) and diastolic rumble of mitral stenosis	RU**P** bu **DUP**RRRRRRU**P** S_1 S_2 OS	bu **DUP**RRRRRRU**P** S_1 S_2 OS
Opening snap, diastolic rumble of mitral stenosis, and mitral regurgitation	RU**P**SHSHSHS**P** **DUP**RRRRRRU**P**SHSHSHS**P** S_1 S_2 OS	**DUP**RRRRRRU**P** S_1 S_2 OS
Continuous murmur of arteriovenous fistula	**Pu**SHSHSH**P**u**S**HSHSHSHSH S_1 S_2	**Pu**SHSHSH**P**u**S**HSHSHSHSH S_1 S_2
Continuous murmur of venous hum or mammary souffle	**Pu**SHSHSHS**Pu**SHSH**S**HSHSH S_1 S_2	**Pu**SHSHSHS**Pu**SHSH**S**HSHSH S_1 S_2

FIGURE 41-4 **Murmurs and onomatopoeia.**

systolic murmur, such as aortic stenosis, mitral regurgitation, or ventricular septal defect. In **combined mitral stenosis and regurgitation,** a high-frequency murmur is combined with a low-frequency one (PUSHSHSHSHP DUPRRRRRRRRUP).

D. GRADING THE INTENSITY OF MURMURS

The intensity of murmurs is graded on a scale of 1 to 6, based on the work of Freeman and Levine, which was later modified by Constant and Lippschutz. (Their work is now collectively referred to as the **Levine grading system**.[16–18]) Although this system was devised for systolic murmurs, it is often applied to all murmurs.

The six categories are the following;

1. **Grade 1 murmurs** are so faint they can be heard only with special effort.
2. **Grade 2 murmurs** can be recognized readily after placing the stethoscope on the chest wall.
3. **Grade 3 murmurs** are very loud. (Murmurs of Grades 1 through 3 all lack thrills, which are palpable vibrations on the body wall resembling the purr of a cat. Murmurs of grades 4 through 6 have associated thrills.)
4. **Grade 4 murmurs** are very loud, although the stethoscope must be in complete contact with the skin to hear them.
5. **Grade 5 murmurs** are very loud and still audible if only the edge of the stethoscope is in contact with the skin; they are not audible after complete removal of the stethoscope from the chest wall.
6. **Grade 6 murmurs** are exceptionally loud and audible even when the stethoscope is just removed from the chest wall.

III. CLINICAL SIGNIFICANCE

A. DETECTING VALVULAR HEART DISEASE

In EBM Box 41-1, a *characteristic murmur* refers to the expected murmur of the specific lesion (as described in Table 41-1 and Chapters 42 to 44). For example, in the detection of aortic regurgitation, a characteristic murmur refers to an early diastolic, high-frequency murmur along the lower sternal border, not just any diastolic murmur. In these studies, trivial regurgitation (a common finding at echocardiography of no clinical significance) was classified as "no regurgitation" (i.e., "no disease").

For five of the lesions in EBM Box 41-1, the finding of the characteristic murmur is a conclusive argument that that lesion is present: tricuspid regurgitation (likelihood ratio [LR] = 14.6; see EBM Box 41-1), ventricular septal defect (LR = 24.9), mitral valve prolapse (LR = 12.1), aortic regurgitation (LR = 9.9), and pulmonary regurgitation (LR = 17.4). For two murmurs, aortic stenosis and mitral regurgitation, the positive LRs are less compelling (LRs = 5.4 to 5.9), primarily because these two murmurs may be confused with each other and other systolic murmurs. (See the section on Differential Diagnosis of Systolic Murmur.)

EBM BOX 41-1
*Murmurs and Valvular Heart Disease**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Functional Murmur				
Detecting normal findings on echocardiography[19,20]	67-98	70-91	**4.7**	NS
Characteristic Systolic Murmur				
Detecting mild or worse aortic stenosis[7]	90	85	**5.9**	**0.1**
Detecting severe aortic stenosis[7,21]	96-98	71-75	**3.6**	**0.06**
Detecting mild mitral regurgitation or worse[22,23]	56-75	89-93	**5.4**	0.4
Detecting moderate-to-severe mitral regurgitation[7,22,23]	73-93	61-76	2.6	**0.3**
Detecting mild tricuspid regurgitation or worse[23]	23	98	**14.6**	0.8
Detecting moderate-to-severe tricuspid regurgitation[7,23]	20-62	94-98	**9.6**	NS
Detecting ventricular septal defect[20]	90	96	**24.9**	NS
Detecting mitral valve prolapse[20]	55	96	**12.1**	0.5
Characteristic Diastolic Murmur				
Detecting mild aortic regurgitation or worse[23–30]	54-87	75-98	**9.9**	**0.3**
Detecting moderate-to-severe aortic regurgitation[23,28–30]	88-98	52-88	**4.3**	**0.1**
Detecting pulmonary regurgitation[23]	15	99	**17.4**	NS

*Diagnostic standards: For all *valvular lesions*, Doppler echocardiography,[7,20,23,28,31] angiography,[22,24–26,29,30,32] or surgery.[21,27] Echocardiographic trivial regurgitation is classified as "absent regurgitation" (i.e., no disease).

†Definition of finding: For *functional murmur*, see text; for all other *murmurs*, the murmur characteristic in quality, location, and timing for that specific diagnosis. For example, the positive LR of 9.9 for aortic regurgitation refers to an early diastolic, high-frequency blowing decrescendo murmur at the lower left sternal border, not any diastolic murmur.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

NS, not significant.

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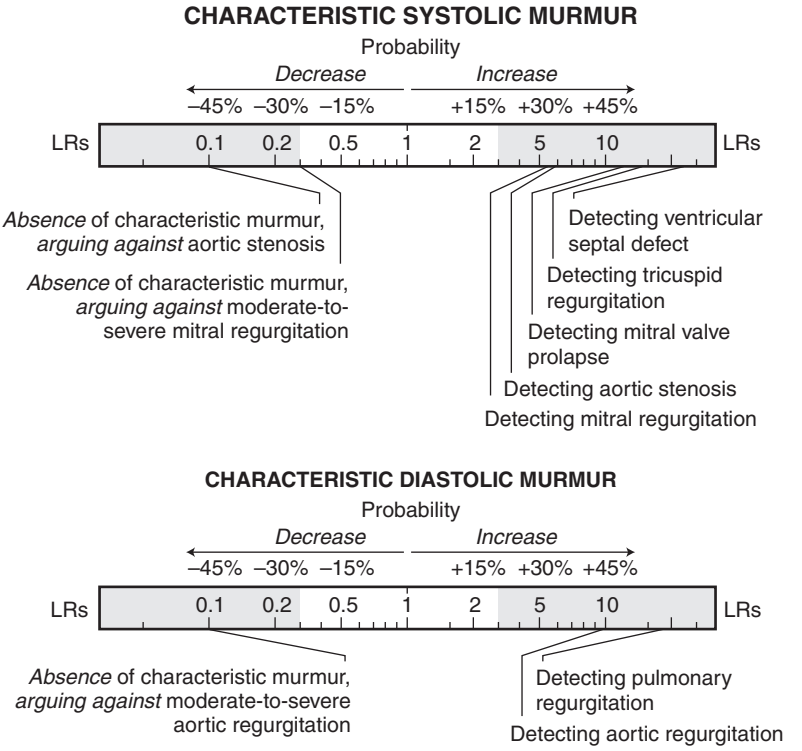

The *absence* of the characteristic murmur *decreases* the probability of significant left-sided valvular lesions: aortic stenosis (negative LR = 0.1), moderate-to-severe mitral regurgitation (negative LR = 0.3), and moderate-to-severe aortic regurgitation (negative LR = 0.1); it does not, however, exclude significant right-sided valvular lesions (the negative LRs for tricuspid regurgitation and pulmonary regurgitation are not significant), probably because pressures on the right side of the heart are lower and thus generate less turbulence and sound than left-sided pressures. Many patients with *mild* mitral regurgitation or *mild* aortic regurgitation also lack murmurs.

B. DIFFERENTIAL DIAGNOSIS OF SYSTOLIC MURMURS

Systolic murmurs are common bedside findings, occurring in 5% to 52% of young adults and 29% to 60% of older persons.[33] Over 90% of younger adults and over half of older adults with systolic murmurs have normal echocardiograms, which means the murmur is "innocent" or "functional."[33]

1. The Functional Murmur

Functional murmurs are short, early systolic or midsystolic murmurs of grade 2/6 or less that are well-localized to the area of the left sternal border and diminish in intensity when the patient stands, sits up, or strains during

the Valsalva maneuver. Patients with functional murmurs have normal neck veins, apical impulse, arterial pulse, and heart tones. The finding of a functional murmur in a patient increases the probability that the echocardiogram does *not* reveal significant valvular disease (LR = 4.7; see EBM Box 41-1).

2. Identifying the Cause of Systolic Murmurs

In patients with abnormal systolic murmurs (i.e., murmurs that are *not* functional), the most important causes are increased aortic velocity (from aortic stenosis or increased flow over an unobstructed valve), mitral regurgitation, and tricuspid regurgitation. In patients with abnormal systolic murmurs, the most important features are distribution of sound on the chest wall (i.e., murmur pattern); intensity of S_1 and S_2; timing, radiation, and quality of sound; murmur intensity during irregular rhythms; and response to maneuvers.

a. Distribution of Murmur (Murmur Pattern; see Fig. 41-1)

EBM Box 41-2 indicates that one of the most important diagnostic signs is the distribution of sound on the chest wall. The broad apical-base pattern increases the probability of increased aortic velocity (LR = 9.7; see EBM Box 41-2), the broad apical pattern increases the probability of mitral regurgitation (LR = 6.8), and the left lower sternal pattern increases the probability of tricuspid regurgitation (LR = 8.4).

In one study, the small apical-base pattern was due to mildly increased aortic velocity (but aortic stenosis was rare); the isolated base pattern usually stemmed from increased flow in the great arteries, not the heart (e.g., anemia, hemodialysis fistula, or subclavian stenosis); and the isolated apical pattern was nondiagnostic.[7]

b. Intensity of S_1 and S_2

If S_1 intensity is determined at the apex and S_2 intensity at the left second parasternal space, and intensity is divided into four levels—inaudible, soft, normal, or loud—the finding of an inaudible S_1 (LR = 5.1; see EBM Box 41-2) or inaudible S_2 (LR = 12.7) in patients with systolic murmurs increases the probability of increased aortic valve velocity, whereas the finding of a loud S_2 increases the probability of mitral regurgitation (LR = 4.7).

c. Timing, Radiation, and Quality of Sound (see also the Section on Specific Timing and Quality of Murmurs Using Onomatopoeia)

Pathologic murmurs have a longer duration (long systolic or holosystolic, LRs 1.7 to 2.2) than nonpathologic ones. Most late systolic murmurs are due to mitral regurgitation.[7] Radiation into the neck (LR = 2.4) and coarse quality (LR = 3.3) increase the probability of increased aortic velocity.

d. Intensity of Systolic Murmur during Irregular Rhythms

One important clue to the etiology of a systolic murmur is how it changes in intensity with changing cycle lengths, as occurs in the irregular pulse of atrial fibrillation or frequent premature beats. Mitral regurgitation

maintains the same intensity whether the beats are quick or delayed.[34] The intensity of aortic stenosis, in contrast, depends on the cycle length: the longer the previous diastole (e.g., beat after a premature beat or after a pause in atrial fibrillation), the louder the murmur.[34,35]

Explaining why these two murmurs behave differently first requires an understanding of the physiology of the pause (Fig. 41-5). The pause causes diastolic filling and contractility to be greater for the next beat than it would have been if the cycle had been quicker (contractility is increased because of Starling forces and, in the case of extrasystoles, postextrasystolic accentuation of contractility). The pause also reduces afterload for the next beat because the aortic pressures have had more time to fall before the next ventricular systole. In aortic stenosis, all three of these changes—increased

EBM BOX 41-2
*Differential Diagnosis of Systolic Murmurs in Adults**

Finding†	Likelihood Ratio for Detecting: *AV Peak Velocity ≥2.5 m/sec*‡	*Mitral Regurgitation*	*Tricuspid Regurgitation*
Murmur Pattern			
Broad apical-base pattern	**9.7**	NS	NS
Broad apical pattern	**0.2**	**6.8**	2.5
LLSB pattern	NS	NS	**8.4**
Heart Tones†			
S_1 inaudible, apex	**5.1**	NS	NS
S_2 inaudible	**12.7**	NS	NS
S_2 loud	NS	**4.7**	**3.6**
Murmur Quality, Timing, and Intensity			
Radiation to neck	2.4	0.6	0.6
Timing midsystolic or early systolic	0.4	0.4	0.5
Timing long systolic or holosystolic	2.2	1.9	1.7
Coarse quality	**3.3**	0.5	0.5
If pulse irregular, murmur intensity same in beat after a pause	0.4	2.5	2.3

*Diagnostic standards: For all *valvular lesions*, Doppler echocardiography[7]; regurgitation severity is moderate or worse.

†Definition of finding: For *murmur pattern*, see Figure 41-1; for *heart tones*, S_1 intensity is determined at the apex, S_2 intensity is determined at the left second parasternal space, and intensity is graded into four levels, as inaudible, soft, normal, or loud; for *quality* and *timing*, see the section on Specific Timing and Quality of Murmurs Using Onomatopoeia in text and Table 41-2.

‡AV peak velocity ≥ 2.5 m/sec indicates aortic stenosis, mild or worse.

NS, not significant.

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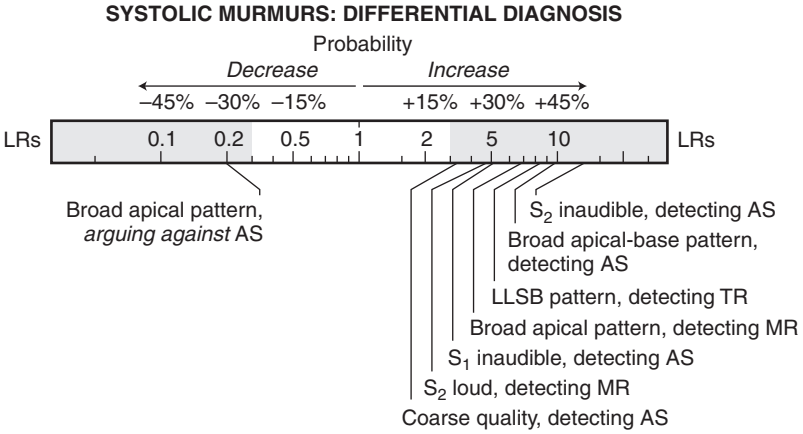

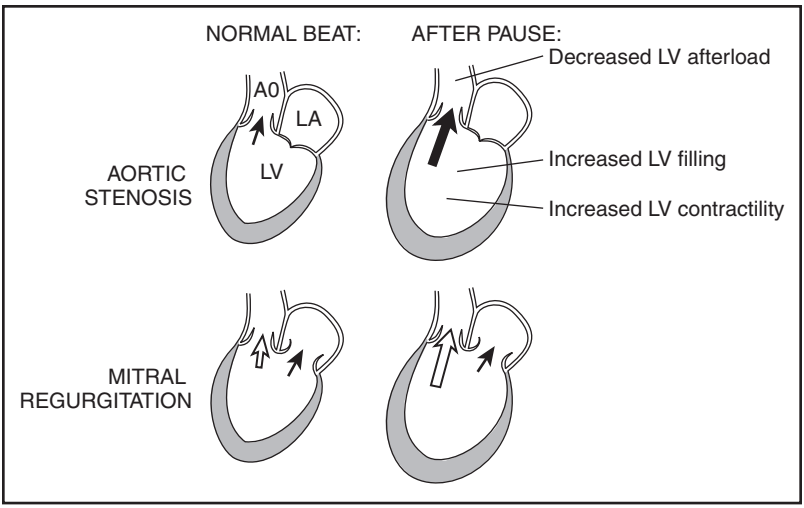

FIGURE 41-5 **Intensity of systolic murmurs and irregular rhythms.** The figure depicts blood flow and intensity of systolic murmurs during normal beats *(left column)* and after pauses in the heart rhythm (from extrasystoles or atrial fibrillation, *right column*). In each drawing, the size of the arrow indicates the volume of blood flow: *black arrows* depict flow *causing* sound, whereas *open arrows* depict flow *not generating* sound. After the pause *(right column),* there is increased left ventricular filling and contractility but *decreased* left ventricular afterload. In aortic stenosis *(top rows),* these changes all favor increased flow across the aortic valve and a louder murmur (i.e., *dark arrow* is larger after the pause). In mitral regurgitation, these same forces again favor increased flow across the aortic valve *(open arrow),* but because this flow is not generating sound, the regurgitant volume *(dark arrow)* and murmur intensity remain unchanged. See text. Ao, aorta; LA, left atrium; LV, left ventricle.

filling, increased contractility, and decreased afterload—promote greater flow across the stenotic valve after pauses than after quick beats, causing the murmur to become louder.[36] In mitral regurgitation, however, the stroke volume is divided between two paths:

1. Blood flowing out the aorta
2. Into the left atrium

The reduced afterload promotes the extra filling from the pause to exit into the aorta, leaving the regurgitant volume the same as with quicker beats and making the intensity of the murmur thus independent of cycle length.

In one study, unchanging intensity of systolic murmurs during irregular rhythms increased the probability of regurgitation (LR = 2.5; see EBM Box 41-2).

Another systolic murmur, hypertrophic cardiomyopathy, responds unpredictably to changing cycle lengths: The long pause may make the murmur louder or softer or may not change it at all.[35]

e. Maneuvers

Several maneuvers help differentiate systolic murmurs (Table 41-3). They are classified into respiratory maneuvers, maneuvers that change venous return (e.g., Valsalva maneuver, squatting-to-standing, standing-to-squatting, and passive leg elevation), and maneuvers that primarily change systemic vascular resistance (isometric hand grip, transient arterial occlusion, and inhalation of amyl nitrite).

(1) Respiration. Inspiration increases venous return to the right side of the heart and decreases it to the left side of the heart.* Murmurs that intensify during inspiration, therefore, characteristically originate in the right side of the heart (e.g., tricuspid regurgitation or pulmonic stenosis; LR = 7.8; EBM Box 41-3). Murmurs that become *softer* during inspiration are most likely *not* right-sided murmurs (LR = 0.2).

Before interpreting the test, however, the clinician should be certain the patient is breathing evenly in and out because irregular breathing or breath-holding makes interpretation impossible. To help direct the patient's breathing, the clinician can move his or her arm slowly up and down and ask the patient to breathe in when the arm is going up and breathe out when it is going down.

Inspiratory intensification of the murmur of tricuspid regurgitation was originally described by Rivero-Carvallo in 1946. (The sign is sometimes called the **Carvallo sign**.[45])

*This occurs because pressures in the right side of the heart diminish with intrathoracic pressures during inspiration, increasing the pressure gradient between the right side of the heart and the systemic veins and causing filling to increase to the right side of the heart. In contrast, inspiration increases the capacitance of pulmonary veins, thus reducing flow to the left side of the heart during inspiration.

TABLE 41-3 Maneuvers and Heart Murmurs

Maneuver*	Technique	When to Note Change in Murmur
Respiration	The patient breathes normally in and out	During inspiration and expiration
MANEUVERS AFFECTING VENOUS RETURN		
Decrease Venous Return		
Valsalva maneuver	The patient exhales against closed glottis for 20 seconds	At end of the strain phase (i.e., at 20 seconds)
Squatting-to-standing	The patient squats for at least 30 seconds and then rapidly stands up	Immediately after standing
Increase Venous Return		
Standing-to-squatting	The patient squats rapidly from the standing position while breathing normally to avoid a Valsalva maneuver	Immediately after squatting
Passive leg elevation	The patient's legs are passively elevated to 45 degrees while the patient is supine	15-20 seconds after leg elevation
MANEUVERS AFFECTING SYSTEMIC VASCULAR RESISTANCE (AFTERLOAD)		
Increase Afterload		
Isometric hand-grip exercise	The patient uses one hand to squeeze the examiner's index and middle fingers together tightly†	After 1 minute of maximal contraction
Transient arterial occlusion	The examiner places blood pressure cuffs around both upper arms of the patient and inflates them to pressures above the patient's systolic blood pressure	20 seconds after cuff inflation
Decrease Afterload		
Amyl nitrite	The patient takes three rapid, deep breaths from a broken amyl nitrite capsule	15-30 seconds after inhalation

*Squatting-to-standing also decreases systemic vascular resistance, and amyl nitrite also diminishes pulmonary vascular resistance by a small amount.

†In clinical studies, a hand dynamometer was used to confirm that at least 75% of maximal hand-grip strength was sustained for 1 minute.[39]

From information cited in references 36 to 40.

(2) Maneuvers Changing Venous Return. Venous return to the heart *decreases* during the straining phase of the Valsalva maneuver and the squatting-to-standing maneuver. Venous return *increases* during passive leg elevation and the standing-to-squatting maneuver (see Table 41-3 for definitions).

These maneuvers are most useful in identifying hypertrophic cardiomyopathy, which, unlike most systolic murmurs, intensifies with decreased

venous return and becomes softer with increased venous return. This paradoxic response occurs because the murmur is caused by obstruction in the outflow tract, below the aortic valve and between the anterior leaflet of the mitral valve and the hypertrophied interventricular septum. Decreased venous return brings the mitral leaflet and septum closer together and aggravates the obstruction; increased return moves them apart and relieves the obstruction.

All four venous return maneuvers are useful in diagnosing hypertrophic cardiomyopathy (LRs = 6 to 14; see EBM Box 41-3), although intensification of the murmur during Valsalva strain increases the probability the most (LR = 14). For three of the maneuvers (squatting-to-standing, standing-to-squatting, and passive leg elevation), the *absence* of the characteristic response decreases the probability of hypertrophic cardiomyopathy (LR = 0.1). Of these four maneuvers, only passive leg elevation can be easily performed with frail patients.

One other systolic murmur, mitral valve prolapse, may intensify during squatting-to-standing, although it does *not* become louder during Valsalva strain. This paradoxic finding, which is further discussed in Chapter 44, may explain why there are more false-positive results for squatting-to-standing (specificity = 84%) than Valsalva strain (specificity = 95%).

(3) Maneuvers Changing Systemic Vascular Resistance (or Afterload). Before employing maneuvers that change afterload in diagnosing systolic murmurs, the clinician has already addressed the possibility of right-sided murmurs (respiratory maneuvers) and hypertrophic cardiomyopathy (venous return maneuvers). The primary remaining diagnostic possibilities are murmurs generated by flow over the aortic valve (e.g., aortic stenosis or increased aortic flow without stenosis) and murmurs from left-sided regurgitant lesions (e.g., mitral regurgitation or ventricular septal defect).

Changing afterload may distinguish these lesions. The murmurs of mitral regurgitation and ventricular septal defect intensify with increased afterload because blood leaving the ventricle, having two paths to potentially follow, encounters more resistance in the aorta and therefore flows more readily through the regurgitant lesion. Similarly, these murmurs become softer when afterload is decreased because enhanced aortic flow reduces the regurgitant volume.

The common techniques of manipulating afterload at the bedside are isometric hand grip and transient arterial occlusion (see Table 41-3), both of which increase afterload. The finding of a systolic murmur that intensifies with either maneuver increases the probability of mitral regurgitation or ventricular septal defect (LR = 5.8 for isometric hand grip and 48.7 for transient arterial occlusion; see EBM Box 41-3). Another maneuver that reduces afterload, amyl nitrite inhalation, was used commonly 40 to 50 years ago but is rarely used today.

EBM BOX 41-3
*Systolic Murmurs and Maneuvers**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Respiration				
LOUDER DURING INSPIRATION				
Detecting right-sided murmurs (tricuspid regurgitation or pulmonic stenosis)[38,41]	78-95	87-97	**7.8**	**0.2**
Changing Venous Return				
LOUDER WITH VALSALVA STRAIN				
Detecting hypertrophic cardiomyopathy[38]	70	95	**14.0**	**0.3**
LOUDER WITH SQUATTING-TO-STANDING				
Detecting hypertrophic cardiomyopathy[38]	95	84	**6.0**	**0.1**
SOFTER WITH STANDING-TO-SQUATTING				
Detecting hypertrophic cardiomyopathy[38,42]	88-95	84-97	**7.6**	**0.1**
SOFTER WITH PASSIVE LEG ELEVATION				
Detecting hypertrophic cardiomyopathy[38]	90	90	**9.0**	**0.1**
Changing Systemic Vascular Resistance (Afterload)				
SOFTER WITH ISOMETRIC HAND GRIP				
Detecting hypertrophic cardiomyopathy[38]	90	75	**3.6**	**0.1**
LOUDER WITH ISOMETRIC HAND GRIP				
Detecting mitral regurgitation or ventricular septal defect[38,39]	70-76	78-93	**5.8**	**0.3**
LOUDER WITH TRANSIENT ARTERIAL OCCLUSION				
Detecting mitral regurgitation or ventricular septal defect[38]	79	98	**48.7**	**0.2**
SOFTER WITH AMYL NITRITE INHALATION				
Detecting mitral regurgitation or ventricular septal defect[38,39,43,44]	41-95	89-95	**10.5**	**0.2**

*Diagnostic standards: Doppler echocardiography or angiography.

†Definition of finding: See text; for amyl nitrite inhalation, the test was interpretable only if it induced tachycardia.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

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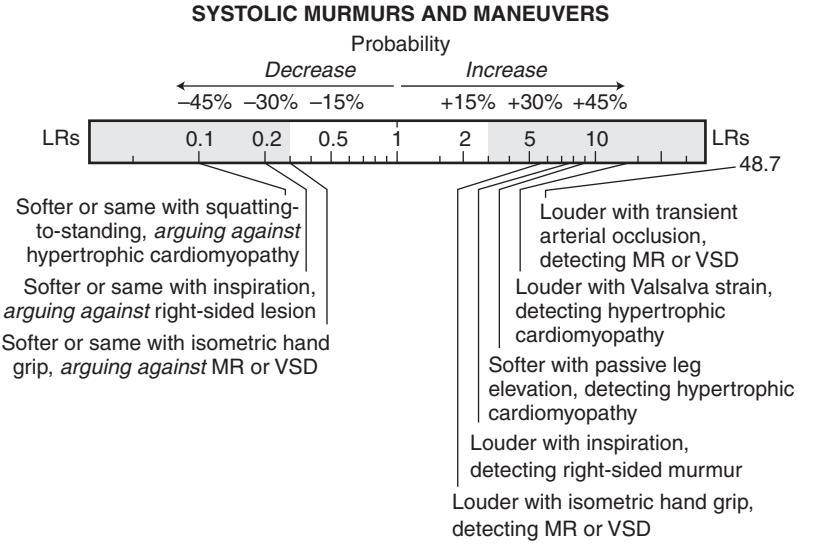

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 42

Aortic Stenosis

I. INTRODUCTION

Aortic stenosis is any disorder of the aortic valve that obstructs the ejection of blood from the left ventricle into the aorta. Its characteristic findings are a systolic murmur, abnormal carotid pulse, and sustained apical impulse.

The pathologic characteristics of aortic stenosis were recognized in the 1600s, but it was James Hope who in 1832 first clearly described the characteristic murmur.[1,2]

II. THE FINDINGS

A. THE MURMUR

The murmur of aortic stenosis is early systolic, midsystolic, or holosystolic. Although it may be loudest at the right second intercostal space (i.e., the classic "aortic" area), most aortic stenosis radiates above and below the third left parasternal space, obliquely and upward toward the right clavicle and downward toward the apex, a distribution mimicked by placing a sash over the patient's right shoulder. Radiation of sound in the neck first appears on the right side (clavicle and neck), but, as the stenosis worsens, the sound appears on *both* sides of the neck and over both clavicles (i.e., isolated radiation to just the *left* clavicle or *left* neck is not characteristic of aortic stenosis and instead suggests stenosis of a great artery; see Chapter 41).

In **calcific aortic stenosis,** the most common modern etiologic type, the murmur at the upper sternal borders contains both high-frequency and low-frequency vibrations, giving it a harsh or rough sound, like that of a person clearing the throat. At the apex, in contrast, the murmur of calcific aortic stenosis sometimes loses its low-frequency components and instead consists of a narrow band of high-frequency sound, thus making it sound like mitral regurgitation. This harmonic distortion of sound—the loss of low-frequency components of sound when the stethoscope is moved "upstream"—is called the **Gallavardin phenomenon.**[3]

B. ASSOCIATED CARDIAC SIGNS

Other traditional findings of severe aortic stenosis are the following:

1. A carotid pulse that is abnormally small in volume and delayed **(pulsus parvus et tardus)**
2. A palpable apical impulse that is abnormally sustained (see Chapter 36 for definition of sustained impulse)

3. Reduced intensity of the second heart sound, which occurs because the inflexible aortic leaflets close with less force than normal

Another traditional finding is a prominent A wave in the neck veins (i.e., the **Bernheim phenomenon**), although this wave is more often seen on pressure tracings than at the bedside. Its mechanism is still disputed.[4]

III. CLINICAL SIGNIFICANCE

A. DETECTING AORTIC STENOSIS

The presence of the characteristic aortic systolic murmur increases the probability of aortic stenosis (likelihood ratio [LR] = 5.9 for mild or worse aortic stenosis; EBM Box 42-1); most patients with false-positive results (i.e., those with a characteristic aortic murmur but no aortic stenosis) have increased aortic flow without obstruction (e.g., from fever, anemia, pregnancy, or turbulence due to nonobstructing calcification). Most important, the *absence* of the aortic flow murmur decreases considerably the probability of aortic stenosis (LR = 0.06 for severe aortic stenosis; LR = 0.1 for stenosis of any severity). Chapter 41 discusses further the differential diagnosis of systolic murmurs, and how the clinician—by observing the location of sound, second heart sound, quality of the murmur, and the way in which the murmur responds to irregular heartbeats and different maneuvers—can be more confident that a systolic murmur indeed represents aortic stenosis and not another valvular lesion.

EBM BOX 42-1
*Aortic Stenosis Murmur**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Arterial Pulse				
Aortic systolic murmur, detecting mild or worse aortic stenosis[5]	90	85	**5.9**	**0.1**
Aortic systolic murmur, detecting severe aortic stenosis[5,6]	96-98	71-75	**3.6**	**0.06**

*Diagnostic standard: For *mild or worse aortic stenosis*, peak aortic velocity ≥2.5 m/sec; for *severe aortic stenosis*, maximal interaortic cusp distance = 8 mm[6] or peak aortic velocity ≥ 4 m/sec.[5]

†Definition of findings: For *aortic systolic murmur,* either the broad apical-base pattern or small apical-base pattern (see Chapter 41).

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

NS, not significant.

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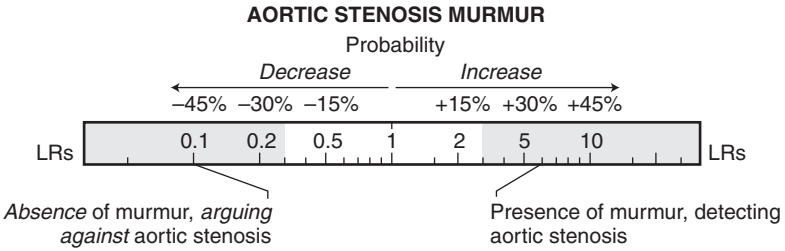

B. SEVERITY OF AORTIC STENOSIS

Once clinicians are confident that a murmur represents an aortic flow murmur, they must decide whether the patient has significant aortic stenosis. **Significant aortic stenosis** refers to those lesions with such severe obstruction that if the patient has symptoms of angina, syncope, or dyspnea, valvular replacement is indicated. (The footnotes of EBM Box 42-2 define severe stenosis.)

Many of the traditional teachings about aortic stenosis appeared during a time when congenital and rheumatic diseases were more common than they are today. Because the primary cause of aortic stenosis today is calcific aortic stenosis, some of these teachings may not be as relevant as they were in the past. In comparison with congenital and rheumatic diseases, calcific aortic stenosis affects older patients, who commonly have aortic flow murmurs *without* stenosis (i.e., aortic sclerosis) and who often have ischemic heart disease, a disorder complicating the bedside evaluation because the patient then has two possible explanations (i.e., severe aortic stenosis or ischemic heart disease) for symptoms of angina or dyspnea.

The patients whose clinical signs are summarized in EBM Box 42-2 (over 1000 patients in all) were all elderly (mean age, 66 years). Importantly, *all had aortic flow murmurs*, and the bedside question was whether the murmur represented *severe* aortic stenosis. Although some had mild aortic regurgitation, other significant valvular disease was excluded from most of these studies. In these studies, syncope was the only classic aortic stenosis symptom that increased the probability of severe aortic stenosis (LR = 3.1; the LRs for the other two classic aortic stenosis symptoms, angina and dyspnea, were not significant).[8,15,16]

1. Individual Findings

The following findings, in descending order of diagnostic accuracy (see EBM Box 42-2), increase the probability of severe aortic stenosis in patients with aortic flow murmurs: late peaking murmur (LR = 4.4), sustained apical impulse (LR = 4.1), delayed carotid artery upstroke (pulsus tardus, LR = 3.3), absent or diminished S_2 (LR = 3.1), prolonged murmur (LR = 3), apical-carotid delay (i.e., a palpable delay between the apical impulse and the carotid impulse, LR = 2.6), brachioradial delay (i.e., palpable delay between the brachial and radial artery pulses, LR = 2.5), reduced carotid artery volume (i.e., pulsus parvus, LR = 2.3), and added humming quality of the murmur (LR = 2.1).

EBM BOX 42-2

Characteristics of Severe Aortic Stenosis (All Patients Have Aortic Murmur)[*]

Finding (Reference)[†]	Sensitivity (%)	Specificity (%)	Likelihood Ratio[‡] if Finding Is	
			Present	*Absent*
Arterial Pulse				
Delayed carotid artery upstroke[5,7–10]	31-90	68-93	**3.3**	0.4
Reduced carotid artery volume[5,8,9]	44-80	65-81	2.3	0.4
Brachioradial delay[11]	97	62	2.5	**0.04**
Apical Impulse				
Sustained apical impulse[8]	78	81	**4.1**	**0.3**
Apical-carotid delay[12]	97	63	2.6	**0.05**
Heart Tones				
Absent or diminished S_2[5,7,9,10,13]	44-90	63-98	**3.1**	0.4
S_4 gallop[10,14]	29-50	57-63	NS	NS
Murmur				
Grade ≥3/6[5,15]	31-89	23-77	NS	NS
Early systolic[5]	4	61	**0.1**	1.6
Prolonged duration[5,7,10]	83-94	49-84	**3.0**	**0.2**
Late peaking[7,8,10]	83-90	72-88	**4.4**	**0.2**
Loudest over aortic area[9,10]	58-75	41-73	1.8	0.6
Radiation to neck[5,9,10]	90-98	11-36	NS	**0.1**
Radiation to both sides of neck[5]	50	74	1.9	NS
Blowing quality[5]	4	67	**0.1**	1.4
Humming quality[5]	62	71	2.1	0.5

*Diagnostic standard: For *severe aortic stenosis*, aortic valve area <0.75 cm^2,[11,13] <0.8 cm^2,[9,12] <0.9 cm^2;[8] peak gradient >50 mm Hg,[9,10] or peak velocity of aortic flow >3.6 m/sec[7] or ≥4 m/sec.[5]

[†]Definition of findings: For *late peaking murmur,* murmur peaks at midsystole or beyond; for *aortic area*, second right intercostal space.

[‡]Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

NS, not significant.

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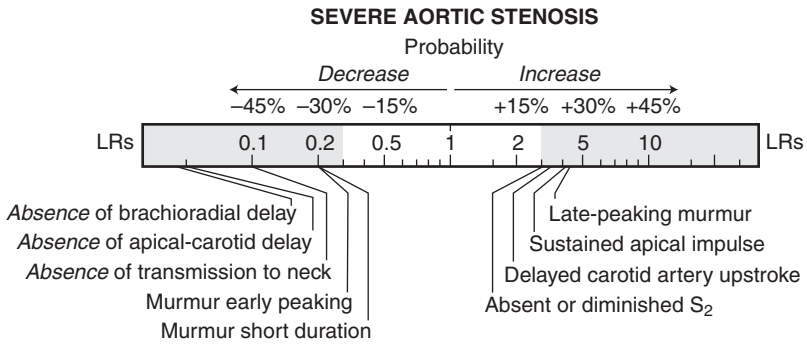

The findings that *decrease* the probability of severe aortic stenosis in patients with aortic flow murmurs are absence of brachioradial delay (LR = 0.04; see EBM Box 42-2), absence of an apical-carotid delay (LR = 0.05), early systolic timing (LR = 0.1), blowing quality throughout (LR = 0.1), lack of radiation to the neck (LR = 0.1), and short duration of the murmur (LR = 0.2). Brachioradial delay and apical-carotid delay were investigated in only single studies and thus require confirmation by others.

Two additional bedside findings are chest radiography and electrocardiography (ECG). The finding of calcification of the aortic valve on chest radiography detects severe stenosis with a sensitivity of 31% to 81%, specificity of 63% to 96%, positive LR of 3.9, and negative LR of 0.5.[9,13,15,16] Left ventricular hypertrophy on ECG detects severe stenosis with a sensitivity of 49% to 94%, specificity of 57% to 86%, positive LR of 2.1, and negative LR of 0.5.[7,9,12,13,15,16]

The following findings are not helpful in identifying patients with severe aortic stenosis: narrow pulse pressure,[17] fourth heart sound, third heart sound,[13] reversed splitting of the second heart sound,[10] aortic ejection click,[10] and intensity of the murmur (see EBM Box 42-2).

2. Why Positive Likelihood Ratios Are So Low

The highest positive LR for the findings listed in EBM Box 42-2 is 4.4 (i.e., late peaking murmur). In general, positive LRs are low when patients *without* disease also demonstrate the physical finding (i.e., specificity is low and there are many *false-positive* results). The cause of false-positive results in the studies of aortic stenosis is principally *moderate* aortic stenosis (defined as aortic valve area of 0.8 to 1.2 cm^2 or peak gradient of 25 to 50 mm Hg).

Therefore, if "disease" is instead defined as "combined moderate-to-severe aortic stenosis," the positive LRs improve dramatically, especially for delayed carotid upstroke (positive LR = 9, negative LR = 0.6), absent or diminished S_2 (positive LR = 7.3, negative LR = 0.5), prolonged duration of murmur (positive LR = 11.4, negative LR = 0.3), and late-peaking murmur (positive LR = 29.5, negative LR = 0.3).[5,7,10,18]

This means that the clinician examining patients with aortic flow murmurs can easily distinguish patients with moderate-to-severe aortic stenosis

from those with milder stenosis or no obstruction, but he or she has greater difficulty distinguishing severe stenosis from moderate stenosis.

3. Combined Findings

One study has validated the use of combined findings in the diagnosis of aortic stenosis.[9] According to this diagnostic scheme, the clinician evaluates five bedside findings and assigns the following points: delayed carotid upstroke (3 points), diminished carotid volume (2 points), murmur loudest at right upper sternal border (2 points), single/absent second heart sound (3 points), and calcification of the aortic valve on chest radiography (4 points).

This diagnostic scheme distinguishes moderate-to-severe aortic stenosis from other causes of aortic flow murmurs. The probability of moderate-to-severe aortic stenosis is low with 0 to 6 points (LR = 0.2) and high with 10 to 14 points (LR = 10.6). Scores from 7 to 9 points are unhelpful (LR not significant).

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 43

Aortic Regurgitation

I. INTRODUCTION

The principal problem in aortic regurgitation is defective closure of the aortic valve, which allows blood to return from the aorta to the left ventricle during diastole. In patients with significant chronic regurgitation, the traditional physical findings are a diastolic murmur, dilated apical impulse, and abnormally forceful and collapsing arterial pulses **(pulsus celer).**

In the 1700s, clinicians associated the postmortem finding of damaged aortic valves with hearts "larger than that of an ordinary ox" (the origin of the phrase *cor bovinum*) and the finding during life of "violently throbbing" carotid arteries. In 1832, Sir Dominic John Corrigan, a Dublin surgeon, taught clinicians how to diagnose the disease during life by emphasizing the importance of these dramatic arterial pulsations and the associated diastolic murmur.[1,2]

II. THE FINDINGS

A. THE MURMUR(S)

Severe aortic regurgitation may cause three distinct murmurs:

1. The early diastolic murmur of aortic regurgitation
2. A systolic aortic flow murmur
3. The apical diastolic rumble of the Austin Flint murmur

1. Early Diastolic Murmur of Regurgitation

The most important physical sign of aortic regurgitation is the early diastolic murmur, which is a blowing, high-frequency murmur with a decrescendo in shape (see Chapter 41.) :

Lub **P**EWWWWWWW

The murmur may occupy all of diastole or just its early part.[3] Pressing firmly against the chest wall with the diaphragm of the stethoscope brings out the murmur, which is usually loudest in the left parasternal area at the third or fourth intercostal space. In some patients, the murmur is only audible when the patient sits up, leans forward, and holds his or her breath in exhalation.

2. Systolic Aortic Flow Murmur

Severe aortic regurgitation also produces a short systolic aortic flow murmur, which results from ejection over the aortic valve of the large stroke volume characteristic of the disease. The combination of this murmur and

the early diastolic one causes a characteristic to-fro sound near the sternum (see Chapter 41.):

Lub SHSHSH **P**EWWWWWWW

This murmur may superficially resemble that of aortic stenosis, although the flow murmur of pure regurgitation is shorter and associated with the peripheral pulse findings of severe regurgitation (see later).

3. Apical Diastolic Rumble: Austin Flint Murmur

a. Definition

The Austin Flint murmur is a diastolic rumbling murmur heard at the apex in patients with severe aortic regurgitation. It resembles mitral stenosis, even though the mitral valve is completely normal. It was first described by the American physician Austin Flint in 1862.[4]

The Austin Flint murmur is found in up to 60% of patients with moderate or severe aortic regurgitation but is rarely heard in mild aortic regurgitation.[5,6] Austin Flint called his murmur *presystolic*, but by this he meant it was loudest before S_1 and thus different from the murmur of aortic regurgitation, which began immediately after S_2 and tapered off during diastole. About half of Austin Flint murmurs have two diastolic components (mid-diastolic and presystolic), whereas the other half have just a presystolic component.[6,7]

b. Pathogenesis

The cause of the Austin Flint murmur is still debated. Although all hypotheses assume that the murmur depends on a strong regurgitant stream of blood being directed back toward the left ventricle during diastole, these hypotheses differ in how this regurgitant stream causes an apical rumbling sound. Proposed mechanisms include fluttering of the anterior leaflet of the mitral valve, premature closure of the mitral valve from elevated left ventricular end-diastolic pressure, collision of the regurgitant stream with the anterior mitral leaflet, ventricular vibrations caused by the regurgitant stream itself, and harmonic distortion of the aortic regurgitant murmur.[6,8,9] Many of these mechanisms may operate together to create the sound.[10] An instructive video showing the blood flow responsible for the Austin Flint murmur is available in reference 11.

B. WATER-HAMMER PULSE AND INCREASED PULSE PRESSURE

Because of the large stroke volume and diastolic emptying of aortic blood into the left ventricle (i.e., aortic runoff), the arterial pulse wave of aortic regurgitation rises suddenly and collapses abruptly. This abnormality has many names, although the most common ones are **collapsing pulse, Corrigan pulse,** and **water-hammer pulse**.* In most patients with aortic regurgitation, the collapsing pulse becomes more prominent as the examiner elevates the patient's wrist.[12,13] This occurs because elevation

*Corrigan actually emphasized the exaggerated *visible* pulsations of aortic regurgitation, not the palpable ones. The term *water-hammer pulse* was coined in 1836 by Sir Thomas Watson, who likened the pulse to a Victorian toy called a water hammer, which imparted to a child's hands the same sensation as that of a collapsing pulse of aortic regurgitation.[2]

of the arm with respect to the heart reduces the diastolic pressure in that arm, causing the vessel to collapse more completely with each beat. (The pounding sensation of the water-hammer pulse is identical to the sensation felt by the examiner when palpating a patient's blood pressure, with the cuff pressure just above the diastolic pressure; see Chapter 16.)

C. ABNORMAL PULSATIONS OF OTHER STRUCTURES: THE AORTIC REGURGITATION EPONYMS

The large stroke volume and aortic runoff of aortic regurgitation often induce pulsations in other parts of the body. This finding has generated many eponyms of what is fundamentally a single physical finding. (The number of eponyms for aortic regurgitation rivals those of some neurologic reflexes.)[1,14–17] These various bobbings include the following:

1. An abnormally conspicuous capillary pulsation, best elicited by blanching a portion of the nail and then observing the border pulsating between the white and red color **(Quincke's capillary pulsations,** described in 1868, although Heinrich Quincke should be known instead for inventing the lumbar puncture)
2. An anterior-posterior bobbing of the head, synchronous with the arterial pulsations **(de Musset sign,** named after the French poet Alfred de Musset, who was afflicted with aortic regurgitation)[18]
3. An alternate blanching and flushing of the forehead and face **(Lighthouse sign)**
4. Pulsations of organs or their parts, including the uvula **(Müller sign,** 1899), retinal arteries **(Becker sign),** larynx **(Oliver-Cardavelli sign),** spleen **(Sailer sign,** 1928),[19] and cervix **(Dennison sign)***[20]

In many of the original descriptions of these eponymous findings, the sign was presented simply as an interesting observation, not one of particular diagnostic value.

D. HILL TEST

In 1909, Leonard Hill of Britain observed that patients with severe aortic regurgitation often have a systolic pressure in the foot that is much greater than a simultaneously measured systolic pressure in the arm.[21,22] The **Hill test** specifically refers to the systolic pressure of the foot minus that of the arm. The correct technique for measuring the pressure in the foot is to wrap the arm cuff around the patient's calf and to measure the systolic pressure in the dorsalis pedis and posterior tibial arteries by palpation. The higher of these two pressures is the "foot pressure."

E. AUSCULTATION OVER ARTERIES

Two auscultatory findings may appear over the peripheral arteries of patients with aortic regurgitation: pistol shot sounds and Duroziez murmur (or Duroziez sign).

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*The eponym does not necessarily indicate priority: Sailer gave credit for the pulsating spleen to Tulp of the 1600s,[19] and Dennison gave credit for the pulsating cervix to Shelly, one of his house officers.[20]

1. Pistol Shot Sound

a. Definition

Pistol shot sounds are short, loud, snapping sounds with each pulse, heard over the femoral, brachial, or radial arteries. They are identical in quality to the Korotkoff sounds heard when measuring blood pressure. Pistol shot sounds are heard with only *light* pressure of the stethoscope and, like the water-hammer pulse, may first appear only after elevation of the patient's arm.[13]

Pistol shot sounds were first described by Traube in 1872.[23,24]

b. Pathogenesis

Pistol shot sounds occur because of sudden expansion and tensing of the walls of the vessels during systole. Consequently, they are not only associated with the collapsing pulses of aortic regurgitation but also are inducible in normal individuals by administering intravenous vasodilator medications.[25] The sounds are analogous to the loud, snapping notes heard when a sail or parachute suddenly fills with wind.[26] The quicker the vessel dilates, the louder the note, and in patients with aortic regurgitation, the intensity of the pistol shot sound correlates with the height of the pulse pressure[27] and the change in pressure over time (dP/dt) of the pulse.[25]

2. Duroziez Murmur or Sign

a. Definition

Duroziez sign[14,23,28–31] is a *double* to-fro murmur heard over the brachial or femoral artery. It is heard only with *firm* pressure from the stethoscope. For the Duroziez sign to be positive, both a systolic murmur and a diastolic murmur must be present. (Many normal persons develop systolic murmurs with pressure on the stethoscope.) The diastolic component often becomes louder with pressure applied distal to the stethoscope.

Although some claim that the Duroziez murmur also may occur in normal individuals who have increased flow because of fever, anemia, or peripheral vasodilatation,[28] the vascular sound produced in these conditions does not have the characteristic to-fro sound of the Duroziez murmur, but instead resembles the continuous murmur of an arteriovenous fistula[30]:

PuSHSHSHSH**Pu**SHSHSHSHSHSHSH

Duroziez described his "double intermittent murmur" in 1861.[23,32]

b. Pathogenesis

The diastolic component of the Duroziez sign results from the blood actually reversing directions in the artery during diastole.[29,30]

III. CLINICAL SIGNIFICANCE

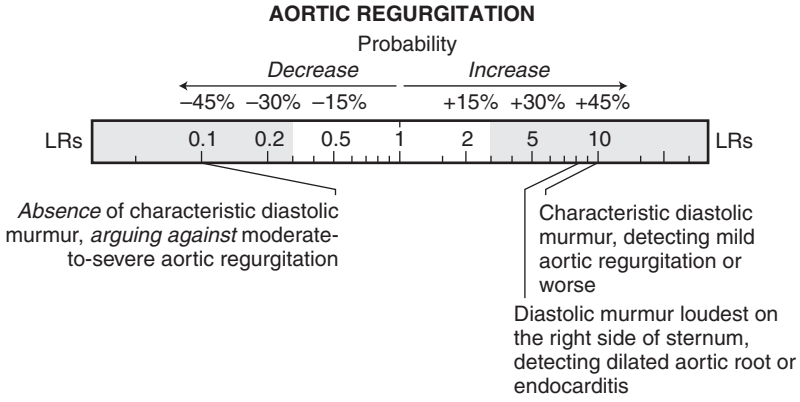
A. DETECTING AORTIC INSUFFICIENCY

The presence of the characteristic early diastolic murmur of aortic insufficiency greatly increases the probability that an aortic leak is actually present (LR = 9.9; EBM Box 43-1). Although some patients with mild regurgitation have no murmur, the *absence* of the characteristic murmur

EBM BOX 43-1
*Aortic Regurgitation**

Finding (Reference)	Sensitivity (%)	Specificity (%)	Likelihood Ratio† if Finding Is	
			Present	*Absent*
Characteristic Diastolic Murmur				
Detecting mild aortic regurgitation or worse[33–40]	54-87	75-98	**9.9**	**0.3**
Detecting moderate-to-severe aortic regurgitation[37–40]	88-98	52-88	**4.3**	**0.1**
Early Diastolic Murmur Loudest on Right Side of Sternum				
Detecting dilated aortic root or endocarditis[3]	29	96	**8.2**	0.7
Early Diastolic Murmur Softer with Amyl Nitrite Inhalation				
Detecting aortic regurgitation (vs. Graham Steell murmur)[41]	95	83	NS	**0.1**

*Diagnostic standard: For *moderate-to-severe aortic regurgitation*, see EBM Box 43-2.
†Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.
NS, not significant.
Click here to access calculator.



greatly *decreases* the probability of moderate-to-severe aortic regurgitation (LR = 0.1; see EBM Box 43-1).

B. DISTINGUISHING AORTIC VALVE DISEASE FROM AORTIC ROOT DISEASE

The early diastolic murmur of aortic regurgitation is usually loudest in the left parasternal area. In some patients, the murmur may be loudest to the right of the sternum, which suggests an eccentric regurgitant stream from dilation of

the aortic root (e.g., Marfan syndrome, aortic dissection, syphilitic aortitis) or damage to a single aortic cusp (e.g., endocarditis). This sign, introduced by Harvey in 1963,[42] increases the probability of a dilated root or endocarditis (LR = 8.2; see EBM Box 43-1); its absence is diagnostically unhelpful (LR = 0.7)*.

C. DISTINGUISHING AORTIC REGURGITATION FROM PULMONARY REGURGITATION

Distinguishing aortic from pulmonary regurgitation was particularly relevant in patients with rheumatic mitral stenosis, who often had associated aortic valve disease but who also could develop pulmonary hypertension and the early diastolic murmur of pulmonary insufficiency (i.e., the **Graham Steell murmur**).

In patients with mitral stenosis who also have an early diastolic murmur of regurgitation heard next to the sternum, the additional lesion is aortic regurgitation at least 80% of the time. Aortic regurgitation is the most common correct diagnosis even when there are no peripheral pulse findings of aortic regurgitation and the patient shows signs of severe pulmonary hypertension.[33,43,44] In the past, patients inhaled amyl nitrite to reduce the afterload so that the clinician could distinguish aortic from pulmonary regurgitation. Amyl nitrite should diminish the intensity of the aortic regurgitation murmur (i.e., less regurgitant flow) but not affect the pulmonary regurgitation murmur. The finding of an early diastolic murmur that instead becomes louder or does not change after amyl nitrite inhalation *decreases* the probability of aortic regurgitation (LR = 0.1; see EBM Box 43-1).

D. SEVERITY OF AORTIC REGURGITATION

This section applies only to patients with the characteristic early diastolic murmur of chronic aortic regurgitation (EBM Box 43-2). It does not apply to acute aortic regurgitation. (See the section on Acute Aortic Regurgitation.) Many of the patients enrolled in the studies also had additional murmurs of aortic stenosis or mitral regurgitation.

1. The Diastolic Murmur

The louder the murmur, the more severe the aortic regurgitation (r = 0.67).[45] Murmurs of grade 3 or more indicate moderate-to-severe aortic regurgitation (LR = 8.2; see EBM Box 43-2).

2. Blood Pressure

Two findings *increasing* the probability of moderate-to-severe regurgitation in these patients are diastolic blood pressure of 50 mm Hg or less (LR = 19.3; see EBM Box 43-2) and pulse pressure of 80 mm Hg or more (LR = 10.9; see EBM Box 43-2). Two findings *decreasing* the probability of significant regurgitation are diastolic blood pressure of more than 70 mm Hg (LR = 0.2) and pulse pressure of less than 60 mm Hg (LR = 0.3). These

*The diagnostic accuracy of the **Harvey sign** is based on patients from the 1960s, when most patients with aortic insufficiency had either rheumatic valvular disease or syphilitic root disease. Whether it is as accurate today is unknown.

signs have no diagnostic value when applied to other patients lacking the characteristic murmur of aortic regurgitation.[36]

3. Hill Test

If the abnormal response in the Hill test is defined as a foot-arm blood pressure difference of 60 mm Hg or more, the positive test significantly increases the probability of significant regurgitation (LR = 17.3; see EBM Box 43-2).

EBM BOX 43-2

*Characteristics of Moderate-to-Severe Aortic Regurgitation**

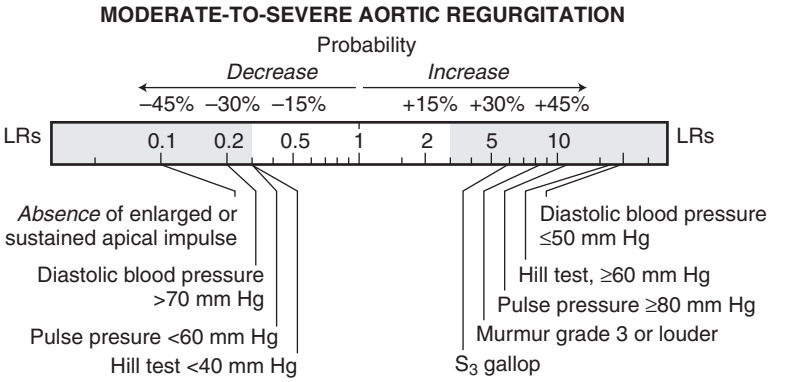
Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Diastolic Murmur				
Murmur grade 3 or louder[36,45]	30-61	86-98	**8.2**	0.6
Blood Pressure				
Diastolic Blood Pressure[33,46]				
>70 mm Hg	8-21	32-55	**0.2**	—
51-70 mm Hg	42-50	—	NS	—
≤50 mm Hg	30-50	98	**19.3**	—
Pulse Pressure[46]				
<60 mm Hg	21	32	**0.3**	—
60-79 mm Hg	21	—	NS	—
≥80 mm Hg	57	95	**10.9**	—
Hill Test[46]				
<40 mm Hg	29	13	**0.3**	—
40-59 mm Hg	29	—	NS	—
≥60 mm Hg	42	98	**17.3**	—
Other Signs				
Enlarged or sustained apical impulse[46]	97	60	2.4	**0.1**
S_3 gallop[47]	20	97	**5.9**	0.8
Duroziez sign, femoral pistol shot, water-hammer pulse[30,46]	37-55	63-98	NS	0.7

*Diagnostic standards: For *moderate-to-severe regurgitation*, regurgitation was either 3+ (moderate) or 4+ (severe) on a 0 to 4+ scale, using angiography,[33–35,39,40,46] Doppler echocardiography,[37,38,45,47] or surgery.[36] Trivial regurgitation on echocardiography was classified as "absent regurgitation."

†Definition of findings: See text.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. NS, not significant.

Click here to access calculator.



Some doubt that the Hill test is accurate, citing experiments showing the intra-arterial pressure in the *femoral arteries* of patients with aortic regurgitation to be identical to that of the brachial arteries.[48,49] The Hill test, however, measures the pressure of the pedal arteries, not the femoral arteries. It is possible that the systolic pressure is augmented in the foot, which is near the point of reflection of the abnormal pulse waveform.

4. Other Signs

The *absence* of an enlarged or sustained apical impulse *decreases* the probability of moderate-to-severe regurgitation (LR = 0.1; see EBM Box 43-2).

In one study of patients with pure aortic regurgitation, the finding of a third heart sound increased the probability of severe regurgitation (LR = 5.9). The S_3 does not reliably indicate elevated left atrial pressure in these patients, however, because regurgitation alone may accelerate early diastolic filling sufficiently to produce the sound (see Chapter 39).[50,51] The Duroziez sign, femoral pistol shots, and water-hammer pulse are all unreliable indicators of severity of regurgitation.

E. ACUTE AORTIC REGURGITATION

Compared with chronic aortic regurgitation, acute aortic regurgitation (e.g., from endocarditis or acute aortic dissection) causes a shorter murmur, faster pulse rate (108 beats/min vs. 71 beats/min, mean values), smaller pulse pressure (55 mm Hg vs. 105 mm Hg), and lower systolic blood pressures (110 mm Hg vs. 155 mm Hg).[52] The murmur of acute aortic regurgitation is shorter because the combination of low arterial pressure and very high ventricular filling pressure eliminates the pressure gradient causing regurgitation by mid-diastole.[52] The first heart sound is faint or absent in acute aortic regurgitation because of premature closure of the mitral valve (see Chapter 38).[53] In patients with aortic regurgitation from endocarditis, an associated pericardial rub often indicates extravalvular extension of the infection.[52]

F. DISTINGUISHING THE AUSTIN FLINT MURMUR FROM MITRAL STENOSIS

Based on an older analysis of 400 patients with severe aortic regurgitation, many of whom also had apical diastolic rumbles, the following findings increase the probability of associated mitral stenosis: atrial fibrillation, loud S_1, absent S_3, and opening snap. Findings suggesting that the apical rumble more likely is an Austin Flint murmur are sinus rhythm, faint S_1, S_3 gallop, and absent opening snap.[54] In addition, inhalation of amyl nitrite, which reduces systemic vascular resistance, makes the Austin Flint murmur (and the aortic regurgitation murmur) softer but the apical rumble of true mitral stenosis louder.[55]

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 44

Miscellaneous Heart Murmurs

HYPERTROPHIC CARDIOMYOPATHY

I. THE MURMUR

The murmur of hypertrophic cardiomyopathy is usually midsystolic, harsh in quality, and loudest at the lower left sternal border or between the lower left sternal border and the apex.[1] The murmur may obliterate the second heart sound and become a late systolic murmur, especially if there is associated mitral regurgitation. The intensity of the murmur behaves in distinctive ways during maneuvers altering venous return to the heart (see Chapter 41).

II. ASSOCIATED FINDINGS

The palpable apex beat may be sustained and the arterial pulse hyperkinetic (see Chapters 14 and 36). Although pulsus bisferiens has been described in hypertrophic cardiomyopathy,[2] this refers to a finding seen on intra-arterial pressure tracings, not a palpable one at the bedside.[3] The second heart sound is usually single or physiologically split, although in 10% of cases, splitting is paradoxic or reversed.[1] Over half of patients have audible fourth heart sounds.[1]

MITRAL REGURGITATION

I. THE FINDING

A. THE MURMUR

The murmur of chronic mitral regurgitation is usually holosystolic, high in frequency, and loudest at the apex.[4] It radiates to the axilla and inferior angle of the left scapula, although in some patients with isolated incompetence of the medial portion of the posterior leaflet, the murmur radiates instead to the right base and even into the neck, thus mimicking aortic stenosis.[4,5]

In 1832, James Hope was the first to describe the apical systolic murmur of mitral regurgitation.[4,6]

B. ASSOCIATED FINDINGS

In chronic mitral regurgitation, the intensity of S_1 is normal 75% of the time, loud 12% of the time, and soft 12% of the time. In 50% of patients, S_2 splitting is wide and physiologic.[4] An associated S_3 is common, appearing in 89% with severe regurgitation. S_4 is rare.

Associated cardiac findings are an enlarged, laterally displaced, palpable apical movement[7]; a palpable lower parasternal movement from an enlarged left atrium or associated tricuspid regurgitation (see Chapter 36)[8]; and, in younger patients, a hyperkinetic arterial pulse (see Chapter 14).[9] Neck veins are normal unless the patient has decompensated heart failure.

II. CLINICAL SIGNIFICANCE

A. DETECTING MITRAL REGURGITATION

The presence of the characteristic murmur of mitral regurgitation increases the probability that regurgitation is present, at least to a mild degree (likelihood ratio [LR] = 5.4; see Chapter 41). Although 25% to 50% of patients with *mild* regurgitation lack a murmur, the absence of the characteristic murmur decreases the probability of *moderate-to-severe* mitral regurgitation (LR = 0.3; see Chapter 41).

B. SEVERITY OF MITRAL REGURGITATION

1. The Murmur

In a very general way, the intensity of the murmur of mitral regurgitation correlates with the severity of regurgitation, especially for rheumatic mitral regurgitation ($r = 0.67$), but less so for ischemic or functional* mitral regurgitation ($r = 0.45$).[10–12] A mitral regurgitation murmur of grade 3 intensity or louder increases the probability of moderate-to-severe regurgitation (LR = 4.4; EBM Box 44-1).

2. Other Findings

Patients with severe mitral regurgitation may have a late-systolic sustained left-lower parasternal impulse from a dilated left atrium. (Chapter 36 discusses how to distinguish this impulse from a right ventricular impulse or atrial impulse.) The degree of this movement correlates well with the severity of regurgitation ($r = 0.93$, $p < .01$), so long as the patient does not have associated mitral stenosis. (The presence of mitral stenosis confounds analysis of the parasternal impulse of patients with mitral regurgitation because the impulse could represent either a large left atrium from severe regurgitation or a hypertensive right ventricle from mitral stenosis.[8,13])

Some studies correlate the third heart sound with severity of mitral regurgitation,[14] whereas others do not.[17] Overall, the pooled LR is not significant (see EBM Box 44-1).

*Functional mitral regurgitation implies that the primary problem is cardiomyopathy, which dilates the atrioventricular ring and renders the valve incompetent. Because of their low ejection fraction, these patients often tolerate valve replacement poorly.

C. DISTINGUISHING ACUTE FROM CHRONIC MITRAL REGURGITATION

The physical signs of acute and chronic mitral regurgitation differ in several ways. In acute lesions, patients are acutely ill with elevated neck veins and signs of pulmonary edema; in chronic lesions, these signs may be absent. In acute lesions, the pulse is rapid and regular; in chronic lesions, it is often slow and irregular (from atrial fibrillation).[18] In acute lesions, the murmur may be short and confined to early systole (40% of patients in one series) because the left atrial pressures are so high they equal ventricular pressures by mid-to-late systole and thus eliminate the regurgitation gradient[19,20]; in chronic lesions, the timing varies, although holosystolic and late systolic murmurs are most common. In acute lesions, the fourth heart sound is common (80% in one series); in chronic lesions, the fourth heart sound is rare, either because the atrial contraction is absent (i.e., atrial fibrillation) or because the atrium is so dilated it cannot contract strongly.[10,18,21]

EBM BOX 44-1
*Severity of Mitral and Tricuspid Regurgitation**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is *Present*	Likelihood Ratio‡ if Finding Is *Absent*
Detecting Moderate-to-Severe Mitral Regurgitation (in Patients with the Characteristic Murmur)				
Murmur grade 3 or louder[12]	85	81	**4.4**	**0.2**
S_3 gallop[13,14]	24-41	77-98	NS	0.8
Detecting Moderate-to-Severe Tricuspid Regurgitation				
INSPECTION OF NECK VEINS				
Early systolic outward movement (CV wave)[15]	37	97	**10.9**	0.7
PRECORDIAL AND HEPATIC PULSATIONS				
Lower sternal precordial pulsations[15]	17	99	**12.5**	0.8
Right ventricular (RV) rock[15]	5	100	**31.4**	NS
Pulsatile liver[15,16]	12-30	92-99	**6.5**	NS

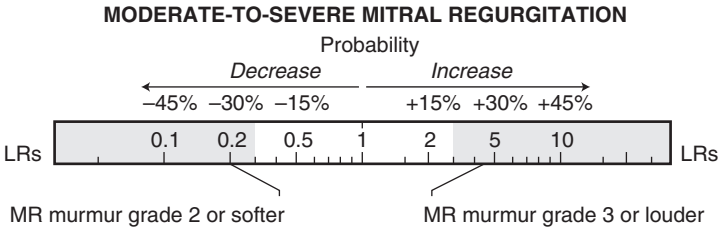
*Diagnostic standard: For *moderate-to-severe mitral regurgitation*, regurgitant fraction >40% by Doppler echocardiography[12,14] or as assessed visually from echocardiography[15] or angiography[13]; for *moderate-to-severe tricuspid regurgitation*, 3+ or 4+ by angiography[16] or as assessed visually from echocardiography.[15]

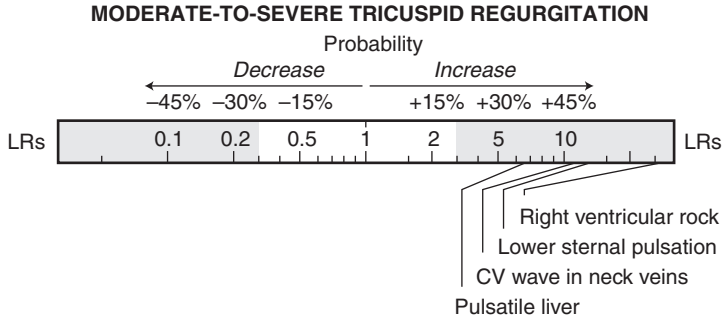
†Definition of findings: for *right ventricular rock*, see text and Chapter 36.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

NS, not significant.

Click here to access calculator.





D. PAPILLARY MUSCLE DYSFUNCTION

Papillary muscle dysfunction refers to a murmur of mitral regurgitation that develops in the setting of myocardial ischemia. The murmur, which is usually transient, may be holosystolic, midsystolic, or late systolic. It appears in up to 20% of patients with myocardial infarction,[22] in whom it is associated with a higher incidence of persistent chest pain in the intensive care unit (45% vs. 26% without murmur) and a higher 1-year mortality rate (18% vs. 10%).[22]

MITRAL VALVE PROLAPSE

I. INTRODUCTION

Mitral valve prolapse describes an abnormal posterosuperior movement of the mitral valve leaflets into the left atrium after they close at the beginning of systole. It is an important cause of late systolic murmurs and mid-to-late systolic clicks,[23–25] and, in developed nations, it is the most common cause of mitral regurgitation.[26]

At the beginning of the 20th century, most clinicians believed that late systolic murmurs were benign and that late systolic clicks were generated outside of the heart.[23,24] In 1963, Barlow[27] performed angiograms in several patients with late systolic murmurs and proved that the cause was mitral prolapse and regurgitation.

II. THE FINDINGS

A. THE MURMUR

The murmur of mitral valve prolapse is loudest at the apex and is sometimes musical (see Chapter 41). It is characteristically a late systolic murmur because the mitral leaflets are well supported by chordae tendineae and competent during early systole but lose this support as the ventricle becomes smaller during late systole, allowing the leaflets to buckle backward toward the left atrium and create a regurgitant leak.[23–25]

B. THE CLICKS

The clicks of mitral valve prolapse occur during mid-to-late systole and are loudest at the apex or left lower sternal border.[23] They are sometimes multiple. In patients with both a click and a murmur, the click introduces the murmur 65% of the time and occurs just after the beginning of the murmur 35% of the time.[23] Sudden deceleration of the billowing mitral leaflet, as it prolapses into the left atrial cavity, causes the sound, which thus resembles the sound produced by a parachute or sail that suddenly tenses as it fills with wind.[28]

C. RESPONSE OF MURMURS AND CLICKS TO MANEUVERS

Bedside maneuvers that alter venous return or afterload (i.e., systemic vascular resistance) change both the timing of the clicks and murmurs and the intensity of the murmurs, although they affect timing and intensity independently.

The *timing* of clicks and murmurs depends on the venous return to the heart (Fig. 44-1). Reductions in venous return—by straining during the Valsalva maneuver or moving from the squatting to the standing position—cause the ventricular chamber to become smaller and the mitral leaflets to prolapse earlier during systole, thus moving the click closer to S_1 and making the murmur longer.[23,25]

In contrast, the *intensity* of the murmur depends more on afterload; in this way, the response resembles that of chronic mitral regurgitation (see Chapter 41). As afterload is reduced with amyl nitrite inhalation, the murmur of mitral valve prolapse becomes fainter.[23] The Valsalva strain also usually makes the murmur *softer*. Squatting-to-standing, however, makes the murmur *louder*, perhaps because the standing position invokes sufficient sympathetic tone to preserve afterload while at the same time making ventricular contractions more vigorous, thus intensifying the sound.*[23]

III. CLINICAL SIGNIFICANCE

A. DETECTION OF MITRAL VALVE PROLAPSE

The presence of the characteristic click and murmur of mitral valve prolapse increases greatly the probability of prolapse, as detected by echocardiography (LR = 12.1; see Chapter 41). In fact, some have argued that

*Mitral valve prolapse is therefore an important cause of the false-positive result when using the squatting-to-standing maneuver to diagnose obstructive cardiomyopathy (see Chapter 41).

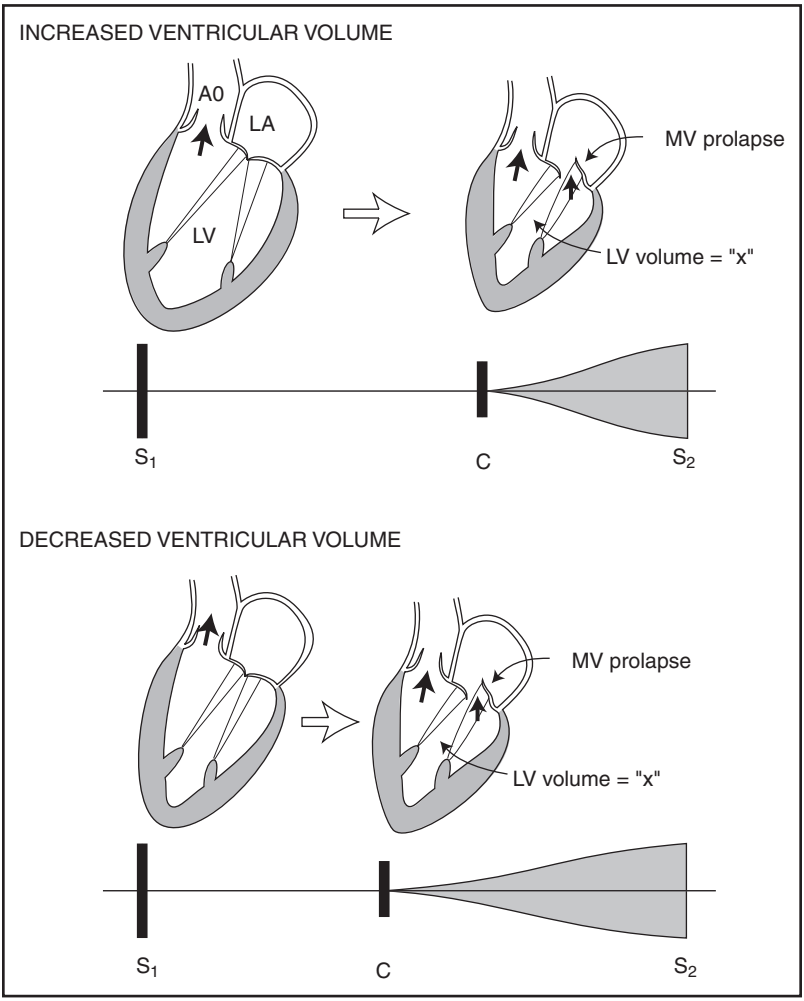


FIGURE 44-1 Timing of mitral valve prolapse. In each example, the left ventricle is ejecting blood during systole and prolapse of the mitral valve occurs at the moment ventricular volume equals "x." If ventricular systole begins with a relatively large ventricular volume *(top row)*, the ventricular volume of "x" is delayed until late systole. If ventricular systole instead begins with a smaller ventricular volume (e.g., by straining during the Valsalva maneuver or moving from a squatting to a standing position, *bottom row*), the ventricular volume of "x" is reached earlier during systole, causing the click and murmur to move toward S_1. Ao, aorta; C, click; LA, left atrium; LV, left ventricle; MV, mitral valve.

the auscultatory criteria alone are sufficient for diagnosis.[29,30] The criterion for diagnosing mitral valve prolapse is the reproducible finding in a young patient of a mid-to-late systolic click or late systolic murmur at or near the apex. These sounds should shift their timing with respect to S_1 and S_2 in response to the Valsalva and squatting-to-standing maneuvers.

(See the section on Response of Murmurs and Clicks to Maneuvers and Fig.44-1.) These criteria can only be applied to young patients; in older patients, there may be confusion with papillary muscle dysfunction, a common cause of late systolic murmurs in these patients.[29] The click should be mobile and occur in mid-to-late systole to eliminate confusion with other short systolic sounds, such as the split S_1 and aortic ejection sound. (See Chapters 39 and 40 for further differentiation of these sounds.[29,30])

B. RISK OF SIGNIFICANT MITRAL REGURGITATION

The risk of significant mitral regurgitation in mitral valve prolapse is low. In one study of 291 patients with a click or murmur presenting to a cardiologist (which biases selection toward more severe cases), none of the patients with an isolated click developed significant mitral regurgitation over 8 years of follow-up, and only 3% of those with murmurs required mitral valve replacement.[31]

TRICUSPID REGURGITATION

I. THE FINDINGS

The physical findings of tricuspid regurgitation depend on the patient's pulmonary pressure, which may be high (high-pressure tricuspid regurgitation) or normal (low-pressure tricuspid regurgitation). **High-pressure tricuspid regurgitation** is commonly due to left-sided heart disease; **low-pressure tricuspid regurgitation** commonly results from endocarditis of the tricuspid valve.

A. THE MURMUR

Whether pulmonary pressures are high or low, the murmur of tricuspid regurgitation is typically loudest at the lower left sternal border, becomes louder during inspiration, and may radiate below the xiphoid process.[32]

1. High-Pressure Tricuspid Regurgitation

The murmur of high-pressure tricuspid regurgitation is holosystolic because the elevated right ventricular pressures exceed right atrial pressures throughout systole. The murmur becomes louder during inspiration **(Carvallo sign)** in 75% of patients and during manual pressure over the liver in 60% of patients.[16,33–37]

In some patients with high-pressure tricuspid regurgitation, the murmur is loudest at the apex because the enlarged right ventricle has replaced the normal position of the left ventricle. At this location, the resulting holosystolic apical murmur resembles mitral regurgitation. In the 1950s, this fact led to the significant bedside error of misdiagnosing mitral regurgitation in some patients with mitral stenosis, thus inappropriately denying them valvuloplasty (a procedure contraindicated with severe mitral regurgitation).[38] Clues that help the clinician correctly recognize the apical holosystolic murmur as tricuspid regurgitation are the

associated findings of an identical murmur at the lower sternal border, inspiratory augmentation of the murmur, elevated neck veins, and pulsatile liver.[38]

2. Low-Pressure Tricuspid Regurgitation

If pulmonary and right ventricular pressures are normal, the murmur of tricuspid regurgitation is confined to early systole because right atrial and right ventricular pressures equilibrate by midsystole, thus eliminating the gradient causing the murmur.[39]

B. OTHER FINDINGS

1. High-Pressure Tricuspid Regurgitation

Other important cardiac findings are elevated neck veins (>90% of patients), a systolic regurgitant wave in the neck veins (51% to 83% of patients), and systolic retraction of the apical impulse (22% of patients).[16,34,36] Thirty percent to 91% of patients have a pulsatile liver, and 90% have edema or ascites, or both.[16,32,34,36] In some patients, there is an outward precordial pulsation of the lower sternum (from ejection of blood into the right atrium and liver). This sternal movement, when combined with simultaneous apical retraction (from right ventricular contraction), creates a distinctive rocking motion (i.e., the apex moves in and the lower sternum moves out at the same time), a motion called **right ventricular rock** (see Chapter 36).[15]

2. Low-Pressure Tricuspid Regurgitation

In these patients, the neck veins and apical impulse are normal. There is no edema, pulsatile liver, or ascites.

C. ESTIMATING VENOUS PRESSURE IN TRICUSPID REGURGITATION

Estimates of venous pressure are useful because they indicate right ventricular *diastolic* pressures (or filling pressures), which provide important clues to the etiology of ascites and edema (see Chapter 34). In tricuspid regurgitation, however, the neck veins characteristically reveal a large *systolic* wave, raising the question of whether bedside estimates of venous pressure still reliably indicate the right heart filling pressures.

In patients with tricuspid regurgitation (and no tricuspid stenosis), catheter measurements of the *mean* pressure in the right atrium correlate closely with right ventricular end-diastolic pressure ($r = 0.94$, $p < .001$, slope = 1).[34] Mean atrial pressure is estimated at the bedside by identifying which patient position brings out the regurgitant waves. If the regurgitant waves are visible when the patient is supine, then venous diastolic pressure must be low (i.e., the waves collapse and become visible because the diastolic venous pressure is below the level of the sternum, or low). The mean atrial pressure (i.e., central venous pressure) in these patients is probably normal. On the other hand, if the regurgitant waves are only visible in the upright position, the diastolic pressure in the veins must be high (otherwise the neck veins would collapse and be visible in lower

positions). The mean atrial and central venous pressures of these patients are probably high.

II. CLINICAL SIGNIFICANCE

A. DETECTING TRICUSPID REGURGITATION

The presence of the characteristic systolic murmur of tricuspid regurgitation increases the probability of tricuspid regurgitation (LR = 14.6; see Chapter 41). Many patients with tricuspid regurgitation, however, lack a murmur, which means that the *absence* of a murmur has less diagnostic significance (i.e., negative LRs either are not significant or are close to the value of 1; see Chapter 41).

B. SEVERITY OF TRICUSPID REGURGITATION

From palpation of the precordium or inspection of neck veins alone, the diagnosis of moderate-to-severe tricuspid regurgitation may be obvious (see EBM Box 44-1). Diagnostic findings include right ventricular rock (LR = 31.4), lower sternal pulsations (LR = 12.5), early systolic outward venous pulsation (i.e., the CV wave, LR = 10.9; see Chapter 34), and hepatic pulsations (LR = 6.5). The absence of any of these findings, however, is diagnostically unhelpful.

PULMONIC REGURGITATION

I. THE FINDING

The murmur of pulmonic regurgitation is a diastolic murmur heard best at the second left intercostal space. Its timing and frequency depend on pulmonary pressures.

A. HIGH-PRESSURE PULMONIC REGURGITATION

Sustained pulmonary hypertension may cause the pulmonic valve to become incompetent, producing an early diastolic, high-frequency murmur at the second left intercostal space. The murmur begins immediately after a loud S_2, and most patients have elevated neck vein pressure and other auscultatory findings of pulmonary hypertension, such as the pulmonary ejection sound, abnormal S_2 splitting, and right ventricular gallops (see Chapters 38 to 40).[40] Chapter 43 discusses how to distinguish this murmur from that of aortic regurgitation.

The high-pressure pulmonic regurgitation murmur was first described by the British clinician Graham Steell in 1888[41] and is often called the **Graham Steell murmur.**

B. LOW-PRESSURE PULMONIC REGURGITATION

When pulmonary pressures are normal, pulmonic regurgitation represents primary valvular disease (e.g., endocarditis). This murmur is mid-diastolic and contains a mixture of low-frequency and high-frequency sound. It begins with a short delay after S_2.[39]

II. CLINICAL SIGNIFICANCE

A. DETECTING PULMONIC REGURGITATION

Although the presence of the characteristic murmur is diagnostic (LR = 17.4; see Chapter 41), the absence of the murmur is unhelpful (LR not significant; see Chapter 41).

B. HEMODIALYSIS PATIENTS

A common cause of an early diastolic murmur at the sternal border in patients with end-stage renal disease is pulmonic regurgitation.[42] This murmur presumably occurs because of volume overload because it is loudest immediately before dialysis and often disappears just after dialysis.

MITRAL STENOSIS

I. THE FINDINGS

A. THE MURMUR

Mitral stenosis causes a low-frequency, rumbling mid-diastolic murmur, which is usually heard with the bell lightly applied to the apex, often only after the patient has turned to the left lateral decubitus position. The murmur peaks during mid diastole and again immediately before the first heart sound **(presystolic accentuation).** The mid-diastolic peak occurs because the mitral leaflets move backward toward the left atrium at this time, narrowing the mitral orifice and causing more turbulence. (An analogy is the difficulty whistling with the mouth open.[43,44]) The importance of these movements to the sound may explain why some patients with severe calcific mitral stenosis and inflexible leaflets lack murmurs.[44]

The traditional explanation for presystolic accentuation is atrial systole, but this is probably incorrect because presystolic accentuation also occurs in patients with atrial fibrillation.[45] Instead, there is some evidence that presystolic accentuation is actually caused by *ventricular* contraction: The crescendo sound occurs because the closing movement of the mitral leaflets, induced by ventricular systole, occurs when a pressure gradient is still maintaining forward flow across the valve. The sound continues and crescendos up until the moment the valves completely close, at the first heart sound. (Therefore, the "presystolic" accentuation is not presystolic at all, but instead is systolic.[43–45])

Because the sound vibrations of mitral stenosis border on the threshold of human hearing, this murmur is indistinct and the most difficult to detect, as reflected in descriptions of the sound as "the faint sound of distant thunder," "the rumbling sound of a ball rolling down a bowling alley," and "the absence of silence."[46]

B. OTHER CARDIAC FINDINGS

Other cardiac findings in mitral stenosis include an irregular pulse (atrial fibrillation), loud first heart sound, opening snap (early diastolic sound), and associated findings of pulmonary hypertension, including elevated

neck veins with an exaggerated A wave, a right ventricular parasternal impulse, and a palpable P_2 (see Chapters 34, 36, and 38).[9] The palpable apical impulse is small or absent because of obstruction of blood flow into the left ventricle.[9]

II. CLINICAL SIGNIFICANCE

A. THE MURMUR

Mitral stenosis has become a rare diagnosis in developed countries, where the characteristic apical diastolic rumble instead may reflect another disorder, such as mitral annular calcification, Austin Flint murmur, atrial myxoma, or flow rumbles (i.e., increased flow over a nonobstructed mitral valve from mitral regurgitation, ventricular septal defect, or high output states; see Chapter 39). In one study of 529 elderly patients living in the United States, an apical diastolic rumble detected *mitral annular calcification* on echocardiography with a sensitivity of 10%, specificity of 99%, and positive LR of 7.5. (Ninety percent of patients with this murmur had *no* mitral stenosis.[47])

B. OTHER CARDIAC FINDINGS

In patients with mitral stenosis, the apical impulse should be absent or small and the arterial pulse should be normal or reduced. Consequently, the finding of a hyperkinetic apical movement in patients with mitral stenosis suggests additional mitral or aortic regurgitation (LR = 11.2; EBM Box 44-2) and the finding of a hyperkinetic arterial pulse strongly suggests additional mitral regurgitation (LR = 14.2; see EBM Box 44-2).

ARTERIOVENOUS FISTULA: THE HEMODIALYSIS FISTULA

The hemodialysis fistula provides a good example of the continuous murmur typical of arteriovenous fistulas: It is a high-frequency murmur, persisting throughout systole and diastole and peaking during late systole:

PuSHSHSHSH**Pu**SHSHSHSHSHSHSH

Venous hums, in contrast, peak during diastole (see Chapter 41). Moving the stethoscope progressively away from the fistula and toward the heart makes the diastolic component of the murmur fainter until only a systolic murmur remains.[49]

The importance of this murmur is that its systolic remnants are transmitted to the upper sternal border, where they can be mistaken for cardiac murmurs unless the clinician traces them to the fistula (see "Isolated Base" murmur pattern in Fig. 41-1).[49]

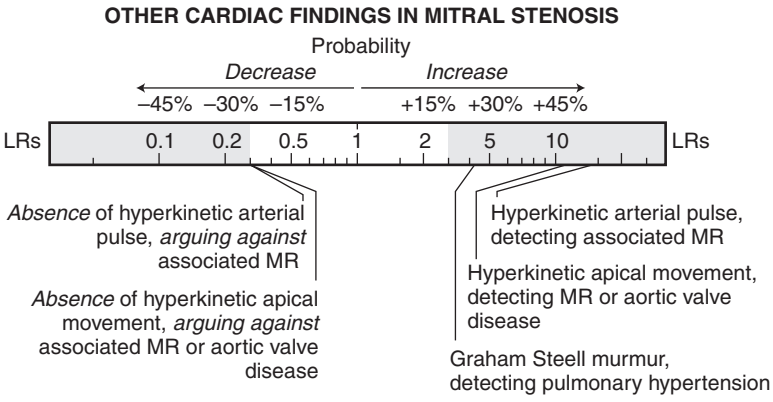
EBM BOX 44-2
*Other Cardiac Findings in Mitral Stenosis**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Graham Steell Murmur				
Detecting pulmonary hypertension[48]	69	83	**4.2**	0.4
Hyperkinetic Apical Movement				
Detecting associated mitral regurgitation or aortic valve disease[9]	74	93	**11.2**	**0.3**
Hyperkinetic Arterial Pulse				
Detecting associated mitral regurgitation[9]	71	95	**14.2**	**0.3**

*Diagnostic standard: For *pulmonary hypertension*, mean pulmonary pressure >50 mm Hg.[48]

†Definition of findings: For *Graham Steell murmur*, early diastolic decrescendo murmur of high-pressure pulmonic regurgitation at second left intercostal space; for *hyperkinetic apical movement*, apical "thrust" (see Chapter 36)[9]; for *hyperkinetic pulse*, arterial pulse strikes fingers abruptly and strongly (see Chapter 14).

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. *Click here to access calculator.*



The references for this chapter can be found on www.expertconsult.com.

CHAPTER 45

Disorders of the Pericardium

PERICARDITIS AND THE PERICARDIAL RUB

I. INTRODUCTION

The **pericardial rub** is a physical sign of **pericarditis,** or inflammation of the pericardium, which is caused by a wide variety of disorders, including infections, connective tissue diseases, myocardial infarction, neoplasia, uremia, and trauma.

In the 1820s, shortly after the introduction of the stethoscope, Collin first described the pericardial rub as a sound "similar to that of the crackling of new leather."[1]

II. THE FINDING

Pericardial rubs are grating, scratching, or creaking sounds that are loudest near the left sternal border and are most apparent when the patient is sitting upright, leaning forward, and holding his or her breath in deep expiration.[2,3] The sound is like two pieces of sandpaper being rubbed together. Compared with heart murmurs, the pericardial rub has more high-frequency energy and sounds closer to the ear,[2] it may completely disappear during inspiration or expiration, and up to one fourth are palpable.[3,4]

In about 50% of patients, the rub has three components per cardiac cycle—one during ventricular systole and two during diastole (mid-diastole and atrial systole).* In about one third of patients, only two components are heard (usually, the atrial and ventricular systolic components of the rub), and, in the remaining 15%, only a single-component ventricular systolic rub is heard.[3]

III. CLINICAL SIGNIFICANCE

A. THE RUB AND PERICARDITIS

Because the diagnosis of pericarditis relies on bedside criteria, one of which is the rub, the diagnostic accuracy of the rub cannot be assessed. The other two criteria for pericarditis are the characteristic pericardial chest pain (precordial pleuritic pain radiating to the trapezius ridge, which is relieved when the patient is sitting up) and the characteristic electrocardiographic

*These three components represent the three moments in the cardiac cycle when the ventricle is moving the most.

changes (diffuse concave ST elevation, PR segment depression, absence of Q waves).[5,6] Most clinical studies of pericarditis require two of these three criteria. Echocardiographic findings are not criteria for pericarditis, because only half of patients with pericarditis have detectable pericardial effusions.[5,6]

B. THE RUB AND PERICARDIAL EFFUSION

Although the pericardial rub suggests the rubbing together of contiguous pericardial surfaces, the sound often persists after accumulation of significant pericardial effusions.[3,7] The rub is heard, for example, in up to one fourth of patients with cardiac tamponade (see later). The *presence* of the rub, therefore, cannot be used to argue *against* the development of pericardial effusion.

C. THE RUB AND NEOPLASTIC DISEASE

In patients with known cancer who subsequently develop pericardial disease, the presence of a rub increases the probability that the pericarditis is idiopathic or radiation induced, not neoplastic (sensitivity 62%, specificity 89%, positive LR = 5.5, negative LR = 0.4).[8]

D. THE RUB AND MYOCARDIAL INFARCTION

A pericardial rub is found in 5% to 20% of patients with acute myocardial infarction, usually appearing between hospital days 1 and 3.[9–13] The incidence is lowest (i.e., 5% to 7%) in patients receiving immediate thrombolytic medications or angioplasty.[11,13] Compared with patients who do not develop rubs, patients with rubs have significantly larger myocardial infarctions, lower ejection fractions, more extensive coronary artery disease, and more complications, including congestive heart failure and atrial arrhythmias.[9,11,12] In these patients, however, tamponade is rare, even if they receive thrombolytic medications.[11]

CARDIAC TAMPONADE

I. INTRODUCTION

Cardiac tamponade occurs when a pericardial effusion has become so large and tense that intrapericardial pressures exceed normal filling (i.e., diastolic) pressures of the heart, thus impairing diastolic filling of the heart and reducing cardiac output.

The history of diagnosing tamponade illustrates well the tension that sometimes exists between older diagnostic standards based on physical signs and newer ones based on clinical imaging. For example, early descriptions of tamponade, which were based on catastrophic acute intrapericardial hemorrhage, emphasized hypotension, elevated neck veins, and the small, quiet heart as diagnostic findings **(Beck triad).**[14,15] Later, after it became obvious that many medical patients with tamponade had normal blood pressure and loud heart tones, the definition of tamponade shifted

to emphasize large pericardial effusions, elevated neck veins, pulsus paradoxus, and relief of symptoms and signs after pericardiocentesis.[16] Finally, in the 1980s, several echocardiographic criteria for tamponade were introduced,[15,17] although studies have subsequently shown that relying solely on these criteria sometimes identifies patients who fail to improve symptomatically or physiologically after pericardiocentesis.[18–20]

The diagnosis of tamponade, therefore, should not rely solely on the echocardiographic report but requires synthesis of all the findings, emphasizing especially the ones from the physical diagnosis—elevated neck veins, tachycardia, and pulsus paradoxus.[21]

II. THE FINDINGS

Table 45-1 presents the physical signs observed in several studies of patients with proven cardiac tamponade; most patients present with shortness of breath.[16,25] The definition and pathogenesis of pulsus paradoxus and elevated neck veins are discussed in Chapters 14 and 34.

The three key findings of tamponade are elevated neck veins (100% of patients), tachycardia (81% to 100% of patients), and pulsus paradoxus

TABLE 45-1 Cardiac Tamponade*

Physical Finding†	Frequency (%)‡
NECK VEINS	
Elevated neck veins	100
Kussmaul sign	0
ARTERIAL PULSE	
Tachycardia (>100 beats/min)	81-100
BLOOD PRESSURE	
Systolic blood pressure >100 mm Hg	58-100
Pulsus paradoxus >10 mm Hg	98
Pulsus paradoxus >20 mm Hg	78
Pulsus paradoxus >30 mm Hg	49
Pulsus paradoxus >40 mm Hg	38
Total paradox	23
AUSCULTATION OF HEART	
Diminished heart tones	36-84
Pericardial rub	27
OTHER FINDINGS	
Hepatomegaly	58
Edema	27

*Diagnostic standard: For *tamponade,* cardiac output improved after drainage of pericardial effusion.
†Definition of finding: For *total paradox,* palpable pulse disappears completely during inspiration.
‡Results are overall mean frequency or, if statistically heterogeneous, the range of values.
Data from 121 patients from references 16 and 22 to 25.

of more than 10 mm Hg (98% of patients). In patients with pericardial effusions, the finding of pulsus paradoxus of more than 12 mm Hg detects tamponade with a sensitivity of 98%, specificity of 83%, positive LR of 5.9, and negative LR of 0.03 (see Chapter 14).[26]

Cardiac tamponade is one of the few causes of elevated neck veins with an absent *y* descent (see Chapter 34). This finding contrasts sharply with the exaggerated *y* descent of constrictive pericarditis (see later).

CONSTRICTIVE PERICARDITIS

I. INTRODUCTION

Constrictive pericarditis is present when calcification or fibrosis of the pericardium impairs diastolic filling, thus causing elevated venous pressure and reduced cardiac output.

II. THE FINDINGS

Table 45-2 presents the physical signs of patients with constrictive pericarditis; most patients present with edema, abdominal swelling, and dyspnea.[31,32,35] The key physical findings are elevated neck veins (98%), prominent *y* descent in venous waveform (57% to 100%), pericardial knock (28% to 94%), and hepatomegaly (87% to 100%).

A. NECK VEINS

In addition to elevated venous pressure, the venous waveform displays an unusually prominent *y* descent, which combined with an exaggerated *x′* descent creates two conspicuous dips per cardiac cycle, making the waveform appear to trace an M or W with each arterial pulse (**Friedreich sign**; see Chapter 34). These movements are sometimes transmitted to the liver, causing it to pulsate inward twice with each cardiac cycle.[36]

The prominent *y* descent occurs because diastolic filling is only impaired during the last two thirds of diastole. At the moment the tricuspid valve opens (beginning of diastole and beginning of *y* descent), the right atrium empties rapidly and without resistance (causing a prominent *y* descent), although eventually the relaxing ventricle meets the limits of the rigid pericardial shell and pressures again increase.[37] This contrasts with tamponade, which impairs diastolic filling throughout diastole and thus eliminates the *y* descent.

B. KUSSMAUL SIGN

The Kussmaul sign is the paradoxic increase in venous pressure during inspiration. This sign, present in 50% of patients with constriction, is discussed fully in Chapter 34. A video of the Kussmaul sign has been published by Koruth and others.[38]

TABLE 45-2 Constrictive Pericarditis*

Physical Finding	Frequency (%)†
NECK VEINS	
Elevated neck veins	98
Prominent y descent (Friedreich sign)	57-100
Kussmaul sign	50
ARTERIAL PULSE	
Irregularly irregular (atrial fibrillation)	36-70
BLOOD PRESSURE	
Pulsus paradoxus >10 mm Hg	17-43
AUSCULTATION OF HEART	
Pericardial knock	28-94
Pericardial rub	3
OTHER FINDINGS	
Hepatomegaly	87-100
Edema	63
Ascites	53-89

*Diagnostic standard: For *constrictive pericarditis*, surgical and postmortem findings,[22,27,28,31] sometimes in combination with hemodynamic findings.[29,30,32–34]
†Results are overall mean frequency or, if statistically heterogeneous, the range of values.
Data from 331 patients from references 22 and 27 to 34.

C. PERICARDIAL KNOCK

The pericardial knock is a loud, high-frequency early diastolic sound heard between the apex and the left lower sternal border. It is discussed in Chapter 40.

D. OTHER FINDINGS

Up to 90% of patients with constrictive pericarditis have systolic retraction of the apical impulse (see Chapter 36).[33,39]

According to traditional teachings, pulsus paradoxus is not a finding of constrictive pericarditis, yet the studies reviewed in Table 45-2 indicate that pulsus paradoxus does appear, occurring in 17% to 43% of patients with constrictive pericarditis.[22,27,32,35] This seeming contradiction probably reflects different definitions of pulsus paradoxus. When pulsus paradoxus is defined as an inspiratory fall in systolic blood pressure of more than 10 mm Hg (i.e., the usual definition), 17% to 43% of patients with constriction have the finding[22,35]; when it is instead defined as an inspiratory fall of more than 20 mm Hg, no patient has the finding.[22] In contrast, the usual pulsus paradoxus in patients with tamponade is 20 to 50 mm Hg (see Table 45-1).[16]

Mild degrees of pulsus paradoxus (10 to 20 mm Hg) are therefore commonly observed in patients with constrictive pericarditis, but larger degrees (>20 mm Hg) are not, and their presence suggests tamponade or another cause of the finding (see Chapter 14).

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 46

Congestive Heart Failure

I. INTRODUCTION

Heart failure is a clinical syndrome characterized by impaired ventricular performance, elevated diastolic filling pressures, and diminished exercise capacity. Patients with heart failure and ventricular disease may have a low ventricular ejection fraction (systolic dysfunction) or normal ejection fraction (diastolic dysfunction).

Clear descriptions of the signs of heart failure date to the Middle Ages.[1] In the 17th century, just after Harvey published his discovery of the circulation of blood, clinicians began to correlate the pathologic observation of large heart chambers and congested lungs with the clinical observations of dyspnea and edema.[2]

II. THE FINDINGS

Many of the findings of heart failure are discussed fully in other chapters of the book, including pulsus alternans and the dicrotic pulse (Chapter 14), Cheyne-Stokes respirations (Chapter 18), crackles (Chapter 28), elevated neck veins (Chapter 34), the abdominojugular test (Chapter 34), the displaced apical impulse (Chapter 36), and the third heart sound (Chapter 39).

This chapter reviews one finding not discussed extensively elsewhere, the abnormal Valsalva response, and then presents the diagnostic accuracy of all findings of congestive heart failure.

III. THE VALSALVA RESPONSE

A. INTRODUCTION

The **Valsalva maneuver** consists of forced expiration against a closed glottis after a full inspiration.[3] The **Valsalva response** refers to the changes in blood pressure and pulse that occur during both the strain phase of the maneuver and the recovery period after the strain is released.

Valsalva introduced his maneuver in 1704 as a technique to expel pus from the middle ear.[3–5] The maneuver was forgotten, however, until 1859, when Weber showed he could use it to interrupt his arterial pulse at will (an experiment he eventually abandoned after fainting and developing convulsions).[4] Beginning in the 1950s, many different investigators reported that the Valsalva response was distinctly abnormal in patients with congestive heart failure.[6–10]

B. TECHNIQUE

To perform the maneuver, the patient should take a deep breath in and bear down, as if straining to have a bowel movement. The clinician measures the Valsalva response by using a blood pressure cuff, as described later. In clinical studies, the straining phase is standardized by having the patient's mouthpiece connected to a pressure transducer, which should demonstrate an increment of 30 to 40 mm Hg for at least 10 seconds.

The Valsalva maneuver is contraindicated in patients with recent eye or central nervous system surgery or hemorrhage. It is also unwise to perform the maneuver in patients with acute coronary ischemia because it may induce arrhythmias, although in patients with chronic ischemic heart disease, the maneuver is safe and was once even used to terminate episodes of angina.[11]

C. THE NORMAL VALSALVA RESPONSE

The normal Valsalva response is divided into four phases (Fig. 46-1).[3] In phase 1, the arterial systolic blood pressure rises briefly because increased intrathoracic pressure is transmitted directly to the aorta. In phase 2, the blood pressure falls because of reduced venous return during continuing straining. In phase 3, just after release of straining, the pressure falls further because of temporary pooling of blood in the pulmonary veins. In phase 4, the arterial pressure overshoots to levels above the control values, primarily because of reflex sympathetic activity induced by previous hypotension. The changes in heart rate are exactly out of phase with the blood pressure: The heart rate increases during phases 2 and 3 and decreases during phase 4.

The clinician identifies these four phases by inflating the blood pressure cuff on the patient's arm 15 mm Hg higher than the patient's resting systolic blood pressure and maintaining this cuff pressure during the straining phase and for 30 seconds afterward, while at the same time listening for Korotkoff sounds just as if measuring the blood pressure. Korotkoff sounds appear whenever the patient's systolic pressure exceeds the cuff pressure. During the normal Valsalva response, therefore, Korotkoff sounds appear during phases 1 and 4 but are absent during phases 2 and 3.

D. THE ABNORMAL VALSALVA RESPONSE (see Fig. 46-1)

In patients with congestive heart failure, there are two abnormal Valsalva responses:

1. **Absent phase 4 overshoot,** in which the arterial pressure fails to rise during phase 4 (Korotkoff sounds during phase 1 only)
2. **Square wave response,** in which the arterial pressure rises in parallel with intrathoracic pressure (Korotkoff sounds during phases 1 and 2 only)

In all three interpretable responses—normal, absent phase 4 overshoot, and square wave response—Korotkoff sounds appear during phase 1. If sounds do not appear during this phase, the intrathoracic pressure did not increase to high enough levels during the maneuver, and the test is therefore *not* interpretable.

β-blocker medications may cause a false-positive response, primarily by eliminating the phase 4 overshoot.[12]

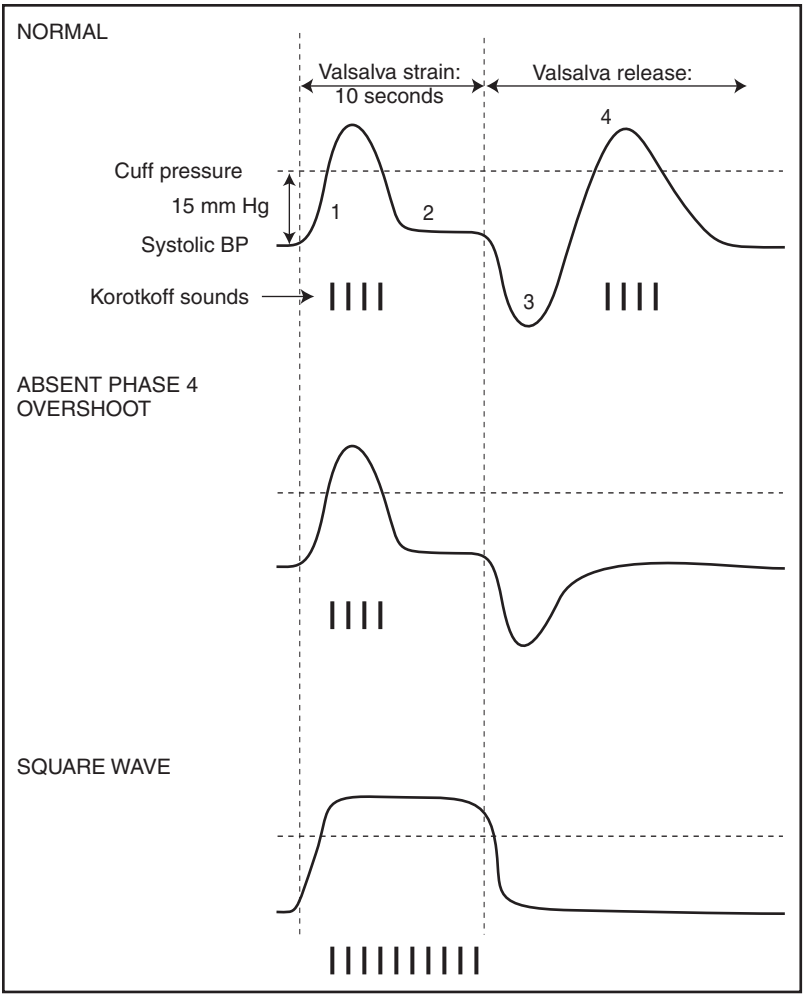


FIGURE 46-1 The Valsalva response. The *solid line* in each drawing depicts changes in systolic blood pressure over time during the Valsalva maneuver. The three types of Valsalva responses are normal *(top),* absent phase 4 overshoot *(middle),* and square wave *(bottom).* The clinician distinguishes these responses by inflating the blood pressure cuff 15 mm Hg above the patient's resting systolic blood pressure *(horizontal dotted line)* and listening for Korotkoff sounds. Korotkoff sounds appear in phases 1 and 4 in the normal response, in phase 1 only in the absent phase 4 overshoot response, and in phases 1 and 2 only in the square wave response. See text.

E. PATHOGENESIS OF THE ABNORMAL VALSALVA RESPONSE

In patients with congestive heart failure, Korotkoff sounds fail to appear during phase 4 because the weakened heart cannot increase cardiac output in response to hypotension. (There is a direct relationship between the degree of overshoot and the patient's ejection fraction; $r = 0.72$.[12]) Although the

cause of the square wave response is still debated, it probably represents the combined effect of neurohormonal activation, peripheral venoconstriction, and increased central blood volume.[8,9,13,14] Phase 2 hypotension may not occur because (1) increased central venous blood volume maintains venous return to the right heart despite the Valsalva strain and (2) the congested lungs have an ample supply of blood for the left heart.*

IV. CLINICAL SIGNIFICANCE

EBM Boxes 46-1 and 46-2 present the diagnostic accuracy of physical signs for congestive heart failure. EBM Box 46-1 refers to the diagnosis of elevated left heart filling pressures and therefore applies to the diagnosis of systolic or diastolic dysfunction. The ability to accurately detect elevated left heart filling pressures is especially important in patients with dyspnea because elevated pressures implicate the heart as the cause of the patient's symptoms. EBM Box 46-2 refers to the diagnosis of a depressed left ventricular ejection fraction and therefore applies only to the diagnosis of systolic dysfunction.

This information should only be applied to patients similar to those enrolled in the studies cited in EBM Boxes 46-1 and 46-2. These patients were all adults presenting to clinicians primarily for evaluation of chest pain or dyspnea. Most had no prior history of congestive heart failure, and many had alternative explanations for dyspnea, such as lung disease.

A. DETECTING ELEVATED LEFT HEART FILLING PRESSURES

In descending order of their likelihood ratios [LRs], the findings *increasing* the probability of elevated filling pressures the most are a positive abdominojugular test (LR = 8; see EBM Box 46-1), abnormal Valsalva response (i.e., either absent phase 4 overshoot or square wave response, LR = 7.6), displaced apical impulse (LR = 5.8), tachycardia (LR = 5.5), third heart sound (LR = 3.9), and elevated venous pressure (LR = 3.9). The findings of a normal Valsalva response (LR = 0.1) and *negative* abdominojugular test (LR = 0.3) *decrease* the probability of elevated left-heart filling pressures. The *absence* of tachycardia, elevated venous pressure, displaced apical impulse, or S_3 gallop is diagnostically unhelpful (LRs not significant).

Because the pulse rate during the Valsalva maneuver is exactly out of phase with the blood pressure changes, the pulse rate should accelerate during phases 2 and 3 of the normal response (i.e., when the systolic blood pressure is falling; see Fig 46-1). In one study, the finding of pulse acceleration during Valsalva strain (i.e., increase in rate of 10%, as detected by rhythm strips) *decreased* the probability of elevated filling pressure (LR = 0.2; see EBM Box 46-1).

The presence of crackles, a fourth heart sound, or edema does not indicate elevated left heart filling pressures in these patients. Crackles are

*The same pathophysiologic characteristics probably explain the finding of reversed pulsus paradoxus in some patients with congestive heart failure receiving positive-pressure ventilation (see Chapter 14).

unhelpful because they are infrequent in chronic heart failure and because many other disorders causing dyspnea also produce crackles. If the finding of crackles is instead applied just to patients with known cardiomyopathy (e.g., those awaiting cardiac transplantation), it becomes a more accurate sign of elevated filling pressure, detecting pulmonary capillary wedge pressures of 20 mm Hg or higher with a sensitivity of 19% to 64%, specificity of 82% to 94%, and positive LR of 3.4. The finding is more accurate in this setting, probably because other diagnoses causing crackles have already been excluded.[19,33,34]

EBM BOX 46-1

*Congestive Heart Failure—Elevated Left Heart Filling Pressures**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Vital Signs				
Heart rate >100 beats/min at rest[15]	6	99	**5.5**	NS
Abnormal Valsalva response[16]	95	88	**7.6**	**0.1**
Pulse increase of ≥10% during Valsalva strain[17]	11	54	**0.2**	1.7
Lung Examination				
Crackles[12,15,18,19]	12-23	88-96	NS	NS
Heart Examination				
Elevated jugular venous pressure[12,15,19]	10-58	96-97	**3.9**	NS
Positive abdominojugular test[19–21]	55-84	83-98	**8.0**	**0.3**
Supine apical impulse lateral to MCL[18]	42	93	**5.8**	NS
S_3 gallop[12,15,18,22]	12-37	85-96	**3.9**	0.8
S_4 gallop[12,23]	35-71	50-70	NS	NS
Other Findings				
Edema[12,15]	10	93-96	NS	NS

*Diagnostic standard: For *elevated left heart filling pressures*, pulmonary capillary wedge pressure >12 mm Hg[18] or >15 mm Hg,[16,19–21] or left ventricular end diastolic pressure >15 mm Hg[12,15,22,23] or >18 mm Hg.[17]

†Definition of findings: For *abnormal Valsalva response*, absent phase 4 overshoot or square wave response (see text); for *positive abdominojugular test*, sustained rise in jugular venous pressure during 10 to 15 seconds of midabdominal pressure (see Chapter 34).

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. MCL, midclavicular line; NS, not significant.

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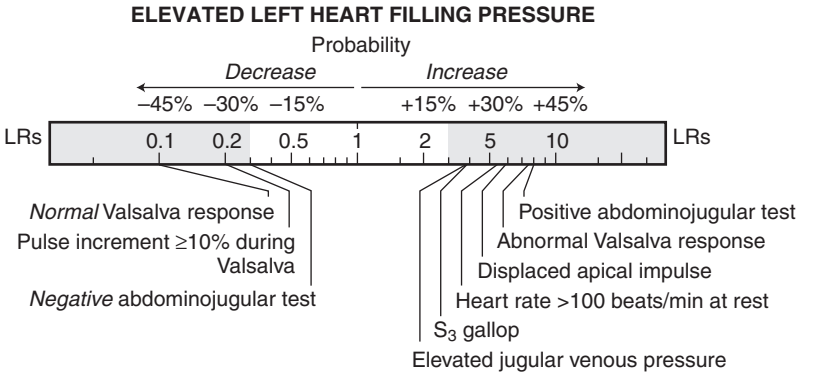

EBM BOX 46-2

*Congestive Heart Failure—Low Ejection Fraction**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Vital Signs				
Heart rate >100 beats/min at rest[24]	22	92	2.8	NS
Abnormal Valsalva response[25,26]	69-88	90-91	**7.6**	**0.3**
Lung Examination				
Crackles[24,27–29]	10-29	77-98	NS	NS
Heart Examination				
Elevated neck veins[24,27,29]	7-25	96-98	**6.3**	NS
Supine apical impulse lateral to MCL[24,27–29]	5-66	93-99	**10.3**	0.7
S_3 gallop[22,27,28,30,31]	11-51	85-98	**3.4**	0.7
S_4 gallop[23,32]	31-67	55-68	NS	NS
Murmur of mitral regurgitation[28]	25	89	NS	NS
Other Findings				
Hepatomegaly[27]	3	97	NS	NS
Edema[27,29,31]	8-33	70-98	NS	NS

*Diagnostic standards: For *low ejection fraction*, radionuclide left ventricular ejection fraction <0.50[25,26,28,30] or <0.53,[27] ejection fraction <0.50 by echocardiography,[22,23,29,31,32] or left ventricular fractional shortening <25% by echocardiography.[24]

†Definition of findings: For *abnormal Valsalva response*, absent phase 4 overshoot or square wave response (see text).

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. MCL, midclavicular line; NS, not significant.

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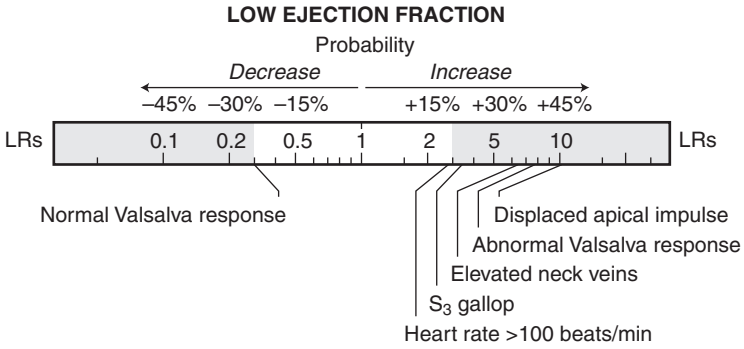

A small instrument similar to a digital pulse oximeter has been designed that measures and records the pulse pressure during the Valsalva maneuver.[35] This instrument calculates the **pulse amplitude ratio,** which is the ratio of the pulse pressure at the end of phase 2 divided by that at the beginning of phase 1. Patients with a normal Valsalva response have a low pulse amplitude ratio (because pulse pressure at the end of phase 2 is much less than that at the beginning of phase 1), whereas those with the square wave response have a higher ratio (near the value of 1). Several studies have shown a direct relationship between the pulse amplitude ratio and the pulmonary capillary wedge pressure (r = 0.81 to 0.92).[14,35–38] In one study, a pulse amplitude ratio or more than 0.7 detected a measured pulmonary capillary wedge pressure of more than 15 mm Hg with a sensitivity of 91%, specificity of 95%, positive LR of 18.2, and negative LR of 0.1,[37] and in another study of elderly patients with heart failure, an elevated pulse amplitude ratio was an independent predictor of the mortality rate.[39]

B. DETECTING DEPRESSED LEFT VENTRICULAR EJECTION FRACTION

Some of the same signs that detect elevated filling pressures also indicate a depressed ejection fraction: displaced apical impulse (LR = 10.3; see EBM Box 46-2), abnormal Valsalva response (either absent phase 4 overshoot or square wave response, LR = 7.6; see EBM Box 46-2), elevated neck veins (LR = 6.3), and third heart sound (LR = 3.4). The *absence* of any of these findings (excepting the Valsalva response) is diagnostically unhelpful (i.e., many patients with ejection fractions <50% lack these findings). Nonetheless, the absence of the third heart sounds does decrease the probability of an ejection fraction of less than 30% (LR = 0.3; see Chapter 39).[28,30]

Some investigators believe that the abnormal Valsalva response is primarily a sign of elevated filling pressure, not a low ejection fraction, citing data correlating the degree of Valsalva abnormality with the left atrial pressure (r = 0.77, p = .005) but not the ejection fraction.[16,35,40] This apparent contradiction may reflect the varying prevalence of diastolic dysfunction in different investigators' practices. Assuming that the sign is primarily one of

elevated filling pressures, it will therefore also be a good sign of a depressed ejection fraction if most patients with heart failure in the clinician's practice have systolic dysfunction (see EBM Box 46-2),[25,26] but it will not predict the ejection fraction if there is a mixture of patients with systolic and diastolic dysfunction.[16,35,40]

Several findings provide no useful diagnostic information when assessing the patient's ejection fraction: crackles, murmur of mitral regurgitation, hepatomegaly, or edema (all LRs not significant; see EBM Box 46-2).

C. PROPORTIONAL PULSE PRESSURE

In patients with known dilated cardiomyopathy and severe left ventricular dysfunction, a proportional pulse pressure (i.e., arterial pulse pressure divided by systolic blood pressure) of less than 0.25 detects a low cardiac index (i.e., ≤2.2 L/min/m^2) with a sensitivity of 70% to 91%, specificity of 83% to 93%, positive LR of 6.9, and negative LR of 0.2.[34,41]

D. PHYSICAL SIGNS AND CONSENSUS DIAGNOSIS OF CONGESTIVE HEART FAILURE

Recent investigations[42–49] into the diagnostic accuracy of B-type natriuretic peptide in patients with acute dyspnea have further addressed the value of the physical examination. In contrast to the studies in EBM Boxes 46-1 and 46-2, however, these studies used expert judgment as the diagnostic standard for heart failure, based on the retrospective review of the patient's presenting findings, laboratory tests, and responses to treatment. These studies confirm the value of the third heart sound (LR = 6.9) and elevated neck vein pressure (LR = 4.8), with both findings surprisingly increasing the probability of heart failure more than a B-type natriuretic peptide level of 100 pg/mL or higher (LR = 3.6). Nonetheless, in these same studies a B-type natriuretic peptide level of less than 100 pg/mL decreases the probability of the consensus diagnosis of heart failure (LR = 0.1) far more than the *absence* of a third heart sound or elevated neck vein pressure (LR 0.7 to 0.9).

Because it is possible that judgments about final diagnosis in these studies were influenced by the physical findings themselves, they are excluded from the EBM boxes.

E. PROGNOSIS IN HEART FAILURE

In patients with clinically suspected ischemic heart disease, the physical signs of heart failure are independent predictors of the mortality rate, adding prognostic information to that already provided by the patient's age, exercise capacity, and measured ejection fraction.[50,51] The 1-year cardiac mortality rate is higher for those with a displaced apical impulse (39% vs. 12% without the finding; p = .005) or a third heart sound (57% vs. 14% without the finding; p = .002).[18]

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 47

Coronary Artery Disease

I. INTRODUCTION

Coronary disease is the leading cause of heart disease and death in the United States,[1] and chest pain accounts for 8% to 10% of complaints of patients presenting to clinics or emergency departments.[2–4] The bedside diagnosis of chest pain is difficult and at times humbling, as illustrated by the fact that up to 1% to 8% of patients with myocardial infarction (confirmed by cardiac biomarkers) are misdiagnosed and then discharged and sent home from emergency departments.[5–10] The focus of this chapter is to identify all aspects of the initial patient encounter—patient interview, physical examination, and electrocardiographic studies—that help distinguish patients with angina and myocardial infarction from those with mimicking disorders.

The first clear description of **angina pectoris** was given in 1768 by William Heberden, who coined the term* and provided a clinical description that has been unsurpassed. Just 8 years later, Edward Jenner linked angina to "ossification" of the coronary arteries and insufficient coronary blood flow,[11] and in 1878 (>50 years before the introduction of electrocardiography), Adam Hammer diagnosed correctly the first case of **myocardial infarction** during life in a young man with sudden collapse, bradycardia, and enfeebled heart tones.[12,13] Coronary disease was once considered to be an uncommon disorder—the great 19th century American cardiologist Austin Flint found only seven cases of angina in his clinical records,[14] and Osler personally observed only 40 cases during his career.[11]

II. THE FINDINGS

A. INTRODUCTION

Unlike other clinical problems in cardiology, such as valvular disease and heart failure, patients with coronary artery disease have few or no physical findings. For over 100 years, the most important aspect of diagnosing coronary disease has been the patient's description of chest pain, whereas the most important element in diagnosing myocardial infarction (at least since 1918) has been the electrocardiogram.

*Heberden based the term *angina* on the Greek *agkhone*, which means "strangling." This Greek root also forms the basis for the English words *anxiety* and *anguish*. Heberden's selection of *angina* was unfortunate, because the term had already been applied to other conditions of the throat, such as Vincent *angina* and Ludwig *angina*.

B. DESCRIPTION OF CHEST PAIN

Heberden wrote that **angina** is a "most disagreeable sensation in the breast" that seizes patients "while they are walking" yet vanishes "the moment they stand still."[15] Modern definitions of **typical angina** retain most of Heberden's essential features, by defining it as substernal discomfort with three characteristics:

1. It is precipitated by exertion.
2. It is improved by rest or nitroglycerin (or both).
3. It lasts less than 10 minutes.

(Many patients also describe radiation of the pain to the shoulders, jaw, or inner aspect of the arm.) In contrast, **atypical angina** is substernal discomfort with atypical features (e.g., it is not always relieved by nitroglycerin, not always brought on by exertion, or not relieved after 15 to 20 minutes of rest), and **nonanginal chest pain** lacks all features of typical angina (i.e., it is unrelated to activity, unrelieved by nitroglycerin, or otherwise not suggestive of angina).

C. HAND GESTURES DURING DESCRIPTION OF CHEST PAIN

According to traditional teachings, patients provide diagnostic clues to the physician by the hand gestures they spontaneously make when describing their chest pain. Four of these gestures are:

1. **Levine sign**—placing a clenched fist against the sternum
2. **Palm sign**—placing the extended palm against the sternum
3. **Arm sign**—gripping the left arm
4. **Pointing sign**—pointing to a single point on the chest with one or two fingers[16]

According to traditional teachings, gestures suggesting deep, poorly localized visceral pain (Levine and palm signs) or pain radiating to the left arm (arm sign) increase the probability of coronary disease, whereas gestures indicating well-localized somatic pain (pointing sign) decrease the probability of disease.

D. PHYSICAL FINDINGS

Some of the findings that appear in EBM Boxes 47-1 and 47-2 are discussed in other chapters: crackles (Chapter 28), displaced precordial pulsation (Chapter 36), and the third heart sound (Chapter 39).

1. Earlobe Crease

The **earlobe crease** is a diagonal crease across the earlobe, connecting the lowest point on the tragus to the outside of the earlobe (Fig. 47-1). Some investigators define the finding as a crease traversing at least one third of the distance from the tragus to the posterior pinna,[35,36] whereas others require the crease to extend the total distance.[27,30,37] In a letter to the editor written in 1973,[66] Frank first presented the "positive ear-lobe sign" as a sign tightly associated with other cardiovascular risk factors. Although its association with coronary disease remains controversial and its pathogenesis a mystery, many investigators have shown that the earlobe crease is a modest risk factor for coronary artery disease, independent of other

EBM BOX 47-1
*Coronary Artery Disease**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Patient Interview				
DESCRIPTION OF CHEST PAIN				
Classification of chest pain[17–24]				
Typical angina	50-91	78-94	**5.8**	—
Atypical angina	8-44	—	1.2	—
Nonanginal chest pain	4-22	14-50	**0.1**	—
Pain duration >30 minutes[25]	1	86	**0.1**	NS
Associated dysphagia[25]	5	80	**0.2**	NS
OTHER FINDINGS				
Male sex[22,23,26–31]	72-86	36-58	1.7	**0.3**
Age[23,26–28,31,32]				
<30 years	0-1	97-98	NS	—
30-49 years	16-38	—	0.6	—
50-70 years	62-73	—	1.3	—
>70 years	2-52	67-99	2.6	—
Prior myocardial infarction[22,24,28,29,31,33,34]	42-69	66-99	**3.8**	0.6
Physical Examination				
Earlobe crease[27,30,35–37]	26-80	33-96	2.3	0.6
Arcus senilis[38]	40	86	**3.0**	0.7
Chest wall tenderness[25,39–41]	1-69	16-97	0.8	NS
Ankle-to-arm pressure index <0.9[42,43]	20-26	93-95	**4.0**	0.8
Laterally displaced apical impulse[44]	5	100	NS	NS
Electrocardiogram				
Normal[24,44,45]	15-33	50-69	NS	NS
ST/T wave abnormalities[17,24,34]	14-44	73-93	NS	NS

*Diagnostic standard: For *coronary artery disease*, coronary angiography reveals >50%,[18,20–22,24,26,27,30,32,33,35–38,40,42,43,45] >60%,[44] or >70% to 75%[17,19,23,25,28,29,31,34] stenosis of any epicardial vessel or positive myocardial perfusion scan.[41]

†Definition of findings: For *classification of chest pain*, *earlobe crease*, and *arcus senilis*, see text.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

NS, not significant.

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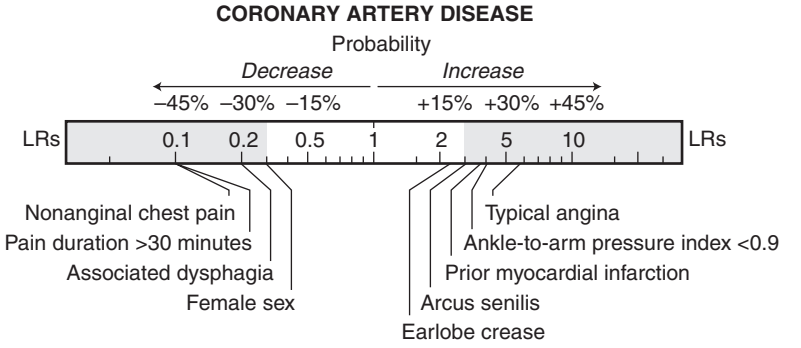

EBM BOX 47-2
*Myocardial Infarction**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Patient Interview				
Male sex[46–54]	59-72	24-61	1.3	0.7
Age[46,51,52]				
<40 years	4	81	**0.2**	—
40-59 years	34	—	NS	—
≥60 years	47-74	54-68	1.5	—
Sharp pain[51,55]	8-16	59-70	**0.3**	1.3
Pleuritic pain[51,52,55]	3-6	74-82	**0.2**	1.2
Positional pain[51,52]	3-11	75-87	**0.3**	1.1
Relief of pain with nitroglycerin[56–59]	35-92	12-59	NS	NS
Physical Examination				
Hand gestures[16]				
Levine sign	7	87	NS	NS
Palm sign	32	63	NS	NS
Arm sign	18	83	NS	NS
Pointing sign	2	95	NS	NS
Chest wall tenderness[51,52,55]	3-15	64-83	**0.3**	1.3
Diaphoretic appearance[52,55,60]	28-53	71-94	2.2	0.7
Pallor[60]	70	49	1.4	0.6
Systolic blood pressure <100 mm Hg[48]	6	98	**3.6**	NS
Jugular venous distention[47]	10	96	2.4	NS

EBM BOX 47-2
Myocardial Infarction—cont'd

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Pulmonary crackles[47,55]	20-38	82-91	2.1	NS
Third heart sound[55]	16	95	**3.2**	NS
Electrocardiogram				
Normal[46,48,51,55,60–64]	1-13	48-77	**0.2**	1.5
Nonspecific ST changes[51,63]	5-8	47-78	**0.2**	1.4
ST elevation[48,51,55,60,62,63,65]	31-56	97-100	**22.3**	0.6
ST depression[48,55,60,62,63]	20-62	79-96	**3.9**	0.8
T wave inversion[48,55,60,62]	9-39	84-94	2.0	NS

*Diagnostic standard: For *myocardial infarction*, development of new electrocardiographic Q waves or elevations of cardiac biomarkers (CK-MB or troponin), or both; except for the studies of nitroglycerin effect, which used a broader definition of "active coronary disease" that combined myocardial infarction, positive stress test, or abnormal coronary arteriogram.[56–58]

†Definition of findings: For *relief of pain with nitroglycerin*, nitroglycerin provided moderate or complete relief. All electrocardiographic abnormalities refer to findings that are new or of unknown duration.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. NS, not significant.

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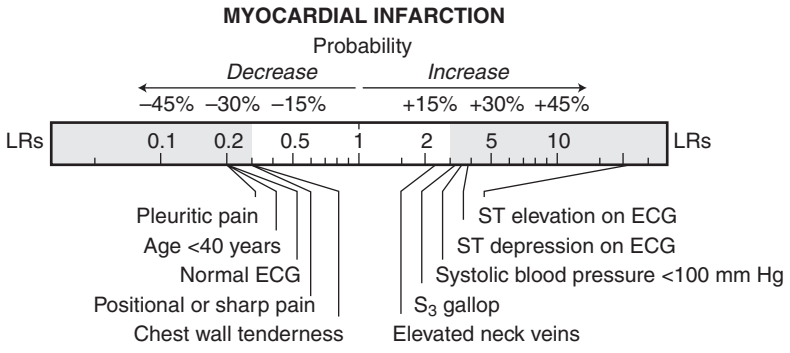

traditional risk factors such as hypertension, age, diabetes mellitus, family history, hyperlipidemia, obesity, and cigarette smoking.[30,35,37,67,68]

2. Arcus Senilis

Arcus senilis is a white or grayish opaque ring about the circumference of the cornea. Since the 1830s, this sign has been associated with both older age (hence, "senilis") and vascular disease. (Virchow considered it

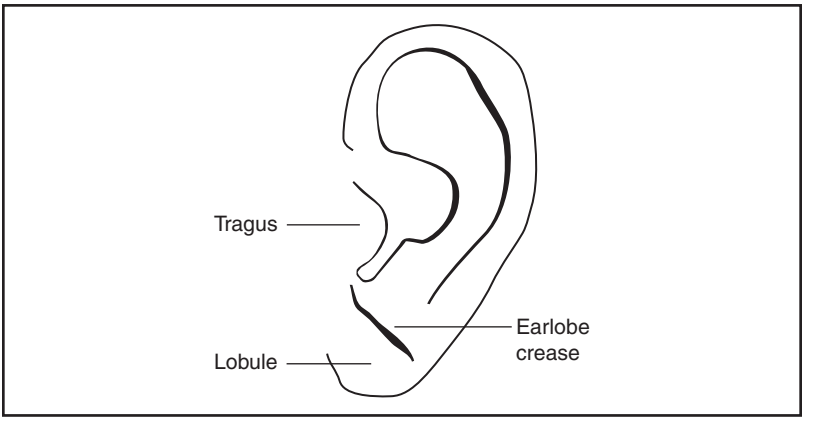

FIGURE 47-1 Earlobe crease. The earlobe crease is a diagonal crease extending from the lowest point on the tragus to the outside of the earlobe. See text.

a definite sign of heart disease.[69]) Modern investigators[70,71] continue to suggest that arcus senilis is linked to coronary disease, independent of its association with hyperlipidemia, although others challenge this view.[69]

3. Ankle-to-Arm Pressure Index

After positioning the patient in the supine position, the clinician uses a hand-held Doppler stethoscope to measure the highest systolic blood pressure in the posterior tibial or dorsalis pedis artery (i.e., the "ankle" pressure). The **ankle-to-arm pressure index** represents this ankle pressure divided by the systolic pressure in the brachial artery (see Chapter 52).

E. GI COCKTAIL

For many years, clinicians working in emergency departments have mixed liquid antacids with other substances (most commonly, viscous lidocaine, a topical anesthetic, and an elixir with the trade name Donnatal, an antispasmodic) to create **GI cocktails,** which are administered orally to patients presenting with chest or upper abdominal discomfort. Because a GI cocktail should act topically only on the gastrointestinal mucosa, prompt relief of a patient's discomfort is said to support a gastrointestinal cause of the pain (and, by inference, argue against a cardiac cause of the pain). Although antacids, lidocaine, and Donnatal are the standard ingredients of the GI cocktail, some investigators have shown that antacid alone (without lidocaine or Donnatal) may relieve pain just as effectively.[72]

III. CLINICAL SIGNIFICANCE

A. DIAGNOSING CORONARY ARTERY DISEASE

EBM Box 47-1 summarizes the accuracy of bedside findings in diagnosing coronary artery disease (based on studies of more than 10,000 patients).[73] Almost all the patients in these studies presented to outpatient clinics with

intermittent chest pain, and the diagnosis of coronary artery disease was based on subsequent cardiac catheterization revealing significant stenosis (>50% to 70% luminal narrowing) in any major epicardial vessel (i.e., single-vessel disease or worse).

According to the likelihood ratios (LRs) in EBM Box 47-1, the findings *increasing* the probability of coronary disease the most in patients with intermittent chest pain are typical angina (LR = 5.8), an ankle-to-arm pressure index of less than 0.9 (LR = 4), previous myocardial infarction (LR = 3.8), arcus senilis (LR = 3), age older than 70 years (LR = 2.6), and a positive earlobe crease (LR = 2.3).

These studies confirm Heberden's original impression that the key diagnostic finding in patients with chest pain is the patient's actual description of the pain. Many investigators have attempted to improve on Heberden's definition of typical angina by dissecting the individual components of the patient's description (e.g., the response to nitroglycerin or the pain's quality) or by creating complicated angina scoring schemes, but each of these attempts to improve the diagnosis is less accurate than the clinician's global perception of whether the patient's pain is typical angina or not.[73]

The findings that *decrease* the probability of coronary artery disease in these studies are chest pain that is nonanginal (i.e., pain unrelated to activity, unrelieved by nitroglycerin, or otherwise not suggestive of angina, LR = 0.1), pain duration of longer than 30 minutes (LR = 0.1), and associated dysphagia (LR = 0.2).

Unhelpful findings include atypical angina, chest wall tenderness, and a displaced apical impulse. Additional descriptors of the pain, such as burning pain, pain made worse by food or emotion, and radiation of the pain to the arms, are also unhelpful (i.e., they appear just as often in patients with coronary disease as in patients with noncardiac chest pain, and the LRs are not different from the value of 1).[73] Neither the Levine sign nor the palm sign affects the probability of coronary disease.[74] Interestingly, electrocardiographic findings (i.e., normal vs. abnormal, presence or absence of nonspecific ST changes) also are diagnostically unhelpful in these studies (LR not significant; see EBM Box 47-1).

Assessment of the patient's traditional risk factors—hypertension, diabetes mellitus, cigarette smoking, or family history, or combinations of these—carry much less diagnostic weight than the patient's description of the pain. Each of these risk factors—except for a cholesterol level higher than 300 mg/dL (LR = 4) and a cholesterol level lower than 200 mg/dL (LR = 0.3)—has an LR between the values of 1.2 and 2.3, thus changing the probability of disease little, if at all.[73,75,76] Even combinations of three or more risk factors change the probability of coronary disease relatively little (LR = 2.2, a value similar to the LR for the earlobe crease).[73]

B. DIAGNOSING MYOCARDIAL INFARCTION

EBM Box 47-2 summarizes the findings in thousands of patients presenting to emergency departments with sustained acute chest pain unrelated to trauma and unexplained by the chest radiograph. The diagnosis of myocardial infarction was confirmed by the development of new Q waves

on the electrocardiogram or elevations of cardiac biomarkers (CK-MB or troponin), or both.

According to the LRs in Table 45-2, the finding *increasing* the probability of myocardial infarction the most is a new electrocardiographic ST elevation (LR = 22.3) or ST depression (LR = 3.9). Several additional physical findings have modest value in diagnosing myocardial infarction: systolic blood pressure lower than 100 mm Hg (LR = 3.6), a third heart sound (LR = 3.2), jugular venous distention (LR = 2.4), diaphoretic appearance (LR = 2.2), and pulmonary crackles (LR = 2.1). Radiation of pain to the right arm (LR = 4.7) increases the probability of myocardial infarction more than radiation to the left arm (LR = 1.8),[46,47,55,73] although fewer patients with infarction have radiation to the right arm (15% to 41% of patients) than the left arm (34% to 55%). The only findings *decreasing* the probability of myocardial infarction in these studies are pain that is pleuritic (LR = 0.2), positional (LR = 0.3), or sharp (LR = 0.3); a normal electrocardiogram (LR = 0.2); chest wall tenderness (LR = 0.3); and age younger than 40 years (LR = 0.2).

The response to nitroglycerin fails to discriminate between cardiac and noncardiac causes of chest pain evaluated (LR not significant; see EBM Box 47-2). This may reflect the temporary nature of most chest pain episodes or perhaps the noncardiac effects of nitroglycerin. Nonetheless, even though the response to nitroglycerin lacks diagnostic value in patients with sustained chest pain, it remains a key element in the definition of typical angina. (See previous discussion in the section on Description of Chest Pain.)

The different hand signs also lack diagnostic value in studies of patients admitted with chest discomfort (see EBM Box 47-2).

One interesting contrast between the diagnosis of coronary disease (see EBM Box 47-1) and myocardial infarction (see EBM Box 47-2) is that chest wall tenderness decreases the probability of myocardial infarction (LR = 0.3; see EBM Box 47-2) but lacks diagnostic value when considering coronary artery disease (LR not significant; see EBM Box 47-1). This difference may reflect a higher prevalence of chest wall disorders in patients without disease in the acute chest pain studies.

C. RISK FACTORS AND CORONARY DISEASE

In patients with sustained chest pain, the presence or absence of traditional cardiovascular risk factors again carries little or no diagnostic weight (positive LRs = 1.2 to 1.7).[73] There are two important reasons why risk factors fail to discriminate well in diagnostic studies. In the first place, traditional cardiovascular risk factors are mostly derived from the study of middle-aged white residents of Framingham, Massachusetts.[77] They may thus overestimate the risk in other populations, something that has been demonstrated in British men,[78] elderly Americans,[79] and Japanese-American, Native American, and Hispanic populations.[80] A second reason is the fundamental difference between risk factors and diagnostic signs. Risk factors precede disease, presumably play a role in causing the disease, and become apparent only after the study of large groups of *asymptomatic* individuals

for long periods of time. Diagnostic signs, in contrast, first appear after the onset of disease, are *caused by* the disease, and become evident after the study of a relatively smaller group of *symptomatic* individuals. It is possible, for example, that certain risk factors associated with coronary disease are also associated with noncardiac causes of pain, which would neutralize any diagnostic value (e.g., cigarette smoking may also increase the risk of chest wall pain, making it appear just as often in patients with noncardiac pain as those with cardiac pain; the resulting LR would therefore have a value near 1).

D. GI COCKTAIL

The existing literature suggests that the GI cocktail has questionable diagnostic value. One problem is that clinicians usually administer the GI cocktail just minutes away from other active medications, such as narcotics, nitroglycerin, antiemetics, histamine blockers, or ketorolac, thus clouding interpretation of the test's results.[81] Another problem is that the viscous lidocaine is absorbed, and even though most patients have levels below 1 μg/mL (usual therapeutic levels are 2 to 5 μg/mL), instances of toxicity and seizures have occurred.[81–83] A final and most troubling problem is the many documented examples of GI cocktail relieving the discomfort of disorders distant from the gastroesophageal mucosa, such as myocardial infarction,[82,84] hepatitis, pancreatitis, or cholecystitis.[85]

E. PROGNOSIS AND ACUTE CHEST PAIN

In patients with acute chest pain, clinicians are interested in diagnosing more than just myocardial infarction because many acute coronary syndromes *without* infarction are also associated with life-threatening complications that require intensive monitoring and treatment. To identify all patients at risk for such complications, Goldman has developed a rule that assesses the patient's electrocardiogram and the presence or absence of three additional bedside findings:

1. Systolic blood pressure of less than 110 mm Hg
2. Crackles heard above the bases bilaterally
3. Chest pain that is either worse than prior angina, the same as prior myocardial infarction, or occurs in the postinfarction or postrevascularization setting[86]

According to this rule, patients have a "high risk" of life-threatening complications in the first 24 hours of hospitalization if there is either

1. Electrocardiographic ST elevation or Q waves (not known to be old) OR
2. Electrocardiographic ST depression or T wave inversion (not known to be old) AND two or more of the three bedside findings

Patients are classified as "very low risk" if the electrocardiogram reveals no ST/T wave changes or Q waves and they lack all three bedside findings.

EBM Box 47-3 indicates that in patients with acute chest pain, a "high-risk" classification increases the likelihood of life-threatening complications in the subsequent 24 hours (LR = 8.7; see EBM Box 47-3), whereas a "very low risk" classification indicates a favorable prognosis (LR = 0.1;

EBM BOX 47-3

Predicting Life-threatening Complications in Patients with Acute Chest Pain

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Goldman Classification				
"High" risk[86,87]	51-88	92-93	**8.7**	—
"Very low" risk[86–88]	7-13	42-53	**0.1**	—

*Diagnostic standard: For *life-threatening complications*, any of the following during the first 24 hours of hospitalization: arrhythmias (ventricular fibrillation, cardiac arrest, new complete heart block, insertion of temporary pacemaker, emergency cardioversion), pump failure (cardiogenic shock, use of intra-aortic balloon pump, intubation), or ischemia (recurrent ischemic chest pain requiring bypass surgery or percutaneous intervention).[86]

†Definition of findings: For *high risk* and *very low risk*, see text.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

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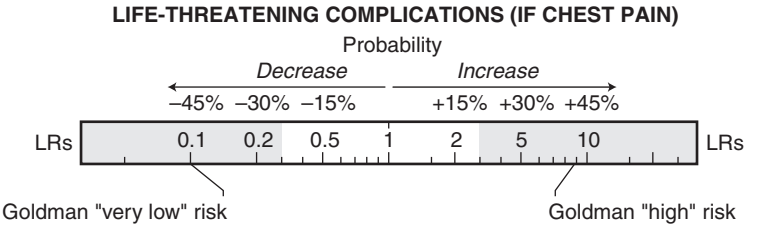

see EBM Box 47-3). This rule compares favorably to the diagnostic accuracy of elevated troponin T levels, drawn at least 6 hours after the onset of chest pain in patients without ST elevation, in predicting cardiac events in the subsequent 30 days (positive LR = 6.1, negative LR = 0.2).[89]

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 48

Inspection of the Abdomen

This chapter reviews two physical signs, ecchymosis of the abdominal wall and Sister Mary Joseph nodule. Other chapters discuss jaundice (Chapter 7), dilated abdominal veins (Chapter 7), signs of malnutrition (Chapter 11), and abnormal respiratory movements of the abdominal wall (Chapter 18).

ECCHYMOSIS OF THE ABDOMINAL WALL

I. THE FINDINGS

Ecchymosis of the abdominal wall is an important sign of retroperitoneal or intraperitoneal hemorrhage. Periumbilical ecchymosis is called the **Cullen sign,** after the American pathologist and clinician who first described the finding in a patient with ectopic pregnancy in 1918.* Flank ecchymosis is often called the **Grey Turner sign** or **Turner sign,** after the British surgeon Gilbert Grey Turner, who described the sign in a patient with hemorrhagic pancreatitis in 1920.[3] Nonetheless, Cullen sign and Turner sign are rare, occurring in less than 1% of patients with ruptured ectopic pregnancy[4] and less than 3% of patients with pancreatitis.[5] Both signs have since been described in a wide variety of other disorders, including intrahepatic hemorrhage from tumor,[6] amebic liver abscess,[7] ischemic bowel,[8] splenic rupture,[9] rectus sheath hematoma,[10] perforated duodenal ulcer,[11] ruptured abdominal aortic aneurysm,[12] percutaneous liver biopsy,[13] and coronary angiography.[14] A patient may sometimes have both Cullen sign and Grey Turner sign.[15,16]

II. PATHOGENESIS

The discoloration of the skin is actually due to the collection of blood in the subcutaneous fascial planes, not the dispersion of red cells within lymphatics, as has been sometimes surmised.[17] In patients with pancreatitis, computed tomography often reveals collections of retroperitoneal blood within the fascial planes behind the kidney, which may then pass to the subcutaneous

*Cullen was well versed in the anatomy of the umbilicus, having just 2 years before his report published the book *Embryology, Anatomy, and Diseases of the Umbilicus, Together with the Urachus*, which contained 27 chapters on the umbilicus.[1]

tissues of the lateral abdominal wall via the lateral border of the quadratus lumborum muscle.[18] Presumably, the mechanism of the Grey Turner sign in other disorders is the same. In most patients with the Cullen sign, blood travels to the periumbilical area through the falciform ligament, which connects to the retroperitoneum via the lesser omentum and transverse mesocolon. (The falciform ligament and lesser omentum are the embryologic remnants of the ventral mesentery, into which the liver has grown.)

In patients with ectopic pregnancy, however, the falciform ligament is probably not responsible for the Cullen sign, because the ecchymosis of these patients is often located on the abdominal wall below the umbilicus, yet the falciform ligament attaches to the abdominal wall above the umbilicus. Some investigators have hypothesized that fascial planes connecting the broad ligament and the lower abdominal wall are responsible for the Cullen sign in ectopic pregnancy,[18] although this does not explain why the sign sometimes appears in patients with free rupture into the peritoneal cavity outside of the broad ligament.[4]

SISTER MARY JOSEPH NODULE

I. THE FINDING

Sister Mary Joseph nodule is metastatic carcinoma of the umbilicus. It usually presents as a hard dermal or subcutaneous nodule, and, in about 20% of patients with the lesion, it represents the initial sign of malignancy.[19] Most patients have metastatic adenocarcinoma, usually from the stomach, large bowel, ovary, or pancreas (usually, the tail of the pancreas, not the head).[19–23] It is an ominous sign, the average survival time after discovery being only 10 to 11 months.[19,22]

The finding is named after Sister Mary Joseph, who, as first surgical assistant to William J. Mayo, noted the association between umbilical nodules and intra-abdominal malignancy. (Sister Mary Joseph was born Julia Dempsey in 1856; before Vatican II in 1965, all Franciscan nuns took the name of Mary as a prefix to an additional name.)[24,25] Dr. Mayo discussed the sign as early as 1928, calling it the **pants-button umbilicus.**[26] It was not until Sir Hamilton Bailey's 1949 edition of *Physical Signs in Clinical Surgery* (10 years after Sister Mary Joseph's death) that the term **Sister Joseph nodule** was used.[27]

A mimic of the Sister Mary Joseph nodule is an omphalith, which is the hardened concretion of keratin and sebum in the umbilicus from inadequate hygiene.[28] Careful examination of these patients, however, manages to extract the debris.

II. PATHOGENESIS

There are many potential avenues of spread to the umbilicus: vascular and lymphatic connections to the retroperitoneum, axilla, and inguinal regions, and embryologic remnants that connect the umbilicus to the bladder and

retroperitoneum.[29] Nonetheless, the umbilicus and periumbilical tissues represent the thinnest part of the abdominal wall, and, in one series of patients, direct spread from peritoneal tumor implants through the abdominal wall was the most common cause of the umbilical nodule.[19]

References for this chapter can be found on www.expertconsult.com.

CHAPTER 49

Palpation and Percussion of the Abdomen

I. INTRODUCTORY COMMENTS ON TECHNIQUE

Palpation of the abdomen may reveal abnormal tenderness, tumors, hernias, aneurysms, or organomegaly (i.e., of the liver, spleen, or gallbladder). To help the patient relax and to minimize pain during palpation, experienced clinicians recommend that the clinician's hands should be warm, the technique soft and gentle, and the expected tender areas palpated last. Other maneuvers designed to help the patient relax include drawing up the patient's knees, encouraging deep breathing, or engaging the patient in conversation.

In the days before clinical imaging, palpation of a relaxed abdomen was so essential that patients with tense abdominal muscles were often re-examined after immersion in a hot bath or after anesthesia had been induced with ether or chloroform, to determine whether an abnormality was present or not.[1]

II. LIVER

A. LIVER SPAN

1. The Finding

The liver span is the distance in centimeters between the upper border of the liver in the right midclavicular line (as determined by percussion, i.e., where lung resonance changes to liver dullness) and the lower border (as determined by either percussion or palpation). Clinicians have been measuring the liver span ever since Piorry introduced topographic percussion in 1828,[2] although after introduction of the x-ray it became apparent that the estimated span often differed from the actual span, leading most clinicians to adopt the view that the percussed liver span was just an index of liver size, not a precise measurement.[3]

2. Clinical Significance

The clinician's assessment of liver span almost always underestimates the actual value. Clinicians place the upper border too low (2 to 5 cm)[4,5] and the lower border too high (>2 cm in about half of patients),[4,6] except in patients with chronic obstructive lung disease, in whom the error with the

top border is less.[4] The liver span is the same whether the patient is percussed during quiet respirations or full held expiration.[7]

Nonetheless, most studies of liver percussion make two points:

1. The estimated span does correlate modestly with the actual span, as determined by ultrasonography or scintigraphy (r = 0.6 to 0.7).[3,5,6,8] This correlation is much better in patients with diseased livers than with healthy livers.[5,8]
2. The percussed liver span is very dependent on the clinician's technique, and, consequently, one clinician's "normal liver span" is not the same as another's. The heavier the clinician's percussion stroke, the smaller the measured span and the greater the error in underestimating the actual liver size (see also Chapter 27).[4,7] This explains why published estimates of the "normal liver span" range from as low as 6 cm to as high as 15 cm*[6,10–12] and why experienced clinicians, each examining the same patient, differ in their estimate of the patient's span, *on average*, by 8 cm.[13]

These comments imply that each clinician could determine his or her own "normal liver span," based on examination of hundreds of healthy persons, and then use this span as a benchmark to indicate whether a patient's span is abnormally large or not. Nonetheless, two studies applying a standardized percussion technique failed to accurately detect hepatomegaly (likelihood ratio [LR] not significant; EBM Box 49-1).

B. PALPABLE LIVER EDGE

1. The Finding

To palpate the liver edge, the clinician begins by gently palpating the patient's right *lower* quadrant. As the patient breathes in and out, the clinician moves the palpating hand upward 1 to 2 cm at a time, at each location searching for a liver edge that moves down during inspiration and strikes the clinician's fingers. Once the edge is located, the clinician should note its consistency (a cirrhotic liver is firmer than a healthy one)[8] and whether the edge has any irregularities or masses.[29]

Anatomically, the normal liver extends on average 5 cm below the right costal margin at the midclavicular line.[5]

2. Clinical Significance

a. Detection of Hepatomegaly

If clinicians palpate what they believe is the patient's liver edge extending below the costal margin, they are virtually always correct (LR = 233.7; see EBM Box 49-1). Nonetheless, the distance between the liver edge and the costal margin correlates poorly with the overall liver size, and the finding of a palpable liver edge is an unreliable sign of hepatomegaly (LR only 1.9; see EBM Box 49-1). Moreover, about half of livers that extend below the costal margin are not palpable.[8,15] The *consistency* of the liver parenchyma probably determines in part whether a liver is palpable, because in patients

*The normal upper limit for the cephalocaudad dimension of the liver on ultrasonography is 13 cm.[9]

with cirrhosis, whose livers are smaller but firmer than normal, the liver's edge is palpable 95% of the time.[8]

b. Palpable Liver and Other Disorders

In patients with chronic liver disease, a few findings modestly increase the probability of cirrhosis: an enlarged palpable liver edge (LR = 2.3; EBM Box 49-2), a palpable liver in the epigastrium (LR = 2.7), and a liver edge that is unusually firm (LR = 2.7). In patients with jaundice, the findings of a palpable liver and liver tenderness are unhelpful, both appearing equally as often in patients with hepatocellular disease (i.e., nonobstructive jaundice) as in those with obstructive jaundice (LR not significant; see Chapter 7). In patients with lymphadenopathy, the finding of a palpable liver fails to distinguish those with serious infections

EBM BOX 49-1
*Detection of Enlarged Liver and Spleen**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Liver				
PERCUSSION SPAN ≥10 CM IN MCL				
Detecting enlarged liver[6,14]	61-92	30-43	NS	NS
PALPABLE LIVER				
Detecting liver edge below costal margin[15]	48	100	**233.7**	0.5
Detecting enlarged liver[14,16–18]	39-71	56-85	1.9	0.6
Spleen				
PALPABLE SPLEEN				
Detecting enlarged spleen[16,17,20–27]	18-78	89-99	**8.5**	0.5
SPLENIC PERCUSSION SIGNS				
Detecting enlarged spleen[21,22,26–28]				
Spleen percussion sign	25-85	32-94	1.7	0.7
Nixon method	25-66	68-95	2.0	0.7
Traube space dullness	11-76	63-95	2.1	0.8

*Diagnostic standard: for *enlarged liver*, liver enlarged by scintigraphy,[16,18] craniocaudal span >13 cm by ultrasonography,[6,14] or postmortem weight of liver >2000 g[17]; for *enlarged spleen*, spleen enlarged by ultrasonography,[21,22,25–27] scintigraphy,[16,20,23,28] or postmortem weight >200 g,[17] *or* >250 g.[24]

†Definition of findings: For *percussed liver span*, using light percussion technique; for *splenic percussion signs*, see text.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. MCL, midclavicular line; NS, not significant.

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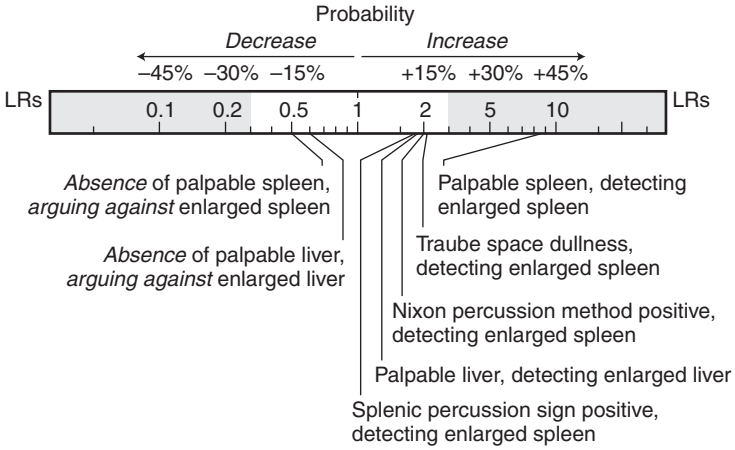
DETECTION OF ENLARGED LIVER AND SPLEEN



EBM BOX 49-2
*Palpation of Liver and Spleen in Various Disorders**

Finding (Reference)	Sensitivity (%)	Specificity (%)	Likelihood Ratio† if Finding Is	
			Present	*Absent*
Liver				
Enlarged palpable liver in patients with chronic liver disease, detecting cirrhosis[30–37]	31-96	20-96	2.3	0.6
Palpable liver in epigastrium in patients with chronic liver disease, detecting cirrhosis[35,37]	50-86	68-88	2.7	**0.3**
Liver edge firm to palpation in patients with chronic liver disease, detecting cirrhosis[31,34]	71-78	71-74	2.7	0.4
Palpable liver in patients with jaundice, detecting hepatocellular disease (nonobstructive jaundice)[38,39]	71-83	15-17	NS	NS
Liver tenderness in patients with jaundice, detecting hepatocellular disease (nonobstructive jaundice)[38,39]	37-38	70-78	NS	NS

Continued

EBM BOX 49-2
Palpation of Liver and Spleen in Various Disorders—cont'd

Finding (Reference)	Sensitivity (%)	Specificity (%)	Likelihood Ratio† if Finding Is	
			Present	*Absent*
Palpable liver in patients with lymphadenopathy, detecting serious disease[40,41]	14-16	86-89	NS	NS
Spleen				
Palpable spleen in returning travelers with fever, detecting malaria[42–44]	19-25	95-98	**6.5**	0.8
Palpable spleen in patients with jaundice, detecting hepatocellular disease (nonobstructive jaundice)[38,39]	29-47	83-90	2.9	0.7
Palpable spleen in patients with chronic liver disease, detecting cirrhosis[31–37,45–48]	5-85	35-100	2.5	0.8
Palpable spleen in patients with lymphadenopathy, detecting serious disease[40,41,49]	5-10	92-96	NS	NS

*Diagnostic standard: for *nonobstructive (vs. obstructive) jaundice*, needle biopsy of liver, surgical exploration, or autopsy; for *cirrhosis*, needle biopsy of liver (see Chapter 7); for *serious disease* (in patients with lymphadenopathy), see Chapter 25.

†Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

MCL, midclavicular line; NS, not significant.

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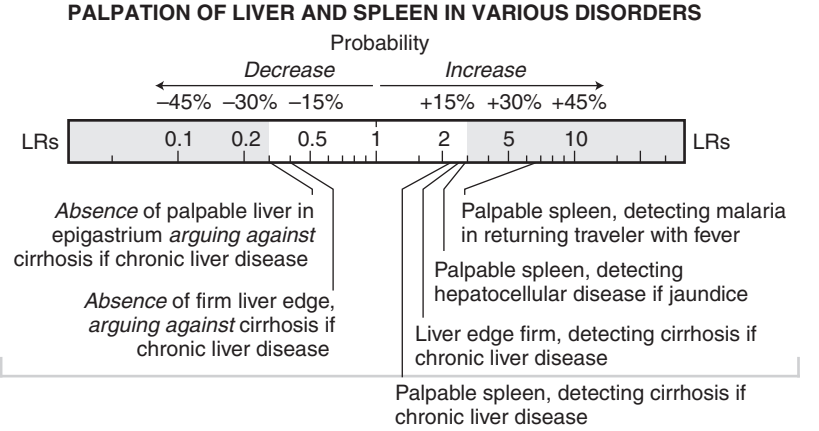


and malignant diseases from those with benign self-limited disorders (LR not significant; see Chapter 25).

C. AUSCULTATORY PERCUSSION: SCRATCH TEST

1. The Finding

Auscultatory percussion (see also Chapter 27) is frequently used to locate the lower border of the liver. According to traditional teachings, the moment the clinician's percussing digit crosses the border of the liver and begins to strike the abdominal wall over the liver, the sound heard through the stethoscope becomes louder.

Nonetheless, the lack of consensus on the proper technique of locating the liver will quickly discourage the serious student of auscultatory percussion. Various experts recommend placing the stethoscope on the xiphoid,[4,50] near the umbilicus,[51] superior to[52] or at the costal margin,[53] at four separate positions over the liver,[54] or above the suspected center.[55] According to various authorities, the clinician should percuss with a finger and pleximeter,[55] a finger alone,[52] a bristle brush,[54] or a corrugated rod.[54] The direction of the stroke should be circular,[1] centripetal,[55] centrifugal,[54] left to right,[53] or always in a longitudinal axis and toward the liver.[4,52]

2. Clinical Significance

The evidence supporting auscultatory percussion of the liver is mixed and meager. Only one study supports the technique, showing that 78% of estimates of the lower border are within 2 cm of the actual border (by ultrasonography), compared with 44% for conventional percussion and palpation.[52] Another study showed that palpation of the liver was more accurate than auscultatory percussion.[4] A third study showed that there was no correlation whatsoever between the distance of the liver edge below the costal margin, located by auscultatory percussion, and the actual distance (by ultrasonography) for any of 11 different examiners.[50]

D. PULSATILE LIVER

The finding of a pulsatile liver has been described in tricuspid regurgitation with high pulmonary pressures (see Chapter 44) and constrictive pericarditis.[56,57] In patients with the holosystolic murmur of tricuspid regurgitation, the finding of a pulsatile liver increases the probability that the regurgitation is moderate-to-severe (LR = 6.5; see EBM Box 44-1).

III. THE SPLEEN

A. PALPABLE SPLEEN

1. The Finding

Experts recommend many different ways to palpate the spleen: Some palpate from the patient's right side and others from the patient's left side (curling the fingers over the costal margin to "hook" the spleen edge); some position the patient supine, others position the patient supine with the

patient's left fist under his or her left posterior chest, and still others position the patient in the right lateral decubitus position. One study comparing the different positions found all three equivalent[22]; the approach clinicians use probably depends most on personal preference.

2. Clinical Significance

a. Detection of Splenomegaly

EBM Box 49-1 indicates that the finding of a palpable spleen increases greatly the probability of splenomegaly (LR = 8.5; see EBM Box 49-1). Although many enlarged spleens are not palpable (sensitivity is only 18% to 78%), virtually all massively enlarged spleens (i.e., weight >1 kg or scintigraphic span >22 cm) are detectable by palpation.[24,58]

b. Etiology of Splenomegaly

The common causes of splenomegaly are hepatic disease (i.e., portal hypertension), hematologic disorders (e.g., leukemias, lymphomas, myelofibrosis), infectious disease (e.g., HIV infection), and primary splenic disorders (e.g., splenic infarction or hematoma).[59,60] The presence of left upper quadrant tenderness and pain increases the probability of a primary splenic disorder or hematologic disorder.[60] Associated lymphadenopathy practically excludes hepatic disease and points to one of the other disorders (LR = 0.04).[60] The finding of a palpable liver increases the probability of an underlying hepatic cause of splenomegaly (LR = 2.7), and the finding of massive splenomegaly (i.e., the spleen extends to the level of the umbilicus) increases the probability of an underlying hematologic disease (LR = 2.1).[60]

c. Palpable Spleen and Other Disorders

In returning travelers from tropical countries who are febrile, the finding of a palpable spleen significantly increases the probability of malaria (LR = 6.5; see EBM Box 49-2). In patients with jaundice, the palpable spleen modestly increases the probability of hepatocellular disease (i.e., nonobstructive jaundice, LR = 2.9; see Chapter 7), and in patients with chronic liver disease, it increases the probability of cirrhosis (LR = 2.5). In patients with lymphadenopathy, a palpable spleen is found just as often in patients with serious infections and malignant diseases as in those with benign, self-limited disorders (LR not significant; see Chapter 25).

B. SPLENIC PERCUSSION SIGNS

1. The Findings

There are three commonly used splenic percussion signs.

a. Spleen Percussion Sign

Castell described this sign in 1967,[11] finding it a useful way to measure splenic size in patients with infectious mononucleosis. The clinician percusses the lowest left intercostal space in the anterior axillary line (usually, the eighth or ninth); if the percussion note in this location, usually resonant, becomes dull with a full inspiration, the test is positive. Since

Castell's original description, other investigators have regarded any dullness at this location as a positive response (i.e., whether during inspiration or expiration).

b. Nixon Method

Nixon described this sign in 1954,[61] finding it accurate in his experience of 60 splenic aspiration biopsies. The patient is positioned in the right lateral decubitus position, and the clinician percusses from the lower level of pulmonary resonance in the posterior axillary line downward obliquely to the lower midanterior costal margin. The test is positive if the border of dullness on this line lies more than 8 cm from the costal margin.

c. Traube Space Dullness

Traube space is the triangular space, normally tympanic, that is over the left lower anterior part of the chest. Its upper border is marked by the limits of cardiac dullness (usually, the sixth rib), its lower border is the costal margin, and its lateral border is the anterior axillary line. Although Traube suggested that dullness in this space was a sign of pleural effusion,[62] Parrino in 1987 suggested that it could be a sign of splenic enlargement.[63]

2. Clinical Significance

Positive percussion signs are much less convincing than palpation (positive LRs = 1.7 to 2.1; see EBM Box 49-1). Traube space dullness becomes even less accurate in overweight patients or those who have recently eaten.[64]

IV. GALLBLADDER: COURVOISIER SIGN

A. THE FINDING

The **Courvoisier sign** is a *palpable nontender* gallbladder in a patient with *jaundice*, a finding that has been traditionally associated with malignant obstruction of the biliary system. Many textbooks call the sign **Courvoisier law,** as if the positive result were pathognomonic of malignancy, although the Swiss surgeon Courvoisier originally presented the finding in 1890 as only an interesting observation.[65] In a monograph on biliary tract disorders, he stated that among 187 patients with jaundice and common duct obstruction, a dilated gallbladder was found in only 20% of patients with stones, compared with 92% of patients having other disorders, mostly malignant diseases.[66]

B. CLINICAL SIGNIFICANCE

Summarizing the information about the Courvoisier sign is difficult because various authors define the sign differently. Some apply it to patients without jaundice (clearly not what Courvoisier intended)[67]; others define the positive sign as any palpable gallbladder, tender or nontender (some patients with cholecystitis have tender enlarged gallbladders)[68–70]; and still others

expand the positive sign to include a dilated gallbladder discovered during surgery, clinical imaging, or even autopsy.[71]

Restricting analysis to those studies defining the positive sign as a palpable gallbladder in a jaundice patient, EBM Box 49-3 indicates that the Courvoisier sign is pathognomonic for extrahepatic obstruction of the biliary system (i.e., stones or malignant disease, LR = 26; i.e., *not* hepatocellular jaundice). Among patients with biliary obstruction, however, the sign increases the probability only modestly *for* malignant disease and *against* stones (LR = 2.6). In one series of 86 hospitalized patients with distended gallbladders (as detected by computed tomography or at laparotomy), only 46 (53%) were palpable at the bedside; 83% had a malignant cause of the obstruction and 17% a benign one.[82]

Consequently, if there is a "law" to the Courvoisier sign, it is that the palpable gallbladder in a jaundiced patient indicates extrahepatic obstruction, not that the obstruction is caused by malignant disease.

C. PATHOGENESIS

Courvoisier's original hypothesis—that the gallbladder of choledocholithiasis fails to dilate because its walls are fibrotic from chronic cholecystitis—is probably incorrect, because experiments with gallbladders of jaundiced patients show that both dilated and nondilated gallbladders have similar wall stiffness.[83] Instead, patients with dilated gallbladders differ from patients without dilated gallbladders in two important ways: Dilated gallbladders are associated with much higher operative intraductal pressures and with a longer duration of jaundice.

The relationship between the duration of jaundice and dilation of the gallbladder explains why Courvoisier's original findings are different from the studies in EBM Box 49-3. When analysis is restricted to just those patients with extrahepatic obstruction, the sensitivity of the dilated gallbladder in malignant obstruction today (25% to 55%) is lower than it was for Courvoisier (i.e., 92%) (although the specificity is similar at 80% to 90%). The reduced sensitivity may simply reflect the fact that patients with malignant obstruction today, compared with those from a century ago, are diagnosed sooner with clinical imaging, before pressures increase enough to enlarge the gallbladder greatly.

V. BLADDER VOLUME

For over a century, clinicians have investigated percussing the suprapubic area to detect the bladder volume, with most studies revealing that the bladder volume must be about 400 to 600 mL before dullness reliably appears.[84] Although the extent of dullness above the symphysis pubis does correlate with the bladder volume,[84,85] overall the sign is unreliable because the results vary tremendously among individual patients and because many patients have inexplicable dullness of the lower abdomen, even without bladder distention.[2,84]

There are few studies of palpation of the bladder. One study has demonstrated that the *absence* of a palpable bladder in the

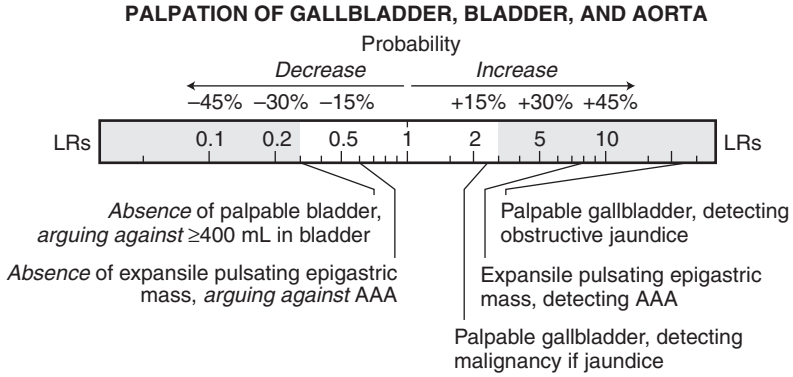
EBM BOX 49-3
*Palpation of Gallbladder, Bladder, and Aorta**

Finding (Reference)	Sensitivity (%)	Specificity (%)	Likelihood Ratio† if Finding Is	
			Present	*Absent*
Gallbladder				
PALPABLE GALLBLADDER				
Detecting obstructed bile ducts in patients with jaundice[38]	31	99	**26.0**	0.7
Detecting malignant obstruction in patients with obstructive jaundice[38,67,69,72]	26-55	83-90	2.6	0.7
Bladder				
PALPABLE BLADDER				
Detecting ≥400 mL urine in bladder[73]	82	56	1.9	**0.3**
Aorta				
EXPANSILE PULSATING EPIGASTRIC MASS				
Detecting abdominal aortic aneurysm[74–81]	22-68	75-99	**8.0**	0.6

*Diagnostic standard: for *obstructive jaundice* and *malignant obstruction*, needle biopsy of liver, surgical exploration, or autopsy; for *≥400 mL urine in bladder*, bladder ultrasound[73]; for *abdominal aortic aneurysm*, ultrasonography revealing focal dilation of infrarenal aorta >3 cm in diameter,[75,76,78–81] >4 cm in diameter,[77] or >1.5 cm larger than proximal aorta.[74]

†Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

Click here to access calculator.



suprapubic area *decreases* probability of bladder volumes > 400 mL[73] (LR = 0.3; see EBM Box 49-3).

VI. ASCITES

A. THE FINDINGS

In supine patients with ascites, peritoneal fluid gravitates to the flanks, and the air-filled intestines float to occupy the periumbilical space. This distribution of fluid and air causes four characteristic signs of ascites:

1. Bulging flanks
2. Flank dullness: Flank dullness is positive if there is a *horizontal* border between dullness in the flank area and resonance (or tympany) in the periumbilical area.
3. Shifting dullness: Shifting dullness describes flank dullness whose position shifts as the patient changes position, usually by rolling on to one side. The sign is based on the principle that air-filled loops of intestine, floating on peritoneal fluid, move to the uppermost position in the abdomen. In a patient with a positive response, the border between resonance and dullness shifts away from the side that is most dependent. To be positive, the shifting border should remain horizontal.
4. Fluid wave: To elicit the fluid wave, the clinician places one hand against the lateral wall of the abdomen and uses the other hand to tap firmly on the opposite lateral wall. In the positive response, the tap generates a wave that is transmitted through the abdomen and felt as a sudden shock by the other hand. Because a false-positive response may result from waves traveling through the subcutaneous tissue of the anterior abdominal wall, the clinician should always use the patient's hand or that of an assistant to apply firm pressure against the anterior abdominal wall.

In addition to these four signs, most patients with ascites also have edema, from hypoalbuminemia and the weight of the peritoneal fluid compressing the veins to the legs.[86]

B. PATHOGENESIS

In experiments with cadavers performed a century ago, Müller showed that 1000 mL of fluid injected into the peritoneal space was undetectable by physical examination (i.e., flank or shifting dullness), 1500 mL resulted in some flank dullness, and 2000 mL was the smallest volume to cause shifting dullness.[84] The living abdominal wall is probably more elastic than the cadaver's, and it is likely that the careful clinician can detect smaller amounts of ascites in patients, but one small study of healthy volunteers still showed that injection of 500 to 1100 mL of fluid was necessary before shifting dullness appeared.[87] A significant cause of false-positive flank dullness or shifting dullness is accumulation of fluid within loops of the colon.[87,88] This condition, called *pseudoascites* in the days before clinical imaging,[88] typically occurred in patients with diarrheal illnesses.

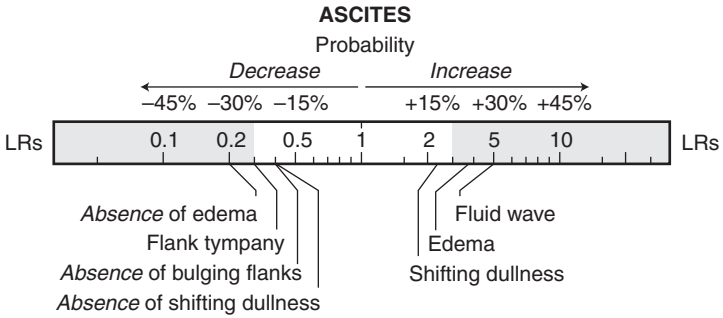
EBM BOX 49-4
*Ascites**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Inspection				
Bulging flanks[89–91]	73-93	44-70	1.9	0.4
Edema[90]	87	77	**3.8**	**0.2**
Palpation and Percussion				
Flank dullness[89,90]	80-94	29-69	NS	**0.3**
Shifting dullness[89–91]	60-87	56-90	2.3	0.4
Fluid wave[89–91]	50-80	82-92	**5.0**	0.5

*Diagnostic standard: for *ascites*, peritoneal fluid by ultrasonography.

†Definition of findings: for *shifting dullness*, border between resonance and dullness "shifts" when patient rolls from supine to left lateral decubitus position or right lateral decubitus position; Cattau required a shift in both positions,[89] Simel in only one of two positions,[90] and Cummings used only the right lateral decubitus position at 45 degrees and required a shift >1 cm.[91]

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.
NS, not significant.
Click here to access calculator.



C. CLINICAL SIGNIFICANCE

In patients with abdominal distention, the findings *increasing* the probability of ascites the most are the positive fluid wave (LR = 5; EBM Box 49-4) and presence of edema (LR = 3.8). The findings *decreasing* the probability of ascites the most are *absence* of edema (LR = 0.2) and *absence* of flank dullness (LR = 0.3). Shifting dullness shifts the probability of ascites modestly upward when present (LR = 2.3) and modestly downward when absent (LR = 0.4). Findings having relatively little diagnostic value are positive flank dullness, positive bulging flanks, and negative fluid wave. The finding of a flat or everted umbilicus was also diagnostically unhelpful in one study.[90]

Auscultatory percussion also has been recommended to detect ascites,[92–94] although only the **puddle sign** (auscultatory percussion of the prone patient) has been formally tested,[89,90] proving to be diagnostically unhelpful.

VII. ABDOMINAL AORTIC ANEURYSM

A. INTRODUCTION

Abdominal aortic aneurysm is a focal ballooning of the infrarenal abdominal aorta, traditionally defined as a diameter greater than 3 to 4 cm. It is a disorder of elderly patients, affecting 1% to 2% of patients over the age of 50 years.[95,96] Abdominal aortic aneurysms tend to enlarge slowly, but some rupture catastrophically with an overall mortality rate of up to 90%.[97]

B. THE FINDING

Because the normal aorta bifurcates at the level of the umbilicus, palpable aortic aneurysms usually are found in the epigastrium or left upper quadrant. The clinician should place one hand on each side of the aorta and measure its diameter, subtracting the estimated thickness of two layers of skin and subcutaneous tissue. Most studies do not specifically define the positive finding (instead stating simply that the positive finding is "aortic aneurysm present by palpation"), although others define it as an estimated diameter of more than 3 cm using the previously described method.[75]

Importantly, an aortic aneurysm pushes the two hands *apart*, a finding called *expansile* pulsation.[98] Other prominent epigastric pulsations sometimes occur in patients with thin abdomens or in those with epigastric masses overlying the normal aorta, but unless these pulsations are expansile, they do not indicate an aneurysm.

C. CLINICAL SIGNIFICANCE

According to EBM Box 49-3, the finding of a palpable epigastric pulsation suggestive of aneurysm increases the probability that one is present (LR = 8; see EBM Box 49-3). In contrast, the absence of this finding is much less helpful (LR is only 0.6), simply because the sensitivity for the finding is as low as 22% (i.e., up to 78% of patients with aneurysms lack a prominent pulsation).

The two most important variables governing whether an aneurysm is palpable are the size of the aneurysm and the girth of the patient's abdomen. Aneurysms between 3 and 5 cm in diameter are the most difficult to detect; if *aneurysm* is instead defined as a focal bulging of more than 5 cm in diameter—the diameter usually indicating surgical repair—the sensitivity of the bedside examination increases to over 80% in almost all series.[75,96,99] Aneurysms are also more difficult to detect in patients with larger abdominal girths.[74,75,99,100] After restricting the analysis to just patients with an abdominal girth of less than 100 cm (measured at the umbilicus)[74,75] or to patients in whom the clinician can palpate the aorta,[75,100,101] the sensitivity of the examination exceeds 88% in all studies. These results indicate that the negative examination significantly decreases the probability of an aneurysm of more than 5 cm in diameter, especially if the patient has a girth of less than 100 cm or has a palpable aorta.

The most common cause of a false-positive examination is an abnormally tortuous aorta.[102,103] Rare causes are a horseshoe kidney, intra-abdominal tumor, or para-aortic adenopathy.[102,103]

References for this chapter can be found on www.expertconsult.com.

CHAPTER 50

Abdominal Pain and Tenderness

ACUTE ABDOMINAL PAIN

I. INTRODUCTION

Among patients presenting with acute abdominal pain and tenderness (i.e., pain lasting <7 days), the most common diagnoses are nonspecific abdominal pain (43% of patients), acute appendicitis (4% to 20%), acute cholecystitis (3% to 9%), small bowel obstruction (4%), and ureterolithiasis (4%).[1–4] The term *acute abdomen* usually refers to those conditions causing abrupt abdominal pain and tenderness and requiring urgent diagnosis and surgical intervention, such as appendicitis, bowel obstruction, and perforated intra-abdominal organs.

Although many patients with acute abdomen undergo computed tomography scanning (to distinguish perforation, abscess, and appendicitis from other disorders), the bedside diagnosis remains a fundamental diagnostic tool in all of these patients.[5] Based just on the bedside findings, some patients can be safely discharged and sent home without further imaging because the probability of peritonitis is so low, whereas others should proceed directly to the operating room because the probability of peritonitis is so high. Those patients whose bedside findings are equivocal or suggest abscess formation benefit most from further imaging.[6]

II. THE FINDINGS

The two most common causes of acute abdomen are the following:

1. **Peritonitis** from inflammation (appendicitis, cholecystitis) or perforation of a viscus (appendix, peptic ulcer of stomach or duodenum, diverticulum)
2. Bowel obstruction

Both peritonitis and obstruction cause abdominal tenderness. Additional findings are discussed later.

A. PERITONITIS

The additional findings of peritonitis are guarding and rigidity, rebound tenderness, percussion tenderness, a positive cough test, and a *negative* abdominal wall tenderness test.

1. Guarding and Rigidity

Guarding refers to *voluntary contraction* of the abdominal wall musculature, usually the result of fear, anxiety, or the laying on of cold hands.[7] **Rigidity** refers to *involuntary contraction* of the abdominal musculature in response to peritoneal inflammation, a reflex that the patient cannot control.[7] Experienced surgeons distinguish these two findings by doing the following:

1. Distracting the patient during examination (e.g., engaging the patient in conversation or using the stethoscope to gently palpate the abdomen)[8,9]
2. Examining the patient repeatedly over time

Guarding, but not rigidity, diminishes with distraction and fluctuates in intensity or even disappears over time.

The first clinician to clearly describe rigidity was the Roman physician Celsus, writing in 30 AD.[10]

2. Rebound Tenderness

To elicit **rebound tenderness,** the clinician maintains pressure over an area of tenderness and then withdraws the hand abruptly. If the patient winces with pain upon withdrawal of the hand, the test is positive. Many expert surgeons discourage the use of the rebound tenderness test, regarding it as "unnecessary,"[7,11] "cruel,"[5] or a "popular and somewhat unkind way of emphasizing what is already obvious."[12]

Rebound tenderness was originally described by J. Moritz Blumberg (1873-1955), a German surgeon and gynecologist, who believed that pain in the lower abdomen after abrupt withdrawal of the hand from the *left* lower abdominal quadrant was a sign of appendicitis (i.e., **Blumberg sign**).[13]

3. Percussion Tenderness

In patients with peritonitis, sudden movements of the abdominal wall cause pain, such as those produced during abdominal percussion. **Percussion tenderness** is present if light percussion causes pain.

4. Cough Test

The **cough test** is based on the same principle as percussion tenderness (i.e., jarring movements of the abdominal wall cause pain in patients with peritonitis). The cough test is positive if the patient, in response to a cough, shows signs of pain, such as flinching, grimacing, or moving the hands toward the abdomen.[14]

5. Abdominal Wall Tenderness Test

In 1926, Carnett introduced the **abdominal wall tenderness test**[15] as a way of diagnosing lesions in the abdominal wall that cause abdominal pain and tenderness and sometimes mimic peritonitis. In this test, the clinician locates the area of maximal tenderness by gentle palpation and then applies enough pressure to elicit moderate tenderness. The patient is asked to fold the arms on the chest and lift the head and shoulders, as if performing a partial sit-up. If this maneuver causes increased tenderness at the site of palpation, the test is positive,[16] a finding traditionally *decreasing* the

probability of peritonitis because tense abdominal wall muscles are protecting the peritoneum from the clinician's hands.

One well-recognized cause of acute abdominal wall tenderness is diabetic neuropathy (i.e., thoracoabdominal neuropathy involving nerve roots T7 to T11; lesions of T1 to T6 cause chest pain).[17–19] In addition to a positive abdominal wall tenderness test, characteristic signs of this disorder are cutaneous hypersensitivity, often of contiguous dermatomes, and weakness of the abdominal muscles causing ipsilateral bulging of the abdominal wall that resembles a hernia.[18,19]

B. APPENDICITIS

1. McBurney Point Tenderness

In a paper read before the New York Surgical Society in 1889, citing the advantages of early operation in appendicitis, Charles McBurney stated that all patients with appendicitis have maximal pain and tenderness "determined by the pressure of the finger (at a point) very exactly between an inch and a half and two inches from the anterior superior spinous process of the ilium on a straight line drawn from that process to the umbilicus."[20,21]

2. Rovsing Sign (Indirect Tenderness)

The **Rovsing sign** (Neils T. Rovsing, 1862-1927, Danish surgeon) is positive when pressure over the patient's *left* lower quadrant causes pain in the right lower quadrant.[7]

3. Rectal Tenderness

In patients with appendicitis and inflammation confined to the pelvis, rectal examination may reveal tenderness, especially on the right side; also, some patients with perforation may have a rectal mass (i.e., pelvic abscess).

4. Psoas Sign

The inflamed appendix may lie against the right psoas muscle, causing the patient to shorten that muscle by drawing up the right knee. To elicit the **psoas sign,** the patient lies down on the left side and the clinician hyperextends the right hip. Painful hip extension is the positive response.[7,11]

5. Obturator Sign

The **obturator sign** is based on the same principle as the psoas sign, that stretching a pelvic muscle irritated by an inflamed appendix causes pain. To stretch the right obturator internus muscle and elicit the sign, the clinician flexes the patient's right hip and knee and then internally rotates the right hip.[7,11]

C. CHOLECYSTITIS AND MURPHY SIGN

Patients with acute cholecystitis present with continuous epigastric or right upper quadrant pain, nausea, and vomiting. The traditional physical signs are fever, right upper quadrant tenderness, and a positive **Murphy**

sign. In 1903, the American surgeon Charles Murphy stated that the hypersensitive gallbladder of cholecystitis prevents the patient from taking in a "full, deep inspiration when the clinician's fingers are hooked up beneath the right costal arch below the hepatic margin. The diaphragm forces the liver down until the sensitive gallbladder reaches the examining fingers, when the inspiration suddenly ceases as though it had been shut off."[22]

Most clinicians elicit the Murphy sign by palpating the right upper quadrant of the supine patient. In his original description, Murphy proposed other methods, such as the **deep-grip palpation technique,** in which the clinician examines the seated patient from behind and curls the fingertips of his or her right hand under the right costal margin, and the **hammer-stroke percussion technique,** in which the clinician strikes a finger pointed into the right upper quadrant with the ulnar aspect of the other hand.[22]

D. SMALL BOWEL OBSTRUCTION

Small bowel obstruction presents with abdominal pain and vomiting. The traditional physical signs are abdominal distention and tenderness, visible peristalsis, and abnormal bowel sounds (initially, high-pitched tickling sounds followed by diminished or absent bowel sounds).[7,11] Signs of peritonitis (e.g., rigidity, rebound) may appear if portions of the bowel become ischemic.

III. CLINICAL SIGNIFICANCE

EBM Boxes 50-1 through 50-4 present the physical findings of acute abdomen. Two of the boxes apply to *all* patients with acute abdominal pain, addressing the diagnosis of peritonitis (see EBM Box 50-1) or small bowel obstruction (see EBM Box 50-4). (Many of these pooled likelihood ratio [LR] estimates are based on >6000 patients.) EBM Box 50-2 addresses bedside findings specific for appendicitis (i.e., focusing on patients with right lower quadrant pain), whereas EBM Box 50-3 applies to patients with right upper quadrant pain and suspected cholecystitis.

A. PERITONITIS

In the studies reviewed in EBM Box 50-1, the principal cause of peritonitis was appendicitis, although some patients had perforated ulcers, perforated diverticula, or cholecystitis. According to these studies, the findings increasing the probability of peritonitis the most are rigidity (LR = 3.7), percussion tenderness (LR = 2.4), and guarding (LR = 2.2). The findings that *decrease* the probability of peritonitis are a *positive* abdominal wall tenderness test (LR = 0.1) and a *negative* cough test (LR = 0.4). The presence or absence of rebound tenderness (positive LR = 2, negative LR = 0.4) shifts the probability relatively little, confirming the long-held opinion of expert surgeons that rebound tenderness adds little to what clinicians already know from gentle palpation.

Unhelpful findings in these studies are fever, characteristics of the bowel sounds, and rectal tenderness.

EBM BOX 50-1
*Acute Abdominal Pain, Signs Detecting Peritonitis**

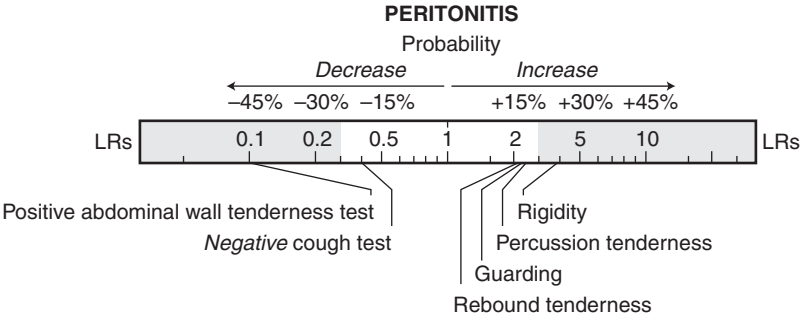
Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Vital Signs				
Fever[23–35]	20-96	11-86	1.4	0.7
Abdominal Examination				
Guarding[2,24,29,31,33,34,36–42]	13-90	40-97	2.2	0.6
Rigidity[2,25,27,37–39,41,43,44]	6-66	76-100	**3.7**	0.7
Rebound tenderness[2,23–25,27–29,31–38,40–42,45–50]	37-95	13-91	2	0.4
Percussion tenderness[27,40,47]	57-65	61-86	2.4	0.5
Abnormal bowel sounds[2,39]	25-61	44-95	NS	0.8
Rectal Examination				
Rectal tenderness[23–25,29,30,32,34,36,37,39–41,48,51]	22-82	41-85	NS	NS
Other Tests				
Positive abdominal wall tenderness test[16,52]	1-5	32-72	**0.1**	NS
Positive cough test[14,27,30,43,47,50]	50-85	38-79	1.6	0.4

*Diagnostic standard: for *peritonitis*, surgical exploration and follow-up of patients not operated on; causes of peritonitis included appendicitis (most common), cholecystitis, and perforated ulcer. One study also included patients with pancreatitis.[39]

†Definition of findings: for *fever,* most studies used >37.3° C; for *abnormal bowel sounds*, absent, diminished, or hyperactive; for *abdominal wall tenderness test,* see text; for *positive cough test*, the patient is asked to cough, and during the cough shows signs of pain or clearly reduces the intensity of the cough to avoid pain.[27]

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. NS, not significant.

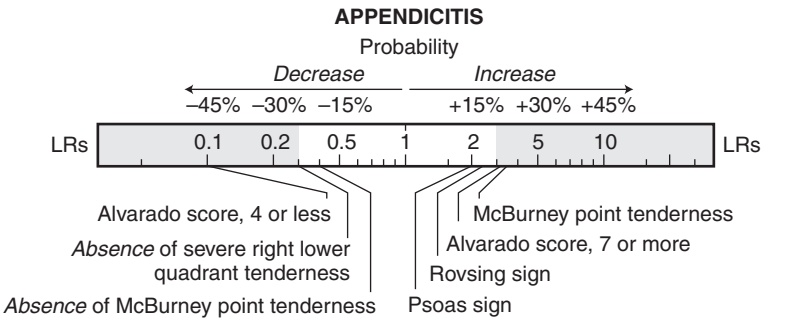
Click here to access calculator.



EBM BOX 50-2
*Acute Abdominal Pain: Findings of Appendicitis**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Abdominal Examination				
Right lower quadrant tenderness[23–25,27–29,33,34,36,37,39,41,47,50,53]	65-100	1-92	1.8	**0.3**
McBurney point tenderness[24,27,54]	50-94	75-86	**3.4**	0.4
Rovsing sign[24,29,30,38]	7-68	58-96	2.3	0.8
Other Signs				
Psoas sign[29,36,40]	13-42	79-97	2.0	NS
Obturator sign[36]	8	94	NS	NS
Combination of Findings—Alvarado Score[4,23,28,55–66]				
7 points or more	24-95	46-99	**3.1**	—
5-6 points	4-43	—	NS	—
4 points or less	0-28	6-87	**0.1**	—

*Diagnostic standard: for *appendicitis*, surgical findings, histologic findings, and follow-up of patients who have not undergone operation.
†Definition of findings: for *Rovsing sign*, see text; for *Alvarado score*, see Table 50-1.
‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.
NS, not significant.
Click here to access calculator.



B. SPECIAL TESTS FOR APPENDICITIS

In patients with acute abdominal pain, the absence of right lower quadrant tenderness decreases the probability of appendicitis (LR = 0.3; see EBM Box 50-2).

1. Individual Findings

For individual findings, see EBM Box 50-2. All of the findings in EBM Box 50-1 apply to patients with suspected appendicitis. (In fact, the most common cause of peritonitis in these studies was appendicitis.)

EBM BOX 50-3

*Acute Right Upper Quadrant Tenderness, Signs Detecting Cholecystitis**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Fever[67–70]	29-44	37-83	NS	NS
Right upper quadrant tenderness[39,53,67,69,71,72]	60-98	1-97	2.7	0.4
Murphy sign[53,71,73,74]	48-97	48-98	**3.2**	0.6
Right upper quadrant mass[67,69,70,72]	2-23	70-99	NS	NS

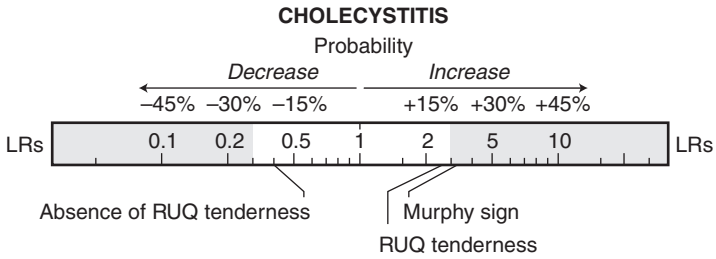
*Diagnostic standard: for *cholecystitis*, positive hepatobiliary scintiscan[71] or surgical findings and histologic findings.[39,53,67,69,70,72–74]

†Definition of findings: for *fever*, temperature >37.5° C,[70] >37.7° C,[68] >38° C,[69] or undefined.[67]

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

NS, not significant.

Click here to access calculator.



Additional special tests that further increase the probability of appendicitis are McBurney point tenderness (LR = 3.4), a positive Rovsing sign (LR = 2.3), and a positive psoas sign (LR = 2). The only special finding decreasing the probability of appendicitis (other than the absence of right lower quadrant tenderness) is the absence of McBurney point tenderness (LR = 0.4).

McBurney point tenderness would have even greater accuracy if every patient's appendix were located precisely at the McBurney point, but radiologic investigation reveals that the normal appendix sometimes lies a short distance away.[75] In one study of patients with acute abdominal pain, clinicians first located the patient's appendix using handheld ultrasound equipment. Maximal pinpoint tenderness over this "sonographic McBurney point" had superior diagnostic accuracy for detecting appendicitis (sensitivity 87%, specificity 90%, positive LR 8.4, negative LR 0.1).[76]

EBM BOX 50-4

*Acute Abdominal Pain, Signs Detecting Bowel Obstruction**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Inspection of Abdomen				
Visible peristalsis[3]	6	100	**18.8**	NS
Distended abdomen[1,3,39]	58-67	89-96	**9.6**	0.4
Palpation of Abdomen				
Guarding[1,2,39]	20-63	47-78	NS	NS
Rigidity[1–3,39]	6-18	75-99	NS	NS
Rebound tenderness[1,2,39]	22-40	52-82	NS	NS
Auscultation of Abdomen				
Hyperactive bowel sounds[3,39]	40-42	89-94	**5.0**	0.6
Abnormal bowel sounds[1–3,39]	63-93	43-88	**3.2**	0.4
Rectal Examination				
Rectal tenderness[1,2,39]	4-26	72-94	NS	NS

*Diagnostic standard: for *small bowel obstruction*, surgical findings, abdominal radiographs, and clinical follow-up.

†Definition of findings: for *abnormal bowel sounds*, hyperactive, absent, or diminished bowel sounds.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

NS, not significant.

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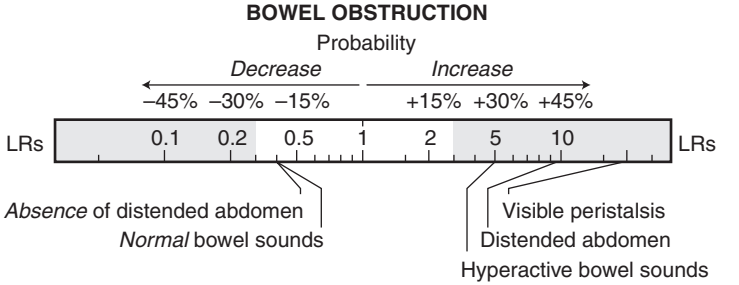

In contrast to a long-held traditional teaching, giving analgesics to patients with acute abdominal pain does not change the accuracy of individual signs or reduce the clinician's overall diagnostic accuracy.[77]

Rectal tenderness (see EBM Box 50-1) and the obturator sign (see EBM Box 50-2) were diagnostically unhelpful in these studies. Nonetheless, a rectal examination should still be performed to detect the rare patient (≤2%) with a pelvic abscess and rectal mass.[37,39]

TABLE 50-1 The Alvarado Score*

Finding†	Points
SYMPTOMS	
Migration	1
Anorexia	1
Nausea and vomiting	1
SIGNS	
Tenderness, right lower quadrant	2
Rebound tenderness	1
Elevation of temperature	1
LABORATORY FINDINGS	
Leukocytosis (white blood cell count >10,000/μL)	2
Shift to the left (>75% neutrophils)	1
TOTAL POSSIBLE POINTS	10

*MANTRELS is an acronym for the Alvarado score; see text for explanation.
†Definition of findings: for *migration,* classic migration of pain from periumbilical or epigastric area to right lower quadrant; for *anorexia*, may substitute acetone in urine; for *elevation of temperature,* oral temperature ≥37.3° C.

2. Combination of Findings: The Alvarado Score

Many scoring systems have been developed to improve diagnostic accuracy and reduce the negative appendectomy rate in patients with acute right lower quadrant tenderness. One of the earliest and most widely used ones is the **Alvarado score** (Table 50-1), which is also called ***MANTRELS* score,** based on the mnemonic **M**igration to the right iliac fossa, **A**norexia, **N**ausea/Vomiting, **T**enderness in the right iliac fossa, **R**ebound pain, **E**levated temperature (fever), **L**eukocytosis, and **S**hift of leukocytes to the left.[23] In 15 studies of more than 3000 patients with acute abdominal pain, an Alvarado score of 7 or more increased the probability of appendicitis (LR = 3.1; see EBM Box 50-2), and a score of 4 or less significantly decreased the probability of appendicitis (LR = 0.1).

C. CHOLECYSTITIS

In patients with right upper quadrant pain and suspected cholecystitis, the findings that increase the probability of cholecystitis (see EBM Box 50-3) are a positive Murphy sign (LR = 3.2) and right upper quadrant tenderness (LR = 2.7). The absence of right upper quadrant tenderness decreases the probability (LR = 0.4). The presence or absence of a right upper quadrant mass is unhelpful, probably because a palpable tender gallbladder is uncommon in cholecystitis (sensitivity <25%) and because the sensation of a right upper quadrant mass may occur in other diagnoses, such as liver disease or localized rigidity of the abdominal wall from other disorders.

There is also a *sonographic Murphy sign,* elicited during ultrasonography of the right upper quadrant, which is simply the finding of maximal tenderness over the gallbladder. Studies of this sign in patients with right upper

quadrant pain reveal much better diagnostic accuracy than conventional palpation: sensitivity 63%, specificity 94%, positive LR = 9.9, and negative LR = 0.4.[78] The superior accuracy of this sign, which also relies on palpation of the abdominal wall, suggests that the poorer accuracy of conventional palpation is due to the difficulty in precisely locating the position of the gallbladder.

The Murphy sign may be less accurate in elderly patients because up to 25% of patients over 60 years of age with cholecystitis lack any abdominal tenderness whatsoever.[79] Although most of these patients have abdominal pain, some lack pain and present instead with altered mental status or sepsis syndrome.

In patients with a pyogenic liver abscess, the presence of the Murphy sign increases the probability of associated biliary tract sepsis (sensitivity 32%, specificity 88%, positive LR = 2.8, negative LR not significant).[80]

D. SMALL BOWEL OBSTRUCTION

In patients with acute abdominal pain, the findings of visible peristalsis (LR = 18.8), abdominal distention (LR = 9.6), and hyperactive bowel sounds (LR = 5) increase the probability of bowel obstruction (though visible peristalsis is rare, occurring in only 6% of affected patients) (see EBM Box 50-4). Diminished or absent bowel sounds also occur in obstruction, being found in one of four patients.[3,39]

The findings that decrease the probability of obstruction slightly are normal bowel sounds (i.e., not hyperactive, absent, or diminished) and the absence of a distended abdomen (both LRs = 0.4). Nonetheless, 30% to 40% of patients with obstruction lack abdominal distention, especially early in the course or if the obstruction is high in the intestines. The findings of peritoneal irritation—rigidity and rebound tenderness—do not change the probability of obstruction.

E. DIVERTICULITIS

In one study of 600 patients with abdominal pain, the finding of left lower quadrant tenderness significantly increased the probability of diverticulitis (sensitivity 22%, specificity 98%, positive LR = 13.8, negative LR = 0.8).[39]

F. RENAL COLIC

In one study of 1333 patients presenting with acute abdominal pain, two findings were accurate signs of ureterolithiasis (as diagnosed by imaging or follow-up): loin tenderness (sensitivity 15%, specificity 99%, positive LR = 27.7, negative LR = 0.9) and renal tenderness (sensitivity 86%, specificity 76%, positive LR = 3.6, negative LR = 0.2). As compelling as these findings are, they are less accurate than the finding of microscopic hematuria, which has a sensitivity of 75%, specificity of 99%, positive LR of 73.1, and negative LR of 0.3.[81]

CHRONIC ABDOMINAL PAIN

In one study of patients with chronic abdominal pain, the abdominal wall tenderness test (see the section on Abdominal Wall Tenderness Test) significantly *decreased* the probability of a visceral cause of the pain (LR = 0.1;

EBM BOX 50-5
*Chronic Upper Abdominal Pain**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Positive abdominal wall tenderness test, detecting visceral pain[82]	11	21	**0.1**	**4.2**
Right upper quadrant tenderness, detecting cholelithiasis[83]	53	51	NS	NS
Lower abdominal tenderness, detecting cholelithiasis[83]	21	57	0.5	1.4
Epigastric tenderness, detecting positive upper endoscopy[84]	63	31	NS	NS

*Diagnostic standard: for *cholelithiasis*, ultrasonography or oral cholecystogram[83]; for *positive upper endoscopy*, findings on upper gastrointestinal endoscopy, most of which were peptic ulcers; for *visceral pain*, pain originating from an intra-abdominal organ or structure (i.e., not abdominal wall).

†Definition of findings: for *abdominal wall tenderness test*, see text.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

NS, not significant.

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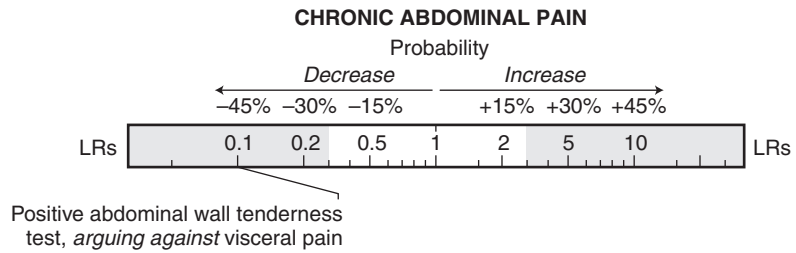

EBM Box 50-5). In these patients, a positive abdominal wall tenderness test increased the probability that the pain would respond to an injection of combined anesthetic/corticosteroid into the tender spot and that *no* serious pathology would be discovered during 3 or more months of follow-up (LR = 7).[82]

Beyond this finding, there is relatively little information on the accuracy of examination in diagnosing chronic abdominal pain. Most studies show that the finding of abdominal tenderness is common in many nonorganic disorders and has little diagnostic value. In patients with suspected biliary colic, right upper quadrant tenderness does not distinguish patients with cholelithiasis from those without it, although lower abdominal tenderness

modestly decreases the probability of cholelithiasis (LR = 0.5; see EBM Box 50-5). In patients with dyspepsia, epigastric tenderness does not help predict whether upper endoscopy will reveal an ulcer, some other abnormality, or normal findings.

Even if the finding of tenderness has little diagnostic value in patients with chronic abdominal pain, abdominal examination is still important to detect masses, organomegaly, and signs of a surgical abdomen.

References for this chapter can be found on www.expertconsult.com.

CHAPTER 51

Auscultation of the Abdomen

ABDOMINAL BRUITS

I. THE FINDING

Abdominal bruits are murmurs heard during auscultation of the abdomen. Like any murmur generated outside the four heart chambers, abdominal bruits may extend beyond the confines of the first and second heart sounds from systole into diastole (i.e., they may be "continuous"; see Chapter 41). Most bruits are detected in the epigastrium or upper abdominal quadrants.

II. CLINICAL SIGNIFICANCE

A. BRUITS IN HEALTHY PERSONS

Bruits occur in 4% to 20% of healthy persons.[1–3] Abdominal bruits are more common in those younger than 40 years of age than in older persons.[1–4]

Characteristically, the abdominal bruit of a healthy individual is systolic, medium-pitched to low-pitched, and audible between the xiphoid process and the umbilicus.[1] Only rarely does it spread to the patient's sides, in contrast to abnormal bruits, which are often loudest away from the epigastrium (see following section). Arteriograms reveal that the most common source for the normal abdominal bruit is the patient's celiac artery.[4]

B. BRUITS IN RENOVASCULAR HYPERTENSION

In patients with renal artery stenosis and renovascular hypertension, an abdominal bruit may be heard in the epigastrium, although the sound sometimes radiates to one side.[1] In one study of patients referred because of severe hypertension that was difficult to control—a setting suggesting renovascular hypertension—the finding of a *systolic/diastolic* abdominal bruit (i.e., continuous bruit) was virtually diagnostic for renovascular hypertension (LR = 38.9; EBM Box 51-1). In contrast, the finding in similar patients of *any* abdominal bruit (i.e., one not necessarily extending into diastole) is less compelling (LR = 5.6), probably because these bruits also occur in persons without renovascular hypertension. (See the section on Bruits in Healthy Persons.)

The abdominal bruit of renovascular hypertension, however, does not always originate in the renal artery. In one study of patients undergoing surgery for renal artery stenosis, intraoperative auscultation localized the bruit to the renal arteries as the sole source only about half the time.[1] In the remaining patients, other vessels generated or contributed to the sound.

EBM BOX 51-1
*Auscultation of Abdomen**

Finding (Reference)	Sensitivity (%)	Specificity (%)	Likelihood Ratio† if Finding Is	
			Present	*Absent*
Abdominal Bruit—Any				
Detecting renovascular hypertension[5–8]	27-56	89-96	**5.6**	0.6
Detecting abdominal aortic aneurysm[9]	11	95	NS	NS
Abdominal Bruit—Systolic/Diastolic				
Detecting renovascular hypertension[10]	39	99	**38.9**	0.6

*Diagnostic standard: for *renovascular hypertension*, renal angiography,[5–8] sometimes combined with renal vein renin ratio >1.5[10] or cure of hypertension after surgery[7]; for *abdominal aortic aneurysm*, ultrasonography revealing focal dilation of infrarenal aorta >1.5 cm larger than proximal aorta.[9]

†Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

NS, not significant.

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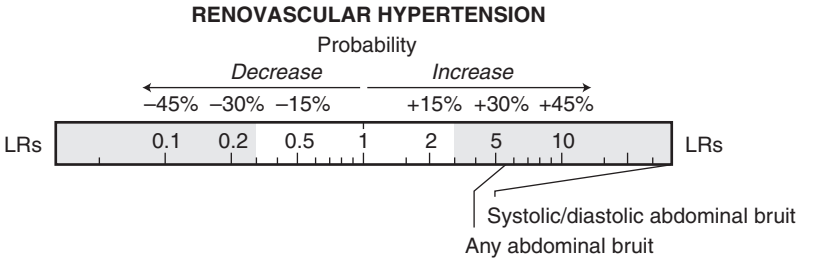

Bruits in these patients may possibly be general markers of vascular disease, just as the finding of a carotid bruit has been associated with disease in other distant vascular beds, such as the coronary vasculature.[11]

C. BRUITS IN OTHER DISORDERS

Harsh, epigastric or right upper quadrant bruits (systolic and continuous) have been repeatedly described in patients with hepatic malignant diseases[12,13] and hepatic cirrhosis.[12,14] In these patients, the sound may represent extrinsic compression of vessels by tumor or regenerating nodules, the hypervascular tumor, or portosystemic collateral vessels. Left upper quadrant bruits occur in patients with carcinoma of the body of the pancreas (8 of 21 patients in one study).[15] Other rare causes of abdominal bruits are renal artery aneurysms,[16] aortocaval fistulas,[17] ischemic bowel disease,[18] and celiac compression syndrome.[19] Although an abdominal bruit is traditionally associated with an abdominal aortic aneurysm, the finding lacked diagnostic value in one study (LR not significant; see EBM Box 51-1).[9]

HEPATIC RUB

In the absence of a recent liver biopsy, the finding of a hepatic friction rub has been repeatedly associated with intrahepatic malignant disease, either hepatoma or metastatic disease.[13,20] In one study of tumors metastatic to the liver, 10% of patients had a hepatic friction rub.[21]

BOWEL SOUNDS

I. THE FINDING

Most clinicians have great difficulty making any sense out of a patient's bowel sounds, for two reasons:

The first reason is that normal bowel sounds, from moment to moment, vary greatly in pitch, intensity, and frequency. One healthy person may have no bowel sounds for up to 4 minutes, but when examined later may have more than 30 discrete sounds per minute.[22] The activity of normal bowel sounds may cycle with peak-to-peak periods as long as 50 to 60 minutes,[23] meaning that any analysis based on even several minutes of bedside auscultation is incomplete.

The second reason is that bowel sounds generated at one point of the intestinal tract radiate widely over the entire abdominal wall.[22,24] The sounds heard in the right lower quadrant, for example, may actually originate in the stomach. This dissemination of bowel sounds makes the practice of listening to them in all four quadrants fundamentally unsound because, as an example, the left lower quadrant may be quieter than the left upper quadrant, not because the descending colon is making less noise than the stomach but instead because the entire abdomen has become quieter, at least for the moment that the clinician is listening to the lower quadrant.

Most bowel sounds are generated in the stomach, followed by the large intestine and then the small bowel.[25] The overall frequency of bowel sounds increases after a meal.[26] The actual cause of bowel sounds is still debated; experiments with exteriorized loops of bowel in dogs show many intestinal contractions to be silent, although sound often occurs when contractions propel contents through a bowel segment that is not relaxed.[22]

II. CLINICAL SIGNIFICANCE

Analysis of the bowel sounds has modest value in diagnosing small bowel obstruction. After experimental complete bowel obstruction in animals, bowel sounds are hyperactive for about 30 minutes before becoming diminished or absent.[23] In patients with small bowel obstruction, clinical observation shows that about 40% have hyperactive bowel sounds and about 25% have diminished or absent bowel sounds.[27,28] Consequently, because most patients with small bowel obstruction have abnormal bowel sounds, the finding of *normal* bowel sounds in a patient with acute abdominal pain

modestly *decreases* the probability of bowel obstruction (LR = 0.4; see EBM Box 50-4 in Chapter 50).

A traditional finding of peritonitis is diminished or absent bowel sounds, although studies of patients with acute abdominal pain show this finding to be unreliable (see Chapter 50).

References for this chapter can be found on www.expertconsult.com.

CHAPTER 52

Peripheral Vascular Disease

I. INTRODUCTION

Chronic arterial disease usually affects the lower limbs in three distinct segments:

1. The aortoiliac segment (especially the infrarenal abdominal aorta and common iliac arteries)
2. The femoropopliteal segment (especially the superficial femoral artery in the adductor canal)
3. The peroneotibial segment (below the knee)[1]

Disease in each segment produces distinct patterns of claudication (Table 52-1). Most patients have aortoiliac disease or femoropopliteal disease, or both.[2] Disease below the knee is uncommon unless the patient is diabetic or has thromboangiitis obliterans.

The diagnostic standard for chronic lower extremity ischemia is the ankle-to-arm systolic pressure index (AAI), which is obtained by measuring the highest systolic blood pressure at the ankle (dorsalis pedis and posterior tibial arteries) with a handheld Doppler flowmeter and dividing it by the blood pressure measurement in the brachial artery. Values of less than 0.97 are abnormal (i.e., the lower 2.5% of measurements from large numbers of young, nonsmoking, asymptomatic persons).[3–5] Most patients with claudication have AAIs between 0.5 and 0.8 and disease in only a single segment; those with limb-threatening ischemia (i.e., rest pain, gangrene) have AAIs of less than 0.5 and disease in at least two segments.[4,5]

II. THE FINDINGS

A. APPEARANCE OF THE FOOT

The earliest clinicians writing about peripheral vascular disease emphasized the physical sign of gangrene, but in 1924, the American surgeon Leo Buerger described in his book *The Circulatory Disturbances of the Extremities* various "prodromal" signs of vascular disease, including toe and foot ulcers, poor capillary refill, impaired nail growth, atrophic skin, foot pallor with elevation, and dependent foot rubor (i.e., redness of the foot first appearing after dangling it in a dependent position, as over the edge of a bed).[6] Clinicians have since regarded these findings as characteristic of chronic lower limb ischemia, although some of them—especially poor capillary refill and dependent rubor—were controversial even in Buerger's time.[7,8]

TABLE 52-1 Diagnosis of Peripheral Arterial Disease: Traditional Approach

		Pulse Examination		
Anatomic Segment	**Location of Claudication**	**Femoral Pulse***	**Popliteal Pulse**	**Pedal Pulse**
Aortoiliac	Buttock, thigh, calf†	Absent	Absent	Absent
Femoropopliteal*	Calf	Present	Absent	Absent
Peroneotibial	None or foot‡	Present	Present	Absent

*The *femoro* of femoropopliteal indicates the superficial femoral artery; the *femoral* of femoral pulse indicates the common femoral artery.
†May cause erectile dysfunction if internal iliac arteries are involved.
‡Disease in this segment usually causes no claudication in patients with diabetes but causes foot pain in those with thromboangiitis obliterans (Buerger disease).
Adapted from reference 1.

B. PULSES

In studies of large numbers of healthy individuals, the dorsalis pedis pulse is not palpable 3% to 14% of the time and the posterior tibial pulse is not palpable 0% to 10% of the time.[9–14] Nonetheless, when one of these arteries is congenitally small or absent, the other enlarges to make up the difference, explaining why only 0% to 2% of healthy persons lack *both* pedal pulses.[9,10,13]

The absence of both pedal pulses is common to vascular disease in each of the three vascular segments and thus represents the best screening test for peripheral vascular disease (see Table 52-1).

C. BRUITS

A traditional finding of vessel stenosis is the limb bruit, which may be in the iliac segment (above the inguinal crease), femoral segment (in the thigh), or popliteal segment. Complete occlusion of a vessel should make bruits disappear.

In patients who have undergone femoral artery puncture for cardiac catheterization, the presence of a continuous femoral bruit (i.e., one extending beyond the second heart sound and thus having both systolic and diastolic components) suggests an abnormal communication between an artery and a vein (i.e., arteriovenous fistula; see Chapter 41).

D. ANCILLARY TESTS

1. Venous Filling Time

In patients with peripheral vascular disease, the veins of the feet fill abnormally slowly once they are emptied. After positioning the patient supine and identifying a prominent vein on the top of the foot, the clinician empties this vein by elevating the patient's leg to 45 degrees above the table surface for 1 minute. The patient then sits up and dangles the foot over the edge of the examining table, and the clinician records how long it takes for the vein to rise above the level of the skin surface. Measurements of more than 20 seconds are abnormal.[15]

2. Capillary Refill Time

To perform this test, the clinician applies firm pressure for 5 seconds to the plantar skin of a distal digit (usually the great toe if one is diagnosing peripheral vascular disease) and then times how long it takes for normal skin color to return after releasing the pressure. Normal values of capillary refill time, based on observation of thousands of persons, average about 2 seconds.[16,17] Women have slightly longer times compared with men, and capillary refill times normally increase in elderly patients and in cooler ambient temperatures.

In the great toe, measurements of more than 5 seconds are regarded as abnormal.[15]

3. Buerger Test

In the **Buerger test,** the clinician observes the color of the patient's leg when it is elevated and again when it is lowered. Abnormal pallor in the elevated leg and deep rubor in the lowered leg are features of vascular disease.[1,6] In Buerger's version of the test, the clinician elevated the leg to produce pallor and then simply recorded the angle at which the reddish hue returned as the limb was lowered (his "angle of circulatory sufficiency").[6] In the only investigated version of this test (see the section on Distribution of Vascular Disease), the clinician elevated the patient's leg 90 degrees from the table surface for 2 minutes and then dangled it perpendicular to the table edge for another 2 minutes. The positive response was abnormal pallor with elevation and the appearance of a dusky red flush spreading proximally from the toes in the dependent position.[18]

III. CLINICAL SIGNIFICANCE

A. DIAGNOSIS OF PERIPHERAL VASCULAR DISEASE

EBM Box 52-1 shows that the following physical signs *increase* the probability of peripheral vascular disease (i.e., AAI <0.9) if it is found in a symptomatic leg: absence of both pedal pulses (likelihood ratio [LR] = 14.9), presence of any limb bruit (LR = 7.3), presence of wounds or sores on the foot (LR = 7), absence of femoral pulse (LR = 6.1), and presence of asymmetrical coolness of the foot (LR = 6.1). In another study,[15] the presence of foot coolness was diagnostically unhelpful, although this study defined the abnormal finding as "foot cooler than ipsilateral calf," which actually is a normal finding (i.e., the skin surface temperature of healthy persons normally diminishes toward the feet, paralleling progressively reduced cutaneous blood flow to conserve body heat).[1]

The only finding that *decreases* the probability of peripheral vascular disease is the presence of one or both pedal pulses (LR = 0.3), although studies show that up to one of three patients with disease have this finding. In these patients, however, the pulses often disappear during exercise (e.g., while running in place, walking, standing on the toes, or flexing the ankles repeatedly against resistance), just as normal resting coronary blood flow in a patient with coronary artery disease may become abnormal after exercise.[23]

Findings that are unhelpful diagnostically are atrophic skin, hairless lower limbs,[24,25] and capillary refill time of more than 5 seconds. Writing soon after Buerger introduced the capillary refill time as a test of peripheral vascular disease (his "expression test"), Lewis[8] and Pickering[7] showed it was an unreliable sign because prompt refill could occur from the veins of a limb rendered completely ischemic experimentally.

Some investigators have wondered whether clinicians could accurately measure the AAI by palpating the pedal pulses distal to the blood pressure cuff instead of using a Doppler flowmeter. In one study,[26] such an AAI <0.9 "by palpation" detected an AAI <0.9 "by Doppler" testing with a sensitivity of 88%, specificity of 82%, positive LR = 5, and negative LR = 0.2. Another

EBM BOX 52-1
*Peripheral Vascular Disease**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Inspection				
Wounds or sores on foot[19]	2	100	**7.0**	NS
Foot color abnormally pale, red, or blue[19]	35	87	2.8	0.7
Atrophic skin[15]	50	70	1.7	NS
Absent lower limb hair[15]	48	71	1.7	NS
Palpation				
Foot asymmetrically cooler[19]	10	98	**6.1**	0.9
Absent femoral pulse[19]	7	99	**6.1**	NS
Absent posterior tibial and dorsalis pedis pulses[19,20]	63-72	92-99	**14.9**	**0.3**
Auscultation				
Limb bruit present[19,21,22]	20-50	95-99	**7.3**	0.7
Ancillary Tests				
Capillary refill time ≥5 seconds[15]	28	85	1.9	NS
Venous filling time >20 seconds[15]	22	94	**3.6**	NS

*Diagnostic standard: for *peripheral vascular disease*, an ankle-to-arm index (AAI) of less than 0.8 to 0.97, except in the study by Boyko (i.e., atrophic skin, absent lower limb hair, capillary refill time, and venous filling time),[15] which recruited diabetic patients exclusively and defined disease as an AAI of less than 0.5.

†Definition of findings: For *limb bruit present*, femoral artery bruit[19,22] or iliac, femoral, or popliteal bruit.[21]

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. NS, not significant.

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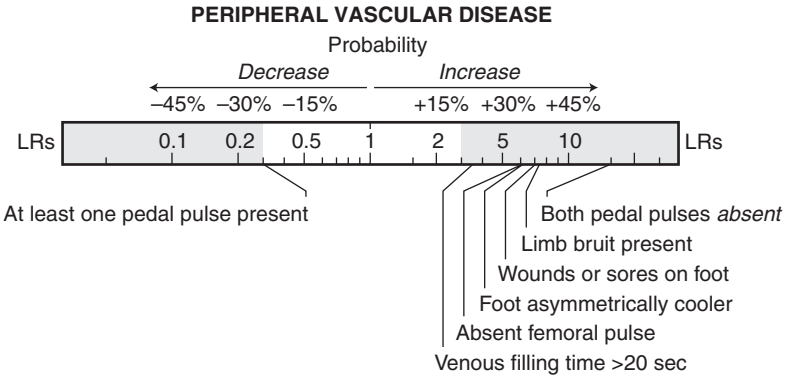


innovative way to detect peripheral vascular disease (without Doppler studies) places a bedside pulse oximeter sequentially on the patient's fingers and great toes: A positive result is either a supine toe measurement 2% lower than the finger measurement *or* a toe measurement that decreases 2% after 12 inches of foot elevation. This test detects vascular disease with a sensitivity of 77%, specificity of 97%, positive LR of 30.5, and negative LR of 0.2.[27] Nonetheless, studies of AAI by palpation and toe pulse oximetry have enrolled mostly asymptomatic patients, and it is unlikely that these studies would be easy to apply in patients with more serious vascular disease, who may lack pedal pulses or have undetectable toe arterial waveforms.

B. DISTRIBUTION OF PERIPHERAL VASCULAR DISEASE

One study showed that vascular surgeons using traditional methods accurately localized the distribution of disease in 96% of 102 symptomatic patients, although the study omitted information about the relative value of specific findings.[28] Of the few studies available, one confirms the traditional teaching (see Table 50-1) that an absent or severely diminished femoral pulse in a symptomatic limb increases the probability of aortoiliac disease (sensitivity 39%, specificity 99%, positive LR = 31, negative LR = 0.6).[29] Also, in symptomatic limbs with preserved popliteal pulses (i.e., a finding arguing against *occlusion* of the aortoiliac or femoropopliteal segments), the presence of a limb bruit argues *for* the presence of stenoses on angiography, a finding of therapeutic importance because these patients may be candidates for angioplasty (sensitivity 80%, specificity 75%, positive LR = 3.2, negative LR = 0.3).[30] Finally, patients who have a positive Buerger test have more extensive disease than those who with a negative test, including more rest pain (60% vs. 8%) and more frequent occurrence of gangrene (23% vs. 0%) and lower AAIs (mean ± standard deviation [SD], 0.37 ± 0.29 vs. 0.62 ± 0.23).[18]

C. COMPLICATIONS OF ARTERIAL PUNCTURE

Femoral artery puncture for cardiac catheterization may be complicated by the formation of false aneurysms or arteriovenous fistulas. In one study of patients with significant groin hematomas or new limb bruits after cardiac

EBM BOX 52-2
*Hypoperfusion in ICU Patients**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Detecting Low Cardiac Output				
Both legs cool (all patients)[32]	23	94	**3.7**	0.8
Both legs cool (patients with sepsis)[32]	30	94	**5.2**	0.7
Combinations of hypoperfusion findings[33]				
0 of 3 findings present	36	24	0.5	—
1 of 3 findings present	52	—	2.3	—
3 or 3 findings present	12	98	**7.5**	—
Detecting Elevated Arterial Lactate Level				
Limb is cool *or* capillary refill time >4.5 seconds[34]	67	69	2.2	0.5
Predicting Multiorgan Dysfunction				
Limb is cool *or* capillary refill time >4.5 seconds[34]	77	70	2.6	**0.3**

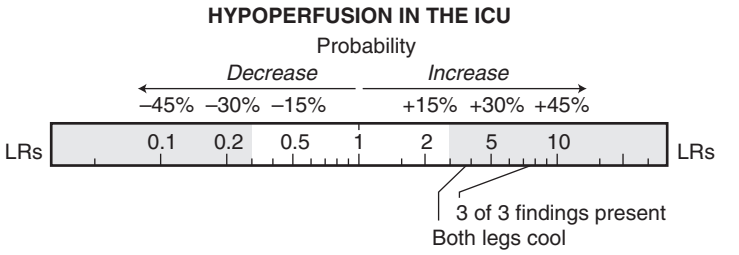
*Diagnostic standard: for *low cardiac output, cardiac index* of less than 2.5 L/min/m^2,[33] or less than 3 L/min/m^2,[32]; for *elevated lactate level,* blood lactate level of more than 2 mmol/L; for *multiorgan dysfunction,* SOFA score that increases during the first 48 hours of hospitalization (**SOFA score** is the Sequential Organ Failure Assessment, a score tabulating the following variables: P_aO_2/F_iO_2, number of vasoactive pressors being administered, bilirubin level, platelet count, Glasgow coma scale score, and creatinine or urine output).

†Definition of findings: For *both legs cool,* either all four limbs have a cool temperature or legs are cool despite arms being warm (patients with known peripheral vascular disease were excluded)[32]; for *hypoperfusion findings*, there are three: (1) capillary refill time of longer than 2 seconds, (2) skin mottling over the knees, and (3) cool limbs.[33]

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

ICU, intensive care unit; NS, not significant.

Click here to access calculator.



catheterization, two findings were diagnostic.[31] A continuous femoral bruit (i.e., one having both systolic and diastolic components) was diagnostic for arteriovenous fistula (sensitivity 96%, specificity 99%, positive LR = 80.8, negative LR = 0.04), and an expansile femoral pulsation (i.e., a dilated arterial pulsation whose walls expanded laterally with each beat) was diagnostic for false aneurysm formation (sensitivity 92%, specificity 93%, positive LR = 13.8, negative LR = 0.1). In this study, the diagnostic standard was duplex scanning or surgery, or both.

D. DETECTING HYPOPERFUSION IN THE INTENSIVE CARE UNIT

The body normally responds to decreased cardiac output by reducing cutaneous blood flow to the limbs, which may produce the findings of cool limbs, prolonged capillary refill, and mottled skin over the knees. In a series of 475 consecutive surgical intensive care unit (ICU) patients, the finding of cool legs increased the probability of low cardiac output (LR = 3.7; EBM Box 52-2), a finding that remained accurate even in the subset of patients with sepsis (LR = 5.2). In another study of intubated patients with acute lung injury, the simultaneous presence of three hypoperfusion findings (i.e., capillary refill time >2 seconds, mottling over the knees, and cool limbs) also increased the probability of a low cardiac output (LR = 7.5), including those patients receiving vasoactive medications to support their blood pressure (LR = 6.5). Finally, in another series of ICU patients, the finding of *either* cool limbs or a capillary refill time of longer than 4.5 seconds increased the probability of an elevated lactate level (LR = 2.2) and predicted future progressive multiorgan dysfunction (LR = 2.6).

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 53

The Diabetic Foot

I. INTRODUCTION

The term *diabetic foot* refers to those complications occurring in a foot rendered hypesthetic from diabetic polyneuropathy. These include ulceration, Charcot arthropathy, and infection. Each year, 2.5% of diabetics develop a foot ulcer,[1] and the diabetic foot is the leading cause of hospitalization among diabetics and the overall leading cause of amputation in the United States.[2]

II. THE FINDINGS

A. FOOT ULCERATION

Most diabetic foot ulcers involve the forefoot, especially the toes or plantar surface of the metatarsal heads. Less often, ulcers develop over the heel, the plantar midfoot, or previous amputation sites. The term *ulcer area* refers to the product of the maximum ulcer width and maximum ulcer length.

B. DIABETIC NEUROPATHY AND SEMMES-WEINSTEIN MONOFILAMENTS

Although neuropathy, ischemia, and infection all contribute to ulceration, the most important is probably neuropathy. Conventional examination often fails to detect diabetic polyneuropathy, however, and about half of patients with diabetic ulceration lack complaints of numbness or pain[3] and can still detect the touch of a cotton wisp or pinprick.[4,5] Consequently, most diabetologists use a simple and more sensitive bedside tool, the **Semmes-Weinstein monofilament,** to identify which patients have neuropathy sufficient to place them at risk for ulceration.

According to traditional teachings, a foot that is able to sense the 5.07 monofilament* is protected from ulceration, whereas one that fails to perceive the 5.07 monofilament is predisposed to ulceration. To use the monofilament, the patient should be lying supine with eyes closed, and the monofilament should be applied perpendicular to the skin with enough force to buckle it for approximately 1 second. The patient responds "yes" each time he or she senses the monofilament, as the clinician randomly

*The nominal value of a monofilament represents the common logarithm of 10 times the force in milligrams required to bow it (e.g., the 5.07 monofilament will buckle with 11.8 g of pressure, $\log_{10}$ [10 × 11,800] = 5.07).[6] Therefore, monofilaments with higher numbers are stiffer and more easily perceived than those with lower numbers.

tests each site on the foot multiple times. In clinical studies, anywhere from 1 to 10 different sites on the foot are tested, but each study defines the abnormal result as inability to consistently sense the monofilament at *any* site. Testing the plantar surface of the first and fifth metatarsal heads may be the most efficient and, overall, the most accurate bedside maneuver.[7]

Monofilaments were first developed in 1898 by von Frey, who glued thorns to hairs of various stiffness and calibrated them with a chemical balance **(von Frey hairs).**[6] Nylon monofilaments were introduced in 1960 by Josephine Semmes and Sidney Weinstein, who used filaments of 20 different diameters (from 0.06 to 1.14 mm) to study sensation in patients with penetrating brain injuries.[8,9] Although the 5.07 monofilament is firmly entrenched as the standard for testing diabetic feet, this standard is based on an older study of patients with neuropathic foot ulcers from diabetes or leprosy, which used just 3 of the 20 monofilaments available.[10] The monofilaments studied were the 4.17 monofilament, which was selected because virtually all normal persons are able to sense it, and the stiffer 5.07 and 6.10 monofilaments. In the study, none of the patients with ulcers could sense the 4.17 or 5.07 monofilaments, although some could sense the 6.10 monofilament. These findings led the investigators to conclude that the ability to sense the 5.07 monofilament was protective (i.e., 6.10 was not protective and 4.17 was normal sensation). It is also possible, however, that a better indicator of protective sensation is one of the other seven monofilaments between 6.10 and 4.17 not used in the study, and in support of this hypothesis, one study has suggested that the 4.21 monofilament may provide a better discriminatory threshold.[4]

C. CHARCOT JOINT

Charcot joint (neuroarthropathy) refers to accelerated degenerative changes and ultimate joint destruction that follows repetitive trauma to insensitive, neuropathic joints. Although historically the most common causes were syphilis (affecting the larger joints of the lower extremity) and syringomyelia (affecting the larger joints of the upper extremity), the most common cause today is diabetes. In diabetic patients, the Charcot joint characteristically affects the foot, including the ankle, tarsometatarsal, and metatarsophalangeal joints.[11,12]

Most patients present with a limp, difficulty in putting on shoes, or soft tissue swelling suggesting fracture, acute arthritis, or sprain.[12,13] The characteristic physical findings are anesthetic or hypesthetic feet (100% of patients), bony deformities (69% of patients), and soft tissue swelling (17% of patients). Many patients also have ulceration and abnormal callus formation. The most common bony deformities are abnormal projections on the plantar arch **(rocker sole)** or other unusual prominence of the dorsal or medial arches of the midfoot or the metatarsophalangeal (MTP) joint. In the acute phase, soft tissue swelling typically appears at the ankle and midfoot, sometimes with marked rubor and warmth mimicking arthritis or cellulitis. (In one study, the affected foot was approximately 5° C [9.2° F] warmer than the unaffected foot.[13])

EBM BOX 53-1
*The Diabetic Foot**

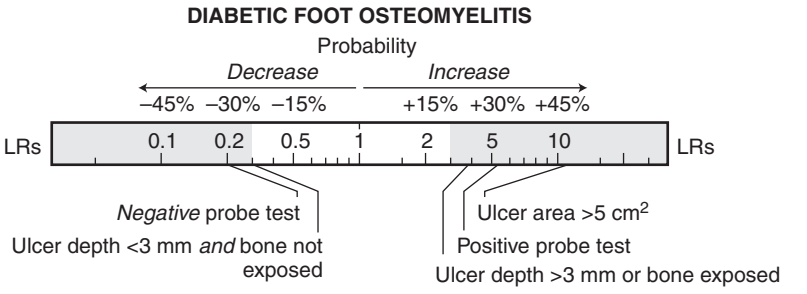
Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Predictors of Subsequent Foot Ulceration				
Insensate to 5.07 monofilament[17–22]	50-90	34-86	2.4	0.5
Predictors of Osteomyelitis, in Patients with Foot Ulcers				
Ulcer area[23–25]				
>2 cm^2	44-88	20-92	NS	NS
>3 cm^2	79	77	**3.5**	0.3
>4 cm^2	67	91	**7.3**	0.4
>5 cm^2	50	95	**11.0**	0.5
Positive probe test[16,24,26–28]	38-98	78-92	**5.3**	**0.2**
Ulcer depth >3 mm or bone exposed[24,25]	65-82	77-85	**3.9**	**0.3**
Erythema, swelling, purulence[24,25]	36-41	77-80	NS	NS
Predictors of Nonhealing Wound at 20 Weeks, in Patients with Foot Ulcers[29]				
0 findings	14	70	0.5	—
1 finding	37	—	0.8	—
2 findings	35	—	1.8	—
3 findings	13	96	**3.5**	—

*Diagnostic standard: for *foot ulceration*, the appearance of an ulcer during 2 to 4 years of follow-up; for *osteomyelitis*, biopsy of the bone (histology or microbiology); a small number of patients in two studies[23,28] underwent MRI to confirm osteomyelitis.

†Definition of findings: for *positive probe test*, *ulcer area*, and *predictors of nonhealing wound*, see text.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. NS, not significant.

Click here to access calculator.



Jean-Martin Charcot described Charcot neuroarthropathy in 1868 in patients with tabes dorsalis,[14] although he credited the American Mitchell (1831) with the original description.[15]

D. OSTEOMYELITIS

In diabetic patients with foot ulceration and underlying radiographic abnormalities of the bone, it is very difficult to distinguish Charcot foot from osteomyelitis. One proposed test is the **probe test,** in which the clinician gently probes the ulcer base with a sterile, blunt, 14-cm 5-Fr, stainless-steel eye probe. The test is positive, suggesting osteomyelitis, if the clinician detects a rock-hard, often gritty structure at the ulcer base without any intervening soft tissue.[16]

III. CLINICAL SIGNIFICANCE

A. THE SEMMES-WEINSTEIN MONOFILAMENT

According to the information presented in EBM Box 53-1, the *inability* to feel the 5.07 monofilament is a modest predictor of ulceration during 2 to 4 years of follow-up (likelihood ratio [LR] = 2.4). Another study has demonstrated that the *presence* of 5.07 monofilament sensation *decreases* the probability of subsequent amputation during 3 to 4 years of follow-up (LR = 0.3).[30] Monofilament sensation predicts complications better than other quantitative measures of sensation, including the 128-Hz tuning fork[31] and graded vibratory or thermal stimuli.[4,32]

B. OSTEOMYELITIS

In diabetic patients with foot ulceration, three findings *increase* the probability of underlying osteomyelitis (defined by bone biopsy): ulcer size (>3 cm^2, LR = 3.5; >4 cm^2, LR = 7.3; >5 cm^2, LR = 11), positive probe test (LR = 5.3), and ulcer depth of more than 3 mm or exposed bone (LR = 3.9). The findings of erythema, swelling, or purulence are unhelpful in diagnosing osteomyelitis.[25] The negative probe-to-bone test decreases the probability of osteomyelitis (LR = 0.2).

C. PREDICTORS OF NONHEALING WOUNDS

In one study of over 27,000 diabetic foot ulcers treated with debridement, moist wound dressings, and measures to reduce pressure on the foot (e.g., special footwear, crutches, or wheelchairs), 53% failed to heal after 20 weeks.[29] This study identified three independent predictors of nonhealing ulcers:

1. Wound age of more than 2 months
2. Wound size of more than 2 cm^2
3. Full-thickness wound associated with either exposed tendons, an exposed joint, an abscess, osteomyelitis, necrotic tissue, or limb gangrene[29]

The presence of all three of these predictors increases the likelihood that a diabetic foot ulcer will not heal by 20 weeks (LR = 3.5).

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 54

Edema and Deep Vein Thrombosis

EDEMA

I. INTRODUCTION

Edema of a limb may occur because of increased venous pressure (e.g., venous insufficiency, congestive heart failure), increased vascular permeability (e.g., inflammation), decreased oncotic pressure (e.g., hypoalbuminemia), lymphatic obstruction (i.e., lymphedema), and deposition of additional tissue (e.g., lipedema). The most common causes of bilateral edema are congestive heart failure, chronic venous insufficiency, pulmonary hypertension without left heart failure, and drug-induced edema (e.g., nifedipine, nonsteroidal anti-inflammatory medications).[1] The most common causes of unilateral swelling of the leg are deep vein thrombosis, Baker cyst, and cellulitis (see later section).[2–4]

II. THE FINDINGS

The pitting characteristics of edema reflect the viscosity of the edema fluid, which in turn depends largely on its protein concentration.[5–8] Edema fluid with low protein levels (e.g., hypoalbuminemia, congestive heart failure) pits easily and recovers relatively quickly compared with edema fluid that has higher protein levels (lymphedema, inflammatory edema).[6,7] A clue to "low-protein edema" (i.e., edema associated with a serum albumin level <3.5 g/dL) is edema that pits easily with just 1 to 2 seconds of thumb pressure over the tibia and then, after removal of the thumb, begins to recover within 2 to 3 seconds.[8]

Lymphedema is painless, firm edema that characteristically causes squaring of the toes and a dorsal hump on the foot. In contrast to venous edema, lymphedema varies little during the day and ulceration is uncommon unless there is secondary infection. Even though lymphedema has high protein levels, clinical experience reveals that lymphedema does pit early in its course, although it eventually becomes nonpitting, hard, and "woody" as secondary fibrosis ensues.[5,9]

Lipedema consists of bilateral deposition of excess subcutaneous fatty tissue in the legs that does not pit with pressure and the most characteristic feature of which is sparing of the feet.[10] Lipedema occurs exclusively in obese women.

III. CLINICAL SIGNIFICANCE

A. PITTING EDEMA

In patients with bilateral pitting edema of the legs, the most important diagnostic finding is the venous pressure, estimated from examination of the neck veins. If the neck veins are abnormally distended, cardiac disease or pulmonary hypertension is at least partly responsible for the patient's edema; if they are normal, another cause is responsible, such as liver disease, nephrosis, chronic venous insufficiency, or one of the patient's medications. Clinicians' estimates of venous pressure are accurate, with studies showing that the finding of elevated neck veins predicts an abnormally increased central venous pressure (i.e., >8 cm of water), with a positive likelihood ratio (LR) of 9.7 (see Chapter 34).

In contrast, the finding of pitting edema by itself and without knowledge of the patient's venous pressure is an unreliable sign of cardiac disease. For example, in patients undergoing cardiac catheterization because of chest pain or dyspnea, the finding of edema (without knowledge of venous pressure) lacked any significant relationship with the patient's left heart pressures (see Chapter 46).

B. LYMPHEDEMA

Lymphedema is classified as "primary" (i.e., congenital abnormality of the lymphatic systems) or "secondary" (damage to the lymphatics from previous radiation or surgery, malignant obstruction, or recurrent episodes of cellulitis). Primary lymphedema begins before the age of 40 years, may be bilateral (50% of cases), and affects women 10 times more often than men.[11] Secondary lymphedema from infection, radiation, or surgery affects men and women of all ages, is usually unilateral, and is preceded by the characteristic history. Malignant obstruction affects patients older than 40 years and is almost always unilateral (>95% of cases).[11] The most common cause of malignant lymphedema in the leg of men is metastatic prostate carcinoma; in women, it is lymphoma.[11] Lymphedema of the arm is almost always due to breast cancer, either the tumor itself or the combined treatment with surgery and irradiation.[12]

DEEP VEIN THROMBOSIS

I. INTRODUCTION

Deep vein thrombosis of the leg is conventionally divided into *proximal* thrombosis (popliteal vein and above) and *distal* thrombosis (calf veins). Several studies have shown that only proximal thrombi are associated with clinically significant pulmonary emboli, and thus only these thrombi require treatment with anticoagulation.[13]

In patients with acutely painful and swollen calves, accurate diagnosis is essential, not only because untreated proximal thrombi may cause fatal pulmonary emboli but also because inappropriate administration of

anticoagulants to persons without proximal thrombi risks unnecessarily life-threatening hemorrhage.

II. THE FINDINGS

A. INSPECTION AND PALPATION

The most important signs of vein thrombosis are tenderness and swelling. Calf asymmetry of more than 1.5 cm is abnormal, indicating significant edema of the larger limb or atrophy of the smaller one.[14]

Other traditional signs associated with deep vein thrombosis are a palpable cord, dilated superficial veins, Homans sign, skin erythema, and altered skin temperature. (Both coolness and warmth have been proposed by different authorities.) The basis for these signs, however, seems dubious. Because large muscles and dense fascial tissues encompass the deep veins of the legs, concealing them from the examiner's eyes and hands, it is difficult to conceive how a clinician could ever palpate the cord of a thrombosed *deep* vein. The increased collateral flow around an obstruction could make the superficial veins more conspicuous, but skin surface temperature and color reflect blood flow and vessel size of the minute vessels *of the dermis*,[15] which should not necessarily be different after venous obstruction.

B. HOMANS SIGN

In his extensive writings about venous thrombosis, the American surgeon John Homans contrasted two forms of the disease: bland thrombosis of the calf veins, which caused few symptoms other than mild swelling and pain, and iliofemoral thrombophlebitis (phlegmasia alba dolens), which caused generalized leg edema and cyanosis.[16–18] Homans believed that most pulmonary emboli originated in the bland calf thrombi and that, once diagnosed, the disorder should be treated by femoral vein ligation to prevent pulmonary emboli. (Anticoagulation was not yet being used.) In 1941, Homans proposed that the **dorsiflexion sign,** defined as "discomfort behind the knee on forced dorsiflexion of the foot," was a sign of these difficult-to-diagnose calf thrombi.[17] Although contemporaries called the sign **Homans sign,**[19] Homans never did and instead later credited another clinician for making the original description.[20]

Surgeons soon learned that there were many examples of a false-positive Homans sign (i.e., positive dorsiflexion sign but no clot found at surgery),[19,21] and in 1944, Homans redefined the positive response, stating that "discomfort need have no part in the reaction." Eventually, Homans became unenthusiastic about the sign[22,23] and has been quoted as saying, "if you wanted to name a sign after me, why didn't you pick a good one?"[24]

C. PSEUDOTHROMBOPHLEBITIS

In a large series of patients presenting with suspected deep vein thrombosis, only one out of every four or five patients actually had the diagnosis.[25–29] An important mimic of deep vein thrombosis (i.e., **pseudothrombophlebitis**) is **Baker cyst,** which is a distended gastrocnemius-semimembranosus bursa that has dissected or ruptured into the calf or is compressing the

popliteal vein.[30,31] A telltale sign of this disorder (and any other cause of calf hematoma) is crescent-shaped ecchymosis near either malleolus.[32,33]

III. CLINICAL SIGNIFICANCE

A. INDIVIDUAL FINDINGS

EBM Box 54-1 presents the diagnostic accuracy of physical signs for deep vein thrombosis of the lower extremity, as applied to thousands of patients with acute calf pain or swelling, or both. Although some studies recruited outpatients[25,35,37–40,42–49] and others both inpatients and outpatients,[27,28,41]

EBM BOX 54-1
*Lower Extremity Deep Vein Thrombosis**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Inspection				
Any calf or ankle swelling[22,23,28,34–38]	41-90	8-74	1.2	0.7
Asymmetrical calf swelling, ≥2 cm difference[27,39]	61-67	69-71	2.1	0.5
Swelling of entire leg[28,37,38,40]	34-57	58-80	1.5	0.8
Superficial venous dilation[23,37,38,40,41]	28-33	79-85	1.6	0.9
Erythema[34,35,41]	16-48	61-87	NS	NS
Superficial thrombophlebitis[36]	5	95	NS	NS
Palpation				
Tenderness[22,23,34–38,40,41]	19-85	10-80	NS	NS
Asymmetrical skin coolness[23]	42	63	NS	NS
Asymmetrical skin warmth[34,41]	29-71	51-77	1.4	NS
Palpable cord[28,41]	15-30	73-85	NS	NS
Other Tests				
Homans sign[22,23,28,34–36,41]	10-54	39-89	NS	NS

*Diagnostic standard: for *deep venous thrombosis*, positive contrast venography[22,23,28,34–36,41] or compression ultrasonography.[27,37–40]

†Definition of findings: All findings refer to the symptomatic leg.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

NS, not significant.

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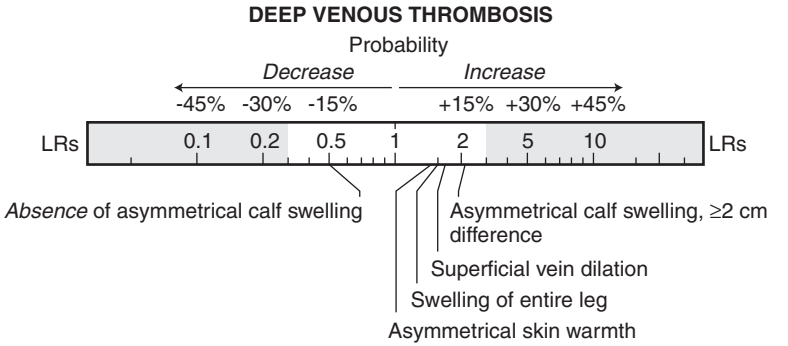

the accuracy of individual signs is the same whether or not inpatients are included in the analysis. In almost all studies, "deep vein thrombosis" refers only to proximal thrombosis (popliteal vein or higher),[28,34,35,37–40,42–49] although a few studies included patients with proximal vein or isolated calf vein thrombosis. (In these studies, however, only 15% to 29% had isolated calf thrombosis.[27,36,41]) Most studies excluded patients with symptoms suggesting pulmonary embolism.

According to these studies, only the findings of asymmetrical calf swelling (≥2 cm difference, LR = 2.1), superficial vein dilation (LR = 1.6), swelling of the entire leg (LR = 1.5), and asymmetrical skin warmth (LR = 1.4) increase the probability of thrombosis, although the discriminatory value of all these signs is slight. The presence or absence of erythema, tenderness, skin coolness, palpable cord, and Homans sign lack diagnostic value. As expected, the finding of superficial thrombophlebitis (i.e., visibly inflamed and tender subcutaneous veins) also lacks any relationship to pathologic findings in the deep veins. No individual finding convincingly *decreases* the probability of thrombosis (i.e., no LR <0.5).

These same studies show that certain risk factors assist the diagnosis, most importantly the presence of active cancer (sensitivity 7% to 39%, specificity 90% to 97%, positive LR = 2.9).[25,27,28,37–40,42,50] The finding of "recent immobilization" or "recent surgery" increased the probability of deep venous thrombosis by a smaller amount. (Positive LR for each finding is 1.6.)

B. COMBINED FINDINGS

Given the meager accuracy of individual findings, Wells and others developed a simple scoring scheme (Table 54-1) that combines findings, stratifying patients into groups of low, moderate, or high probability for deep vein thrombosis of the leg.[25] The findings entering his model were all proven to be independent predictors in an earlier analysis.[26,51] This model has now been validated in many studies enrolling more than 6000 patients with suspected deep venous thrombosis: A low pretest probability (0 or fewer points by this model) decreases the probability of deep vein thrombosis (LR = 0.2; EBM Box 54-2), and a high pretest probability (3 or more points)

TABLE 54-1 Wells Scoring Scheme for Pretest Probability of Deep Vein Thrombosis*[25]

Clinical Feature	Points
RISK FACTORS	
Active cancer	1
Paralysis, paresis, or recent plaster immobilization of the lower extremities	1
Recently bedridden >3 days or major surgery, within 4 weeks	1
SIGNS	
Localized tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Asymmetrical calf swelling (>3 cm difference, 10 cm below tibial tuberosity)	1
Asymmetrical pitting edema	1
Collateral superficial veins (nonvaricose veins)	1
ALTERNATIVE DIAGNOSIS	
Alternative diagnosis as likely or more likely than deep venous thrombosis	−2

*Interpretation of score: high probability if 3 points or more, moderate probability if 1 or 2 points, and low probability if 0 points or less.

EBM BOX 54-2
*Leg Deep Vein Thrombosis (Wells Score)**

Pretest Probability†[25,29,43,45–49,52–54]	Sensitivity (%)	Specificity (%)	Positive LR‡
Low pretest probability	2-21	24-77	**0.2**
Moderate pretest probability	13-46	—	NS
High pretest probability	38-87	71-99	**6.3**

*Diagnostic standard: for *deep vein thrombosis*, proximal vein clot by compression ultrasonography,[25,29,42,43,45–49,53,54] sometimes with contrast venography.[25,53] In some studies,[42,46,48,53,54] deep venous thrombosis was excluded without compression ultrasonography in patients with low clinical risk, normal D-dimer assay, and absence of venous thromboembolism during 3 months of follow-up.

†Definition of findings: for *pretest probability*, see Table 54-1.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

NS, not significant.

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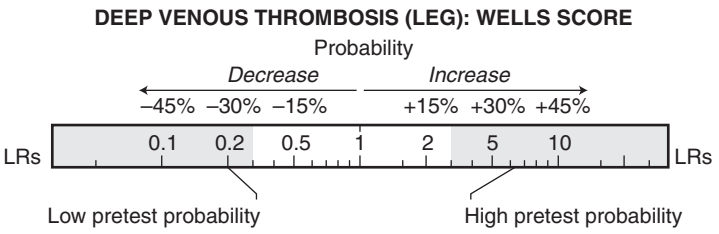


significantly increases the probability of deep vein thrombosis (LR = 6.3). The finding of a moderate pretest probability is diagnostically unhelpful.

If the clinical probability (using the Wells rule) is low and the D-dimer measurement is normal, the probability of deep vein thrombosis is so low (i.e., <1% in six of seven studies) that anticoagulants and further testing may safely be withheld.[42,46,47,50,55–57] Randomized studies show that this approach is as accurate and safe as performing compression ultrasonography in all patients.[58]

C. DIAGNOSING UPPER EXTREMITY DEEP VENOUS THROMBOSIS

Constans and others have derived and validated a bedside rule to diagnose deep venous thrombosis of the upper extremity.[59] According to this rule, the clinician adds one point for each of three clinical findings:

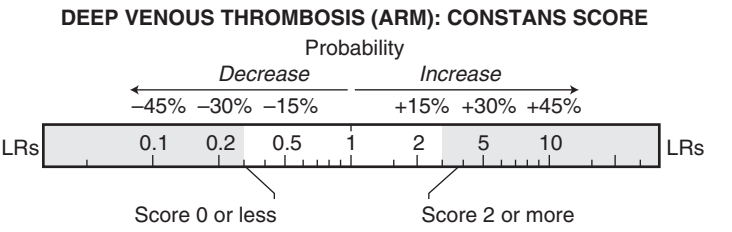
1. Venous material (i.e., catheter, pacemaker, or access device in a subclavian or jugular vein)
2. Pitting edema of arm
3. Localized pain of the arm

and then *subtracts* one point if another diagnosis is at least as plausible as arm deep venous thrombosis. (Possible scores thus range from −1 to 3.) A **Constans score** of 0 or lower decreases the probability of arm thrombosis (LR = 0.3; EBM Box 54-3), and a score of 2 or higher increases the probability of thrombosis (LR = 3.8).

EBM BOX 54-3
*Arm Deep Vein Thrombosis**[59]

Finding†	Sensitivity (%)	Specificity (%)	Positive LR‡
Constans score ≤0	12	50	**0.3**
Constans score 1	29	—	NS
Constans score ≥2	58	85	**3.8**

*Diagnostic standard: for *arm deep vein thrombosis*, compression ultrasonography.
†Definition of findings: for *Constans score*, see text.
‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.
Click here to access calculator.



The references for this chapter can be found on www.expertconsult.com.

CHAPTER 55

Examination of the Musculoskeletal System

Examination of the musculoskeletal system includes *inspection* (for joint swelling, redness, and deformity), *palpation* (for joint warmth, tenderness, and crepitus*), and investigation of the joint's *range of motion*. Of these tests, range of motion is the most sensitive indicator of joint disease. The normal range of motion of joints is presented in Table 55-1.[1]

Joint pain may originate in the joint itself (i.e., articular disease) or in extra-articular structures such as tendons, ligaments, bursas, or nerves. Articular disease characteristically causes swelling and tenderness that surrounds the entire joint and limits its entire repertoire of motion, during both active and passive movements. Extra-articular disease, in contrast, causes swelling and tenderness localized to particular regions of the joint, affecting some aspects of the joint's range of motion while sparing others. Extra-articular disease also tends to limit active joint movements (i.e., voluntary movements) more than passive ones (i.e., movements with the muscles relaxed).

In joints lacking normal alignment, **dislocation** implies complete lack of contact between the two articular surfaces, whereas **subluxation** implies residual contact but abnormal alignment. In a **valgus deformity,** the distal part of the limb is directed *away* from the body midline (e.g., **genu valgum** of knock-knees, or **hallux valgus** of bunions). In a **varus deformity,** the distal part is directed *toward* the body midline (e.g., genu varum of bowlegs). A **recurvatum deformity** describes abnormal hyperextension of a joint (e.g., **genu recurvatum** of back-kneed individuals, common in patients with chronic quadriceps weakness; see Chapter 6).

An attentive physical examination is fundamental to musculoskeletal diagnosis because, in contrast to other organ systems, the diagnostic standard for many musculoskeletal disorders *is* the bedside findings (Table 55-2 and see Chapter 1). For example, in patients with symmetrical arthritis of the wrists and hands, ulnar deviation of the metacarpophalangeal joints, and swan neck deformities of the fingers, the diagnosis of rheumatoid arthritis is almost certain whether or not the serologic rheumatoid factor is present. (If the factor is absent, the patient has **seronegative rheumatoid arthritis**.) Instead of focusing on such syndrome-defining findings (for which calculating likelihood ratios [LRs] is impossible), this chapter will focus on those disorders of the shoulder, hip, knee, and ankle for which the diagnosis relies on clinical imaging or surgical findings (e.g., osteoarthritis and orthopedic injuries). Other chapters of this book review stance

*__Crepitus__ is a vibratory sensation felt over joints during movement.

TABLE 55-1 Normal Range of Motion of Joints*

Joint	Flexion/Extension	Abduction/ Adduction	Rotation
Shoulder	180 degrees	180 degrees (abduction) 45 degrees (adduction, across body)	90 degrees (internal rotation) 90 degrees (external rotation)
Elbow	150 degrees (humeroulnar)		180 degrees (radiohumeral)
Wrist and carpal joints	70 degrees (wrist extension) 80-90 degrees (palmar flexion)	50 degrees (ulnar deviation) 20-30 degrees (radial deviation)	
Fingers (MCP, PIP, and DIP joints)	90 degrees (MCP) 120 degrees (PIP) 80 degrees (DIP)	30-40 degrees (MCP combined abduction/ adduction)	
Hip	10-20 degrees (extension) 120 degrees (flexion, knee flexed)	40 degrees (abduction) 25 degrees (adduction)	40 degrees (internal rotation) 45 degrees (external rotation)†
Knee	130 degrees		
Ankle and feet	45 degrees (plantar flexion) 20 degrees (dorsiflexion)		30 degrees (inversion) 20 degrees (eversion)

*From reference 1.
†Internal and external rotation if hip and knee flexed; less if hip and knee extended.
DIP, distal interphalangeal; MCP, metacarpophalangeal; PIP, proximal interphalangeal.

and gait (see Chapter 6), back pain (see Chapter 62), and hand pain (see Chapter 62).

THE SHOULDER

I. INTRODUCTION

Shoulder pain is the third most common musculoskeletal complaint. (The first two are back pain and knee pain.[2]) The shoulder is vulnerable to pain because it is the only location in the human body where tendons (i.e., the rotator cuff tendons*) pass between moving bones (i.e., the acromion and humerus). This anatomy grants the shoulder great flexibility but also renders the rotator cuff tendons and accompanying bursa susceptible to inflammation, degeneration, and tears.

*The tendons of the supraspinatus, infraspinatus, subscapularis, and teres minor muscles make up the rotator cuff.

TABLE 55-2 Abnormal Articular Findings and Implied Diagnosis*

Finding	Diagnosis
SHOULDER	
Inspection	
Flattening of rounded lateral aspect of shoulder	Anterior dislocation
Swelling over anterior aspect	Glenohumeral synovitis; synovial cyst
ELBOW	
Inspection	
Localized cystic swelling over olecranon	Olecranon bursitis
Swelling obscuring paraolecranon grooves	Elbow synovitis
Nodules over extensor surface of ulna	Gouty tophi; rheumatoid nodules
Palpation	
Elbow pain and tenderness over lateral epicondyle	Lateral epicondylitis (tennis elbow)
Elbow pain and tenderness over medial epicondyle	Medial epicondylitis (golfer's elbow)
WRISTS AND CARPAL JOINTS	
Inspection	
Firm, painless cystic swelling, often located over volar or dorsal wrist	Ganglion (synovial cyst)
Thickening of palmar aponeurosis, causing flexion deformity of MCP joints (fourth finger > fifth finger > third finger)	Dupuytren contracture
Abnormal prominence of distal ulna	Subluxation of ulna (from chronic inflammatory arthritis, especially rheumatoid arthritis)
Nonpitting swelling proximal to wrist joint, sparing joint itself; associated clubbing of digits	Hypertrophic osteoarthropathy
Special Tests	
Flexion and extension of digits causes snapping or catching sensation in palm	Trigger finger (flexor tenosynovitis)
Finkelstein test: pain when patient makes fist with fingers over thumb and bends the wrist in an ulnar direction	Tenosynovitis of long abductor and short extensor tendons of thumb, or de Quervain stenosing tenosynovitis)
FINGERS	
Inspection	
Loss of normal knuckle wrinkles	PIP or DIP synovitis
Loss of "hills and valleys" between metacarpal heads	MCP synovitis
Ulnar deviation at MCP joints	Chronic inflammatory arthritis
Swan neck deformity (flexion at MCP joint, hyperextension of PIP joint, flexion of DIP joint)	Chronic inflammatory arthritis, especially rheumatoid arthritis
Boutonniere deformity (flexion of PIP, hyperextension of DIP)	Detachment of central slip of extensor tendon to PIP, common in rheumatoid arthritis

Continued

TABLE 55-2 Abnormal Articular Findings and Implied Diagnosis*—cont'd

Finding	Diagnosis
Osteophytes: Heberden nodes at DIP, Bouchard nodes at PIP	Osteoarthritis
Mallet finger: flexion deformity of DIP	Detachment of extensor tendon from base of distal phalanx or fracture
"Telescoping" or "opera glass hand": shortening of digits and destruction of IP joints	Arthritis mutilans, in rheumatoid or psoriatic arthritis
HIP	
Inspection	
Trauma, hip externally rotated	Femoral neck fracture; anterior dislocation
Trauma, hip internally rotated	Posterior dislocation
Pelvic tilt (imaginary line through the anterior iliac spines is not horizontal)	Scoliosis; anatomic leg-length discrepancy; hip disease
Palpation	
Hip pain, tenderness localized over greater trochanter	Trochanteric bursitis
Hip pain, tenderness localized over middle third of inguinal ligament, lateral to femoral pulse	Iliopsoas bursitis
Hip pain and tenderness localized over ischial tuberosity	Ischiogluteal bursitis (weaver's bottom)
KNEE	
Inspection	
Localized tenderness and swelling over patella	Prepatellar bursitis (housemaid's knees)
Generalized swelling of popliteal space	Baker cyst (enlarged semimembranosus bursa, which communicates with knee joint)
Genu varum and genu valgum	See text
Palpation	
Knee pain and tenderness localized over medial aspect of upper tibia	Anserine bursitis
Distressed reaction if patella moved laterally (apprehension test)	Recurrent patellar dislocation
ANKLES AND FEET	
Inspection	
Flattening of longitudinal arch	Pes planus
Abnormal elevation of medial longitudinal arch	Pes cavus
Outward angulation of great toe with prominence over medial first MTP joint (bunion)	Hallux valgus
Hyperextension of MTP joints and flexion of PIP joints	Hammer toes
Palpation	
Nodules within Achilles tendon	Tendon xanthoma
Foot pain, localized tenderness over calcaneal origin of plantar fascia	Plantar fasciitis

Continued

TABLE 55-2 Abnormal Articular Findings and Implied Diagnosis*—cont'd

Finding	Diagnosis
Foot pain, localized tenderness over plantar surface of MT heads	Metatarsalgia
Forefoot pain, tenderness between second and third toes or between third and fourth toes	Morton interdigital neuroma
Ankle pain, dysesthesias of sole, aggravated by forced dorsiflexion and eversion of foot	Tarsal tunnel syndrome

*Special tests of the shoulder, hip, knee, and ankle are discussed in the text.
DIP, distal interphalangeal; MCP, metacarpophalangeal; MT, metatarsal; MTP, metatarsophalangeal; PIP, proximal interphalangeal.

TABLE 55-3 Shoulder Syndromes*

Syndrome	Location of Pain	Range of Passive Motion	Other Findings
Capsular syndromes Adhesive capsulitis Glenohumeral arthritis	Outer arm	Limited† (all motions limited, especially external rotation and abduction)	
Acute bursitis‡	Outer arm	Limited† (abduction especially limited)	
Acromioclavicular pain	Point of shoulder	Normal	Tenderness of acromioclavicular joint Pain worse during adduction of arm across body
Subacromial syndromes‡ Rotator cuff tendinitis Rotator cuff tear	Outer arm	Normal	Painful arc Rotator cuff muscle strength: Normal in tendinitis Weak in rotator cuff tears

*From references 3 to 5.
†One way to test for limitation of passive motion is to ask the patient to bend over and try to touch his or her toes. In those with normal shoulder passive motion, the arms dangle toward the floor.
‡*Acute bursitis* and *subacromial disorders* both represent disorders of the subacromial space, but *bursitis* causes inflammation and swelling that is more acute and severe, thus limiting motion.

One popular method of classifying shoulder pain (Table 55-3), based on the work of the British orthopedic surgeon James Cyriax,[3,4] distinguishes the causes of shoulder pain by location of pain, range of passive motion, strength of rotator cuff muscles, and **painful arc** (i.e., pain during arm elevation between the angles of 70 degrees and 100 degrees, angles at which compression of the subacromial tissues is the greatest). Using this classification, 5% to 12% of patients with shoulder pain have capsular syndromes,

17% acute bursitis, 5% to 11% acromioclavicular syndromes, 47% to 65% subacromial syndromes, and 5% to 10% referred shoulder pain (e.g., cervical disc disease or myofascial pain).[5–8]

Nonetheless, some clinicians have questioned the utility and accuracy of this classification, for several reasons:

1. Most shoulder syndromes are treated similarly with anti-inflammatory medications, injections, and physical therapy, no matter what the diagnosis is.[5]
2. Different shoulder syndromes are indistinguishable from the patient's perspective, causing similar pain and disability over time.[5,6]
3. If patients are examined a second time, the specific diagnosis often changes.[6]
4. Legions of bedside tests have been proposed to diagnose shoulder disorders (one website lists 113 tests)[9] and new ones continue to appear,[10] suggesting that a comprehensive understanding of shoulder pain is still lacking.

Nonetheless, the bedside examination continues to play an important role in patients with shoulder pain, especially in distinguishing intrinsic shoulder syndromes from disorders causing referred pain, and in identifying rotator cuff tears, a condition sometimes requiring surgical repair. These subjects are the focus of this section.

II. THE FINDINGS

A. IMPINGEMENT SIGNS

Impingement signs reproduce subacromial pain by compressing the rotator cuff tendons between the head of the humerus and the acromion. Of the many different impingement signs, the most popular are the **Neer impingement sign** and **Hawkins impingement sign** (Figs. 55-1 and 55-2).

Both of these maneuvers were originally introduced to select patients for specific surgical procedures. The Neer maneuver forces the humerus (and overlying rotator cuff tendons) against the anterior acromion, which Neer proposed resecting (i.e., anterior acromioplasty) in patients with persistent pain.[11] The Hawkins maneuver forces the greater tuberosity of the humerus against the coracoacromial ligament (the ligament forming the anterior roof over the rotator cuff). If patients develop pain during this maneuver and surgery is contemplated, Hawkins believed the coracoacromial ligament should be resected.[13]

B. YERGASON SIGN

The **Yergason sign** (Fig. 55-3) has traditionally been associated with bicipital tendinitis, as if that were an isolated entity, but in fact most patients with inflammation of the biceps tendon also have disease of the rotator cuff. This occurs because progressive subacromial impingement causes wearing away of the supraspinatus tendon and underlying capsule, which then exposes the long head of the biceps tendon and subjects it to the same injurious forces. In fact, most tears of the biceps tendon are associated with advanced rotator cuff disease.[11,15,16]

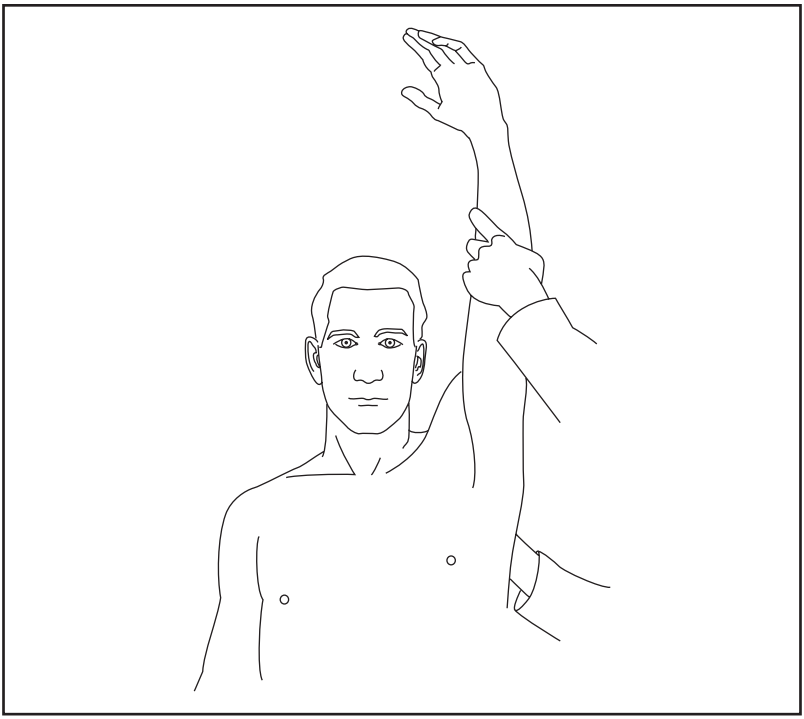


FIGURE 55-1 Neer impingement sign.[11] The clinician prevents scapular motion with one hand and uses the other hand to raise the patient's arm in forward flexion, a position that presses the greater tuberosity of the humerus against the acromion.[11,12] Neer believed his sign was nonspecific (i.e., shoulder pains of all types worsened with this maneuver), but he taught that subacromial pain was the only shoulder syndrome whose positive impingement sign disappeared after injection of the subacromial space with lidocaine.

C. SPEED TEST

Like the Yergason sign, the Speed **test** (Fig. 55-4) was originally developed to identify pain originating in the bicipital tendon,[17] but studies apply the test now to the diagnosis of subacromial impingement syndromes in general.

D. MUSCLE ATROPHY

The clinician detects atrophy of the supraspinatus or infraspinatus muscles by inspecting the posterior scapula on the symptomatic side and noting any increased prominence of the scapular spine when compared with the contralateral side. Atrophy of these muscles may appear as soon as 2 to 3 weeks after a rotator cuff tear.

E. MUSCLE TESTING

The most important muscles to test in suspected tears of the rotator cuff are the supraspinatus muscle (involved in most rotator cuff tears) and infraspinatus muscle (involved in 11% to 45% of tears).[16,18] The supraspinatus

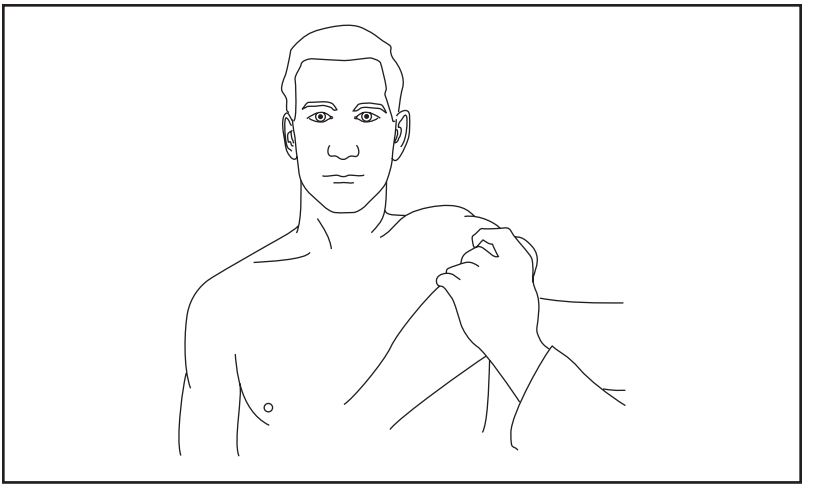


FIGURE 55-2 Hawkins impingement sign.[13] The clinician stands in front of the patient, flexes both the patient's shoulder and elbow to 90 degrees, and then internally rotates the patient's arm, a position that presses the greater tuberosity against the coracoacromial ligament.[12]

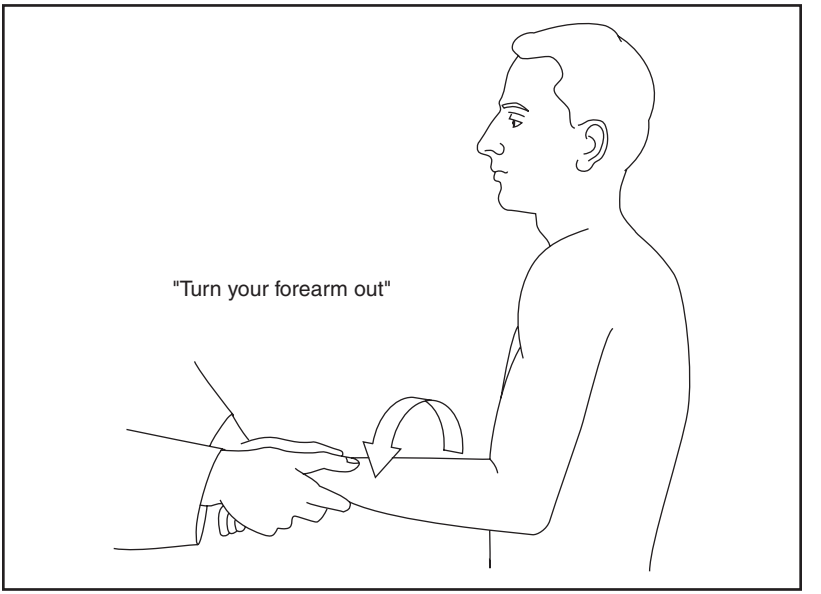


FIGURE 55-3 Yergason sign.[14] The clinician stands in front of the patient, flexes the patient's forearm 90 degrees at the elbow, and pronates the patient's wrist. The clinician then asks the patient to supinate the forearm against resistance (i.e., turn the forearm in the direction of the *arrow*). Pain indicates a positive test, implying inflammation of the long head of the biceps tendon (the main supinator of the forearm).

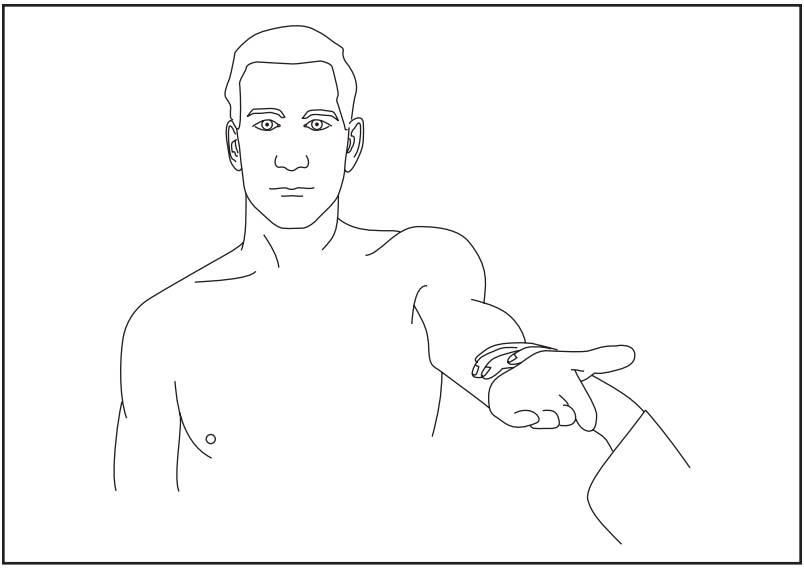


FIGURE 55-4 Speed test. The patient flexes the shoulder forward to 60- to 90 degrees, with his or her elbow extended and arm fully supinated (i.e., palm up) as the clinician applies a downward force. Pain in the shoulder (in the bicipital groove) is the positive response.

muscle abducts the shoulder, and the infraspinatus muscle externally rotates it. Figures 55-5 and 55-6 describe testing the strength of these muscles.

F. DROPPED ARM TEST

The examiner abducts the patient's arm as far as possible and releases it, asking the patient to lower the arm slowly back down to the side. In patients with a positive test, indicating rotator cuff tear, the patient lowers the arm smoothly to about 100 degrees, after which the smooth movements become irregular and the arm may fall suddenly to the side.[22]

The dropped arm test becomes positive below angles of 100 degrees, not because the supraspinatus muscle is the most powerful abductor at this angle* but because the rotator cuff muscles must be intact to pull the humeral head tightly against the glenoid fossa, creating a fulcrum that allows the deltoid muscle to smoothly lower the arm.

G. PALPATING ROTATOR CUFF TEARS

Early descriptions of rotator cuff tears emphasized the importance of actually palpating the tear, just anterior to the acromial edge and through the deltoid muscle (Fig. 55-7).[23]

*The supraspinatus muscle is responsible for only the initial 30 degrees of abduction, whereas the deltoid muscle (uninvolved in rotator cuff disease) accounts for abduction between 30 degrees and 180 degrees.

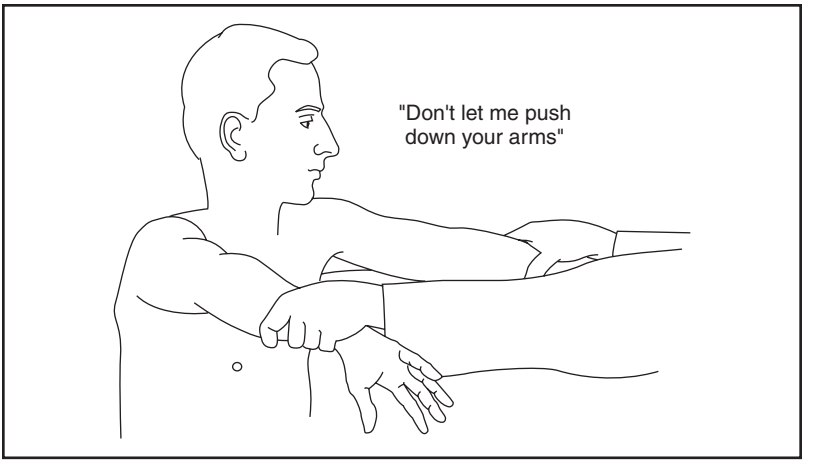


FIGURE 55-5 Supraspinatus test (empty can test, Jobe test).[19] The clinician stands in front of the patient and elevates the patient's arms to 90 degrees in the plane of the scapula (i.e., *scaption,* midway between forward flexion and sideways abduction). The patient's arms are internally rotated with the thumbs pointing down (as if emptying a can). The patient is asked to hold this position and resist attempts to lower the arms to the side. Some investigators propose testing the supraspinatus muscle in a slightly different way, with the arms externally rotated and the thumbs pointing up (i.e., **full can test**) because this position causes less pain than the empty can test. In clinical studies, both versions have similar diagnostic accuracy.[18,20]

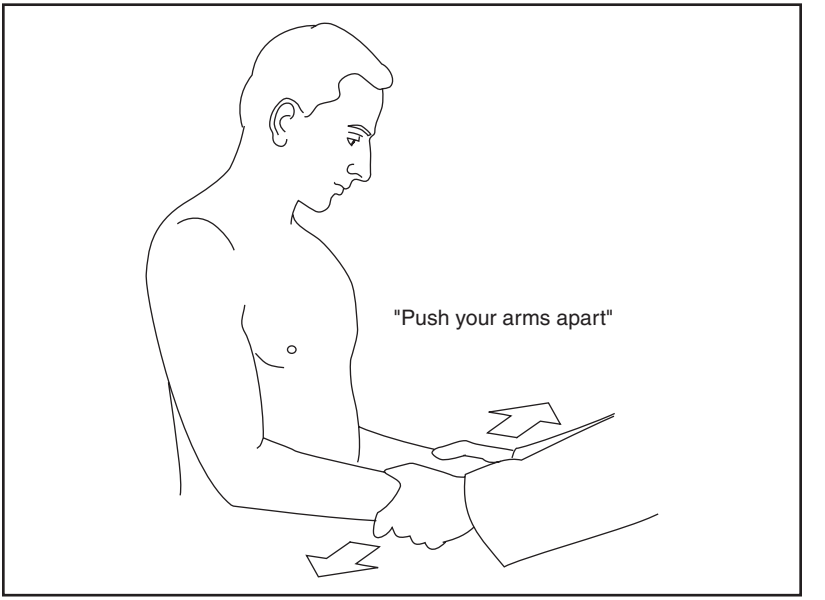


FIGURE 55-6 Infraspinatus test. The clinician stands in front of the patient, and the patient's arms are at his or her side with the elbows flexed 90 degrees and the thumbs up. The examiner places his or her hands outside the patient's hands and directs the patient to move his or her arms out (i.e., in the direction of the *arrow*), resisting the clinician's opposing inward pressure.[21]

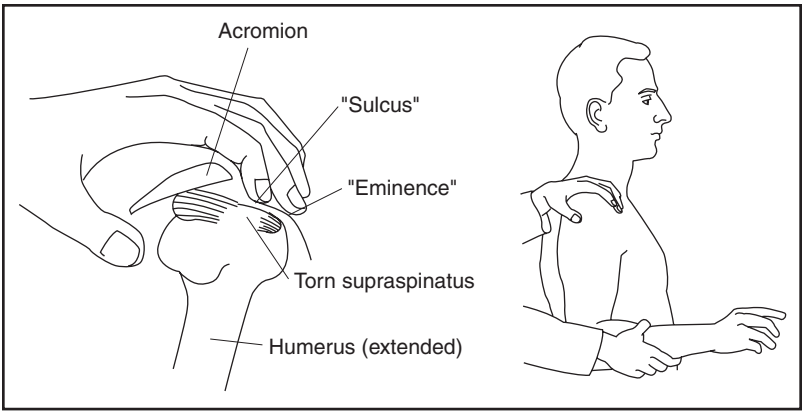


FIGURE 55-7 Palpation of rotator cuff tears. The clinician stands behind the patient, and the patient's arm is relaxed at the side with the elbow flexed 90 degrees. The clinician palpates just below the patient's acromion with one hand and holds the patient's forearm with the other hand. The clinician then gently extends the patient's arm as far as possible and rotates the shoulder internally and externally to fully reveal the greater tuberosity and attached tissues. In patients with tears of the supraspinatus tendon (which inserts on the greater tuberosity), the clinician detects both an abnormal eminence and an abnormal sulcus posterior to this eminence. The abnormal eminence is the greater tuberosity with an attached remnant of tendon, and the sulcus just behind it is the actual rent in the supraspinatus tendon. Comparison with the contralateral shoulder helps determine whether the suspected tear is real or not.

H. CROSSED BODY ADDUCTION TEST (SCARF TEST)

By crossing the arm horizontally maximally across the chest (Fig. 55-8), compression of the ipsilateral acromioclavicular joint occurs, a maneuver that aggravates pain from acromioclavicular disease.

III. CLINICAL SIGNIFICANCE

A. ACROMIOCLAVICULAR JOINT PAIN

In patients with shoulder pain, a positive crossed body adduction test increases the probability of acromioclavicular joint pain (LR = 3.7; EBM Box 55-1) and its absence decreases it (LR = 0.3). Acromioclavicular joint tenderness and compression tenderness are not helpful diagnostically (LRs not significant).

B. ROTATOR CUFF TENDINITIS

According to the LRs in EBM Box 55-1, the findings that increase the probability of rotator cuff tendinitis the most are a positive Yergason sign (LR = 2.8), painful arc (LR = 2.8), and a positive Speed test (LR = 1.9). The diagnostic accuracy of the Yergason sign and Speed test emphasizes again the association between biceps tendon pain and rotator cuff disease. (See the section on Yergason Sign.)

The presence of the Neer or Hawkins impingement sign fails to change the probability of rotator cuff tendinitis much (LR = 1.6), simply because shoulder pain of all types worsens during these maneuvers (i.e., specificity is low and there are many false-positive tests). Nonetheless, these studies did not repeat

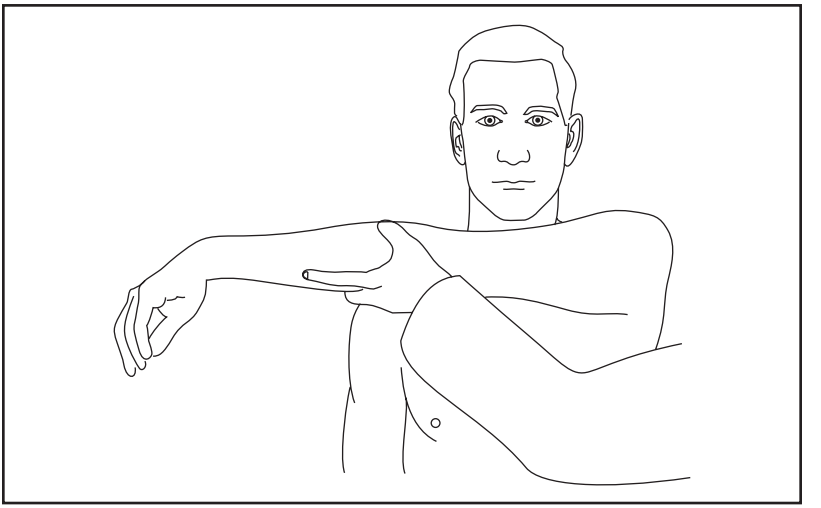


FIGURE 55-8 Crossed body adduction test. The clinician maximally adducts the patient's arm (ipsilateral to the symptomatic shoulder) across the patient's chest. Pain in the symptomatic acromioclavicular joint is the positive response.

the impingement signs after lidocaine injection as Neer originally proposed, which might have improved specificity. The *absence* of both impingement signs significantly *decreases* the probability of subacromial disease (LR = 0.1).

C. ROTATOR CUFF TEARS

1. Individual Findings

In patients with shoulder pain, the bedside findings increasing the probability the most are age of 60 years or older (LR = 3.2), positive dropped arm test (LR = 2.9), and infraspinatus muscle weakness (LR = 2.3). The positive supraspinatus test increases the probability slightly, and diagnostic accuracy is similar whether the clinician regards the positive response to be weakness (LR = 2.1) or pain (LR = 1.7). Age of 39 years or younger (LR = 0.1) and negative impingement signs (LR = 0.3) decrease the probability of a rotator cuff tear.

Although the reported diagnostic accuracy of palpating actual rents in the supraspinatus tendon is impressive (positive LR = 10.2, negative LR = 0.1; see EBM Box 55-1), these LRs have been derived from examinations by orthopedic surgeons who have comprehensive understanding of the anatomy of the shoulder and considerable experience in treating shoulder pain.[30,31] Whether other practitioners will duplicate this accuracy is unknown.

2. Combined Findings

Two investigations of rotator cuff tears that combined clinical findings demonstrate superior diagnostic accuracy. Each focused on three clinical findings. Murrell[22] combined impingement signs, supraspinatus muscle weakness, and infraspinatus muscle weakness, and Park[27] combined the Hawkins sign, a painful arc, and infraspinatus muscle weakness. When all three signs are

EBM BOX 55-1
*Shoulder Pain: Individual Findings**

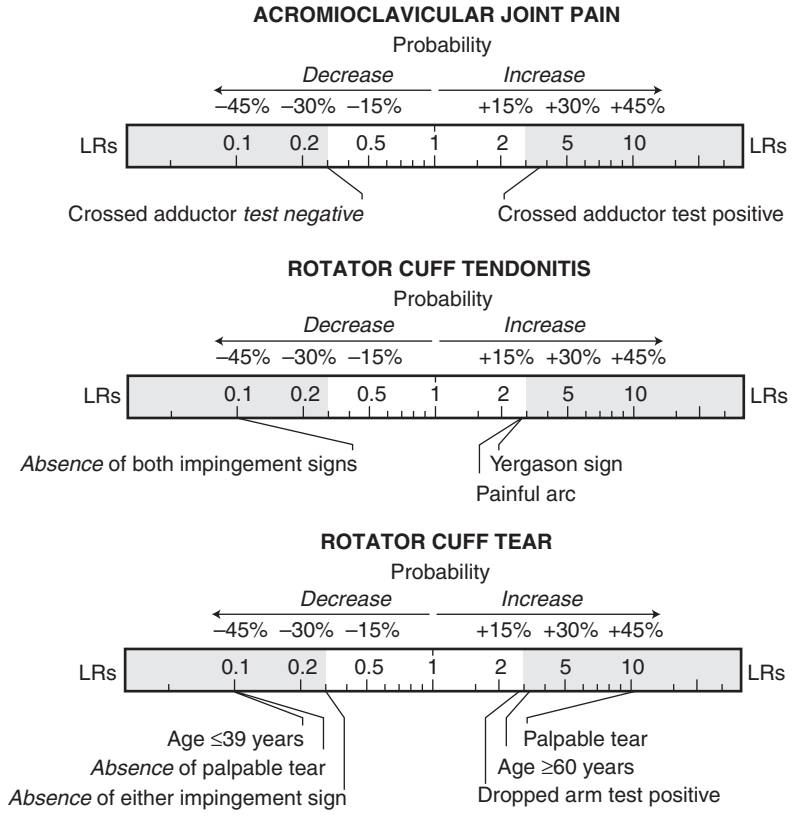
Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is Present	Likelihood Ratio‡ if Finding Is Absent
Detecting Acromioclavicular Joint Pain				
Acromioclavicular joint tenderness[8]	96	10	NS	NS
Tenderness with compression of acromioclavicular joint[8]	79	50	NS	NS
Crossed body adduction test[8,24]	77	79	**3.7**	**0.3**
Detecting Rotator Cuff Tendinitis				
Neer impingement sign[25–27]	68-89	32-69	1.6	0.5
Hawkins impingement sign[25–27]	72-92	26-66	1.6	0.4
Hawkins or Neer impingement sign[26]	96	41	1.6	**0.1**
Yergason sign[25]	37	87	2.8	0.7
Speed test[25,27]	38-69	55-83	1.9	0.7
Painful arc[25,27]	32-74	81-82	2.8	NS
Detecting Rotator Cuff Tear: Individual Findings				
Age[22]				
≤39 years	5	58	**0.1**	—
40-59 years	34	—	NS	—
≥60 years	62	81	**3.2**	—
Supraspinatus atrophy[21]	55	73	2.0	0.6
Infraspinatus atrophy[21]	55	73	2.0	0.6
Painful arc[21,27]	76-97	10-62	NS	0.4
Neer impingement sign[26]	88	43	1.5	**0.3**
Hawkins impingement sign[26]	83	51	1.7	**0.3**
Supraspinatus testing causes pain[16,18,20]	63-85	52-60	1.7	0.4
Supraspinatus weakness[18,20,21,27–29]	32-84	51-89	2.1	0.5
Infraspinatus weakness[21,27]	51-76	57-84	2.3	0.5
Dropped arm test[22,27]	10-35	88-98	2.9	NS
Palpable tear[30,31]	91-96	75-97	**10.2**	**0.1**

*Diagnostic standard: for *acromioclavicular joint pain*, reduction of pain after injecting lidocaine into the acromioclavicular joint; for *rotator cuff tendinitis*, reduction of pain after injection of the subacromial space with lidocaine[25] or subacromial bursitis at arthroscopy[26,27]; for *rotator cuff tear*, arthrography,[21,27] magnetic resonance imaging,[18,20] ultrasonography,[29] or surgery (arthroscopy or open repair).[16,22,26,28,30–32]

†Definition of findings: for *tenderness with compression of the acromioclavicular joint*, the clinician stands behind the patient and compresses the joint by placing his or her thumb over the patient's posterolateral acromion and index/middle fingers on the patient's midclavicle.[8]

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. NS, not significant.

Click here to access calculator.



present, the probability of rotator cuff tear is greatly increased (LR = 48 for the Murrell findings; LR = 15.9 for the Park findings; EBM Box 55-2), whereas when all three signs are absent, the probability is greatly diminished (LR = 0.02 for the Murrell findings; LR = 0.2 for the Park findings).

THE HIP

I. INTRODUCTION

Hip pain may result from a variety of disorders, including hip arthritis, sacroiliac disease, extra-articular disease (e.g., trochanteric bursitis, iliopsoas bursitis), neurogenic causes (e.g., meralgia paresthetica, sciatica), and, rarely, miscellaneous distant disorders (e.g., hernia).

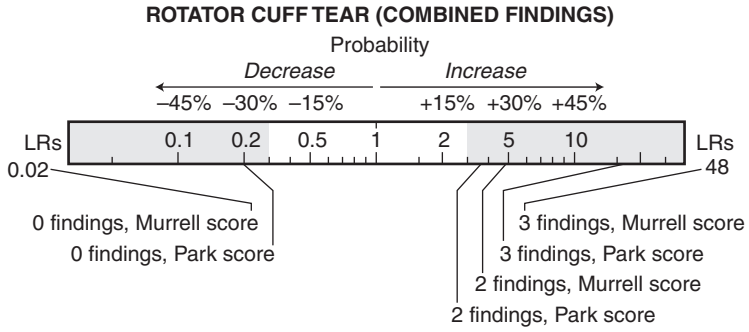
II. THE FINDINGS

The hip joint lies deep in the lower pelvis, surrounded by large muscles that protect it from direct contact with the external world, thus limiting the development of well-localized somatic sensations. Consequently, some patients

EBM BOX 55-2
*Rotator Cuff Tear: Combined Findings**

Finding (Reference)	Sensitivity (%)	Specificity (%)	Likelihood Ratio† if Finding Is	
			Present	*Absent*
Number of Findings Present (Murrell): (1) impingement signs, (2) supraspinatus weakness, (3) infraspinatus weakness[22]				
3 findings	24	100	**48.0**	—
2 findings	37	—	**4.9**	—
1 finding	39	—	NS	—
0 findings	1	52	**0.02**	
Number of Findings Present (Park): (1) Hawkins sign, (2) painful arc, (3) infraspinatus weakness[27]				
3 findings	33	98	**15.9**	—
2 findings	35	—	**3.6**	—
1 finding	24	—	NS	—
0 findings	9	42	**0.2**	

*Diagnostic standard: for *rotator cuff tear,* arthroscopy.[22,27]
†Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. *Click here to access calculator.*



with hip arthritis develop groin pain, but many experience pain at distant sites in the cutaneous distribution of nerves innervating the joint capsule, such as the thigh and knee (obturator and femoral nerves) or buttock (sciatic nerve). Unlike extra-articular causes of hip pain (e.g., trochanteric bursitis), hip disease affects the entire repertoire of hip motion, including flexion, extension, abduction, adduction, and rotation (both internal and external).

Many patients with hip disease develop a characteristic limp, the **coxalgic gait** (see Chapter 6).

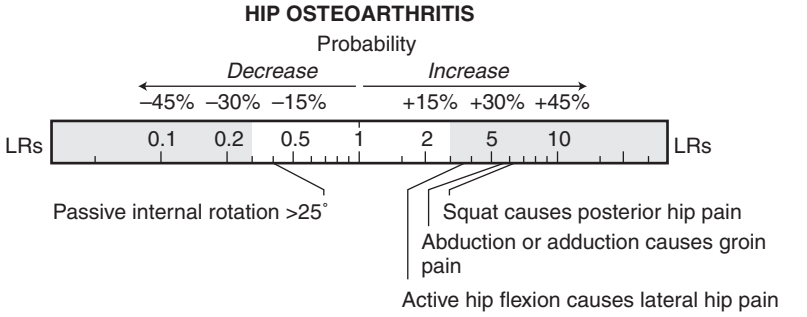
III. CLINICAL SIGNIFICANCE

In a study of 78 patients presenting with unilateral hip pain,[33] pain localized to the ipsilateral buttock (LR = 6.7) or groin (LR = 3.6) increased the probability of hip osteoarthritis. Additional findings increasing the

EBM BOX 55-3
*Diagnosis of Osteoarthritis in Patients with Hip Pain**[33]

Finding	Sensitivity (%)	Specificity (%)	Likelihood Ratio† if Finding Is	
			Present	*Absent*
Squat causes pain in posterior hip	24	96	**6.1**	NS
Abduction or adduction causes groin pain	33	94	**5.7**	NS
Active hip flexion causes lateral hip pain	43	88	**3.6**	NS
Active hip extension causes hip pain	52	80	2.7	0.6
Passive internal rotation ≤25 degrees	76	61	1.9	0.4

*Diagnostic standard: for *diagnosis of osteoarthritis*, Kellgren-Lawrence score on plain radiographs ≥2.
†Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. NS, not significant.
Click here to access calculator.



probability of hip disease were posterior hip pain with squatting (LR = 6.1; EBM Box 55-3), groin pain with abduction or adduction (LR = 5.7), and hip pain with active flexion (LR = 3.6) or extension (LR = 2.7).

THE KNEE

I. INTRODUCTION

Knee pain affects up to 13% of the adult population and is second only to back pain among musculoskeletal complaints.[34] Common causes include arthritis (osteoarthritis, rheumatoid arthritis, gout, and pseudogout), bursitis (prepatellar and anserine bursitis), and injuries to ligaments or menisci.

TABLE 55-4 Ottawa Rule for Knee Fracture[35,36]

A knee radiograph is indicated (and the rule is positive) if *any* of the following are present:
- Age ≥55 years
- Tenderness at head of fibula
- Isolated tenderness of patella*
- Inability to flex to 90 degrees
- Inability to bear weight both immediately and in the emergency department (four steps)†

*No bone tenderness of knee other than patella.
†Unable to transfer weight twice onto each lower limb regardless of limping.

Among patients presenting with knee trauma, 6% to 12% have significant fractures on knee radiographs[35–42] and the most frequently injured internal structures are the medial collateral ligament, anterior cruciate ligament, and menisci. (Injuries of the medial meniscus outnumber lateral ones by at least three to one.)[43–48]

II. THE FINDINGS

A. OTTAWA RULES FOR KNEE FRACTURE

Based on a study of over 1000 patients with acute blunt injury to the knee, Stiell and others have identified five independent predictors of clinically significant knee trauma (Table 55-4).[36] In this study, the *knee* was broadly considered to include the patella, head and neck of the fibula, proximal 8 cm of the tibia, and distal 8 cm of the femur; *significant trauma* implied an injury requiring orthopedic consultation, splinting, or surgery.

B. TESTS OF LIGAMENT INJURIES

The stability of the knee depends on the joint capsule and two pairs of ligaments: the medial and lateral collateral ligaments, and the anterior cruciate ligament (ACL) and posterior cruciate ligament (PCL).* The clinician tests each of these four ligaments by stressing the knee in a direction that the intact ligament would normally resist (specific tests appear below). If no movement occurs during stress testing or if small movements occur but abruptly end with a firm stop (i.e., a "hard" end point), the ligament is intact. If there is excessive laxity of movement or a "soft" or "mushy" end point, the ligament is damaged.

Blunt trauma to the outside of the knee is associated with injury of the medial collateral ligament; trauma to the inside of the knee suggests injury of the lateral collateral ligament. Twisting of the knee after planting the foot is the characteristic mechanism of ACL injury, whereas deceleration of the flexed knee on a hard surface (e.g., striking the knee against the dashboard in an automobile accident) often precedes PCL injury. The mechanism of meniscal injuries resembles that of ACL injuries—twisting

*The crossed cruciate ligaments are named for their attachment to the *tibial* surface, that is, the *anterior* cruciate ligament (ACL) crosses from the posterior femur to the *anterior* tibia and the *posterior* cruciate ligament (PCL) crosses from the anterior femur to the *posterior* tibia. *Cruciate* derives from the Latin *cruciatus*, meaning "cross-shaped."

the knee after planting the foot—but unlike ACL injuries, which are associated with immediate knee swelling, meniscal injuries are associated with swelling that appears only after a delay of several hours (because the menisci are relatively avascular).[49,50]

1. Anterior Cruciate Ligament

The ACL prevents anterior subluxation of the tibia on the femoral head. There are three common tests for this ligament: the anterior drawer sign, Lachman sign, and pivot shift sign (Figs. 55-9 to 55-11).

The **pivot shift sign** refers to the tendency of the tibia to sublux anteriorly in an ACL-deficient knee when the knee is between 0 degrees and 30 degrees of flexion and to the spontaneous reduction of the subluxed tibia as the knee is flexed past 40 degrees.[53,54] Patients with ACL injuries notice the pivot shift phenomenon themselves when they plant the foot with extended knee

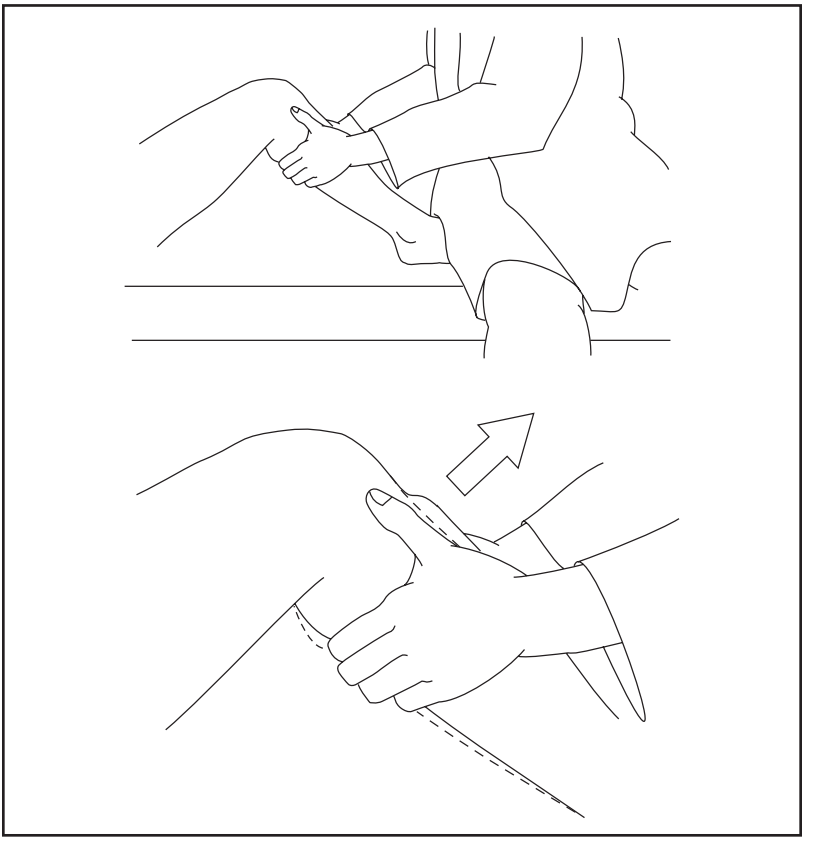


FIGURE 55-9 Anterior drawer sign. The patient lies supine with the hip flexed at 45 degrees, knee flexed at 90 degrees, and foot flat on the table. The clinician sits on top of the patient's foot to stabilize it and stresses the ACL ligament by grasping the patient's upper calf and pulling forward. Abnormal anterior subluxation of the tibia *(arrow)* with a soft end point is a positive test.

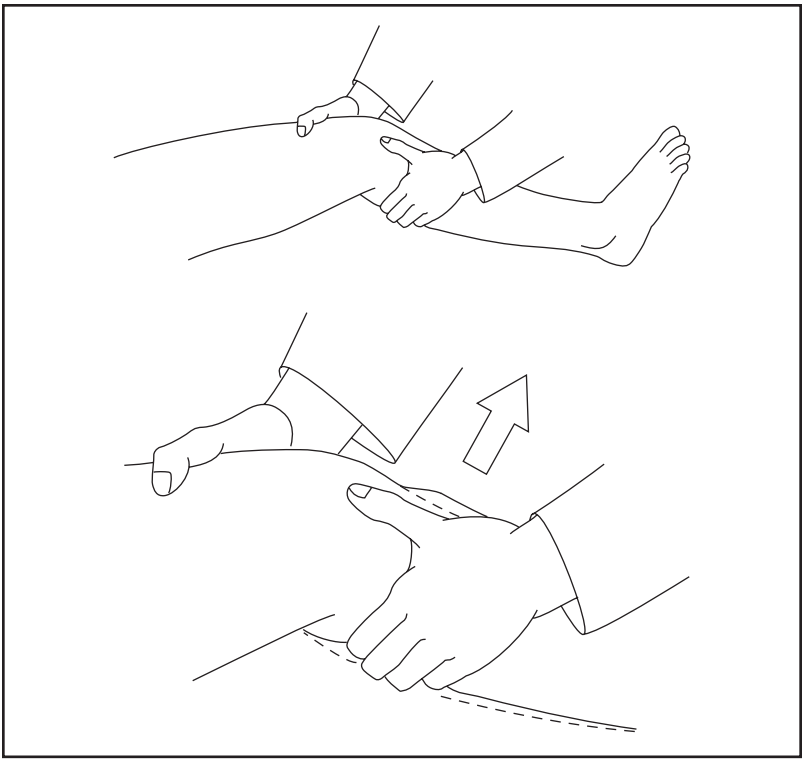


FIGURE 55-10 Lachman sign. The Lachman sign differs from the anterior drawer sign (see Fig. 55-9) by the position of the knee during testing. In the Lachman test, the hip is extended and the knee flexed at only 20 degrees. The clinician grasps the lower thigh with one hand and the upper calf with the other, pulling forward on the tibia to stress the ligament and reveal the abnormal anterior subluxation of the tibia *(arrow)*.

in front of them (e.g., stopping suddenly from a run causes the tibia to shift forward, producing the sensation of the knee "giving way"). Figure 55-12 explains the mechanism of the pivot shift phenomenon. What specifically is responsible for the sudden reduction at 40 to 50 degrees is controversial, but most experts believe it is the pull of the iliotibial tract (whose action abruptly changes from knee extension to knee flexion beyond 40 degrees of flexion)[53,55,56] and the geometric peculiarities of the convex tibial surface.[54,57]

Descriptions of the **anterior drawer sign** have been found in writings from the 1870s.[58] The **Lachman test** was attributed to the American orthopedic surgeon John Lachman by one of his students in 1976,[59] although the same sign was described a century earlier by European clinicians.[58] Photographs of patients demonstrating their own pivot shift phenomena were published in 1920,[60] but the pivot shift test was formerly described in 1972.[61] The term itself is confusing, but according to Liorzou,[55] it originated from an interview with a hockey player who stated "When I pivot, my knee shifts."

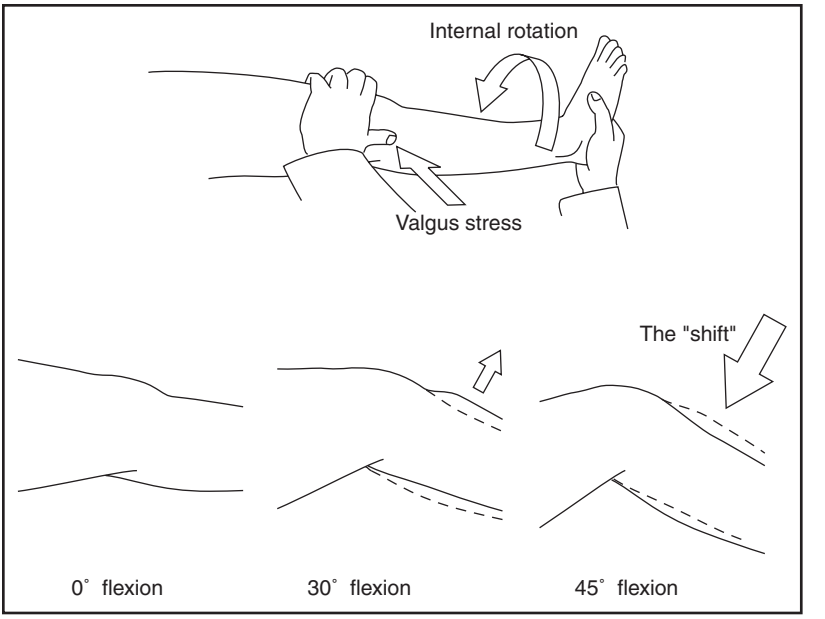


FIGURE 55-11 Pivot shift sign. Many variations of this test have been published,[51] but the most common version begins with the patient supine with the hip and knee extended. The clinician lifts the patient's leg, one hand over the fibula and the other at the ankle, pushing medially on the fibula (i.e., providing a valgus stress) and rotating internally the ankle and foot (and, thus, the tibia). While maintaining these valgus and rotational stresses, the examiner slowly flexes the patient's knee. In the ACL-deficient knee, the tibia subluxes anteriorly, almost imperceptibly, during the initial 0 to 30 degrees of flexion with these applied forces *(small arrow)*. At 40 to 50 degrees, however, the tibia suddenly subluxes posteriorly (the shift), which constitutes a positive pivot shift test (and recalls for many patients the sensation of their "knee giving way."[52]

2. Posterior Cruciate Ligament

The PCL is the least likely internal structure of the knee to be injured.[44] Because this ligament resists posterior subluxation of the tibia on the femur, the conventional test is the **posterior drawer sign** (Fig. 55-13).

3. Collateral Ligaments

Injury to either collateral ligament is identified by applying a varus or valgus stress to the knee and noting abnormal movement when compared with the contralateral side. Testing is performed with the knee straight and at 20 degrees of flexion. Excessive movement during valgus stress indicates injury to the medial collateral ligament; excessive movement during varus stress indicates injury to the lateral collateral ligament.

C. TESTS OF MENISCAL INJURIES: MCMURRAY TEST

Tears of the *anterior* meniscus or large bucket-handle tears often displace tissue between the articular surfaces of the anterior tibia and femur, thus preventing full extension of the knee (or **locking**), a characteristic sign of meniscal injury.

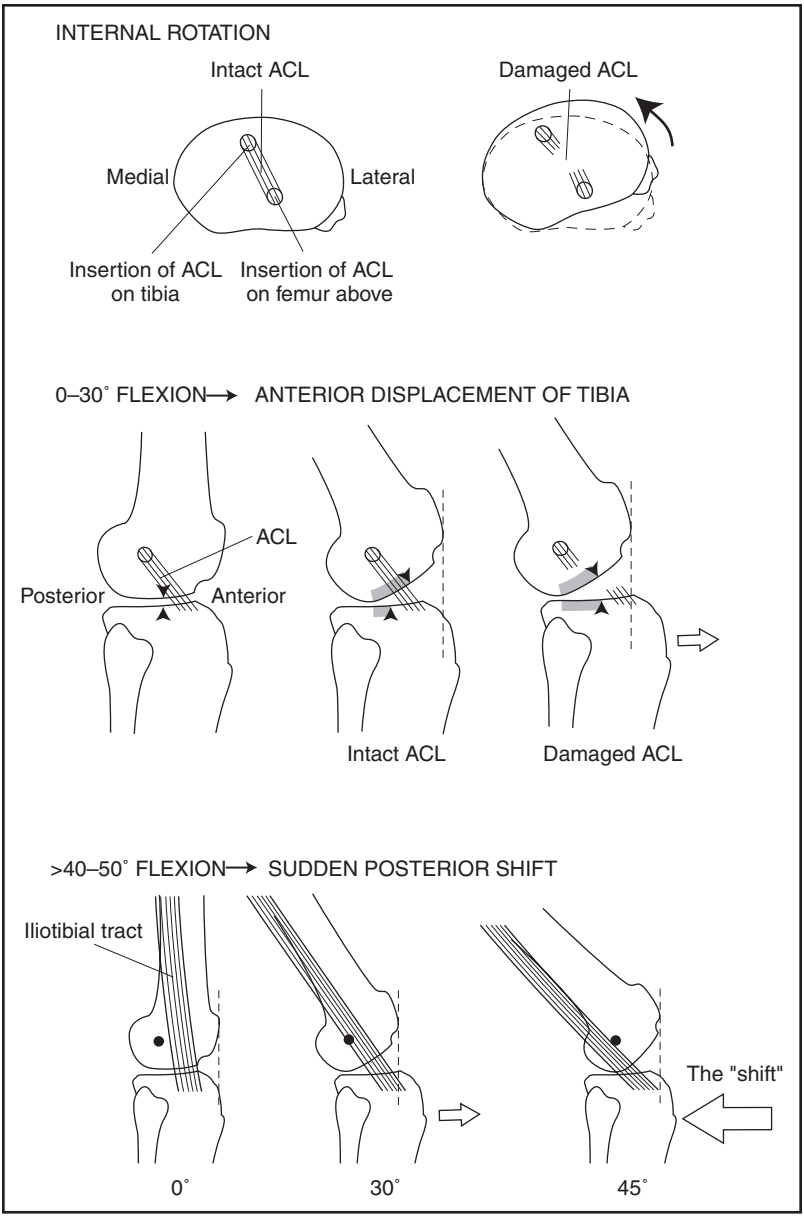


FIGURE 55-12 **Mechanism of the pivot shift.** The **pivot shift phenomenon** (i.e., positive test) refers to anterior displacement of the tibia with respect to the distal femur during the first 30 degrees of flexion and the sudden backward return of the tibia to its normal position after about 40 to 50 degrees of flexion (see Fig. 55-11). This figure depicts what happens during internal rotation *(top row)*, 0 to 30 degrees of flexion *(middle row)*, and beyond 40 to 50 degrees of flexion *(bottom row)* in the ACL-deficient knee.

Continued

FIGURE 55-12, cont'd *Top row* (view of the tibial plateau from above): Because of its oblique orientation *(left),* the ACL is the key ligament resisting internal rotation of the tibia. (This also explains why many ACL injuries occur after the athlete plants the foot and then rotates the knee.) If the ACL is torn *(right),* internal rotation causes excessive anterior movement of the tibia (with respect to the femur).[2] *Middle row* (0 to 30 degrees of flexion): The *left* figure shows the orientation of the ACL, and the *black arrowheads* mark contiguous points on the femur and tibia when the knee is fully extended. During flexion of the knee when the ACL is intact *(middle figure),* the femur glides on the tibia, which results in a large surface area of the femur *(gray shading)* contacting a relatively small area on the tibia. If the ACL is damaged *(right figure),* such gliding does not occur and instead the femur rolls back on the tibia, which displaces the tibia anteriorly (see *vertical dotted line*). A valgus stress is applied during the pivot shift test because it ensures contact between the lateral femoral condyle and lateral tibial plateau, as occurs during normal weight bearing.[3] *Bottom row:* When the knee is extended *(left),* the iliotibial tract is relaxed and lies in front of the axis of flexion *(dark circle).* At 30 degrees of flexion *(middle),* the iliotibial tract is still in front of the axis of flexion, but it becomes taut in the ACL-deficient knee as the tibia is displaced anteriorly. At 45 degrees of flexion *(right),* the iliotibial tract suddenly falls behind the axis of flexion, thus shifting from being an extensor of the knee to being a flexor and pulling the tibia backward into its normal alignment (the shift).

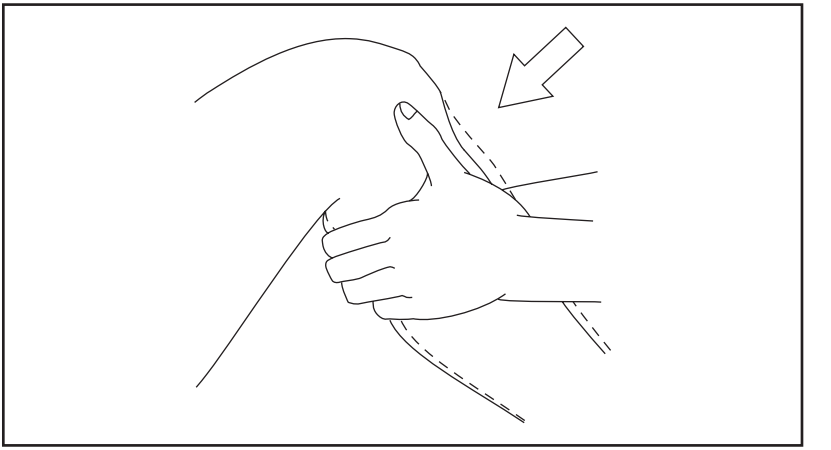


FIGURE 55-13 Posterior drawer sign. With the patient positioned as for the anterior drawer sign (see Fig. 55-9), the clinician pushes posteriorly on the patient's upper calf. In the PCL-deficient knee, this force reveals an abnormal posterior tibial movement *(arrow)* with a soft end point.

Because tears of the posterior half of the meniscus are unlikely to cause locking and are therefore more difficult to detect, the British orthopedic surgeon McMurray proposed in 1949 additional diagnostic tests, one of which is now called the **McMurray test** (Fig. 55-14).*[48]

*One way to help recall the correct positioning of the McMurray test is the following: Testing the medial (i.e., *inner*) meniscus is analogous to the patient squatting with both feet *externally* rotated; testing the lateral (*outer*) meniscus is analogous to the patient squatting with both feet *internally* rotated (i.e., pigeon toed). One author has converted this squatting maneuver into a clinical test, the **Ege test**.[62]

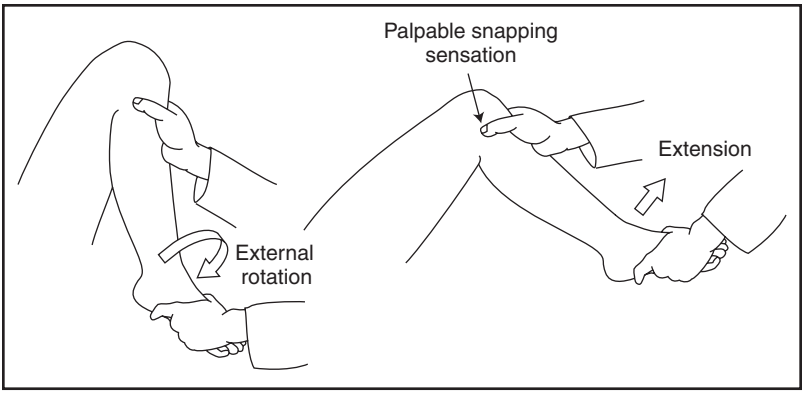


FIGURE 55-14 The McMurray test. The clinician flexes the patient's knee fully against the buttock and rotates the tibia (by grasping the patient's foot and ankle). The purpose of rotation is to bring the torn meniscal fragment, located on the posterior half of the meniscus, *anterior* to the curved surface of the femoral condyle: *External* rotation brings forward the *medial* meniscus; *internal* rotation, the *lateral* meniscus. This figure, therefore, depicts testing of the medial meniscus: The clinician places a free hand over the medial joint line, fully flexes the patient's knee, and then rotates the tibia externally. The clinician slowly extends the knee while maintaining this rotational force, thereby forcing the medial femoral condyle to glide forward on the tibia and *over* any torn fragment of meniscus. When the femur passes over the torn fragment, a palpable snapping sensation may be detected at the medial joint line (a positive test). To test the lateral meniscus, the clinician repeats the test while internally rotating the knee and palpating the lateral joint line. Popular orthopedic textbooks[63] and review articles[50,64,65] add varus and valgus stresses to their definitions of the McMurray test, although McMurray did not include these in his original description nor were they used in clinical studies testing the sign's accuracy (see EBM Box 55-6).

III. CLINICAL SIGNIFICANCE

A. DETECTING OSTEOARTHRITIS

In a study of 237 patients with various forms of chronic knee pain (i.e., osteoarthritis, rheumatoid arthritis, meniscal or ligament injuries, osteonecrosis, gout, septic arthritis, and other assorted connective tissue disorders), the following findings increased the probability of osteoarthritis in the knee: palpable bony enlargement (LR = 11.8; EBM Box 55-4), genu varum deformity (LR = 3.4), stiffness lasting for less than 30 minutes (LR = 3), and the presence of at least three of six characteristic findings listed in EBM Box 55-4 (LR = 3.1). The findings that decrease the probability of osteoarthritis in the knee are fewer than three characteristic findings (LR = 0.1), morning stiffness lasting for more than 30 minutes (LR = 0.2), and absence of crepitus (LR = 0.2). The presence of valgus deformity is diagnostically unhelpful (LR not significant), occurring just as often in patients with osteoarthritis as alternative diagnoses.

B. DETECTING KNEE FRACTURE

In patients presenting to emergency departments with knee trauma, the following findings increase the probability of a clinically significant knee fracture: inability to flex the knee beyond 60 degrees (LR = 4.7; EBM Box 55-5),

EBM BOX 55-4

*Diagnosis of Osteoarthritis in Patients with Chronic Knee Pain**[66]

Finding†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Individual Findings				
Stiffness <30 minutes	85	72	**3.0**	**0.2**
Crepitus, passive motion	89	58	2.1	**0.2**
Bony enlargement	55	95	**11.8**	0.5
Palpable increase in temperature	14	52	**0.3**	1.6
Valgus deformity	24	83	NS	NS
Varus deformity	22	93	**3.4**	0.8
Combined Findings				
At least 3 out of 6: (1) age >50 years; (2) stiffness <30 minutes; (3) Crepitus; (4) bony tenderness along margins of joint; (5) bone enlargement; (6) no palpable warmth				
	95	69	**3.1**	**0.1**

*Diagnostic standard: for *diagnosis of osteoarthritis*, consensus of experts after review of patient's course, laboratory tests, and radiographs.

†Definition of findings: for *morning stiffness <30 minutes*, when applied only to patients complaining of morning stiffness and knee pain.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. NS, not significant.

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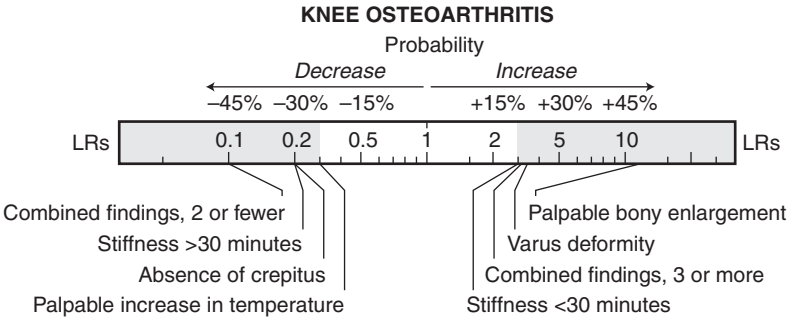

inability to bear weight immediately after the injury and in the emergency department (LR = 3.6), tenderness at the head of the fibula (LR = 3.4), and age of 55 years or older (LR = 3). A negative Ottawa knee rule (i.e., lacking all five predictors from Table 55-4) greatly decreases the probability of knee fracture (LR = 0.1).

EBM BOX 55-5
*Clinically Significant Knee Fracture**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Individual Findings				
Age ≥55 years[35,37]	23-48	87-88	**3.0**	NS
Joint effusion[35–37,67]	54-79	71-81	2.5	0.5
Ecchymosis[37]	19	91	NS	NS
Limitation of knee flexion[35–37]				
Not able to flex beyond 90 degrees	42-65	78-80	2.9	0.5
Not able to flex beyond 60 degrees	46-49	90	**4.7**	0.6
Isolated tenderness of patella[35–37]	25-31	85-89	2.2	0.8
Tenderness at head of fibula[35–37]	12-32	92-95	**3.4**	NS
Inability to bear weight, immediately and in emergency department[35–37]	46-58	81-89	**3.6**	0.6
Combined Findings				
Ottawa rule positive[35–42]	83-99	19-54	1.7	**0.1**

*Diagnostic standard: for *clinically significant knee fracture*, one requiring orthopedic consultation, splinting, or surgery (i.e., one >5 mm in breadth or one associated with complete tendon or ligament disruption).

†Definition of findings: for *isolated tenderness of the patella*, no bony tenderness elsewhere on the knee[35]; for *inability to bear weight immediately and in emergency department*, unable to transfer weight twice onto each lower limb regardless of limping; for *Ottawa rule positive*, see Table 55-4.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

NS, not significant.

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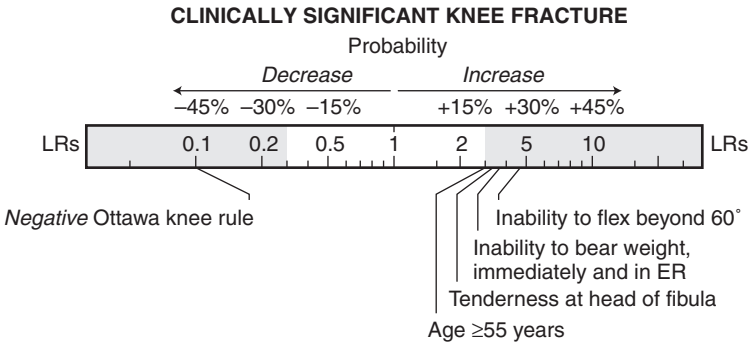

C. DETECTING LIGAMENT AND MENISCAL INJURIES

Most studies of soft tissue injuries of the knee are vulnerable to both *selection bias* (i.e., only patients scheduled for surgery are enrolled) and *verification bias* (i.e., the surgeons who operated on the patients are also the clinicians who examined the patients). These biases may be less important than expected, however, because other studies using independent diagnostic standards (e.g., magnetic resonance imaging [MRI])[68,69] reveal a similar diagnostic accuracy for these clinical signs.

1. Anterior Cruciate Ligament Injury

Any of the three physical tests of ACL injury, when positive, indicate an increased probability of injury: the Lachman sign (LR = 17; EBM Box 55-6), anterior drawer sign (LR = 11.5), and pivot shift sign (LR = 8). Only the *absence* of the Lachman sign, however, significantly decreases the probability of ACL injury (LR = 0.2).

The Lachman sign is more sensitive than the anterior drawer sign for three reasons:[59]

1. Hemarthrosis from acute ACL injury impairs knee flexion and thus prevents testing by means of the anterior drawer test.
2. Tense hamstring muscles, irritated from pain, directly oppose forward subluxation of the tibia during the anterior drawer sign (knee at 90 degrees) but not when the knee is at 20 degrees (i.e., at this angle, the pull of the hamstring muscle is almost perpendicular to the anterior subluxation of the tibia).
3. The thick posterior edge of the medial meniscus acts as a wedge against the curved femoral condyles and prevents anterior subluxation of the tibia when the knee is at 90 degrees (i.e., anterior drawer sign) but not when it is at 20 degrees (i.e., the Lachman sign). In support of this last hypothesis, the sensitivity of the anterior drawer sign in one study increased from 50% to 100% after medial meniscectomy.[59]

In two clinical studies, expert clinicians combining the patient interview and clinical examination accurately diagnosed ACL tears (as detected by subsequent arthroscopy: sensitivity 96%, specificity 98% to 99%, positive LR = 74.7, negative LR = 0.04).[44,77]

2. Posterior Cruciate Tear

Two studies demonstrated the accuracy of bedside examination for posterior cruciate tears (positive LR = 97.8, negative LR = 0.1; see EBM Box 55-6). Unfortunately, neither study specifically identified the technique used at the bedside, although it almost certainly included the posterior drawer sign.

3. Meniscal Injury

Both the positive McMurray sign (LR = 4.5) and block to full extension of the knee (LR = 3.2) increase the probability of a meniscal tear. No finding, however, significantly decreases the probability, except for the absence of joint line tenderness (LR = 0.5), which decreases the probability only slightly. It is possible that the presence of joint line tenderness reflects

EBM BOX 55-6
*Ligament and Meniscal Injuries**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Detecting Anterior Cruciate Ligament Tear				
Anterior drawer sign[45,59,68–71]	27-88	91-99	**11.5**	0.5
Lachman sign[45,59,68–70]	48-96	90-99	**17.0**	**0.2**
Pivot shift sign[45,68,70]	6-32	96-99	**8.0**	NS
Detecting Posterior Cruciate Ligament Tear				
Posterior drawer sign[44,72]	90-95	99	**97.8**	**0.1**
Detecting Meniscal Injury				
McMurray sign[46,47,73,74]	17-52	77-98	**4.5**	0.8
Joint line tenderness[47,73–75]	55-92	30-67	1.5	0.5
Block to full extension[47]	44	86	**3.2**	0.7
Pain on forced extension[47,73]	47-51	67-70	1.6	0.7
Detecting Medial Collateral Ligament Injury				
Valgus stress laxity[45,76]	79-89	49-99	NS	**0.2**

*Diagnostic standard: for *anterior cruciate tear*, MRI,[68,69] arthroscopy[45,70] or surgery[59,71]; for *posterior cruciate tear*, arthroscopy; for *meniscal tear*, arthroscopy[46,47,73–75]; for *medial collateral ligament tear*, arthroscopy[45] or MRI.[76]

†Definition of findings: See text.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

NS, not significant.

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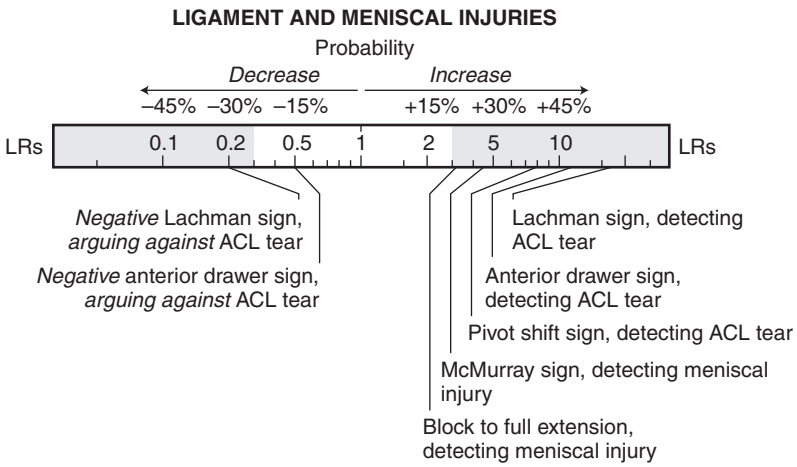


accompanying injury of the joint capsule or collateral ligaments rather than injury to the meniscus per se.

The above studies address the diagnosis of *any* meniscus injury. Two studies have addressed the question of whether expert clinicians who combine the patient interview with the clinical examination can accurately diagnose *and localize* the injured meniscus. In these studies, clinicians *were* slightly more accurate in *ruling out* medial meniscus injury (sensitivity 88% to 95%, specificity 56% to 77%, positive LR = 2.9, negative LR = 0.1) and *ruling in* lateral meniscus injury (sensitivity 51% to 55%, specificity 90% to 94%, positive LR = 5.9, negative LR = 0.5).[44,77]

4. Medial Collateral Ligament

One study of valgus laxity (at 0 degrees and 20 degrees of flexion) demonstrated superior clinical accuracy,[45] whereas another testing for valgus laxity at 30 degrees of flexion demonstrated poor accuracy.[76] The pooled LR is not significant. In both studies, *absence* of valgus laxity *decreased* the probability of medial collateral ligament injury (LR = 0.2; see EBM Box 55-6).

5. Variables Affecting Sensitivity of Signs

Signs of ligament injury are more likely to be positive if:

1. The ligament tear is complete, not partial.[64]
2. The injury is chronic, not acute.[78,79]
3. Multiple ligaments are injured (e.g., in ACL-deficient knees, the anterior drawer sign is more likely to be positive if the medial collateral ligament is also injured).[80]

Also, the degree to which the patient is relaxed influences the sensitivity of these signs, as illustrated by the observation that the sensitivity of most tests increases when patients are examined under anesthesia.[45,64,78,80]

6. Predicting the Need for Knee Surgery

If all knee injuries were managed conservatively (e.g., by rest, bracing, and physical therapy), the detailed bedside examination described above would have limited clinical utility. One study, however, enrolled patients with knee pain and demonstrated that many of these physical signs—limited knee flexion (<120 degrees) or extension, medial or lateral joint line tenderness, a positive McMurray test, a positive Lachman test, and a positive anterior drawer sign—independently predicted whether an experienced orthopedic surgeon would recommend nonarthroplasty knee surgery to the patient.[81]

THE ANKLE

I. INTRODUCTION

In patients presenting with ankle or foot injuries to emergency departments, 8% to 14% are found to have a clinically significant fracture.[82–88] Achilles tendon rupture typically occurs during sports activities when the

athlete forcibly plantarflexes the ankle (e.g., "pushes off" during running or jumping) or dorsiflexes it forcibly.[89]

II. THE FINDING

A. OTTAWA ANKLE AND MIDFOOT RULES

Stiell and others have developed a prediction rule for clinically significant injuries called the **Ottawa ankle rule.**[90,91] This rule focuses on the presence of tenderness at four locations and on whether the patient is able to bear weight both immediately after the accident and later in the emergency department (Fig. 55-15). Importantly, the rule applies only to patients with injury of the ankle (i.e., the distal 6 cm of the tibia, fibula, and talus) and midfoot (i.e., the navicular, cuboid, and cuneiform bones, anterior process of the calcaneus, and base of the fifth metatarsal) and *not* to injury of the body and tuberosities of the calcaneus or injury more than 10 days old.

B. ACHILLES TENDON RUPTURE

Many patients with ruptured Achilles tendons can still plantarflex the ankle, thus potentially misleading clinicians into thinking the Achilles tendon is intact (i.e., the tibialis posterior and peroneus muscles, which attach to the midfoot bones, also plantarflex the ankle). Consequently, special tests for Achilles tendon rupture have been developed. These tests, illustrated in Figure 55-16, rely on palpation of the injured tendon **(palpable gap)** or demonstration of disrupted tendon integrity (**calf squeeze test** and **knee flexion test**).

III. CLINICAL SIGNIFICANCE

A. ANKLE AND MIDFOOT FRACTURES

In patients with ankle injury, the finding of tenderness of the posterior medial malleolus increases the probability of fracture (LR = 4.8; EBM Box 55-7), and the findings of a negative Ottawa ankle rule (LR = 0.1) and ability to bear weight for four steps in the emergency room (LR = 0.3) decrease the probability. Specificity of the Ottawa ankle rule may improve by substituting "tuning-fork tenderness" for "tenderness with palpation."[101]

In patients with midfoot pain, tenderness at the base of the fifth metatarsal bone increases the probability of fracture by a small amount (LR = 2.9). A negative Ottawa foot rule greatly decreases the probability of midfoot fracture (LR = 0.1), although much of this argument rests on the absence of tenderness at the base of the fifth metatarsal (LR = 0.1).

Other studies combining the ankle and foot rules have confirmed their accuracy[82–88,102,103] and shown they reduce the need for radiographs by 14% to 34% and decrease medical costs and patient waiting times.[83,85–87,90,96,104–107]

B. ACHILLES TENDON RUPTURE

All three signs of Achilles tendon rupture accurately increase the probability of a torn tendon if present (LRs = 6.2 to 13.5; EBM Box 55-8) and decrease the probability if absent (LRs = 0.05 to 0.3)

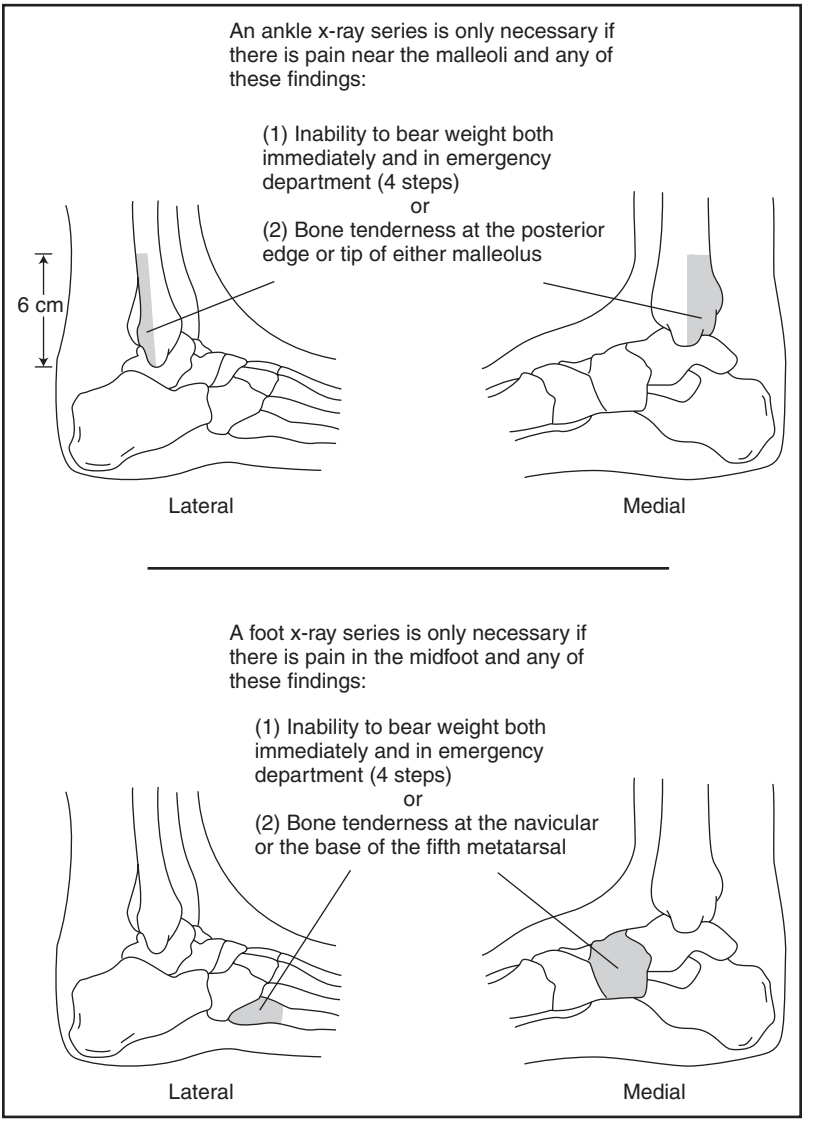


FIGURE 55-15 **Ottawa rule for ankle or midfoot fracture.** The rule for ankle pain is the top figure; the rule for midfoot pain is the bottom figure. The rule is positive if any indication for radiography is met. "Inability to take four steps" means the patient is unable to transfer weight twice onto each lower limb regardless of limping. Importantly, these rules apply *only* to patients with injury of the ankle or midfoot, and they exclude patients with injury to the body or tuberosities of the calcaneus. *Adapted from reference 90 with permission.*

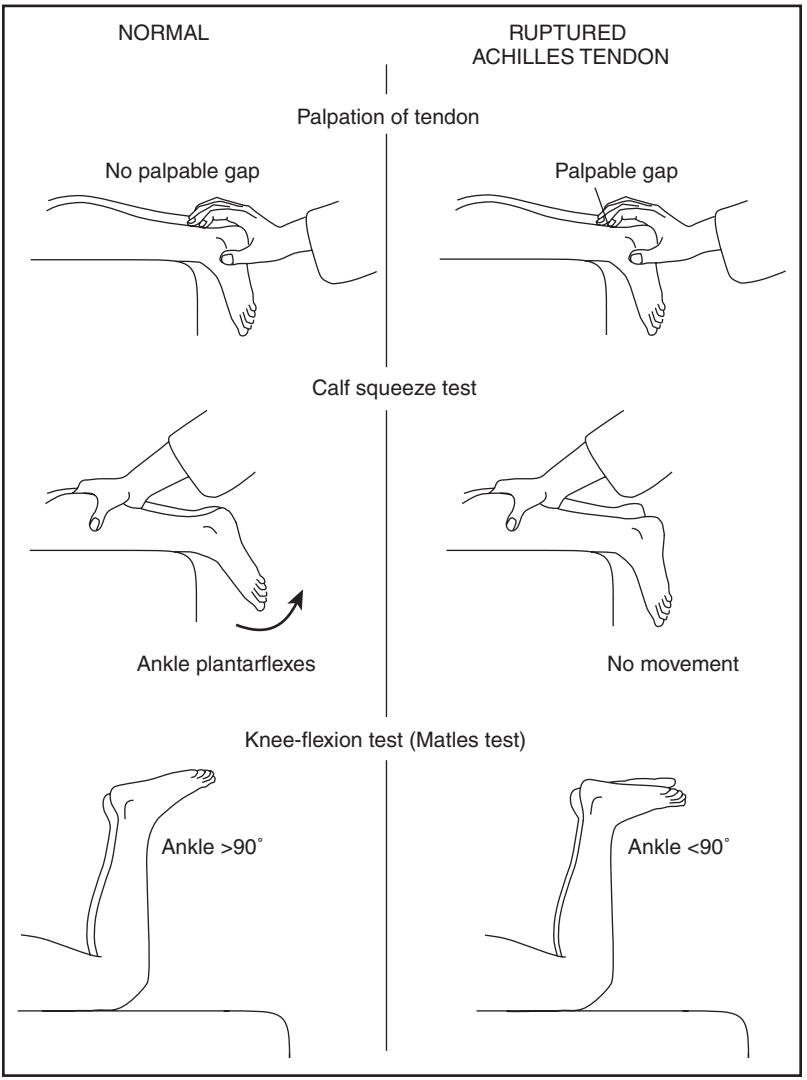
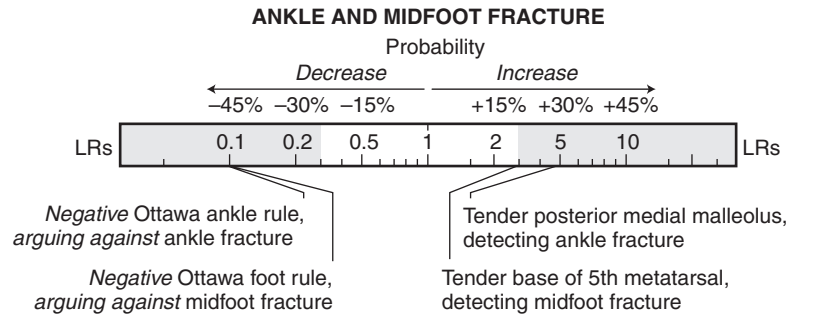


FIGURE 55-16 **Tests for rupture of the Achilles tendon.**[92] All tests are performed with the patient lying prone and his or her feet extending over the end of the examination table. The patient's asymptomatic side serves as a control. (For each test, a patient with an intact Achilles tendon is depicted on the *left,* compared with a patient with a ruptured Achilles tendon on the *right.*) **(1) Palpable gap in tendon** *(top):* The clinician gently palpates the course of the tendon, searching for gaps, which if present usually lie between 2 to 6 cm from the calcaneus.[89] (2) **Calf squeeze test** (**Simmonds-Thompson test**, *middle*)**:** The clinician gently squeezes the patient's calf in its middle third and just below the place of widest girth, observing the ankle for movement. If the tendon is intact, the ankle should plantarflex. Absence of movement or minimal movement is a positive response. The normal plantar flexion of the ankle results from compression of the soleus muscle, which bows the Achilles tendon posteriorly.[93] (3) **Knee flexion test** (**Matles test,** *bottom*)**:** The clinician observes the position of the patient's ankles as the patient flexes both knees to 90 degrees. (The knees may be flexed individually or simultaneously.) The ankle remains slightly plantarflexed if the tendon is intact; slight dorsiflexion or a neutral position of the ankle is the positive response. Thompson described the calf squeeze test in 1962,[89] pointing out that the test could be performed with the patient prone or kneeling on a chair. Simmonds described the identical test in 1957.[94] Matles described the knee flexion test in 1975.[95]

EBM BOX 55-7
*Ankle and Midfoot Fracture**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Detecting Ankle Fracture				
Tenderness over posterior lateral malleolus[90, 91]	69-76	65-74	2.4	0.4
Tenderness over posterior medial malleolus[90,91]	34-47	87-95	**4.8**	0.6
Inability to bear weight immediately after injury[90,91]	61-68	72-79	2.6	0.5
Inability to bear weight for four steps in the emergency room[90,91]	80-85	64-70	2.5	**0.3**
Ottawa ankle rule[83,85,90,96–99]	94-100	16-44	1.5	**0.1**
Detecting Midfoot Fracture				
Tenderness at the base of the fifth metatarsal[90,91]	92-94	66-69	2.9	**0.1**
Tenderness of navicular bone[90,91]	3-12	74-90	0.4	NS
Inability to bear weight immediately[90,91]	18-28	74-82	NS	NS
Inability to bear weight for four steps in the emergency room[90,91]	38-45	58-67	NS	NS
Ottawa foot rule[85,90,96–98,100]	88-99	21-79	2.1	**0.1**

*Diagnostic standard: for *clinically significant ankle or midfoot fracture*, bone fragments >3 mm in breadth (i.e., a size that might require plaster immobilization).
†Definition of findings: for *Ottawa ankle and foot rules*, see Figure 55-15.
‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. NS, not significant.
Click here to access calculator.

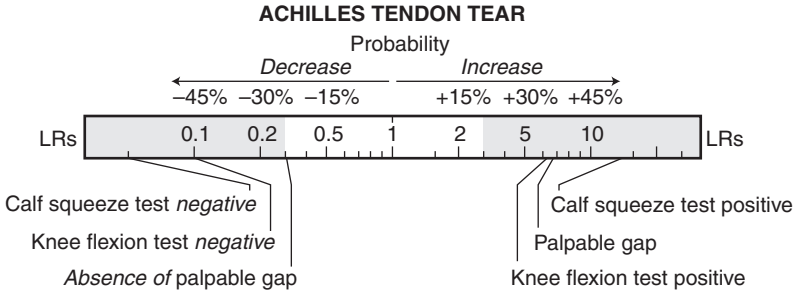


EBM BOX 55-8
Achilles Tendon Tear[*92]

Finding	Sensitivity (%)	Specificity (%)	Likelihood Ratio[†] if Finding Is	
			Present	*Absent*
Palpable gap in Achilles tendon	73	89	6.8	0.3
Calf squeeze test	96	93	13.5	0.05
Knee flexion test	88	86	6.2	0.1

*Diagnostic standard: for *Achilles tendon tear*, surgical findings or (in patients without surgery) ultrasonography or magnetic resonance imaging.

[†]Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. *Click here to access calculator.*



The references for this chapter can be found on www.expertconsult.com.

CHAPTER 56

Visual Field Testing

I. INTRODUCTION

Abnormalities of peripheral vision are called **visual field defects.** These defects, many of which can be detected at the bedside, provide important clues to the diagnosis of lesions throughout the visual pathways—the retina, optic nerve, optic chiasm, optic tracts, optic radiations (parietal and temporal lobes), and occipital cortex (Fig. 56-1).

II. DEFINITION

The term **hemianopia** describes visual defects that occupy about one-half of an eye's visual space. **Quadrantanopia** describes defects confined mostly to about one-fourth of an eye's visual space. **Homonymous** describes defects that affect the same side of the vertical meridian (i.e., right or left side) of both eyes. For example, a right homonymous hemianopia affects the right visual space of both eyes (i.e., the temporal field of the right eye and the nasal field of the left eye). Homonymous implies that the defect does not cross the vertical meridian.

III. THE ANATOMY OF THE VISUAL PATHWAYS

The key anatomic points in Figure 56-1 are the following:

1. Images from the visual fields are inverted throughout the retina and all neural pathways. Images from the temporal visual field fall on the nasal retina, and those from the nasal field on the temporal retina. Images from the *superior* visual fields are transmitted throughout the *inferior* visual pathways (inferior retina, inferior optic nerve and chiasm, and temporal lobe), and those from the *inferior* visual fields throughout the *superior* visual pathways (superior retina, superior optic nerve and chiasm, parietal lobe).
2. The nasal retinal fibers cross in the optic chiasm; therefore, disease of the optic chiasm causes defects in both temporal visual fields **(bitemporal hemianopia).**
3. The visual pathways posterior to the optic chiasm contain information from the same visual space of each eye: Lesions in the *right* postchiasmal pathways cause defects in the *left* visual space of each eye (i.e., temporal field of left eye and nasal field of right eye), and those of the *left* postchiasmal pathways cause defects in the *right* visual

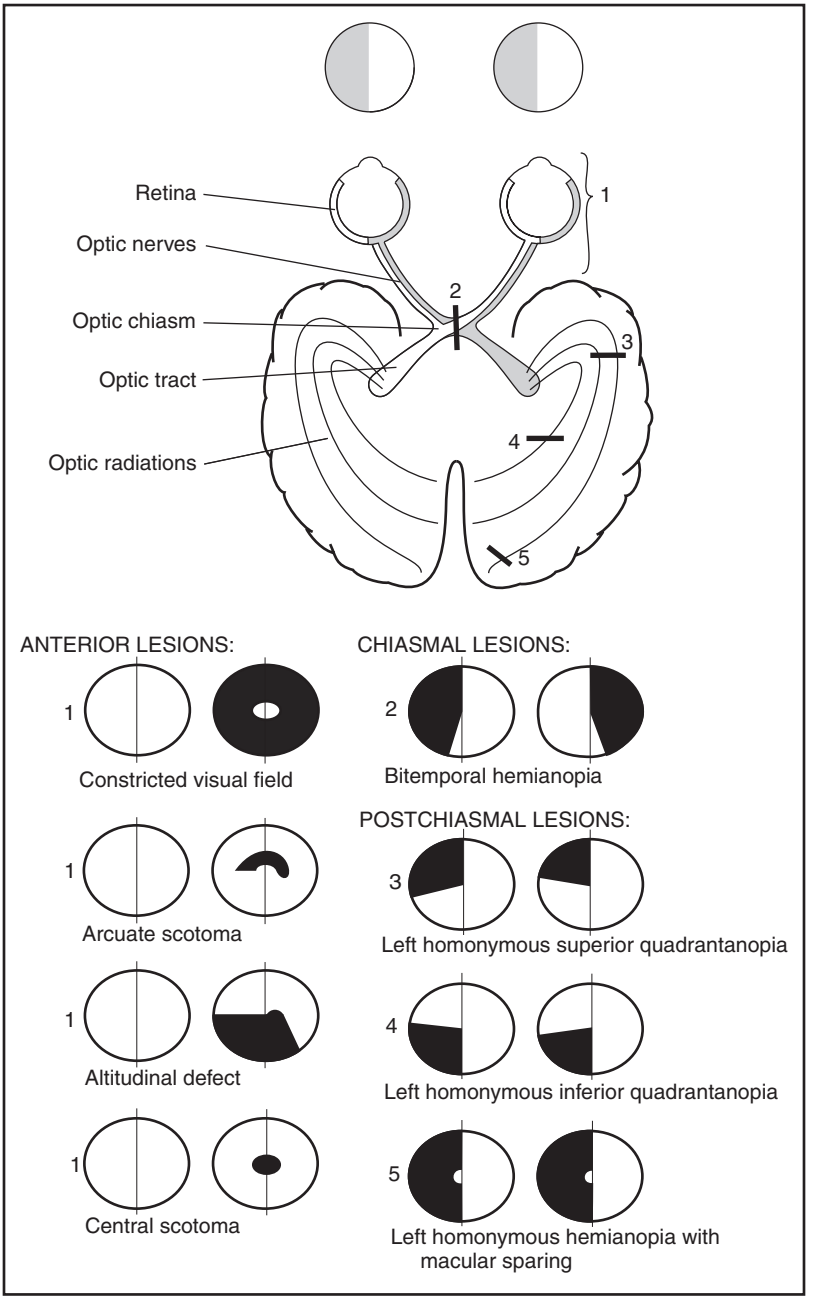


FIGURE 56-1 **Anatomy of the visual pathways.** The anatomy of the visual pathways appears at the top of the figure, the *light gray shading* indicating how visual information from the left visual space eventually courses to the right brain. Visual field defects are at the bottom of the figure. Anterior defects (labeled "1," from disease of the optic nerve or retina) characteristically affect one eye and cause defects *(black shading)* that may cross the vertical meridian (i.e., the vertical meridian is the vertical line bisecting each visual field). Chiasmal defects (labeled "2") and postchiasmal defects (labeled "3" for a lesion in the anterior temporal lobe, "4" for the parietal lobe, and "5" for the occipital cortex) characteristically affect both eyes and respect the vertical meridian.

space. Such defects, respecting the vertical meridian in each eye, are called *homonymous*.

4. The visual pathways in the occipital cortex that contain information from the macula (point of fixation) are distant from those connected to the more peripheral fields.[1] Therefore, lesions of the occipital cortex may cause either homonymous defects sparing the macula or visual defects confined to central vision.

IV. TECHNIQUE

There are many ways to test visual fields at the bedside,[2] but the two traditional techniques are static confrontational testing and kinetic confrontational testing. In all techniques, the patient sits about 70 to 100 cm from the clinician and fixes on the clinician's own eye. Only one eye of the patient is tested at a time; the other is occluded with a card or the patient's hand.

A. STATIC TECHNIQUE

Using this technique, the clinician presents objects at a fixed point in the visual field, usually about 20 to 30 degrees from fixation. The clinician presents one, two, or five fingers to each visual quadrant and asks the patient to count the number of fingers. Testing two quadrants simultaneously (by asking the patient either to count the total number of fingers or to identify which finger is wiggling) has the advantage of detecting some parietal lobe lesions, which may allow patients to see an object in the contralateral field if it appears alone but not if another object is presented simultaneously to the healthy visual field (i.e., visual extinction).

Throughout the examination, the clinician focuses on whether a defect respects the vertical or horizontal meridians of the visual field (see later). Defects crossing the vertical meridian are due to anterior disease (see later), whereas those respecting the vertical meridian are due to chiasmal disease (if the defect is bitemporal) or postchiasmal disease (if it is homonymous).

B. KINETIC TECHNIQUE

In this technique, the clinician tests one quadrant at a time by slowly moving an object (e.g., a wiggling finger, <5 degrees of oscillation) from an extreme peripheral field toward fixation, the patient then indicating the moment he or she sees the object. The trajectory of the moving object is an imaginary line bisecting the horizontal and vertical meridians (e.g., 45, 135, 225, and 315 degrees from the vertical meridian), and the direction of movement is from periphery to central fixation.

V. THE FINDINGS

Visual field defects are classified as prechiasmal defects (from disease in the retina or optic nerves, often called anterior defects), chiasmal defects, and postchiasmal defects (optic tracts, optic radiations, and occipital cortex).

A. ANTERIOR OR PRECHIASMAL DEFECTS

The characteristic features are the following:

1. One eye is affected (unless the retinal or optic nerve disorder is bilateral).
2. Visual acuity is poor. Most patients have diminished acuity or, if acuity is normal, other signs of anterior disease, such as an afferent pupillary defect (see Chapter 20), red color desaturation, abnormal retina examination, or an abnormal optic disc (drusen, cupping, or atrophy).
3. The defects may cross the vertical meridian. This occurs because retinal nerve fibers from the temporal retina arch across the vertical meridian to reach the optic disc and nerve (which lie on the nasal side of the retina). Damage to these fibers thus may cause a defect that crosses the vertical meridian. Small nerve fiber defects may cause an arcuate defect (see Fig. 56-1) and larger ones an altitudinal defect (having a sharp horizontal border in the nasal field). Damage to fibers from the macula may cause central scotomas and, to those preferentially affecting the most peripheral vision, constricted visual fields.[3]

B. CHIASMAL DEFECTS

These defects are bitemporal hemianopias (see Fig. 56-1).

C. POSTCHIASMAL DEFECTS

The characteristics of these defects are the following:

1. Both eyes are affected, causing homonymous hemianopias or quadrantanopias.
2. **Visual acuity is normal.** This is true in more than 90% of cases. If visual acuity is abnormal, it is because of bilateral disease, and thus the acuity in both eyes is the same.[4]
3. **Pupil and retinal examinations are normal.** One important exception is the occasional finding of papilledema, caused by brain tumors affecting the optic radiations.

VI. CLINICAL SIGNIFICANCE

A. ETIOLOGY

Most anterior defects are caused by severe glaucoma, retinal emboli, and optic neuritis.[2] Chiasmal defects are usually from a pituitary tumor just below the optic chiasm. Over 95% of postchiasmal defects are due to lesions of the temporal, parietal, and occipital lobes. Lesions of the optic tracts are rare.[4]

Although parietal and temporal lobe disease may cause inferior and superior quadrantanopias, respectively (see Fig. 56-1), lesions in these areas more often cause dense hemianopias or hemianopias that are denser inferiorly or superiorly, respectively.[4,5]

B. DIAGNOSTIC ACCURACY

EBM Box 56-1 summarizes the diagnostic accuracy of the confrontational technique for diagnosing visual field defects. According to these likelihood ratios [LRs], the finding of a visual field defect by confrontation significantly

increases the probability that one is actually present (i.e., by perimetry, LRs = 5.7 to 9.6). The absence of a defect on bedside testing, however, only modestly decreases the probability of an actual defect (especially for anterior defects, LR = 0.7). Sensitivity is lower for anterior defects because anterior defects are much less dense than posterior ones. (See the section on Improving Detection of Visual Defects.[2])

C. DIFFERENTIAL DIAGNOSIS OF POSTCHIASMAL DEFECTS

Homonymous hemianopias may be either an isolated finding or associated with other neurologic findings. The most common cause of an *isolated* homonymous hemianopia is an ischemic infarct of the occipital cortex.[6,7] In patients with associated hemiparesis, aphasia, or asymmetrical optokinetic nystagmus, the most common diagnosis is parietal lobe disease.[4,7–9] Optokinetic nystagmus is a normal horizontal nystagmus that occurs when patients look at a vertically striped tape moving in front of them. The clinician moves the tape first to one side and then the other, comparing the

EBM BOX 56-1
*Visual Field Defects**

Finding (Reference)	Sensitivity (%)	Specificity (%)	Likelihood Ratio† if Finding Is	
			Present	*Absent*
Confrontation Technique, Detecting the Following Visual Field Defects‡[2,13–18]				
Anterior defects (retina and optic nerve)	11-58	93-99	**5.7**	0.7
Patchy defects	6			
Constriction of visual fields	58			
Arcuate defects	20-51			
Altitudinal defects	88			
Posterior defects (optic chiasm to occipital cortex)	43-86	86-98	**9.6**	0.4
Bitemporal hemianopia	45			
Homonymous hemianopia	80			
Patients with Homonymous Hemianopias, Detecting Parietal Lobe Disease				
Asymmetrical optokinetic nystagmus[4]	93	84	**5.7**	**0.1**
Associated hemiparesis or aphasia[7]	90	95	**18.3**	**0.1**

*Diagnostic standard: for *visual field defects*, conventional perimetry.
†Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.
‡Definition of findings: abnormal static finger counting, static kinetic finger testing, kinetic finger boundary testing, or combinations of these tests.
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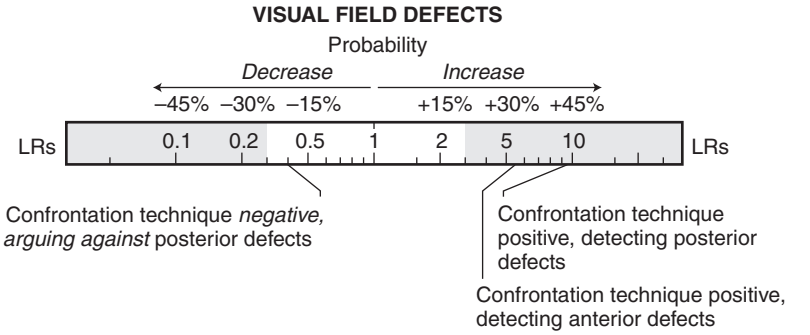
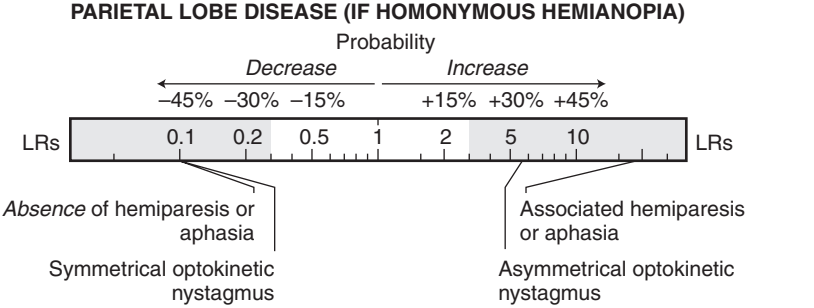




amplitude of horizontal nystagmus produced, which should be equal in each direction. Parietal lobe lesions reduce or eliminate optokinetic nystagmus when the tape is moved *toward* the side with the lesion. (Barany first made this observation in 1921.)

In patients undergoing computed tomography of the head (because of stroke, headache, seizures), the finding of a homonymous hemianopia increases the probability of contralateral focal cerebral disease (sensitivity 22% to 30%, specificity 93% to 98%, positive LR = 4.3; see Chapter 59).[10,11] In those patients with homonymous defects, the presence of asymmetrical optokinetic nystagmus, associated aphasia, or hemiparesis increases the probability of a parietal lobe lesion (LR = 5.7 for optokinetic nystagmus and LR = 18.3 for hemiparesis or aphasia), whereas the absence of these findings decreases the probability of a parietal lobe lesion (both LRs = 0.1) and thus makes occipital or temporal lobe disease more likely.

D. IMPROVING DETECTION OF VISUAL FIELD DEFECTS

Confrontation fails to detect some defects because they are too small, lack a sharp linear border (e.g., patchy defects of anterior disease), or are too peripheral (e.g., constricted visual fields; confrontation only tests the most central 20 to 30 degrees of visual space). To increase the sensitivity of bedside examination, some experts have proposed increasing the distance during testing from 1 m to 4 m, which may improve the detection of subtle arcuate scotomas (glaucoma or optic nerve disease) or macular sparing (some occipital cortex lesions).[12] Additional techniques include:

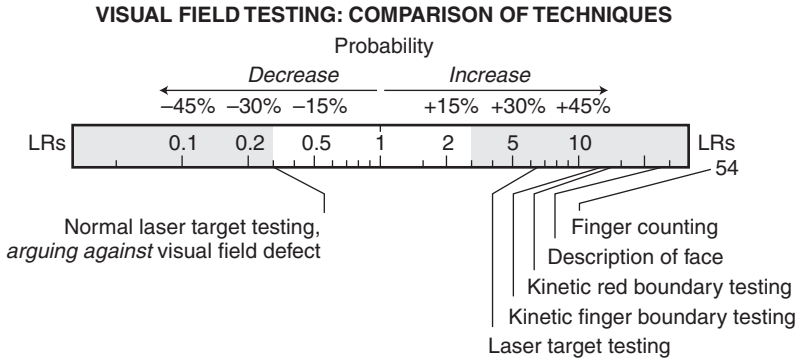
EBM BOX 56-2
*Visual Field Testing: Comparison of Techniques**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Finger counting[2,17]	25-35	99-100	**54.4**	0.7
Kinetic finger boundary testing[2,17]	39-41	97-99	**13.3**	0.6
Description of face[2,17]	36-44	99	**26.4**	0.6
Kinetic red boundary testing[2,17]	56-74	93-99	**13.6**	0.4
Laser target testing[13]	71	89	**6.3**	**0.3**
Red target comparison[2,17]	59-77	27-99	NS	NS

*Diagnostic standard: for *visual field defect*, conventional perimetry testing. (Most patients in these studies had anterior visual field defects.)

†Definition of findings: for *kinetic red boundary testing*, the moving target was either 5 mm^2 or 20 mm^2[17] in diameter and the patient was asked to report when it first appeared red. For all other findings, see text.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.
NS, not significant.
Click here to access calculator.



1. **Description of face:** The patient is asked to report if any part of the examiner's face is distorted or missing.
2. **Kinetic red boundary testing:** The patient is asked to report when the *color red first appears* in a moving target (5 to 20 mm in diameter) as it is moved inward from the periphery.
3. **Red target comparison:** The examiner presents two 20-mm red targets (often the caps of mydriatic solutions) to two quadrants simultaneously and asks the patient if the bottle tops appear equally red.
4. **Laser target testing:** The clinician uses a conventional red laser pointer and projects it in front of the patient on a dark screen 1 m away.[13]

According to studies comparing these various techniques (EBM Box 56-2), static finger counting, kinetic finger boundary testing, and description of

the clinician's face have similar diagnostic accuracy (LRs = 13.3 to 54.4). Kinetic testing with a red target and laser pointer testing improve sensitivity but at the cost of diminished specificity. In these studies, the red target comparison test was diagnostically unhelpful (LRs not significant).

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 57

Nerves of the Eye Muscles (III, IV, and VI): Approach to Diplopia

DIPLOPIA

I. INTRODUCTION

Patients with lesions of cranial nerves III, IV, and VI have paralysis of one or more ocular muscles, which prevents the eyes from aligning properly and causes double vision, or **diplopia.** The most common mistake in analyzing diplopia, however, is to prematurely conclude that the affected patient must have neuropathy of one of these three nerves. Because less than half of patients with diplopia actually have a cranial neuropathy, this chapter first emphasizes the general approach to *all* causes of diplopia.

II. DEFINITIONS

Diplopia may be monocular or binocular. **Monocular diplopia** persists after occluding one eye. **Binocular diplopia** depends on the visual axes of each eye being out of alignment and therefore disappears when one eye is occluded.

Several other terms are used to describe the findings of patients with binocular diplopia. **Heterotropia** is a general term for the finding of visual axes that are not parallel. (Synonyms are **squint** or **strabismus.**) **Esotropia** means that one eye is converging or is deviated toward the nose (e.g., a left esotropia means that the left eye is deviated toward the nose). **Exotropia** means that one eye is diverging or is deviated toward the temple (e.g., a right exotropia means that the right eye is deviated out). **Hypertropia** means that one eye is deviated upward (e.g., a left hypertropia means that the left eye is elevated with respect to the right eye). Diplopia may be **horizontal**, with the two images side by side, or **vertical**, with one image higher than the other. (The term **vertical diplopia** also encompasses diplopia with images separated both vertically and horizontally.)

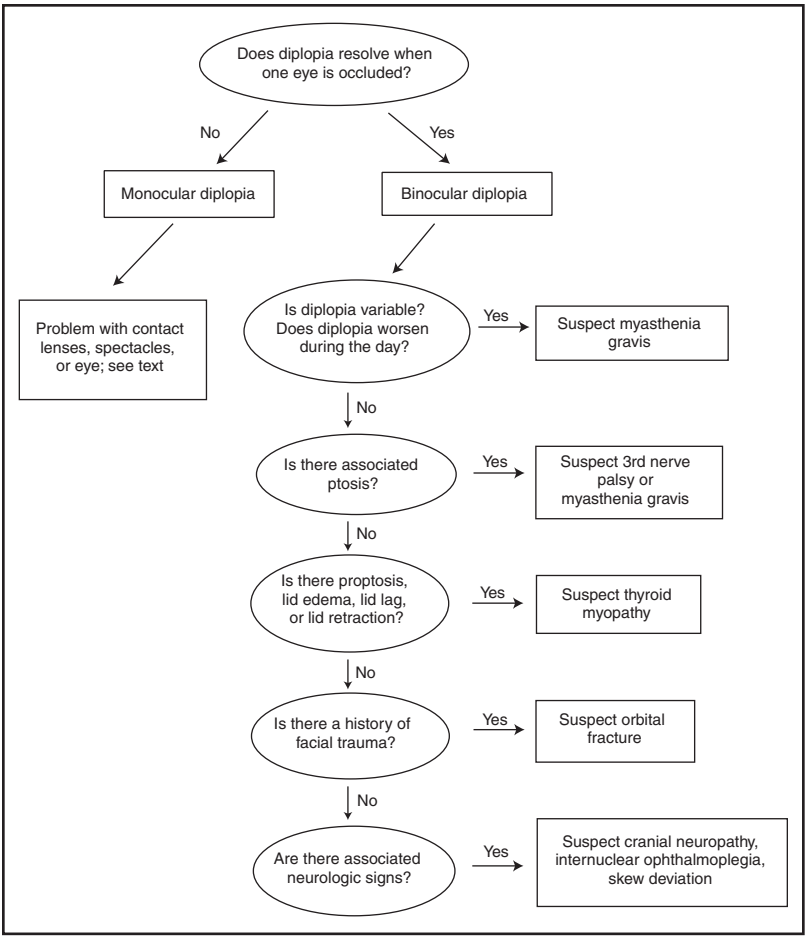


FIGURE 57-1 General approach to diplopia. The clinician should first distinguish monocular from binocular diplopia and, in patients with binocular diplopia, address the five questions on the right side of the figure. Only then should the clinician identify which muscle is weak, although this is unnecessary if the clinician already suspects myasthenia (from fatigability) or full third nerve palsy (from weakness of the medial rectus, superior rectus, inferior rectus, and inferior oblique muscles, with or without a dilated pupil). Uncommon causes of diplopia and associated *ptosis*, not presented in the figure, are botulism, the Fisher variant of Guillain-Barré syndrome, and aberrant regeneration of the third nerve.[1,2] Uncommon causes of diplopia and associated *orbital findings* (e.g., proptosis) are carotid-cavernous fistula (which causes an orbital bruit),[3] orbital tumor, and pseudotumor.

III. TECHNIQUE

A. GENERAL APPROACH

Figure 57-1 outlines the general approach to diplopia. The most important initial question is whether the diplopia is monocular or binocular, which can easily be addressed by covering one of the patient's eyes. Overall, 12% to 25% of all cases of diplopia are monocular and 75% to 88% are binocular.[4,5]

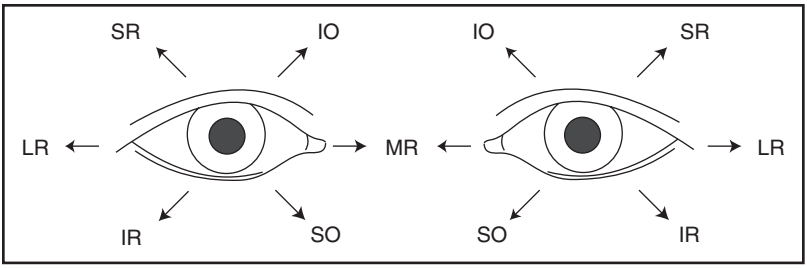


FIGURE 57-2 Principal actions of ocular muscles. There are 12 ocular muscles, 6 in each eye. The actions of the medial rectus (MR) and lateral rectus (LR) muscles are simple right and left lateral movements, respectively. Although the actions of the four vertical eye muscles—the superior rectus (SR), inferior rectus (IR), superior oblique (SO), and inferior oblique (IO) muscles—are more complex, there is one direction of gaze, indicated in the figure, in which weakness is most apparent.

In patients with binocular diplopia, the clinician can avoid misdiagnosing cranial neuropathy by first addressing the five questions listed in Figure 57-1. Only after asking these questions should the clinician attempt to identify which eye muscle is weak.

B. IDENTIFYING THE WEAK MUSCLE

When examining the eye muscles, the clinician holds up his or her index finger or penlight and asks the patient to track it toward each of the six cardinal directions of gaze (i.e., left, left and up, left and down, right, right and up, right and down). These directions parallel the principal action of the six eye muscles, as described in Figure 57-2.

There are two steps in identifying which eye muscle is weak. Step 1 reduces the number of possible weak eye muscles from 12 to 2. Step 2 then identifies which of these two muscles is causing the diplopia.

1. Step 1: The Worst Diplopia (and Heterotropia) Occurs When the Patient Looks in the Direction of the Weak Muscle

The clinician asks the patient which of the six cardinal directions aggravates the diplopia the most. According to this rule, the weak muscle is one of the two muscles responsible for this movement, one of which moves the right eye and the other the left eye. For example, diplopia that is worse on far right lateral gaze indicates weakness of the right lateral rectus muscle or left medial rectus muscle. Diplopia that is worse when the patient looks to the left and down indicates a problem of the left inferior rectus muscle or right superior oblique muscle.*

*Because the actions of the four vertical muscles are sometimes difficult to recall, a mnemonic by Maddox (1907) may be helpful: The affected muscle is "either the same-named rectus muscle or the most crossed-named oblique muscle." For example, if diplopia is worse when the patient looks to the *left* in a *superior* direction, the affected muscles are either the *left superior* rectus muscle or *right inferior* oblique muscle.

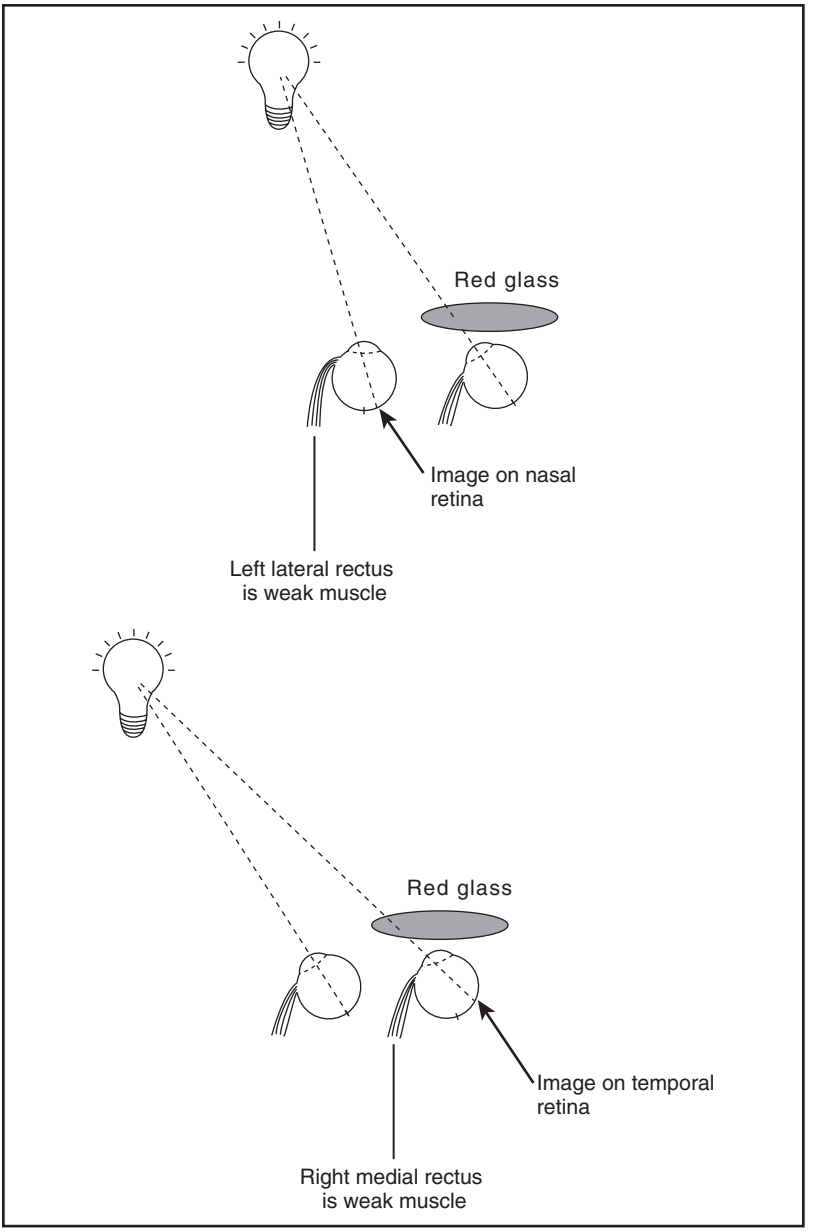

Red glass
Image on nasal retina
Left lateral rectus is weak muscle
Red glass
Image on temporal retina
Right medial rectus is weak muscle

FIGURE 57-3 Use of a red glass to identify the weak muscle. In this example, the patient has horizontal binocular diplopia when looking to the left, indicating that the possible weak muscle is either the left lateral rectus or right medial rectus muscle (see Fig. 57-2). A red glass is placed in front of the right eye, causing the image seen by the right eye to be red and that by the left eye to be white. Importantly, images projecting on the nasal side of the retina are perceived to belong to the temporal visual space (see Chapter 56) and those on the temporal side of the retina to belong to the nasal visual space. If the left lateral rectus muscle is the weak muscle (*top* figure), the image in the left eye falls on the nasal retina, whereas that of the right eye falls on the fovea; therefore, the white image is more *peripheral* than the red image (i.e., it is farther leftward in the patient's left visual field). If the right medial rectus muscle is the weak muscle (*bottom* figure), the image in the left eye falls on the fovea and that of the right eye falls on the temporal retina; therefore, the red image is more *peripheral* than the white image (i.e., it is farther leftward in the patient's left visual space). In both cases, the most peripheral image belongs to the paralyzed eye. In both of these examples, it is the stronger eye that is fixing on the target (i.e., the image falls on the fovea of the stronger eye), but the results are the same if it is the weaker eye that fixates on the object (i.e., the more peripheral image belongs to the weaker eye). See text.

2. Step 2: The Clinician Identifies Which of the Two Identified Muscles Is Weak

There are three techniques (a, b, and c following).

a. Simple Inspection of the Eyes

In patients with diplopia on far right lateral gaze, the weak muscle is the right lateral rectus muscle if there is an esotropia but it is the left medial rectus muscle if there is an exotropia. In patients with diplopia that is worse when looking up and to the right, the weak muscle is the right superior rectus muscle if there is a left hypertropia but the left inferior oblique muscle if there is a right hypertropia.

Often, however, the heterotropia is not obvious, either because the visual axes are out of line only by a degree or two (too small a distance to observe) or because the patient can compensate and temporarily pull the visual axes back into line. In these patients, the following techniques are helpful:

b. The Affected Eye is the One with the Most Peripheral Image

By placing a red glass over one eye (usually the right eye), the patient is less likely to fuse the images, and, when the patient looks at a penlight in the direction of maximal diplopia, he or she sees two images, one red and one white. The most peripheral image belongs to the weak eye (Fig. 57-3).

For example, in a patient whose maximal diplopia is to the left and down (and who has the red glass over the right eye), the weak muscle is the right superior oblique muscle if the red image is most peripheral but the left inferior rectus muscle if the white image is most peripheral.

c. The Cover/Uncover Test

To perform this test, the clinician covers one eye while the patient looks in the direction of maximal diplopia. Covering one eye prevents fusion of the images, and any heterotropia that exists will return, although it is now obscured by occlusion of the eye. The clinician then observes which

way that eye moves to pick up the image after it is uncovered. If it moves out, there was an esotropia; if it moves in, there was an exotropia; and if it moves down, that eye had a hypertropia.

IV. CLINICAL SIGNIFICANCE

A. MONOCULAR DIPLOPIA

Almost all patients with monocular diplopia have "extraocular" or "ocular" causes.[4,6] Common extraocular causes are the patient's spectacles (e.g., reflections off one or both surfaces of the lenses) or contact lenses (e.g., air bubble in the pupillary area, abnormal curves, or uneven thicknesses). This diplopia resolves after removal of the lenses and, in patients with spectacles, varies as the spectacles are moved in and out or up and down. Common ocular causes include problems in the lens (e.g., fluid clefts, early cataracts), cornea (e.g., astigmatism, keratitis), and eyelids (e.g., chalazion, prolonged reading that may allow drooping lids to temporarily deform the cornea). The diplopia of these patients resolves when patients look through a pinhole or when a card is held over half of the pupillary aperture. (It resolves because the diplopia depends on irregularities of the optic media acting as tiny prisms that divert some rays off the fovea; the pinhole or card blocks these wayward rays and thus eliminates the problem.)

Rare patients with monocular diplopia have cerebral disease.[7] Despite traditional teachings, hysteria is a rare cause of monocular diplopia.

B. BINOCULAR DIPLOPIA

1. Etiology

Among patients with binocular diplopia, common final diagnoses are cranial neuropathy (III, IV, or VI; 39% to 67% of patients), eye muscle disease (thyroid ophthalmopathy, myasthenia gravis; 13% of patients), trauma (12%), supranuclear causes (internuclear ophthalmoplegia, skew deviation, 5%), other causes (4% to 16%), and unknown causes (4% to 11%).[4,5]

2. Weak Muscles and Their Clinical Significance

Incomplete palsies of the third cranial nerve are rare. (In one study of 579 third nerve palsies, <1% were partial.[8,9]) If only one or two of the third nerve muscles (i.e., superior rectus, inferior rectus, medial rectus, and inferior oblique muscles) are weak, therefore, the diagnosis is almost certainly *not* a partial third nerve palsy but instead one of the diagnoses listed below.

a. Weak Superior Rectus Muscle

The clinician should consider **myasthenia gravis** (see Fig. 57-4). Most patients with myasthenia gravis present with ocular symptoms, usually diplopia and ptosis,[10] although the pupils are always normal. Symptoms often fluctuate, worsening at the end of the day or even alternating between the eyes. Ocular myasthenia may mimic any ocular misalignment, although the most commonly affected muscles are the superior or medial rectus muscles, in which weakness is provoked by having the patient sustain an upward or far lateral gaze for 30 seconds or more.

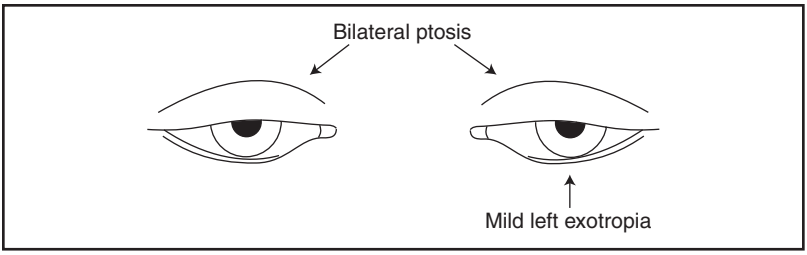


FIGURE 57-4 **Myasthenia gravis.** Myasthenia gravis may mimic any ocular disorder causing diplopia, although most often it mimics weakness of the superior rectus muscle or medial rectus muscle (i.e., difficulty with sustained elevation or adduction of the eye, respectively). Clues to the diagnosis of myasthenia gravis are associated ptosis, fluctuating course, and *normal* pupils.

One important bedside test for myasthenia is the ice pack test. (See the section on Ice Pack Test for Myasthenia Gravis.)

b. Weak Inferior Rectus Muscle

The clinician should consider thyroid myopathy and orbital floor fracture.

(1) Thyroid Myopathy. Patients may have associated proptosis, lid lag, lid retraction, chemosis, and hyperemia at the insertions of the rectus muscles (see Chapter 23). These findings are sometimes subtle, and because many patients are also clinically euthyroid, the only finding of thyroid myopathy may be heterotropia. The cause of diplopia is mechanical restriction of the eye muscles, which ophthalmologists confirm using the forced duction test (i.e., after anesthetization of the conjunctiva, the ophthalmologist grasps the conjunctiva with toothed forceps and attempts to passively rotate the eye, detecting abnormal resistance in patients with thyroid myopathy).[8]

(2) Orbital Fracture. Diplopia is a complication of 58% of blowout fractures of the orbit and 20% of all midfacial fractures.[11] The heterotropia occurs because of swelling or entrapment of one of the eye muscles, most often the inferior rectus muscle. In addition to the history of previous trauma, some patients have an additional clue, hypesthesia of the ipsilateral infraorbital area, which results from accompanying injury to the infraorbital branch of the trigeminal nerve. Diplopia may first become a problem for the patient days after the injury, when the swelling has had time to partially resolve.[8]

c. Weak Medial Rectus Muscle

The clinician should consider internuclear ophthalmoplegia and myasthenia gravis.

(1) Internuclear Ophthalmoplegia. Lesions in the medial longitudinal fasciculus (the periaqueductal pathway in the brainstem that links the nuclei of cranial nerves III, IV, and VI and coordinates conjugate eye

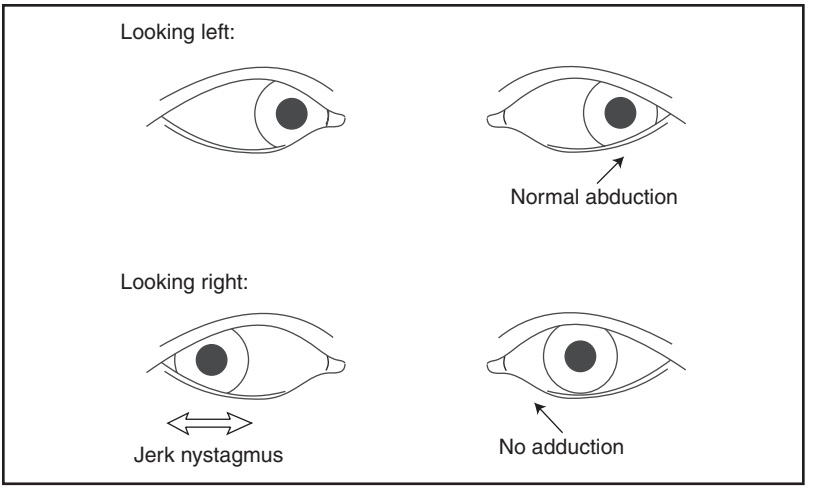


FIGURE 57-5 Internuclear ophthalmoplegia. When the patient in the figure looks to the left *(top row)*, both eyes move normally, but when the patient looks to the right *(bottom row)*, the left eye fails to adduct ("weak" medial rectus muscle) and the contralateral eye develops a jerk nystagmus. The finding is named for the side with weak adduction (i.e., in this example, a *left* internuclear ophthalmoplegia), and the lesion is in the *ipsilateral* medial longitudinal fasciculus (i.e., *left* medial longitudinal fasciculus in this example). See text.

movements) cause **internuclear ophthalmoplegia (INO)**[12–14] (Fig. 57-5). The features of INO are the following:

1. Incomplete adduction of one eye on lateral gaze (i.e., the "weak" medial rectus muscle)
2. Jerk nystagmus of the contralateral abducting eye

Many patients also have vertical nystagmus on upward gaze. The finding is named according to the side with weak adduction. For example, in efforts to look to the far right, if the patient's left eye is unable to completely adduct and the right eye develops a jerk nystagmus, the patient has a left internuclear ophthalmoplegia (and a lesion in the left medial longitudinal fasciculus).

Ninety-seven percent of patients with *bilateral* INOs have multiple sclerosis, whereas *unilateral* INO has many causes, although the most common one is vertebrobasilar cerebrovascular disease.[13]

(2) Myasthenia Gravis. Myasthenia gravis (see the section on Weak Superior Rectus Muscle) sometimes causes medial rectus muscle weakness. In contrast to the finding in patients with internuclear ophthalmoplegia, there is no jerk nystagmus of the abducting eye.

d. Weak Lateral Rectus Muscle

Weakness of this muscle almost always indicates damage to the **sixth cranial nerve** (see later), although conditions that mimic nerve damage include myasthenia gravis and thyroid myopathy.[15]

e. Weak Superior Oblique Muscle

A weak superior oblique muscle indicates damage to the **fourth cranial nerve** (see later).

f. Weak Inferior Oblique Muscle

A weak inferior oblique muscle usually indicates **Brown syndrome**.[16,17] These patients appear to have a weak inferior oblique muscle, but the problem actually is in the superior oblique muscle and tendon, which are unable to move freely through their pulley (i.e., the trochlea). In some patients, Brown syndrome is congenital. Acquired Brown syndrome is a complication of orbital inflammation, surgery, and metastases.

3. Skew Deviation

Skew deviation has the following diagnostic features:

1. Acquired hypertropia
2. Associated cerebellar or brainstem disease
3. Lack of an alternative cause of hypertropia

Skew deviation mimics a weak inferior rectus muscle 40% of the time, a weak inferior oblique muscle 25% of the time, a weak superior rectus muscle 17% of the time, and a weak superior oblique muscle 17% of the time (although the head tilt test, described later, is negative).[8,18] Skew deviation is believed to represent an abnormal ocular tilt reaction (Fig. 57-6).[19]

C. ICE PACK TEST FOR MYASTHENIA GRAVIS

Clinicians have observed that sunlight may aggravate the ptosis of myasthenic patients and that hot liquids (vs. cold liquids) may provoke myasthenic dysphagia.[20] Based on these observations and the fact that results of electromyography in myasthenia are temperature dependent, Salvedra devised the ice pack test in 1979[21] as a test for ptosis. In this test, the clinician places a surgical glove filled with crushed ice for 2 minutes over the patient's closed eye and then compares the ptosis before application of the ice (by measuring the palpebral fissure, i.e., the vertical height of eye opening, to the nearest 0.5 mm) to that after application of the ice. Digital pressure is applied on the forehead just above the eyebrow to avoid contributions from the frontalis muscle in elevating the lid. Because cold temperature improves the weakness of myasthenia, the positive result is *diminished* ptosis after application of the ice (i.e., the palpebral fissure increases 2 mm or more).

Several investigators have studied this test in patients presenting with ptosis, demonstrating that the positive ice test greatly increases the probability of myasthenia (likelihood ratio [LR] = 19.3; EBM Box 57-1) and the negative result greatly decreases the probability (LR = 0.2). One investigator has also applied the ice pack test to patients with ophthalmoplegia, showing that improved ophthalmoplegia (and diplopia) after application of ice is diagnostic (positive LR = 31, negative LR = 0.03; see EBM Box 57-1).

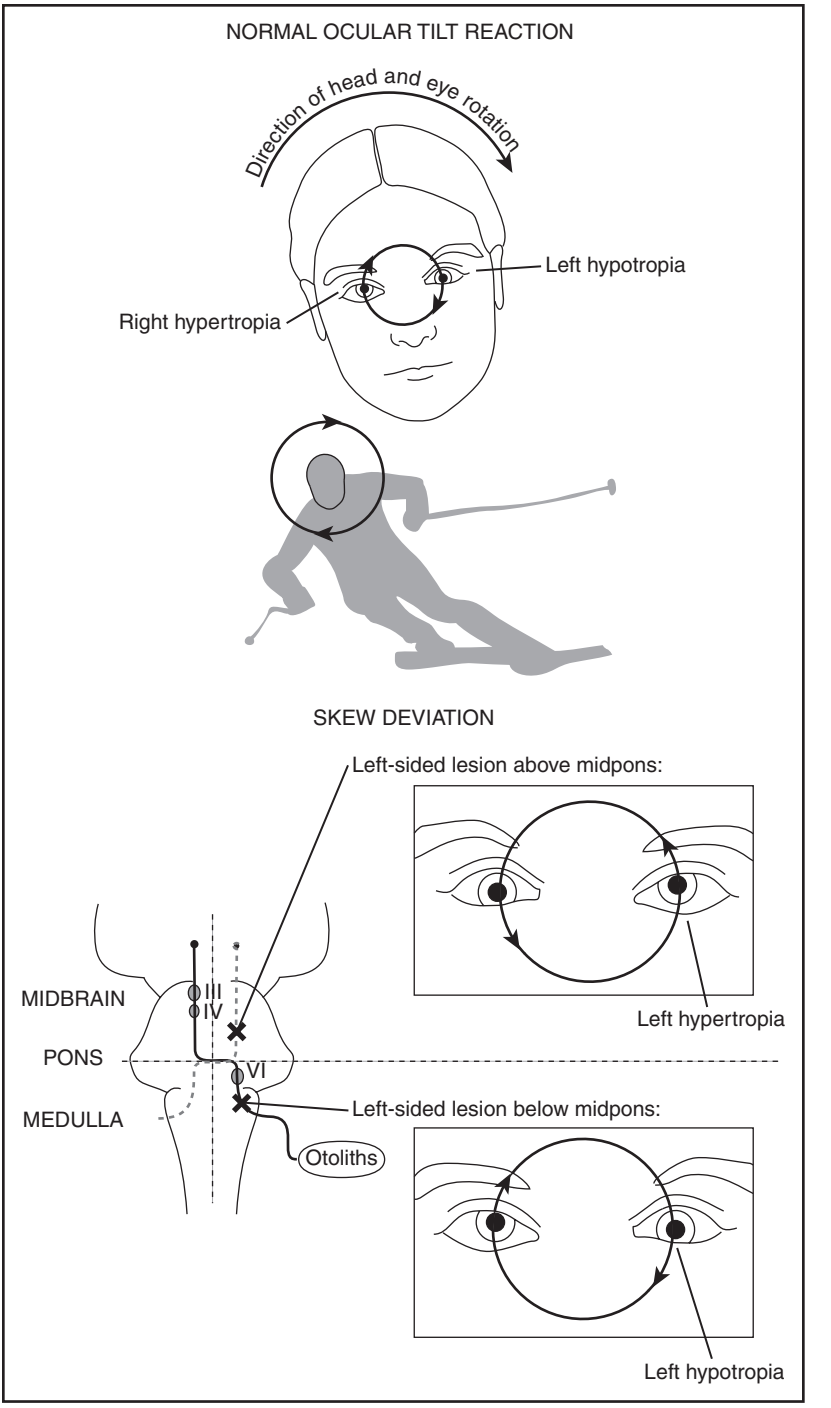

NORMAL OCULAR TILT REACTION
Direction of head and eye rotation
Left hypotropia
Right hypertropia
SKEW DEVIATION
Left-sided lesion above midpons:
Left hypertropia
MIDBRAIN
III
IV
PONS
VI
MEDULLA
Left-sided lesion below midpons:
Otoliths
Left hypotropia

FIGURE 57-6 Skew deviation and the ocular tilt reaction. When a person leans to one side, his or her head and eyes normally compensate by rotating in the opposite direction. For example, in the skier in the top figure, whose body is leaning to the right, the natural compensatory movements are tilting of the head to the left, elevation of the right eye and depression of the left eye, and torsion of both eyes (right eye *intorts* and left eye *extorts*), all movements that restore the normal vertical position of the head and eyes (*left* side of figure). All of these compensatory movements are part of the ocular tilt reaction, a normal reflex that stabilizes retinal images and is mediated by the otolith organs (especially the gravity-sensing utricle and its connections to the ocular motor nuclei and the vestibulospinal tract). Skew deviation (*bottom* figure) is the abnormal heterotropia that appears in disorders (especially cerebellar or brainstem lesions) that produce asymmetry in these pathways.[19] Unilateral lesions below the midpons, the point where these gravity-adjusting pathways cross in the brainstem, cause *ipsiversive* tilt reactions (i.e., the patient's *lowermost eye* indicates the side of the lesion; *right bottom;* see Wallenberg stroke in Chapter 60); lesions above the midpons cause *contraversive* tilt reactions (i.e., the *uppermost eye* indicates the side of the patient's lesion; *right top*). (III, oculomotor nucleus; IV, trochlear nucleus; VI, abducens nucleus.)

EBM BOX 57-1
*Ice Pack Test, Detecting Myasthenia**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Improvement in ptosis after application of ice[20–27]	77-96	83-98	**19.3**	**0.2**
Improvement in diplopia and ophthalmoplegia after application of ice[20]	97	97	**31.0**	**0.03**

*Diagnostic standard: for *myasthenia gravis*, a positive edrophonium (Tensilon) test, positive anti–acetylcholine receptor antibody, electromyography, or combinations of these tests.

†Definition of findings: for *ice pack test*, see text. The ice was applied to the eye for 2 minutes[22–24] or 5 minutes[20] before determining the results of the test.

‡"Likelihood ratio (LR) if finding present" = positive LR; "LR if finding absent" = negative LR.

Click here to access calculator.

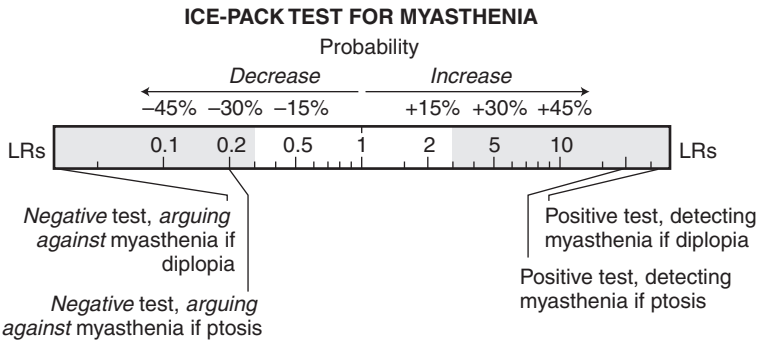


TABLE 57-1 Etiology of Isolated Palsies of Cranial Nerves III, IV, and VI

	Oculomotor Nerve	Trochlear Nerve	Abducens Nerve	Mixed*
Proportion (%)†	31	11	45	13
Etiology (%)				
Head trauma	13	34	11	18
Neoplasm	11	5	19	29
Ischemic cause	25	22	20	7
Aneurysm	17	1	3	11
Other cause	14	8	21	19
Idiopathic palsy	20	30	26	16

**Mixed* refers to combinations of cranial nerves III, IV, and VI.
†*Proportion* is ratio of palsies affecting designated cranial nerve to total number of palsies affecting cranial nerves III, IV, and VI.
Based on references 28 to 40.

DISORDERS OF CRANIAL NERVES III, IV, AND VI

I. INTRODUCTION

Table 57-1 reviews the causes of *isolated* palsies of these three cranial nerves, based on analysis of over 3500 patients reported in the literature. Major causes are ischemic infarcts (all three nerves), intracranial aneurysms (especially the third cranial nerve), head trauma (especially the fourth cranial nerve), and tumors (especially when more than one of these nerves are affected). At least one-fourth of isolated cranial neuropathies affecting these nerves remain idiopathic, even in the modern era of clinical imaging.[36]

II. RULES FOR DIAGNOSING ISCHEMIC INFARCTS

One of the most common causes of *isolated* palsies of cranial nerves III, IV, and VI is ischemic infarction, a diagnosis made at the bedside based on the following criteria:

1. The palsy is isolated (i.e., no other neurologic or ophthalmologic findings).
2. The onset is abrupt.
3. The patient has risk factors for cerebrovascular disease (i.e., age >50 years, hypertension, and diabetes).
4. No other cause is apparent.
5. The palsy is self limited (i.e., resolves over several months).

Seventy-five percent of ischemic mononeuropathies resolve within 4 months; persistence beyond this should prompt evaluation for other causes.

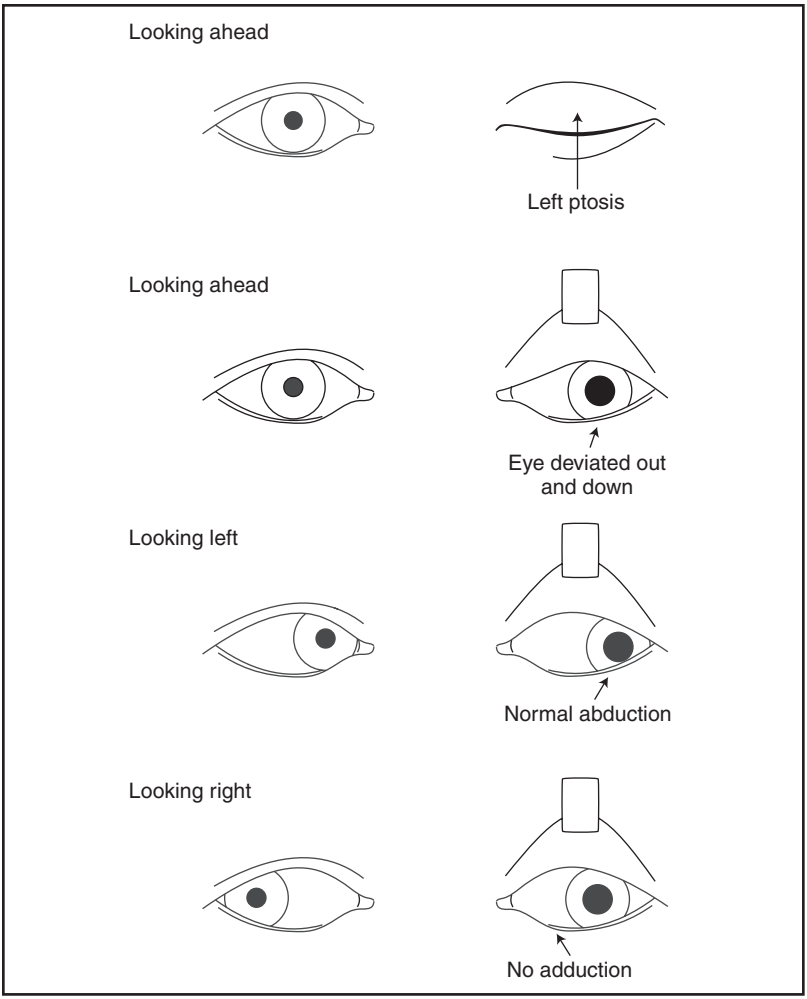


FIGURE 57-7 **Third nerve palsy.** Complete third nerve palsy (of the left eye in this example) causes ptosis that obscures the position of the eye *(first row).* When the lid is held open (by a piece of tape in this example), the eye appears deviated outward and slightly downward *(second row),* because of unopposed action of the lateral rectus muscle (abducting the eye) and superior oblique muscle (depressing the eye). In this example of third nerve palsy, the pupil is dilated because the cause is an intracranial aneurysm: Many ischemic third nerve palsies spare the pupil. (See the section on the Pupil-Sparing Rule in the text.) When the patient looks to the left *(third row),* the intact lateral rectus muscle abducts the eye normally. When the patient looks to the right *(fourth row),* the left eye fails to adduct past the midline. Further tests would also demonstrate that the left eye cannot look up or down.

III. OCULOMOTOR NERVE (CRANIAL NERVE III)

A. THE FINDING

Complete weakness causes downward and outward deviation of the affected eye and ptosis (Fig. 57-7). The pupil may or may not be dilated, depending on the cause of the patient's neuropathy.

B. CLINICAL SIGNIFICANCE

1. Pupil-Sparing Rule[41,42]

The most common identified causes of *isolated nontraumatic* third nerve paralysis are posterior communicating artery aneurysm (which must be managed aggressively) and ischemic infarction of the third nerve (which is managed conservatively). In over 95% of aneurysmal palsies, the pupil reacts sluggishly to light or is fixed and dilated, but in 73% of ischemic palsies, the pupil is spared.[30,31,33,40,43–52] These observations have led to the **pupil-sparing rule,** which states that patients with third nerve palsies sparing the pupil do not have aneurysms and can be safely managed expectantly.

Before applying this rule, however, there are three important caveats.

1. The rule applies only to patients with *complete* paralysis of the ocular muscles of the third nerve and *complete* sparing of the pupil. Up to 4% of patients with aneurysms do have sparing of the pupil, although the third nerve muscles are only partially paralyzed.
2. The rule should be applied sparingly to patients aged 20 to 50 years, an age-group in which ischemic infarcts are uncommon.
3. The rule only applies to patients with isolated third nerve palsies. Any other neurologic or ophthalmologic finding (e.g., hemiparesis, proptosis, other cranial neuropathy) invalidates the rule.

Nonetheless, the pupil-sparing rule had greater value in an earlier era when the only diagnostic test for intracranial aneurysms was catheter angiography (a test carrying a 2% risk of stroke), a time when clinicians sought ways to identify who could safely avoid this potentially dangerous test. Today, with the availability of safer noninvasive testing methods (computed tomographic angiography and magnetic resonance imaging), some experts recommend noninvasive vascular imaging of all patients with new-onset isolated nontraumatic third nerve palsies, whether or not the pupil is spared.[53]

2. Clinical Syndromes

Associated findings distinguish the different causes of third nerve palsy.[54]

a. Ipsilateral Brainstem Damage

Damage to the third nerve fascicle as it exits the ipsilateral brainstem causes accompanying ipsilateral cerebellar signs (**Nothnagel syndrome,** involving the superior cerebellar peduncle), contralateral hemitremor (**Benedikt syndrome,** involving the red nucleus), or contralateral hemiparesis (**Weber syndrome,** involving the cerebral peduncle).

b. Damage to the Nerve in the Subarachnoid Space

Important causes include uncal herniation (i.e., patient is comatose) and internal carotid–posterior communicating artery aneurysm (i.e., the third nerve palsy is isolated).

c. Ipsilateral Cavernous Sinus or Orbit Damage

Lesions of the cavernous sinus or orbit cause simultaneous injury to cranial nerves III, IV, and VI (which causes total ophthalmoplegia), to the

sympathetic nerves of the iris (contributing to a pupil that is small and unreactive), and to the ophthalmic distribution of the trigeminal nerve (causing hypesthesia of the upper third of the face). Orbital disease also causes early, prominent proptosis.

d. Ischemic Infarcts

Ischemic infarction causes isolated third nerve palsy. (See the sections on Rules for Diagnosing Ischemic Infarcts and Pupil-Sparing Rule.)

IV. TROCHLEAR NERVE (CRANIAL NERVE IV)

A. THE FINDING

1. Isolated Cranial Nerve IV Palsy

Paralysis of cranial nerve IV causes vertical diplopia and hypertropia of the affected eye. The hypertropia may not be evident on examination, however, and often the clinician will have to tilt the patient's head toward the affected side to bring out the finding (Fig. 57-8). Tilting the head aggravates the diplopia because it requires the ipsilateral eye to intort, which calls upon simultaneous contraction of the superior oblique and superior rectus muscles. These two muscles work together, and the tendency of the superior oblique muscle to depress the eye is normally balanced by that of the superior rectus muscle to elevate the eye. If the superior oblique muscle is weak, however, attempts to intort the eye (e.g., during tilting of the head) instead bring about unopposed action of the superior rectus muscle, which elevates the eye and aggravates the vertical diplopia and hypertropia.

2. Palsy of Both Cranial Nerves III and IV

In patients with third nerve palsy, testing cranial nerve IV is particularly difficult because the eye is already deviated outward and down (see Fig. 57-7). If cranial nerve IV is intact in these patients, however, the eye will *intort* as the patient is asked to look down. Absence of intorsion (which is apparent by observing the medial conjunctival vessels) indicates palsy of both the third and fourth nerves. An instructive video of this finding appears in the reference by Reich.[55]

B. CLINICAL SIGNIFICANCE

1. Head Position

Studies have shown that in patients with isolated third nerve palsies, 45% actually habitually tilt their head away from the side of the lesion (to minimize any need for intorsion in the affected eye).[35,56,57] This habitual head tilting is often apparent in old photographs of patients with chronic fourth nerve palsies. As expected, when the head is tilted toward the affected side, the diplopia and hypertropia worsen in 96% of patients.[35,57]

2. Clinical Syndromes

The trochlear nerve has the longest intracranial course of any cranial nerve, in part explaining why trauma is the most common explanation for isolated lesions. Associated findings distinguish the different clinical syndromes.

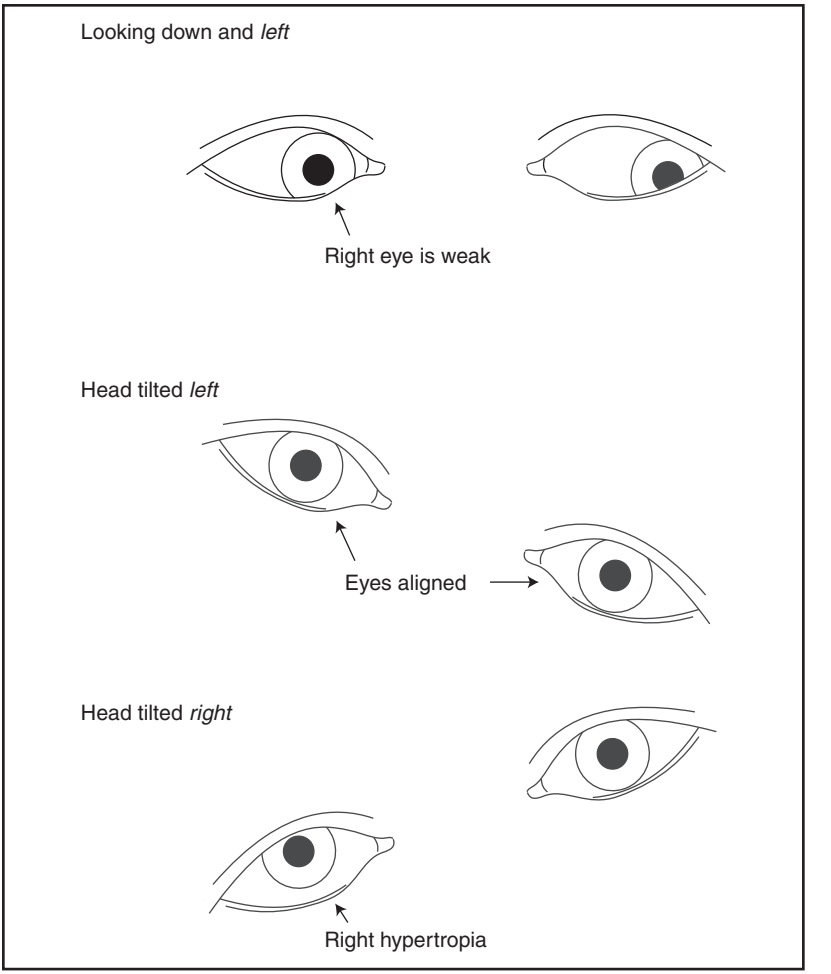


FIGURE 57-8 Fourth nerve palsy. The patient in this example has a right fourth nerve palsy. Diplopia is worst when the patient is looking down and to the left, indicating that the weak muscle is either the left inferior rectus muscle or right superior oblique muscle (see Fig. 57-2 for principal actions of eye muscles). Simple inspection *(first row)* reveals that the right eye lags behind the left eye, indicating that the weak muscle is indeed on the right side (i.e., right superior oblique muscle). Tilting the head *away* from the affected side (i.e., to the *left* side, away from the weak *right* superior oblique muscle; *second row*) aligns the eyes normally, but tilting the head toward the *affected* side (i.e., to the right side, *third row*) brings out a prominent right hypertropia (i.e., the right eye is higher than the left eye). See text.

a. Contralateral Midbrain Lesions

Associated findings are contralateral **Horner syndrome,** contralateral dysmetria, and contralateral internuclear ophthalmoplegia. In all of these syndromes, the associated findings are contralateral because the trochlear nerves cross on their way to the eyes (i.e., the fourth cranial nerve innervating the right eye originates in the left brainstem).[54]

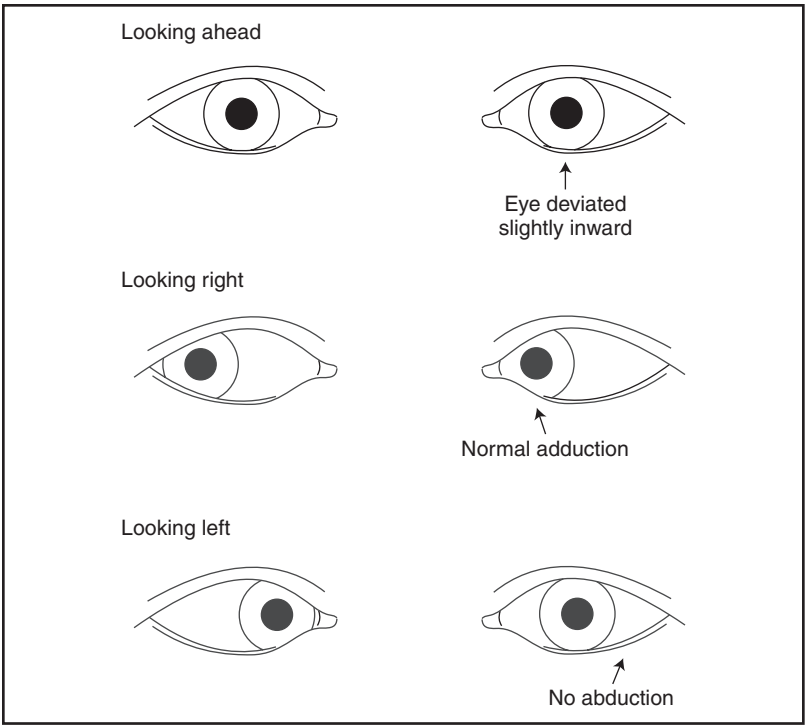


FIGURE 57-9 Sixth nerve palsy. When the patient in this example (who has a *left* sixth nerve palsy) looks ahead, there is a mild left esotropia (i.e., left eye is deviated toward the nose, *first row*). When looking to the right, the affected eye adducts normally *(second row)*. When looking to the left, the left eye fails to abduct *(third row)*.

b. Ipsilateral Cavernous Sinus or Orbit Damage

These lesions cause combinations of findings discussed previously in section III.B.2.c. Ipsilateral Cavernous Sinus or Orbit Damage.

c. Ischemic Infarcts

Ischemic infarcts cause isolated fourth nerve palsy. (See the section on Rules for Diagnosing Ischemic Infarcts.)

V. ABDUCENS NERVE (CRANIAL NERVE VI)

A. THE FINDING

Paralysis of the sixth cranial nerve causes esotropia and an inability to fully abduct the affected eye (Fig. 57-9).

B. CLINICAL SIGNIFICANCE

The various clinical syndromes are distinguished by their associated findings.

1. Ipsilateral Pons Damage

Associated findings are contralateral hemiparesis **(Raymond syndrome),** ipsilateral seventh nerve palsy and contralateral hemiparesis **(Millard-Gubler syndrome),** or ipsilateral **Horner syndrome,** ipsilateral horizontal gaze palsy, and ipsilateral involvement of cranial nerves V, VII, and VIII **(Foville syndrome).**

2. Damage to the Nerve in the Subarachnoid Space

Damage to the nerve in the subarachnoid space often causes isolated sixth nerve palsy. Examples are meningitis, recent lumbar puncture (with subsequent leak of cerebrospinal fluid that leads to stretching of the nerve), and pseudotumor cerebri (also from stretching of the nerve, brought on by elevated intracranial pressure; these patients may have associated papilledema).

3. Damage at the Petrous Apex

Examples are complicated otitis media (**Gradenigo syndrome,** which has associated ipsilateral decreased hearing, facial pain from involvement of the fifth cranial nerve, and ipsilateral seventh nerve palsy), petrous bone fracture (associated hemotympanum and **Battle sign**), and nasopharyngeal carcinoma.

4. Ipsilateral Cavernous Sinus or Orbit Damage

These lesions cause combinations of findings discussed previously in section III.B.2.c. Ipsilateral Cavernous Sinus or Orbit Damage.

5. Ischemic Infarcts

Ischemic infarction causes isolated sixth nerve palsy. (See the section on Rules for Diagnosing Ischemic Infarcts.)

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 58

Miscellaneous Cranial Nerves

Table 58-1 reviews the physical examination of the 12 cranial nerves. Only cranial nerves I, V, VII, and IX through XII are discussed in this chapter. Cranial nerve II is discussed in Chapters 20 and 56; cranial nerve VIII, in Chapter 22; and cranial nerves III, IV, and VI, in Chapter 57.

OLFACTORY NERVE (I)

I. TECHNIQUE

The usual test for the sense of smell is placing a nonirritative substance, such as wintergreen or cloves, under one nostril at a time. One simple method uses the standard 70% isopropyl alcohol pad available in most clinics and wards.[1] Pungent substances such as ammonia should be avoided because they stimulate trigeminal nerve endings (i.e., cranial nerve V).

II. CLINICAL SIGNIFICANCE

A. ANOSMIA

Anosmia is the complete absence of smell. The most common causes are upper respiratory infection and sinus disease (which obstruct the nasal passages) and previous head trauma (which damages the olfactory fibers).[2,3] Less common causes are **Kallman syndrome** (hypogonadotropic hypogonadism) and sphenoid ridge masses (e.g., meningioma, which causes the **Foster Kennedy syndrome**—ipsilateral anosmia, ipsilateral optic atrophy, and contralateral papilledema).[2,4]

B. OLFACTORY DYSFUNCTION

Patients with olfactory dysfunction are able to detect odors but frequently misidentify them. Olfactory dysfunction is common in patients with Parkinson disease or after frontal or temporal lobectomies.[5,6] Patients with Parkinson disease are much more likely to have olfactory dysfunction than patients with other parkinsonian syndromes such as vascular parkinsonism and progressive supranuclear palsy (see Chapter 64).[6–8]

TABLE 58-1 The Twelve Cranial Nerves

Cranial Nerve	Motor Examination	Sensory Examination	Reflex Examination
Olfactory nerve (I)		Detection of nonirritating odors	
Optic nerve (II)		Visual acuity Retinal examination	Afferent pupillary defect (swinging flashlight test)
Nerves of the eye muscles: Oculomotor nerve (III) Trochlear nerve (IV) Abducens nerve (VI)	Extraocular movements (III, IV, and VI) Lid elevation (III only)		Pupillary constriction (III only)
Trigeminal nerve (V)	Masseter muscle Lateral pterygoid muscle	Pain, temperature, and touch sensation of the ipsilateral face	Corneal reflex (afferent limb) Jaw jerk (afferent and efferent limb) Glabellar reflex (afferent limb)
Facial nerve (VII)	All facial movements except lid elevation	Taste sensation to anterior two-thirds of the tongue	Corneal reflex (efferent limb) Glabellar reflex (efferent limb)
Vestibulocochlear nerve (VIII)		Tests of hearing (cochlear component)	Vestibulo-ocular reflex (vestibular component)
Glossopharyngeal nerve (IX)	Ipsilateral palate elevation (with X)	Sensation posterior pharynx Taste sensation to posterior two-thirds of tongue	Gag reflex (afferent limb and, with X, efferent limb)
Vagus nerve (X)	Ipsilateral palate elevation (with IX)		Gag reflex (efferent limb with IX)
Spinal accessory nerve (XI)	Trapezius muscle Sternocleidomastoid muscle		
Hypoglossal nerve (XII)	Genioglossus muscle		

TRIGEMINAL NERVE (V)

I. INTRODUCTION

The trigeminal sensory and motor nuclei are located in the pons, although the sensory nucleus extends through the medulla into the cervical spinal cord. The sensory branches of the trigeminal nerve innervate the upper

face (V_1, ophthalmic division), midface (V_2, maxillary division), and lower face (V_3, mandibular division). The motor fibers to the masseter and lateral pterygoid muscles travel with the mandibular division (V_3).

II. THE FINDING

A. MOTOR WEAKNESS

Lesions of the motor component of the trigeminal nerve affect the masseter muscle (causing difficulty in clenching that side of the jaw, sometimes with atrophy that flattens the contour of the cheek) and lateral pterygoid muscle (causing difficulty in deviating the jaw to the opposite side; at rest, the jaw may deviate toward the weak side).

B. SENSORY LOSS

Lesions of the sensory component cause diminished pain, temperature, and touch sensation in any or all of the three divisions on one side of the face. Sensation to most of the external ear (excluding the tragus) and the angle of the jaw is preserved in trigeminal lesions because these areas are supplied by cervical sensory roots (see Fig. 60-1 in Chapter 60).

C. CORNEAL REFLEX

Unilateral gentle stimulation of the cornea normally causes bilateral blinking. The afferent limb of this reflex is the ipsilateral trigeminal nerve (only V_1 and V_2) and the efferent limb is both facial nerves (i.e., both eyes blink after stimulation of one cornea).

III. CLINICAL SIGNIFICANCE

A. MOTOR WEAKNESS

Unilateral weakness of the trigeminal muscles indicates disease of the proximal mandibular division (e.g., skull metastases) or a lesion in the ipsilateral pons. (Patients with pontine lesions have other associated neurologic findings, such as abnormalities of cranial nerve VI or VII or contralateral hemiparesis.) Unilateral weakness of the trigeminal muscles does not occur with cerebral hemispheric lesions, because each trigeminal nucleus receives bilateral cortical innervation.[9] *Bilateral* weakness, however, may occur in bilateral cerebral hemispheric disease and cause great difficulty in chewing. (See the section on Pseudobulbar Palsy.)

B. SENSORY LOSS

Sensory loss of the face may be part of a broader neurologic syndrome affecting sensation of the whole body and other neurologic functions (lesions of the cerebral hemisphere, thalamus, or brainstem) or may be isolated to the face (lesions of the peripheral nerve and its branches).

1. Sensory Loss of Face and Body

In thalamic and cerebral hemispheric lesions, sensation of the face and body is abnormal on the *same* side, contralateral to the lesion. There is often associated hemiparesis or aphasia, or both. In brainstem lesions, the

sensory abnormalities of the face and body are on *opposite* sides: Sensation is diminished on the *ipsilateral* face but *contralateral* body (see Fig. 60-2 and Table 60-2 in Chapter 60). Pontine lesions affect intraoral more than facial sensation, whereas medullary lesions affect facial more than intraoral sensation.[10]

2. Sensory Loss Isolated to the Face

Sensory loss isolated to the face is part of syndromes affecting the apex of the temporal bone (see Chapter 57, cranial nerve VI), the cavernous sinus syndrome (V_1 division only; see Chapter 57), and the numb chin syndrome. The **numb chin syndrome** describes the loss of sensation on the lower lip and chin, an ominous finding in cancer patients because it suggests metastatic disease to the ipsilateral mandible, base of the skull, or leptomeninges.[11,12] Some affected patients also have other cranial nerve abnormalities.

C. ABNORMAL CORNEAL REFLEX

The two limbs of the corneal reflex are cranial nerves V and VII. According to traditional teachings, unilateral trigeminal nerve dysfunction (i.e., in the ipsilateral brainstem, V_1, or V_2 divisions) prevents both eyes from blinking after stimulation of the ipsilateral cornea, whereas unilateral facial nerve dysfunction prevents the ipsilateral eye from blinking when its cornea is stimulated, although the contralateral eye blinks normally. The absent corneal reflex is felt to be particularly important in patients with unilateral sensorineural hearing loss, in whom it raises the possibility of cerebellopontine angle tumors such as acoustic neuroma.

Nonetheless, the clinical utility of the asymmetrical corneal reflex is limited. The reflex is inexplicably absent unilaterally in 8% of healthy elderly patients,[13] and the sensitivity of the absent reflex for acoustic neuroma is only 33%, the finding usually indicating the tumor has already grown to a large size (>2 cm in diameter).[14]

D. HERPES ZOSTER INFECTION AND THE NASOCILIARY BRANCH OF THE TRIGEMINAL NERVE (HUTCHINSON SIGN)

About half of patients with herpes zoster infection of the ophthalmic division of the trigeminal nerve **(herpes zoster ophthalmicus)** develop vision-threatening complications such as uveitis and keratitis within 1 to 4 weeks of the onset of the rash. (Mean onset of ocular complications is 11 to 13 days.[15–17]) In 1865, Hutchinson noted that the tip of the nose, cornea, and iris all share the same branch of the trigeminal nerve (the nasociliary nerve) and that if patients with herpes zoster ophthalmicus developed vesicles on the tip of the nose (i.e., **Hutchinson sign**), they were at increased risk of ocular complications.[18] The clinical utility of this sign, however, is limited: Its accuracy is only modest (sensitivity 43% to 85%, specificity 77% to 82%, positive LR = 3, negative LR = 0.4),[15,16] and today all patients with herpes zoster ophthalmicus, whether or not the tip of the nose or the eye is involved, should receive antiviral medications and be monitored for ophthalmologic complications.

FACIAL NERVE (VII)

I. THE FINDING

Lesions of the facial nerve may cause facial asymmetry (diminished ipsilateral nasolabial fold and widened ipsilateral palpebral fissure) and weakness of most ipsilateral facial muscles (muscles used during speaking, blinking, raising eyebrows, smiling, wrinkling the forehead, closing the eyes, showing the teeth, and retracting the chin). There may be abnormalities of ipsilateral tearing (lacrimal gland), hearing (stapedius muscle), taste (anterior two-thirds of the tongue), and the corneal and glabellar reflexes.

Facial nerve lesions do not cause ptosis, because the lid muscles are not innervated by the facial nerve but rather by sympathetic nerves and cranial nerve III.

II. CLINICAL SIGNIFICANCE

A. CENTRAL VERSUS PERIPHERAL FACIAL WEAKNESS

Unilateral facial weakness may be *central* (i.e., in upper motor neurons, from lesions in the contralateral motor cortex or descending pyramidal tracts) or *peripheral* (i.e., in lower motor neurons, from lesions in the peripheral nerve or facial nucleus in the ipsilateral pons).* These lesions are distinguished by the following two features:

1. Distribution of Weakness

Peripheral lesions affect both upper and lower facial muscles, whereas central lesions affect predominately the lower facial muscles. Wrinkling of the forehead is relatively spared in central lesions because the facial nuclei innervating these muscles receive bilateral cortical innervation.

2. Movements Affected

Peripheral lesions paralyze all facial movements on the side affected, whereas central lesions affect voluntary movements but spare emotional ones. The patient with central weakness (e.g., cerebral hemispheric stroke) may be unable to wrinkle one corner of the mouth volitionally yet move it briskly during laughter or crying. This occurs because emotional input to the facial nuclei does not come from the motor cortex.†[19,20]

B. PERIPHERAL NERVE LESIONS

1. Etiology

The causes of isolated peripheral facial palsies are idiopathic (50% to 87%), surgical or accidental trauma (5% to 22%), herpes zoster infections (**Ramsay Hunt syndrome,** 7% to 13%), tumors (e.g., cholesteatoma,

*Chapter 59 defines upper and lower motor neurons.

†The opposite clinical finding, emotional paralysis without volitional paralysis, occurs with lesions of the thalamus or frontal lobe.[19]

parotid tumors, 1% to 6%), and miscellaneous disorders (8% to 11%) (These figures originate in specialty referral centers and may overrepresent unusual etiologies.)[21–26] **Bell palsy** refers to the idiopathic disorders, although evidence is mounting that it represents a viral infection.[27]

2. Associated Findings

In patients with Bell palsy, associated findings are diminished taste (52%), hyperacusis (8% to 30%), increased tearing (19% to 34%), and decreased tearing (2% to 17%).[22–25,28–30] Increased tear production occurs because the weak orbicularis oculi muscle cannot contain and direct the tears down the nasolacrimal duct; decreased tearing reflects lacrimal gland dysfunction. Although 23% of patients also have sensory complaints, the finding of hypesthesia of the face (i.e., cranial nerve V) is variable: Some investigators, arguing that Bell palsy is part of a multiple cranial neuropathy, have found hypesthesia in as many as 48% of patients,[24,28] whereas other investigators have never found associated hypesthesia of the face.[22]

3. Topographic Diagnosis

The branches of the facial nerve diverge from the main trunk in a predictable order: They are, proximally to distally, branches to the lacrimal gland, stapedius muscle, tongue (taste), and facial muscles.[24] Therefore, tests of tearing **(Schirmer tear test),** stapedius function (stapedius reflex during audiometry), and taste should pinpoint the location of the lesion, although this is only accurate when the nerve is completely severed. In patients with patchy lesions (Bell palsy or partial injuries), topographic diagnosis is often nonsensical (e.g., tearing is reduced but taste and stapedius function are preserved) and has minimal clinical value.[24,28,31,32]

4. Complications of Bell palsy

Three complications occur after recovery from Bell palsy.[23,25,29,30]

a. Associated Movements

Associated movements, or **synkinesis,** occur in 55% to 94% of patients. These are unexpected movements that probably result from aberrant regeneration. Examples are narrowing of the palpebral fissure when the patient smiles, or motion of the corner of the mouth when the patient closes the eyes tightly.

b. Contracture

Contracture occurs in 3% to 36% of patients. Despite the name, this is increased muscle tone, not a fibrotic scar, which often restores facial symmetry even though some weakness persists.

c. Crocodile Tears

Crocodile tears are seen in 2% to 6% of patients, from aberrant regeneration of salivary gland fibers to the lacrimal gland. When affected patients eat, tears form and run down the cheek or collect in the nose.

GLOSSOPHARYNGEAL (IX) AND VAGUS (X) NERVES

I. FINDING

These nerves are considered together because their functions are difficult to separate at the bedside and because clinical disorders usually affect both nerves simultaneously. There are three abnormal findings.

1. **Absent pharyngeal sensation.** This is usually tested with a cotton applicator stick touching the posterior oropharynx.
2. **Diminished velar movement.** The posterior edge of the soft palate is called the **velum** and its elevation, **velar movement.** The soft palate should elevate as the patient vocalizes a prolonged "ah."
3. **Abnormal gag reflex.** During stimulation of the posterior tongue, pharynx, or soft palate, there is reflex elevation of the tongue and soft palate and constriction of the pharyngeal muscles. The gag reflex is labeled abnormal when it is diminished, absent, hyperactive, or asymmetrical.

II. CLINICAL SIGNIFICANCE

Abnormalities of these nerves may occur because of *bilateral* cerebral hemispheric disease or because of disease in the *ipsilateral* medulla or peripheral nerves (i.e., cranial nerves IX and X). *Unilateral* cerebral hemispheric disease does not ordinarily cause palatal weakness, because the nuclei of these nerves receive bilateral corticobulbar innervation.

A. BILATERAL CEREBRAL HEMISPHERIC LESIONS: PSEUDOBULBAR PALSY

Bilateral lesions above the level of the pons that disrupt the descending pyramidal tracts innervating brainstem motor nuclei may cause significant paralysis of the palate and pharynx, along with paralysis of the tongue, face, and muscles of chewing. This syndrome, **pseudobulbar palsy,** affects about 4% of patients with cerebrovascular disease, who mostly have lacunar infarcts in both internal capsules.[33,34] The main clinical features are dysarthria, dysphagia, and paralysis of voluntary movements of the face.[35] Other findings are hyperactive jaw jerk (70% of patients), absent gag reflex (70%), and hyperactive emotional reflexes that cause spasmodic and often inappropriate crying and laughing (24%).[33,34] The animated facial movements during laughter or uncontrollable crying contrast markedly with the lack of voluntary facial movement and the patient's inability to mimic gestures.

The term *pseudobulbar,* coined by Lepine in 1877,[34] is used because the lesion is supranuclear, to distinguish this syndrome from a similar motor paralysis that may occur after damage to the brainstem nuclei themselves (i.e., **bulbar paralysis**). The term is a misnomer, however, because *bulbar* refers to the medulla; two of the motor nuclei prominently affected in pseudobulbar palsy—those of the facial muscles (VII) and of chewing (V)—reside in the pons.

B. BEDSIDE PREDICTORS OF RISK OF ASPIRATION AFTER STROKE

In patients who have suffered bilateral strokes, significant dysfunction of cranial nerves IX and X makes the airway vulnerable to aspiration during swallowing. EBM Box 58-1 presents the accuracy of several bedside signs of aspiration in patients after strokes. The findings that increase the probability of aspiration risk the most are drowsiness (likelihood ratio [LR] = 3.4), abnormal water swallow test (LR = 3.2), and oxygen desaturation of 2% or more after the patient swallows a liquid (LR = 3.1; see footnote to EBM Box 58-1 for definitions of findings). The findings *decreasing* the risk of aspiration the most are normal pharyngeal sensation (LR = 0.03), absence of oxygen desaturation following a swallow (LR = 0.3), a normal water swallow test (LR = 0.4), and the absence of dysphonia (LR = 0.4). The accuracy of other findings, including the abnormal gag reflex, presence of dysphonia, and abnormal cough, is only modest. Findings without predictive value are abnormal sensation of the face and tongue, tongue weakness, bilateral cranial nerve findings, and abnormal chest radiograph.[36]

The poor predictive value of the gag reflex is not surprising, because the pharyngeal muscles involved in this reflex are not necessarily the same ones activated during normal swallowing to protect the airway. Moreover, the gag reflex is often absent in normal individuals, especially elderly patients.[51,52] Pharyngeal sensation, on the other hand, is rarely absent in normal individuals.[51]

C. LESIONS OF IPSILATERAL BRAINSTEM OR PERIPHERAL NERVE

The lateral medullary syndrome causes ipsilateral absence of pharyngeal sensation and reduced velar elevation, associated with **Horner syndrome** and other sensory and cerebellar signs (see Table 60-2 in Chapter 60). The **jugular foramen syndrome** (e.g., basilar skull fracture or glomus jugulare tumors) simultaneously disrupts cranial nerves IX, X, and XI, causing ipsilateral paralysis of the palate, vocal cords (hoarseness), and trapezius and sternocleidomastoid muscles.

SPINAL ACCESSORY NERVE (XI)

I. FINDING

The primary findings are a weakness or atrophy, or both, of the sternocleidomastoid muscle (which turns the head to the opposite side) and trapezius muscle (which elevates the ipsilateral shoulder).

II. CLINICAL SIGNIFICANCE

Unilateral weakness of these muscles may represent disease of the cerebral hemispheres, brainstem, spinal cord, or peripheral nerve. Atrophy indicates that the lesion is in the nucleus (i.e., brainstem or high cervical

spinal cord) or peripheral nerve (i.e., the lesion is *not* in the cerebral hemispheres).

A. CEREBRAL HEMISPHERE

Lesions of the cerebral hemispheres affect the trapezius and sternocleidomastoid muscles differently: Lesions in one cerebral hemisphere weaken the *contralateral* trapezius muscle but the *ipsilateral* sternocleidomastoid

EBM BOX 58-1
*Aspiration after Stroke**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Voice and Cough				
Abnormal voluntary cough[36–44]	48-89	36-94	1.9	0.6
Dysphonia[36–41,43,45]	59-98	13-67	1.3	0.4
Dysarthria[39,43,46]	60-77	53-57	1.6	0.5
Neurologic Examination				
Drowsiness[44,47]	50-76	65-92	**3.4**	0.5
Abnormal sensation face and tongue[36]	22	52	NS	NS
Absent pharyngeal sensation[47]	98	60	2.4	**0.03**
Tongue weakness[44,45]	50-72	47-91	NS	0.6
Bilateral cranial nerve signs[36,41]	71-73	30-39	NS	NS
Abnormal gag reflex[36–41,43–46]	53-91	18-82	1.5	0.6
Other Tests				
Water swallow test[42–45,47,48]	47-85	58-93	**3.2**	0.4
Oxygen desaturation 0-2 minutes after swallowing[42,49,50]	73-87	39-88	**3.1**	**0.3**

*Diagnostic standard: for *aspiration*, fiberoptic examination[42] or videofluoroscopy (all other studies).

†Definition of findings: for *abnormal voluntary cough*, the patient is asked to cough as hard as possible and the resulting cough is absent, weak, breathy, or sluggish; for *dysphonia*, the patient is asked to sing a prolonged "ah," and the voice is breathy, hoarse, wet, harsh, or strained; for *absent pharyngeal sensation*, the patient cannot sense an applicator stick applied to the posterior oropharynx, on one or both sides; for *abnormal gag reflex*, the gag reflex is diminished, absent, hyperactive, or asymmetrical; for *water swallow test*, drinking 5 to 90 mL of water in 5-mL to 10-mL sips causes coughing, choking, or alteration of the voice; for *oxygen desaturation after swallowing*, oxygen saturation decreases ≥2% 0 to 2 minutes after swallowing 10 mL of water[42] or 20 mL[50] to 150 mL[49] of liquid barium.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. NS, not significant.

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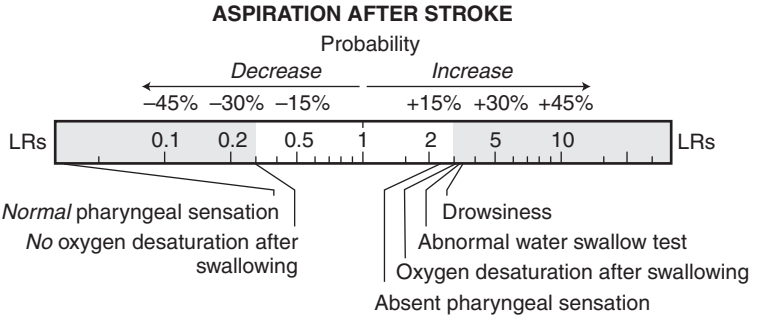


muscle.*[53] Therefore, in a hemispheric stroke, the patient may demonstrate weakness when turning the head toward the hemiparetic side.[54] In a focal seizure, the head often deviates toward the seizing limbs.

B. BRAINSTEM OR HIGH CERVICAL SPINAL CORD

Lesions of the accessory nucleus, located in the medulla and high cervical spinal cord, may cause atrophy and weakness of the *ipsilateral* trapezius and sternocleidomastoid muscles (e.g., **syringomyelia**).

C. PERIPHERAL NERVE

Injuries to the peripheral nerve, which occur from trauma to the posterior triangle of the neck (e.g., surgical excision of lymph nodes, blunt trauma), may paralyze the *ipsilateral* trapezius or sternocleidomastoid muscle, although the sternocleidomastoid muscle is often spared because its branches diverge early from the main trunk of the nerve.[55] The **jugular foramen syndrome,** discussed above under the glossopharyngeal nerve, also affects cranial nerve XI, along with cranial nerves IX and X.

HYPOGLOSSAL NERVE (XII)

I. FINDING

During protrusion of the tongue, each genioglossus muscle acts to push the tongue out and toward the opposite side. Normally, these laterally directed forces balance each other and the tongue remains in the midline. With unilateral hypoglossal weakness, however, the intact genioglossus muscle acts to deviate the tongue toward the opposite, or weak, side.

*Descending corticobulbar fibers to the sternocleidomastoid muscle are believed to cross twice to innervate the ipsilateral side. This innervation makes teleologic sense because the sternocleidomastoid muscle turns the head to the opposite side and the cerebral hemisphere is interested in turning the head to the same side for which it controls visual fields, eye movements, and motor function.[53]

II. CLINICAL SIGNIFICANCE

Weakness of the genioglossus muscle may represent disease in the cerebral hemisphere, brainstem, or peripheral nerve. Atrophy or fasciculations of the tongue indicate the lesion is in either the hypoglossal nucleus (brainstem) or the hypoglossal nerve (i.e., *not* cerebral hemispheres).

A. CEREBRAL HEMISPHERE

Lesions of the cerebral hemisphere may cause weakness of the contralateral genioglossus muscle. Therefore, the tongue deviates *toward* the side of the weak arm and leg.[56]

B. BRAINSTEM

The medial medullary syndrome causes ipsilateral hypoglossal paralysis, contralateral hemiparesis, and contralateral loss of proprioceptive and vibratory sensation (preserving pain and temperature sensation). Therefore, the tongue deviates *away* from the side of the weak arm and leg.

C. PERIPHERAL NERVE

The most common causes of lesions of the hypoglossal nerve are metastatic cancer (to the base of the skull, subarachnoid space, or neck) and trauma (e.g., gunshot wounds to the neck, radical neck surgery, carotid endarterectomy).[57]

Hypoglossal palsy in association with other cranial nerve findings occurs with both brainstem and peripheral nerve disorders and therefore has little localizing value.[57]

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 59

Examination of the Motor System: Approach to Weakness

THE MOTOR EXAMINATION

Examination of the muscles includes inspection (for atrophy, hypertrophy, fasciculations, and tremor), percussion (for myotonia), palpation (for abnormal tone), full flexion and extension of the elbows and knees (for abnormal tone and nonneurologic restrictions to movement, such as contractures or joint disease), and tests of muscle strength.

I. MUSCLE STRENGTH

A. DEFINITIONS

Paralysis refers to loss of power of any degree, from mild weakness to complete loss. The suffixes **plegia** and **paresis** also indicate paralysis (e.g., hemiplegia), although paresis is usually used to indicate incomplete paralysis. **Tetraparesis** indicates weakness of all four limbs. (Specialists in spinal cord disorders prefer this term over *quadriparesis*.) **Paraparesis** indicates weakness of both legs; **hemiparesis**, weakness of an arm and a leg on one side of the body; and **monoparesis**, weakness of just one arm or leg.

B. THE FINDINGS

1. Technique

The clinician tests single muscles at a time by asking the patient to contract the muscle strongly while the clinician tries to resist any movement. Unilateral weakness is recognized by comparing the muscle to its companion on the opposite side; bilateral weakness, by comparing the strength to some standard recalled from clinical experience. The clinician grades the muscle's strength according to a six-point system (0 through 5), as described later. (See the section on Grading Muscle Strength.)

In patients with weakness, the clinician should systematically test all the muscles from head to foot, paying particular attention to which muscles are weak, whether proximal and distal muscles of a limb differ in strength, and whether the weakness of a monoparetic limb involves only muscles from a single spinal segment or peripheral nerve (see Chapter 62). An excellent,

TABLE 59-1 Grading Muscle Strength

Grade	Finding
0	No contraction
1	Flicker or trace of contraction
2	Active movement with gravity eliminated
3	Active movement against gravity
4	Active movement against gravity and resistance
5	Normal power

From reference 1.

inexpensive handbook describes the proper technique for testing all of the important muscles of the arms and legs.[1]

Testing muscles by resisting their action, however, tends to overlook significant weakness at the hips and knees, where powerful antigravity muscles can easily overcome the physician's resistance even when significant weakness is present.[2] A better way to test these muscles is to use the patient's own body weight as the load the muscle must lift. For example, quadriceps weakness is more apparent by asking the patient to arise from a chair on the symptomatic leg than by manually resisting the patient's attempt to extend the knee.[3] Another method measures the time required by the patient to rise up from a chair and sit down 10 times. Patients without weakness accomplish this in 20 to 25 seconds (<20 seconds if 50 years old and <25 seconds if 75 years old). If patients require more time, proximal weakness of the legs is present unless an alternative explanation is present, such as joint or bone disease.[4]

2. Grading Muscle Strength

Muscle strength is graded using a conventional scale developed by the British Medical Research Council (MRC) during World War II (Table 59-1).[1] This scale, which is used universally, has one important drawback: It assigns a disproportionate amount of a muscle's power to grade 4 strength. For example, the biceps muscle uses just 2% of its full power to overcome gravity (i.e., grade 3 strength), meaning that almost 98% of the remaining range of power is grade 4.[5] Because of this drawback, many neurologists subdivide grade 4 into three grades: 4 minus (i.e., moves barely against resistance), 4, and 4 plus (i.e., almost full power).

3. Special Tests for Unilateral Cerebral Lesions

In patients with cerebral lesions, measures of muscle power alone often underestimate the size of the lesion and the patient's functional disability. Special tests have been developed as more sensitive tests of motor function in these patients: the upper limb drift test (pronator drift), the forearm rolling test (and its variants, the index finger test and little finger test),[6] and the rapid finger tapping and foot tapping tests (Fig. 59-1).

C. CLINICAL SIGNIFICANCE

See the section on Approach to Weakness, later.

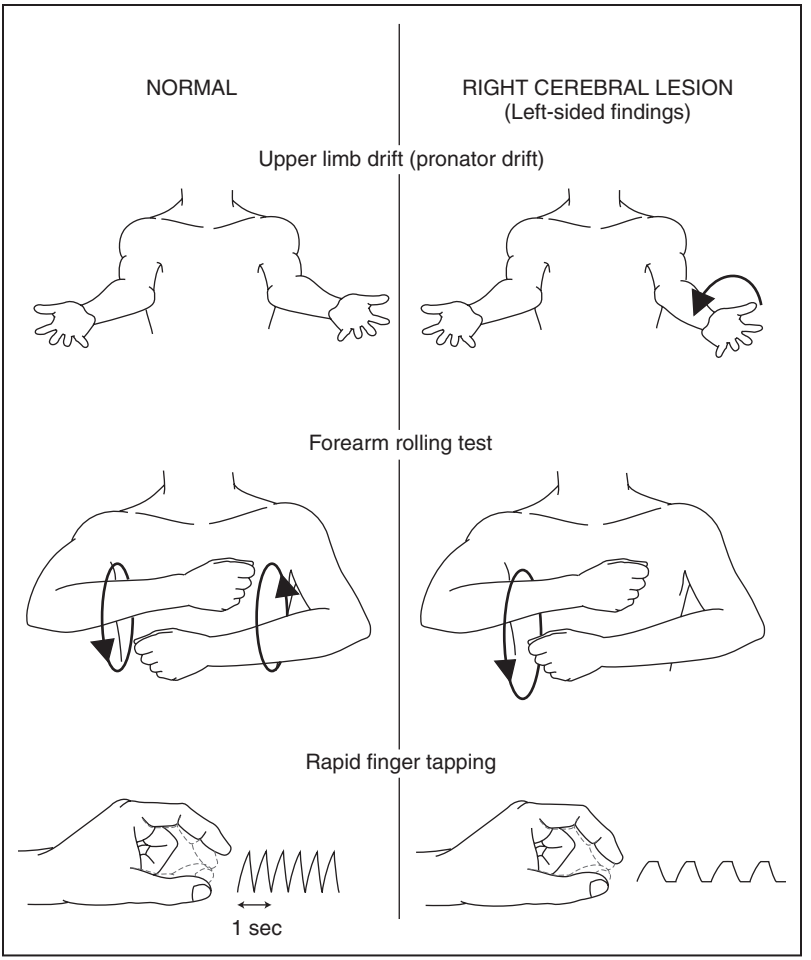


FIGURE 59-1 Special tests for unilateral cerebral lesions. The depicted patient has a right cerebral lesion with left-sided findings during three different tests: **1. Upper limb drift test** (**pronator drift,** *top row).* The patient stretches out both arms directly in front of him or her with palms upright (i.e., forearms supinated) and closes his or her eyes. This position is held for 45 seconds.[7] The arm contralateral to the hemispheric lesion drifts downward and pronates. **2. Forearm rolling test** *(middle row).*[6] The patient bends each elbow and places both forearms parallel to each other. He or she then rotates the forearms about each other in a rapid rolling motion for 5 to 10 seconds in each direction. In the abnormal response, the forearm contralateral to the lesion is held still while the other arm "orbits" around it. **3. Rapid finger tapping test** *(bottom row).* The patient rapidly taps the thumb and index finger repeatedly at a speed of about two taps per second. In normal persons, the movement has an even rhythm and large amplitude. Hemispheric lesions cause the contralateral finger and thumb to tap more slowly and with diminished amplitude, as if the finger and thumb are sticking together.[7] The index finger rolling test and little finger rolling test are similar to the forearm rolling test. (Each index finger or little finger is rotated about the other for 5 seconds in both directions.) In the foot tapping test, the seated patient taps one forefoot at a time for 10 seconds on the floor, as fast as possible, while the heel maintains contact with the floor. A discrepancy of more than five taps between the left and right foot indicates cerebral disease contralateral to the slower foot.[8]

II. ATROPHY AND HYPERTROPHY

A. ATROPHY

1. Definition

Atrophy describes muscles that are emaciated or wasted.

2. Technique

Atrophy is detected during inspection of the muscle. Examples are as follows:

1. An abnormally flat thenar eminence, when viewed from the side (e.g., cervical radiculopathy or carpal tunnel syndrome)
2. Missing shadows on the anterior neck from atrophic sternocleidomastoid muscles (e.g., syringomyelia)
3. Metacarpal bones appearing unusually prominent on the back of the hand, from atrophic intrinsic muscles (e.g., polyneuropathy)

Significant asymmetry of the circumference of the arms or legs indicates atrophy of the smaller side (or edema of the other side). In normal persons, the difference in calf circumference between the right and left sides is less than 1 cm in 90% and less than 1.5 cm in 100% (measured 10 cm below the tibial tuberosity).[9]

3. Clinical Significance

Atrophy is a feature of lower motor neuron disease* or muscle disuse (especially from adjacent joint disease or trauma). In patients with sciatica, the finding of ipsilateral calf wasting (i.e., maximum circumference at least 1 cm less than the contralateral side) accurately indicates lumbosacral nerve compression from disc herniation (likelihood ratio [LR] = 5.2. see Chapter 62).

B. HYPERTROPHY

Hypertrophy describes abnormal enlargement of a muscle. Bilateral calf hypertrophy is a typical feature of some muscular dystrophies, although it is found in a wide variety of neuromuscular diseases.[11]

III. FASCICULATIONS

A. DEFINITION

Fasciculations are involuntary rapid muscle twitches that are too weak to move a limb but are easily felt by patients and seen or palpated by clinicians.[12] Most healthy people experience fasciculations at some time, especially in the eyelid muscles.

*In the evaluation of weakness, a fundamental distinction is the separation of upper motor neuron lesions (i.e., located in the cerebral cortex, brainstem, or descending motor pathways of the spinal cord) from lower motor neuron lesions (i.e., located in the peripheral nerves and anterior horn cells of the spinal cord). William Gowers first distinguished the upper and lower motor segments in his 1888 work *Manual of Diseases of the Nervous System*.[10] See Figure 59-2 and the section on Approach to Weakness later in this chapter.

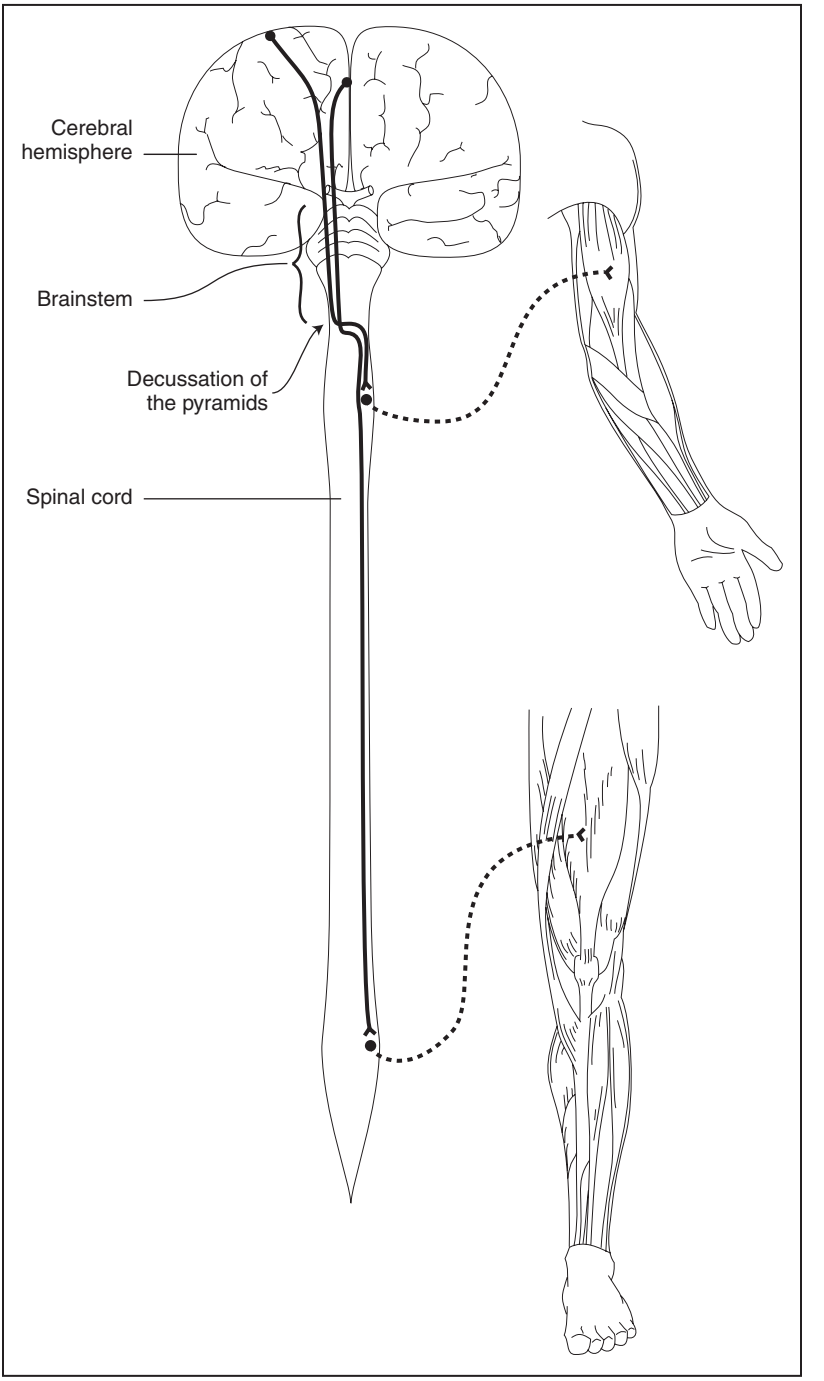

Cerebral hemisphere
Brainstem
Decussation of the pyramids
Spinal cord

FIGURE 59-2 Anatomy of upper motor and lower motor neurons. The figure illustrates the entire pathway of nerves responsible for movement, from cerebral cortex to muscle. *Upper motor neurons (solid line)* extend from the cerebral cortex through the brainstem to the spinal cord. *Lower motor neurons (dotted line)* originate in the spinal cord and travel to muscles within peripheral nerves. Because the upper motor neurons cross to the contralateral side at the border between the brainstem and the spinal cord (decussation of the pyramids), weakness of the upper motor neuron type may result from lesions in the *ipsilateral* spinal cord, *contralateral* brainstem, or *contralateral* cerebral hemisphere. Lesions of the spinal cord, where both upper and lower motor neurons reside, may cause weakness of both types: of the *lower motor neuron* type *at* the level of the lesion and of the *upper motor neuron* type in muscles whose peripheral nerves originate *below* the level of the lesion.

B. CLINICAL SIGNIFICANCE

Isolated fasciculations without other neurologic findings are benign.[13] When accompanied by weakness or atrophy, however, fasciculations indicate lower motor neuron disease, usually of the anterior horn cell or proximal peripheral nerve. Tongue fasciculations occur in up to one-third of patients with amyotrophic lateral sclerosis.[14] (See the section on Approach to Weakness, later.)

IV. MUSCLE TONE

Muscle tone refers to the involuntary muscle tension perceived by clinicians repeatedly flexing and extending one of the patient's limbs. Assessing muscle tone assumes that the patient is relaxed and that there are no bone or joint limitations to movement. Muscle tone may be increased (e.g., in spasticity, rigidity, or paratonia) or diminished (e.g., in flaccidity).

A. INCREASED MUSCLE TONE

1. Spasticity

a. Definition

Spasticity is increased muscle tone that develops in patients with upper motor neuron lesions.[15] The increased muscle tone of spasticity has three characteristics.

1. **Velocity-dependence.** The amount of muscle tone depends on the velocity of movement: The more rapid the movement, the greater the resistance; the slower the movement, the less the resistance.
2. **Flexor and extensor tones differ.** The tone in the flexors and extensors of a limb is not balanced, which commonly causes characteristic resting postures of that limb (see later).
3. **Associated weakness.** The muscle with spasticity is also weak. If left untreated, muscles shortened by spasticity may eventually develop fixed contractures.

b. Characteristic Postures

In spasticity, an imbalance in flexor and extensor tone commonly causes abnormal postures of the resting limb. In hemiplegia, for example, there is excess tone in the *flexors* of the arms and *extensors* of the legs, which

causes the arm and hand to be fixed against the chest, flexed and internally rotated, and the leg to extend with the foot pointed (see Fig. 6-4 in Chapter 6).[16] In contrast, some patients with complete spinal cord lesions have excess tone in the *flexors* of the legs, which causes the legs to flex up onto the abdomen **(paraplegia-in-flexion).***[17]

c. Clasp-Knife Phenomenon

Up to half of patients with spasticity have the **clasp-knife phenomenon,** a finding usually observed in the knee extensors and less often in the elbow flexors.[16,18] To elicit this phenomenon, the clinician extends the patient's knee using a constant velocity, but as the patient's knee nears full extension, the muscle tone of the quadriceps muscles increases dramatically and completes the movement, just as the blade of a pocket knife opens under the influence of its spring.[10] The clasp-knife phenomenon occurs because muscle tone is dependent on the muscle's length, the tone diminishing with stretching and increasing with shortening.

d. Relationship of Spasticity to Weakness

Although spasticity is a sign of upper motor neuron disease, its severity correlates poorly with the degree of weakness or hyperreflexia. Patients with slowly developing cerebral hemisphere lesions usually develop spasticity and weakness in concert.[19] Patients with strokes or spinal cord injury, in contrast, develop immediate weakness and flaccidity, spasticity appearing only days to weeks later.[16] Some elderly patients with large strokes have persistent **flaccid hemiplegia,** in which the paralyzed muscles never develop increased muscle tone despite being hyperreflexic.[19]

2. Rigidity

a. Definition

Rigidity is increased muscle tension with three characteristic features.

1. **No velocity-dependence.** The resistance to movement is the same with slow and rapid movements.
2. **Flexor and extensor tones are the same**.
3. **No associated weakness.** Patients with rigidity lack the clasp-knife phenomenon.[15]

Cogwheel rigidity refers to rigidity that gives way intermittently as if the patient's limb were the lever pulling over a ratchet.

*These hemiplegic and paraplegic postures recall the neurologic development of normal infants. Paraplegia-in-flexion resembles the initial posture of babies, their legs flexed against their chest. The infant eventually is able to extend the leg and stand (resembling the extensor tone of hemiplegia) after descending pathways from the brainstem mature enough to overcome the spinal reflexes responsible for the flexed position. The infant eventually walks after cerebral connections are mature enough to provide fine motor control. Damage to the cerebral hemispheres (e.g., stroke) disrupts this fine motor control and uncovers the extensor posture; damage to the spinal cord (e.g., severe multiple sclerosis or complete spinal cord transection) removes all supraspinal input, uncovering the original flexed posture of the legs.[15]

b. Distinguishing Spasticity from Rigidity

Most clinicians distinguish spasticity from rigidity by repeatedly extending and flexing the patient's limbs and observing the characteristics already noted. In the 1950s, Wartenberg* introduced a simple bedside test to assess motor tone and to distinguish spasticity from rigidity.[20,21] In this test, the patient is seated on the edge of the examining table, which is open underneath to allow the legs to swing unobstructed back and forth. The clinician lifts both feet to extend the knees, instructs the patient to relax, and then releases the legs. The normal lower limb swings back and forth six or seven times, smoothly and regularly in a perfect sagittal plane. In patients with spasticity, the limbs drop with normal velocity but their movements are jerky and fall out of the sagittal plane, the great toe tracing zigzags or ellipses. In patients with rigidity, the swinging time and velocity are significantly reduced, resulting in a total of only one or two swings. Others have confirmed Wartenberg's findings.[22]

c. Clinical Significance

Rigidity is a common finding of extrapyramidal disease, the most common example of which is Parkinson disease (see Chapter 64).

3. Paratonia

a. Definition

Paratonia is excess muscle tension that is *not present at rest* but develops when the patient's limb *contacts* another object, as if such contact makes the patient unable to relax. There are two forms: **oppositional paratonia (gegenhalten)** and **facilitatory paratonia (mitgehen).** In patients with oppositional paratonia, the clinician feels a stiffening of the limb with every applied movement, but unlike in rigidity, the stiffening depends entirely on contact and its force is proportional and opposite to the examiner's movements. Patients with facilitatory paratonia, in contrast, actively aid movements guided by the examiner.

b. Technique

One simple test of facilitatory paratonia is to take the arm of the seated patient and bend the elbow back and forth three times, from full flexion to 90 degrees of extension. The clinician then releases the arm at the patient's lap and scores any further movement, 0 being no movement, 4 full flexion or more, and 1 to 3 intermediate movements.[23]

c. Clinical Significance

Both oppositional and facilitatory paratonias are associated with extensive frontal lobe disease and often appear in dementing illnesses.[23] Among patients with dementia, the severity of oppositional or facilitatory paratonia (including the score for the paratonia test described in the previous section) correlates inversely with the Folstein Mini-Mental Status Examination score ($r = -0.5$ to -0.7, $p < .05$).[23]

*Robert Wartenberg, who wrote many popular neurology textbooks in the 1950s, was an ardent opponent of eponyms and called his test the "test for pendulousness of the legs."

B. DECREASED MUSCLE TONE: HYPOTONIA (FLACCIDITY)

1. Definition

Hypotonia refers to reduced or absent muscle tension.

2. Technique

There are many ways to detect the flaccid muscle: The limb feels like a "rag doll," the muscles feel soft and flabby, the outstretched arm when tapped demonstrates wider than normal excursions, or the knee jerks are abnormally pendular. The original definition of abnormally pendular knee jerks—more than three back-and-forth swings of the patient's leg during testing of the knee jerk—should be revised, however, because many normal individuals have this finding.[24]

3. Clinical Significance

Hypotonia is a feature of lower motor neuron disease and cerebellar disease.

4. Pathogenesis

There is some evidence that "normal" muscle tone actually consists of tiny muscle contractions that assist the clinician in moving the extremity (even though the patient is trying to relax).[25] Clinicians perceive reduced muscle tension in hypotonic limbs because these contractions are absent.

V. MUSCLE PERCUSSION

Striking the muscle with a reflex hammer may elicit two abnormal findings, percussion myotonia and myoedema.

A. PERCUSSION MYOTONIA

1. The Finding

Percussion myotonia is a prolonged muscle contraction that lasts several seconds and causes a sustained dimple to appear on the skin. Percussion myotonia of the thenar eminence may actually draw the thumb into sustained opposition with the fingers.

2. Clinical Significance

Percussion myotonia is a feature of some myotonic syndromes, such as myotonia congenita and myotonic dystrophy.[26]

B. MYOEDEMA

1. The Finding

Myoedema is a focal mounding of muscle lasting seconds at the point of percussion. Unlike myotonia, myoedema causes a lump instead of a dimple, and the lump may be oriented crosswise or diagonal to the direction of muscle fibers.[27]

Graves and Stokes originally described myoedema in 1830.

2. Clinical Significance

Myoedema is a normal physiologic response and does not indicate disease.[28] Its historical association with undernourished patients simply reflects the ease with which the response appears when there is no intervening subcutaneous fat.[27,28]

APPROACH TO WEAKNESS

I. CAUSE OF WEAKNESS

Neuromuscular weakness has four principal causes.

1. Upper motor neuron disease ("pyramidal tract disease" or "central weakness")
2. Lower motor neuron disease ("denervation disease" or "peripheral weakness")
3. Neuromuscular junction disorders
4. Muscle disease

Each disorder is associated with distinct physical signs (Table 59-2), neuroanatomy (see Fig. 59-2), and causes (Table 59-3).

Most patients with weakness have lesions of the upper and lower motor neurons. Clinicians should consider muscle disease in any patient with *symmetrical* weakness of the *proximal* muscles of the arms and legs (sometimes associated with muscle pain, dysphagia, and weakness of the neck muscles). Disorders of the neuromuscular junction should be considered in patients in whom weakness *varies* during the day or in whom *ptosis* or

TABLE 59-2 Differential Diagnosis of Weakness*

	Motor Examination				
Location of Lesion	**Muscle Tone**	**Atrophy or Fasciculations?**	**Sensory Findings**	**Muscle Stretch Reflexes**	**Other Findings**
Upper motor neuron	Spasticity	No	Sometimes	Increased	Babinski sign
Lower motor neuron	Hypotonia	Yes	Usually†	Decreased/absent	
Neuromuscular junction	Normal or hypotonia	No	No	Normal/decreased	Ptosis, diplopia
Muscle	Normal	No‡	No	Normal/decreased	Myotonia

*These characteristics are *specific* but not *sensitive*, and thus are helpful when *present*, not when absent. See text.

†Sensory findings are in the distribution of the spinal segment, plexus, or peripheral nerve. See Chapter 62.

‡Atrophy may be a late finding.

TABLE 59-3 Common Etiologies of Neuromuscular Weakness

Location of Lesion	Common Etiology
Upper motor neuron	Cerebrovascular disease Multiple sclerosis Brain tumor
Lower motor neuron	Polyneuropathy (diabetes, alcoholism) Entrapment neuropathy Trauma
Neuromuscular junction	Myasthenia gravis
Muscle	Drug-induced myopathy Thyroid disease Polymyositis

diplopia is present. Associated abnormalities of sensation, tone, or reflexes of the weak limb exclude muscle or neuromuscular junction disease and indicate instead upper or lower motor neuron lesions.

II. THE FINDINGS

A. UPPER VERSUS LOWER MOTOR NEURON LESIONS

Both upper motor neuron weakness and lower motor neuron weakness tend to affect *distal* muscles in either a symmetrical or an asymmetrical pattern. The bedside findings that distinguish these two disorders are other neurologic findings in the weak limb, certain localizing signs of upper motor neuron disease, the Babinski sign, and the type of weakness produced.

1. Associated Findings in the Weak Limb (see Table 59-2)

Spasticity and hyperreflexia indicate central weakness; hypotonia, atrophy, fasciculations, and absent muscle stretch reflexes indicate peripheral weakness. In patients with central weakness, sensory abnormalities vary from the isolated loss of cortical sensations in the distal limb to dense loss of all sensation throughout the limb; if sensory abnormalities occur in peripheral weakness, they follow the distribution of spinal segments or peripheral nerves (see Chapter 62).

2. Localizing Signs of Upper Motor Neuron Weakness

The upper motor neuron pathway extends from the cerebral cortex down through the spinal cord (see Fig. 59-2), traveling in tight quarters with central neurons innervating other structures. Consequently, in addition to producing central weakness, lesions along this pathway cause characteristic additional physical signs (Table 59-4) that confirm that the weakness is of the central type and pinpoint its location.

3. Babinski Sign

The **Babinski sign** (see Chapter 61) indicates central weakness. In the positive response, the great toe moves upward after a scratching stimulus to the sole of the patient's foot.

TABLE 59-4 Localizing Signs in Upper Motor Neuron Weakness

Anatomic Location	Associated Finding
Cerebral hemisphere	Seizures Hemianopia Aphasia (right hemiparesis) Inattention to left body, apraxia (left hemiparesis) Cortical sensory loss* Hyperactive jaw jerk
Brainstem	Crossed motor findings† Contralateral third nerve palsy (midbrain) Contralateral sixth nerve palsy (pons) Sensory loss on contralateral face*
Spinal cord	Sensory level* Pain and temperature sensory loss on contralateral arm and leg* No sensory or motor findings in face Additional lower motor neuron findings (atrophy, fasciculations)

*Chapter 60 describes the different sensory syndromes.
†Crossed motor findings refers to unilateral cranial nerve palsy opposite the side of weakness.

4. Distribution of Weakness

a. Limbs Affected

The findings of monoparesis, paraparesis, and tetraparesis are, by themselves, unhelpful because they may occur in either central or peripheral weakness. Only hemiparesis is specific, indicating a central lesion.

b. Movement versus Muscle

Central lesions paralyze *movements*; peripheral lesions paralyze *muscles*. This occurs because neurons from a single area of the cerebral cortex connect with many different spinal cord segments and muscles to accomplish a particular movement. A single muscle has many movements and thus receives information from many different upper segments, all of which converge on the single peripheral nerve traveling to the muscle. A lesion in that nerve, therefore, obliterates a muscle's entire repertoire of movement; a lesion in an upper segment eliminates only one of many possible movements.[21]

One example of this is the contrast between peripheral facial weakness **(Bell palsy),** which paralyzes all ipsilateral facial movements, and central facial weakness (e.g., strokes), which paralyzes voluntary movements but spares emotional ones (e.g., during laughing or crying; see Chapter 58).[29] Another example is the contrast between the peripheral paraparesis of Guillain-Barré syndrome, which paralyzes all leg movements, and the central paraparesis of spinal cord injury, which eliminates volitional movements of the legs but allows the powerful flexor spasms induced by a mild scratching of the patient's foot.[17]

B. THE DIAGNOSTIC PROCESS

1. Upper Motor Neuron Weakness

In patients with upper motor neuron weakness, associated neurologic findings indicate the *level* of the lesion (see Table 59-4); the distribution of weakness indicates the *side* of the lesion. For example, bilateral weakness

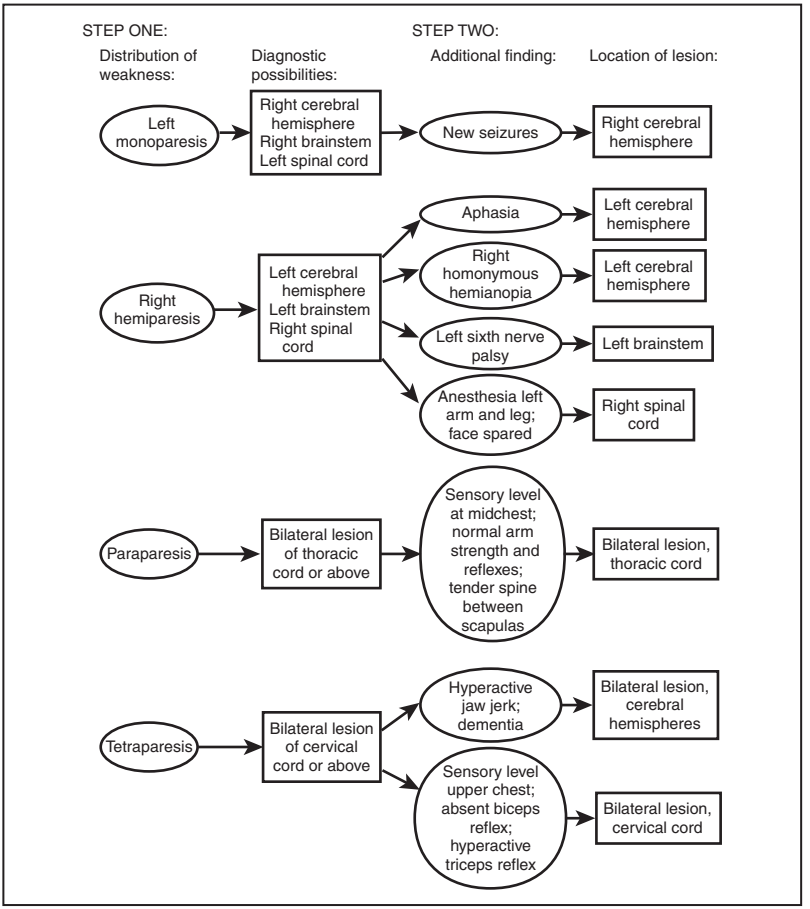


FIGURE 59-3 Diagnostic approach to upper motor neuron weakness. The figure illustrates the sequential steps in identifying the location of an upper motor neuron lesion. See text.

(paraparesis or tetraparesis) indicates *bilateral* lesions (in the thoracic cord or higher if paraparesis, and in the cervical cord or higher if tetraparesis). Monoparesis or hemiparesis indicates a *unilateral* lesion, either in the *contralateral* cerebral hemisphere or brainstem or in the *ipsilateral* spinal cord.*

Figure 59-3 illustrates this diagnostic process in the analysis of central weakness. In the first column is the distribution of central weakness for hypothetical patients, which narrows the diagnostic possibilities to a smaller region of the central motor pathway (second column). The associated findings (third column) identify the level of the lesion within that region, thus pinpointing the lesion's location (fourth column).

*It is the contralateral cerebral hemisphere and brainstem because the descending central motor pathways originate in the contralateral hemisphere, but it is the ipsilateral spinal cord because these pathways cross just below the brainstem (see Fig. 59-2).

TABLE 59-5 Segmental Innervation of Muscles*

Spinal Level	Muscles
ARM	
C5	Elbow flexors (biceps, brachialis)
C6	Wrist extensors (extensor carpi radialis longus and brevis)
C7	Elbow extensors (triceps)
C8	Finger flexors (flexor digitorum profundus of middle finger)
T1	Small finger abductors (abductor digiti minimi)
LEG	
L2	Hip flexors (iliopsoas)
L3	Knee extensors (quadriceps)
L4	Ankle dorsiflexors (tibialis anterior)
L5	Long toe extensors (extensor hallucis longus)
S1	Ankle plantar flexors (gastrocnemius, soleus)

*Most muscles are innervated by nerves from more than one spinal root. This table, based on reference 31, simplifies this innervation to standardize the description of spinal cord injury. A more thorough description of segmental innervation of muscle appears in Figures 62-1 and 62-6 of Chapter 62.

2. Lower Motor Neuron Weakness

In patients with monoparesis of the lower motor neuron type, the clinician should determine whether the muscles affected are supplied by a single spinal segment **(radiculopathy)** or a peripheral nerve **(peripheral neuropathy),** or a combination of the two **(plexopathy).** Further evaluation of these patients is discussed in Chapter 62.

In lower motor neuron weakness, the lesion is always *ipsilateral* to the side of the weakness.

3. Combined Upper and Lower Motor Neuron Weakness

Combined upper and lower motor neuron findings indicate disease in the spinal cord, the only anatomic location where both segments reside. Common causes are myelopathy and amyotrophic lateral sclerosis.

a. Myelopathy

Myelopathy is a term describing a spinal cord lesion confined to a discrete level (e.g., trauma, tumor, disc disease). The lesion causes motor, sensory, and reflex abnormalities *at* the level of the lesion and *below* it. The weakness is of the peripheral type *at* the level of the lesion (from damage to anterior horn cells and spinal roots),* and of the central type *below* the level of the lesion (from damage to the descending upper motor neuron paths).

Identifying the level of the lesion requires knowledge of which spinal segments innervate which muscle. Table 59-5 presents the standardized segmental innervation used internationally by spinal cord specialists.

*Exceptions to this are lesions at the foramen magnum and C3 to C4 level, which sometimes produce atrophy in the hands.[30]

(Chapter 62 discusses the derivation of this table.) For example, in a patient with a lesion involving the C7 segment of the spinal cord, there is peripheral weakness in the C7 muscles (i.e., atrophy and weakness of the elbow extensors) but central weakness of all the muscles below this level (hyperreflexia and increased tone of the hands, legs, and feet and a positive Babinski sign). The muscles from segments above C7, the biceps and wrist extensors, are normal.*

b. Amyotrophic Lateral Sclerosis

Amyotrophic lateral sclerosis is a degenerative disorder of descending motor tracts and motor nuclei of the spinal cord. The disorder causes both lower motor neuron findings (atrophy, fasciculations) and upper motor neuron findings (hyperreflexia). About half of patients have a Babinski response.[14] The disease may start in the arms (44%), legs (37%), or bulbar muscles (causing tongue fasciculations, change in voice, and difficulty swallowing, 19%).[14] There are no sensory findings.

Amyotrophic lateral sclerosis and cervical myelopathy are commonly confused at the bedside, even by experienced neurologists.[32] In patients with both upper and lower motor neuron signs, findings that increase the probability of amyotrophic lateral sclerosis include the following:

1. Prominent fasciculations
2. Absence of sensory findings
3. Signs of lower motor neuron degeneration affecting more than one level of the spinal cord simultaneously†[33,34]

III. CLINICAL SIGNIFICANCE

The clinical significance of the motor examination cannot be tested in the conventional manner of this book, because bedside criteria alone are sufficient to diagnose many causes of weakness (e.g., cerebrovascular disease, amyotrophic lateral sclerosis, and peripheral nerve injuries are routinely diagnosed by bedside criteria; see Chapter 1).

Nonetheless, several investigations allow a few conclusions.

A. CLINICAL SYNDROMES ARE OFTEN INCOMPLETE

Most studies show that the full lower motor or upper motor neuron syndromes, as depicted in Table 59-2, are often incomplete. In upper motor neuron weakness, up to 25% of patients lack exaggerated reflexes[35,36] and the absence of spasticity is common, especially in acute lesions (see earlier discussion). Similarly, in many examples of lower motor weakness, the nerve affected does not even innervate a clinical reflex (e.g., median or ulnar neuropathy) and the reflexes of the limbs are thus preserved.

*By convention, the neurologic level in spinal cord injury refers to the most caudal level with *normal* function, rather than the first level with abnormal function.[31] The motor level for this hypothetical patient is therefore C6.

†The four spinal cord "levels" are bulbar (jaw, face, tongue, larynx), cervical (neck, arm, hand, diaphragm), thoracic (back, abdomen), and lumbosacral (back, abdomen, leg, and foot).

Therefore, in the evaluation of weak patients, the *absence* of spasticity or hyperreflexia does *not* argue against the presence of upper motor neuron disease nor does the *absence* of hypotonicity or hyporeflexia argue against the presence of lower motor neuron disease.

On the other hand, the *presence* of abnormal reflexes is very helpful: In one study of patients with weakness, 87% had abnormal reflexes and in every case, areflexia correctly predicted lower motor neuron disease and hyperreflexia correctly predicted upper motor neuron disease.[36]

The fact that syndromes are often incomplete emphasizes the importance of the complete neurologic examination. For example, in a patient with weakness of the fingertips, in whom the absence of sensory or reflex changes prevents classifying the weakness as peripheral or central using the criteria of Table 59-2, the discovery of any additional neurologic finding from Table 59-4 indicates that the lesion is central and pinpoints its location precisely.

B. PROXIMAL WEAKNESS INDICATES MUSCLE DISEASE

If *proximal weakness* is defined as the strength of a limb's proximal muscles being one MRC grade less than that of the distal muscles, proximal weakness appears in 92% of patients with muscle disease.[36] The *absence* of proximal weakness, therefore, decreases the probability of muscle disease.

C. FOR CEREBRAL HEMISPHERIC LESIONS, THE SPECIAL TESTS ARE VERY SENSITIVE

EBM Box 59-1 presents the diagnostic accuracy of various physical signs for detecting unilateral cerebral hemispheric lesions in patients undergoing computed tomography or magnetic resonance imaging of the head. Most of the patients in these studies lacked motor weakness by conventional power testing, and the neuroimaging was performed to assess headaches, seizures, or other neurologic symptoms. In these patients, the findings that increase the probability of *contralateral* cerebral hemispheric lesions the most are a positive forearm rolling test (LR = 15.6), pronator drift (LR = 9.6), Babinski response (LR = 8.5), index finger rolling test (LR = 6), hyperreflexia (LR = 5.3), positive finger tapping test (LR = 4.7), and hemianopia (LR = 4.3). The *absence* of pronator drift (LR = 0.3) diminishes the probability of contralateral cerebral disease.

D. DIAGNOSIS OF PERIPHERAL NERVE DISORDERS

Chapter 62 discusses the clinical significance of muscle weakness and its localizing value to the diagnosis of peripheral nerve disorders.

The references for this chapter can be found on www.expertconsult.com.

EBM BOX 59-1
*Unilateral Cerebral Hemispheric Disease**

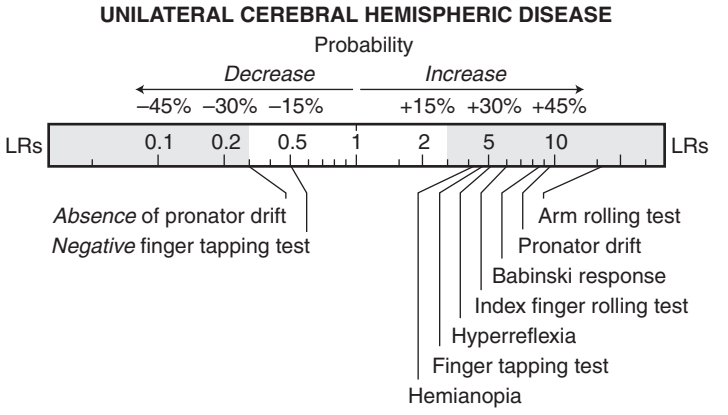
Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Cranial Nerves				
Hemianopia[6,37]	22-30	93-98	**4.3**	0.8
Motor Examination				
Pronator drift[6–8,37]	22-91	90-98	**9.6**	**0.3**
Arm rolling test[6–8,37]	17-87	97-98	**15.6**	0.6
Index finger rolling test[8,37]	33-42	92-98	**6.0**	0.7
Little finger rolling test[8]	7	95	NS	NS
Finger tapping test[6,7]	16-79	88-98	**4.7**	0.5
Foot tapping test[8,37]	11-23	89-93	NS	NS
Sensory Examination				
Hemisensory disturbance[6]	29	98	NS	0.7
Reflex Examination				
Hyperreflexia[7,37]	11-69	88-95	**5.3**	NS
Babinski response[6,8]	9-45	98	**8.5**	NS

*Diagnostic standard: for *unilateral cerebral hemispheric disease*, magnetic resonance imaging or computed tomography.

†Definition of findings: for *arm rolling test*, *pronator drift*, and *finger tapping test*, see Figure 59-1.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. NS, not significant.

Click here to access calculator.



CHAPTER 60

Examination of the Sensory System

SIMPLE SENSATIONS

I. DEFINITIONS

There are four simple sensations: pain, temperature, touch, and vibration. These sensations are all called *simple* because their perception does not require a healthy contralateral cerebral cortex. Excepting the sense of vibration, the simple sensations have distinct sensory organs in the skin and, excepting touch, their pathways in the spinal cord are well defined.

Hypesthesia refers to diminished ability to perceive a simple sensation; **anesthesia** refers to the complete inability to perceive a simple sensation. Although both hypesthesia and anesthesia originally referred only to the sensation of touch, many clinicians use the terms when reporting any of the simple sensations. **Hypalgesia** means there is a decreased sensitivity to painful stimuli; **analgesia**, a complete insensitivity. **Hyperpathia**, **hyperesthesia**, and **allodynia** all refer to an increased sensitivity to sensory stimuli, often with unpleasant qualities, although some experts restrict hyperpathia to increased sensitivity from *painful* stimuli and allodynia to discomfort from *tactile* stimuli.

II. TECHNIQUE

Deciding which sensory tests to include in the physical examination depends on the clinical setting. For screening examinations of patients without sensory complaints, testing only touch sensation on all four extremities should suffice. If there are sensory complaints confined to one limb, testing for touch and pain sensation is usually performed, although testing pain sensation has a better chance of detecting subtle radiculopathies and peripheral nerve disorders. (See the section on Dermatomes.[1,2]) For screening diabetic feet and limbs at risk for neuropathic ulcers and arthropathy, clinicians should use Semmes-Weinstein monofilaments (see Chapter 53). Finally, for any patient with sensory complaints involving large portions of a limb or the trunk, testing for all simple sensations is necessary to uncover **sensory dissociation** (i.e., perception of one modality

but not another), a finding suggesting spinal cord disease. (See the section on Sensory Syndromes.)

During sensory testing, the patient's perceptions are compared either with a known standard of normal sensation (e.g., Semmes-Weinstein monofilaments for tactile sensation and tuning fork tests for vibratory sensation), with the contralateral companion part of the patient's body, or with the clinician's own sense of what is normal, as gathered from previous experience.

A. TOUCH

The sensation of touch is usually tested qualitatively by stimulating the patient's skin lightly with a cotton wisp, a piece of tissue paper, or the clinician's finger, or quantitatively by using Semmes-Weinstein monofilaments (see Chapter 53).

B. PAIN AND TEMPERATURE

The usual techniques for testing pain sensation are a safety pin bent at right angles or the sharp edge of a broken wooden applicator stick, both of which must be discarded after use to prevent the transmission of infection.[3] It is no longer permissible to use the built-in pin of many reflex hammers or the traditional tailor's pinwheel, because of the risk of transmitting infection.

The traditional test for temperature sensation uses tubes of warm and cold water, although testing the patient's ability to distinguish the cold stem of the tuning fork from the warmer index finger is much simpler.[4]

C. VIBRATION

Vibratory sensation is tested with a tuning fork (usually, 128 Hz; less often, 256 Hz). There is no compelling reason for using one tuning fork over the other, except that standards have been developed for the 128-Hz fork. Humans are most sensitive to vibration frequencies of 200 to 300 Hz and have difficulty consistently detecting frequencies below 100 Hz.[5,6] Traditionally, the tuning fork is applied against bony prominences, although this is based on the mistaken belief that bones contain the "vibration receptors"; vibratory sensation is just as good, or even better, over soft tissues without underlying bone. (The clinician can easily demonstrate this by testing sensation on the abdominal wall.[7])

When a 128-Hz tuning fork is struck from a distance of 20 cm against the heel of the clinician's palm, a healthy 40-year-old person should perceive vibrations for at least 11 seconds when the stem of the fork is held against the lateral malleolus, and for at least 15 seconds when it is held against the ulnar styloid.[8] These values decrease 2 seconds for every decade of age greater than 40 years.

One disadvantage to vibratory testing is the conduction of the vibrating impulse away from the tuning fork, thus preventing precise definition of sensory boundaries in patients with peripheral nerve injuries.[7]

Rumpf introduced the tuning fork to bedside neurology in 1889.[9]

III. CLINICAL SIGNIFICANCE

A. TOUCH, PAIN, AND TEMPERATURE SENSATION

Abnormalities of simple sensations define all important clinical sensory syndromes: peripheral nerve injury, radiculopathy, spinal cord syndromes, lateral medullary infarction, and thalamic and cerebral hemispheric syndromes. (See the section on Sensory Syndromes.) No diagnostic test has proved superior to bedside examination. The finding of diminished pain sensation (to a safety pin) detects small nerve fiber loss on skin biopsies with a sensitivity of 88%, specificity of 81%, positive LR of 4.6, and negative LR of 0.2,[10] and the clinician's bedside assessment of hypesthesia is a more specific predictor of nerve fiber loss than automated touch-pressure esthesiometers.[11] Physical examination may even be superior to nerve conduction testing, a test of only the large myelinated peripheral nerve fibers, not the smaller unmyelinated fibers that carry pain and temperature sensations and from which many uncomfortable sensory syndromes originate.[12]

Diabetic feet insensate to the 5.07 monofilament have an increased risk of subsequent foot ulceration and amputation (see Chapter 53).

B. VIBRATORY SENSATION

Vibratory sensation is often diminished in peripheral neuropathy and spinal cord disease but spared in disease confined to the cerebral cortex.[7] Although it is a highly developed sensation—Helen Keller could interpret speech by feeling the vibrations of the speaker's larynx, lips, and nose—it lacks distinct sense organs and its neuroanatomic pathways remain obscure.[7,13] Traditionally, it is associated with proprioception because impulses from both sensations ascend in the posterior columns of the spinal cord, but there are many clinical examples of dissociation of vibratory and proprioceptive loss, both in peripheral neuropathy and spinal cord disease. (See the section on Proprioception.[7,14])

C. HYPERPATHIA AND ALLODYNIA ARE NONSPECIFIC FINDINGS

Hyperpathia and allodynia occur in many different painful conditions, including peripheral neuropathy, brainstem infarction, and thalamic stroke; by themselves, they have no localizing value.[15,16]

PROPRIOCEPTION

I. DEFINITION

Proprioception allows individuals to detect joint motion and limb position when their eyes are closed.[17] Like most of the simple sensations, proprioception has distinct sense organs and ascending pathways in the spinal cord. Unlike simple sensations, however, full perception requires a healthy contralateral cerebral cortex; in this way, it resembles cortical sensations. (See the section on Cortical Sensations.[18,19])

Sir Charles Bell originally called proprioception the "sixth sense." In 1906, Sherrington introduced the term "proprioception" to describe this sensation.[17,20]

II. TECHNIQUE

The conventional test of proprioception is to lightly hold the sides of the patient's finger or toe and bend it slowly up and down. The patient is asked to indicate any sensation of movement and the movement's direction. Because normal persons perceive motion much more easily than direction, a normal person may accurately indicate the presence of motion all of the time but indicate the wrong direction up to 10% of the time.[21] Normal individuals can detect 1 to 2 degrees of movement in most joints, the hips being the most sensitive.[21,22]

Another test of proprioception tests the ability to direct a limb to a given point, again with the eyes closed. In one version, the clinician positions the patient's outstretched index finger on the clinician's own index finger. The patient then drops the arm to the side and attempts to find the previous position. Normal individuals consistently come within 5 cm of the target.[20]

Patients with severe proprioceptive loss depend on vision for balance and thus become very unstable when they close their eyes or walk in darkness. This dependence on vision forms the basis for another test of proprioceptive loss, Romberg sign, which is discussed fully in Chapter 6.

III. CLINICAL SIGNIFICANCE

Proprioceptive loss is common in peripheral neuropathy (e.g., diabetes mellitus), spinal cord disease (e.g., multiple sclerosis, vitamin B_{12} deficiency, tabes dorsalis), and severe hemispheric disease. In unilateral disease of the spinal cord (e.g., the **Brown-Séquard syndrome**), proprioception is lost on the side of weakness, opposite the side with pain and temperature loss. (See the section on Sensory Syndromes.) In patients who have had a stroke, proprioceptive loss indicates extensive damage and correlates with a poorer functional recovery rate and higher mortality rate.[23]

According to traditional teachings, a disproportionate loss of vibration sensation and proprioception (compared with pain and temperature sensation) occurs in diseases of the dorsal columns of the spinal cord (e.g., tabes dorsalis, multiple sclerosis, vitamin B_{12} deficiency) and some peripheral neuropathies (e.g., diabetic polyneuropathy). Although this teaching is true, most patients with these disorders have abnormalities of pain and temperature sensation as well.[7,24]

CORTICAL SENSATIONS

I. DEFINITION

Cortical sensations are those sensations requiring higher integration and processing for them to be perceived properly. Consequently, perception of cortical sensations requires a healthy contralateral cerebral cortex. Cortical

sensations may become abnormal in cerebral hemispheric disease, *even though* the simple sensations are preserved.

II. TECHNIQUE

Testing for cortical sensations has three requirements:

1. The patient's eyes are closed.
2. The patient lacks dementia.
3. Most of the simple sensations, especially touch, are preserved.

If the simple sensations are profoundly altered, as in severe peripheral neuropathy, no sensory information will reach the cerebral hemisphere and tests for cortical sensation become uninterpretable.

A. TWO-POINT DISCRIMINATION

Two-point discrimination is the ability to distinguish two compass points simultaneously applied to the skin. The normal minimal distance is 3 cm for the hand or foot and 0.6 cm for the fingertips.[14,18,25,26]

B. TACTILE RECOGNITION (STEREOGNOSIS)

Tactile recognition is the ability to recognize common objects such as a key, paper clip, coin, tweezers, or rubber ball placed in the hand. Normal individuals can name more than 90% of objects within 5 seconds or less.[27,28]

C. GRAPHESTHESIA

Graphesthesia is the ability to identify letters or numbers traced on the hand or foot. Normal individuals can easily recognize symbols 1 cm in height on the fingertips and 6 cm tall elsewhere.[18]

D. LOCALIZATION

Localization is the ability to accurately point to a spot on the body just touched by the clinician.

E. BILATERAL SIMULTANEOUS TACTILE STIMULATION

Bilateral simultaneous tactile stimulation tests the patient's ability to recognize that both sides of the body are being touched simultaneously. The term **tactile extinction** refers to the patient's consistent failure to detect the stimulus on one side of the body.[29]

F. APPRECIATION OF WEIGHTS

Appreciation of weights is the ability to perceive differences in weight between two objects, placed sequentially in the patient's hand. This test was used more often several decades ago than it is now.[30]

III. CLINICAL SIGNIFICANCE

Lesions of the posterior parietal lobe may preserve the simple sensations but eliminate proprioception and cortical sensations. The loss is typically confined to just the contralateral distal parts of the limbs, sparing the face and trunk.[19,30–32]

It is important to note that cortical disease also may eliminate any or all of the simple sensations, especially if the lesion involves the anterior parietal lobe (postcentral gyrus) or deeper white matter.[7,19,30,33] These lesions often cause a dense sensory loss on the opposite side of the body, involving the trunk, limbs, and face, sometimes referred to as the **pseudothalamic syndrome** because of its resemblance to the sensory loss of thalamic disease. (See the section on Sensory Syndromes.[19])

DERMATOMES

I. DEFINITION

Dermatomes define the area of skin innervated by a single nerve root or spinal segment. They are primarily used to determine whether the sensory loss on a limb corresponds to a single spinal segment, implying that the lesion is of that nerve root (i.e., radiculopathy), and to assign the neurologic "level" to a spinal cord lesion.

II. DERIVATION OF THE DERMATOMAL MAPS

The original human dermatomal maps emerged from Sherrington's experiments with monkeys and Head's observations of patients with herpes zoster infection.[2,34] These maps have been subsequently revised, based on several types of evidence collected over the last century, including neurosurgical observations (by Cushing, Foester, and Keegan), experiments injecting novocaine next to the nerve roots of medical student volunteers, and electrical stimulation of the skin while recording potentials at the nerve roots.[1,2,34–36] Differences among dermatomal maps, which are minor and primarily deal with how far proximally some limb dermatomes extend, probably reflect biologic variation and differences in experimental method (i.e., sensory loss from a herniated disc or novocaine injection is not necessarily the same as that from root resection).

III. TECHNIQUE

The dermatomal map in Figure 60-1 is the international standard used for classifying patients with spinal cord injury; Table 60-1 provides additional information about dermatomes.[37] Two principles apply when evaluating the dermatomal pattern of sensory loss:

1. Contiguous dermatomes overlap, which means that damage to one nerve root may cause either no anesthesia or a sensory loss confined to a small area. These small areas, which are referred to as **signature zones,** define the sensory level in patients with spinal cord disease.*

*In sensory testing, as in motor testing, the neurologic "level" refers to the most caudal level with *normal* function, rather than the first level with abnormal function. For example, a patient with sensation in the nipple line, but none below it, has a T4 sensory level.

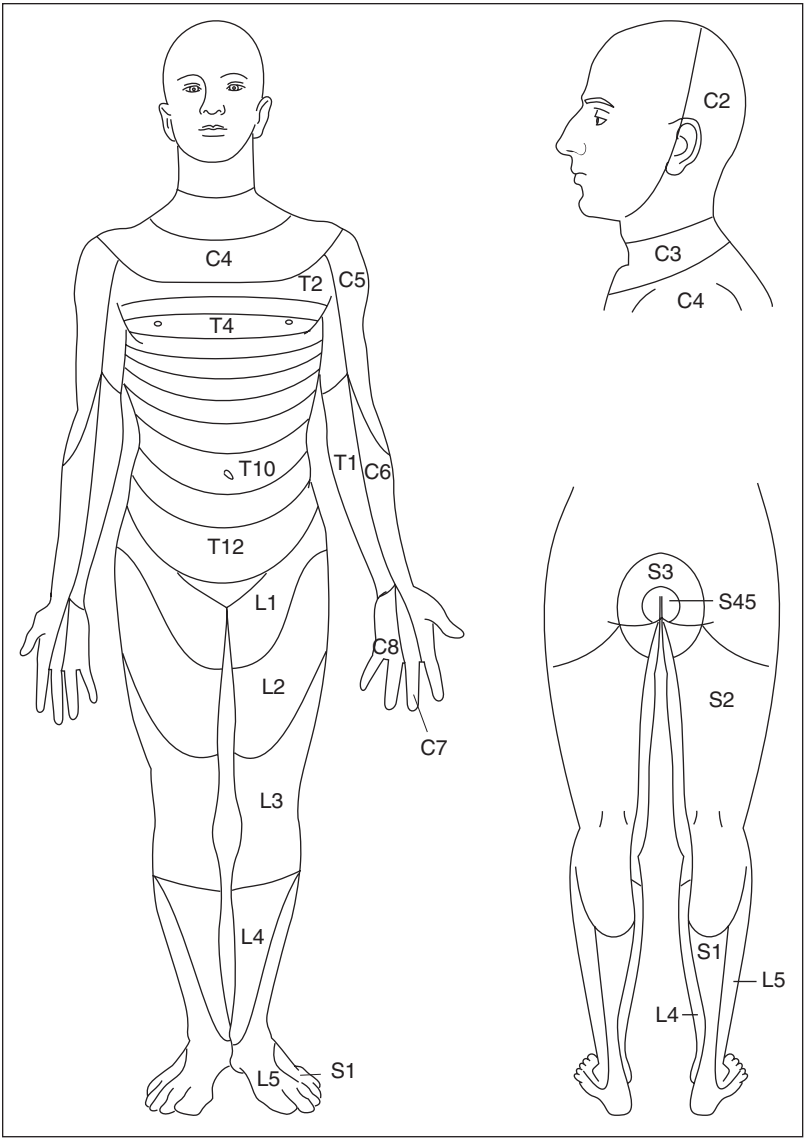


FIGURE 60-1 Dermatomes. This is the dermatome map recommended by the American Spinal Injury Association.[37] A printable copy is available at asia-spinalinjury.org/publications/2006_Classif_worksheet.pdf. Note that the C2 dermatome includes the angle of the jaw and most of the ear. The precise boundaries of the S1 and S2 dermatomes are the most controversial.[35]

TABLE 60-1 Dermatomes and Their Signature Zones

Spinal Level	Signature Zone
CERVICAL	
C3	Supraclavicular fossa
C4	Top of acromioclavicular joint
C5	Lateral side of antecubital fossa
C6	Thumb
C7	Middle finger
C8	Little finger
THORACIC (SELECTED LEVELS)	
T1	Medial (ulnar) side of the antecubital fossa
T2	Apex of axilla
T4	Fourth intercostal space (nipple line)
T10	Tenth intercostal space (umbilicus)
T12	Inguinal ligament at midpoint
LUMBAR	
L1	Half the distance between T12 and L2
L2	Midanterior thigh
L3	Medial femoral condyle
L4	Medial malleolus
L5	Dorsum of the foot at the third metatarsophalangeal joint
SACRAL	
S1	Lateral heel
S2	Popliteal fossa in the midline
S3	Ischial tuberosity
S4-5	Perianal level

Based on reference 37 and original work cited in text.

2. Tactile dermatomes are larger than pain dermatomes. This suggests that, when only one or two segments are affected, testing for pain sensibility is a more sensitive method of examination than testing for abnormal touch.[1,2]

IV. CLINICAL SIGNIFICANCE

A. THE SENSORY LEVEL IN SPINAL CORD DISEASE

The patient's sensory level is often several segments *below* the actual level of the lesion in the spine (e.g., the patient with a T8 sensory level may have a lesion in the T3 segment of the spinal cord).*[38–41] There are two explanations for this phenomenon:

*During the first successful operation to remove a spinal tumor, in 1887, the surgeon's initial incision, which had been based on the patient's sensory level at T5, had to be revised upward twice before the tumor was found at the T2 level.[42]

1. The organization of the ascending spinothalamic pathway (carrying pain and temperature sensation) makes the more lateral fibers carrying lower body sensations more vulnerable to external injury.
2. Instead of directly damaging the contiguous cord, the spinal lesion causes injury at a more distant segment by compromising the cord's blood supply.[38,39]

When the sensory and motor levels disagree, the motor level is a more reliable indicator of level of injury and future disability.[43] In some patients with spinal cord disease, the most accurate indicator of the spinal segment affected is the site of the patient's vertebral pain and tenderness or the level of the patient's radicular pain.[40,44]

B. DERMATOMAL LOSS IN RADICULOPATHY

The clinical significance of dermatomal sensory loss in disorders of the nerve roots is discussed in Chapter 62.

SENSORY SYNDROMES

I. TECHNIQUE

Figure 60-2 depicts the sensory loss of the important sensory syndromes. Sensory loss confined to a *portion* of a limb suggests injury to a peripheral nerve, plexus, or spinal root, subjects discussed in Chapter 62. When sensory loss involves *most of a limb* or the *trunk*, a systematic approach using the following questions defines the syndrome:

A. DOES THE SENSORY LOSS INVOLVE BOTH SIDES OF THE BODY?

Involvement of *both* sides indicates polyneuropathy or spinal cord disease. Involvement of *one* side indicates contralateral disease of the brainstem, thalamus, or cerebral cortex. In patients with pure hemisection of the spinal cord (i.e., Brown-Séquard syndrome), there is sensory loss on both sides of the body, although pain and temperature sensation is lost on the side *opposite to* the lesion and tactile sensation is lost on the side *of* the lesion.

B. IS THERE A SENSORY LEVEL?

A sensory level is a distinct border on the trunk, below which sensory testing is abnormal and above which it is normal. A sensory level indicates spinal cord disease, although the finding sometimes also occurs in lateral medullary infarction.[15,45–48]

C. IS THERE SENSORY DISSOCIATION?

Sensory dissociation is a disproportionate loss of one or more simple sensations with preservation of others. Loss of pain and temperature sensation with preservation of touch and vibration sensation is a feature of some *incomplete* spinal cord syndromes (e.g., syringomyelia, spinal stroke, and Brown-Séquard syndrome).

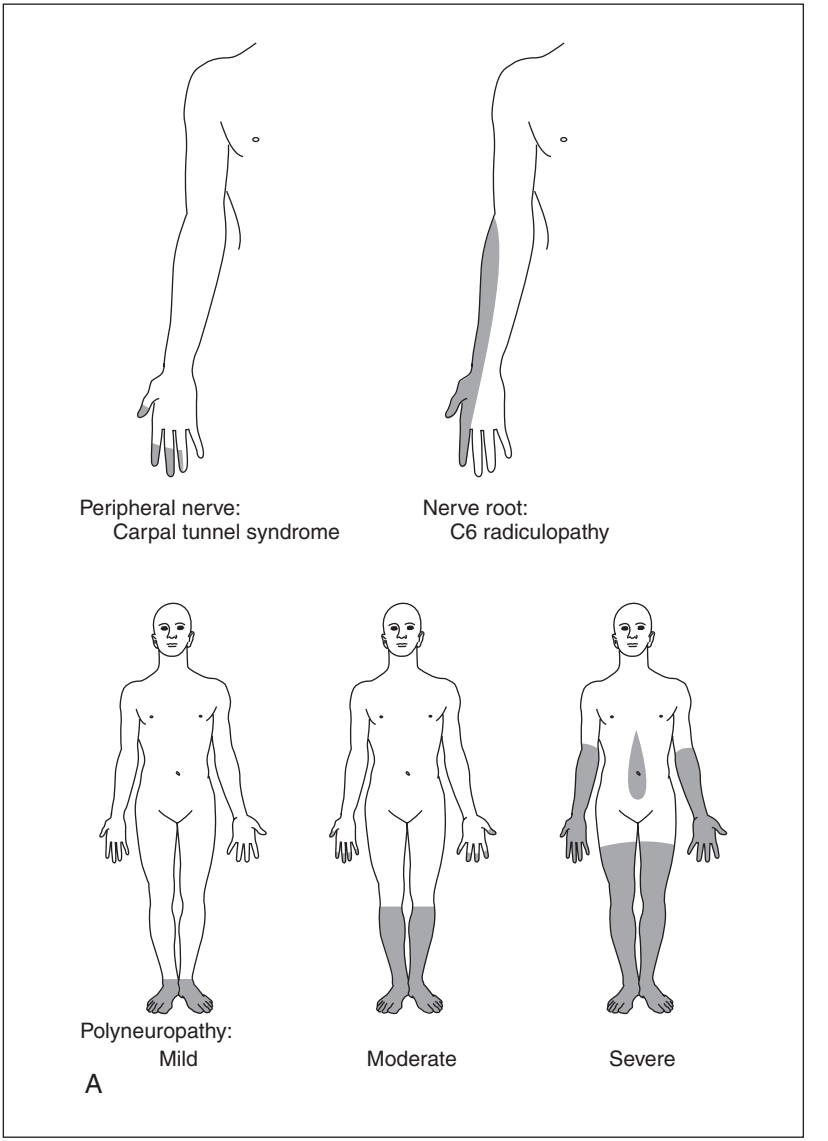


FIGURE 60-2 Sensory syndromes. In these figures, the *gray shading* indicates hypalgesia (loss of pain and temperature sensation) and the *arrows* indicate limbs with significant accompanying weakness. In the Brown-Séquard syndrome (hemisection of the cord, *top row,* Fig. 60-2B), there is often diminished tactile sensation on the side of weakness and opposite the side with hypalgesia.

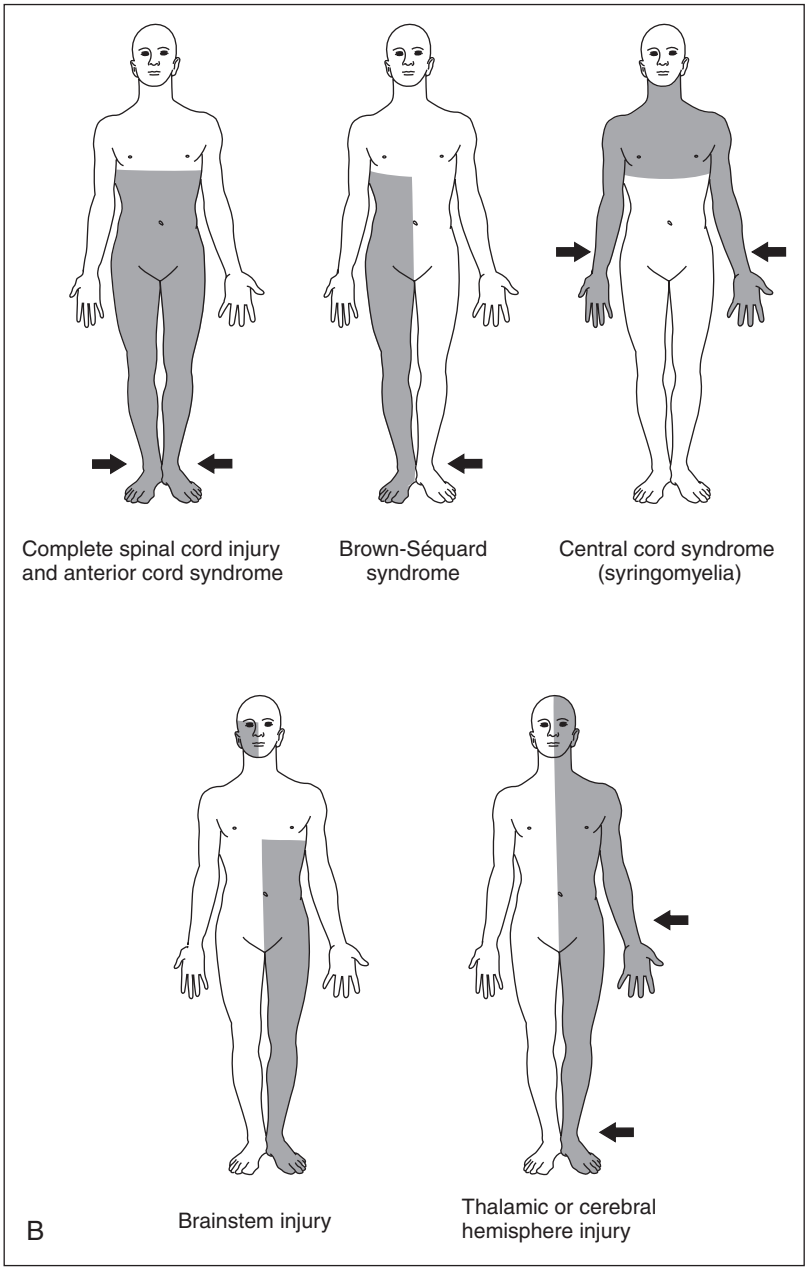


FIGURE 60-2, cont'd

D. IS THERE SENSORY LOSS ON THE FACE?

Sensory loss on the face indicates disease above the spinal cord, in the brainstem, thalamus, or cerebral hemispheres. In brainstem disease (e.g., lateral medullary syndrome), the sensory loss on the patient's face is *opposite* to the side of sensory loss on the body; in disease of the thalamus or cerebral hemisphere, the sensory losses on the face and body are on the *same* side.

E. ARE THERE ASSOCIATED NEUROLOGIC SIGNS?

Most disorders causing the sensory syndromes depicted in Figure 60-2 also cause significant weakness (indicated by the arrows in Fig. 60-2), a major exception being the lateral medullary syndrome.

The presence of an associated **Horner syndrome** (see Chapter 20 for definition) indicates disease of the ipsilateral brainstem or cervical spinal cord.[49]

II. DEFINITION OF THE SENSORY SYNDROMES

Peripheral nerve and spinal root disorders are discussed in Chapter 62.

A. POLYNEUROPATHY

Polyneuropathy is a bilateral **stocking-glove sensory loss** that spares the face. (The sensory loss resembles the pattern of a stocking or glove because polyneuropathy affects all nerves of the same length equally.) Because the sensory loss of polyneuropathy affects the longest nerves first, hypesthesia initially appears in the feet; later in the fingertips; and only after extensive involvement of the arms and legs, in the anterior trunk.[50] Atrophy of the small muscles of the feet and hands and absent ankle reflexes are common. Distal weakness may occur, but because the nerves to the foot dorsiflexors are longer than those to plantar flexors, patients with polyneuropathy have more trouble walking on their heels than on their toes. (The opposite finding, trouble walking on toes but not on heels, suggests an alternative diagnosis.[51])

B. SPINAL CORD SYNDROMES

1. Complete Spinal Cord Lesion

A complete spinal cord lesion causes a sensory level with loss of all simple sensations below that level, weakness (tetraparesis or paraparesis), and urinary retention.

2. Incomplete Spinal Cord Lesions

a. Anterior Cord Syndrome

Spinal stroke, which may follow prolonged hypotension or trauma to the aorta, resembles the complete spinal cord lesion, except there is a disproportionate loss of pain and temperature sensation and relative sparing of touch and vibration, owing to the more vulnerable blood supply of the ventral cord.[52]

b. Brown-Séquard Syndrome

Brown-Séquard syndrome describes injury to one-half of the cord, causing *contralateral* loss of pain and temperature sensation but *ipsilateral* paralysis and diminished touch sensation.[49] Unilateral disease of the cervicothoracic region may involve the ascending sympathetic fibers and cause an ipsilateral Horner syndrome.[49]

The pure Brown-Séquard syndrome is rare. Instead, most patients with unilateral disease of the spinal cord present with bilateral weakness and sensory loss, although the weakness is greatest on the side of the lesion and the hypalgesia is greatest opposite the lesion.[49]

c. Central Cord Syndrome

In syringomyelia, the sensory loss typically involves one or both arms. Seventy-five percent of patients have atrophy and weakness of one or both hands or sternocleidomastoid muscles.[53,54]

C. LATERAL MEDULLARY INFARCTION

Lateral medullary infarction (Wallenberg syndrome) is a dramatic syndrome presenting with dizziness and sensory loss on opposite sides of face and body but no weakness. (The lesion is ipsilateral to the facial analgesia.) Common associated signs are diminished corneal reflex, ipsilateral limb ataxia, nystagmus, ipsilateral Horner syndrome, gait ataxia, and ipsilateral palate weakness (Table 60-2).

D. THALAMIC DISEASE

A lesion in the thalamus may cause loss of all simple sensations on the opposite side of the body, associated with hemiparesis, vertical gaze abnormalities, miosis, and aphasia.[33,55,56]

TABLE 60-2 Lateral Medullary Infarction (Wallenberg Syndrome)

Physical Finding	Frequency (%)*
CRANIAL NERVES	
Diminished corneal reflex (V and VII)	91
Ipsilateral Horner syndrome†	71-95
Ipsilateral face analgesia (V)	50-86
Nystagmus	56-100
Ipsilateral palate weakness (IX, X)	52-86
Ipsilateral facial weakness (VII)	21-43
SENSORY	
Contralateral body analgesia	88
COORDINATION	
Ipsilateral limb ataxia	55-95
Gait ataxia	91

*Results are overall mean frequency or, if statistically heterogeneous, the range of values.
†Strictly speaking, Horner syndrome does not involve the cranial nerves, although it is discovered during examination of the pupils and eyelids.
Data obtained from 290 patients from references 47 and 57 to 61.

E. CEREBRAL HEMISPHERIC DISEASE

Cerebral hemispheral disease may cause a dense sensory loss and hemiparesis identical to thalamic disease **(pseudothalamic syndrome),**[19] or the selective loss of cortical sensations in the distal parts of the extremities. (See the section on Cortical Sensations.)

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 61

Examination of the Reflexes

Reflexes are involuntary contractions of muscles induced by specific stimuli. In the neurologic examination, there are three types of reflexes:

1. Muscle stretch reflexes (deep tendon, or myotatic, reflexes)
2. Cutaneous reflexes
3. Primitive reflexes (release reflexes)

This chapter also discusses the **Babinski response,** which is an abnormal cutaneous reflex of the foot that appears in upper motor neuron disease.

REFLEX HAMMERS

I. TYPES OF REFLEX HAMMERS

Early in the history of reflex testing,* clinicians used various implements to elicit reflexes: The great British neurologist Gowers used the ulnar aspect of his hand or his rigid stethoscope. Other clinicians were less selective, using paper weights, laboratory stands, or even table lamps.[2–4] In the late 1800s and early 1900s, many different reflex hammers were produced, some of which remain popular today.

A. TAYLOR HAMMER

The **Taylor hammer** was developed in 1888 by J.M. Taylor, personal assistant to S. Weir Mitchell at the Philadelphia Orthopedic Hospital and Infirmary for Nervous Disease. This tomahawk-shaped soft rubber hammer has a broad edge for percussing most tendons and a rounded point for reaching the biceps tendon or percussing muscles directly. The original handle ended in an open loop; the pointed end was added in about 1920 for use in eliciting cutaneous reflexes.[4]

B. QUEEN SQUARE HAMMER

The **Queen Square hammer** was developed by a Miss Wintle, head nurse at the National Hospital for Nervous Diseases at Queen's Square, London, who for years made hammers from ring pessaries, solid brass wheels, and bamboo rods to sell to resident medical officers. This hammer has a rubber-lined disc attached to the end of a long rod, like a wheel on an axle.[2]

*Reflex testing became common after Erb and Westphal simultaneously discovered the value of muscle stretch reflexes in 1875.[1]

C. BABINSKI HAMMER (BABINSKI/RABINER HAMMER)

The **Babinski hammer** has a handle that can be removed and attached either perpendicularly or parallel to the disc-shaped head. Babinski's name probably reflects marketing more than innovation.[4]

D. TROEMNER HAMMER

The **Troemner hammer,** the only one of the four that actually resembles a hammer, was made popular in this country by the Mayo Clinic, where the neurologist Woltman introduced it in 1927.[5]

II. CLINICAL SIGNIFICANCE

No study has demonstrated any hammer to be superior to another, and selection depends more on personal preference and tradition. The Taylor hammer is popular in America, the Queen Square hammer in England, and the Troemner hammer in continental Europe.[6] The built-in pins of some models (e.g., the Babinski hammer), designed for testing pain sensation and cutaneous reflexes, should not be used, because they could transmit infections.[7]

MUSCLE STRETCH REFLEXES

I. DEFINITION

Muscle stretch reflexes are involuntary contractions of muscles induced by a brisk stretch of the muscles. Muscle stretch reflexes are usually named after the muscle being tested (Table 61-1), the one notable exception being the Achilles reflex (or ankle jerk). Although these reflexes are often called **deep tendon reflexes,** this name is a misnomer because tendons have little to do with the response, other than being responsible for mechanically transmitting the sudden stretch from the reflex hammer to the muscle spindle. In addition, some muscles with stretch reflexes have no tendons (e.g., "jaw jerk" of the masseter muscle).

TABLE 61-1 Common Muscle Stretch Reflexes

Name of Reflex	Peripheral Nerve	Spinal Level
Brachioradialis	Radial	C5-C6
Biceps	Musculocutaneous	C5-C6
Triceps	Radial	C7-C8
Quadriceps (patellar)	Femoral	L2-L4
Medial hamstring*	Sciatic	L5
Achilles (ankle)	Tibial	S1

*An online video demonstrating the medial hamstring reflex is available in reference 91.
Based on references 21, 26, and 81 to 90.

Most healthy persons have the muscle stretch reflexes listed in Table 61-1 (except for perhaps the medial hamstring reflex, which is not traditionally tested).

II. TECHNIQUE

A. METHOD

The usual stimulus is a sharp tap with the reflex hammer on the muscle's tendon, near where the tendon inserts distally on bone. The Achilles reflex is also elicited sometimes by the plantar strike method, in which the reflex hammer strikes the clinician's hand, which is resting on the ball of the foot. In clinical studies of the Achilles reflex, the plantar strike method and the tendon strike method are equivalent.[8–10]

B. GRADING REFLEX AMPLITUDE

The most important observation during reflex examination is the reflex's amplitude. Unlike examination of motor strength, examination of reflexes lacks a single universally accepted grading system. Proposed schemes range from S. Weir Mitchell's original four grades[4] to the Mayo Clinic's nine grades.[11] A five-point grading system (i.e., grades 0 through 4), reproduced in Table 61-2, is recommended by the National Institute of Neurological Disorders and Stroke (NINDS).[12]

C. REINFORCEMENT: THE JENDRASSIK MANEUVER

According to the NINDS scale (see Table 61-2), grade 1 reflexes describe reflexes made conspicuous by reinforcement maneuvers and grade 0 reflexes are those that are absent despite reinforcement. The most common method of reinforcing reflexes is the **Jendrassik maneuver.** In 1885, Erno Jendrassik reported that having the patient "hook together the flexed fingers of his right and left hands and pull them apart as strongly as possible" while the clinician taps on the tendon enhances the reflexes of normal patients.[2] Reflex enhancement with this maneuver persists as long as the patient is pulling apart the arms, up to 10 seconds in some studies.[13,14] In one study of normal elderly patients, the absent ankle jerk was made to appear 70% of the time using reinforcing maneuvers.[15]

TABLE 61-2 NINDS* Muscle Stretch Reflex Scale

Grade	Finding
0	Reflex absent
1	Reflex small, less than normal; includes a trace response or a response brought out only with reinforcement
2	Reflex in lower half of normal range
3	Reflex in upper half of normal range
4	Reflex enhanced, more than normal; includes clonus if present, which optionally can be noted in an added verbal description of the reflex

*NINDS, National Institute of Neurological Disorders and Stroke, from reference 12.

III. CLINICAL SIGNIFICANCE

A. AMPLITUDE OF REFLEX

The amplitude of muscle stretch reflexes depends on the integrity of the lower and upper motor neurons innervating the reflex (see Fig. 59-2 in Chapter 59 for definitions of lower and upper motor neurons).

1. The lower motor neurons of a reflex are its peripheral nerve (second column in Table 61-1) and its spinal segment (third column in Table 61-1): Disease at either of these locations *reduces* or *abolishes* the relevant reflex.
2. The upper motor neurons are the descending corticospinal pathways innervating the reflex: Disease anywhere along this pathway (e.g., cerebral hemisphere, brainstem) *exaggerates* the reflex.
3. Disease of the *spinal cord*, where both upper and lower motor neurons reside, abolishes the reflex *at* the level of the lesion (lower motor neuron response) and exaggerates all reflexes from spinal levels *below* the level of the lesion (upper motor neuron response).

Nonetheless, absent or exaggerated reflexes, by themselves, do not signify neurologic disease.[16–18] For example, 6% to 50% of elderly persons without neurologic disease lack the ankle jerk bilaterally, despite the Jendrassik maneuver,[15,19] and a small percentage of normal individuals have generalized hyperreflexia.[16–18,20] Instead, the absent or exaggerated reflex is significant only when it is associated with one of the following clinical settings:

1. The absent reflex is associated with other findings of lower motor neuron disease (weakness, atrophy, fasciculations).
2. The exaggerated reflex is associated with other findings of upper motor neuron disease (i.e., weakness, spasticity, Babinski sign).
3. The reflex amplitude is asymmetrical, which suggests either lower motor neuron disease of the side with the diminished reflex or upper motor neuron disease of the side with the exaggerated reflex.
4. The reflex is unusually brisk compared with reflexes from a higher spinal level. This finding raises the possibility of disease at some level of the spinal cord between the segments with exaggerated reflexes and those with diminished ones.

B. LOCALIZING VALUE OF DIMINISHED REFLEXES

In patients with nerve complaints of the arm or leg suggesting disorders of the cervical or lumbosacral nerve roots, the diminished reflex has an important localizing value that indicates a lesion of the reflex's respective spinal root (see Table 61-1). A diminished biceps or brachioradialis reflex indicates C6 radiculopathy (likelihood ratio [LR] = 14.2),[21] a diminished triceps reflex indicates C7 radiculopathy* (LR = 3),[21,22] a diminished quadriceps reflex indicates L3 or L4 radiculopathy (LR = 8.7),[23–25] a diminished medial hamstring reflex indicates L5 disease (LR = 6.2),[26] and a diminished Achilles reflex indicates S1 radiculopathy (though only modestly) (LR=2.7) (see Chapter 62).[23–25,27–29]

*C6 and C7 radiculopathies are much more common than C5 or C8 radiculopathies (see Chapter 62).

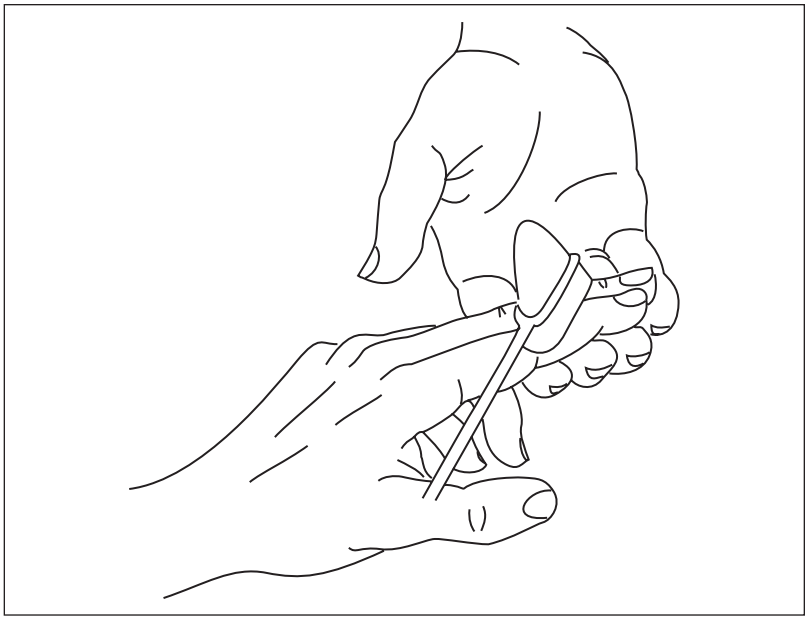


FIGURE 61-1 Finger flexion reflex. After positioning the patient's hand in the supinated position with fingers slightly flexed, the clinician places his own index and middle fingers across the tips of the patient's fingers and taps them with the reflex hammer. Reflex contraction of the patient's finger flexor muscles is a positive response.

C. ADDITIONAL FINDINGS IN THE HYPERREFLEXIC PATIENT

The physical finding of hyperreflexia has generated more eponyms in physical diagnosis than any other physical finding,* even though the basic pathophysiology for all exaggerated reflexes is the same (i.e., loss of corticospinal inhibition) and the reflexes differ only according to which muscle is stretched and which method the clinician uses to stretch the muscle. Of the many findings that have been described in hyperreflexic patients, commonly recognized ones are finger flexion reflexes, jaw jerks, clonus, and "irradiating" reflexes.

1. Finger Flexion Reflexes

Finger flexion reflexes were introduced by Hoffman about 1900. In a positive response, sudden stretching of the finger flexors causes them to involuntarily contract. (The finger flexion reflex, therefore, is no different from any other muscle stretch reflex.) There are many ways to elicit this finding, each with its own eponym (e.g., **Hoffman sign, finger Rossolimo sign, Troemner sign, von Bechterew reflex**). One of these methods is described in Figure 61-1. Like other exaggerated reflexes, finger flexion reflexes by

*_Dorland's Illustrated Medical Dictionary_ lists 115 neurologic reflexes, 46 having eponyms.[30]

themselves have little diagnostic value (i.e., they are detectable in 3% of healthy college students),[20] and, to be significant, they must accompany one of the settings described previously in the section on Amplitude of Reflex.

2. Jaw Jerk Reflex

The **jaw jerk reflex** was originally described by Lewis in 1882.[31] In a positive response, sudden stretching of the masseter muscle causes reflex contraction, moving the jaw briskly upward. With the patient's jaw slightly open, the clinician can elicit the reflex by tapping with a reflex hammer directly on the chin or on a tongue blade resting on the lower teeth or tongue. An exaggerated jaw jerk, sometimes appearing with clonus (see below), implies bilateral disease above the level of the pons (e.g., pseudobulbar palsy).[16] In patients with spastic tetraparesis, for example, an exaggerated jaw jerk excludes cervical cord disease and points to pyramidal tract disease above the pons.

3. Clonus

Clonus is a self-sustained, oscillating stretch reflex induced when the clinician briskly stretches a hyperreflexic muscle and then continues to apply stretching force to that muscle. Each time the muscle relaxes from the previous reflex contraction, the applied stretching force renews the reflex, setting up a rhythmic series of muscle contractions that continues as long as the tension is applied. These rhythmic oscillations (clonus) are most easily elicited in the foot (usually with oscillations of 5 to 8 Hz), by briskly dorsiflexing the patient's ankle. Clonus also may be elicited in the quadriceps muscle, finger flexors, jaw muscles, and other muscles.

As expected mathematically, the frequency of clonus varies inversely with the length of the reflex path ($r = -0.80$, $p < .001$). Clonus of the wrist has a higher frequency than that of the ankle, simply because the nerves to the forearm are shorter than those to the calf.[32]

4. "Irradiation" of Reflexes

In some hyperreflexic patients, the blow of the reflex hammer is conducted mechanically through bone and tissues, where it may stretch hyperexcitable muscles at distant sites, thus producing additional, unexpected movements (e.g., crossed adductor reflex).[17,33] Also, if this distant irradiation of a reflex is combined with paralysis of the reflex of interest, paradoxic movements, or "inverted" reflexes, may appear.

a. Crossed Adductor Reflex

Tapping on the medial femoral condyle, patella, or patellar tendon causes the contralateral adductor muscle to contract, moving the contralateral knee medially.[34]

b. Inverted Supinator Reflex

The **inverted supinator reflex** (the **supinator reflex** is the brachioradialis reflex) was introduced by Babinski in 1910. This sign indicates spinal cord disease at the C5 to C6 level.[17,35,36] In a positive response, tapping on the

brachioradialis muscle causes no flexion at the elbow but, instead, flexion of the fingers. The lesion at C5 to C6 eliminates the brachioradialis reflex (lower motor neuron reflex) but exaggerates all reflexes below that level (upper motor neuron reflex), including the finger flexion reflexes (C8), which are stimulated by mechanical conduction of the blow on the brachioradialis muscle.

c. Inverted Knee Jerk

The **inverted knee jerk**[37] indicates spinal cord disease at the L2 to L4 level. In the positive response, attempts to elicit the knee jerk instead cause paradoxic knee flexion. Its two components are denervation of L2 to L4 (thus paralyzing the quadriceps jerk) and conduction of the blow to the muscle spindles of the hamstrings (innervated by the L5 to S1 level and made hyperexcitable by the same lesion).

CUTANEOUS REFLEXES (SUPERFICIAL REFLEXES)

I. DEFINITION

Cutaneous reflexes are involuntary muscle contractions that follow stimulation of the skin surface by scratching, stroking, or pinching.

II. SUPERFICIAL ABDOMINAL REFLEX (T6 TO T11)

A. TECHNIQUE

In the superficial abdominal reflexes, stroking the skin of the abdomen causes the underlying abdominal wall muscle to contract, sometimes pulling the umbilicus toward the stimulus. The clinician usually tests one abdominal quadrant at a time using a side-to-side motion with a wooden applicator stick or the pointed end of the reflex hammer handle. The abdominal reflexes appear just as often whether the direction is medial to lateral or lateral to medial.[38]

B. CLINICAL SIGNIFICANCE

According to traditional teachings, superficial abdominal reflexes disappear with both upper and lower motor neuron disease. Their clinical value is slight, however, because they are also absent in about 20% of normal individuals, more so in the elderly.[38,39] Moreover, the observation of asymmetrical reflexes or ones preserved only in the upper quadrants, patterns traditionally associated with neurologic disease, also are a common finding in healthy persons.[38–40]

III. BULBOCAVERNOSUS REFLEX (S2 TO S4)

A. TECHNIQUE

After positioning the patient in the lithotomy position, sudden manual compression of the glans penis or clitoris causes reflex contraction of the bulbocavernosus muscle and external anal sphincter. The reflex is detected either

by palpating the skin behind the scrotum (bulbocavernosus muscle) or, more commonly, by placing the index finger in the anal canal (external anal sphincter). Other effective stimuli are percussing the suprapubic area[41] or pulling the retention balloon of an indwelling Foley catheter against the bladder neck.[42]

B. CLINICAL SIGNIFICANCE

The bulbocavernosus reflex is one of the few ways to test the conus medullaris (distal end of the spinal cord) and the S2 to S4 pelvic nerves (the only other bedside test of this region is testing sensation in the perineal, or "saddle," area).[42–44] This reflex is particularly important in patients with urinary retention, therefore, which may be caused by disease of the pelvic nerves or cauda equina. In one study of consecutive patients referred for urodynamic studies,[42] most of whom had difficulty with urination, an *absent* reflex predicted disease in the S2 to S4 segments only modestly in women (LR = 2.7) but much better in men (LR = 13). The modest accuracy of the sign in women may reflect damage to the pudendal nerve from having given birth or having had pelvic surgery.[42] In this study, the *presence* of a bulbocavernosus reflex was unhelpful: Although the positive response is expected in patients with urinary retention from common disorders such as prostate hypertrophy, it also is commonly found in incomplete lesions of the sacral nerves.

In spinal cord injury above the S2 to S4 level (i.e., upper motor neuron lesion to the S2 to S4 segment), the bulbocavernosus reflex also disappears, but only temporarily, for a period of 1 to 6 weeks.[42]

BABINSKI RESPONSE

I. DEFINITION

The **Babinski response** is an abnormal cutaneous reflex found in upper motor neuron disease affecting the muscles of the foot. In these patients, scratching the sole of the patient's foot causes an upward movement of the great toe, instead of the normal downward movement (Fig. 61-2). Much revered and researched, this reflex was originally described by Babinski in

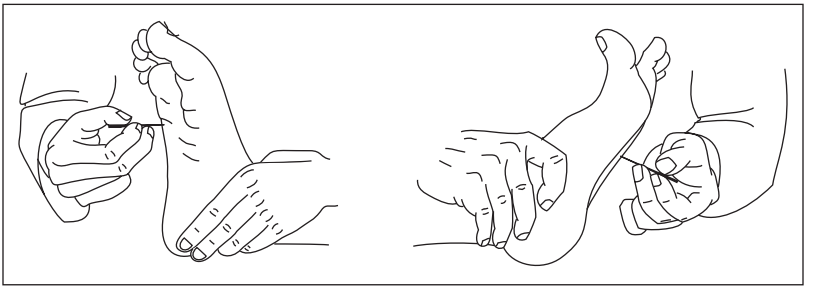


FIGURE 61-2 Babinski response. Drawing of the normal plantar cutaneous reflex *(left)* and the Babinski response *(right),* adapted from photographs taken by Babinski himself in 1900.[45]

1896.[45,46] It goes by various names, including the Babinski response, sign, or reflex; the upgoing toe; and the extensor response.

In some patients with bilateral corticospinal tract disease, scratching the foot may even cause the contralateral great toe to move upward, a response termed **crossed dorsiflexion** or **crossed extensor response.**[45]

II. PATHOGENESIS

In response to painful stimuli applied to the lower limbs, most mammals rapidly withdraw that limb by flexing the hips and knees and dorsiflexing the feet and toes. This primitive reflex, the **flexion response,** also occurs in human infants until the age of 1 or 2 years, after which time the developing pyramidal tracts cause two important changes.

1. The flexion response becomes less brisk.
2. The toes no longer move upward but instead move downward because of the interval development of a normal plantar cutaneous reflex.[47]

If pyramidal tract disease develops later in the person's life, the normal plantar cutaneous reflex disappears, and, instead, painful stimulation of the foot causes the great toe to again move upward.

The use of the term *extensor response* to describe the Babinski response is unfortunate and confusing: Even though anatomists have always named the upward movement "extension" (e.g., the great toe extensor muscle), physiologists have named the same upward movement "flexion" (e.g., the primitive flexion response discussed earlier).

III. TECHNIQUE

A. ELICITING THE RESPONSE

Of the many ways to elicit this reflex,[48] a slow (i.e., 5- to 6-second) hockey-stick stroke beginning at the lateral plantar surface is best, using a wooden applicator stick, key, or pointed handle of the reflex hammer (see Fig. 61-2). This method is superior to other methods, including scratching the lateral sole, scratching below the lateral malleolus **(Chaddock method),** rubbing the anterior shin **(Oppenheim method),** or—the least effective stimulus—squeezing the calf **(Gordon method).**[49,50]

B. INTERPRETING THE RESPONSE

Helpful guidelines in assessing an equivocal toe response, based on careful electrodiagnostic studies and patient follow-up, are as follows:

1. The pathologic upgoing toe results from contraction of the extensor hallucis longus muscle, the tendon of which is conspicuous under the skin on top of the great toe.[51,52] Movement of the toe per se is not critical and may be prevented by joint disease. Moreover, the toe may seem to be upgoing—without contraction of the extensor hallucis longus muscle—when the ankle dorsiflexes or when the toe returns from an initial downward movement.
2. Over 90% of the time, the foot with the pathologic upgoing toe is weak or has difficulty with fine motor movements. An excellent test

of fine motor movement is rapid foot tapping against the examiner's hand: Normal persons accomplish 20 to 40 taps per 10 seconds.
3. The pathologic upgoing toe coincides with a flexion response in the whole limb, which may be slight but is evident in the ipsilateral tensor fascia lata and hamstring muscles.
4. The pathologic upgoing toe is reproducible.[47,53,54]

As Babinski himself pointed out, fanning of the toes is a normal phenomenon and not part of the pathologic response.[45,47]

IV. CLINICAL SIGNIFICANCE

A. ASSOCIATED CONDITIONS

The Babinski response is found in both destructive lesions of the pyramidal tracts (see Chapter 59) and in many metabolic disorders affecting these tracts, most of which are associated with altered mental status, such as seizures, meningitis, drug overdose, or renal and hepatic failure.[45]

B. FALSE-NEGATIVE RESPONSE

Patients may have pyramidal tract disease yet lack the upgoing toe (i.e., false-negative response) because they have the following:
1. Spinal shock[51]
2. A peroneal palsy denervating the muscles that dorsiflex the great toe (a common problem in bedridden patients due to pressure against the head of the fibula)[51]
3. Pyramidal tract disease sparing the muscles of the foot (e.g., upper motor neuron weakness that is confined to the arm of that side)[55]

PRIMITIVE REFLEXES

I. DEFINITION

Primitive reflexes (or release reflexes) are a hodgepodge of reflexes that are normally present in infants but disappear during normal development of the central nervous system, only to reappear sometimes later in life when neurologic disease or aging removes (or "releases") the inhibiting influences of the central nervous system.[56] Among many primitive reflexes,[57] the more common ones are the palmomental reflex, glabellar reflex, grasp reflex, snout reflex, and suck reflex.

II. TECHNIQUE

A. PALMOMENTAL REFLEX

In the **palmomental reflex,** a key or other blunt object is used to apply an unpleasant stimulus to the patient's thenar eminence, stroking it briskly in a proximal-to-distal direction. A positive response is a brief contraction of the ipsilateral mentalis muscle, causing the ipsilateral lower lip to protrude, rise, or wrinkle.[58]

The wrinkle response at the corner of the mouth is probably the beginnings of a wince that would develop with more painful stimuli.[59] Theoretically, the stimulus could be applied anywhere on the skin of the patient's body, and, in fact, descriptions of a similar response after stimulation of the patient's arm, chest, trunk, sole of the foot, and tongue have all appeared.[59] The most sensitive area, however, is the thenar eminence.[60]

Marinesco and Radovici discovered the palmomental reflex in 1920.[59]

B. GLABELLAR REFLEX

The stimulus for the **glabellar reflex** is light taps with the finger or a soft rubber reflex hammer, about two times per second, over the patient's glabella. Although most normal persons respond to this by blinking bilaterally, the blinking stops after the first few taps in normal individuals. Persistent blinking is a positive response, although there is no consensus as to whether habituation should be indefinite or just beyond a certain number of blinks (e.g., more than four successive blinks).

The glabellar reflex is sometimes called the **blink reflex** or **Myerson reflex,** although the original description was by Overend in 1896.[61]

C. GRASP REFLEX

In the **grasp reflex,** the clinician places his index and middle fingers over the thenar aspect of the patient's wrist and exerts pressure on the skin while withdrawing the fingers between the patient's thumb and index finger. In a positive response, the patient grasps the clinician's fingers, and the grasp progressively increases as the clinician attempts to withdraw.[57]

III. CLINICAL SIGNIFICANCE

A. GENERAL COMMENTS

Primitive reflexes are common findings in frontal lobe disease,[62] parkinsonism,[63–66] dementias,[67–71] and advanced human immunodeficiency virus (HIV) infection.[72] Other than the grasp reflex (see below), the precise neuroanatomic cause of these reflexes is unknown.

B. PALMOMENTAL REFLEX

The palmomental reflex is bilateral 38% to 75% of the time and unilateral 25% to 62% of the time.[73,74] The side of the reflex does not correlate with the side of the lesion.[58,73] In one study of 39 patients with a unilateral palmomental reflex, 44% had an ipsilateral cerebral hemispheric lesion, 36% a contralateral lesion, 10% bilateral lesions, and 10% no lesions.[74] In patients with Parkinson disease, the palmomental reflex correlates with the degree of akinesia, and the reflex often disappears with the onset of levodopa-induced dyskinesias.[63]

C. GLABELLAR REFLEX

The afferent limb of the glabellar reflex is the trigeminal nerve, and the efferent limb is the facial nerve. Lesions of either nerve may interrupt the reflex (although in facial nerve palsy, the blinking continues on the sound

side). This reflex is also a common finding in Parkinson disease, and in these patients, the positive response may reverse after administration of levodopa.[64]

D. GRASP REFLEX

A positive grasp reflex is common in frontal lobe disease and, if both arms can be tested (i.e., no paralysis), the grasp reflex, when present, is usually bilateral.[62] In patients with dementia, the sign correlates with more severe cognitive and functional impairment and greater loss of pyramidal cells in the frontal lobe.[67,68,71] Among patients admitted to a neurologic ward, a positive grasp reflex (defined as no habituation with three successive strokes) predicted discrete lesions in the frontal lobe or deep nuclei and subcortical white matter with a sensitivity of 13% to 50%, specificity of 99%, and positive LR of 19.1.[62,75]

E. PRIMITIVE REFLEXES AND NORMAL AGING

The palmomental and glabellar reflexes, but not the grasp reflex, also occur in normal persons, although the reported frequencies from different studies vary widely.[69,70,72,76] The reported frequency for the palmomental sign in normal persons varies from 3% to 70%; that for the glabellar sign, from 3% to 33%.[63,70,72,76–79] A few of these "normal" persons with primitive reflexes undoubtedly have subclinical disease, as indicated by lesions in the basal ganglia or subcortical white matter on magnetic resonance imaging (MRI).[77] Others, however, have no evidence of neurologic disease, although importantly, their findings differ from the pathologic response in two important ways, as follows:

1. The primitive reflex of patients without neurologic lesions is weak and fatigable, disappearing after the first few repetitive stimuli spaced evenly apart.[56]
2. The primitive reflex of patients without neurologic lesions is an isolated finding. For example, less than 1% of normal persons have a positive palmomental reflex, if it is defined as persistence beyond five or more strokes of the thenar eminence.[60,63] And, even if the definition of a positive response includes fatigable primitive reflexes, less than 12% of normal persons have two primitive reflexes and less than 2% have three or more primitive reflexes.[72,76,78–80]

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 62

Disorders of the Nerve Roots, Plexuses, and Peripheral Nerves

I. INTRODUCTION

Nerve roots destined to innervate the limbs exit through vertebral foramina and intermingle in plexuses (i.e., the brachial and lumbosacral plexuses) before emerging as peripheral nerves that extend to the fingers and toes. Lesions anywhere along this pathway—from spinal nerve roots to the final peripheral nerve branch—produce combinations of pain, *lower* motor neuron weakness, and sensory loss.

A lesion in the nerve root is called **radiculopathy;** one in the plexus, **plexopathy;** and one in the peripheral nerve, **peripheral neuropathy.** This chapter emphasizes how to distinguish these lesions in patients with nerve complaints of the arms or legs. Because the neuroanatomy of these lesions is complex, accurate diagnosis requires systematic examination of all the limb's muscles, sensations, and reflexes.

II. THE ARM

A. INTRODUCTION

In patients presenting with upper extremity nerve complaints, the most common neurologic diagnosis is carpal tunnel syndrome, followed by polyneuropathy, ulnar neuropathy, and cervical radiculopathy.[1–3] Other focal neuropathies and plexopathies are less common. Most cervical radiculopathies affect the C6 or C7 root.[4–7]

B. NEUROLOGIC FINDINGS

1. Motor Nerves

Most muscles of the arm are innervated by nerves from more than one spinal segment. Figure 62-1 presents the relationship between the different peripheral nerves (grouped in rows) and their corresponding spinal roots (in columns). The spinal levels listed in Figure 62-1 are based on several lines of evidence, including Bolk's detailed dissection of a single human subject,[8,9] electrodiagnostic studies,[10,11] and bedside observations of patients with documented spinal root lesions.[5,12]

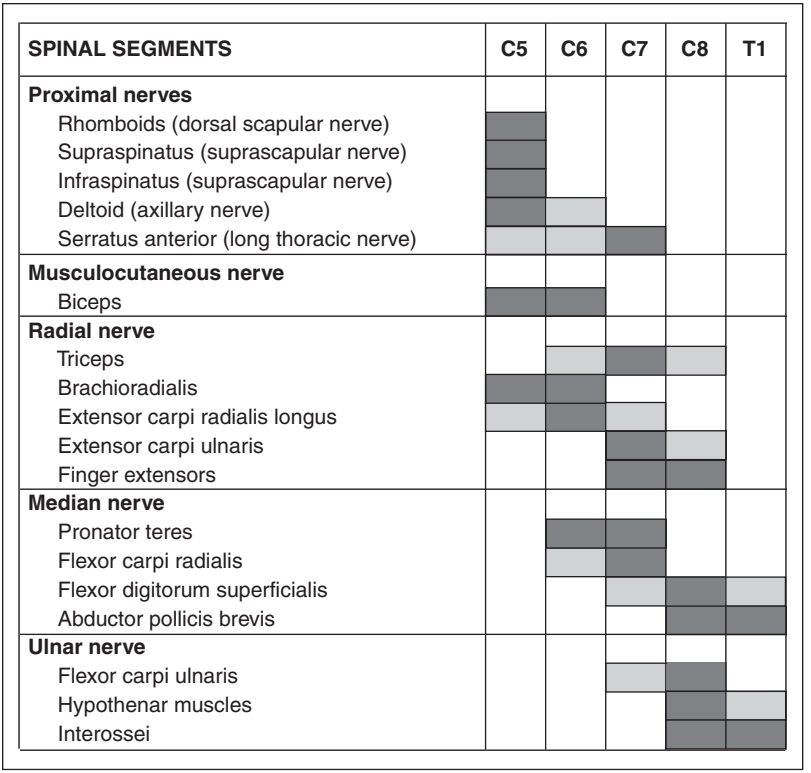


FIGURE 62-1 Innervation of muscles of the arm. This figure indicates those spinal levels that usually *(dark gray shade)* and sometimes *(light grey shade)* contribute to the corresponding muscle; based on references 4, 5, and 8 to 14.

a. Radiculopathy

Even though most muscles receive innervation from more than one spinal nerve root, injury to one root is usually sufficient to cause significant loss of power. The motor examination of radiculopathy has two characteristics.

1. Weakness affects two or more muscles from the same spinal segment but different peripheral nerves (i.e., all of the weak muscles are in the same *column* in Fig. 62-1). For example, a C6 radiculopathy may simultaneously weaken the elbow flexion (biceps muscle and musculocutaneous nerve) and wrist extension (radial and ulnar wrist extensors and radial nerve).[5]
2. Weakness may involve muscles innervated by "proximal nerves," which are listed in the top rows of Figure 62-1. Proximal nerves originate from the nerve roots but then promptly innervate muscles of the shoulder, thus moving away from the course of the peripheral nerves of the arm. If, therefore, a muscle innervated by one of these nerves is weak in a patient with nerve complaints of the arm or hand, the lesion must be a proximal one near the nerve roots. A common example is

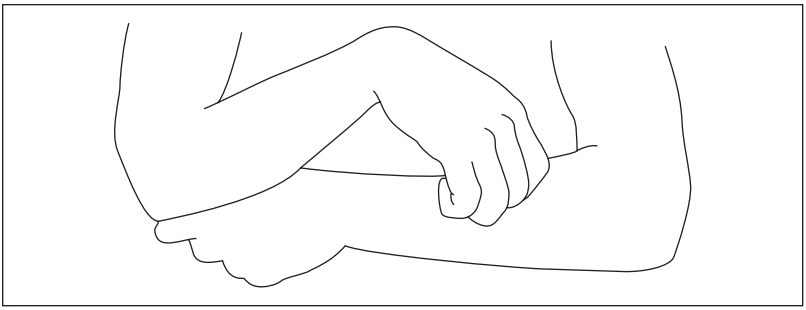


FIGURE 62-2 Wrist drop of radial neuropathy. This patient has a right radial nerve palsy, which eliminates the wrist and finger extensor strength and causes the hand to droop downward from its own weight.

the finding of scapular winging (i.e., weak serratus anterior muscle and long thoracic nerve) in a patient with arm pain and triceps muscle weakness. Involvement of the serratus anterior muscle points to the C7 root and away from the radial nerve or brachial plexus.[13]

b. Brachial Plexopathy

Lesions of the brachial plexus cause simultaneous weakness of muscles from two or more adjacent spinal segments (i.e., adjacent *columns* in Fig. 62-1) and from two or more peripheral nerves. Brachial plexus lesions usually affect either the upper plexus (C5 to C6) as a group, causing weakness of the shoulder and upper arm but sparing all muscles of the hand, or the lower plexus (C7 to T1) as a group, affecting all muscles of the hand but sparing those of the shoulder and upper arm.

c. Peripheral Nerve Disorders

These lesions weaken two or more muscles from a *single* peripheral nerve (which may have different spinal segments) and spare muscles from other nerves. For example, a complete radial nerve injury weakens the brachioradialis muscle (C5 to C6),* elbow extension (triceps, C7), wrist extension (wrist extensors, C6 to C7), and finger extension (finger extensors, C8).

In Figure 62-1, the muscles belonging to each peripheral nerve are listed in the order that their branches diverge from the main trunk. A proximal lesion of the radial nerve in the axilla would therefore cause the findings described in the previous paragraph, but a lesion of the radial nerve at the elbow, after the branch to the brachioradialis muscle, spares the triceps and brachioradialis muscles but weakens more distal muscles (i.e., wrist and finger extensors).

Some peripheral nerve lesions can be recognized at a glance, such as the wrist drop of radial neuropathy (Fig. 62-2) and the claw hand appearance of ulnar neuropathy (Fig. 62-3). A callus over the hypothenar eminence in

*Testing elbow flexion with the forearm midway between supination and pronation reveals brachioradialis weakness.[14]

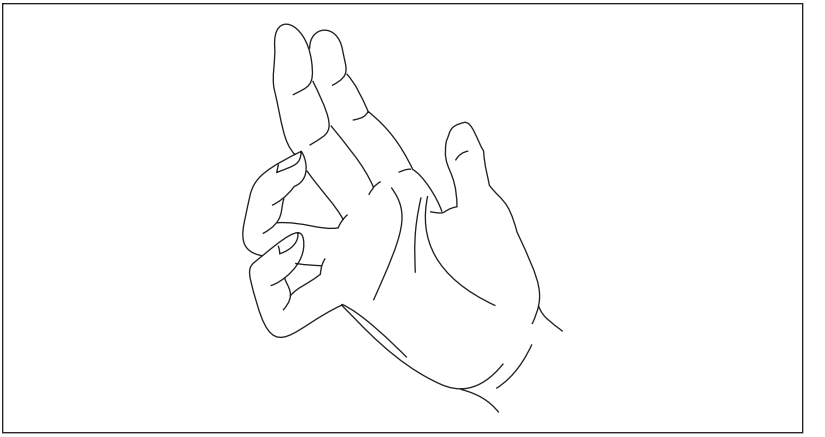


FIGURE 62-3 Claw hand of ulnar nerve palsy. All metacarpophalangeal joints are hyperextended because of paralysis of all of the interosseous muscles and unopposed action of the finger extensors (radial nerve). The hyperextension is less prominent in the index and middle fingers because the lumbricals of these digits, innervated by the median nerve, act to flex the joint. Tethering from the flexor tendons causes all interphalangeal joints to flex.

a patient with ulnar muscle weakness suggests damage to the deep branch of the ulnar nerve, caused by chronic pressure on the heel of the hand from bicycling or using a walker.[15,16]

2. Sensory Findings

Radiculopathy causes sensory loss in a dermatomal pattern (see Table 60-1 and Fig. 60-1 in Chapter 60). Brachial plexus lesions cause sensory loss from adjacent dermatomes. Peripheral nerve lesions cause the sensory loss described in Figure 62-4.

One purely sensory syndrome of the arm is **cheiralgia paresthetica,** resulting from injury to the superficial branch of the radial nerve, usually because of too tight a wristband or handcuffs. Sensory findings are confined to the radial aspect of the dorsal hand (Fig. 62-4).[17]

3. Reflexes

The three muscle stretch reflexes of the arm are the biceps muscle (musculocutaneous nerve, C5 to C6), brachioradialis muscle (radial nerve, C5 to C6), and triceps muscle (radial nerve, C7 to C8).* The finding of abnormal reflexes therefore *excludes* median and ulnar neuropathies (nerves lacking reflexes) and instead *increases* the probability of radiculopathy or plexopathy. Radial nerve lesions usually spare the brachioradialis and triceps reflexes because the branches to these muscles diverge from the main trunk proximally in the axilla and most injuries to this nerve occur at a more distal point (e.g., humeral fracture, or **Saturday night palsy**).

*Even though weakness of the triceps muscle may follow lesions in the C6 or C7 roots (C7 is most common; see Fig. 62-1), the absent triceps jerk usually results from C7 or C8 lesions.[5]

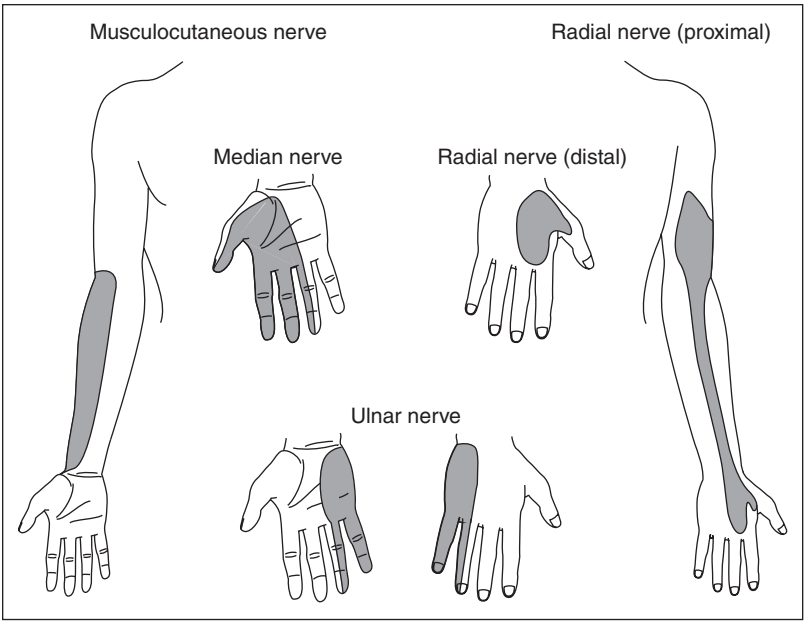


FIGURE 62-4 Sensory branches of peripheral nerves of the arm. The three figures on the left depict the *volar* surface of the arm; the three on the right, the *dorsal* surface. Proximal lesions of the radial nerve *(upper right),* near the axilla (and above the origin of the posterior cutaneous nerves of the arm and forearm) affect sensation of the posterior arm, forearm, *and* hand; more distal lesions in the radial nerve (e.g., at the elbow) affect only the dorsal hand. Proximal lesions of the median nerve affect both the palm and fingers; more distal ones (e.g., in the carpal tunnel) affect just the fingers. The sensory innervation of the medial arm and forearm derives from cutaneous nerves that branch directly off the brachial plexus.

4. Provocative Tests

One traditional test for cervical radiculopathy is the **Spurling test,** or **neck compression test.** In this test, the clinician turns and tilts the patient's head and neck toward the painful side and then adds a compressive force to the top of the head.[18] Aggravation of pain is a positive response. The **Tinel sign** and **Phalen sign** are provocative tests traditionally used to diagnose carpal tunnel syndrome. (See the section on Diagnosis of Carpal Tunnel Syndrome.) The Katz hand diagram (for carpal tunnel syndrome) appears in Figure 62-5.

C. ADDITIONAL DIAGNOSTIC CLUES

1. The Clavicle

The brachial plexus lies just behind the clavicle. Therefore, additional physical findings in the supraclavicular space, such as a mass, an adenopathy, a hemorrhage, or other evidence of trauma, suggest injury to the brachial plexus. Trauma *above* the clavicle injures roots; that *below* the clavicle injures peripheral nerves.

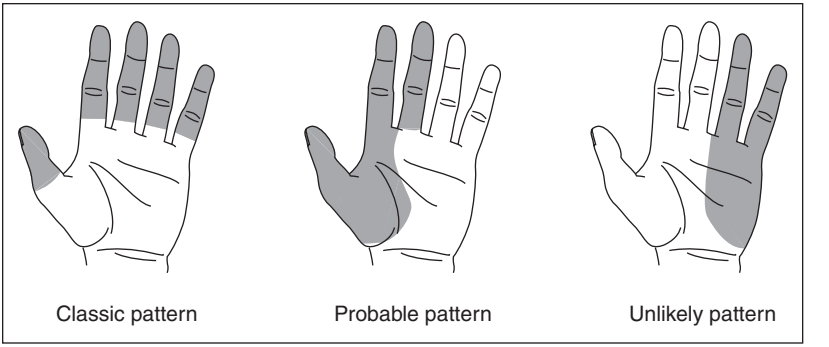


FIGURE 62-5 Katz hand diagram. The Katz hand diagram is a self-administered diagram of the hand that depicts the patient's symptoms: The "classic" pattern (example, *left*) describes symptoms affecting at least two of digits 1, 2, or 3 but sparing the palm and dorsum of the hand (digit 1 is the thumb; digit 5 is the little finger); the "probable" pattern is similar to the classic pattern, although palm symptoms are allowed; the "unlikely" pattern depicts symptoms not involving digits 1, 2, or 3.[19] Palm symptoms are not part of the "classic" pattern, because the palmar cutaneous branch of the median nerve does not travel through the carpal tunnel.[20]

2. Horner Syndrome

An associated Horner syndrome (i.e., ipsilateral small pupil and ptosis; see Chapter 20) indicates radiculopathy (C8 to T1) or a lesion of the lower brachial plexus.

D. CLINICAL SIGNIFICANCE

1. Diagnosing Cervical Radiculopathy

EBM Box 62-1 presents the diagnostic accuracy of bedside examination for cervical radiculopathy, as applied to patients presenting with neck pain or arm pain, or both. In these patients, the findings that *increase* the probability of radiculopathy the most are a reduced biceps reflex (likelihood ratio [LR] = 9.1; see EBM Box 62-1), a positive Spurling test (LR = 4.2), and reduction of any arm reflex (i.e., biceps, brachioradialis, or triceps reflex, LR = 3.6). Findings that *decrease* the probability of radiculopathy are normal rotation of the neck (i.e., can rotate to affected side >60 degrees, LR = 0.2) and the absence of arm muscle weakness (LR = 0.4).

Despite its modest accuracy, however, the Spurling test should probably *not* be performed. In other studies of cervical radiculopathy, its sensitivity is only 9% to 16%,[24,25] and in patients with rheumatoid arthritis, cervical malformations, or metastatic disease, the test risks serious injury to the spine.

2. Localizing Cervical Radiculopathy

EBM Box 62-2 presents the diagnostic accuracy of the motor, sensory, and reflex examination in patients with known cervical radiculopathy, illustrating the accuracy of findings in predicting the exact level of the lesion. According to these LRs, the best indicator of C5 radiculopathy is weak elbow flexion (LR = 5.3). A diminished biceps or brachioradialis reflex

EBM BOX 62-1

*Diagnosing Cervical Radiculopathy in Patients with Neck and Arm Pain**

Finding†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Motor Examination				
Weakness of any arm muscle[6]	73	61	1.9	0.4
Sensory Examination				
Reduced vibration or pinprick sensation in arm[6]	38	46	NS	NS
Reflex Examination				
Reduced biceps reflex[6]	10	99	**9.1**	NS
Reduced brachioradialis reflex[6]	8	99	NS	NS
Reduced triceps reflex[6]	10	95	NS	NS
Reduced biceps, triceps, or brachioradialis reflex[6]	21	94	**3.6**	0.8
Other Tests				
Spurling test[7,21–23]	21-92	84-93	**4.2**	0.6
Rotation of neck to involved side <60 degrees[7]	89	48	1.7	**0.2**

*Diagnostic standard: for *cervical radiculopathy,* nerve conduction studies,[7,21] magnetic resonance imaging (MRI),[23] or MRI and surgery.[22]

†Definition of findings: for *Spurling test,* see text.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. NS, not significant.

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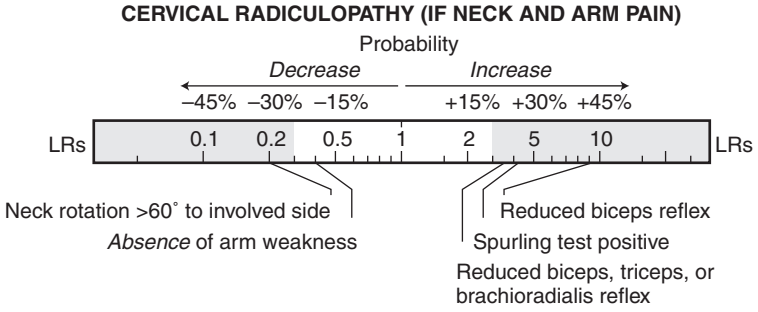

(LR = 14.2), sensory loss affecting the thumb (LR = 8.5), and weak wrist extension (LR = 2.3) indicate C6 radiculopathy. Weak elbow extension (LR = 4) and a diminished triceps reflex (LR = 3) indicate C7 radiculopathy, whereas normal elbow extensor strength modestly decreases the probability of this diagnosis (LR = 0.4). Sensory loss affecting the little finger (LR = 41.4) and weak finger flexion (LR = 3.8) indicate C8 radiculopathy.

These LRs show that each of the indicator muscles discussed in Chapter 59 (i.e., elbow flexion for C5, wrist extension for C6, elbow extension for C7, and finger flexion for C8) predict the level involved (LRs = 2.3 to 5.3). The weaker a muscle is, the more significant its localizing value.[5] Also, although certain sensory findings are diagnostic (e.g., sensory loss affecting the little finger caused by C8 radiculopathy, LR = 41.4), fewer than one in three patients with cervical radiculopathy have any sensory loss, and therefore the finding of *normal* sensation is never a compelling argument *against* cervical radiculopathy (i.e., negative LRs for all sensory findings are not significant).

Importantly, the LRs in EBM Box 62-2 apply only to patients with cervical radiculopathy. Patients with carpal tunnel syndrome may also develop hypesthesia of the thumb and those with ulnar neuropathy may develop hypesthesia of the little finger, although in these patients, the arm reflexes and arm and wrist strength are normal.

3. Plexopathy in Cancer Patients

If brachial plexopathy develops in a patient with cancer who has received radiation therapy near the shoulder, the question arises as to whether the plexopathy is due to metastatic disease or radiation injury. Findings increasing the probability of *metastatic* involvement are motor and sensory findings confined to C7 to T1 (LR = 30.9) and Horner syndrome (LR = 4.1). Findings increasing the probability of *radiation* injury are motor and sensory findings confined to C5 to C6 (LR = 8.8) and lymphedema of the ipsilateral arm (LR = 4.9).[26]

4. Peripheral Nerve Injury: Diagnosis of Carpal Tunnel Syndrome

EBM Box 62-3 summarizes the diagnostic accuracy of findings for the most common peripheral neuropathy of the arm, carpal tunnel syndrome. According to this EBM box, three findings modestly increase the probability of carpal tunnel syndrome: diminished pain sensation in the distribution of the median nerve (LR = 3.1), a square wrist ratio (defined in a footnote of EBM Box 62-3; LR = 2.7), and a "classic" or "probable" hand diagram (LR = 2.4). The finding *decreasing* the probability of carpal tunnel syndrome the most is an "unlikely" hand diagram (LR = 0.2). Several traditional tests such as the Tinel sign and Phalen sign and other novel ones such as the pressure provocation sign and flick sign (defined in a footnote in EBM Box 62-3) do not distinguish carpal tunnel syndrome from other common disorders causing hand dysesthesias (such as polyneuropathy, ulnar neuropathy, or radiculopathy, using electrodiagnosis as the diagnostic standard).[1,41]

III. THE LEG

A. INTRODUCTION

Among patients presenting with lower extremity nerve complaints, the most common neurologic diagnosis is lumbosacral radiculopathy, which almost always affects the L5 or S1 roots. (Both are affected with a similar frequency.[4,43–48])

EBM BOX 62-2
*Localizing Cervical Radiculopathy**

Finding	Sensitivity (%)	Specificity (%)	Likelihood Ratio† if Finding Is	
			Present	*Absent*
Motor Examination				
Weak elbow flexion, detecting C5 radiculopathy[5]	83	84	**5.3**	NS
Weak wrist extension, detecting C6 radiculopathy[5]	37	84	2.3	NS
Weak elbow extension, detecting C7 radiculopathy[5]	65	84	**4.0**	0.4
Weak finger flexion, detecting C8 radiculopathy[5]	50	87	**3.8**	NS
Sensory Examination				
Sensory loss affecting thumb, detecting C6 radiculopathy[5]	32	96	**8.5**	NS
Sensory loss affecting middle finger, detecting C7 radiculopathy[5]	5	98	NS	NS
Sensory loss affecting little finger, detecting C8 radiculopathy[5]	23	99	**41.4**	NS
Reflex Examination				
Diminished biceps or brachioradialis reflex, detecting C6 radiculopathy[5]	53	96	**14.2**	0.5
Diminished triceps reflex, detecting C7 radiculopathy[5,6]	15-65	81-93	**3.0**	NS

*Diagnostic standard: for *level of radiculopathy,* surgical findings[5] or electrodiagnosis.[6]
†Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.
NS, not significant.
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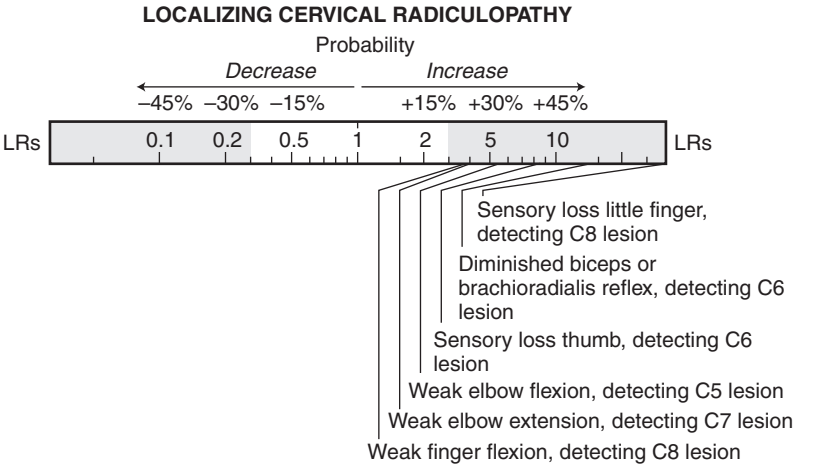

EBM BOX 62-3

*Diagnosing Carpal Tunnel Syndrome**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Hand Diagram				
"Classic" or "probable"[19]	64	73	2.4	—
"Unlikely"[19]	4	—	**0.2**	—
Motor Examination				
Weak thumb abduction[27,28]	63-66	62-66	1.8	0.5
Thenar atrophy[28–30]	4-28	82-99	NS	NS
Sensory Examination (Median Distribution)				
Hypalgesia[27,29]	15-51	85-93	**3.1**	NS
Diminished two-point discrimination[28,30,31]	6-32	64-99	NS	NS
Abnormal vibration sensation[28,31]	20-61	71-81	NS	NS
Diminished monofilament sensation[31,32]	59-98	15-59	NS	NS
Other Tests				
Tinel sign[27–31,33,34]	23-60	64-91	1.5	NS
Phalen sign[27–31,33–37]	10-91	33-86	1.4	0.7
Pressure provocation test[27,31,35,36,38]	28-63	33-74	NS	NS
Square wrist ratio[27,39]	47-69	73-83	2.7	0.5
Flick sign[34,40]	37-93	74-96	NS	NS

*Diagnostic standard: for *carpal tunnel syndrome*, abnormal motor or sensory conduction within the carpal tunnel, measured by nerve conduction testing.

†Definition of findings: for *hand diagram*, see Figure 62-5; for all *sensory findings*, perception diminished in index finger compared with ipsilateral little finger (*two-point discrimination* used compass points separated by 4 to 6 mm, *vibratory* sensation used 126-Hz or 256-Hz tuning fork, *monofilament* sensation abnormal if >2.83); for *Tinel sign*, *Phalen sign*, and *pressure provocation test*, the positive response is paresthesias in distribution of median nerve, although each test uses a different stimulus—tapping on the distal wrist crease over the median nerve (*Tinel sign*), maximal wrist flexion for 60 seconds (*Phalen sign*), and firm pressure with examiner's thumbs on palmar aspect of patient's distal wrist crease for 60 seconds (*pressure provocation test*)[41]; for *square wrist ratio*, anteroposterior dimension of wrist divided by mediolateral dimension, measured with calipers at distal wrist crease, is ≥0.70[42]; and for *flick sign*, upon asking the patient, "What do you actually do with your hand(s) when the symptoms are at their worst?" the patient demonstrates a flicking movement of the wrist and hand, similar to that employed in shaking down a thermometer.[40]

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. NS, not significant.

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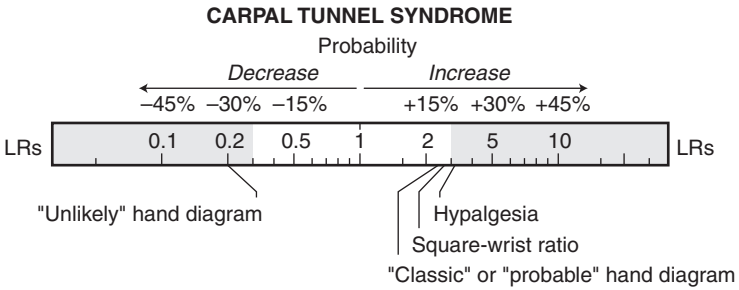

B. NEUROLOGIC FINDINGS

1. Motor Findings

Figure 62-6 presents the innervation of the muscles of the leg, showing the relationship between the different spinal roots (in columns) and the different peripheral nerves (grouped in rows).

a. Radiculopathy

Like radiculopathy of the arm, radiculopathy of the leg has two characteristics.

1. Weakness affects two or more muscles from the same spinal segment but different peripheral nerves (i.e., all muscles innervated by the same *column* in Fig. 62-6). For example, an L5 radiculopathy may affect both the dorsiflexors of the foot and toes (peroneal nerve) and inversion of the foot (tibial nerve).
2. Weakness may involve "proximal nerves" to the gluteus muscles (which cause characteristic abnormalities of the gait [i.e., either the gluteus maximus gait or Trendelenburg gait]; see Chapter 6).

b. Lumbosacral Plexopathy

Unlike brachial plexus lesions, lumbosacral plexopathies tend to affect the entire leg (L2 to S1) simultaneously, and discrete upper and lower plexus syndromes are rare.[51,52]

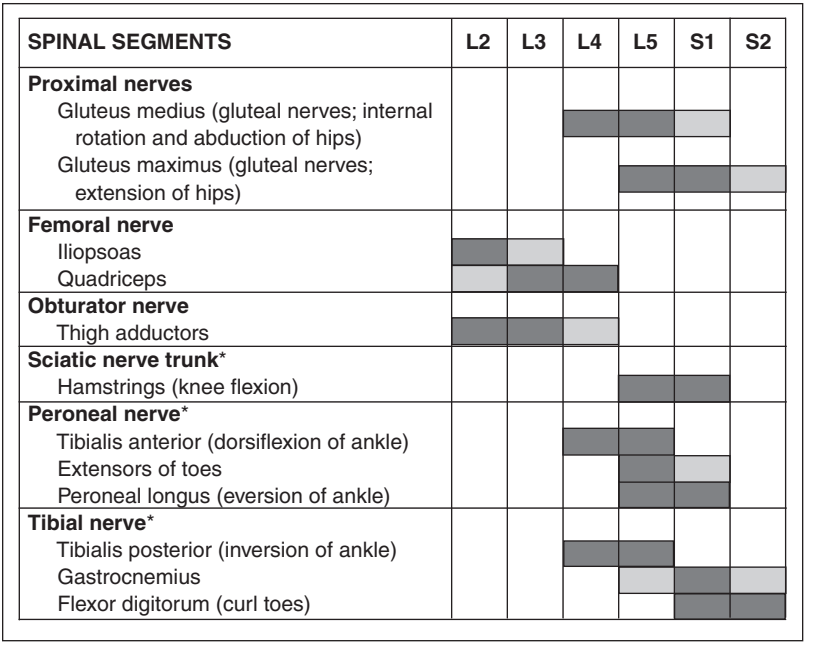

FIGURE 62-6 Innervation of the muscles of the leg. This figure indicates the spinal levels that usually *(dark gray shade)* and sometimes *(light grey shade)* contribute to the corresponding muscle; based on references 4, 8, 9, 12, 14, 49, and 50. The sciatic nerve trunk divides above the knee into the peroneal and tibial nerves; therefore, lesions of the sciatic nerve trunk affect muscles of all three branches (indicated by the asterisk in the figure; see text).

c. Peripheral Nerve Disorders

Peripheral nerve lesions weaken two or more muscles from a *single* peripheral nerve (which may belong to different spinal segments) and spare muscles from other nerves. For example, over 85% of patients with foot drop due to peroneal nerve injury have weak ankle dorsiflexion (L4 to L5) and eversion (L5 to S1) but preservation of inversion (i.e., same spinal segments but a different nerve, the tibial nerve).[53]

The sciatic trunk divides into the peroneal and tibial nerves just above the knee. Lesions of the sciatic trunk may therefore affect any of the muscles listed under sciatic trunk, peroneal nerve, and tibial nerve in Figure 62-6. Most patients with sciatic neuropathy have either greater involvement of the peroneal division (75% of patients) or equal involvement of the peroneal and tibial divisions (20% of patients). A sciatic neuropathy with greater involvement of the tibial nerve muscles is uncommon.[54]

The finding of weakness predominantly of the proximal leg muscles is unlikely in sciatic, peroneal, or tibial neuropathy because all of these nerves innervate muscles below the knee. Therefore, proximal weakness suggests femoral or obturator neuropathy; lumbosacral plexopathy or radiculopathy; or, if sensory findings are absent, muscle disease.

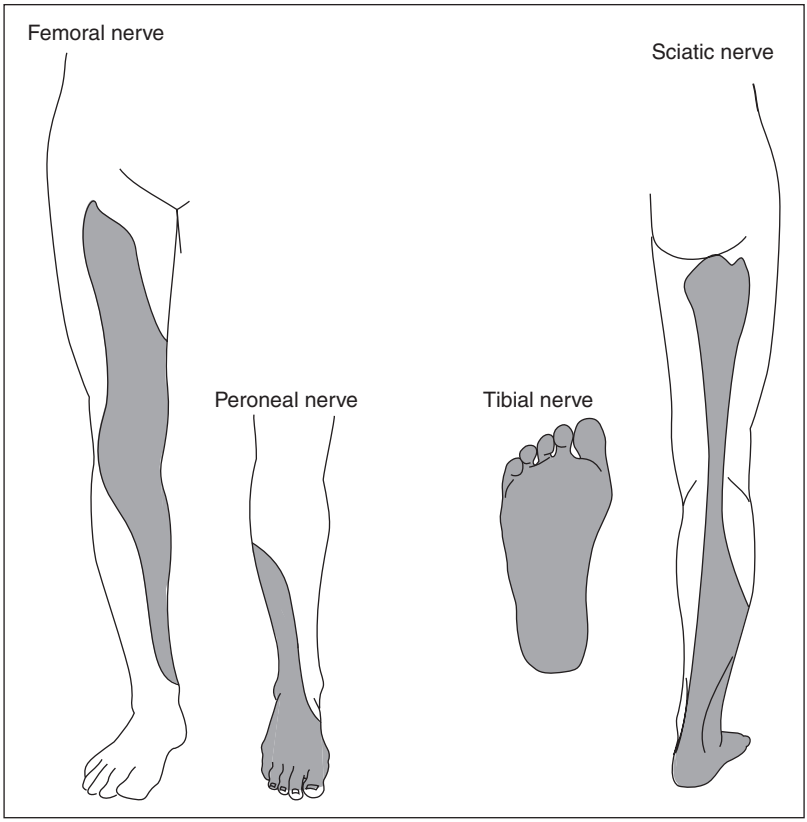

FIGURE 62-7 Sensory branches of peripheral nerves of the leg. The two figures on the left depict the *front* surface of the leg; the two on the right, the sole of the foot and *back* of the leg. The sciatic nerve trunk divides above the knee into the peroneal and tibial nerves; therefore, lesions of the sciatic nerve trunk affect sensation from all three branches (i.e., *posterior thigh,* posterior cutaneous nerve of the thigh; *lateral calf and top of foot,* peroneal nerve; and *sole of foot,* tibial nerve).

2. Sensory Findings

Radiculopathy causes sensory loss in a dermatomal pattern (see Table 60-1 and Fig. 60-1 in Chapter 60), peripheral nerve lesions cause the sensory loss described in Figure 62-7, and lumbosacral plexopathies tend to affect the entire leg.

A purely sensory syndrome is **meralgia paresthetica,** which consists of hypesthesia of the anterior and lateral thigh, usually caused by mechanical compression of the lateral femoral cutaneous nerve (e.g., obesity, pregnancy, or carpenter's belts).[55]

3. Reflexes

The muscle stretch reflexes of the leg are the quadriceps reflex (femoral nerve, L2 to L4), medial hamstring reflex (sciatic nerve, L5), and Achilles reflex (tibial nerve, S1). The peroneal nerve does not contribute to the

Achilles reflex. Consequently, in patients with foot drop, the finding of an asymmetrically diminished or absent ankle jerk *decreases* the probability of peroneal palsy and *increases* the probability of sciatic neuropathy (87% have abnormal ankle jerk)[54] or lumbosacral radiculopathy (14% to 48% have an abnormal ankle jerk).[12,43,47,56,57]

4. Provocative Tests

The **straight leg–raising test** is a traditional maneuver used to diagnose lumbosacral radiculopathy, which is usually caused by disc herniation. In the maneuver, the clinician lifts the extended leg of the supine patient, flexing the leg at the hip. In a positive response, the patient develops pain down the ipsilateral leg. (If pain develops just in the hip or back, the test is considered negative.) The **crossed straight leg–raising maneuver** consists of pain in the affected leg when the clinician lifts the contralateral healthy limb. The pathogenesis of the sign is believed to be stretching of the sciatic nerve and its nerve roots.[58]

A positive straight leg–raising test is sometimes called **Lasègue's sign,** after the French clinician Charles Lasègue (1816 to 1883), although Lasègue never published a description of the sign. His student Forst described the maneuver in his 1881 doctoral thesis, crediting Lasègue. An earlier description of the sign was published by Yugoslavian physician Lazarevic in 1880.[59–61]

C. CLINICAL SIGNIFICANCE

1. Lumbosacral Radiculopathy

EBM Boxes 62-4 and 62-5 review the diagnostic accuracy of the bedside examination in patients with nerve pain of one leg (i.e., sciatica). EBM Box 62-4 applies to all patients with sciatica. EBM Box 62-5 applies only to patients with known lumbosacral radiculopathy and addresses how accurately findings localize the level of the lesion.

In patients with sciatica, the findings that *increase* the probability of disc herniation and lumbosacral radiculopathy* are calf wasting (LR = 5.2), weak ankle dorsiflexion (LR = 4.9), the *crossed* straight leg–raising maneuver (LR = 3.4), and the absent ankle jerk (LR = 2.1). A *negative* straight leg–raising maneuver modestly *decreases* the probability of disc herniation (LR = 0.4).

Some clinicians propose performing the straight leg–raising maneuver in the seated patient whose hip is already flexed at 90 degrees; the maneuver then consists of simply extending the knee. Two studies,[73,74] however, have demonstrated that this maneuver has diminished sensitivity compared with the traditional maneuver performed in the supine patient.

In patients with sciatica and lumbosacral radiculopathy (see EBM Box 62-5), an abnormal quadriceps reflex (LR = 8.7) or weak knee extension (LR = 3.7) indicates the L3 or L4 level. The best test for L5 radiculopathy is a diminished medial hamstring reflex (LR = 6.2) or L5 sensory loss (dorsum of the foot, LR = 3.1). The best predictors for the S1 level are sensory

* An L4 to L5 disc compresses the L5 root, and an L5 to S1 disc compresses the S1 root.

EBM BOX 62-4

*Diagnosing Lumbosacral Radiculopathy in Patients with Sciatica**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Motor Examination				
Weak ankle dorsiflexion[47]	54	89	**4.9**	0.5
Ipsilateral calf wasting[47]	29	94	**5.2**	0.8
Sensory Examination				
Leg sensation abnormal[47,56,57]	16-50	62-86	NS	NS
Reflex Examination				
Abnormal ankle jerk[47,56,57,62]	14-48	73-93	2.1	0.8
Other Tests				
Straight leg–raising maneuver[44,47,57,62–66]	53-98	11-89	1.5	0.4
Crossed straight leg–raising maneuver[47,63–65,67]	22-43	88-98	**3.4**	0.8

*Diagnostic standard: for *lumbosacral radiculopathy,* surgical findings,[44,47,63,64] electrodiagnosis,[56] or magnetic resonance imaging or computed tomography[57,62,65,66] indicating lumbosacral nerve root compression.

†Definition of findings: for *ipsilateral calf wasting,* maximum calf circumference at least 1 cm smaller than contralateral side[47]; for *straight leg–raising maneuvers,* flexion at hip of supine patient's leg, extended at the knee, causes radiating pain in affected leg (pain confined to back or hip is negative response); for *crossed straight leg–raising maneuver,* raising contralateral leg provokes pain in affected leg.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. NS, not significant.

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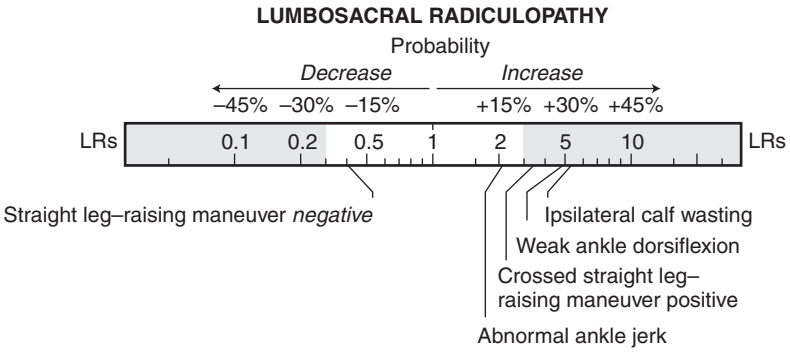

EBM BOX 62-5
*Localizing Lumbosacral Radiculopathy**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Motor Examination				
Weak knee extension, detecting L3 or L4 radiculopathy[56,68]	38-42	89	**3.7**	0.7
Weak hallux extension, detecting L5 radiculopathy[43,47,56]	12-61	54-91	1.6	NS
Weak ankle dorsiflexion, detecting L5 radiculopathy[47,69]	37-62	51-77	NS	NS
Weak ankle plantar flexion, detecting S1 radiculopathy[47,56]	26-45	75-99	NS	0.7
Ipsilateral calf wasting, detecting S1 radiculopathy[47]	43	82	2.4	0.7
Sensory Examination				
Sensory loss L5 distribution, detecting L5 radiculopathy[43,47,69]	20-53	77-98	**3.1**	0.8
Sensory loss S1 distribution, detecting S1 radiculopathy[43,47,69]	32-49	70-90	2.4	0.7
Reflex Examination				
Asymmetrical quadriceps reflex, detecting L3 or L4 radiculopathy[43,56,70]	30-57	93-96	**8.7**	0.6
Asymmetrical medial hamstring reflex, detecting L5 radiculopathy[71]	57	91	**6.2**	0.5
Asymmetrical Achilles reflex, detecting S1 radiculopathy[43,47,56,69,70,72]	45-91	53-94	2.7	0.5

*Diagnostic standard: for *level of radiculopathy,* surgical findings and preoperative myelography,[43,47,69,70,72] myelography, magnetic resonance imaging,[68] or electrodiagnosis.[56]

†Definition of findings: for *ipsilateral calf wasting,* maximum calf circumference at least 1 cm smaller than contralateral side.[47]

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

NS, not significant.

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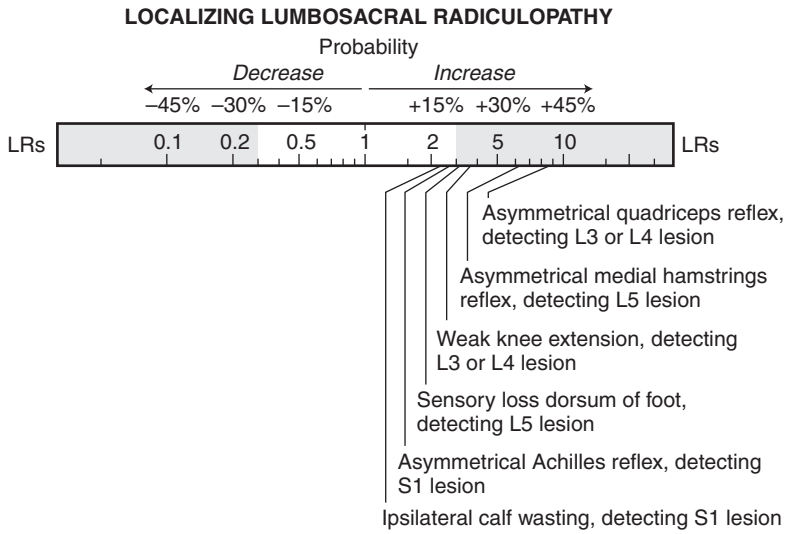

loss in the S1 distribution (lateral heel, LR = 2.4), reduced Achilles reflex (LR = 2.7), and ipsilateral calf wasting (LR = 2.4).

2. Lumbosacral Plexopathy

a. Cancer Patients

In patients with known cancer and prior pelvic irradiation who present with lumbosacral plexopathy, findings confined to one leg increase the probability of *recurrent tumor* (LR = 4.5), whereas findings in both legs increase the probability of *radiation plexopathy* (LR = 7.5).[51]

b. Diabetic Amyotrophy

Diabetic amyotrophy[75–79] (or **diabetic proximal neuropathy**) is a lumbosacral plexopathy of diabetic patients with presenting symptoms of weak thigh muscles and severe pain in the thighs or back, or both. The quadriceps, adductor, and iliopsoas muscles are weak 100% of the time, and the gluteus and hamstring muscles 50% of the time. (All are proximal muscles.) The weakness may be unilateral or bilateral, but it is always asymmetrical. Sensation is normal (70% of the time) or diminished over the thigh (30% of the time). The quadriceps reflex is absent in 80% of patients.

Although patients with diabetes also develop femoral neuropathy,[80] it affects only thigh flexion and knee extension and spares other proximal leg muscles.

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 63

Coordination and Cerebellar Testing

I. INTRODUCTION

In the 1920s, after closely observing patients with cerebellar tumors and World War I soldiers with gunshot wounds to the posterior fossa, the British neurologist Gordon Holmes concluded that four physical signs were fundamental to cerebellar disease: ataxia, nystagmus, hypotonia, and dysarthria.[1–5]

II. THE FINDINGS

A. ATAXIA

Ataxia refers to uncoordinated voluntary movements that lack the speed, smoothness, and appropriate direction seen in normal persons. Because the cerebellum's role is to organize and administer movement, testing for ataxia is only possible in patients with adequate motor strength (i.e., 4 or 5 on the MRC scale; see Chapter 59). Tests of ataxia include observation of the patient's gait (see Chapter 6) and the finger-nose-finger test, heel-knee-shin test, and rapid alternating movements test.

1. Finger-Nose-Finger Test

In this test, the seated patient takes the index finger of his outstretched hand and alternately touches his own nose and the clinician's index finger being held a couple of feet away. The patient with cerebellar disease may misjudge the range of movement (i.e., **dysmetria**), overshooting the target (i.e., **hypermetria**, as in missing the nose and slapping the hand into the patient's own face), or undershooting the target (i.e., **hypometria**, as in stopping before reaching the clinician's finger). The patient's finger also may deviate from a smooth course, especially if the clinician shifts the target during the test. As the patient's finger approaches the target, an increasing side-to-side tremor may appear (i.e., **intention tremor,** or kinetic tremor). Nonetheless, the term intention tremor can be confusing because it is applied to two distinct tremors, one of cerebellar disease and another of any action tremor that worsens as the hand approaches a target (e.g., the essential tremor that worsens as a soup spoon or cup approaches the patient's mouth; see Chapter 64). The intention tremor of cerebellar disease, however, is markedly *irregular*, of large amplitude and low frequency (e.g., <5 Hz), and associated with

dysmetria; whereas the intention tremor of essential tremor is *regular*, fine, rapid (8 to 12 Hz), and unassociated with dysmetria.[6]

2. Heel-Knee-Shin Test

In this test, the supine patient places the heel of one leg on the opposite knee and then slides it down the shin. Like the finger-to-nose test, a positive response may reveal any combination of ataxia, dysmetria, and intention tremor.

Decomposition of movement denotes an abnormal sequence of actions. For example, during the heel-knee-shin test, the patient may completely flex the hip before beginning to bend the knee, thus lifting the heel abnormally high in the air before lowering it to complete the movement.[2]

3. Rapid Alternating Movements

Difficulty with rapid alternating movements is called **dysdiadochokinesia.** (Babinski coined the original term *adiadochokinesis*.[3]) The usual test is rapid pronation and supination of the forearm, but other tasks such as clapping the hands, tapping a table, or stamping the foot are just as adequate.[3] In all these tests, the movements of patients with cerebellar disease are slower and significantly more irregular in rhythm, range, and accuracy.

B. NYSTAGMUS

1. Definition

Nystagmus is an involuntary to-and-fro oscillation of the eyes. Nystagmus may be congenital or acquired, and the movements may affect both eyes (bilateral) or just one eye (unilateral). Bilateral nystagmus may be conjugate, which means that both eyes have identical movements, or dissociated, which implies separate movements. Nystagmus may be pendular, which means that the to-and fro-movements have the same velocity, or rhythmic, which means that the movement is slow in one direction and quick in the other. (Rhythmic nystagmus is usually called jerk nystagmus.) **Jerk nystagmus** is named after the direction of the quick component (e.g., right conjugate jerk nystagmus). Finally, the direction of the nystagmus may be horizontal, vertical, or rotatory.

2. Patterns of Nystagmus

Although nystagmus is a complicated subject that sometimes defies general principles,* several well-recognized patterns are described below.

a. Cerebellar Nystagmus

The most common nystagmus of cerebellar disease is a conjugate horizontal jerk nystagmus on lateral gaze. (See the section on Clinical Significance.)

One rare type of nystagmus, **rebound nystagmus,** has been described only in patients with cerebellar disease.[8–10] To test for this nystagmus, the patient first looks in one direction (say, to the right). In patients with a

*One famous neuro-ophthalmologist once advised his students to "never write on nystagmus, it will lead you nowhere."[7]

positive response, a brisk nystagmus with its fast component to the right appears. If the patient continues looking in this direction for about 20 seconds, the nystagmus fatigues and disappears (sometimes even reversing direction). The patient then returns his eyes to the primary position (i.e., straight ahead), and nystagmus to the left, not present initially, appears, although it fatigues over time. In these patients, the direction of the nystagmus in primary gaze can be reversed at will, depending on whether the patient looks first to the left or to the right.[8]

b. Other Patterns of Nystagmus

Other useful patterns of nystagmus are optokinetic nystagmus (see Chapter 56), the nystagmus of internuclear ophthalmoplegia (see Chapter 57), and the nystagmus of vestibular disease (see Chapter 66).

3. Effect of Retinal Fixation

Retinal fixation means the patient is focusing his or her eyes on an object. Spontaneous nystagmus that diminishes during retinal fixation argues that the responsible lesion is located in the peripheral vestibular system; nystagmus that increases or remains unchanged during fixation argues that the lesion is in the central nervous system (i.e., the brainstem or cerebellum). Neuro-ophthalmologists usually use electronystagmography to detect the effects of fixation (by comparing eye movements with the eyes open with those with the eyes closed), but general clinicians can accomplish the same examination during direct ophthalmoscopy: In a dimly lit room, the clinician examines the optic disc of one eye and compares its movements as the patient fixes the opposite eye on a distant target with those when the patient's opposite eye is covered. If rhythmic movements of the optic disc first appear or worsen when the fixating eye is occluded, a peripheral vestibular disturbance is likely.[11] A simpler version of this test, using just a penlight without ophthalmoscopy, has been proposed.[12]

C. HYPOTONIA

The limbs of patients with cerebellar disease offer no resistance to passive displacement (hypotonia; see Chapter 59), sometimes resembling (in the words of Gordon Holmes) the "muscles of a person deeply under an anaesthetic, or of a corpse recently dead."[1] Holding the forearms vertically causes the wrist to bend to an angle much more acute than normal. Displacing the patient's outstretched arm downward causes abnormally wide and prolonged up-and-down oscillations, even when the patient is requested to resist such movements. Striking the patellar tendon causes pendular knee jerks, traditionally defined as three or more swings,[13] although, as already stated in Chapter 59, this threshold will have to be revised upward because many normal persons also demonstrate three or more swings.[14]

D. DYSARTHRIA

The speech of patients with cerebellar disease is slow, slurred, and irregular in volume and rhythm, findings that are collectively referred to as **dysarthria.** In contrast to patients with aphasia, however, patients with

TABLE 63-1 Unilateral Cerebellar Lesions*

Physical Finding†	Frequency (%)‡
Ataxia	
Gait ataxia	80-93
Limb ataxia	
Dysmetria	71-86
Intention tremor	29
Dysdiadochokinesia	47-69
Nystagmus	54-84
Hypotonia	76
Pendular knee jerks	37
Dysarthria	10-25

*Diagnostic standard: clinical imaging, surgical findings, or postmortem examination.
†Definition of findings: see text.
‡Results are overall mean frequency or, if statistically heterogeneous, the range of values.
Data from 444 patients from references 13 and 15.

dysarthria can name objects, repeat words, comprehend language, and speak sentences with words whose order makes sense.

III. CLINICAL SIGNIFICANCE

A. INDIVIDUAL FINDINGS

1. Ataxia

Ataxia of gait is the most common finding in all cerebellar syndromes (Table 63-1), and, therefore, examination of the gait should be part of the survey of every patient with suspected cerebellar disease. Many patients with cerebellar disease have difficulty walking, despite the absence of all other findings of limb ataxia.

Simple measurements of the patient's dysdiadochokinesia—such as how quickly and accurately the patient can alternately tap two buttons spaced about 12 inches apart*—are accurate measures of ataxia that correlate well with other measures of disability.[16]

2. Nystagmus

Seventy-five percent of patients with cerebellar nystagmus have a conjugate horizontal jerk nystagmus that appears on lateral gaze (15% of cases are rotatory nystagmus and 10% vertical nystagmus). Nonetheless, a horizontal jerk nystagmus is not specific for cerebellar disease and also occurs in peripheral vestibular disease and other central nervous system disorders. The direction of the jerk nystagmus has less localizing value than tests of ataxia. (See the section on Cerebellar Hemisphere Syndrome.)

*Ninety percent of normal persons can accomplish at least 32 taps within 15 seconds, whereas 90% of patients with cerebellar ataxia cannot.[16]

The clinical utility of rebound nystagmus is limited because it is a late finding, and all patients described with the finding have had many other obvious cerebellar signs.[8,9]

3. Dysarthria

Dysarthria, the least common of the fundamental cerebellar signs (see Table 63-1), appears more often with lesions of the left cerebellar hemisphere than with those of the right hemisphere.[17]

B. CEREBELLAR SYNDROMES

Most patients with cerebellar disease present with difficulty in walking or a headache, or both.[13,15] In adults, there are four common cerebellar syndromes, each of which is characterized by a different distribution of the principal cerebellar signs.

1. Cerebellar Hemisphere Syndrome

a. Cerebellar Findings

Table 63-1 presents the physical findings of 444 patients with focal lesions (mostly tumors) confined to one hemisphere.[13,15] According to traditional teachings, cerebellar signs appear on the side of the body *ipsilateral* to the lesion. This teaching proved generally correct in the patients of Table 63-1, in whom signs of limb ataxia (i.e., dysmetria, intention tremor, dysdiadochokinesia) were unilateral 85% of the time, and, if unilateral, were on the side ipsilateral to the lesion 80% to 90% of the time. These patients also had more hypotonia on the side of the lesion and tended to fall toward the side of the lesion when walking.

Nystagmus has less localizing value. When present, nystagmus is unilateral in only 65% of patients, and in these patients, the direction of nystagmus points to the side of the lesion only 70% of the time.

b. Associated Findings

Despite having a lesion confined to the cerebellum, patients with structural cerebellar lesions may also have the following:

1. Cranial nerve findings (10% to 20% of patients; usually of cranial nerves V, VI, VII, or VIII, ipsilateral to the side of the lesion 75% of the time)[13,15]
2. Altered mental status (38% of patients, from compression of the brainstem or complicating hydrocephalus)
3. Upper motor neuron signs such as hyperactive reflexes and the Babinski sign (28% of patients)
4. Papilledema (68% of patients)

In contrast, severe weakness and sensory disturbance are both uncommon, affecting only 4% of patients.

2. Anterior Cerebellar Degeneration (Rostral Vermis Syndrome)

In contrast to the cerebellar hemisphere syndrome, patients with anterior cerebellar degeneration (rostral vermis syndrome)[18] have ataxia of gait (100%) and of both legs (88%), with relative sparing of the arms (only

16% of patients). Nystagmus and dysarthria also are much less frequent (9% for both findings). This syndrome most often results from chronic alcohol ingestion.

3. Pancerebellar Syndrome

This syndrome causes the same signs as those listed in Table 63-1, but instead of being on one side of the body, the cerebellar signs are symmetrical. Causes include drug intoxication (e.g., phenytoin), inherited disorders, and paraneoplastic syndromes.

4. Cerebellar Infarction

The physical signs of cerebellar infarction resemble those of the cerebellar hemisphere syndrome described above, with three exceptions. In infarction,

1. All signs appear *abruptly*.
2. Dysarthria is more prominent (44% of patients).
3. Weakness occurs more often (22% have hemiparesis; 24% have tetraparesis).[19–22]

The three main arteries supplying the cerebellum are the superior cerebellar artery, anterior inferior cerebellar artery, and posterior inferior cerebellar artery.[23] An associated lateral medullary syndrome (see Table 60-2 in Chapter 60) suggests an infarct in the distribution of the posterior inferior cerebellar artery.[21,24]

The **acute vestibular syndrome**—the abrupt onset of sustained vertigo, nausea and vomiting, and imbalance—raises the possibility of cerebellar infarction as well as peripheral vestibular disease. This subject is fully discussed in Chapter 66.

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 64

Tremor and Parkinson Disease

I. INTRODUCTION

In a remarkably concise essay written almost 200 years ago, the British physician James Parkinson described in nine pages most of the features we now associate with **Parkinson disease**—insidious onset, asymmetrical resting tremor, bradykinesia, postural instability, sialorrhea, flexed posture, shuffling steps, and festinating gait.[1] One sign Parkinson failed to describe was rigidity, an oversight leading many historians to suggest that Parkinson had actually never touched a patient and instead had based his conclusions solely on observation.[2] In 1877, Charcot provided the first full account of Parkinson disease that included rigidity.[2]

II. THE FINDING

The three cardinal findings in Parkinson disease are resting tremor, bradykinesia, and cogwheel rigidity (rigidity is discussed fully in Chapter 59). A patient with two of these three findings is said to have **parkinsonism.**

A. TREMOR

A **tremor** is a rhythmic involuntary oscillation of a body part. There are two basic tremors: (1) resting tremor and (2) action tremor.[3,4]

Resting tremors occur when muscles are inactive and the body part is completely supported against gravity. Action tremors occur during voluntary contraction of muscle and are further subdivided into **postural tremors** (e.g., when holding the arms outstretched), **intention tremors** (e.g., when a limb approaches a visually guided target as in finger-nose-finger testing), **task-related tremors** (e.g., when pouring water from cup to cup), and **isometric tremors** (e.g., when making a fist or gripping the examiner's fingers).* One confusing tremor is a postural tremor (i.e., action tremor) that continues after the examiner supports the outstretched arms (thus mimicking a resting tremor): If such patients are given a glass of water to drink, the amplitude of a true postural tremor increases or remains the same as the glass approaches the patient's mouth, whereas that of a genuine resting tremor diminishes in amplitude.

Intention tremor and *task-related tremor* are sometimes collectively called *kinetic tremors* (i.e., action tremors appearing during movement).

Movement disorder specialists have identified at least a dozen types of tremor, the most common being essential tremor and parkinsonian resting tremor.[3,4] **Essential tremor** is a 4- to 12-Hz* bilateral postural tremor that usually involves the hands or forearms. It may be asymmetrical and have an associated kinetic component (i.e., associated intention or task-related component). In contrast, the **parkinsonian resting tremor** (which is only one of the different tremors that may appear in Parkinson disease) is a 4- to 6-Hz "pill-rolling" tremor of the fingertips, hand, or forearm. It begins *asymmetrically,* initially in one hand, followed years later by involvement of the contralateral hand. Essential tremor may involve the jaw, tongue, or head (producing a characteristic rhythmic "nodding yes" or "shaking no" motion); the parkinsonian tremor may involve the jaw, lips, or tongue but spares the head.

B. BRADYKINESIA

Patients with bradykinesia have a reduced blink rate. Normal persons blink about 24 ± 15 times per minute, whereas patients with Parkinson disease blink more slowly, about 12 ± 10 times per minute. Severely symptomatic patients blink only 5 to 6 times per minute.[5,6] The contrast between the reduced spontaneous blink rate but exaggerated reflex blink rate (during glabellar reflex testing; see Chapter 61) is striking in Parkinson disease. During treatment with levodopa, the spontaneous blink rate increases as the reflex rate during glabellar testing diminishes.[7,8]

C. ATYPICAL FEATURES OF PARKINSON DISEASE

Confirming the diagnosis of Parkinson disease during life is difficult because the disorder still lacks biochemical, genetic, or imaging diagnostic standards. In patients diagnosed during life with Parkinson disease, 10% to 25% have an alternative diagnosis discovered at postmortem examination.[9–12] These alternative mimicking conditions consist of a variety of neurodegenerative disorders collectively referred to as **Parkinson-plus syndromes,** disorders that tend to progress more rapidly, present more symmetrically, and respond less well to levodopa than does Parkinson disease.[13] Several clinical clues, called atypical features, suggest one of the following mimicking Parkinson-plus Disorders[9]:

1. Marked autonomic dysfunction (e.g., postural hypotension, neurogenic bladder or bowel)
2. Early severe dementia
3. Pyramidal tract findings (i.e., hyperreflexia, spasticity, or the Babinski sign; see Chapter 59)
4. Cerebellar findings (i.e., limb ataxia, gait ataxia, or nystagmus; see Chapter 63)
5. Supranuclear gaze palsy (i.e., difficulty looking down)

*Hz indicates hertz, a unit of frequency equal to one cycle per second. A parkinsonian tremor of 5 Hz, therefore, has 300 oscillations per minute (i.e., 5 × 60), thus explaining why this tremor sometimes produces electrocardiographic artifacts mimicking tachyarrhythmias (e.g., atrial flutter or ventricular tachycardia).

6. Use of neuroleptic medications
7. Multiple prior strokes
8. Encephalitis at the time of onset of symptoms

The most common Parkinson-plus syndromes are multiple system atrophy, progressive supranuclear palsy, and vascular parkinsonism.*

D. TANDEM GAIT TESTING

The gait of patients with Parkinson disease has a much narrower base than that of most Parkinson-plus patients, leading neurologists to wonder whether tandem gait testing might more easily provoke imbalance in patients with Parkinson-plus disorders, thus distinguishing them from Parkinson disease. According to this hypothesis, inability to complete 10 tandem steps would suggest a Parkinson-plus disorder, not Parkinson disease (see also Chapter 6).

E. APPLAUSE SIGN (CLAPPING TEST)

The **applause sign** refers to the tendency of some patients to continue clapping their hands in response to instructions to clap three times. Initially, the sign was proposed as a way to distinguish progressive supranuclear palsy (more than three claps, or a positive applause sign) from Parkinson disease (only three claps),[14] although subsequently a positive applause sign has been noticed in many other Parkinson-plus disorders.[15] To elicit the sign, the clinician asks the patient to clap three times as quickly as possible and then demonstrates the clapping. The patient's response is normal if he or she claps just three times and "abnormal" if the patient claps more than three times. The exact cause of the abnormal applause sign is unknown, although many believe it could be related to frontal disinhibition.[16]

III. CLINICAL SIGNIFICANCE: DIAGNOSING PARKINSON DISEASE

In patients with combinations of tremor, bradykinesia, and rigidity (i.e., patients with parkinsonism), the probability of pathologic Parkinson disease is increased (likelihood ratio [LR] = 4.1; EBM Box 64-1) if all three of the following additional features are present:

1. All three cardinal findings are present
2. Asymmetrical onset
3. Absence of atypical features (as defined earlier)

Also, the following three symptoms increase the probability of Parkinson disease: the complaint of feet suddenly freezing in doorways (LR = 4.4), voice progressively becoming softer (LR = 3.2), or handwriting becoming progressively smaller (i.e., micrographia, LR = 2.7).[26,27] The inability to

*__Multiple system atrophy__ has three phenotypes: *Shy-Drager syndrome* (early autonomic insufficiency is prominent), *olivopontocerebellar atrophy* (cerebellar signs are prominent), and *striatonigral degeneration*. (Both cerebellar and pyramidal tract signs are prominent.) **Vascular parkinsonism** refers to parkinsonism that appears abruptly after a stroke; neuroimaging reveals subcortical or deep brain infarction.

EBM BOX 64-1
*Suspected Parkinson Disease**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Diagnosing Parkinson Disease				
Unable to perform 10 tandem steps[17]	8	18	**0.1**	**5.0**
Positive applause sign[14–16]	3-30	29-42	**0.3**	2.3
Tremor, bradykinesia, rigidity[9]				
3 of 3 present	64	71	2.2	0.5
3 of 3 present, asymmetry, no atypical features	68	83	**4.1**	0.4
Good response to levodopa[18]	77	58	1.8	0.4
Diagnosing Multiple System Atrophy				
Rapid progression[18,19]	54-64	78	2.5	0.6
Absence of tremor[18–20]	39-91	39-76	NS	NS
Speech and/or bulbar signs[18]	87	79	**4.1**	**0.2**
Autonomic dysfunction[18–20]	73-84	74-90	**4.3**	**0.3**
Cerebellar signs[18,20]	32-44	90-99	**9.5**	0.7
Pyramidal signs[18,20]	31-50	85-93	**4.0**	NS
Dementia[18,20]	17-25	36-45	**0.3**	1.9
Diagnosing Progressive Supranuclear Palsy				
Downgaze palsy AND postural instability within first year of symptoms[21]	50	99	**60.0**	0.5
Diagnosing Vascular Parkinsonism				
Pyramidal tract signs[22–25]	26-68	95-99	**21.3**	0.5
Lower body parkinsonism[22–24]	59-69	88-91	**6.1**	0.4

*Diagnostic standard: for *Parkinson disease*, careful clinical observation[14–17] or postmortem examination of brain revealing depletion of nigral pigmented neurons with Lewy bodies in remaining nerve cells (all other studies); for *vascular parkinsonism*, infarction on neuroimaging or postmortem examination revealing cerebrovascular disease and absence of depigmentation and Lewy bodies.[25]

†Definition of findings: for *atypical features*, see text; for *rapid progression*, the appearance of unsteadiness and tendency to fall at initial visit[18] or within 3 years of onset of first symptom[19]; for *speech or bulbar findings*, dysarthria, dysphagia, and excessive sialorrhea; for *autonomic dysfunction*, symptomatic postural hypotension, urinary urge or fecal incontinence, or neurogenic bladder[18] or abnormalities on formal testing of cardiovascular reflexes[19]; for *cerebellar findings*, *applause sign*, and *pyramidal tract findings*, see text.

All LRs apply *only* to patients with suspected Parkinson disease (i.e., some combination of tremor, bradykinesia, and rigidity).

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

NS, not significant.

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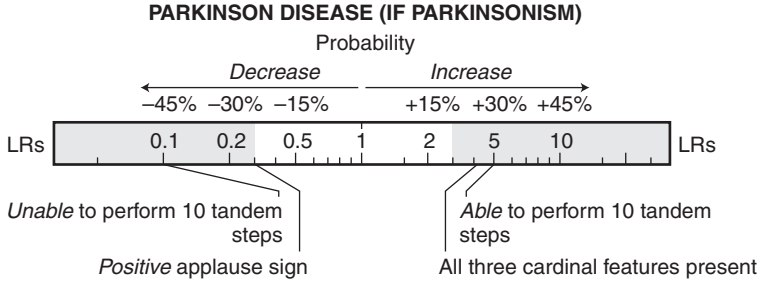

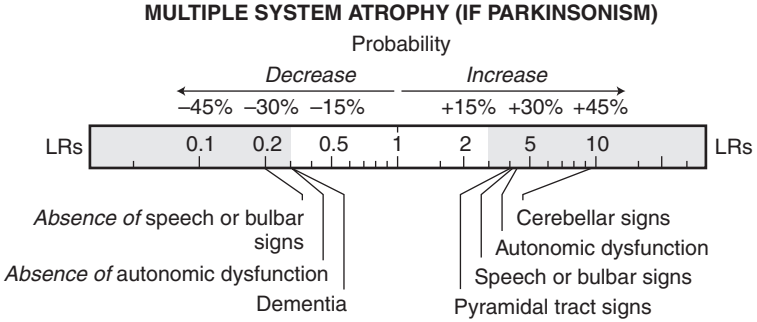

perform 10 tandem steps (LR = 0.1) and a positive applause sign (LR = 0.3) decrease the probability of Parkinson disease.

In patients with parkinsonism, the presence of cerebellar signs (LR = 9.5; see EBM Box 64-1), autonomic dysfunction (LR = 4.3), or speech/bulbar signs (LR = 4.1) increase the probability of multiple system atrophy. The combination of a downgaze palsy and early postural instability from axial rigidity is pathognomonic for progressive supranuclear palsy (LR = 60). The presence of pyramidal tract signs increases the probability of vascular parkinsonism (LR = 21.3) and multiple system atrophy (LR = 4). Parkinsonian findings confined to the legs suggest vascular parkinsonism (LR = 6.1), as does abrupt onset of parkinsonian findings (LR = 21.9).[23,24]

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 65

Hemorrhagic versus Ischemic Stroke

I. INTRODUCTION

Stroke is the third leading cause of death in the United States.[1] The two fundamental subtypes of strokes are **hemorrhagic stroke** (intracerebral hemorrhage or subarachnoid hemorrhage) and **ischemic stroke** (infarction from thrombosis or embolism). In the United States, 87% of strokes are ischemic and 13% are hemorrhagic (10% are intracerebral and 3% are subarachnoid),[1] but in some developing nations, more than 50% of strokes are hemorrhagic.[2] All patients with stroke require prompt neuroimaging to distinguish these subtypes and direct management, although bedside examination is still helpful when neuroimaging is unavailable and while patients are being monitored during treatment.[3]

Since the times of ancient Babylonia, Greece, and Rome, clinicians have recognized stroke, calling it *apoplexy*.[4,5] Although ancient physicians understood that damage to one cerebral hemisphere produced weakness on the opposite side of the body, modern concepts of cerebrovascular disease were lacking until 1655, when Johann Jakob Wepfer, a Swiss physician, first described intracranial hemorrhage, both its clinical features and postmortem findings.[6]

II. FINDINGS

Both cerebral hemorrhage and infarction cause abrupt *deficits* of neurologic function, such as hemiparesis, aphasia, hemisensory disturbance, ophthalmoplegia, visual field defects, and ataxia. Nonetheless, cerebral hemorrhage differs from infarction by the presence of an *expanding* hemorrhage within the brain, which may produce *additional* symptoms beyond neurologic deficits (Fig. 65-1). Examples of additional symptoms are prominent vomiting (from increased intracranial pressure), severe headache (from meningeal irrigation or increased intracranial pressure), rapid progression of neurologic deficits (from expansion of the hematoma), coma (from bilateral cerebral dysfunction, uncal herniation, or posterior fossa mass effect), and bilateral Babinski signs (from bilateral dysfunction).

Over the last several decades, clinicians have developed several different stroke scores to distinguish hemorrhagic from ischemic infarction,[3] but

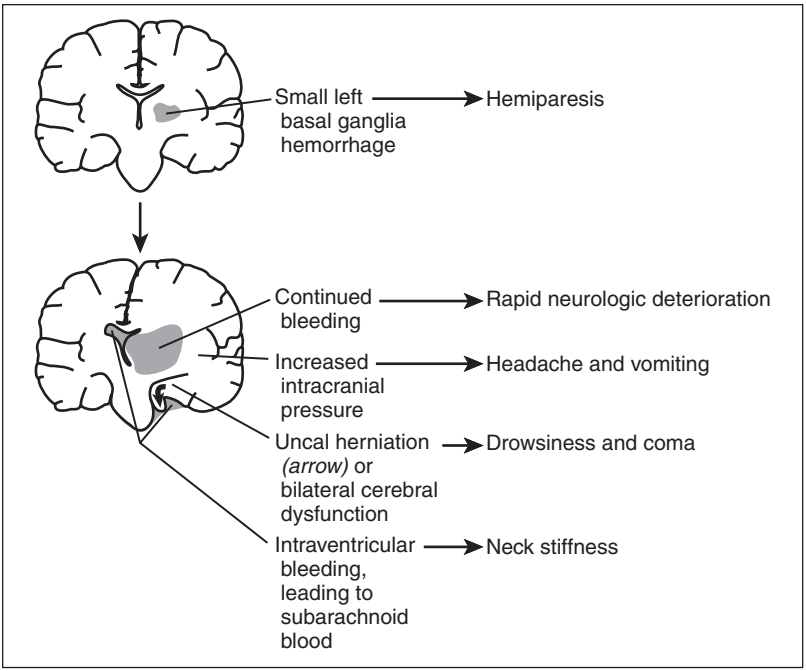

FIGURE 65-1 "Additional" findings of hemorrhagic stroke (coronary section of brain). *Top half:* There is a small hemorrhage in the left basal ganglia, causing hemiparesis and clinical findings indistinguishable from ischemic stroke. *Bottom half:* Progressive intracranial hemorrhage causes the "additional" findings of hemorrhage, including rapid neurologic deterioration, headache, vomiting, coma, and neck stiffness. Intraventricular blood follows the normal path of cerebrospinal circulation through the median and lateral apertures of the fourth ventricle to reach the subarachnoid space at the base of the brain. (Only rarely does intracerebral hemorrhage directly rupture in the subarachnoid space.)

the most widely used is the Siriraj stroke score, developed by Poungvarin and others[7] in 1991 (Table 65-1).

III. CLINICAL SIGNIFICANCE

The data in EBM Boxes 65-1 and 65-2 stem from the analysis of 35 studies enrolling more than 9000 patients with stroke from across the globe. The diagnosis of hemorrhagic stroke in these studies includes both intracranial and subarachnoid hemorrhage, although relatively few patients had subarachnoid hemorrhage. Diagnostic accuracy of bedside findings is the same if patients with subarachnoid hemorrhage are excluded.[3]

A. SYMPTOMS

According to a systematic review,[3] the following symptoms increase the probability of hemorrhagic stroke: seizures accompanying the neurologic deficit (likelihood ratio [LR] = 4.7), vomiting (LR = 3), severe headache

TABLE 65-1 Siriraj Stroke Score*

Characteristic	Points
Mental status†	
Coma or semicoma	+ 5
Drowsy or stupor	+ 2.5
Vomiting	+ 2
Headache within 2 hours	+ 2
Diastolic blood pressure	+ 0.1 × DBP in mm Hg
Diabetes, angina, or intermittent claudication	−3
Correction factor	−12

*From reference 7. Interpretation of total score: >1, hemorrhage; −1 to 1, uncertain; <−1, infarction.
†*Alert mental status* receives 0 points.
DBP, diastolic blood pressure.

EBM BOX 65-1
*Hemorrhagic Stroke**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Vital Signs				
Systolic BP >220 mm Hg[8]	17	96	**4.0**	NS
Systolic BP <160 mm Hg[9]	29	30	0.4	2.4
Additional Findings				
Mental status[7,10–14]				
Coma	18-51	90-99	**6.3**	—
Drowsy	17-59	—	1.7	—
Alert	21-54	21-41	0.5	—
Neurologic deterioration during first 3 hours[15]	77-81	85-88	**5.8**	**0.2**
Kernig sign or Brudzinski sign[15,16]	3-15	98	NS	NS
Neck stiffness[2,7,9,15–17]	16-48	81-98	**5.4**	0.7
Babinski response[7,17,18]				
Both toes extensor	12-22	90-95	2.4	—
Single toe extensor	30-73	—	NS	—
Both toes flexor	8-48	40-75	0.5	—

EBM BOX 65-1
Hemorrhagic Stroke—cont'd

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Neurologic Deficits				
Deviation of eyes[11,12,17,18]	27-62	64-81	1.9	0.7
Hemiparesis[10–12,17–19]	17-87	12-73	NS	NS
Aphasia[11,12,17,20]	12-35	62-92	NS	NS
Hemisensory disturbance[10–12,17,18]	0-80	40-98	1.3	NS
Hemianopia[11,12]	35	73	1.3	NS
Ataxia[11,12]	15	80	NS	NS
Other Findings				
Cervical bruit[9,11,12]	1	81-93	**0.1**	NS
Atrial fibrillation on ECG[10,15,17,18]	1-21	69-91	0.4	1.2

*Diagnostic standard: for *hemorrhagic stroke*, computed tomography (all studies), sometimes with magnetic resonance imaging[14,21] or autopsy.[14,22]

†Definition of findings: for *both toes extensor*, the Babinski response is *present* on both feet; for *both toes flexor*, the Babinski response is *absent* in both feet.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

ECG, electrocardiogram; NS, not significant.

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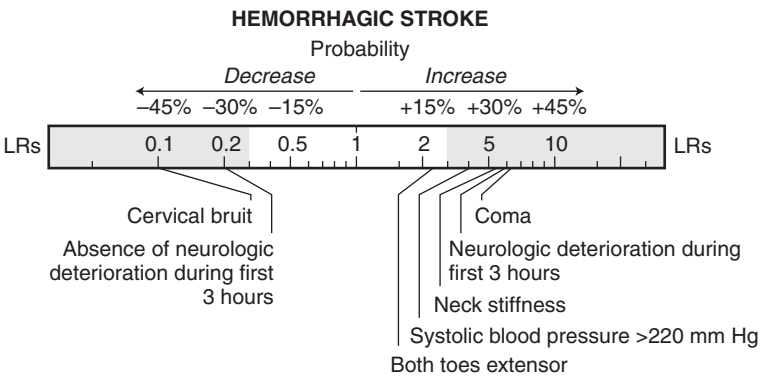

(LR = 2.9), and loss of consciousness (LR = 2.6). Chronic anticoagulation with warfarin also increases the probability of hemorrhagic stroke (LR = 5.4).[8,20] A history of prior transient ischemic attack decreases the probability of hemorrhagic stroke (LR = 0.3).

EBM BOX 65-2
*Siriraj Score for Hemorrhagic Stroke**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Siriraj score "hemorrhage" (>1)	23-87	65-99	**5.4**	—
Siriraj score "uncertain" (−1 to 1)	1-51	—	NS	—
Siriraj score "infarction" (<−1)	3-53	13-60	**0.3**	—

*Based on references 2, 7, 15–17, 19, and 22–38.
†For calculation of *Siriraj score*, see Table 65-1.
‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.
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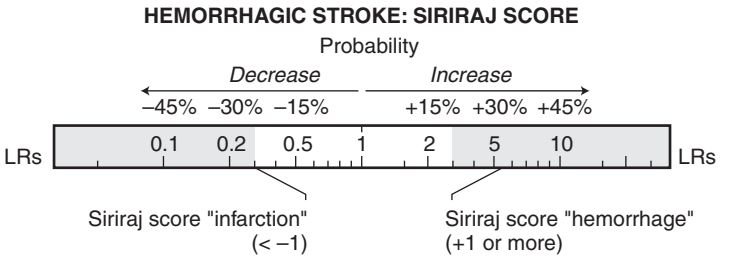

B. INDIVIDUAL PHYSICAL FINDINGS

According to the LRs in EBM Box 65-1, the physical findings that increase the probability of hemorrhagic stroke are coma (LR = 6.3), neurologic deterioration during the first 3 hours (LR = 5.8), neck stiffness (LR = 5.4), systolic blood pressure higher than 220 mm Hg (LR = 4), and Babinski response in both toes (LR = 2.4).

The findings that decrease the probability of hemorrhagic stroke are cervical bruit (LR = 0.1) and absence of neurologic deterioration during the first 3 hours (LR = 0.2).

As expected (see the section on Findings), the presence or absence of neurologic *deficits*—hemiparesis, hemisensory disturbance, deviation of eyes, aphasia, hemianopia, and ataxia—fail to distinguish hemorrhagic stroke from ischemic stroke.

C. COMBINED FINDINGS (SIRIRAJ STROKE SCORE)

A Siriraj score greater than 1 (hemorrhage) increases the probability of hemorrhagic stroke (LR = 5.4; see EBM Box 65-2), whereas a score less than −1 (infarction) decreases the probability (LR = 0.3). Nonetheless, in these studies, an average of 20% of patients with stroke (range, 8% to 48%) were classified as "uncertain" by the Siriraj score, a score lacking diagnostic value. (LR is not significant.)

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 66

Acute Vertigo and Imbalance

I. INTRODUCTION

Acute, sustained vertigo and imbalance, often associated with nausea and vomiting, is collectively called the **acute vestibular syndrome** (or **acute vestibulopathy**). Most affected patients have benign disorders of the peripheral vestibular system, dysfunction of either the vestibular nerve **(vestibular neuritis)** or the labyrinth **(labyrinthitis).** A few affected patients, however, are experiencing serious strokes of the cerebellum or brainstem, problems that may rapidly cause coma and death from acute hydrocephalus or brainstem compression.[1]

The full syndrome of brainstem stroke causing vertigo is described in Chapter 60 (see lateral medullary, or Wallenberg, stroke) and that of cerebellar infarction appears in Chapter 63. Nonetheless, about 10% of strokes causing dizziness (especially cerebellar infarctions) present as *isolated* dizziness or vertigo, and they lack other telltale cerebellar and brainstem findings.[2] This chapter focuses on these patients and discusses additional bedside findings that help distinguish stroke from peripheral vestibular disease.

II. THE FINDINGS

The additional findings that suggest stroke in acutely dizzy patients are *normal* bilateral vestibulo-ocular reflexes (detected by the head impulse test), skew deviation, abnormal visual tracking (saccadic pursuit), and direction-changing nystagmus.

A. THE VESTIBULO-OCULAR REFLEX

In healthy humans, any head movement is involuntarily matched by opposing conjugate movements of the eyes through the actions of the **vestibulo-ocular reflex.** Without this reflex, it would be impossible to focus on objects when walking, riding, or even breathing.* The accuracy and efficiency of this reflex can be easily demonstrated by holding a pencil vertically in front of the face and moving it side to side through a 10-degree

*A dramatic description of life without the vestibulo-ocular reflex appears in the story "Living without a Balancing Mechanism,"[3] written by a physician with bilateral vestibular damage after long-term streptomycin treatment. He describes difficulty reading in bed and having to brace his "head between two metal bars at the head of the bed (to) minimize the effect of the pulse beat, which made the letters on the page jump and blur."

arc, five times per second. The pencil will appear blurred because the retina cannot compensate quickly enough for the shifting image. If the experiment is repeated with the pencil stationary and the head moved back and forth through the same arc and with the same frequency, the pencil remains sharply defined. The eye movements are *identical* in the two examples, yet only in the second experiment is the vestibulo-ocular reflex employed to keep the pencil in focus.[4]

The vestibulo-ocular reflex stabilizes retinal images by specific connections between the semicircular canals and eye muscles (Fig. 66-1). When there is unilateral damage to the neural pathways of this reflex, two consequences follow:

1. Unopposed stimulation of six eye muscles, three on each side, causes prominent vertigo and nystagmus.
2. A deficient vestibulo-ocular reflex is conspicuous when the head is turned to the affected side, a disorder detected by the head impulse test.

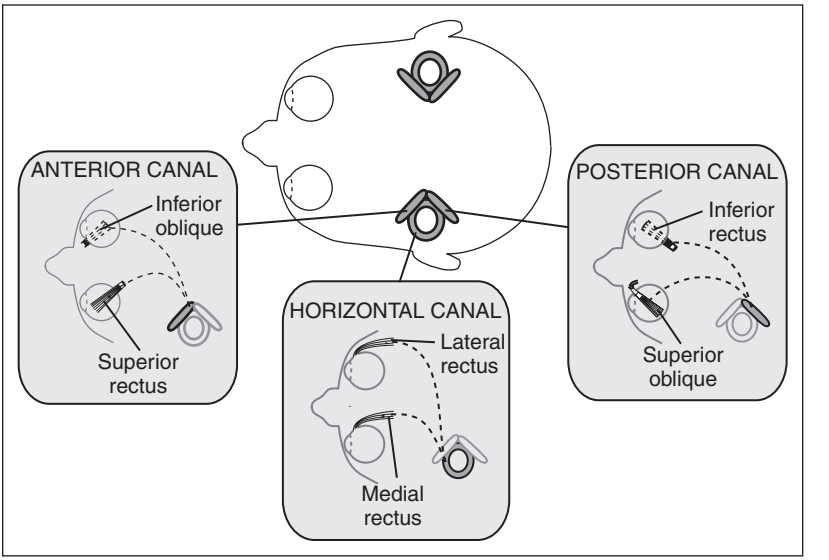

FIGURE 66-1 Connections between semicircular canals and eye muscles. Each of the *gray-shaded* boxes illustrates the orientation and specific connections between the semicircular canals—anterior canal on the *left,* horizontal canal in the *middle*, and posterior canal on the *right*—and specific eye muscles. (In these drawings, the semicircular canals are greatly magnified.) Importantly, there are six semicircular canals (three on each side) and twelve eye muscles (six on each side). Therefore, each semicircular canal is yoked to two eye muscles, one on each side, muscles that pull the eyes conjugately *in the same plane* as the paired canal. The anterior canal is linked to the ipsilateral superior rectus muscle and the contralateral inferior oblique muscle (both muscles are oriented in the same plane as the canal); the horizontal canal, to the ipsilateral medial rectus muscle and the contralateral lateral rectus muscle; and the posterior semicircular canal, to the ipsilateral superior oblique muscle and the contralateral inferior rectus muscle. If a person's head rotates in a plane perpendicular to the right posterior semicircular canal, for example, movements of the right superior oblique muscle and left inferior rectus muscle (muscles in the same plane of the right posterior semicircular canal) move the eyes in the exact opposite direction, thus stabilizing the retinal image. From information in reference 5.

B. HEAD IMPULSE TEST

First described by Halmagyi in 1988,[7] the head impulse test (Fig. 66-2) demonstrates the integrity of the vestibulo-ocular reflex. The clinician sits in front of the patient and places his or her hands on each side of the patient's head. Throughout the test, the patient focuses on the clinician's nose while the clinician focuses on the patient's eyes. If the vestibulo-ocular reflex is intact, the patient can maintain gaze on the clinician's nose during rapid head movements to both sides, and no corrective saccades are observed at the end of the head movement. If the peripheral vestibular system and vestibulo-ocular reflex are abnormal, however, the eyes move away with the

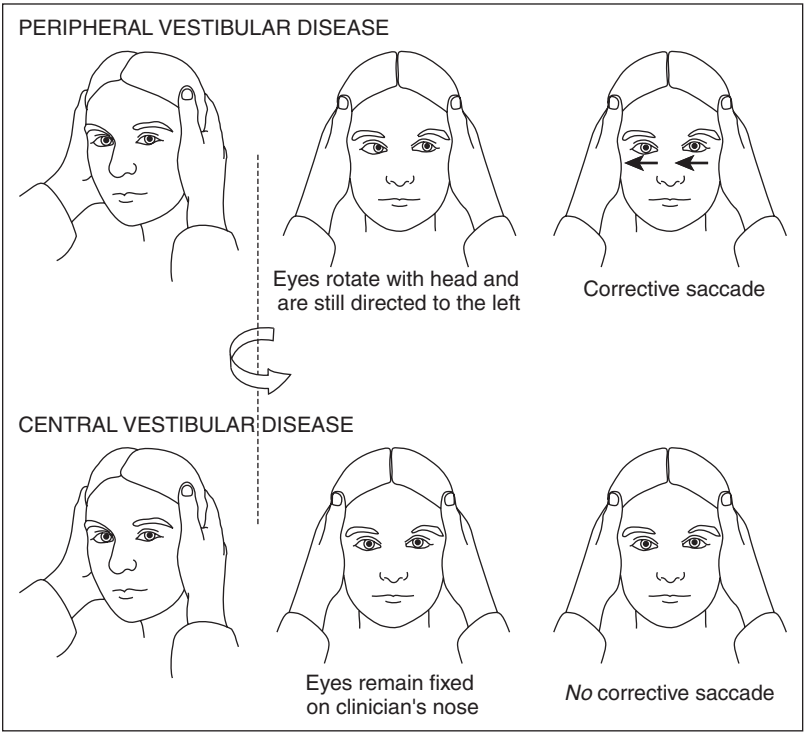

FIGURE 66-2 Head impulse test. The *top row* depicts the head impulse test in left-sided *peripheral* vestibular disease; the bottom row, in *central* vestibular disease (e.g., stroke). In this example, the clinician is testing the left ear (and left vestibulo-ocular reflex) by first turning the patient's head 20 degrees to the *patient's* right (*left* column) and then rapidly rotating the head to the straight-ahead position (*middle* column). Importantly, the clinician should focus on the patient's eyes immediately following head rotation (*right* column): In peripheral vestibular disease, there is a *corrective saccade (arrows)* revealing a deficient vestibulo-ocular reflex and the patient's attempt to focus again on the clinician's nose; in central vestibular disease, the intact vestibulo-ocular reflex allows the patient's eyes to track the clinician's nose throughout the rotation, and no corrective saccade appears. When performing the test, neuro-otologists usually start with a warm-up period of slow movements back and forth to help the patient relax, thus permitting the more rapid movements necessary for the test. Most experts perform many trials, randomly to one side or the other; the test is abnormal if most trials to one side (e.g., two out of three) reveal the corrective saccade. In patients with peripheral disease, the more rapid the initial head movement, the greater the amplitude of the corrective saccade.[6]

rotating head when turned to the abnormal side and, at the end of rotation, the patient's eyes quickly move back to pick up the image of the clinician's nose (i.e., the clinician observes a **corrective saccade**). When compared with the traditional definition of unilateral peripheral vestibular disease (asymmetrical caloric responses), an abnormal head impulse test (i.e., corrective saccade present) has a sensitivity of 35% to 57%, specificity of 90% to 99%, positive LR = 6.7, and negative LR = 0.6.[8–10]

In patients with acute vertigo or dizziness, a *normal* vestibulo-ocular reflex bilaterally (i.e., *no* corrective saccades observed) exonerates the peripheral vestibular system and suggests that the cause of the dizziness is central (e.g., stroke).

An excellent online video of the abnormal head impulse test (with corrective saccades) appears in the supplementary material of reference 11 and at the NOVEL website.[12] The only reported complication of the test is complete heart block, observed in a single patient, presumably induced by vasovagal reaction.*[13]

C. SKEW DEVIATION

Skew deviation refers to an acquired hypertropia, which means one eye is aligned higher than the other, a sign of cerebellar or brainstem disease. It is best revealed by the alternate cover test, which is discussed in Chapter 57.

D. ABNORMAL VISUAL TRACKING: SACCADIC PURSUIT

The patient is asked to follow a slowly moving small target (e.g., the clinician's finger) both horizontally and vertically, while holding the head still. Most patients have no difficulty following the target (i.e., the pursuit is smooth), but some patients with cerebellar or brainstem disease instead reveal conspicuous quick "catch-up" movements, called **saccadic pursuit.**

E. DIRECTION-CHANGING NYSTAGMUS

Many patients with acute vertigo have a spontaneous conjugate jerk nystagmus when looking straight ahead. (Chapter 63 defines the terms used to describe nystagmus.)† In most patients, whether the disorder is peripheral or central, the nystagmus will persist or worsen when a patient looks *in the direction* of the quick component of the nystagmus. The distinguishing finding appears when the patient looks in the *opposite* direction (i.e., contralateral to the quick component of the nystagmus). In patients with peripheral disease, the nystagmus diminishes or disappears. In 20% to 56% of patients with stroke, it *reverses directions*, a finding called **direction-changing nystagmus** (Fig. 66-3).

A second distinguishing feature of nystagmus is the effect of retinal fixation, which means that the patient is focusing on an object (see Chapter 63). In peripheral disease, nystagmus diminishes during fixation; in central disease, it is unchanged.

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*The authors of this report confirmed that the heart block was not due to carotid sinus hypersensitivity.

†In peripheral vestibular disease, the direction of the nystagmus (i.e., its quick component) is *away* from the abnormal side.

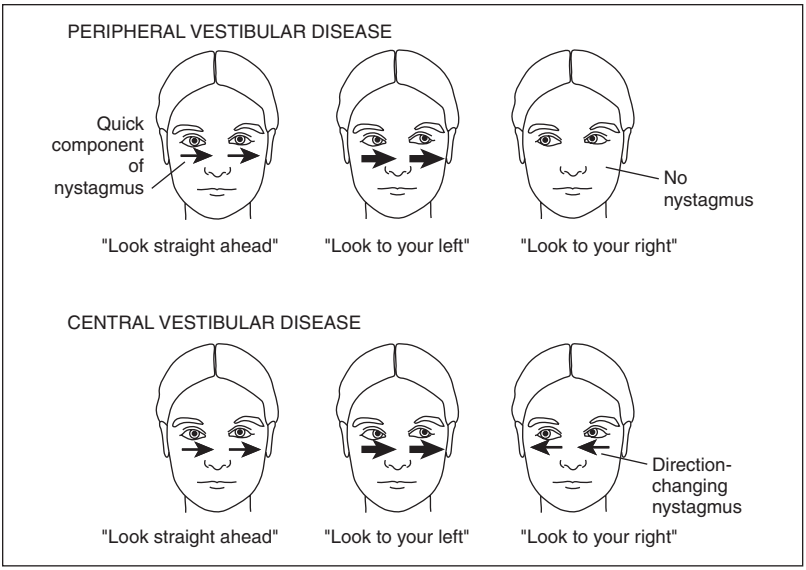


FIGURE 66-3 Direction-changing nystagmus. In this example, the patient has a spontaneous conjugate left-beating jerk nystagmus (*left,* "look straight ahead"; in each example, the *arrows* indicate the direction of the *quick* component of the nystagmus). The patient is asked to look "to your left" (i.e., the direction of the nystagmus, *middle*) and then "to your right" (the contralateral direction, *right*). In both peripheral *(top row)* and central nystagmus *(bottom row),* the nystagmus increases when looking in the direction of the nystagmus ("to your left," *middle*). The distinguishing feature appears when the patient looks in the direction contralateral to the nystagmus ("to your right," *right*). In peripheral disease, nystagmus diminishes or disappears; in central disease, it may *change* directions (direction-changing nystagmus). Importantly, the direction-changing nystagmus is more likely to represent central disease if it appears before extreme lateral gaze, is sustained, and is documented during the first few hours of the acute vestibular syndrome. Normal persons may have a small amplitude jerk nystagmus on *extreme* lateral gaze, although it is rarely sustained.

III. CLINICAL SIGNIFICANCE

Most patients presenting to emergency departments with dizziness, vertigo, or imbalance have benign peripheral disease. In one study of 1666 patients with acute vertigo or dizziness, only 3.2% of patients had a final diagnosis of stroke: If the dizziness was unaccompanied by other neurologic signs (e.g., no dysarthria, ataxia, lethargy, or paresis), only 0.7% had stroke.[14]

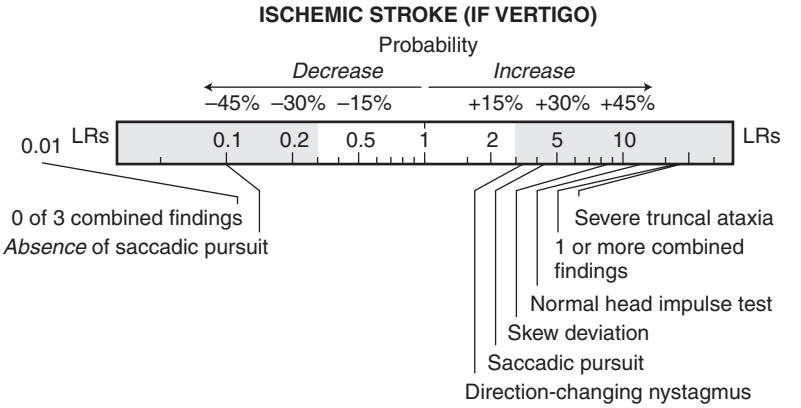
A. INDIVIDUAL FINDINGS

EBM Box 66-1 presents the accuracy of additional bedside findings in 184 patients with acute vertigo and imbalance, all of whom underwent neuroimaging. The findings that increase the probability of stroke are severe truncal ataxia (unable to sit unassisted, LR = 17.9), *normal* vestibulo-ocular reflex during the head impulse test (i.e., *no* corrective saccades, LR = 11.9), skew deviation (LR = 8.5), saccadic pursuit (LR = 4.4), and direction-changing nystagmus (LR = 3.3). The presence of smooth pursuit (i.e., absence of saccadic pursuit) decreases the probability of stroke

EBM BOX 66-1
*Acute Vertigo, Detecting Ischemic Stroke**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Individual Findings				
Severe truncal ataxia[15]	34	98	**17.9**	0.7
Skew deviation present[15,16]	24-40	94-99	**8.5**	0.7
Saccadic pursuit[16]	88	80	**4.4**	**0.1**
Direction-changing nystagmus[15,16]	20-56	82-98	**3.3**	NS
Normal head impulse test (i.e., no corrective saccade)[15,16]	60-93	91-98	**11.9**	NS
Combined Findings				
1 or more of the following: (1) normal head impulse test (no corrective saccades); (2) direction-changing nystagmus; (3) skew deviation[15]	99	94	**17.2**	**0.01**

*Diagnostic standard: for *ischemic stroke*, magnetic resonance imaging of cerebellum and brainstem.
†Definition of findings: see text
‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR
NS, not significant.
Click here to access calculator.



(LR = 0.1). Importantly, the accuracy of these signs has only been demonstrated in patients presenting within 1 to 2 days of the onset of symptoms.

B. COMBINED FINDINGS

Three oculomotor signs—normal vestibulo-ocular reflex on head impulse test (i.e., no corrective saccades), direction-changing nystagmus, and skew deviation—are all characteristic of stroke. In one study of acutely dizzy patients, the presence of *any* of these findings increased the probability of stroke (LR = 17.2; see EBM Box 66-1) and, more importantly, the *absence of all three* findings markedly decreased the probability of stroke (LR = 0.01). This LR (0.01) is lower than the LR for a *normal* (diffusion-weighted) image obtained by magnetic resonance imaging (MRI) (LR = 0.2; i.e., the probability of stroke decreases *more* with the absence of these three findings than it does with a normal MRI result).*[15]

The references for this chapter can be found on www.expertconsult.com.

*In this study, the diagnostic accuracy of the initial magnetic resonance/diffusion weight imaging for stroke was a sensitivity of 85%, specificity of 98%, positive LR = 44.2, and negative LR = 0.2. The eight patients with falsely negative MRIs (five lateral medullary, one lateral pontomedullary, and two middle cerebellar peduncle infarctions) all had positive repeat MRIs an average of 3 days later.[15]

CHAPTER 67

Examination of Nonorganic Neurologic Disorders

I. TRADITIONAL PHYSICAL FINDINGS OF NONORGANIC DISEASE

Nonorganic neurologic disorders (also called hysterical, psychogenic, or functional disorders) occur commonly, accounting for up to 9% of admissions to a neurologic service[1] and 30% of outpatient referrals to neurologists.[2] Of the many proposed findings of nonorganic neurologic disease,* the most prominent are findings whose severity fluctuates during the examination, findings that defy neuroanatomic explanation, bizarre movements not normally seen in organic disease, and findings elicited during special tests.

A. FINDINGS WHOSE SEVERITY FLUCTUATES DURING THE EXAMINATION

Examples are the patient who falls suddenly while walking but catches himself or herself with the knees and hips flexed, a position that requires considerable strength, or the patient whose stance is unstable until he or she is distracted when asked to perform the finger-nose test.[5]

Two examples of formal bedside tests designed to demonstrate fluctuating findings are the knee-lift test (Fig. 67-1) and chair test. The **chair test** is used in patients with gait disorders: The clinician first asks the patient to walk 20 to 30 feet and back again and then places the patient in a wheeled swivel chair (with back) and asks the patient to propel himself or herself (using the legs) over the same distance in the chair. Marked improvement when using the chair (compared with walking) is a positive test.

B. FINDINGS THAT DEFY NEUROANATOMIC EXPLANATION

Findings that defy neuroanatomic explanation[7,8] include the following:

1. **Hysterical hemianopia,** as in the patient who has right hemianopia with both eyes open or just the right eye open but normal visual fields when just the left eye is open[9,10]

*Review articles by Stone[3] and Lanska[4] and the entire issue of *Seminars in Neurology* 2006, volume 26, exhaustively review nonorganic neurologic signs.

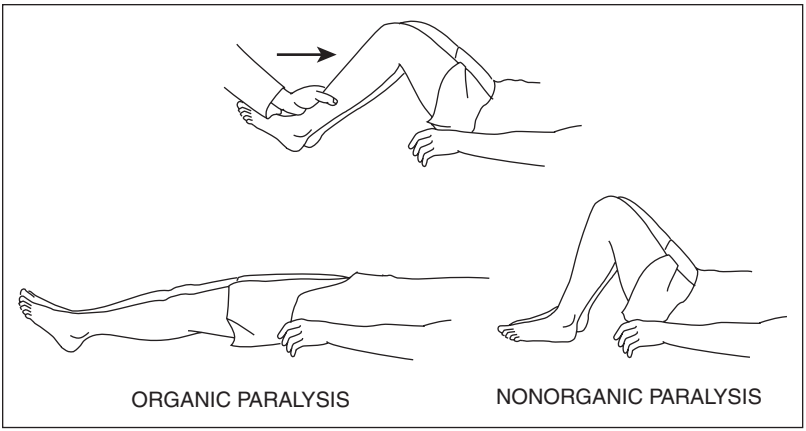


FIGURE 67-1 Knee-lift test for nonorganic paraparesis. The knee-lift test is designed to test patients with leg weakness from suspected spinal cord lesions; it is interpretable only if the supine patient cannot lift his or her knees off the examination table. The clinician raises both of the patient's knees *(top)* and then gently releases the patient's legs. Patients with organic paralysis cannot hold the knees upright (negative test, *lower left*). If the patient maintains the knees upright, the test is positive (for nonorganic paralysis, *lower right*).[6]

2. **Wrong-way tongue deviation,** which describes a tongue deviating *away* from the hemiparetic side. (In cerebral hemispheric disease, the tongue deviates toward the hemiparetic side; see Chapter 58.)[11]
3. **Peripheral facial palsy and ipsilateral hemiparesis** (if a single lesion causes peripheral facial weakness and hemiparesis, the lesion is in the brainstem and the findings should be on opposite sides of the body[12]

C. BIZARRE MOVEMENTS NOT NORMALLY SEEN IN ORGANIC DISEASE

Examples are the patient who drags a hemiparetic leg after himself or herself as if it were an inanimate object[5,13] or the ataxic patient who sways dramatically without falling.[10]

D. FINDINGS ELICITED DURING SPECIAL TESTS

Findings elicited during special tests include the following:

1. **Optokinetic nystagmus** (for functional blindness); because patients with intact vision cannot suppress this nystagmus (see Chapter 56), the presence of optokinetic nystagmus indicates that the blindness is functional
2. **Procedures that confuse the patient of sidedness,** such as a maneuver that mixes up the fingers to uncover hysterical hemianalgesia (Fig. 67-2)[14]
3. **The Hoover sign of nonorganic weakness** (Fig. 67-3), first described by the American physician Charles Hoover in 1908[15]

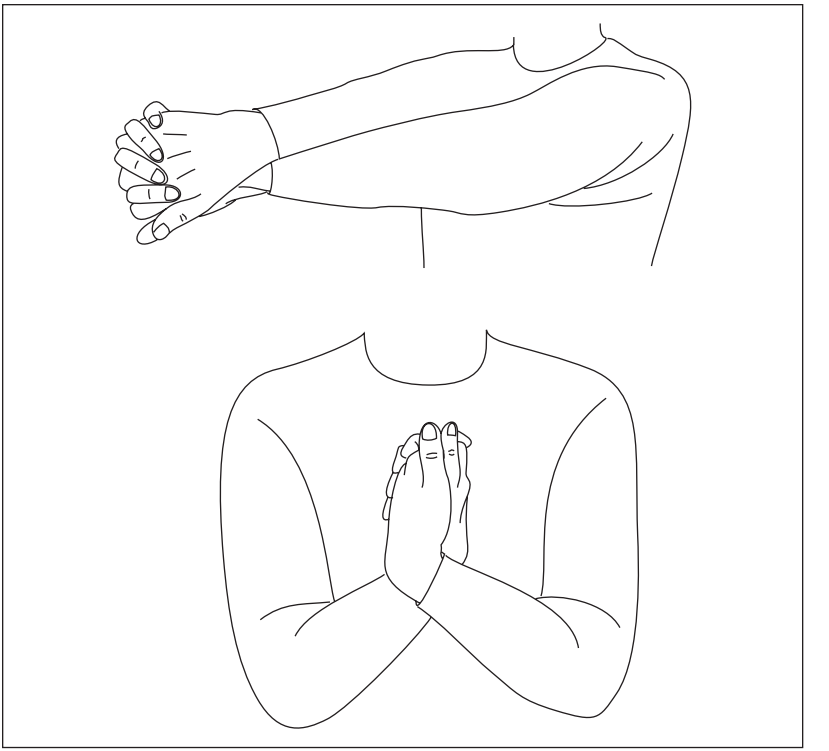


FIGURE 67-2 Test for hysterical hemianalgesia. This test simply mixes up the fingers and confuses the body image. In the first step *(top row),* the patient's hands are pronated with the little fingers on top, the palms are outward, and fingers are interlocked. In the second step *(bottom row),* the hands are rotated downward, inward, and upward, so the interlocked fingers are positioned in front of the chest. The clinician then repeats the sensory examination to determine if the patient is consistent in describing his or her sensory loss. In the final position, the fingertips end up on the same side of the body as their respective arms, and the thumbs (which are not interlocked) end up on the side opposite the fingers.

II. CLINICAL SIGNIFICANCE

A. DIAGNOSTIC ACCURACY

According to the likelihood ratios [LRs] in EBM Box 67-1, tests of nonorganic weakness are quite accurate: The chair test identifies functional gait disorder (positive LR = 17, negative LR = 0.2); the knee-lift test identifies nonorganic paraparesis (positive LR = 7.1, negative LR = 0.04); and the Hoover sign identifies nonorganic leg weakness (positive LR = 30.7, negative LR = 0.2). Nonetheless, these impressive LRs may overestimate the diagnostic accuracy because the clinician performing the tests was probably familiar with the final diagnosis, a diagnosis that in turn was probably determined by the same clinician using clinical criteria. (See footnote to EBM Box 67-1.)

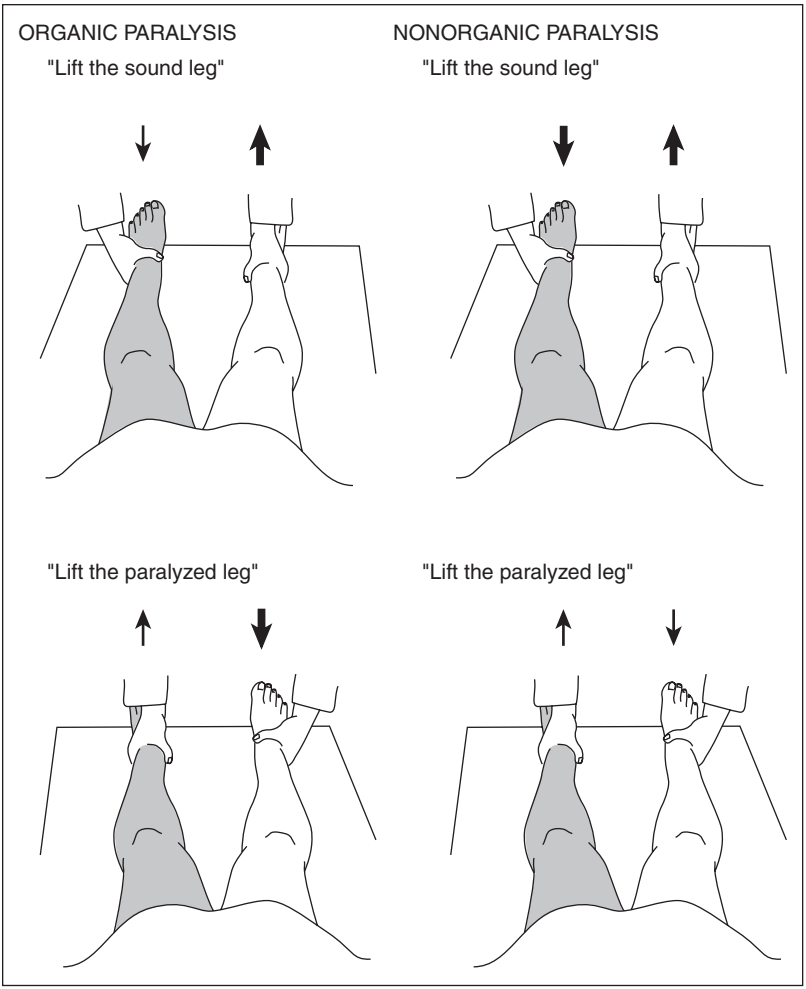
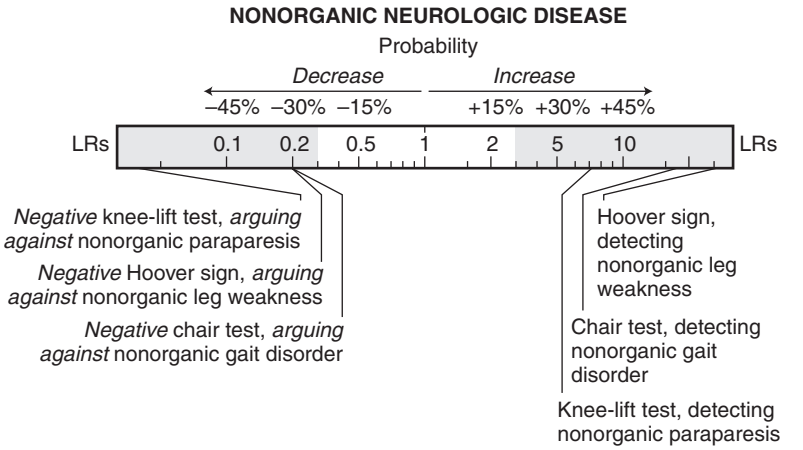


FIGURE 67-3 The Hoover sign of nonorganic paralysis. The left half of the figure depicts *organic* paralysis and the right half, *nonorganic* paralysis; in each drawing, the patient's right leg is the sound leg and the left leg *(shaded gray)* is the paretic leg. In the *top rows*, the clinician stands at the foot of the bed and, with his or her hands around the patient's ankles, asks the patient to *lift the sound leg* as strongly as possible while the clinician resists the movement. (The size of *arrows* indicates the power perceived by the clinician.) In organic paralysis, the downward force of the paretic leg is weak; in nonorganic weakness, the *downward* force of the paretic leg is *strong*. Then (in the *bottom rows*), the patient is asked to lift the *paretic* leg as strongly as possible. In organic weakness, the downward force of the strong leg is strong, whereas in nonorganic weakness, the *downward* force is *weak*. The Hoover test relies on the principle that strong muscular contractions of healthy persons are involuntarily matched by opposing movements of the opposite limb, unless organic weakness intervenes. The appeal of the Hoover test is that its interpretation relies on observation of the leg *opposite* of the one being tested (i.e., in the first test—*top row*—the patient is focused on the sound leg but the clinician observes the paretic leg; in the second test—*bottom row*—the patient is focused on the paretic leg but the clinician observes the sound leg).

EBM BOX 67-1
*Nonorganic Neurologic Disease**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Diagnosing Nonorganic Gait Disorder				
Chair test positive[16]	85	95	17.0	0.2
Diagnosing Nonorganic Paraparesis				
Knee-lift test positive[6]	97	86	7.1	0.04
Diagnosing Nonorganic Leg Weakness				
Hoover sign positive[17]	85	97	30.7	0.2

*Diagnostic standard: for *nonorganic gait disorder*, the Haye criteria[16]; for *nonorganic paraparesis*, disproportionate motor paralysis, nonanatomic sensory loss, and normal neuroimaging; for *nonorganic weakness*, neurologic examination and observation over time.
†Definition of findings: for *chair test*, see text; for *knee-lift test*, see Figure 67-1.
‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR. *Click here to access calculator.*



B. CAVEATS TO THE DIAGNOSIS OF NONORGANIC DISORDERS

Clinicians should be reluctant to diagnose nonorganic disease, primarily because many "nonorganic" findings, when subjected to serious study, also appear in patients with organic disease. For example, in studies of patients with known organic disorders, 8% "split" their sensory findings precisely at the midline, up to 85% feel vibration less in numb areas, 48% have sensory findings that change between examinations or make no sense neuroanatomically, and 33% have "give-away" weakness.[18,19] All of these findings, at one point in time, have been presented as reliable markers of psychogenic disease.[20]

Rare disorders also will trip up the unwary clinician. For example, patients with the medial medullary syndrome also may point the tongue to the "wrong" side, and patients with advanced Huntington disease are often regarded as having a nonorganic gait when it is viewed in isolation.[13]

In clinical studies, 6% to 40% of patients given a diagnosis of nonorganic neurologic disease are subsequently found to have genuine organic neurologic disease to account for their findings.[21,22] The diagnosis of nonorganic illness, therefore, is a diagnostic snare, best left to the experts who are paid to take on such risks.

The references for this chapter can be found on www.expertconsult.com.

CHAPTER 68

Examination of Patients in the Intensive Care Unit

I. INTRODUCTION

The traditional physical examination meets many challenges in the intensive care unit (ICU). First, it must compete with legions of additional sensory information, including continuous telemetry of vital signs, heart rhythm displays, ventilator parameters, and flow sheets of urine output, mental status, and intravenous medications. Second, there are many barriers to traditional inspection, palpation, percussion, and auscultation: Central lines and dressings conceal neck veins, anasarca limits normal palpation, and cardiac leads and ventilator noise obscure heart and lung sounds. Even so, the careful examination retains value in the ICU patient because it is the only way, among many examples, to detect purulence around intravenous lines, the warmth of infected joints, the purpuric skin lesions of septic emboli, the wheezing of bronchospasm, the neck stiffness of meningitis, or the absent doll's eyes of cerebellar stroke.

This chapter brings together both those aspects of the physical examination relevant to critically ill patients already discussed in previous chapters and presents several findings not previously reviewed.

II. THE FINDINGS

Other chapters in this book discuss vital signs (Chapters 14 to 19), asynchronous breathing (Chapter 18), anisocoria (Chapter 20), and neck stiffness (Chapters 24 and 65). This chapter describes three additional findings: modified early warning score, assessment of peripheral perfusion in the ICU, and pulse pressure changes with leg elevation.

A. MODIFIED EARLY WARNING SCORE (TABLE 68-1)

Developed in 2001 by Subbe,[1] who simplified previous scores used in critically ill surgical patients, the **modified early warning score** relies on measurements of four vital signs (systolic blood pressure, heart rate, respiratory rate, and temperature) and the mental status (using the acronym **AVPU**, which stands for **A**lert, responsive to **V**oice, responsive to **P**ain, or **U**nresponsive). In Figure 68-1, normal parameters are shaded grey; the greater the deviation from these normal measurements, in either direction,

Points	3	2	1	0	1	2	3
Systolic blood pressure (mm Hg)	<70	71-80	81-100	101-199		≥200	
Heart rate (beats/min)		<40	41-50	51-100	101-110	111-129	≥130
Respiratory rate (breaths/min)		<9		9-14	15-20	21-29	≥30
Temperature (degrees C)		<35		35-38.4		≥38.5	
Neurologic score				Alert	Voice	Pain	Unresponsive

FIGURE 68-1 Modified Early Warning Score. From reference 1.

the greater the score and presumed risk of hospital death. Patients at highest risk may benefit from observation in an ICU.

B. ASSESSMENT OF PERIPHERAL PERFUSION IN THE ICU

There are three findings of peripheral perfusion in ICU patients.[2]

1. Temperature of limbs, which should reflect the volume of blood circulating in the most superficial vessels of the skin[3]
2. Capillary refill time (see Chapter 52)
3. Mottled skin, especially of the knees

Mottling describes a lacy purplish netlike discoloration of the skin, a sign indicating sluggish blood flow in dilated superficial postcapillary venules.[3]

C. PULSE PRESSURE CHANGES WITH LEG ELEVATION

Critical care physicians have long sought ways to anticipate which patients would benefit from intravascular saline infusions. Based on the hypothesis that pulse pressure reflects stroke volume (see Chapter 16) and the idea that passive elevation of the patient's legs reversibly transfers blood from the legs to the thorax, clinicians have investigated whether changes in pulse pressure after passive leg elevation might predict volume responsiveness.

The methods of this test are not standardized, but the procedures used in the studies from EBM Box 68-1 are as follows: The clinician measures the baseline blood pressure with the patient's legs horizontal on the bed.* After baseline measurements, the clinician lifts the patient's legs to a 45-degree angle. Both the baseline and postelevation blood pressure measurements are made using intra-arterial catheters, and multiple readings over 1 to 4 minutes in both positions are averaged. (After leg elevation, changes in the blood pressure usually appear within 1 minute.) An increase in the mean pulse pressure of 12% or more after elevating the legs signifies that the test is positive (e.g., if the average

*The position of the trunk during baseline measurements was supine in one study[10] and elevated at a 45-degree angle in another.[9] After leg elevation, the trunk was supine in both studies.

EBM BOX 68-1
*Examination of Patients in the Intensive Care Unit**

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Vital Signs				
Modified early warning score ≥5, predicting hospital mortality[4–7]	22-62	79-97	**3.7**	0.7
Peripheral Perfusion and Response to Volume Expansion				
Cool extremities in ICU patients, detecting low cardiac index[8]	23	94	**3.7**	0.8
Number of findings present: (1) cool skin temperature of extremities, (2) capillary refill time >2 seconds, (3) skin mottling over the knees, detecting low cardiac index[2]				
0 of 3 findings present	36	24	0.5	—
1 of 3 findings present	52	—	2.3	—
3 of 3 findings present	12	98	**7.5**	—
Pulse pressure increase ≥12%, detecting patients who respond to fluid challenge[9,10]	59-70	85-92	**4.6**	0.4
Lungs				
Asynchronous breathing during COPD exacerbation, predicting intubation or death[11]	64	80	**3.2**	NS
Asymmetrical breath sounds after intubation, detecting right main-stem bronchus intubation[12,13]	28-41	98-99	**24.4**	0.7
Absent breath sounds in patients with ARDS, detecting underlying pleural effusion[14]	42	90	**4.3**	0.6

Continued

EBM BOX 68-1
Examination of Patients in the Intensive Care Unit—cont'd

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Neurologic Findings				
Anisocoria in patients with coma, detecting structural intracranial lesion[15]	39	96	**9.0**	0.6
Neck stiffness in patients with stroke, detecting hemorrhagic stroke[16–21]	16-48	81-98	**5.4**	0.7

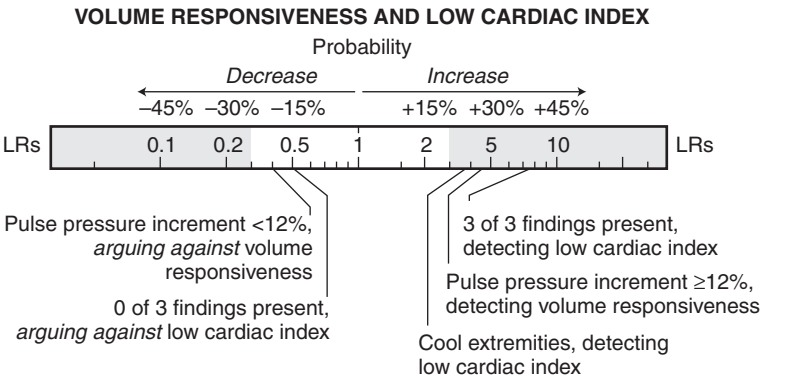
*Diagnostic standard: for *response to fluid challenge*, ≥15% increase in aortic blood flow after 500-mL intravenous saline challenge; *low cardiac index*, <2.5 L/min/m^2 [2] or <3 L/min/m^2 [8]; for *structural lesion*, supratentorial and subtentorial lesions with gross anatomic abnormality, including cerebrovascular disease, intracranial hematoma, tumor, and contusion.

†Definition of findings: for *capillary refill time >2 seconds*, gentle pressure is applied to one of the fingers (not the thumb), over either the distal nail or the pulp, sufficient to cause blanching; the return of normal color after removal of pressure exceeds 2 seconds; for *pulse pressure increase ≥12%*, see text; for *asynchronous breathing*, see Chapter 18 and Figure 18-2.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

ARDS, acute respiratory distress syndrome; COPD, chronic obstructive pulmonary disease; NS, not significant.

Click here to access calculator.



blood pressure is 100/54 mm Hg at baseline and 114/61 mm Hg after leg elevation, the pulse pressure has risen from 46 mm Hg to 53 mm Hg, an increase of 7/46 mm Hg, or 15%).

Patients with deep venous thrombosis of either leg were excluded from these trials.

III. CLINICAL SIGNIFICANCE

A. MODIFIED EARLY WARNING SCORE

In four studies of over 2800 patients with acute medical illness (i.e., trauma excluded), a modified early warning score of 5 or more predicted an increased risk of hospital death (likelihood ratio [LR] = 3.7; see EBM Box 68-1). This finding would identify patients who may benefit from intensive monitoring. (The baseline mortality rate was 4% to 15% in these studies.) In one study of 1100 patients, a score of 0 (i.e., all parameters within the gray-shaded area of Figure 68-1) predicted a reduced risk of death (LR = 0.3).[6]

B. ASSESSMENT OF PERIPHERAL PERFUSION IN THE ICU

In one study of 475 admissions to a surgical ICU,[8] the finding of cool extremities increased the probability of a low cardiac index (LR = 3.7; see EBM Box 68-1). In a subset of 195 patients with sepsis, the finding was even more accurate (LR = 5.2).

In a study of 405 patients with acute lung injury, the presence of all three findings of poor perfusion—cool skin, capillary refill time of more than 2 seconds, and mottling over the knees—increased the probability of a low cardiac index (LR = 7.5). This combination of findings was also accurate in patients receiving intravenous vasopressor medications (LR = 6.5). The absence of all three findings modestly decreased the probability of a low cardiac index (LR = 0.5).

Another study of critically ill patients showed that the presence of *either* a cool arm *or* a capillary refill time of the index finger of more than 4.5 seconds (measured with a stopwatch) increased the probability of an elevated blood lactate level (>2 mmol/L; LR = 2.2).[22]

C. PULSE PRESSURE CHANGES WITH LEG ELEVATION

In two studies of 93 critically patients, all of whom were mechanically ventilated and judged to warrant a trial of volume expansion (because of hypotension, tachycardia, oliguria, mottled limbs, or a requirement for vasopressor medications), a pulse pressure increase of 12% or more after passive leg elevation increased the probability that the patient would subsequently respond to an infusion of 500 mL of intravenous saline (LR = 4.6); the absence of this increment in pulse pressure decreased the probability of volume responsiveness (LR = 0.4).

One cause of a false-negative result (i.e., the patient's pulse pressure increment is <12% yet he or she responds positively to intravenous fluid) is intra-abdominal hypertension (i.e., bladder pressure >16 mm Hg).[23] Presumably, the high pressures within the abdomen of these patients interfere with the normal increment of central blood volume after leg elevation, thus producing the negative test result.

D. LUNG FINDINGS

In patients hospitalized with exacerbations of chronic obstructive pulmonary disease, the finding of asynchronous breathing (see Chapter 18)

accurately predicts the subsequent need for intubation or the rate of hospital mortality (LR = 3.2). In patients examined after intubation, asymmetrical breath sounds are pathognomonic for endobronchial intubation (LR = 24.4), although physical examination *never excludes* this important complication and confirmation of appropriate tube placement by other means is always indicated. In patients mechanically ventilated for acute respiratory distress syndrome, the finding of absent vesicular breath sounds increases the probability of underlying pleural effusion (LR = 4.3).

E. NEUROLOGIC FINDINGS

The finding of anisocoria in an unresponsive patient raises concern for the **Hutchinson pupil** (see Chapter 20), the abnormal larger pupil representing an early sign of an ipsilateral expanding cerebral mass (LR = 9). A common mimic of this finding in the ICU is the **pharmacologic pupil,** resulting from nebulized bronchodilators, which can be distinguished from the Hutchinson pupil by its lack of response to topical pilocarpine (see Chapter 20).

Neck stiffness raises concern for meningeal irritation, caused either by purulent secretions (meningitis) or by blood (intracranial or subarachnoid hemorrhage). In patients with stroke, the finding of neck stiffness increases the probability of intracranial or subarachnoid hemorrhage (LR = 5.4).

The references for this chapter can be found on www.expertconsult.com.

EVIDENCE-BASED PHYSICAL DIAGNOSIS

3rd Edition

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INTRODUCTION TO THE FIRST EDITION

The purpose of this book is to explore the origins, pathophysiology, and diagnostic accuracy of many of the physical signs used today in adult patients. We have a wonderfully rich tradition of physical diagnosis, and my hope is that this book will help square this tradition, now almost 2 centuries old, with the realities of modern diagnosis, which often rely more on technologic tests such as clinical imaging and laboratory testing. The tension between physical diagnosis and technologic tests has never been greater. Having taught physical diagnosis for 20 years, I frequently observe medical students purchasing textbooks of physical diagnosis during their preclinical years, to study and master traditional physical signs, but then neglecting or even discarding this knowledge during their clinical years, after observing that modern diagnosis often takes place at a distance from the bedside. One can hardly fault a student who, caring for a patient with pneumonia, does not talk seriously about crackles and diminished breath sounds when all of his teachers are focused on the subtleties of the patient's chest radiograph. Disregard for physical diagnosis also pervades our residency programs, most of which have formal x-ray rounds, pathology rounds, microbiology rounds, and clinical conferences addressing the nuances of laboratory tests. Very few have formal physical diagnosis rounds.

Reconciling traditional physical diagnosis with contemporary diagnostic standards has been a continuous process throughout the history of physical diagnosis. In the 1830s, the inventor of topographic percussion, Professor Pierre Adolphe Piorry, taught that there were nine distinct percussion sounds, which he used to outline the patient's liver, heart, lungs, stomach, and even individual heart chambers or lung cavities. Piorry's methods flourished for over a century and once filled 200-page manuals,[1] although today, thanks to the introduction of clinical imaging in the early 1900s, the only vestige of his methods is percussion of the liver span. In his 1819 *A Treatise on Diseases of the Chest*,[2] Laennec wrote that lung auscultation could detect "every possible case" of pneumonia. It was only a matter of 20 years before other careful physical diagnosticians tempered Laennec's enthusiasm and pointed out that the stethoscope had diagnostic limitations.[3] And, for most of the 20th century, expert clinicians believed that all late systolic murmurs were benign, until Barlow in 1963 showed they often represented mitral regurgitation, sometimes of significant severity.[4]

There are two contemporary polar opinions of physical diagnosis. Holding the less common position are clinicians who believe that all traditional physical signs remain accurate today, and these clinicians continue to quiz students about the Krönig isthmus and splenic percussion signs. A more common position is that physical diagnosis has little to offer the modern clinician and that traditional signs, though interesting, cannot compete with the accuracy of our more technologic diagnostic tools. Neither position, of course, is completely correct. I hope this book, by examining the

best evidence comparing physical signs to current diagnostic standards, will bring clinicians to a more appropriate middle ground, understanding that physical diagnosis is a reliable diagnostic tool that can still help clinicians with many, but not all, clinical problems.

Although some regard evidence-based medicine as "cookbook medicine," this is incorrect, because there are immeasurable subtleties in our interactions with patients that clinical studies cannot address (at least, not as yet) and because the diagnostic power of any physical sign (or any test, for that matter) depends in part on our ideas about disease prevalence, which in turn depend on our own personal interviewing skills and clinical experience.* Instead, evidence-based physical diagnosis simply summarizes the best evidence available, whether a physical sign is accurate or not. The clinician who understands this evidence can then approach his or her own patients with the confidence and wisdom that would have developed had the clinician personally examined and learned from the thousands of patients reviewed in the studies of this book.

Sometimes, comparing physical signs with modern diagnostic standards reveals that the physical sign is outdated and perhaps best discarded (e.g., topographic percussion of diaphragm excursion). Other times, the comparison reveals that physical signs are extremely accurate and probably underused (e.g., early diastolic murmur at the left lower sternal area for aortic regurgitation, conjunctival rim pallor for anemia, or a palpable gallbladder for extrahepatic obstruction of the biliary ducts). And still other times, the comparison reveals that the physical sign *is* the diagnostic standard, just as most of physical examination was a century ago (e.g., systolic murmur and click of mitral valve prolapse, hemiparesis for stroke, neovascularization for proliferative diabetic retinopathy). For some diagnoses, a tension remains between physical signs and technologic tests, making it still unclear which should be the diagnostic standard (e.g., the diagnoses of cardiac tamponade or carpal tunnel syndrome). And for still others, the comparison is impossible because clinical studies comparing physical signs with traditional diagnostic standards do not exist.

My hope is that the material in this book will allow clinicians of all levels—students, house officers, and seasoned clinicians alike—to examine patients more confidently and accurately, thus restoring physical diagnosis to its appropriate, and often pivotal, diagnostic role. Once they are well-versed in evidence-based physical diagnosis, clinicians can settle most important clinical questions at the time and place they should be first addressed—the patient's bedside.

Steven McGee, MD
July 2000

*These subjects are discussed fully in Chapters 2 and 4.

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To Rosalie, Connor, and Matt

PREFACE TO THE THIRD EDITION

There are countless new studies of bedside examination and its accuracy in detecting disease, solving clinical problems, and predicting the patient's course. This third edition of *Evidence-Based Physical Diagnosis* summarizes all of this knowledge, both old and new, by updating every chapter from the second edition, adding over 250 new studies to the book's evidence-based medicine (EBM) boxes, and presenting new information on many subjects, including stance and gait, systolic murmurs, Schamroth sign (for clubbing), diagnosis of dementia, prediction of falls, hepatopulmonary syndrome, atrial fibrillation, relative bradycardia, tourniquet test (for dengue infections), acute stroke, pleural effusion, osteoarthritis, and acute vertigo. There is even a new chapter on examination of patients in the intensive care unit, an excellent example of how traditional physical examination and modern technology work together.

I am indebted to many investigators who contributed extra information not included in their published work. These include Dr. Waldo de Mattos (who provided his original data on patients with chronic obstructive lung disease), Dr. Aisha Lateef (who provided raw data from her study on relative bradycardia and dengue), Dr. Newman-Toker (for his explanation of the head impulse test and for directing me to the NOVEL website), Dr. Colin Grissom (who supplied additional information on his technique of capillary refill time), Dr. G. LeGal (who answered questions about the modified Geneva score), Dr. J. D. Chiche (who provided additional information regarding the correct technique of passive leg elevation), Dr. C. Subbe (who explained the derivation of the MEWS score), Dr. Torres-Russotto (who described the correct technique for the finger rub test), and Dr. S. Kalantri (who helped me understand the physical findings of pleural effusion).

Through the efforts of these and other investigators, physical examination remains an essential clinical skill, one that complements the advanced technology of modern medicine and one vital to good patient care.

Steven McGee, MD

Likelihood Ratios, Confidence Intervals, and Pretest Probability

Appendix Table 1 displays the point estimates and 95% confidence intervals (CIs) for all of the likelihood ratios (LRs) presented in this book. Also, the table presents the range of pretest probabilities observed in the studies used to calculate the LRs (for pretest probability of disease, see Chapter 2). Chapter 3 presents the methods used to obtain the point estimates of LRs and their confidence intervals, and individual chapters define each physical finding and further discuss its significance.

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
EBM BOX 5-1 DEMENTIA AND DELIRIUM			
Abnormal clock-drawing test	5.3 (2.5, 11.2)	0.5 (0.3, 0.7)	22-57
Mini-Cog score 2 or less	9.5 (4.5, 19.9)	0.1 (0, 1.6)	6-52
Mini-Mental Status Examination (MMSE) score 23 or less	8.9 (6.7, 11.9)	0.2 (0.2, 0.3)	4-77
MMSE score 20 or less	14.4 (8, 26.1)	—	9-35
MMSE score 21-25	2.1 (1.7, 2.6)	—	14-35
MMSE score 26 or more	0.1 (0.1, 0.2)	—	14-77
Confusion assessment method	10.7 (5.6, 20.7)	0.2 (0.1, 0.4)	14-64
CHAPTER 6 STANCE AND GAIT			
Positive Trendelenburg sign and gait, detecting gluteus medius muscle tear	3.2 (1.1, 9.1)	0.4 (0.1, 1)	46
Asymmetrical arm swing, detecting focal cerebral disease	2.1 (0.5, 9.6)	0.9 (0.7, 1.0)	71
Prior fall in last year, predicting future fall	2.4 (2, 2.9)	0.6 (0.4, 0.9)	19-53
EBM BOX 6-1 GAIT ABNORMALITIES			
Unable to perform perfect 10 tandem steps, detecting Parkinson disease	0.1 (0, 0.3)	5 (2.7, 9.1)	42

Continued

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
Any gait or balance disorder, detecting Alzheimer dementia	0.2 (0.1, 0.3)	3.4 (1.9, 5.8)	75
Parkinsonian gait, detecting Lewy body dementia or Parkinson disease with dementia	8.8 (4.3, 18.1)	0.2 (0.2, 0.4)	50
Nutt frontal gait or frontal disequilibrium	6.1 (3.2, 11.3)	0.5 (0.3, 0.7)	25
EBM BOX 6-2 PREDICTING FALLS			
Palmomental reflex present	2.8 (1.7, 4.4)	0.8 (0.7, 0.9)	32
Failure to stand with feet together and eyes open for 10 seconds	4.5 (2.1, 9.8)	1 (0.9, 1)	19
Failure in tandem walk (>2 errors)	1.7 (1.5, 2)	0.7 (0.6, 0.8)	19
Stops walking when talking	3 (1.3, 6.8)	0.8 (0.7, 1)	36-48
Timed up and go <15 seconds	0.1 (0, 0.3)	—	53
Timed up and go 15-35 seconds	1.1 (0.9, 1.4)	—	53
Timed up and go ≥35 seconds	2.6 (1.4, 4.7)	—	53
Timed chair stands (get up and sit down 3 times) >10 seconds	1.5 (1.2, 2)	0.9 (0.8, 1)	15
CHAPTER 7 JAUNDICE			
Ascites, detecting varices	1.5 (1.2, 2)	0.7 (0.6, 0.8)	13-58
EBM BOX 7-1 HEPATOCELLULAR JAUNDICE			
Weight loss	0.8 (0.2, 3.2)	1.3 (0.5, 3.3)	65-67
Spider angiomas	4.7 (1, 22.4)	0.6 (0.5, 0.9)	65-67
Palmar erythema	9.8 (1.4, 67.6)	0.5 (0.4, 0.7)	67
Dilated abdominal veins	17.5 (1.1, 277)	0.6 (0.5, 0.8)	67
Ascites	4.4 (1.1, 17.1)	0.6 (0.5, 0.8)	67
Palpable spleen	2.9 (1.2, 6.8)	0.7 (0.6, 0.9)	65-67
Palpable gallbladder	0.04 (0, 0.7)	1.4 (1.1, 1.9)	67
Palpable liver	0.9 (0.8, 1.1)	1.4 (0.6, 3.4)	65-67
Liver tenderness	1.4 (0.8, 2.6)	0.8 (0.7, 1.1)	65-67
EBM BOX 7-2 CIRRHOSIS			
Spider angiomas	4.5 (2.4, 8.3)	0.5 (0.4, 0.7)	7-67
Palmar erythema	4.3 (1.4, 12.7)	0.6 (0.4, 0.9)	11-67
Gynecomastia	7 (5.2, 9.4)	0.6 (0.3, 1.1)	11-16
Reduction of body or pubic hair	8.8 (6.3, 12.5)	0.6 (0.4, 1)	11-16
Jaundice	3.8 (2, 7.2)	0.8 (0.8, 0.9)	11-53
Dilated abdominal wall veins	9.5 (1.8, 49.2)	0.8 (0.6, 1)	11-55
Hepatomegaly	2.3 (1.6, 3.3)	0.6 (0.4, 0.7)	7-67
Palpable liver in epigastrium	2.7 (1.9, 3.9)	0.3 (0.1, 0.9)	7-37
Liver edge firm to palpation	2.7 (2.2, 3.3)	0.4 (0.3, 0.5)	54-67

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
Splenomegaly	2.5 (1.6, 3.8)	0.8 (0.7, 0.9)	18-67
Ascites	6.6 (3.6, 12.1)	0.8 (0.7, 0.8)	16-55
Peripheral edema	3 (1.9, 4.8)	0.7 (0.6, 0.9)	16-55
Encephalopathy	8.8 (3.3, 23.7)	0.9 (0.8, 1)	16-39
EBM BOX 7-3 HEPATOPULMONARY SYNDROME			
Clubbing	4.6 (1.8, 11.7)	0.6 (0.3, 0.9)	16-32
Cyanosis	4.3 (2.4, 7.8)	0.5 (0.1, 2.4)	19-32
Palmar erythema	1.8 (0.8, 3.9)	0.6 (0.2, 1.5)	14-19
Spider angiomas	1.4 (1.1, 1.9)	0.5 (0.3, 1)	14-32
Ascites	1 (0.8, 1.3)	0.9 (0.5, 1.6)	16-18
EBM BOX 8-1 CYANOSIS			
Central cyanosis	7.4 (1.5, 36.8)	0.2 (0.1, 0.5)	9-12
EBM BOX 9-1			
Pallor at any site	4 (2.4, 6.7)	0.5 (0.3, 0.7)	2-71
Facial pallor	3.8 (2.5, 5.8)	0.6 (0.5, 0.7)	39
Nailbed pallor	3.9 (0.8, 18.6)	0.5 (0.4, 0.7)	39-71
Palmar pallor	5.6 (1.1, 29.1)	0.4 (0.4, 0.5)	39-71
Palmar crease pallor	7.9 (1.8, 35.3)	0.9 (0.9, 1)	39
Conjunctival pallor	4.7 (1.9, 11.5)	0.6 (0.4, 0.9)	39-71
Tongue pallor	3.7 (2.5, 5.4)	0.6 (0.5, 0.7)	21
Conjunctival rim pallor present	16.7 (2.2, 125)	—	47
Conjunctival rim pallor borderline	2.3 (1.5, 3.5)	—	47
Conjunctival rim pallor absent	0.6 (0.5, 0.8)	—	47
EBM BOX 10-1 HYPOVOLEMIA			
Dry axilla	2.8 (1.4, 5.4)	0.6 (0.4, 1)	23
Dry mucous membranes of mouth and nose	3.1 (1.6, 5.8)	0.4 (0.2, 0.9)	33-77
Longitudinal furrows on tongue	2 (1, 4)	0.3 (0.1, 0.6)	77
Sunken eyes	3.4 (1, 12.2)	0.5 (0.3, 0.7)	79
Abnormal skin turgor	3.5 (2.7, 4.4)	0.3 (0.3, 0.4)	33
Confusion	10 (0.5, 222.8)	0.5 (0.4, 0.6)	33-77
Weakness	2.3 (0.6, 8.6)	0.7 (0.5, 1)	78
Speech unclear or rambling	3.1 (0.9, 11.1)	0.5 (0.3, 0.8)	80
CHAPTER 11 MALNUTRITION AND WEIGHT LOSS			
Alcoholism, detecting organic disease	4.5 (1.1, 18.9)	0.8 (0.7, 1)	55
Cigarette smoking, detecting organic cause	2.2 (1.1, 4.4)	0.6 (0.4, 0.9)	55
Prior psychiatric disease, detecting organic cause	0.2 (0.1, 0.5)	1.8 (1.3, 2.5)	55

Continued

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
Normal physical examination, detecting organic cause	0.4 (0.3, 0.6)	20.3 (2.9, 143)	55
Underestimation, predicting organic cause	5.4 (2, 14.5)	0.6 (0.5, 0.8)	50
Overestimation, predicting nonorganic cause	3.6 (2, 6.5)	0.4 (0.2, 0.6)	50
EBM BOX 11-1 MALNUTRITION AND COMPLICATIONS			
Weight loss >10%	1.4 (1.1, 1.8)	0.9 (0.9, 1)	13-51
Low body weight	2 (1.4, 2.9)	0.9 (0.8, 1)	13-40
Upper arm muscle circumference <85% predicted	2.5 (1.7, 3.6)	0.8 (0.7, 0.9)	13-40
Forearm muscle circumference <85% predicted	3.2 (2, 5.1)	0.8 (0.6, 0.9)	14-40
Reduced grip strength	2.2 (1.7, 2.8)	0.4 (0.2, 0.6)	13-59
CHAPTER 13 CUSHING SYNDROME			
Osteoporosis, detecting Cushing syndrome	17.6 (7.8, 39.4)	0.4 (0.3, 0.5)	25-69
Weight loss, detecting ectopic adrenocorticotropic hormone (ACTH) syndrome	20 (1.2, 341)	0.5 (0.2, 1.1)	24
Symptom duration <18 months, detecting ectopic ACTH syndrome	15 (3.2, 71.4)	0.1 (0, 1)	23
EBM BOX 13-1 CUSHING SYNDROME			
Hypertension	2.3 (1.5, 3.7)	0.8 (0.6, 0.9)	25-56
Moon facies	1.6 (1.1, 2.5)	0.1 (0, 0.9)	58
Central obesity	3 (2, 4.4)	0.2 (0.1, 0.3)	25-56
Generalized obesity	0.1 (0, 0.2)	2.5 (2.1, 3.1)	25
Skinfold thickness <1.8 mm	115.6 (7, 1854)	0.2 (0.1, 0.6)	17
Plethora	2.7 (2.1, 3.5)	0.3 (0.1, 0.5)	25
Hirsutism, in women	1.7 (1.2, 2.5)	0.7 (0.5, 0.9)	22-65
Ecchymoses	4.5 (1.2, 16.4)	0.5 (0.4, 0.6)	25-57
Red or blue striae	1.9 (1.3, 2.7)	0.7 (0.6, 0.9)	25-57
Acne	2.2 (1.5, 3.2)	0.6 (0.5, 0.8)	25
Proximal muscle weakness	4.4 (1, 19.6)	0.4 (0.3, 0.6)	25-57
Edema	1.8 (1.1, 3.1)	0.7 (0.6, 0.9)	25-57
CHAPTER 14 PULSE RATE AND CONTOUR			
Pulsus paradoxus >12 mm Hg, detecting cardiac tamponade	5.9 (2.4, 14.3)	0.03 (0, 0.2)	63
Carotid upstroke delayed, detecting severe aortic stenosis	3.3 (2.4, 4.5)	0.4 (0.2, 0.8)	5-69

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
Hyperkinetic pulse in patients with mitral stenosis, detecting additional valvular disease	14.2 (7.4, 27.2)	0.3 (0.2, 0.4)	35
EBM BOX 14-1 TACHYCARDIA			
Heart rate >90 beats/min, predicting hospital mortality in trauma patients with hypotension	1.5 (1.4, 1.7)	0.2 (0.1, 0.5)	10
Heart rate >95 beats/min, predicting hospital mortality in patients with septic shock	2 (1.3, 3.3)	0.1 (0, 0.5)	60
Heart rate >100 beats/min, predicting mortality in patients with pneumonia	2.1 (1.1, 3.8)	0.7 (0.5, 1)	31
Heart rate >100 beats/min, predicting hospital mortality in patients with myocardial infarction	3 (2.3, 4)	1 (0.9, 1)	2-9
Heart rate >100 beats/min, predicting complications in patients with gallstone pancreatitis	6.8 (3.7, 12.5)	0.2 (0, 1)	7
Heart rate >100 beats/min, predicting hospital mortality in patients with pontine hemorrhage	25.4 (1.6, 396)	0.3 (0.2, 0.6)	55
EBM BOX 14-2 PULSUS PARADOXUS AND ASTHMA			
Pulsus paradoxus >10 mm Hg, detecting severe asthma	2.7 (1.7, 4.3)	0.5 (0.4, 0.7)	36-77
Pulsus paradoxus >20 mm Hg, detecting severe asthma	8.2 (1.7, 40.3)	0.8 (0.7, 0.9)	36-67
Pulsus paradoxus >25 mm Hg, detecting severe asthma	22.6 (1.4, 364)	0.8 (0.8, 0.9)	77
EBM BOX 14-3 PULSES AND HYPOVOLEMIC SHOCK			
Carotid pulse present, detecting systolic blood pressure ≥60 mm Hg	1.2 (0.9, 1.8)	0.2 (0, 2.1)	70
Femoral pulse present, detecting systolic blood pressure ≥60 mm Hg	2.9 (1.1, 7.2)	0.1 (0, 0.5)	70
Radial pulse present, detecting systolic blood pressure ≥60 mm Hg	4.7 (0.7, 31.3)	0.5 (0.3, 0.9)	70
CHAPTER 15 ABNORMALITIES OF PULSE RHYTHM			
Rapid regular pounding in neck, detecting atrioventricular nodal reentrant tachycardia	351 (22, 5594)	0.1 (0, 0.2)	22

Continued

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
EBM BOX 15-1 ATRIOVENTRICULAR (AV) DISSOCIATION AND VENTRICULAR TACHYCARDIA			
Varying arterial pulse, detecting AV dissociation of ventricular tachycardia	2.1 (1, 4.4)	0.5 (0.3, 1)	55
Intermittent cannon a waves in neck veins, detecting AV dissociation of ventricular tachycardia	3.8 (1.8, 8.2)	0.1 (0, 0.4)	55
Changing intensity S_1, detecting AV dissociation of ventricular tachycardia	24.4 (1.5, 385)	0.4 (0.3, 0.7)	55
EBM BOX 15-2 ATRIAL FIBRILLATION			
Radial pulse not regular	3.3 (3, 3.7)	0.1 (0.1, 0.2)	5-30
Chaotic pulse	24.1 (15.2, 38)	0.5 (0.4, 0.6)	6
CHAPTER 16 BLOOD PRESSURE			
Mediastinal widening on chest x-ray, detecting aortic dissection	2 (1.2, 3.4)	0.3 (0.2, 0.4)	45-51
Systolic blood pressure <100 mm Hg, detecting type A dissection	5 (1.8, 14)	0.9 (0.9, 1)	61
Murmur of aortic regurgitation, detecting type A dissection	5 (2.6, 9.8)	0.6 (0.5, 0.8)	43-91
Pulse deficit, detecting type A dissection	2.3 (1.6, 3.2)	0.9 (0.8, 1)	43-91
Findings of aortic coarctation, detecting coarctation	242 (89.3, 657)	0.2 (0.1, 0.4)	2
Proportional pulse pressure <0.25, detecting low cardiac index	6.9 (3, 15.8)	0.2 (0.1, 0.6)	50-64
Pulse pressure ≥80 mm Hg, detecting moderate-to-severe aortic regurgitation	10.9 (1.5, 77.1)	0.5 (0.2, 0.8)	42
Positive tourniquet test, detecting dengue infection	7.4 (2.8, 19.2)	0.6 (0.6, 0.7)	89
EBM BOX 16-1 HYPOTENSION AND PROGNOSIS			
Systolic blood pressure <90 mm Hg, predicting mortality in intensive care patients	3.1 (1.9, 5.1)	0.5 (0.2, 1.3)	21-37
Systolic blood pressure <90 mm Hg, predicting mortality in patients with bacteremia	4.9 (4.2, 5.7)	0.6 (0.2, 1.4)	5-13
Systolic blood pressure <90 mm Hg, predicting mortality in patients with pneumonia	7.6 (3.8, 15.3)	0.8 (0.6, 0.9)	4-10

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
Systolic blood pressure <80 mm Hg, predicting mortality in patients with acute myocardial infarction	15.5 (12.2, 20)	0.7 (0.7, 0.7)	18
Systolic blood pressure ≤90 mm Hg, detecting adverse outcomes in hospitalized patients	4.7 (3.4, 6.5)	0.7 (0.7, 0.8)	49
Systolic blood pressure ≤85 mm Hg, detecting adverse outcomes in hospitalized patients	9 (5.3, 15.2)	0.8 (0.7, 0.8)	49
Systolic blood pressure ≤80 mm Hg, detecting adverse outcomes in hospitalized patients	16.7 (7.6, 36.4)	0.8 (0.8, 0.8)	49
EBM BOX 16-2 AORTIC DISSECTION			
Pulse deficit	6 (1.1, 32.5)	0.7 (0.5, 1)	45-76
Aortic regurgitation murmur	1.4 (0.9, 2.2)	0.9 (0.8, 1)	45-76
Focal neurologic signs	33.4 (2, 549)	0.9 (0.8, 0.9)	51
0 predictors	0.1 (0, 0.2)	—	51
1 predictor	0.5 (0.4, 0.8)	—	51
2 predictors	5.3 (3, 9.4)	—	51
3 predictors	65.8 (4.1, 1061.5)	—	51
EBM BOX 16-3 SYSTOLIC BLOOD PRESSURE AND IMPAIRED CONSCIOUSNESS			
Systolic blood pressure ≥160 mm Hg in patients with impaired consciousness, detecting structural brain lesions	7.3 (3.6, 14.6)	0.6 (0.4, 0.8)	46-59
CHAPTER 17 TEMPERATURE			
White blood cell (WBC) count >15,000/μL, detecting bacteremia	1.6 (1.2, 2.2)	0.8 (0.8, 0.9)	9-37
Band count >1500/μL, detecting bacteremia	2.6 (1.3, 5.1)	0.7 (0.6, 0.9)	8-19
Chills, detecting bacteremia	2 (1.7, 2.2)	0.7 (0.6, 0.8)	7-37
Shaking chills, detecting bacteremia	4.7 (3, 7.2)	0.6 (0.5, 0.8)	8
Stepladder pattern of fever, detecting enteric fever	177 (11, 2842)	0.5 (0.4, 0.6)	38
Pulse rate ≤90 beats/min, detecting dengue infection	3.3 (1.8, 5.9)	0.4 (0.3, 0.6)	50
Pulse rate ≤80 beats/min, detecting dengue infection	5.3 (1.7, 17.2)	0.7 (0.6, 0.9)	50
EBM BOX 17-1 DETECTION OF FEVER			
Patient's report of fever	2.9 (1.1, 8)	0.3 (0.2, 0.5)	6-45
Patient's forehead abnormally warm	2.8 (2.4, 3.3)	0.3 (0.2, 0.5)	24-49

Continued

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
EBM BOX 17-2 DETECTION OF BACTEREMIA			
Age 50 years or more	1.4 (1.2, 1.6)	0.3 (0.1, 0.8)	16-19
Renal failure	4.6 (2.6, 8.1)	0.8 (0.7, 0.9)	14-21
Hospitalization for trauma	3 (2.4, 3.8)	0.7 (0.3, 1.3)	16-18
Intravenous drug use	2.9 (1.1, 7.3)	1 (0.9, 1)	7
Previous stroke	2.8 (1.2, 6.2)	0.9 (0.8, 1)	21
Diabetes mellitus	1.6 (1.2, 2.1)	0.9 (0.9, 1)	8-37
Poor functional performance	3.6 (2.2, 5.9)	0.6 (0.4, 0.8)	14-21
Rapidly fatal disease (<1 month)	2.7 (1.4, 5.2)	0.9 (0.9, 1)	7-19
Indwelling urinary catheter present	2.4 (1.2, 4.7)	0.8 (0.7, 1)	8-37
Central intravenous line present	1.9 (1.5, 2.5)	0.9 (0.9, 1)	18-32
Temperature ≥38.5° C	1.2 (1.1, 1.4)	0.7 (0.6, 0.9)	8-19
Tachycardia	1.3 (1.2, 1.5)	0.7 (0.6, 0.8)	18-37
Respiratory rate >20 breaths/min	0.9 (0.8, 1.1)	1.2 (0.8, 1.7)	37
Hypotension	2.2 (1.7, 2.8)	0.9 (0.8, 1)	7-37
Acute abdomen	1.7 (1.3, 2.3)	1 (0.9, 1)	7-32
Confusion or depressed sensorium	1.5 (1.3, 1.8)	0.9 (0.9, 1)	8-37
EBM BOX 17-3 EXTREMES OF TEMPERATURE			
Hyperthermia, predicting death if pontine hemorrhage	23.7 (1.5, 371)	0.4 (0.2, 0.6)	55
Hypothermia, predicting death if congestive heart failure	6.7 (2.7, 16.9)	0.7 (0.5, 1)	6
Hypothermia, predicting death if pneumonia	3.5 (1.1, 10.9)	0.8 (0.5, 1.2)	4-9
Hypothermia, predicting death if systemic inflammatory response syndrome (SIRS)	3.3 (1.1, 10)	0.9 (0.8, 1)	43
CHAPTER 18 RESPIRATORY RATE AND PATTERNS			
Kussmaul respirations, detecting severe metabolic acidosis in patients with malaria	4.8 (3.4, 6.7)	0.1 (0.1, 0.2)	51
Asynchronous breathing, predicting need for intubation or hospital mortality in hospitalized patients with chronic obstructive pulmonary disease (COPD)	3.2 (1.3, 7.8)	0.5 (0.2, 1)	31
Paradoxic abdominal movements, detecting diaphragmatic weakness	3.2 (1.7, 5.9)	0.1 (0, 1.1)	27
Orthopnea, detecting ejection fraction <50%	2.7 (1.5, 4.9)	0.04 (0, 0.7)	46

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
EBM BOX 18-1 TACHYPNEA			
Respirations >24 breaths/min, predicting failure of weaning from mechanical ventilation	2.9 (1.2, 7.1)	0.1 (0, 1.4)	41
Respirations >27 breaths/min, predicting cardiopulmonary arrest, in medical inpatients	3.1 (1.9, 5.1)	0.6 (0.4, 0.7)	39
Respirations >28 breaths/min, detecting pneumonia in outpatients with cough and fever	2.7 (1.4, 5.1)	0.9 (0.8, 0.9)	9-38
Respirations >30 breaths/min, predicting hospital mortality in patients with pneumonia	2.1 (1.7, 2.6)	0.6 (0.5, 0.8)	6-17
EBM BOX 19-1 PULSE OXIMETRY			
O_2 saturation <90%, predicting hospital mortality	4.5 (1.9, 10.5)	0.8 (0.7, 0.9)	6-15
O_2 saturation <96%, detecting hepatopulmonary syndrome in patients with chronic liver disease	6.7 (2.6, 17.1)	0.6 (0.5, 0.8)	32
O_2 saturation <95%, detecting pneumonia in outpatients with cough and fever	3.1 (2.6, 3.7)	0.7 (0.5, 0.8)	11-13
CHAPTER 20 THE PUPILS			
Both pupils nonreactive to light, detecting unfavorable outcome after craniotomy for subdural hematoma	3.4 (1.5, 7.6)	0.4 (0.4, 0.5)	45-53
EBM BOX 20-1 PUPILS			
Anisocoria >1 mm, detecting intracranial structural lesion in patients with coma	9 (2.8, 28.8)	0.6 (0.5, 0.8)	40
Absent light reflex in at least one eye, detecting intracranial structural lesion in patients with coma	3.6 (2.3, 5.6)	0.2 (0.1, 0.4)	40
Anisocoria and 3rd nerve palsy, detecting intracranial hemorrhage in patients with stroke	3.2 (1.5, 7.1)	0.7 (0.6, 0.9)	48
Anisocoria or abnormal light reaction, detecting intracranial aneurysm in patients with 3rd nerve palsy	2.4 (1.9, 3.1)	0.2 (0.1, 0.4)	17-38
Anisocoria >1 mm following administration of topical cocaine, detecting Horner syndrome	96.8 (6.1, 1527)	0.1 (0, 0.1)	68

Continued

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
Small pupil dilates with hydroxyamphetamine, detecting 1st or 2nd neuron lesion in patients with Horner syndrome	9.2 (2, 43.6)	0.2 (0.1, 0.3)	45-52
Small pupil fails to dilate with topical phenylephrine, detecting 1st or 2nd neuron lesion in patients with Horner syndrome	4.2 (1.3, 13.4)	0.2 (0, 2.1)	21
Asymmetrical facial sweating, detecting 1st or 2nd neuron lesion in patients with Horner syndrome	2.4 (0.9, 6.1)	0.6 (0.4, 0.9)	63
Anisocoria ≥1 mm, small pupil in red eye, detecting serious eye disease	6.5 (2.6, 16.3)	0.8 (0.8, 0.9)	47
EBM BOX 21-1 DIABETIC RETINOPATHY			
Abnormal visual acuity 20/40 or worse	1.5 (1.3, 1.7)	0.9 (0.9, 1)	2-24
Direct ophthalmoscopy, nondilated pupils	6.2 (2.5, 14.9)	0.5 (0.3, 0.8)	21
Direct ophthalmoscopy, dilated pupils general providers	10.2 (6, 17.4)	0.4 (0.3, 0.5)	5-15
Direct ophthalmoscopy, dilated pupils, specialists	25.5 (8.2, 79.1)	0.3 (0.2, 0.5)	5-15
Nonmydriatic three-view digital photographs	31.5 (13, 76.6)	0.2 (0.1, 0.5)	8-10
EBM BOX 22-1 HEARING TESTS			
Abnormal whispered voice test	6 (4.4, 8.2)	0.03 (0, 0.3)	43-64
Cannot hear strong finger rub	355 (22, 5685)	0.4 (0.3, 0.5)	34
Cannot hear faint finger rub	3.9 (3.2, 4.8)	0.02 (0, 0.1)	34
Rinne test	16.8 (13.8, 20)	0.2 (0.1, 0.8)	6-46
Weber test lateralizes to good ear, detecting neurosensory loss	2.7 (1.2, 6.4)	0.5 (0.3, 1.1)	30
Weber test lateralizes to bad ear, detecting conductive loss	6.4 (1, 43.3)	0.5 (0.3, 0.8)	70
CHAPTER 23 THYROID DISEASE			
Half relaxation time >380 ms, detecting hypothyroidism	18.7 (13.3, 26)	0.1 (0, 0.2)	9-15
EBM BOX 23-1 GOITER			
No goiter by palpation or inspection	0.4 (0.3, 0.5)	—	37-79
Goiter by palpation, visible only after neck extension	0.9 (0.4, 2.1)	—	52
Goiter by palpation and inspection with neck in normal position	26.3 (5.2, 132)	—	37-65

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
EBM BOX 23-2 GOITER AND THYROID NODULES PREDICTING CARCINOMA			
Goiter, vocal cord paralysis	45.2 (2.7, 762)	0.8 (0.6, 0.9)	27
Goiter, cervical adenopathy	15.4 (4.8, 49)	0.6 (0.4, 0.7)	32
Goiter, fixation to tissues	10.5 (4.7, 23.5)	0.4 (0.3, 0.6)	32
Goiter, nodular (vs. diffuse)	1.5 (1.2, 1.9)	0.4 (0.2, 0.8)	31
Goiter, pyramidal lobe present	0.2 (0, 1.7)	1.1 (1, 1.2)	31
Thyroid nodule, vocal cord paralysis	17.9 (3.9, 81.1)	0.9 (0.9, 1)	15-23
Thyroid nodule, fixation to surrounding tissues	7.8 (3.3, 18.3)	0.8 (0.6, 1)	23-46
Thyroid nodule, cervical adenopathy	7.2 (4.3, 12)	0.8 (0.7, 0.9)	15-23
Thyroid nodule, ≥4 cm diameter	1.9 (1.4, 2.7)	0.5 (0.4, 0.7)	46
Thyroid nodule, very firm nodule	3.3 (0.2, 52.1)	1 (0.9, 1)	23
EBM BOX 23-2 HYPOTHYROIDISM			
Cool and dry skin	4.7 (3.1, 7.1)	0.9 (0.8, 0.9)	12
Coarse skin	3.4 (1.4, 8)	0.7 (0.5, 0.9)	18
Cold palms	1.6 (1, 2.7)	0.8 (0.6, 1.1)	18
Dry palms	1.5 (1, 2.4)	0.8 (0.6, 1.1)	18
Puffiness of face	1.7 (0.7, 4.2)	0.6 (0.4, 0.8)	18
Puffiness of wrists	2.9 (1.7, 4.9)	0.7 (0.5, 0.9)	18
Hair loss of eyebrows	1.9 (1.1, 3.6)	0.8 (0.7, 1)	18
Pretibial edema	1.1 (0.9, 1.5)	0.7 (0.3, 1.6)	18
Hypothyroid speech	5.4 (2.7, 10.7)	0.7 (0.5, 0.9)	18
Slow pulse rate	4.2 (3.2, 5.4)	0.7 (0.7, 0.8)	12-20
Enlarged thyroid	2.8 (2.3, 3.4)	0.6 (0.6, 0.7)	12
Delayed ankle reflex	3.4 (1.8, 6.4)	0.6 (0.4, 0.9)	18
Slow movements	1 (0.8, 1.2)	1 (0.3, 3.2)	18
Billewicz score <−15 points	0.1 (0, 0.2)	—	30-37
Billewicz score −15 to +29 points	0.9 (0.4, 2.1)	—	30-37
Billewicz score +30 points or more	18.8 (1.2, 301)	—	30-37
EBM BOX 23-4 HYPERTHYROIDISM			
Pulse rate ≥90 beats/min	4.5 (3.9, 5.2)	0.2 (0.2, 0.3)	50
Skin moist and warm	6.8 (5, 9.2)	0.7 (0.7, 0.7)	50
Thyroid enlargement	2.3 (2.1, 2.5)	0.1 (0.1, 0.2)	50
Eyelid retraction	33.2 (17.2, 64)	0.7 (0.6, 0.7)	50
Eyelid lag	18.6 (9.6, 36.1)	0.8 (0.8, 0.8)	50
Fine finger tremor	11.5 (8.8, 14.9)	0.3 (0.3, 0.4)	50
Wayne index <11 points	0.04 (0, 0.3)	—	32-43
Wayne index 11-19 points	1.2 (0.7, 2)	—	32-43
Wayne index ≥20 points	18.2 (2.9, 114)	—	32-43

Continued

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
CHAPTER 24 MENINGES			
Lack of focal neurologic findings, detecting subarachnoid hemorrhage in stroke	5.9 (3.5, 9.9)	0.4 (0.2, 0.7)	11
EBM BOX 24-1 MENINGEAL SIGNS			
Nuchal rigidity, detecting cerebrospinal fluid (CSF) white blood cell (WBC) count >100/μL	1.5 (1.1, 2.1)	0.8 (0.7, 1)	10-35
Kernig sign, detecting CSF WBC count >100/μL	2.4 (1.2, 4.9)	0.9 (0.8, 1)	10-35
Brudzinski sign, detecting CSF WBC count >100/μL	2.1 (0.97, 4.5)	0.9 (0.9, 1)	10-35
Neck stiffness, detecting intracranial hemorrhage in stroke	5.4 (2.5, 11.3)	0.7 (0.7, 0.9)	18-59
Kernig sign, detecting intracranial hemorrhage in stroke	2.9 (0.6, 14.1)	1 (0.9, 1.1)	18-46
CHAPTER 25 LYMPHADENOPATHY			
Generalized pruritus, detecting serious disease	4.9 (1.8, 13.1)	0.9 (0.9, 1)	26
Ear, nose, and throat symptoms, detecting serious disease	0.2 (0.1, 0.4)	1.4 (1.2, 1.6)	26-71
Epitrochlear nodes >0.5 cm, detecting human immunodeficiency virus (HIV) infection	4.5 (3.1, 6.7)	0.2 (0.1, 0.3)	56
Axillary adenopathy if tuberculosis, detecting HIV infection	4.9 (2.2, 11.2)	0.7 (0.5, 0.9)	9-56
EBM BOX 25-1 LYMPHADENOPATHY			
Male sex	1.3 (1.1, 1.6)	0.8 (0.7, 0.9)	26-60
Age ≥40 years	2.4 (1.7, 3.5)	0.4 (0.3, 0.6)	26-63
Weight loss	3.4 (2.2, 5.4)	0.8 (0.8, 0.9)	26-53
Fever	0.7 (0.5, 1)	1.1 (1, 1.2)	26-53
Head and neck nodes (not supraclavicular)	0.9 (0.8, 1.1)	1.1 (0.9, 1.2)	17-70
Supraclavicular nodes	3.2 (2.3, 4.3)	0.8 (0.7, 0.9)	17-70
Axillary nodes	0.8 (0.6, 0.9)	1.1 (1, 1.1)	17-70
Inguinal nodes	0.6 (0.4, 0.7)	1.1 (1, 1.1)	17-70
Epitrochlear nodes	0.7 (0.1, 7.6)	1 (1, 1.1)	41
Generalized lymphadenopathy	1.3 (0.6, 2.9)	1 (0.7, 1.4)	17-60
Node size <4 cm^2	0.4 (0.3, 0.7)	—	26
Node size 4-8.99 cm^2	2 (0.4, 9.2)	—	26
Node size ≥9 cm^2	8.4 (2.1, 32.8)	—	26
Hard texture	3.2 (2.4, 4.3)	0.6 (0.4, 0.7)	26
Lymph node tenderness	0.4 (0.3, 0.6)	1.3 (1.1, 1.5)	26-53

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
Fixed lymph node	10.9 (2, 59.2)	0.7 (0.3, 1.3)	26-53
Rash	0.6 (0.3, 1.4)	1 (1, 1.1)	26-41
Palpable spleen	1.2 (0.6, 2.5)	1 (0.9, 1)	26-41
Palpable liver	1.2 (0.7, 1.9)	1 (0.9, 1.1)	26-41
Score −3 or less	0.04 (0, 0.2)	—	24-26
Score −2 or −1	0.1 (0, 0.3)	—	24-26
Score 0 to 4	1.1 (0.5, 2.3)	—	24-26
Score 5 or 6	5.1 (2.9, 8.8)	—	24-26
Score 7 or more	21.9 (2.7, 179)	—	24-26
CHAPTER 26 INSPECTION OF THE CHEST			
Schamroth sign positive, detecting interphalangeal ratio >1	8 (5.1, 12.5)	0.2 (0.1, 0.3)	38
EBM BOX 26-1 CLUBBING			
Finger clubbing, detecting hypoxemia	3.2 (1.7, 6.1)	0.1 (0.1, 0.3)	75
Finger clubbing, detecting endocarditis	5.1 (2.9, 9.2)	0.9 (0.9, 1)	20
Finger clubbing, detecting hepatopulmonary syndrome	4.6 (1.8, 11.7)	0.6 (0.3, 0.9)	16-32
EBM BOX 26-2 INSPECTION OF THE CHEST			
Barrel chest, detecting chronic obstructive disease	1.5 (1.2, 2)	0.6 (0.4, 0.8)	49
Anteroposterior/lateral (AP/L) chest diameter ratio ≥0.9, detecting chronic obstructive disease	2 (1.1, 3.3)	0.8 (0.7, 1)	49
Pursed-lips breathing, detecting chronic obstructive disease	2.7 (1.8, 4)	0.5 (0.4, 0.7)	49
Scalene/sternomastoid muscle use, detecting chronic obstructive disease	3.3 (1.8, 5.9)	0.7 (0.6, 0.8)	49
Accessory muscle use in patients with amyotrophic lateral sclerosis (ALS) detecting respiratory neuromuscular weakness	4.9 (0.4, 61.7)	0.2 (0.1, 0.6)	92
Accessory muscle use, detecting pulmonary embolism	1.5 (0.6, 3.6)	0.9 (0.8, 1.1)	21
EBM BOX 27-1 PALPATION OF THE CHEST			
Asymmetrical chest expansion, detecting pneumonia	44.1 (2.1, 905)	1 (0.9, 1)	10
Asymmetrical chest expansion, detecting pleural effusion	8.1 (5.2, 12.7)	0.3 (0.2, 0.4)	21
Asymmetrical chest expansion, detecting right main-stem bronchus intubation	15.7 (4, 60.8)	0.7 (0.5, 1.1)	5

Continued

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
Diminished tactile fremitus, detecting pleural effusion	5.7 (4, 8)	0.2 (0.1, 0.4)	20
Chest wall tenderness, detecting pneumonia	1.2 (0.3, 5.3)	1 (0.9, 1.1)	16
Chest wall tenderness, detecting pulmonary embolism	0.8 (0.6, 1.1)	1.1 (1, 1.1)	21-23
Chest wall tenderness, detecting coronary artery disease	0.8 (0.7, 0.9)	1.1 (1, 1.3)	44-62
Chest wall tenderness, detecting myocardial infarction	0.3 (0.2, 0.4)	1.3 (1.1, 1.4)	12-17
EBM BOX 27-2 PERCUSSION OF THE CHEST			
Percussion dullness, detecting pneumonia	3 (1.7, 5.2)	0.9 (0.8, 1)	3-38
Percussion dullness, detecting chest radiograph abnormality	3 (1.4, 6.3)	0.9 (0.9, 1)	26-46
Percussion dullness, detecting pleural effusion	4.8 (3.6, 6.4)	0.1 (0.1, 0.3)	21
Hyperresonance in upper right anterior chest, detecting chronic obstructive disease	5.1 (1.7, 15.6)	0.7 (0.5, 1)	16
Reduced diaphragm excursion, detecting chronic airflow obstruction	5.3 (0.8, 35)	0.9 (0.7, 1.1)	16
Auscultatory percussion abnormal, detecting chest radiograph abnormality	1.7 (1, 3)	0.8 (0.6, 1.1)	26-46
Auscultatory percussion abnormal, detecting pleural effusion	8.3 (1.8, 38.7)	0.2 (0, 1.6)	21-40
CHAPTER 28 AUSCULTATION OF THE LUNGS			
Any crackles, predicting 30-day mortality in myocardial infarction	4.5 (3.9, 5.3)	0.7 (0.6, 0.8)	4
EBM BOX 28-1 BREATH SOUNDS AND VOCAL RESONANCE			
Breath sound score ≤9	10.2 (4.6, 22.7)	—	19-56
Breath sound score 10-12	3.6 (1.4, 9.5)	—	19-56
Breath sound score 13-15	0.7 (0.3, 1.5)	—	19-56
Breath sound score ≥16	0.1 (0, 0.3)	—	19-56
Diminished or absent breath sounds, detecting pleural effusion in hospitalized patients	5.2 (3.8, 7.1)	0.1 (0.1, 0.3)	21
Diminished breath sounds, detecting obstructive lung disease	3.2 (1.8, 5.5)	0.5 (0.3, 0.8)	15-49
Diminished breath sounds, detecting underlying pleural effusion in mechanically ventilated patients	4.3 (2.8, 6.5)	0.6 (0.5, 0.8)	26

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
Diminished breath sounds, detecting asthma during methacholine challenge	4.2 (1.9, 9.5)	0.3 (0.1, 0.6)	50
Diminished breath sounds, detecting pneumonia in patients with cough and fever	2.3 (1.9, 2.8)	0.8 (0.7, 0.9)	5-38
Asymmetrical breath sounds, detecting endobronchial intubation	24.4 (7.7, 77.8)	0.7 (0.5, 0.9)	5-16
Bronchial breath sounds, detecting pneumonia in patients with cough and fever	3.3 (2, 5.6)	0.9 (0.8, 1)	14
Egophony, detecting pneumonia in patients with cough and fever	4.1 (2.1, 7.8)	0.9 (0.9, 1)	3-38
Reduced vocal resonance, detecting pleural effusion in hospitalized patients	6.5 (4.4, 9.6)	0.3 (0.2, 0.4)	20
EBM BOX 28-2 CRACKLES AND WHEEZES			
Crackles, detecting pulmonary fibrosis in asbestos workers	5.9 (2, 17.2)	0.2 (0.1, 0.5)	58
Crackles, detecting elevated left atrial pressure in patients with cardiomyopathy	3.4 (1.6, 7.2)	0.7 (0.6, 1)	54-86
Crackles, detecting myocardial infarction in patients with chest pain	2.1 (1.6, 2.8)	0.8 (0.7, 1)	6-12
Crackles, detecting pneumonia in patients with cough and fever	1.8 (1.2, 2.7)	0.8 (0.7, 0.9)	3-38
Early inspiratory crackles, detecting airway obstruction in patients with crackles	14.6 (3, 70)	0.4 (0.1, 1.4)	15-55
Early inspiratory crackles, detecting severe disease in patients with chronic airflow obstruction	20.8 (3, 142.2)	0.1 (0, 0.4)	48
Unforced wheezing, detecting chronic airflow obstruction	2.8 (1.5, 5)	0.8 (0.7, 0.9)	13-83
Wheezing, detecting pneumonia in patients with cough and fever	0.8 (0.7, 0.9)	1.1 (1, 1.1)	5-38
Wheezing, detecting pulmonary embolism	0.4 (0.1, 0.97)	1.1 (1, 1.2)	23-40
Wheezing during methacholine challenge testing, detecting asthma	6 (1.5, 24.3)	0.6 (0.4, 0.9)	50

Continued

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
Pleural rub, detecting pulmonary embolism	1.4 (0.6, 3.1)	1 (1, 1)	21-23
Pleural rub, detecting pleural effusion	3.9 (0.8, 18.7)	1 (0.9, 1)	21
EBM BOX 29-1 ANCILLARY TESTS			
Forced expiratory time <3 seconds, detecting chronic obstruction	0.2 (0.1, 0.3)	—	55-71
Forced expiratory time 3-9 seconds, detecting chronic obstruction	1.3 (0.5, 2.9)	—	55-71
Forced expiratory time 9 or more seconds, detecting chronic obstruction	4.1 (2.6, 6.4)	—	55-71
Unable to blow out the match, detecting forced expiratory volume in 1 second (FEV_1) ≤1.6 L	9.6 (5.5, 16.6)	0.2 (0.1, 0.8)	37-56
CHAPTER 30 PNEUMONIA			
Absence of sore throat	1.8 (1.3, 2.5)	0.7 (0.6, 0.9)	5-10
Absence of rhinorrhea	2.2 (1.5, 3.2)	0.8 (0.7, 0.9)	5-10
CRB-65 0, predicting mortality	0.1 (0.1, 0.3)	1.4 (1.2, 1.6)	4-13
CRB 2 or 3, predicting mortality	5 (3.3, 7.5)	0.7 (0.6, 0.8)	4-10
EBM BOX 30-1 PNEUMONIA			
Cachexia	4 (1.7, 9.6)	0.9 (0.8, 1)	3
Abnormal mental status	1.9 (1.2, 3)	0.9 (0.9, 1)	14-38
Pulse rate >100 beats/min	1.7 (1.5, 1.8)	0.8 (0.7, 0.9)	3-38
Temperature >37.8° C	2.2 (1.7, 2.8)	0.7 (0.7, 0.8)	3-51
Respiratory rate >28 breaths/min	2.7 (1.4, 5.1)	0.9 (0.8, 0.9)	9-38
Oxygen saturation <95%	3.1 (2.6, 3.7)	0.7 (0.5, 0.8)	11-13
All vital signs normal	0.3 (0.1, 0.6)	2.2 (1.3, 3.8)	7-38
Asymmetrical chest expansion	44.1 (2.1, 905)	1 (0.9, 1)	10
Chest wall tenderness	1.2 (0.3, 5.3)	1 (0.9, 1.1)	16
Percussion dullness	3 (1.7, 5.2)	0.9 (0.8, 1)	3-38
Diminished breath sounds	2.3 (1.9, 2.8)	0.8 (0.7, 0.9)	5-38
Bronchial breath sounds	3.3 (2, 5.6)	0.9 (0.8, 1)	14
Egophony	4.1 (2.1, 7.8)	0.9 (0.9, 1)	3-38
Crackles	1.8 (1.2, 2.7)	0.8 (0.7, 0.9)	3-38
Wheezing	0.8 (0.7, 0.9)	1.1 (1, 1.1)	5-38
0 or 1 findings	0.3 (0.2, 0.4)	—	7-35
2 or 3 findings	1 (0.9, 1.2)	—	15-35
4 or 5 findings	8.2 (5.8, 11.5)	—	15-35

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
EBM BOX 30-2: PNEUMONIA AND MORTALITY			
Abnormal mental status	2.7 (2.1, 3.4)	0.6 (0.5, 0.7)	8-31
Heart rate >100 beats/min	2.1 (1.1, 3.8)	0.7 (0.5, 1)	31
Systolic blood pressure <90 mm Hg	7.6 (3.8, 15.3)	0.8 (0.6, 0.9)	4-10
Hypothermia	3.5 (1.1, 10.9)	0.8 (0.5, 1.2)	4-9
Respiratory rate ≥30 breaths/min	2.1 (1.7, 2.6)	0.6 (0.5, 0.8)	6-17
CURB-65 0	0.2 (0.1, 0.3)	—	4-15
CURB-65 1	0.4 (0.3, 0.6)	—	4-15
CURB-65 2	1 (0.8, 1.2)	—	4-15
CURB-65 3	2.5 (1.9, 3.2)	—	4-15
CURB-65 4	5.4 (4, 7.1)	—	4-13
CURB-65 5	11.2 (6.3, 20)	—	4-13
CHAPTER 31 CHRONIC OBSTRUCTIVE LUNG DISEASE			
Early inspiratory crackles, detecting severe disease	20.8 (3, 142.2)	0.1 (0, 0.4)	48
EBM BOX 31-1 CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
Barrel chest	1.5 (1.2, 2)	0.6 (0.4, 0.8)	49
Anteroposterior/lateral (AP/L) chest diameter ratio ≥0.9	2 (1.1, 3.3)	0.8 (0.7, 1)	49
Pursed-lips breathing	2.7 (1.8, 4)	0.5 (0.4, 0.7)	49
Scalene/sternomastoid muscle use	3.3 (1.8, 5.9)	0.7 (0.6, 0.8)	49
Maximum laryngeal height ≤4 cm	3.6 (2.1, 6)	0.7 (0.6, 0.8)	52
Laryngeal descent, >3 cm	0.9 (0.5, 1.4)	1 (0.9, 1.1)	52
Hoover sign	4.2 (2.5, 7)	0.5 (0.4, 0.7)	37
Subxiphoid cardiac impulse	7.4 (2, 27.1)	0.9 (0.7, 1.1)	16-44
Absent cardiac dullness, left lower sternum	11.8 (1.2, 121)	0.9 (0.7, 1.1)	14
Hyperresonance, upper right anterior chest	5.1 (1.7, 15.6)	0.7 (0.5, 1)	16
Diaphragm excursion <2 cm	5.3 (0.8, 35)	0.9 (0.7, 1.1)	16
Reduced breath sounds	3.2 (1.8, 5.5)	0.5 (0.3, 0.8)	15-49
Breath sound score ≤9	10.2 (4.6, 22.7)	—	19-56
Breath sound score 10-12	3.6 (1.4, 9.5)	—	19-56
Breath sound score 13-15	0.7 (0.3, 1.5)	—	19-56
Breath sound score ≥16	0.1 (0, 0.3)	—	19-56
Early inspiratory crackles	14.6 (3, 70)	0.4 (0.1, 1.4)	15-55
Any unforced wheeze	2.8 (1.5, 5)	0.8 (0.7, 0.9)	13-83
Forced expiratory time 9 or more seconds	4.1 (2.6, 6.4)	—	55-71
Forced expiratory time 3-9 seconds	1.3 (0.5, 2.9)	—	55-71

Continued

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
Forced expiratory time <3 seconds	0.2 (0.1, 0.3)	—	55-71
≥2 combined findings	25.7 (6.2, 106)	0.3 (0.2, 0.7)	16
EBM BOX 31-2 PROGNOSIS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)			
BAP-65 class 1	0.3 (0.3, 0.4)	—	3
BAP-65 class 2	0.4 (0.4, 0.5)	—	3
BAP-65 class 3	1.2 (1.2, 1.2)	—	3
BAP-65 class 4	3.8 (3.6, 4.1)	—	3
BAP-65 class 5	8.9 (7.4, 10.7)	—	3
CHAPTER 32 PULMONARY EMBOLISM			
Sudden dyspnea	2.4 (2, 2.9)	0.3 (0.2, 0.3)	40-43
Syncope	2 (1.6, 2.5)	0.9 (0.8, 1)	19-40
Hemoptysis	1.9 (1.5, 2.5)	1 (0.9, 1)	19-43
Pulse <90 beats/min	0.3 (0.1, 0.8)	1.8 (1.3, 2.5)	33
PaO_2 <80 mm Hg	1.1 (1, 1.3)	0.7 (0.4, 1.1)	28-36
A-a gradient <20 mm Hg	1.2 (0.9, 1.5)	0.6 (0.4, 1.01)	27-36
EBM BOX 32-1 PULMONARY EMBOLISM			
Diaphoresis	0.6 (0.3, 1.4)	1 (1, 1.1)	23
Cyanosis	2.3 (0.4, 15.6)	1 (1, 1)	21-23
Pulse rate >100 beats/min	1.3 (1, 1.6)	0.9 (0.8, 1)	23-43
Systolic blood pressure ≤100 mm Hg	1.9 (1.1, 3)	1 (0.9, 1)	27
Temperature >38° C	0.5 (0.3, 0.9)	1.1 (1, 1.1)	21-43
Respiratory rate >30 breaths/min	2 (1.5, 2.8)	0.9 (0.8, 0.9)	28
Accessory muscle use	1.5 (0.6, 3.6)	0.9 (0.8, 1.1)	21
Crackles	0.8 (0.4, 1.6)	1.1 (0.7, 1.8)	23-38
Wheezes	0.4 (0.1, 0.97)	1.1 (1, 1.2)	23-40
Pleural friction rub	1.4 (0.6, 3.1)	1 (1, 1)	21-23
Elevated neck veins	1.7 (1.1, 2.6)	1 (0.9, 1)	21-38
Left parasternal heave	2.4 (1.03, 5.5)	1 (1, 1)	21-23
Loud P_2	2 (0.8, 5.1)	0.9 (0.8, 1)	22-33
New gallop (S_3 or S_4)	2.7 (1, 7)	0.8 (0.6, 1)	33
Chest wall tenderness	0.8 (0.6, 1.1)	1.1 (1, 1.1)	21-23
Unilateral calf pain or swelling	2.2 (1.8, 2.7)	0.8 (0.7, 0.9)	19-43
Simplified Wells score low probability	0.3 (0.2, 0.4)	—	9-43
Simplified Wells score moderate probability	1.5 (1.3, 1.8)	—	9-43
Simplified Wells score high probability	6.7 (4.2, 10.6)	—	9-43
Modified Geneva score low probability	0.3 (0.3, 0.5)	—	15-32

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
Modified Geneva score moderate probability	1.1 (0.9, 1.4)	—	15-32
Modified Geneva score high probability	8.5 (6, 12.1)	—	15-32
CHAPTER 33 PLEURAL EFFUSION			
Absent vesicular breath sounds in acute respiratory distress syndrome (ARDS), detecting underlying pleural effusion	4.3 (2.8, 6.5)	0.6 (0.5, 0.8)	26
EBM BOX 33-1 PLEURAL EFFUSION			
Asymmetrical chest expansion	8.1 (5.2, 12.7)	0.3 (0.2, 0.4)	21
Reduced tactile fremitus	5.7 (4, 8)	0.2 (0.1, 0.4)	20
Dullness by conventional percussion	4.8 (3.6, 6.4)	0.1 (0.1, 0.3)	21
Auscultatory percussion (Guarino method)	8.3 (1.8, 38.7)	0.2 (0, 1.6)	21-40
Decreased or absent breath sounds	5.2 (3.8, 7.1)	0.1 (0.1, 0.3)	21
Reduced vocal resonance	6.5 (4.4, 9.6)	0.3 (0.2, 0.4)	20
Crackles	0.7 (0.5, 1)	1.5 (1.1, 2)	21
Pleural rub	3.9 (0.8, 18.7)	1 (0.9, 1)	21
CHAPTER 34 INSPECTION OF NECK VEINS			
Measured right atrial pressure ≥10 mm Hg, detecting pulmonary capillary wedge pressure ≥22 mm Hg	4.5 (3.6, 5.7)	0.3 (0.2, 0.3)	62
EBM BOX 34-1 INSPECTION OF NECK VEINS			
Elevated venous pressure, detecting central venous pressure (CVP) >8 cm water	9.7 (4.8, 19.7)	0.3 (0.2, 0.6)	30-55
Elevated venous pressure, detecting CVP >12 cm water	10.4 (5.5, 19.9)	0.1 (0, 0.6)	17-44
Elevated venous pressure, detecting elevated left heart diastolic pressures	3.9 (1.6, 9.4)	0.7 (0.5, 1)	19-75
Elevated venous pressure, detecting low left ventricular ejection fraction	6.3 (3.5, 11.3)	0.9 (0.8, 1)	8-69
Elevated venous pressure, detecting myocardial infarction in patients with chest pain	2.4 (1.4, 4.2)	0.9 (0.9, 1)	6
Elevated venous pressure, predicting postoperative pulmonary edema	11.3 (5, 25.8)	0.8 (0.7, 1)	4

Continued

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
Elevated venous pressure, predicting postoperative myocardial infarction or congestive heart failure (CHF)	9.4 (4, 22.4)	0.8 (0.7, 1)	4
Estimated venous pressure ≤5 cm water, detecting measured venous pressure ≤5 cm water	8.4 (2.8, 25)	0.1 (0, 0.7)	26
Positive abdominojugular test, detecting elevated left heart diastolic pressures	8 (2.1, 31.2)	0.3 (0.2, 0.6)	17-75
Early systolic outward movement, detecting moderate-to-severe tricuspid regurgitation	10.9 (5.5, 21.7)	0.7 (0.5, 0.8)	18
EBM BOX 35-1 PERCUSSION OF THE HEART			
Cardiac dullness >10.5 cm from midsternal line (patient supine), detecting cardiothoracic ratio >0.5	2.5 (1.8, 3.4)	0.05 (0, 0.3)	36
Cardiac dullness extending >10.5 cm from midsternal line (patient supine), detecting increased left ventricular end-diastolic volume	1.4 (1.1, 1.7)	0.2 (0, 1.3)	17
Cardiac dullness extending beyond midclavicular line (patient upright), detecting cardiothoracic ratio >0.5	2.4 (1.1, 5.2)	0.05 (0, 0.4)	76
EBM BOX 36-1 SIZE AND POSITION OF APICAL IMPULSE			
Supine apical impulse lateral to midclavicular line (MCL), detecting cardiothoracic ratio >0.5	3.4 (1.6, 7.3)	0.6 (0.5, 0.8)	25-28
Supine apical impulse lateral to MCL, detecting low ejection fraction	10.3 (5, 21.1)	0.7 (0.6, 0.9)	8-69
Supine apical impulse lateral to MCL, detecting increased left ventricular end-diastolic volume	5.1 (2.7, 9.7)	0.7 (0.6, 0.8)	15-48
Supine apical impulse lateral to MCL, detecting pulmonary capillary wedge pressure >12 mm Hg	5.8 (1.3, 26)	0.6 (0.4, 1)	30
Supine apical impulse >10 cm from midsternal line, detecting cardiothoracic ratio >0.5	4.3 (0.3, 70.8)	0.5 (0.3, 0.8)	25-36

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
Apical beat diameter ≥4 cm in left lateral decubitus position at 45 degrees, detecting increased left ventricular end-diastolic volume	4.7 (2.1, 10.2)	0.4 (0.2, 1)	32-50
EBM BOX 36-2 ABNORMAL PALPABLE MOVEMENTS			
Hyperkinetic apical movement, detecting associated mitral regurgitation or aortic valve disease in patients with mitral stenosis	11.2 (6.4, 19.5)	0.3 (0.2, 0.4)	39
Sustained or double supine apical impulse, detecting left ventricular hypertrophy	5.6 (3.3, 9.5)	0.5 (0.3, 0.7)	27
Sustained apical movement detecting aortic stenosis in patients with aortic flow murmurs	4.1 (1.7, 10.1)	0.3 (0.1, 0.5)	69
Sustained apical movement, detecting moderate-to-severe aortic regurgitation in patients with basal early diastolic murmurs	2.4 (1.4, 4)	0.1 (0, 0.9)	41
Lower sternal movements, detecting moderate-to-severe tricuspid regurgitation	12.5 (4.1, 38)	0.8 (0.8, 0.9)	18
Sustained left lower parasternal movement, detecting right ventricular peak pressure ≥50 mm Hg	3.6 (1.4, 8.9)	0.4 (0.2, 0.7)	51
Right ventricular rock, detecting moderate-to-severe tricuspid regurgitation	31.4 (1.6, 601)	0.9 (0.9, 1)	18
Pulsatile liver, detecting moderate-to-severe tricuspid regurgitation	6.5 (2.2, 19.3)	0.8 (0.7, 1)	18-41
Palpable S_2, detecting pulmonary hypertension in patients with mitral stenosis	3.6 (1.5, 8.8)	0.05 (0, 0.8)	52
EBM BOX 38-1 FIRST AND SECOND HEART SOUNDS			
Varying intensity of S_1, detecting atrioventricular dissociation	24.4 (1.5, 385)	0.4 (0.3, 0.7)	55
Fixed wide splitting of S_2, detecting atrial septal defect	2.6 (1.6, 4.3)	0.1 (0, 0.8)	30
Paradoxic splitting of S_2, detecting significant aortic stenosis	2.4 (0.8, 7)	0.6 (0.2, 1.7)	5
Loud P_2, detecting pulmonary hypertension	1.2 (0.9, 1.5)	0.8 (0.3, 1.9)	32-52

Continued

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
Palpable P_2, detecting pulmonary hypertension	3.6 (1.5, 8.8)	0.05 (0, 0.8)	52
Absent or soft S_2, detecting severe aortic stenosis in patients with aortic flow murmurs	3.1 (2.1, 4.7)	0.4 (0.3, 0.6)	5-60
CHAPTER 39 THIRD AND FOURTH HEART SOUNDS			
S_3 in aortic stenosis, detecting pulmonary capillary wedge pressure >12 mm Hg	2.3 (1.3, 4)	0.9 (0.8, 1)	46
S_3 in aortic stenosis, detecting ejection fraction <0.5	5.7 (2.7, 12)	0.8 (0.7, 0.9)	41
S_3 in aortic regurgitation, detecting severe regurgitation	5.9 (1.4, 25.3)	0.8 (0.7, 0.9)	50
EBM BOX 39-1 THIRD AND FOURTH HEART SOUNDS			
S_3, detecting ejection fraction <0.5	3.4 (2.6, 4.4)	0.7 (0.5, 0.8)	30-80
S_3, detecting ejection fraction <0.3	4.1 (2.3, 7.3)	0.3 (0.2, 0.5)	19-47
S_3, detecting elevated left heart filling pressure	3.9 (2.1, 7.1)	0.8 (0.7, 0.9)	19-68
S_3, detecting elevated B-type natriuretic peptide (BNP) level	10.1 (4.2, 23.9)	0.5 (0.3, 0.8)	50-61
S_3, detecting myocardial infarction in patients with acute chest pain	3.2 (1.6, 6.5)	0.9 (0.8, 1)	12
S_3, predicting postoperative pulmonary edema	14.6 (5.7, 37.3)	0.8 (0.7, 1)	4
S_3, predicting postoperative myocardial infarction or cardiac death	8 (2.7, 23.4)	0.9 (0.8, 1)	4
S_4, predicting 5-year mortality in patients after myocardial infarction	3.2 (1.3, 7.8)	0.8 (0.6, 1.1)	9
S_4, detecting elevated left heart filling pressures	1.3 (0.8, 1.9)	0.9 (0.7, 1.2)	46-67
S_4, detecting severe aortic stenosis	0.9 (0.5, 1.9)	1.1 (0.6, 1.9)	5-90
EBM BOX 41-1 MURMURS AND VALVULAR HEART DISEASE			
Functional murmur, detecting normal echocardiogram	4.7 (2.1, 10.7)	0.1 (0, 1.4)	21-77
Characteristic murmur, detecting mild or worse aortic stenosis	5.9 (4.5, 7.8)	0.1 (0.1, 0.2)	20
Characteristic murmur, detecting severe aortic stenosis	3.6 (3, 4.3)	0.06 (0, 0.1)	7-26

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
Characteristic murmur, detecting mild or worse mitral regurgitation	5.4 (3.7, 8.1)	0.4 (0.2, 0.7)	43-57
Characteristic murmur, detecting moderate or severe mitral regurgitation	2.6 (1.6, 4)	0.3 (0.2, 0.6)	10-20
Characteristic murmur, detecting mild or worse tricuspid regurgitation	14.6 (4.5, 47.1)	0.8 (0.7, 0.9)	39
Characteristic murmur, detecting moderate or severe tricuspid regurgitation	9.6 (6, 15.4)	0.6 (0.3, 1.2)	7-18
Characteristic murmur, detecting ventricular septal defect	24.9 (8.6, 72.7)	0.1 (0, 1.4)	4
Characteristic murmur, detecting mitral valve prolapse	12.1 (4, 36.4)	0.5 (0.2, 0.9)	11
Characteristic murmur, detecting mild aortic regurgitation or worse	9.9 (4.9, 20)	0.3 (0.2, 0.4)	29-88
Characteristic murmur, detecting moderate or severe aortic regurgitation	4.3 (2.1, 8.6)	0.1 (0.1, 0.2)	8-35
Characteristic murmur, detecting pulmonic regurgitation	17.4 (3.6, 83.2)	0.9 (0.8, 1)	15
EBM BOX 41-2 DIFFERENTIAL DIAGNOSIS OF SYSTOLIC MURMURS IN ADULTS			
Detecting aortic velocity ≥2.5 m/sec			
Broad apical-base murmur pattern	9.7 (6.7, 14)	0.1 (0.1, 0.2)	20
Broad apical murmur pattern	0.2 (0.1, 0.9)	1.1 (1.1, 1.2)	20
Left lower sternal border (LLSB) murmur pattern	0.7 (0.2, 2.4)	1 (1, 1.1)	20
S_1 inaudible	5.1 (3.5, 7.4)	0.5 (0.4, 0.6)	20
S_2 inaudible	12.7 (5.3, 30.4)	0.7 (0.6, 0.8)	21
S_2 loud	1.7 (0.9, 3.1)	0.9 (0.8, 1)	21
Radiation to neck	2.4 (1.9, 3)	0.2 (0.1, 0.3)	33
Timing midsystolic or early systolic	0.4 (0.3, 0.6)	2 (1.5, 2.5)	33
Timing long systolic or holosystolic	2.2 (1.7, 2.8)	0.4 (0.3, 0.6)	33
Coarse quality murmur	3.3 (2.4, 4.5)	0.3 (0.2, 0.4)	33
Murmur same intensity in beat after pause	0.4 (0.2, 0.7)	1.9 (1.3, 2.8)	36
Detecting moderate or severe mitral regurgitation			
Broad apical-base murmur pattern	1.1 (0.7, 1.7)	1 (0.8, 1.1)	20

Continued

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
Broad apical murmur pattern	6.8 (3.9, 11.9)	0.7 (0.6, 0.8)	20
LLSB murmur pattern	1.1 (0.4, 3.4)	1 (0.9, 1.1)	20
S_1 inaudible	1.4 (0.9, 2.2)	0.9 (0.8, 1.1)	20
S_2 inaudible	0.5 (0.2, 1.6)	1.1 (1, 1.1)	20
S_2 loud	4.7 (2.7, 8.3)	0.7 (0.6, 0.9)	20
Radiation to neck	0.6 (0.4, 0.9)	1.6 (1.2, 2.1)	28
Timing midsystolic or early systolic	0.4 (0.2, 0.6)	1.9 (1.5, 2.5)	28
Timing long systolic or holosystolic	1.9 (1.5, 2.4)	0.5 (0.3, 0.7)	28
Coarse quality murmur	0.5 (0.3, 0.8)	1.5 (1.2, 1.8)	28
Murmur same intensity in beat after pause	2.5 (1.5, 4.3)	0.4 (0.3, 0.7)	44
Detecting moderate or severe tricuspid regurgitation			
Broad apical-base murmur pattern	0.8 (0.4, 1.3)	1.1 (0.9, 1.3)	18
Broad apical murmur pattern	2.5 (1.4, 4.5)	0.8 (0.7, 1)	18
LLSB murmur pattern	8.4 (3.5, 20.3)	0.8 (0.7, 0.9)	18
S_1 inaudible	1 (0.6, 1.7)	1 (0.9, 1.1)	18
S_2 inaudible	1.4 (0.6, 3.3)	1 (0.9, 1.1)	18
S_2 loud	3.6 (2.1, 6.3)	0.7 (0.6, 0.9)	18
Radiation to neck	0.6 (0.4, 0.9)	1.5 (1.2, 2)	22
Timing midsystolic or early systolic	0.5 (0.3, 0.8)	1.7 (1.3, 2.1)	22
Timing long systolic or holosystolic	1.7 (1.3, 2.2)	0.5 (0.3, 0.8)	22
Coarse quality murmur	0.5 (0.3, 0.9)	1.4 (1.2, 1.8)	22
Murmur same intensity in beat after pause	2.3 (1.4, 3.6)	0.4 (0.2, 0.8)	35
EBM BOX 41-3 SYSTOLIC MURMURS AND MANEUVERS			
Murmur louder with inspiration, detecting right-sided murmur	7.8 (3.7, 16.7)	0.2 (0.1, 0.5)	20-50
Murmur louder with Valsalva strain, detecting hypertrophic cardiomyopathy	14 (3.4, 57.4)	0.3 (0.1, 0.8)	20
Murmur louder with squatting-to-standing, detecting hypertrophic cardiomyopathy	6 (2.9, 12.3)	0.1 (0, 0.8)	20
Murmur softer with standing-to-squatting, detecting hypertrophic cardiomyopathy	7.6 (2.5, 22.7)	0.1 (0, 0.4)	20-41
Murmur softer with passive leg elevation, detecting hypertrophic cardiomyopathy	9 (3.5, 23.3)	0.1 (0, 0.7)	20

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
Murmur softer with hand grip, detecting hypertrophic cardiomyopathy	3.6 (2, 6.4)	0.1 (0, 0.9)	20
Murmur louder with hand grip, detecting mitral regurgitation or ventricular septal defect	5.8 (1.9, 17.3)	0.3 (0.2, 0.5)	40-65
Murmur louder with transient arterial occlusion, detecting mitral regurgitation or ventricular septal defect	48.7 (3.1, 769)	0.2 (0.1, 0.5)	40
Murmur softer with amyl nitrite inhalation, detecting mitral regurgitation or ventricular septal defect	10.5 (5.1, 21.5)	0.2 (0.1, 0.6)	40-71
CHAPTER 42 AORTIC STENOSIS			
Effort syncope and aortic murmur, detecting severe aortic stenosis	3.1 (1.3, 7.3)	0.9 (0.8, 1)	70-75
Angina and aortic murmur, detecting severe aortic stenosis	0.9 (0.7, 1)	1.3 (0.9, 1.9)	70
Dyspnea and aortic murmur, detecting severe aortic stenosis	1.4 (0.6, 3.1)	0.8 (0.4, 1.5)	70
Calcification of aortic valve on chest x-ray, detecting severe aortic stenosis	3.9 (2.1, 7.3)	0.5 (0.4, 0.7)	49-70
ECG left ventricular hypertrophy, detecting severe aortic stenosis	2.1 (1.7, 2.7)	0.5 (0.4, 0.6)	13-70
Delayed carotid artery upstroke, detecting moderate-to-severe aortic stenosis	9 (3.2, 25.2)	0.6 (0.5, 0.7)	13-57
Absent or diminished S_2, detecting moderate-to-severe aortic stenosis	7.3 (2.3, 23.3)	0.5 (0.4, 0.7)	13-57
Murmur late peaking, detecting moderate-to-severe aortic stenosis	29.5 (9.6, 91.1)	0.3 (0.2, 0.4)	24-49
Murmur prolonged duration, detecting moderate-to-severe aortic stenosis	11.4 (1.3, 97.2)	0.3 (0.2, 0.4)	24-57
EBM BOX 42-1 AORTIC STENOSIS MURMUR			
Aortic systolic murmur, detecting mild or worse aortic stenosis	5.9 (4.5, 7.8)	0.1 (0.1, 0.2)	20
Aortic systolic murmur, detecting severe aortic stenosis	3.6 (3, 4.3)	0.06 (0, 0.1)	7-26

Continued

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
EBM BOX 42-2 SEVERE AORTIC STENOSIS			
Delayed carotid artery upstroke	3.3 (2.4, 4.5)	0.4 (0.2, 0.8)	5-69
Reduced carotid artery volume	2.3 (1.8, 2.9)	0.4 (0.3, 0.7)	28-69
Brachioradial delay	2.5 (1.4, 4.7)	0.04 (0, 0.7)	52
Sustained apical impulse	4.1 (1.7, 10.1)	0.3 (0.1, 0.5)	69
Apical-carotid delay	2.6 (1.4, 5.2)	0.05 (0, 0.7)	53
Absent or soft S_2	3.1 (2.1, 4.7)	0.4 (0.3, 0.6)	5-60
S_4 gallop	0.9 (0.5, 1.9)	1.1 (0.6, 1.9)	5-90
Murmur grade ≥3/6	1.2 (1, 1.4)	0.8 (0.5, 1.3)	29-70
Murmur early systolic	0.1 (0, 0.7)	1.6 (1.3, 2)	28
Murmur prolonged duration	3 (1.7, 5.2)	0.2 (0.1, 0.4)	5-28
Murmur late peaking	4.4 (2.5, 7.6)	0.2 (0.1, 0.3)	5-75
Murmur loudest over aortic area	1.8 (1.1, 2.9)	0.6 (0.4, 0.7)	5-49
Murmur radiates to neck	1.3 (1, 1.6)	0.1 (0, 0.3)	5-49
Murmur radiates to both sides of neck	1.9 (1.1, 3.4)	0.7 (0.4, 1)	28
Murmur quality blowing	0.1 (0, 0.8)	1.4 (1.2, 1.7)	28
Murmur with humming quality	2.1 (1.3, 3.5)	0.5 (0.3, 0.9)	28
EBM BOX 43-1 AORTIC REGURGITATION			
Characteristic diastolic murmur, detecting mild aortic regurgitation or worse	9.9 (4.9, 20)	0.3 (0.2, 0.4)	29-88
Characteristic diastolic murmur, detecting moderate or severe aortic regurgitation	4.3 (2.1, 8.6)	0.1 (0.1, 0.2)	8-35
Murmur loudest on right side of sternum, detecting dilated aortic root or endocarditis	8.2 (5, 13.3)	0.7 (0.7, 0.8)	14
Murmur softer with amyl nitrite, detecting aortic regurgitation (vs. Graham Steell murmur)	5.7 (0.5, 71.4)	0.1 (0, 0.3)	93
EBM BOX 43-2 MODERATE-TO-SEVERE AORTIC REGURGITATION			
Murmur grade 3 or louder	8.2 (2.2, 31.1)	0.6 (0.4, 0.9)	24-45
Diastolic blood pressure >70 mm Hg	0.2 (0.1, 0.9)	—	41-56
Diastolic blood pressure 51-70 mm Hg	1.1 (0.7, 1.7)	—	41-56
Diastolic blood pressure ≤50 mm Hg	19.3 (2.7, 141)	—	41-56
Pulse pressure <60 mm Hg	0.3 (0.1, 0.9)	—	42
Pulse pressure 60-79 mm Hg	0.8 (0.2, 2.9)	—	42
Pulse pressure ≥80 mm Hg	10.9 (1.5, 77.1)	—	42
Hill test <40 mm Hg	0.3 (0.2, 0.8)	—	42
Hill test 40-59 mm Hg	2.4 (0.6, 9.7)	—	42

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
Hill test ≥60 mm Hg	17.3 (1.1, 284)	—	42
Enlarged or sustained apical impulse	2.4 (1.4, 4)	0.1 (0, 0.9)	41
S_3 gallop	5.9 (1.4, 25.3)	0.8 (0.7, 0.9)	50
Duroziez sign, femoral pistol shot, water-hammer pulse	3.4 (0.4, 31)	0.7 (0.5, 0.9)	41-75
CHAPTER 44 MISCELLANEOUS HEART MURMURS			
Apical systolic murmur, detecting mild or worse mitral regurgitation	5.4 (3.7, 8.1)	0.4 (0.2, 0.7)	43-57
Apical systolic murmur, detecting moderate-to-severe mitral regurgitation	2.6 (1.6, 4)	0.3 (0.2, 0.6)	10-20
Characteristic mitral valve prolapse (MVP) murmur, detecting MVP	12.1 (4, 36.4)	0.5 (0.2, 0.9)	11
Characteristic murmur of pulmonic regurgitation (PR), detecting PR	17.4 (3.6, 83.2)	0.9 (0.8, 1)	15
Characteristic tricuspid regurgitation murmur, detecting mild or worse tricuspid regurgitation	14.6 (4.5, 47.1)	0.8 (0.7, 0.9)	39
Characteristic tricuspid regurgitation murmur, detecting moderate-to-severe tricuspid regurgitation	9.6 (6, 15.4)	0.6 (0.3, 1.2)	7-18
Apical mid-diastolic rumble, detecting mitral annular calcification	7.5 (2.3, 24.4)	0.9 (0.9, 1)	55
EBM BOX 44-1 MODERATE-TO-SEVERE MITRAL OR TRICUSPID REGURGITATION			
Mitral regurgitation (MR) murmur grade 3 or louder	4.4 (2.9, 6.7)	0.2 (0.1, 0.3)	42
S_3 gallop (MR)	4.4 (0.6, 31.8)	0.8 (0.7, 0.8)	49-62
CV wave, neck veins (tricuspid regurgitation [TR])	10.9 (5.5, 21.7)	0.7 (0.5, 0.8)	18
Lower sternal precordial pulsation (TR)	12.5 (4.1, 38)	0.8 (0.8, 0.9)	18
Right ventricular rock (TR)	31.4 (1.6, 601)	0.9 (0.9, 1)	18
Pulsatile liver (TR)	6.5 (2.2, 19.3)	0.8 (0.7, 1)	18-41
EBM BOX 44-2 OTHER FINDINGS IN MITRAL STENOSIS			
Graham Steell murmur, detecting pulmonary hypertension	4.2 (1.1, 15.5)	0.4 (0.2, 0.9)	52
Hyperkinetic apical movement, detecting associated mitral regurgitation or aortic valve disease	11.2 (6.4, 19.5)	0.3 (0.2, 0.4)	39

Continued

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
Hyperkinetic arterial pulse, detecting associated mitral regurgitation	14.2 (7.4, 27.2)	0.3 (0.2, 0.4)	35
CHAPTER 45 DISORDERS OF THE PERICARDIUM			
Pericardial rub in patient with cancer, detecting idiopathic or radiation-induced pericarditis (not neoplastic)	5.5 (1.4, 21.9)	0.4 (0.2, 0.9)	42
Pulsus paradoxus >12 mm Hg, detecting cardiac tamponade	5.9 (2.4, 14.3)	0.03 (0, 0.2)	63
CHAPTER 46 CONGESTIVE HEART FAILURE			
Crackles, detecting elevated filling pressure in patients with known cardiomyopathy	3.4 (1.6, 7.2)	0.7 (0.6, 1)	54-86
Pulse amplitude ratio >0.7, detecting wedge pressure >15 mm Hg	18.2 (2.7, 123)	0.1 (0, 0.4)	52
S_3 gallop, detecting ejection fraction <30%	4.1 (2.3, 7.3)	0.3 (0.2, 0.5)	19-47
Proportional pulse pressure ≤25%, detecting low cardiac index	6.9 (3, 15.8)	0.2 (0.1, 0.6)	50-64
Elevated neck veins, detecting consensus diagnosis of heart failure	4.8 (3.9, 6)	0.7 (0.7, 0.8)	35-71
S_3, detecting consensus diagnosis of heart failure	6.9 (4.8, 9.9)	0.9 (0.8, 0.9)	35-55
B-type natriuretic peptide (BNP) ≥100 pg/mL, detecting consensus diagnosis of heart failure	3.6 (2.1, 6.3)	0.1 (0.1, 0.1)	39-55
EBM BOX 46-1 DETECTING ELEVATED LEFT HEART FILLING PRESSURE			
Heart rate >100 beats/min at rest	5.5 (1.3, 24.1)	0.9 (0.9, 1)	19
Abnormal Valsalva response	7.6 (1.7, 34.3)	0.1 (0, 0.8)	48
Pulse increase of 10% during Valsalva strain	0.2 (0.1, 0.9)	1.7 (1.3, 2.2)	25
Crackles	1.6 (0.8, 2.9)	0.9 (0.9, 1)	19-77
Elevated jugular venous pressure	3.9 (1.6, 9.4)	0.7 (0.5, 1)	19-75
Positive abdominojugular test	8 (2.1, 31.2)	0.3 (0.2, 0.6)	17-75
Supine apical impulse lateral to midclavicular line (MCL)	5.8 (1.3, 26)	0.6 (0.4, 1)	30
S_3 gallop	3.9 (2.1, 7.1)	0.8 (0.7, 0.9)	19-68
S_4 gallop	1.3 (0.8, 1.9)	0.9 (0.7, 1.2)	46-67
Edema	1.4 (0.6, 3.2)	1 (0.9, 1)	19-68

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
EBM BOX 46-2 DETECTING LOW EJECTION FRACTION			
Heart rate >100 beats/min at rest	2.8 (1.3, 5.9)	0.8 (0.7, 1)	16
Abnormal Valsalva response	7.6 (4.9, 11.8)	0.3 (0.2, 0.4)	41-46
Crackles	1.5 (0.9, 2.4)	0.9 (0.8, 1)	8-69
Elevated jugular venous pressure	6.3 (3.5, 11.3)	0.9 (0.8, 1)	8-69
Supine apical impulse lateral to midclavicular line (MCL)	10.3 (5, 21.1)	0.7 (0.6, 0.9)	8-69
S_3 gallop	3.4 (2.6, 4.4)	0.7 (0.5, 0.8)	30-80
S_4 gallop	1.2 (0.8, 1.9)	0.9 (0.5, 1.4)	30-60
Murmur of mitral regurgitation	2.2 (0.9, 5.7)	0.8 (0.7, 1)	56
Hepatomegaly	0.9 (0.1, 9.4)	1 (0.9, 1.1)	69
Edema	1.2 (0.8, 1.8)	0.9 (0.9, 1)	8-69
CHAPTER 47 CORONARY ARTERY DISEASE			
Troponin T positive (>6 hours after onset of chest pain), predicting cardiac events	6.1 (4.7, 7.9)	0.2 (0.1, 0.5)	4
EBM BOX 47-1 CORONARY ARTERY DISEASE			
Typical angina	5.8 (4.2, 7.8)	—	44-65
Atypical angina	1.2 (1.1, 1.3)	—	44-58
Nonanginal chest pain	0.1 (0.1, 0.2)	—	44-58
Pain duration >30 minutes	0.1 (0, 0.9)	1.2 (1, 1.3)	50
Associated dysphagia	0.2 (0.1, 0.8)	1.2 (1, 1.4)	50
Male sex	1.7 (1.6, 1.8)	0.3 (0.3, 0.4)	51-83
Age <30 years	0.1 (0, 1.1)	—	51-68
Age 30-49 years	0.6 (0.5, 0.7)	—	51-83
Age 50-70 years	1.3 (1.3, 1.4)	—	51-83
Age >70 years	2.6 (1.8, 4)	—	51-90
Prior myocardial infarction	3.8 (2.1, 6.8)	0.6 (0.5, 0.6)	58-83
Earlobe crease	2.3 (1.3, 4.1)	0.6 (0.4, 0.8)	60-85
Arcus senilis	3 (1.02, 8.6)	0.7 (0.6, 0.8)	89
Chest wall tenderness	0.8 (0.7, 0.9)	1.1 (1, 1.3)	44-62
Ankle-to-arm pressure index <0.9	4 (2.3, 6.9)	0.8 (0.8, 0.8)	75-82
Laterally displaced apical impulse	13 (0.7, 228.3)	1 (0.9, 1)	50
ECG normal	0.6 (0.3, 1.1)	1.2 (1, 1.6)	44-58
ECG with ST/T wave abnormalities	1.4 (1, 1.9)	0.9 (0.9, 1)	44-76
EBM BOX 47-2 MYOCARDIAL INFARCTION			
Male sex	1.3 (1.2, 1.3)	0.7 (0.7, 0.7)	6-36
Age, <40 years	0.2 (0.1, 0.5)	1.2 (1.1, 1.3)	17
Age, 40-59 years	0.8 (0.6, 1.1)	1.2 (1, 1.4)	17

Continued

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
Age, ≥ 60 years	1.5 (1.4, 1.6)	0.6 (0.5, 0.8)	14-36
Sharp pain	0.3 (0.2, 0.5)	1.3 (1.3, 1.4)	12-17
Pleuritic pain	0.2 (0.2, 0.3)	1.2 (1.2, 1.3)	12-17
Positional pain	0.3 (0.2, 0.5)	1.1 (1.1, 1.2)	14-17
Relief of pain with nitroglycerin	1 (0.9, 1.1)	1 (0.9, 1.2)	18-34
Levine sign	0.5 (0.2, 1.6)	1.1 (1, 1.2)	22
Palm sign	0.9 (0.5, 1.4)	1.1 (0.9, 1.4)	22
Arm sign	1.1 (0.5, 2.2)	1 (0.8, 1.2)	22
Pointing sign	0.4 (0.1, 3.5)	1 (1, 1.1)	22
Chest wall tenderness	0.3 (0.2, 0.4)	1.3 (1.1, 1.4)	12-17
Diaphoretic appearance	2.2 (1.7, 2.9)	0.7 (0.6, 0.8)	12-29
Pallor	1.4 (1.2, 1.6)	0.6 (0.5, 0.8)	29
Systolic blood pressure <100 mm Hg	3.6 (2, 6.5)	1 (0.9, 1)	18
Jugular venous distention	2.4 (1.4, 4.2)	0.9 (0.9, 1)	6
Pulmonary crackles	2.1 (1.6, 2.8)	0.8 (0.7, 1)	6-12
Third heart sound	3.2 (1.6, 6.5)	0.9 (0.8, 1)	12
ECG normal	0.2 (0.1, 0.3)	1.5 (1.4, 1.6)	14-42
ECG nonspecific ST changes	0.2 (0.1, 0.4)	1.4 (1.1, 1.9)	14-29
ECG ST elevation	22.3 (16.7, 30)	0.6 (0.5, 0.6)	12-29
ECG ST depression	3.9 (3, 5.2)	0.8 (0.7, 0.8)	12-29
ECG T wave inversion	2 (1.5, 2.5)	0.9 (0.9, 1)	12-29
EBM BOX 47-3 PREDICTING COMPLICATIONS			
Goldman "high" risk	8.7 (4.4, 17.1)	0.5 (0.3, 0.8)	1
Goldman "very low" risk	0.1 (0.1, 0.2)	2 (1.7, 2.4)	1
CHAPTER 49 PALPATION AND PERCUSSION OF THE ABDOMEN			
Lymphadenopathy, detecting hepatic cause of splenomegaly	0.04 (0, 0.6)	1.3 (1.1, 1.4)	42
Hepatomegaly, detecting hepatic cause of splenomegaly	2.7 (1.8, 3.9)	0.4 (0.3, 0.6)	42
Massive splenomegaly, detecting hematologic cause of splenomegaly	2.1 (1.1, 3.8)	0.8 (0.7, 1)	40
EBM BOX 49-1 DETECTING ENLARGED LIVER AND SPLEEN			
Percussion span ≥10 cm, detecting enlarged liver	1.2 (1, 1.5)	0.5 (0.2, 1.7)	20-74
Palpable liver, detecting liver edge	234 (15, 3737)	0.5 (0.5, 0.6)	51
Palpable liver, detecting enlarged liver	1.9 (1.6, 2.3)	0.6 (0.5, 0.8)	20-44
Palpable spleen, detecting enlarged spleen	8.5 (6.2, 11.8)	0.5 (0.4, 0.7)	7-84

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
Spleen percussion sign, detecting enlarged spleen	1.7 (1.2, 2.2)	0.7 (0.5, 0.9)	26-61
Nixon method, detecting enlarged spleen	2 (1.2, 3.5)	0.7 (0.6, 0.9)	26-61
Traube space dullness, detecting enlarged spleen	2.1 (1.7, 2.6)	0.8 (0.6, 0.9)	36-61
EBM BOX 49-2 PALPATION OF LIVER AND SPLEEN			
Palpable enlarged liver, detecting cirrhosis	2.3 (1.6, 3.3)	0.6 (0.4, 0.7)	7-67
Palpable liver in epigastrium, detecting cirrhosis	2.7 (1.9, 3.9)	0.3 (0.1, 0.9)	7-37
Liver edge firm, detecting cirrhosis	2.7 (2.2, 3.3)	0.4 (0.3, 0.5)	54-67
Palpable liver (in jaundiced patients), detecting hepatocellular disease	0.9 (0.8, 1.1)	1.4 (0.6, 3.4)	65-67
Liver tenderness (in jaundiced patients), detecting hepatocellular disease	1.4 (0.8, 2.6)	0.8 (0.7, 1.1)	65-67
Palpable liver (in patients with lymphadenopathy), detecting serious disease	1.2 (0.7, 1.9)	1 (0.9, 1.1)	26-41
Palpable spleen in returning travelers with fever, detecting malaria	6.5 (3.9, 10.7)	0.8 (0.8, 0.8)	27-29
Palpable spleen (in patients with jaundice), detecting hepatocellular disease	2.9 (1.2, 6.8)	0.7 (0.6, 0.9)	65-67
Palpable spleen, detecting cirrhosis	2.5 (1.6, 3.8)	0.8 (0.7, 0.9)	18-67
Palpable spleen (in patients with lymphadenopathy), detecting serious disease	1.2 (0.6, 2.5)	1 (0.9, 1)	26-41
EBM BOX 49-3 PALPATION OF GALLBLADDER, BLADDER, AND AORTA			
Palpable gallbladder (in jaundiced patients), detecting extrahepatic obstruction	26 (1.5, 439.9)	0.7 (0.5, 0.9)	33
Palpable gallbladder, detecting malignant extrahepatic obstruction	2.6 (1.5, 4.6)	0.7 (0.6, 0.9)	32-80
Palpable bladder, detecting ≥400 mL urine	1.9 (1.4, 2.6)	0.3 (0.1, 0.7)	29
Expansile pulsating epigastric mass, detecting abdominal aortic aneurysm	8 (4.2, 15.3)	0.6 (0.5, 0.7)	2-50

Continued

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
EBM BOX 49-4 ASCITES			
Bulging flanks	1.9 (1.4, 2.6)	0.4 (0.2, 0.6)	24-33
Edema	3.8 (2.2, 6.6)	0.2 (0, 0.6)	24
Flank dullness	1.8 (0.9, 3.4)	0.3 (0.1, 0.7)	24-29
Shifting dullness	2.3 (1.5, 3.5)	0.4 (0.2, 0.6)	24-33
Fluid wave	5 (2.5, 9.9)	0.5 (0.3, 0.7)	24-33
CHAPTER 50 ABDOMINAL PAIN AND TENDERNESS			
Sonographic McBurney point tenderness, detecting appendicitis	8.4 (2.9, 24.6)	0.1 (0.1, 0.3)	67
Sonographic Murphy sign, detecting cholecystitis	9.9 (5.4, 18.3)	0.4 (0.3, 0.6)	21
Murphy sign in patients with liver abscess, detecting biliary tract sepsis	2.8 (1.1, 6.9)	0.8 (0.6, 1)	40
Left lower quadrant tenderness, detecting diverticulitis	13.8 (6.3, 30)	0.8 (0.7, 0.9)	17
Loin tenderness, detecting ureterolithiasis	27.7 (10.7, 71.9)	0.9 (0.8, 0.9)	4
Renal tenderness, detecting ureterolithiasis	3.6 (3.1, 4.1)	0.2 (0.1, 0.3)	4
Microscopic hematuria, detecting ureterolithiasis	73.1 (41.7, 128)	0.3 (0.2, 0.4)	4
EBM BOX 50-1 ACUTE ABDOMINAL PAIN, DETECTING PERITONITIS			
Fever	1.4 (1.2, 1.7)	0.7 (0.6, 0.8)	31-88
Guarding	2.2 (1.8, 2.7)	0.6 (0.5, 0.7)	13-88
Rigidity	3.7 (2.6, 5.1)	0.7 (0.7, 0.8)	13-75
Rebound tenderness	2 (1.7, 2.3)	0.4 (0.4, 0.5)	13-88
Percussion tenderness	2.4 (1.5, 3.8)	0.5 (0.4, 0.6)	30-50
Abnormal bowel sounds	2.2 (0.5, 9.7)	0.8 (0.7, 0.9)	13-82
Rectal tenderness	1.2 (1, 1.5)	0.9 (0.7, 1)	20-82
Positive abdominal wall tenderness test	0.1 (0, 0.7)	1.9 (0.9, 4.4)	58-72
Positive cough test	1.6 (1.4, 1.9)	0.4 (0.3, 0.5)	30-46
EBM BOX 50-2 ACUTE ABDOMINAL PAIN, DETECTING APPENDICITIS			
Right lower quadrant tenderness	1.8 (1.5, 2.2)	0.3 (0.2, 0.4)	17-85
McBurney point tenderness	3.4 (1.6, 7.2)	0.4 (0.2, 0.7)	39-65
Rovsing sign	2.3 (1.4, 3.8)	0.8 (0.6, 0.9)	36-58
Psoas sign	2 (1.4, 2.8)	0.9 (0.8, 1)	36-82
Obturator sign	1.4 (0.4, 4.5)	1 (0.9, 1.1)	82
Alvarado score, 7 or more	3.1 (2.3, 4.3)	—	17-82
Alvarado score, 5-6	0.8 (0.5, 1.3)	—	17-82
Alvarado score, 4 or less	0.1 (0, 0.2)	—	17-82

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
EBM BOX 50-3 ACUTE RIGHT UPPER QUADRANT PAIN, SIGNS DETECTING CHOLECYSTITIS			
Fever	1.1 (0.8, 1.7)	0.9 (0.8, 1.1)	26-78
Right upper quadrant tenderness	2.7 (1.8, 4)	0.4 (0.3, 0.6)	10-80
Murphy sign (inspiratory arrest)	3.2 (1.6, 6.6)	0.6 (0.4, 0.8)	10-52
Right upper quadrant mass	0.8 (0.5, 1.2)	1 (1, 1)	26-80
EBM BOX 50-4 ACUTE ABDOMINAL PAIN, SIGNS DETECTING BOWEL OBSTRUCTION			
Visible peristalsis	18.8 (4.3, 81.9)	0.9 (0.9, 1)	4
Distended abdomen	9.6 (5, 18.6)	0.4 (0.3, 0.5)	4-8
Guarding	1 (0.6, 1.7)	1 (0.7, 1.4)	4-8
Rigidity	1.2 (0.4, 3.6)	1 (0.9, 1.2)	4-8
Rebound tenderness	0.9 (0.7, 1.1)	1.1 (1, 1.2)	4-8
Hyperactive bowel sounds	5 (2.4, 10.6)	0.6 (0.5, 0.8)	4-8
Abnormal bowel sounds	3.2 (1.7, 6.1)	0.4 (0.3, 0.5)	4-8
Rectal tenderness	0.9 (0.6, 1.5)	1 (1, 1.1)	4-8
EBM BOX 50-5 CHRONIC UPPER ABDOMINAL PAIN			
Positive abdominal wall tenderness test, detecting visceral pain	0.1 (0.1, 0.3)	4.2 (2.2, 8.1)	65
Right upper quadrant tenderness, detecting cholelithiasis	1.1 (0.9, 1.4)	0.9 (0.7, 1.2)	41
Lower abdominal tenderness, detecting cholelithiasis	0.5 (0.3, 0.7)	1.4 (1.2, 1.6)	41
Epigastric tenderness, detecting positive upper endoscopy	0.9 (0.7, 1.3)	1.2 (0.6, 2.3)	61
CHAPTER 51 AUSCULTATION OF ABDOMEN			
Abnormal bowel sounds, detecting bowel obstruction	3.2 (1.7, 6.1)	0.4 (0.3, 0.5)	4-8
EBM BOX 51-1 AUSCULTATION OF ABDOMEN			
Any abdominal bruit, detecting renovascular hypertension	5.6 (4, 7.7)	0.6 (0.5, 0.8)	18-36
Any abdominal bruit, detecting abdominal aortic aneurysm	2 (0.5, 8.6)	0.9 (0.8, 1.1)	9
Systolic/diastolic abdominal bruit, detecting renovascular hypertension	38.9 (9.5, 160)	0.6 (0.5, 0.7)	24
CHAPTER 52 PERIPHERAL VASCULAR DISEASE			
Ankle-to-arm index (AAI) <0.9 by palpation	5 (3.3, 7.5)	0.2 (0, 0.9)	4
Pulse oximetry positive (supine toe 2% less than finger OR toe O_2 saturation decreases 2% on 12-inch elevation of foot)	30.5 (7.7, 121)	0.2 (0.1, 0.4)	31

Continued

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
Absent or severely diminished femoral pulse, detecting aortoiliac disease	31 (1.9, 500.6)	0.6 (0.5, 0.8)	50
Limb bruit (with preserved popliteal pulse), detecting limb stenosis	3.2 (1.2, 8.7)	0.3 (0.1, 0.6)	68
Continuous femoral bruit, detecting arteriovenous fistula	80.8 (5.1, 1273)	0.04 (0, 0.6)	23
Expansile femoral pulsation, detecting false aneurysm	13.8 (3.6, 52.7)	0.1 (0, 0.3)	44
EBM BOX 52-1 PERIPHERAL VASCULAR DISEASE			
Wounds or sores on foot	7 (3.2, 15.6)	1 (1, 1)	11
Foot color abnormally pale, red, or blue	2.8 (2.4, 3.2)	0.7 (0.7, 0.8)	9
Atrophic skin	1.7 (1.2, 2.3)	0.7 (0.5, 1)	8
Absent lower limb hair	1.7 (1.2, 2.3)	0.7 (0.6, 1)	8
Foot asymmetrically cooler	6.1 (4.2, 8.9)	0.9 (0.9, 0.9)	8
Absent femoral pulse	6.1 (3.8, 10)	0.9 (0.9, 1)	9
Both pedal pulses absent (posterior tibial [PT] and dorsal pedal [DP] pulses)	14.9 (3.3, 66.3)	0.3 (0.3, 0.4)	7-71
Limb bruit present	7.3 (3.6, 14.9)	0.7 (0.5, 0.9)	9-67
Capillary refill time ≥5 seconds	1.9 (1.2, 3.2)	0.8 (0.7, 1)	8
Venous filling time >20 seconds	3.6 (1.9, 6.8)	0.8 (0.7, 1)	8
EBM BOX 52-2 HYPOPERFUSION IN ICU PATIENTS			
Cool extremities in ICU patients, detecting low cardiac index	3.7 (2.1, 6.5)	0.8 (0.8, 0.9)	55
Cool extremities in septic ICU patients, detecting low cardiac index	5.2 (2.3, 12.1)	0.7 (0.6, 0.9)	47
0 of 3 findings present, detecting low cardiac index	0.5 (0.3, 0.8)	—	8
1 of 3 findings present, detecting low cardiac index	2.3 (1.6, 3.4)	—	8
All 3 findings present, detecting low cardiac index	7.5 (2.2, 25.3)	—	8
All 3 findings present, detecting low cardiac index (subset receiving vasopressors)	6.5 (2.6, 16.5)	0.8 (0.7, 1)	8
Limb is cool or capillary refill time >4.5 seconds, detecting elevated lactate levels	2.2 (1.6, 3)	0.5 (0.4, 0.7)	50
Limb is cool or capillary refill time >4.5 seconds, predicting multiorgan dysfunction	2.6 (1.9, 3.5)	0.3 (0.2, 0.5)	50

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
CHAPTER 53 THE DIABETIC FOOT			
Insensate to 5.07 monofilament, predicting amputation during 3-4 years of follow-up	1.7 (1.4, 2)	0.3 (0.1, 0.7)	4
EBM BOX 53-1 THE DIABETIC FOOT			
Insensate to the 5.07 monofilament, predicting future foot ulceration	2.4 (1.7, 3.4)	0.5 (0.5, 0.6)	4-29
Ulcer area ≥2 cm^2, detecting osteomyelitis	2.2 (0.4, 11.4)	0.6 (0.2, 2.4)	52-68
Ulcer area ≥3 cm^2, detecting osteomyelitis	3.5 (1.6, 7.7)	0.3 (0.1, 0.6)	52
Ulcer area ≥4 cm^2, detecting osteomyelitis	7.3 (1.9, 28.3)	0.4 (0.2, 0.7)	52
Ulcer area ≥5 cm^2, detecting osteomyelitis	11 (1.6, 77.8)	0.5 (0.3, 0.8)	52
Probe-to-bone positive, detecting osteomyelitis	5.3 (3.7, 7.8)	0.2 (0.1, 0.4)	12-80
Ulcer depth >3 mm or bone exposed, detecting osteomyelitis	3.9 (1.9, 8.1)	0.3 (0.2, 0.6)	63-68
Erythema, swelling, purulence, detecting osteomyelitis	1.8 (0.9, 3.8)	0.8 (0.6, 1)	63-68
0 findings, predicting nonhealing wound	0.5 (0.4, 0.5)	—	53
1 finding, predicting nonhealing wound	0.8 (0.8, 0.8)	—	53
2 findings, predicting nonhealing wound	1.8 (1.7, 1.8)	—	53
3 findings, predicting nonhealing wound	3.5 (3.2, 3.8)	—	53
CHAPTER 54—EDEMA AND DEEP VEIN THROMBOSIS			
Active cancer, detecting proximal leg deep vein thrombosis (DVT)	2.9 (2.4, 3.6)	0.9 (0.8, 0.9)	13-34
Recent immobilization, detecting proximal leg DVT	1.6 (1.3, 2.1)	0.9 (0.8, 0.9)	13-34
Recent surgery, detecting proximal leg DVT	1.6 (1.3, 1.9)	0.9 (0.9, 1)	13-29
EBM BOX 54-1 LOWER EXTREMITY DEEP VEIN THROMBOSIS			
Any calf or ankle swelling	1.2 (1.1, 1.3)	0.7 (0.6, 0.8)	25-54
Asymmetrical calf swelling, ≥2 cm difference	2.1 (1.8, 2.5)	0.5 (0.4, 0.7)	13-16
Swelling of entire leg	1.5 (1.2, 1.8)	0.8 (0.6, 0.9)	22-34
Superficial venous dilation	1.6 (1.4, 1.9)	0.9 (0.8, 0.9)	22-44

Continued

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
Erythema	1 (0.6, 1.7)	1 (0.8, 1.2)	27-45
Superficial thrombophlebitis	0.9 (0.2, 5.1)	1 (0.9, 1.1)	43
Tenderness	1 (1, 1.1)	1 (0.9, 1.1)	22-54
Asymmetrical skin coolness	1.2 (0.6, 2.2)	0.9 (0.6, 1.4)	46
Asymmetrical skin warmth	1.4 (1.2, 1.7)	0.7 (0.5, 1.2)	27-45
Palpable cord	1.1 (0.7, 1.6)	1 (0.9, 1.1)	27-34
Homan sign	1.1 (0.9, 1.3)	1 (0.9, 1.1)	27-58
EBM BOX 54-2 LEG DEEP VEIN THROMBOSIS (WELLS SCORE)			
Wells score, low probability	0.2 (0.1, 0.3)	—	13-43
Wells score, moderate probability	0.9 (0.7, 1.3)	—	13-39
Wells score, high probability	6.3 (3.9, 10.3)	—	10-39
EBM BOX 54-3, ARM DEEP VEIN THROMBOSIS			
Constans score ≤0	0.3 (0.2, 0.4)	—	35
Constans score 1	0.8 (0.6, 1.1)	—	35
Constans score ≥2	3.8 (2.8, 5.2)	—	35
CHAPTER 55 EXAMINATION OF THE MUSCULOSKELETAL SYSTEM			
Constant pain in low back and buttock, detecting hip osteoarthritis	6.7 (2.4, 18.6)	0.5 (0.3, 0.8)	29
Pain in ipsilateral groin, detecting hip osteoarthritis	3.6 (1.1, 11.6)	0.8 (0.6, 1)	29
Overall clinical impression, detecting anterior cruciate ligament (ACL) tear	74.7 (18.8, 297)	0.04 (0, 0.1)	13-43
Clinical impression medial meniscal injury, detecting medial meniscal injury	2.9 (1.6, 5.1)	0.1 (0.1, 0.2)	44-66
Clinical impression lateral meniscal injury, detecting lateral meniscal injury	5.9 (3.3, 10.4)	0.5 (0.4, 0.6)	31-47
EBM BOX 55-1 SHOULDER PAIN			
Detecting acromioclavicular joint pain			
Acromioclavicular joint tenderness	1.1 (0.9, 1.3)	0.4 (0, 5.2)	74
Tenderness with acromioclavicular joint compression	1.6 (0.8, 3)	0.4 (0.2, 1.1)	74
Crossed body adduction causes pain	3.7 (2.9, 4.7)	0.3 (0.2, 0.5)	6
Detecting rotator cuff tendonitis			
Neer impingement sign	1.6 (1.1, 2.3)	0.5 (0.4, 0.5)	28-70
Hawkins impingement sign	1.6 (1.2, 2.3)	0.4 (0.3, 0.5)	28-70

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
Neer or Hawkins impingement sign	1.6 (1.3, 2)	0.1 (0, 0.7)	28
Yergason sign	2.8 (1.2, 6.6)	0.7 (0.6, 0.9)	70
Speed test	1.9 (1.3, 2.8)	0.7 (0.6, 0.9)	65-70
Painful arc	2.8 (1.3, 6.2)	0.5 (0.2, 1.3)	65-70
Detecting rotator cuff tear			
Age ≤39 years	0.1 (0.1, 0.2)	—	50
Age 40-59 years	0.9 (0.7, 1.1)	—	50
Age ≥60 years	3.2 (2.4, 4.3)	—	50
Supraspinatus atrophy	2 (1.5, 2.7)	0.6 (0.5, 0.7)	67
Infraspinatus atrophy	2 (1.5, 2.7)	0.6 (0.5, 0.7)	67
Painful arc	1.5 (0.8, 2.6)	0.4 (0.3, 0.5)	39-67
Supraspinatus test causes pain	1.7 (1.3, 2.2)	0.4 (0.2, 0.7)	24-69
Supraspinatus test reveals weakness	2.1 (1.4, 3.1)	0.5 (0.4, 0.7)	23-72
Infraspinatus weakness	2.3 (1.3, 4.1)	0.5 (0.4, 0.7)	39-67
Dropped arm test	2.9 (2.1, 4)	0.8 (0.7, 1)	39-50
Palpable tear	10.2 (1.3, 80.9)	0.1 (0, 0.2)	42-81
EBM BOX 55-2 ROTATOR CUFF TEAR			
3 findings (Murrell)	48 (6.7, 344.4)	—	50
2 findings (Murrell)	4.9 (2.9, 8.3)	—	50
1 finding (Murrell)	0.9 (0.7, 1.1)	—	50
0 findings (Murrell)	0.02 (0, 0.1)	—	50
3 findings (Park)	15.9 (5.9, 43.1)	—	44
2 findings (Park)	3.6 (2.2, 5.7)	—	44
1 finding (Park)	0.8 (0.6, 1.1)	—	44
0 findings (Park)	0.2 (0.1, 0.3)	—	44
EBM BOX 55-3 HIP OSTEOARTHRITIS			
Squat causes pain in posterior hip	6.1 (1.3, 28.9)	0.8 (0.6, 1)	29
Abduction or adduction causes groin pain	5.7 (1.6, 19.8)	0.7 (0.5, 1)	29
Active hip flexion causes lateral hip pain	3.6 (1.5, 9)	0.6 (0.4, 1)	29
Active hip extension causes hip pain	2.7 (1.3, 5.3)	0.6 (0.4, 0.9)	29
Passive internal rotation ≤25 degrees	1.9 (1.3, 2.9)	0.4 (0.2, 0.9)	29
EBM BOX 55-4 KNEE OSTEOARTHRITIS			
Stiffness <30 minutes	3 (2.1, 4.4)	0.2 (0.1, 0.3)	55
Crepitus, passive motion	2.1 (1.7, 2.7)	0.2 (0.1, 0.3)	52
Bony enlargement	11.8 (4.9, 28.2)	0.5 (0.4, 0.6)	52
Palpable increase in temperature	0.3 (0.2, 0.5)	1.6 (1.4, 2)	52

Continued

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
Valgus deformity	1.4 (0.8, 2.4)	0.9 (0.8, 1)	52
Varus deformity	3.4 (1.6, 7.6)	0.8 (0.7, 0.9)	52
At least 3 out of 6 findings	3.1 (2.3, 4.1)	0.1 (0, 0.1)	55
EBM BOX 55-5 KNEE FRACTURE			
Age ≥55 years	3 (1.6, 5.3)	0.7 (0.5, 1)	6-9
Joint effusion	2.5 (2, 3)	0.5 (0.3, 0.7)	6-9
Ecchymosis	2.2 (0.9, 5.3)	0.9 (0.7, 1.1)	9
Cannot flex beyond 90 degrees	2.9 (2.5, 3.4)	0.5 (0.4, 0.7)	6-9
Cannot flex beyond 60 degrees	4.7 (3.8, 5.9)	0.6 (0.5, 0.7)	6
Isolated tenderness of patella	2.2 (1.6, 2.9)	0.8 (0.8, 0.9)	6-9
Tenderness at head of fibula	3.4 (2.5, 4.7)	0.9 (0.8, 1)	6-9
Inability to bear weight, immediately and in emergency department	3.6 (3, 4.3)	0.6 (0.5, 0.7)	6-9
Ottawa knee rule positive	1.7 (1.4, 2)	0.1 (0, 0.2)	6-12
EBM BOX 55-6 LIGAMENT AND MENISCAL INJURIES			
Anterior drawer sign, detecting anterior cruciate ligament (ACL) tear	11.5 (5, 26.2)	0.5 (0.4, 0.7)	26-76
Lachman sign, detecting ACL tear	17 (5.4, 53.1)	0.2 (0.1, 0.4)	26-76
Pivot shift sign, detecting ACL tear	8 (3.5, 18.3)	0.8 (0.7, 1)	26-76
Posterior drawer sign, detecting posterior cruciate ligament (PCL) tear	97.8 (24.2, 396)	0.1 (0, 0.5)	3-13
McMurray sign, detecting meniscal injury	4.5 (1.7, 11.8)	0.8 (0.7, 0.9)	39-81
Joint line tenderness, detecting meniscal injury	1.5 (1.1, 2.1)	0.5 (0.3, 0.9)	40-81
Block to full extension, detecting meniscal injury	3.2 (1.8, 5.9)	0.7 (0.5, 0.8)	50
Pain on forced extension, detecting meniscal injury	1.6 (1.2, 2.2)	0.7 (0.6, 0.9)	50-81
Valgus laxity, detecting medial collateral ligament injury	12.8 (0.2, 959)	0.2 (0.1, 0.3)	25-44
EBM BOX 55-7 ANKLE AND MIDFOOT FRACTURE			
Detecting ankle fracture			
Tenderness over posterior lateral malleolus	2.4 (1.9, 2.8)	0.4 (0.3, 0.5)	10-14
Tenderness over posterior medial malleolus	4.8 (2.6, 9)	0.6 (0.6, 0.7)	10-14
Inability to bear weight immediately after injury	2.6 (2.2, 3.1)	0.5 (0.4, 0.6)	10-14

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
Inability to bear weight for four steps in the emergency room	2.5 (2.2, 2.8)	0.3 (0.2, 0.4)	10-14
Ottawa ankle rule	1.5 (1.3, 1.7)	0.1 (0, 0.1)	9-16
Detecting midfoot fracture			
Tenderness at the base of the 5th metatarsal	2.9 (2.5, 3.3)	0.1 (0.1, 0.2)	12-14
Tenderness of navicular bone	0.4 (0.2, 0.9)	1.1 (1, 1.2)	12-14
Inability to bear weight immediately after injury	1 (0.5, 2.3)	1 (0.8, 1.3)	12-14
Inability to bear weight for four steps in the emergency room	1.1 (0.8, 1.4)	0.9 (0.8, 1.1)	12-14
Ottawa foot rule	2.1 (1.3, 3.3)	0.1 (0, 0.2)	2-23
EBM BOX 55-8 ACHILLES TENDON TEAR			
Palpable gap in Achilles tendon	6.8 (2.3, 19.9)	0.3 (0.2, 0.4)	83
Calf squeeze test	13.5 (3.5, 51.2)	0.05 (0, 0.1)	83
Matles test	6.2 (2.5, 15.4)	0.1 (0.1, 0.3)	73
CHAPTER 56 VISUAL FIELD TESTING			
Visual field defect, detecting focal cerebral defect	4.3 (1.1, 17.6)	0.8 (0.7, 0.9)	71-75
EBM BOX 56-1 VISUAL FIELD DEFECTS			
Confrontation technique, detecting anterior visual field defects	5.7 (3.7, 8.7)	0.7 (0.6, 0.8)	26-85
Confrontation technique, detecting posterior visual field defects	9.6 (3.9, 23.8)	0.4 (0.3, 0.6)	11-53
Asymmetrical optokinetic nystagmus, detecting parietal lobe disease	5.7 (3.2, 10.1)	0.1 (0, 0.3)	33
Associated hemiparesis or aphasia, detecting parietal lobe disease	18.3 (6, 56.2)	0.1 (0, 0.7)	14
EBM BOX 56-2 VISUAL FIELD TESTING			
Finger counting	54.4 (7.6, 388)	0.7 (0.6, 0.8)	45-64
Kinetic finger boundary	13.3 (5.9, 29.8)	0.6 (0.6, 0.7)	45-64
Description of face	26.4 (8.5, 82.6)	0.6 (0.5, 0.7)	45-64
Kinetic red boundary testing	13.6 (3.6, 50.7)	0.4 (0.2, 0.6)	45-64
Laser target testing	6.3 (3.4, 12)	0.3 (0.2, 0.5)	47
Red target comparison	6.2 (0.1, 314)	0.6 (0.3, 1.2)	45-64
EBM BOX 57-1 ICE PACK TEST FOR MYASTHENIA			
Improvement in ptosis after application of ice	19.3 (7.5, 50.2)	0.2 (0.1, 0.3)	35-75
Improvement in diplopia and ophthalmoplegia after application of ice	31 (2, 475.1)	0.03 (0, 0.5)	50

Continued

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
CHAPTER 58 MISCELLANEOUS CRANIAL NERVES			
Hutchinson sign in varicella zoster virus infection, detecting ocular complications	3 (2, 4.6)	0.4 (0.2, 0.8)	50-64
EBM BOX 58-1 ASPIRATION AFTER STROKE			
Abnormal voluntary cough	1.9 (1.3, 2.7)	0.6 (0.5, 0.7)	19-71
Dysphonia	1.3 (1.2, 1.5)	0.4 (0.3, 0.7)	26-71
Dysarthria	1.6 (1.2, 2.2)	0.5 (0.3, 0.8)	37-68
Drowsiness	3.4 (1.2, 9.5)	0.5 (0.3, 0.7)	21-42
Abnormal sensation face and tongue	0.5 (0.2, 1.2)	1.5 (0.9, 2.4)	46
Absent pharyngeal sensation	2.4 (1.6, 3.6)	0.03 (0, 0.5)	42
Tongue weakness	2.5 (0.7, 9.6)	0.6 (0.4, 0.9)	18-30
Bilateral cranial nerve signs	1.1 (0.8, 1.6)	0.8 (0.4, 1.6)	51-52
Abnormal gag reflex	1.5 (1.2, 1.8)	0.6 (0.4, 0.7)	19-71
Water swallow test	3.2 (2.1, 4.7)	0.4 (0.3, 0.5)	19-52
Oxygen desaturation 0-2 minutes after swallowing	3.1 (1.1, 8.6)	0.3 (0.2, 0.5)	28-52
EBM BOX 59-1 UNILATERAL CEREBRAL HEMISPHERIC DISEASE			
Hemianopia	4.3 (1.1, 17.6)	0.8 (0.7, 0.9)	71-75
Pronator drift	9.6 (5.4, 16.9)	0.3 (0.2, 0.7)	51-76
Arm rolling test	15.6 (5.8, 41.5)	0.6 (0.4, 0.8)	51-76
Index finger rolling test	6 (2, 18.5)	0.7 (0.6, 0.8)	67-71
Little finger rolling test	1.5 (0.1, 15.2)	1 (0.9, 1.1)	58
Finger tapping test	4.7 (2.1, 10.3)	0.5 (0.3, 0.8)	51-76
Foot tapping test	2 (0.6, 6.5)	0.9 (0.7, 1.1)	67-71
Hemisensory disturbance	12.3 (0.8, 196)	0.7 (0.6, 0.9)	76
Hyperreflexia	5.3 (3, 9.5)	0.6 (0.2, 1.5)	51-71
Babinski response	8.5 (1.7, 43.3)	0.8 (0.6, 1)	67-76
CHAPTER 60 EXAMINATION OF THE SENSORY SYSTEM			
Diminished pinprick sensation, detecting nerve fiber density <8 epidermal nerve fibers/mm	4.6 (2.4, 8.6)	0.2 (0.1, 0.3)	60
CHAPTER 61 EXAMINATION OF THE REFLEXES			
Diminished biceps or brachioradialis reflex, detecting C6 radiculopathy	14.2 (4.3, 46.7)	0.5 (0.3, 0.8)	19
Diminished triceps reflex, detecting C7 radiculopathy	3 (1.6, 5.6)	0.6 (0.3, 1.4)	54-69
Asymmetrical quadriceps reflex, detecting L3 or L4 radiculopathy	8.7 (4.9, 15.5)	0.6 (0.5, 0.8)	2-25

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
Abnormal medial hamstring reflex, detecting L5 root disease	6.2 (1.6, 24.2)	0.5 (0.3, 0.7)	58
Asymmetrical Achilles reflex, detecting S1 radiculopathy	2.7 (1.9, 3.8)	0.5 (0.4, 0.6)	20-66
Bulbocavernosus reflex in men, detecting S2-S4 lesion	13 (5.9, 28.9)	0.3 (0.2, 0.5)	27
Bulbocavernosus reflex in women, detecting S2-S4 lesion	2.7 (1.6, 4.6)	0.6 (0.5, 0.9)	22
Positive grasp reflex, detecting discrete lesion in the frontal lobe, deep nuclei, or subcortical white matter	19.1 (5.9, 61.7)	0.7 (0.4, 1.2)	21-37
CHAPTER 62 DISORDERS OF NERVE ROOTS, PLEXUSES, AND PERIPHERAL NERVES			
Motor and sensory findings confined to C7-T1, detecting malignant plexopathy	30.9 (2, 483.8)	0.3 (0.2, 0.5)	61
Horner syndrome, detecting malignant plexopathy	4.1 (1.4, 12.2)	0.5 (0.3, 0.8)	61
Motor and sensory findings confined to C5-C6, detecting radiation plexopathy	8.8 (2.9, 26.4)	0.2 (0.1, 0.5)	39
Lymphedema of arm, detecting radiation plexopathy	4.9 (2.1, 11.6)	0.3 (0.2, 0.6)	39
Unilateral involvement, detecting malignant lumbosacral plexopathy	4.5 (1.8, 10.8)	0.1 (0, 0.4)	58
Bilateral involvement, detecting radiation lumbosacral plexopathy	7.5 (2.5, 22.2)	0.2 (0.1, 0.5)	42
EBM BOX 62-1 DIAGNOSING CERVICAL RADICULOPATHY			
Weakness of any arm muscle	1.9 (1.4, 2.5)	0.4 (0.3, 0.6)	52
Reduced sensation in arm	0.7 (0.5, 1)	1.4 (1, 1.8)	52
Reduced biceps reflex	9.1 (1.2, 69.4)	0.9 (0.8, 1)	52
Reduced brachioradialis reflex	7.3 (0.9, 56.8)	0.9 (0.9, 1)	52
Reduced triceps reflex	2.3 (0.7, 7)	0.9 (0.9, 1)	52
Reduced biceps, triceps, or brachioradialis reflex	3.6 (1.4, 9.2)	0.8 (0.7, 0.9)	52
Spurling test	4.2 (2.5, 7)	0.6 (0.4, 0.9)	10-58
Rotation of neck to involved side <60 degrees	1.7 (1.3, 2.3)	0.2 (0.1, 0.9)	22
EBM BOX 62-2 LOCALIZING CERVICAL RADICULOPATHY			
Weak elbow flexion, detecting C5 radiculopathy	5.3 (2.7, 10.5)	0.2 (0, 2.5)	2
Weak wrist extension, detecting C6 radiculopathy	2.3 (1.1, 5)	0.8 (0.5, 1.1)	19

Continued

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
Weak elbow extension, detecting C7 radiculopathy	4 (1.8, 9.2)	0.4 (0.3, 0.6)	69
Weak finger flexion, detecting C8 radiculopathy	3.8 (1.7, 8.5)	0.6 (0.3, 1.1)	10
Sensory loss of thumb, detecting C6 radiculopathy	8.5 (2.3, 31.1)	0.7 (0.5, 1)	19
Sensory loss of middle finger, detecting C7 radiculopathy	3.2 (0.2, 60.1)	1 (0.9, 1)	69
Sensory loss of little finger, detecting C8 radiculopathy	41.4 (2.1, 807)	0.8 (0.6, 1.1)	10
Diminished biceps or brachioradialis reflex, detecting C6 radiculopathy	14.2 (4.3, 46.7)	0.5 (0.3, 0.8)	19
Diminished triceps reflex, detecting C7 radiculopathy	3 (1.6, 5.6)	0.6 (0.3, 1.4)	54-69
EBM BOX 62-3 CARPAL TUNNEL SYNDROME			
"Classic" or "probable" Katz hand diagram	2.4 (1.6, 3.5)	—	37
"Unlikely" Katz hand diagram	0.2 (0, 0.7)	—	37
Weak thumb abduction	1.8 (1.4, 2.3)	0.5 (0.4, 0.7)	50-62
Thenar atrophy	1.6 (0.9, 2.8)	1 (0.9, 1)	35-50
Hypalgesia	3.1 (2, 5.1)	0.7 (0.5, 1.1)	35-62
Diminished 2-point discrimination	1.3 (0.6, 2.7)	1 (0.9, 1.1)	40-57
Abnormal vibration sensation	1.6 (0.8, 3)	0.8 (0.4, 1.3)	50-57
Diminished monofilament sensation	1.2 (1, 1.5)	0.4 (0.1, 2)	53-56
Tinel sign	1.5 (1.1, 2.1)	0.8 (0.7, 1)	35-73
Phalen sign	1.4 (1.2, 1.6)	0.7 (0.6, 0.9)	35-88
Pressure provocation test	1 (0.9, 1.2)	0.9 (0.8, 1.1)	58-88
Square wrist ratio	2.7 (2.2, 3.4)	0.5 (0.4, 0.8)	60-62
Flick sign	5.5 (0.4, 77.4)	0.3 (0, 2.8)	54-67
EBM BOX 62-4 DIAGNOSING LUMBOSACRAL RADICULOPATHY			
Weak ankle dorsiflexion	4.9 (1.9, 12.5)	0.5 (0.4, 0.7)	74
Ipsilateral calf wasting	5.2 (1.3, 20.8)	0.8 (0.6, 0.9)	74
Leg sensation abnormal	1.1 (0.9, 1.5)	0.9 (0.8, 1.1)	47-74
Abnormal ankle jerk	2.1 (1.4, 3.1)	0.8 (0.7, 0.9)	47-74
Straight leg–raising maneuver	1.5 (1.2, 1.9)	0.4 (0.3, 0.6)	47-87
Crossed straight leg–raising maneuver	3.4 (1.8, 6.4)	0.8 (0.7, 0.9)	55-87
EBM BOX 62-5 LOCALIZING LUMBOSACRAL RADICULOPATHY			
Weak knee extension, detecting L3 or L4 radiculopathy	3.7 (1.9, 7.6)	0.7 (0.5, 0.8)	25-63
Weak hallux extension, detecting L5 radiculopathy	1.6 (1.3, 2)	0.8 (0.6, 1)	52-57

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
Weak ankle dorsiflexion, detecting L5 radiculopathy	1.3 (0.9, 1.8)	0.8 (0.6, 1)	52-58
Weak ankle plantar flexion, detecting S1 radiculopathy	4.8 (0.4, 60.4)	0.7 (0.6, 0.9)	20-48
Ipsilateral calf wasting, detecting S1 radiculopathy	2.4 (1.2, 4.7)	0.7 (0.5, 0.9)	48
Sensory loss L5 distribution, detecting L5 radiculopathy	3.1 (1.8, 5.6)	0.8 (0.7, 0.9)	52-58
Sensory loss S1 distribution, detecting S1 radiculopathy	2.4 (1.3, 4.2)	0.7 (0.6, 0.9)	41-48
Asymmetrical quadriceps reflex, detecting L3 or L4 radiculopathy	8.7 (4.9, 15.5)	0.6 (0.5, 0.8)	2-25
Asymmetrical medial hamstring reflex, detecting L5 radiculopathy	6.2 (1.6, 24.2)	0.5 (0.3, 0.7)	58
Asymmetrical Achilles reflex, detecting S1 radiculopathy	2.7 (1.9, 3.8)	0.5 (0.4, 0.6)	20-66
CHAPTER 64 TREMOR AND PARKINSON DISEASE			
Micrographia, detecting Parkinson disease	2.7 (1.8, 4)	0.7 (0.3, 1.3)	28-32
Voice becoming softer, detecting Parkinson disease	3.2 (1.8, 5.8)	0.5 (0.1, 1.9)	28-32
Feet suddenly freezing in doorway, detecting Parkinson disease	4.4 (1.5, 12.4)	0.7 (0.5, 1)	28-32
Acute-onset parkinsonism, detecting vascular parkinsonism	21.9 (3, 161.8)	0.7 (0.6, 0.9)	24-58
EBM BOX 64-1 SUSPECTED PARKINSON DISEASE			
Diagnosing Parkinson disease			
Unable to perform perfect 10 tandem steps	0.1 (0, 0.3)	5 (2.7, 9.1)	42
Positive applause sign	0.3 (0.1, 0.7)	2.3 (1.6, 3.2)	29-48
3 of 3 cardinal features present	2.2 (1.2, 4.2)	0.5 (0.3, 0.7)	76
3 of 3 cardinal features, asymmetry	4.1 (1.7, 10.2)	0.4 (0.3, 0.6)	76
Good response to levodopa,	1.8 (1.2, 2.8)	0.4 (0.3, 0.6)	75
Detecting multisystem atrophy			
Rapid progression	2.5 (1.6, 4.1)	0.6 (0.4, 0.8)	20-55
Absence of tremor	1.4 (1, 2)	0.7 (0.5, 1.1)	15-55
Speech and/or bulbar signs	4.1 (2.7, 6.1)	0.2 (0.1, 0.4)	28
Autonomic dysfunction	4.3 (2.3, 7.8)	0.3 (0.2, 0.4)	15-55
Cerebellar signs	9.5 (1.4, 64.7)	0.7 (0.5, 0.8)	15-27

Continued

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
Pyramidal tract signs	4 (1.2, 12.8)	0.7 (0.4, 1)	15-27
Dementia	0.3 (0.2, 0.6)	1.9 (1.5, 2.4)	15-27
Diagnosing progressive supranuclear palsy			
Down-gaze palsy and early postural instability	60 (3.7, 974.9)	0.5 (0.3, 0.7)	29
Detecting vascular parkinsonism			
Pyramidal tract signs	21.3 (9.3, 48.5)	0.5 (0.4, 0.8)	20-58
Lower body parkinsonism	6.1 (4.3, 8.7)	0.4 (0.3, 0.5)	20-58
CHAPTER 65 HEMORRHAGIC VERSUS ISCHEMIC STROKE			
Warfarin therapy	5.4 (1.3, 23.3)	0.9 (0.8, 1.1)	13-53
Seizures at onset	4.7 (1.6, 14.1)	0.9 (0.9, 1)	12-39
Vomiting	3 (1.7, 5.5)	0.7 (0.6, 0.9)	16-46
Severe headache	2.9 (1.7, 4.8)	0.7 (0.6, 0.8)	12-46
Loss of consciousness	2.6 (1.6, 4.2)	0.7 (0.5, 0.8)	43
Previous transient ischemic attack (TIA)	0.3 (0.2, 0.7)	1.2 (1.1, 1.3)	12-17
EBM BOX 65-1 HEMORRHAGIC STROKE			
Systolic blood pressure >220 mm Hg	4 (1.1, 15.4)	0.9 (0.7, 1.1)	13
Systolic blood pressure <160 mm Hg	0.4 (0.3, 0.6)	2.4 (1.7, 3.5)	43
Mental status coma	6.3 (3.4, 11.7)	—	12-48
Mental status drowsy	1.7 (1.2, 2.4)	—	12-48
Mental status alert	0.5 (0.3, 0.7)	—	16-48
Neurologic deterioration during first 3 hours	5.8 (4.3, 7.8)	0.2 (0.2, 0.4)	18
Kernig or Brudzinski sign	2.9 (0.6, 14.1)	1 (0.9, 1.1)	18-46
Neck stiffness	5.4 (2.5, 11.3)	0.7 (0.7, 0.9)	18-59
Babinski sign present, bilateral toes	2.4 (1.6, 3.6)	—	17-43
Babinski sign present, single toe	1 (0.9, 1.2)	—	17-43
Babinski sign absent, both toes	0.5 (0.3, 0.9)	—	17-43
Deviation of eyes	1.9 (1.6, 2.3)	0.7 (0.5, 0.9)	15-17
Hemiparesis	0.9 (0.8, 1.1)	1.2 (0.8, 1.7)	12-19
Aphasia	1.1 (0.9, 1.3)	1 (0.9, 1)	14-53
Hemisensory disturbance	1.3 (1.2, 1.4)	0.8 (0.7, 1.1)	12-17
Hemianopia	1.3 (1.1, 1.6)	0.9 (0.8, 1)	16
Ataxia	0.7 (0.5, 1)	1.1 (1, 1.1)	16
Cervical bruit	0.1 (0, 0.4)	1.1 (1, 1.3)	16-43
Atrial fibrillation, ECG	0.4 (0.2, 0.6)	1.2 (1.1, 1.3)	12-19
Siriraj score "hemorrhage" (>1)	5.4 (4.3, 6.9)	—	13-69
Siriraj score "uncertain" (−1 to 1)	1.1 (0.9, 1.2)	—	13-69
Siriraj score "infarction" (<−1)	0.3 (0.3, 0.4)	—	13-69

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
CHAPTER 66 ACUTE VERTIGO			
Head impulse test positive (corrective saccades), detecting abnormal caloric testing	6.7 (3.7, 12.1)	0.6 (0.5, 0.8)	19-52
Acute infarct on diffusion MRI, detecting ischemic stroke	44.2 (2.8, 690)	0.2 (0.1, 0.3)	75
EBM BOX 66-1 ACUTE VERTIGO, DETECTING ISCHEMIC STROKE			
Severe truncal ataxia	17.9 (1.1, 283)	0.7 (0.6, 0.8)	75
Skew deviation present	8.5 (1.3, 56.7)	0.7 (0.5, 0.9)	52-73
Saccadic "smooth" pursuit	4.4 (2.4, 8.3)	0.1 (0.1, 0.3)	52
Direction-changing nystagmus	3.3 (1.7, 6.4)	0.7 (0.5, 1)	52-75
Normal head impulse test (i.e., no corrective saccade)	11.9 (2.2, 63.7)	0.2 (0, 1.1)	52-75
Combined findings, 1 or more	17.2 (3.6, 81.4)	0.01 (0, 0.1)	75
EBM BOX 67-1 NONORGANIC NEUROLOGIC DISEASE			
Chair test positive	17 (1.1, 256.6)	0.2 (0, 0.7)	50
Knee-lift test positive	7.1 (1.6, 31.5)	0.04 (0, 0.6)	58
Hoover sign for nonorganic weakness	30.7 (2, 475.6)	0.2 (0, 0.5)	48
CHAPTER 68 EXAMINATION IN THE ICU			
Modified Early Warning Score (MEWS) = 0, predicting hospital death	0.3 (0.2, 0.4)	2.1 (1.9, 2.4)	9
Cool extremities in septic ICU patients, detecting low cardiac index	5.2 (2.3, 12.1)	0.7 (0.6, 0.9)	47
All 3 findings present in patients with acute respiratory distress syndrome (ARDS) and on vasopressor medications, detecting low cardiac index	6.5 (2.6, 16.5)	0.8 (0.7, 1)	8
Peripheral perfusion abnormal (extremity cool or capillary refill time >4.5 seconds), detecting elevated lactate	2.2 (1.6, 3)	0.5 (0.4, 0.7)	50
BOX 68-1 EXAMINATION IN THE ICU			
MEWS ≥ 5, predicting death	3.7 (2.3, 5.7)	0.7 (0.5, 0.9)	4-15
Cool extremities in ICU patients, detecting low cardiac index	3.7 (2.1, 6.5)	0.8 (0.8, 0.9)	55
0 of 3 findings present in patients with acute respiratory distress syndrome (ARDS), detecting low cardiac index	0.5 (0.3, 0.8)	—	8

Continued

APPENDIX TABLE 1 Likelihood Ratios, Confidence Intervals, and Pretest Probability—cont'd

Finding	Positive LR (95% CI)	Negative LR (95% CI)	Pretest Probability (Range)
1 of 3 findings present in patients with ARDS, detecting low cardiac index	2.3 (1.6, 3.4)	—	8
All 3 findings present in patients with ARDS, detecting low cardiac index	7.5 (2.2, 25.3)	—	8
Pulse pressure increase ≥12%, detecting patients who respond to fluid challenge	4.6 (2.1, 9.9)	0.4 (0.3, 0.7)	45-52
Asynchronous breathing during chronic obstructive pulmonary disease (COPD) exacerbation, predicting intubation or death	3.2 (1.3, 7.8)	0.5 (0.2, 1)	31
Asymmetrical breath sounds, detecting endobronchial intubation	24.4 (7.7, 77.8)	0.7 (0.5, 0.9)	5-16
Absent breath sounds in patients with ARDS, detecting underlying pleural effusion	4.3 (2.8, 6.5)	0.6 (0.5, 0.8)	26
Anisocoria in patients with coma, detecting structural intracranial lesion	9 (2.8, 28.8)	0.6 (0.5, 0.8)	40
Neck stiffness in patients with stroke, detecting hemorrhagic stroke	5.4 (2.5, 11.3)	0.7 (0.7, 0.9)	18-59

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