Bacteriology for Nurses

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SECOND EDITION

William Heinemann Medical Books Limited
London

First published 1964

Second edition 1968

Reprinted 1968

Reprinted 1971

ISBN 0 433 32150 4

Printed in Great Britain by The Whitefriars Press Ltd
London and Tonbridge

PREFACE

The intention of this book is to provide nurses and others who are associated with medicine with a simple outline of basic bacteriology and the applications of bacteriology to medicine and to nursing. Explanation of the fundamentals of medical bacteriology, namely the anatomy and physiology of bacteria, infection and the body defences against infection, is kept to the minimum considered necessary to understand the later chapters. There is no attempt to present systematic bacteriology, genus by genus, and after an introduction to bacterial nomenclature, the bacteria which cause common diseases of various sites in the body are considered together. Thus those bacteria which are found in diseases of the respiratory tract are considered in one chapter. Similarly there are chapters on infections of the gastro-intestinal tract and of the nervous system. Other infections are discussed in chapters on pyogenic infections, chronic bacterial infections, and on generalised infections. Only common and important infections are included, and no attempt has been made to provide a complete study of all the infections of man. A chapter on common parasites has been included because, with the increase in international travel and in immigration, such infections are now more commonly seen.

I would like to thank my wife for the considerable secretarial assistance which she has provided, and also Dr. Louis B. Quesnel for very kindly providing the line drawings from which the figures have been prepared.

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January 1964

PREFACE TO SECOND EDITION

In preparing this edition, the aim has been to retain simplicity of explanation without sacrificing accuracy in order to provide an easily understood outline of the subject. The requirements of the intended reader—the nurse and others closely associated with clinical medicine and surgery, being the prime consideration.

The layout of the book has not been changed, but alterations and additions to the text have been made either in the light of modern developments or in order to more clearly explain a point. Although changes have been made in every chapter, the major additions are in the chapters on the biology of bacteria, body defences against infection and on the destruction of bacteria.

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Chapter I

A BRIEF HISTORY OF BACTERIOLOGY

The first clear description of bacteria was that of a Dutch draper named Leeuwenhoek in the 17th century. Using a very simple form of microscope he was able to see objects which he called "animalcules" in rain water, and in the scrapings from between the teeth. He noted that some were actively moving, and described stick-like shapes and spirals. He did not associate his animalcules with disease. The animalcules have since been variously known as germs, microbes, bacteria, micro-organisms or simply "organisms".

The observations of Leeuwenhoek were soon confirmed but because it was difficult at that time to conceive of so small a life-form, a bitter controversy ensued. The rival factions argued as to whether the animalcules were produced spontaneously under suitable conditions—the theory of spontaneous generation, or whether like other known living things they arose from others like them. The argument resulted in experiments which often gave conflicting results. Thus bacteria could be found in sealed containers of meat extract which had been heated. We would recognise today that the heating was insufficient to sterilise. The problem was solved by Spallanzani, an Italian priest, who showed that if meat extracts were thoroughly heated for a sufficient length of time and then sealed they would not contain bacteria however long they were kept. In addition he showed that such meat extracts would support the growth of bacteria if these were later admitted.

With the improvement of the microscope the study of bacteria continued and many differing shapes were described. It was not however until the mid-19th century that significant progress was made. Pasteur, a French chemist, was

engaged in an investigation into the faulty fermentation of wine. He was able to show that it was a microscopic organism—a yeast, which caused the fermentation whereby sugar was converted into alcohol, and also that the presence of a rod-shaped micro-organism was spoiling the wine. Pasteur next investigated a silk worm disease which was seriously damaging the silk industry. Again he was successful. He was able to show that a living microscopic organism (subsequently shown to be a protozoan and not a bacterium) spread from worm to worm and caused the disease. This observation led to the germ theory of disease.

That living organisms, invisible to the naked eye, could cause disease was not easily accepted, and many ridiculed Pasteur. However, Lister who was Professor of Surgery in Glasgow, took up these new ideas. He believed that the bacteria present in the air might be responsible for the very high rate of post-operative sepsis. He introduced the spraying of carbolic acid (phenol) solutions over the operative area and by this means greatly reduced the incidence of infection. This was antiseptic surgery and it led eventually to modern aseptic surgery in which the aim is to exclude bacteria rather than admit them and then kill them.

The next important name in the history of bacteriology is that of Koch, a German doctor. His first important investigation was into the cause of anthrax, a primary disease of cattle and sheep which sometimes infects man. It had been found some time before that the blood of animals suffering from this disease contained rod-shaped bacteria, but it remained for Koch to prove beyond any doubt that they were the cause of the disease. This fact was confirmed a little later by Pasteur who also discovered a means of preventing the disease. He had previously discovered that under some conditions disease-causing bacteria could be made innocuous and unable to produce disease if given to a susceptible animal. These are known as attenuated strains of bacteria. This discovery he applied to the prevention of anthrax. By giving injections of cultures of

attenuated anthrax bacteria to sheep he was able to prevent them developing the disease when later injected with a culture of bacteria which would kill unprotected sheep. This was the beginning of the prevention of infectious disease by means of vaccines.

Koch continued to make important bacteriological discoveries. He introduced the use of dyes to colour bacteria and so make them more easily seen under the microscope. He also produced the first satisfactory solid media for the growth of bacteria. Up to this time bacteria had been grown in solutions of various nutrients. Koch made these solutions solid by the addition of gelatine. This enabled cultures of a single strain of bacterium to be obtained much more readily. He was able to demonstrate in 1882 that tuberculosis was a bacterial disease. In doing so he propounded his now famous postulates: that a bacterium should always be found in association with its own particular disease, that it should be isolated in pure growth from that disease and that if then given to a suitable animal should reproduce the disease from which it was isolated. This clear thinking was of great value in checking claims that a particular bacterium caused a certain disease, ensuring that the causative nature of the bacterium had been proven to the full.

In subsequent years the causes of many infectious diseases were discovered; leprosy, gonorrhoea, typhoid, cholera and diphtheria were all found to be caused by bacteria within a short time of each other. A further important advance was the discovery in 1888 that the symptoms of diphtheria were not caused directly by the bacteria but by a substance produced by the bacteria. This substance, known as a toxin, diffused throughout the body from the site of bacterial infection and was able to produce tissue damage. Six years later it was found that antibody to the toxin—anti-toxin could neutralise the effects of toxin and could be used in the treatment of diphtheria.

It was found several years later, in 1898, that some infectious diseases were not caused by bacteria but by much

smaller, microscopically invisible bodies which would pass through very fine filters known to arrest the smallest bacteria. These became known as filterable viruses or simply as viruses. They have since been shown to cause a large variety of diseases.

Progress in bacteriology was extremely rapid in the latter part of the 19th century and the following years saw much of the knowledge confirmed and extended; the detailed structure and physiology of bacteria was investigated, the ways in which animals become immune to infectious diseases were studied, and later it became possible to cultivate and examine viruses. Perhaps the most important advances in bacteriology in recent years have been the advent of substances—chemotherapeutic agents and antibiotics, which will kill bacteria in the tissues, and so cure many infections, and the very rapid advances in the study of the viruses which now is a science in its own right—virology.

Chapter II

THE BIOLOGY OF BACTERIA

Bacteria are very widely distributed in nature. They are to be found not only in relationship to man and the animals, but in soil, in water including the sea, and in the air. Only a very small proportion of bacteria can cause disease of animals or of man, others may cause disease in plants or live independently of living things. Many bacteria perform useful functions by altering the chemical structure of substances so that they may be more easily utilised by plants; without this service most of the vegetable kingdom and indirectly the animal kingdom, could not continue to live. In medicine we are concerned only with those bacteria which cause human disease; it is, however, important to realise that the vast majority of bacteria are harmless to us. The biology of bacteria is considered under three headings: their structure—anatomy; the way in which they obtain their energy and use food materials—physiology; and the growth and reproduction of bacteria.

THE ANATOMY OF BACTERIA

Bacteria are extremely small living organisms quite invisible to the naked eye. Very strong magnification, usually provided by a microscope, is required in order to see them. The unit of measurement used in the examination of bacteria is the micron (abbreviated as μ) which is 1/1000 part of a millimetre or approximately 1/25,000 inch. Bacteria vary in size from 0·5 μ in diameter up to 10–12 μ in length for the longer rod-shaped varieties. Bacteria may be examined microscopically in the living state in suspension in a fluid when some types will be found to be actively moving (motile) and others still (non-motile). When

examined in this way bacteria appear as almost clear bodies and details of shape are not easily seen. It is therefore usual to use a dye or STAIN to colour them. Examined in

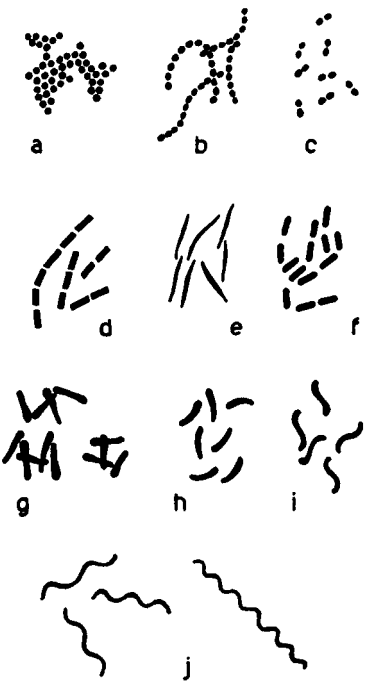

FIG. 1. The shape of bacterial cells.

(*a*) Staphylococcus, (*b*) Streptococcus, (*c*) Diplococcus (pneumococcus), (*d*) Bacillus, (*e*) Mycobacterium, (*f*) Escherichia (coliform), (*g*) Corynebacterium, (*h*) Vibrio, (*i*) Spirillum, (*j*) Two types of Spirochaete.

this way bacteria are found to exist in a variety of shapes, the commonest being either spherical or rod-shaped. These are named a COCCUS and a BACILLUS respectively. Others are in the form of a sharply curved rod shaped rather like

a comma and are termed VIBRIOS, or are elongated flexible organisms twisted spirally about the long axis and are known as SPIROCHAETES (Fig. 1).

As well as enabling the shape of bacteria to be seen more easily, stains assist in the division of bacteria into groups. The two most important differential stains are the GRAM stain and the ZIEHL-NEELSEN (Z-N) stain. In the Gram stain the smear of bacteria is first killed by heating and then stained with a dye such as methyl violet or crystal violet.

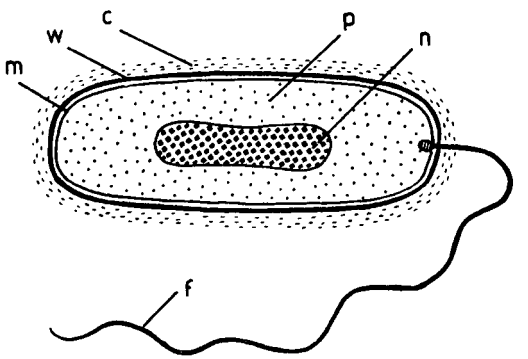

FIG. 2. Schematic drawing of a bacterial cell.
f—flagellum, c—capsule, w—cell wall, m—cytoplasmic membrane, p—protoplasm, n—nucleus.

The bacteria all become blue. They are next treated with dilute iodine which deposits the blue dye within the bacterial cell and converts them from blue to a dense opaque black. The stained film is now treated with either alcohol or acetone when, in some types of bacteria, the black deposit of stain is removed whilst in others it remains. Those retaining the stain are known as Gram positive, whilst those losing it are Gram negative. It is usual to counterstain the film with a weak red dye so that the decolorised Gram negative bacteria are visable as red objects. The difference in staining is related to differences in the structure of the bacterial cell-

wall. The Z-N stain differentiates those bacteria which, once stained, will retain the colour after treatment with strong acids and often also with alcohol. These are known as ACID-FAST or ACID-ALCOHOL FAST bacteria and include the causative organisms of tuberculosis and leprosy. Other disease-causing bacteria are non-acid-fast.

The strains so far described colour the whole bacterial cell which appears as a uniform structure, but by other methods of examination greater detail may be demonstrated. The cell can be shown to consist of a rigid CELL-WALL surrounding a central core of bacterial PROTOPLASM. By special techniques a structure may be demonstrated in the cytoplasm of rapidly-growing bacterial cells which is believed to be similar to the nucleus of higher animal and plant cells. This has been confirmed by other techniques, including electron microscopy. The bacterial nucleus is made up of similar materials to those forming the nuclei of higher life forms, but differs from these in not possessing a nuclear membrane. Like the nucleus of higher animals and plants the bacterial nucleus divides at cell division. Some types of bacteria are found to contain granules within the cytoplasm. These are thought to represent reserve food material. The cell-wall of bacteria may be covered with a mucoid material which is known as the CAPSULE. It is probably secreted by the cell-wall. The ability to produce capsules is often lost after prolonged growth in the laboratory, but is considerable in some strains freshly isolated from an infection. Figure 2 shows diagrammatically the structure of a typical bacillus.

Other important structures to be found in some bacteria are FLAGELLA (flagellum—singular). These are thread-like structures arising from the surface of the bacterial cell which by moving in an undulant manner propel the bacterium through a fluid medium. They may be arranged in various ways as shown in Fig. 3. Most bacteria not possessing flagella can only move by means of outside forces such as currents in the medium. The exception to this rule

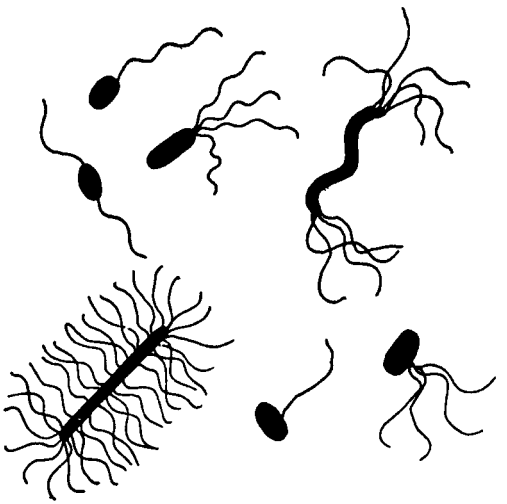

FIG. 3. The various arrangements of flagella in different species of bacteria.

are the spirochaetes which are motile by a corkscrew type of motion without the use of flagella. Flagella are not visible in the unstained state and special stains are required for their demonstration.

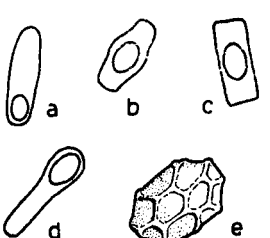

FIG. 4. Bacterial spores.

(*a*) Subterminal spore (Bacillus species), (*b*) Central spore (Clostidium species) (*c*) Central spore (Bacillus species), (*d*) Terminal spore (Clostridium species), (*e*) Detail of the structure of a spore wall.

Some bacteria in the course of their life history produce another important bacterial structure. This is the SPORE. Spores are found as oval or spherical bodies within the substance of the bacterial cell. They have a thick, tough surrounding membrane which enables them to survive adverse conditions of heat or dryness which would kill the unaltered bacterial cell. When the adverse conditions have passed the spore GERMINATES and a bacterial population is re-established. Spores may be positioned in several ways within the cell (Fig. 4), and may have a greater or lesser diameter than the bacterial cell from which they arose. Of the medically important genera only the rod-shaped species of bacteria (bacilli) produce spores.

THE PHYSIOLOGY OF BACTERIA

In discussing the physiology of any living organism we must consider how it obtains the energy for its bodily activities and growth, how it obtains a supply of nutrients, what nutrients are necessary and how it removes waste products. Higher animals have complex organs for the absorption of food materials and for the removal of waste products; bacteria are able to carry out both processes by diffusion through the cell-wall. The higher animals obtain their energy in a process of RESPIRATION by which complex chemical substances are reduced in complexity and energy is liberated. Oxygen is used up in this process and the complex chemical substance is said to be OXIDISED. The higher animals also use complex substances derived from other animals and plants to build up and repair their tissues. Bacteria obtain their energy in a similar way although in many bacteria the substances from which the energy is released may be simple in chemical structure, and oxygen is not always required. The entire food requirements of bacteria such as those living in soil or water may be only simple substances such as water and a mixture of simple salts. From these simple substances these bacteria obtain energy and build up their cell constituents. Many of

the disease-causing bacteria require in addition amino-acids, proteins and sugars and other complex substances of animal or plant origin. This difference in food requirements is mainly due to the ability or lack of ability to make, or SYNTHESISE, more complex chemical substances themselves. Thus given a solution of simple salts some bacteria are able to synthesise their own bacterial protoplasm whilst others are dependent on having the building bricks of protoplasm already made for them.

Oxygen is not always necessary in the respiration of bacteria. Some bacteria are able to grow only in the complete absence of oxygen and are termed ANAEROBES, others will grow only with oxygen and are known as OBLIGATE AEROBES, the rest will grow under either AEROBIC or ANAEROBIC conditions and are called FACULTATIVE ANAEROBES.

Important sources of energy are the carbohydrates (sugars) which bacteria use by the process of FERMENTATION. This process releases energy and results in end products such as alcohols and simple organic acids together with carbon dioxide and hydrogen. Yeasts, which are fungi and not bacteria, ferment sugars in a similar way and are used in the commercial production of alcoholic beverages. It should be noted that fermentation is quite different from the way in which the higher animals use carbohydrates. Bacteria are often able to ferment a great variety of carbohydrates and tests of this ability are used extensively in their identification.

Proteins are also attacked by some bacteria. They obtain energy and also fragments of proteins which they may use to build up or repair their own protoplasm. In nature the bacterial breakdown of proteins is usually termed PUTREFACTION in the absence of oxygen and DECAY in its presence; both often occur together. These processes are essential in nature for the removal of dead organic matter.

In addition to the nutrients already mentioned some

bacteria require the presence of traces of substances which can be considered in much the same way as vitamins in the higher animals. These are known as GROWTH FACTORS. Without the appropriate growth factor some types of bacteria will grow only poorly or not at all. The growth factors are substances which the bacterium cannot make for itself and which play an essential part in the physiology of the organism.

THE GROWTH AND CULTIVATION OF BACTERIA

Bacteria reproduce by simply splitting into two. Two new cells now exist where before there was only one. This type of reproduction is known as BINARY FISSION (Fig. 5). It is

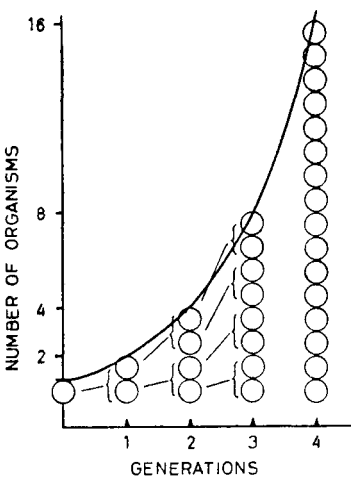

FIG. 5. The figure illustrates the rapid (logarithmic) increase in total cell population produced by binary fission.

asexual and does not therefore involve the exchange of genetic material between two different bacteria. Recently it has been discovered that a type of sexual reproduction may

take place in bacteria under some circumstances. Genetic material is passed from one organism to another via a conjugation canal. The progeny of such a CONJUGATION may differ from the parent stains just as the offspring of a higher animal mating may have some characteristics from the female and some from the male. Bacterial conjugation is probably of little significance in clinical bacteriology.

The rate at which a bacterium multiplies depends on whether the prevailing conditions are favourable to the bacterium. Given ideal conditions a single bacterium may become two in as short a time as 20 minutes. At this rate about a quarter of a million cells will exist after six hours. The growth of bacteria does not continue at this rate indefinitely. Food materials are used up and substances produced by the bacteria themselves are often damaging once a sufficiently high concentration is reached. These factors reduce the rate of multiplication until eventually more bacteria die than are produced and the total population falls.

The study of bacteria is most easily carried on in the laboratory by cultivating them under suitable conditions. Several factors must be taken into consideration. These are: (i) suitable food materials must be provided which will vary from bacterium to bacterium, (ii) appropriate atmospheric conditions which may be presence or absence of oxygen, and (iii) the temperature must be suitable.

MEDIA

The mixtures of food materials and chemicals on or in which bacteria grow in the laboratory are known as media. They provide the nutrients. They may be either solid or liquid, the former made into stiff jelly usually by the addition of a seaweed extract known as AGAR (or agar-agar). Nutrients are provided in many different forms; meat extracts, serum or whole blood are commonly used. In addition to providing the food for the organisms the acidity or alkalinity of the medium must be corrected and maintained correct by the addition of simple chemicals.

The resulting media will be known as meat extract broth (nutrient broth), serum broth, etc., if liquid, or if made solid by the addition of agar, nutrient agar, serum agar and blood agar. Liquid media are usually provided for use in either a screw-capped bottle or in a cotton-wool plugged tube. The cotton-wool plug acts as a filter and prevents the entry of bacteria from the air. Solid media are usually used as a flat sheet of medium in a round shallow covered dish known as a Petri dish. The top of the dish has a slightly greater diameter than the base and when applied prevents contamination of the medium by entry of bacteria from the air (Fig. 6).

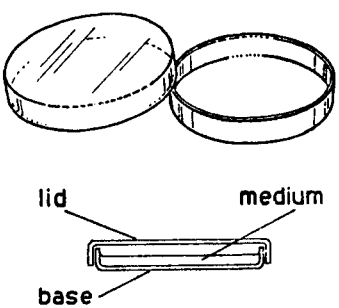

FIG. 6. The Petri dish.

The lower illustration is of a section of the dish to show the overlapping of the base by the lid.

Solid media are essential for the isolation of a pure strain of bacterium. The usual method is to inoculate one part of the dish of medium (usually called a "plate"), and then to spread the inoculum over the remainder of the plate in the manner shown in Fig. 7. In this way in some part of the plate bacteria will be present, separated from each other. After growth has occurred each bacterium will form a group; this when large enough to be visible is known as a BACTERIAL COLONY. Figure 8 shows the appearances of several types of bacterial colony. As the colony has

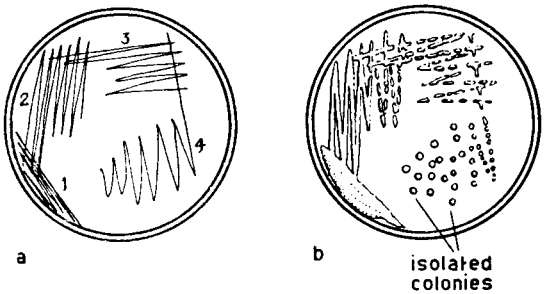

FIG. 7. (*a*) Illustrates the method commonly used to inoculate a Petri dish of medium with a bacterial culture. The groups of strokes labelled 1–4 are performed in this order. The loop is sterilised by flaming between each series of strokes to avoid carrying over too many bacteria.

(*b*) Illustrates the appearances of the plate of medium after incubation. Note the isolated colonies from which a pure growth may be obtained on sub-culture.

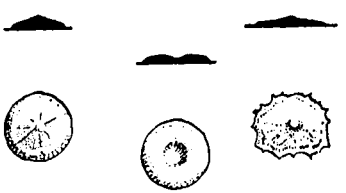

FIG. 8. The illustration shows the surface appearance and vertical section of three types of bacterial colony.

developed from a single bacterium, a pure strain can be obtained by taking a small sample from a single colony and re-culturing it. Liquid media are often used to investigate a bacterium once a pure culture has been obtained.

Many special media have been developed by bacteriologists for particular purposes. Some, known as *selective* media, are designed to stop the growth of some types of bacterium but to permit the growth of those which it is

desired to isolate. Selective media are for instance used to isolate pathogenic bacteria from amongst the great mixture of bacteria present in faeces. *Indicator* media undergo some obvious change when particular bacteria are grown on or in them. These are used for identification purposes. Other specialised media contain food materials without which particularly fastidious bacteria will not grow.

ATMOSPHERIC CONDITIONS

As already mentioned (p. 11) the presence or absence of oxygen is of great importance in the growth of some species of bacterium. No special precautions are necessary when growing facultative anaerobic bacteria which will grow both with or without oxygen. In the growth of anaerobic bacteria oxygen must be removed and then excluded. The commonest method is to enclose the inoculated media in a sealed steel container which is then exhausted to remove most of the air. The partial vacuum produced is replaced with hydrogen gas which combines with the remaining oxygen to form water. This chemical reaction is encouraged by incorporating a catalyst inside the container. Some bacteria prefer to grow in an atmosphere in which there is a little oxygen and an increased amount of carbon dioxide. These are known as MICROAEROPHILIC bacteria.

TEMPERATURE

A strain of bacterium grows best at a temperature which is peculiar to that particular strain. This depends mainly on the temperature of the habitat in which it usually lives. Thus by and large it can be said that those bacteria causing disease in man grow best at body temperature, 37°C, whilst those living in soil and water will grow well at much lower temperatures. The temperature at which a strain grows best is known as its OPTIMUM temperature. In the laboratory this is provided by the use of incubators which can be set to maintain a suitable temperature.

At low temperatures below 0°C bacteria cease to divide

but will often survive in a dormant state for long periods. When the temperature is raised they again begin to multiply. Although some types of bacteria, notably those isolated from the water of hot springs, will grow at as high a temperature as 60°C, most bacteria are killed by exposure to this temperature for a sufficiently long time. Boiling will kill all but the sporing bacteria. Bacterial spores are very resistant to heat and will survive 100°C, i.e. boiling water, for several hours. In order to kill spores quickly temperatures of 120°C are necessary.

Chapter III

THE CLASSIFICATION OF BACTERIA

Animals and plants are classified and given individual names so that in a discussion involving them the participants know exactly what is meant. Thus, in unscientific language, a lion or a buttercup mean more or less the same thing to everyone. Scientific classification goes further than this. It divides animals or plants into closely related groups and gives them all the same GENERIC NAME followed by a SPECIES NAME which is the animal or plant's own. Thus a lion is known as *Panthera leo*—*Panthera* is the generic name and implies that the lion is related to the other members of the genus, the tiger *Panthera tigris* and the leopard *Panthera pardus; leo* is the lion's own species name. Note that the name of the genus takes a capital letter whilst the species name does not. In addition to grouping into genera which contain only a small number of closely related living things, larger, less related groups may be formed. The contents of any group will have some structure or function in common. Thus the family to which the lion belongs is the *Felidae*; the cat family, including the domestic cat.

Bacteria belong to the group of life-forms which cannot with any certainty be called either animal or plant, although usually they are considered as very simple plants. Their classification is very difficult and although many systems of classification have been produced none is entirely satisfactory. The anatomy and detailed physiology are taken into account in their classification. An explanation of the details of bacterial classification is beyond the scope of this book, and all that is attempted is to introduce the names of some medically important bacteria. They are grouped according

to shape and gram staining reaction and many of the less important ones are omitted.

GRAM-POSITIVE COCCI

Staphylococcus—gram positive cocci arranged in clusters rather like bunches of grapes; some types cause wound and other infections such as boils (see Fig. 1a).

Streptococcus—gram positive cocci arranged in chains, many strains live in close association with man; some cause infections such as tonsilitis and erysipelas (see Fig. 1b).

Pneumococcus (*Streptococcus pneumoniae*)—very closely allied to the streptococci; usually arranged in pairs, sometimes called diplococci; may live harmlessly in the upper respiratory tract of man; can cause lobar pneumonia or acute bronchitis (see Fig. 1c).

GRAM-NEGATIVE COCCI

Neisseria—gram negative cocci often arranged in pairs; some species found in the upper respiratory tract of man where they do no harm; two important disease-causing species—*N. gonorrhoea* which causes the venereal disease gonorrhoea and *N. meningitidis* which causes a type of meningitis.

GRAM-POSITIVE BACILLI

Corynebacterium—gram positive bacilli which, when stained, often contain characteristic granules; often arranged in groups rather like "chinese letters"; commonly found on the skin and other sites in man; some types, notably *C. diphtheriae*, produce a powerful toxin and cause diphtheria (see Fig. 1g).

Bacillus—large gram positive rods which grow aerobically and produce spores; widely distributed in nature in soil and water; only one member of the species causes disease of man (*B. anthracis* causing anthrax) (see Fig. 1d).

Clostridium—gram positive anaerobic spore-bearing rods; found especially in manured soils; some species cause gas gangrene and tetanus in man.

Mycobacterium—acid-fast bacilli difficult to stain by gram stain but are gram positive if stained; some harmless species found in water and on grasses; two important human disease-causing species are *M. tuberculosis* and *M. leprae* causing tuberculosis and leprosy respectively (see Fig. 1e).

GRAM NEGATIVE BACILLI

Pseudomonas—motile gram negative rods growing easily on ordinary media; produce green or yellow pigments.

Proteus—actively motile gram negative rods which often spread over the surface of solid media in the surface film of water; attack urea to produce ammonia.

Salmonella—gram negative motile rods characterised mainly by their fermentation of certain sugars; cause enteric fever (*Salm. typhi* and *Salm. paratyphi A*, *B* and *C*) and food poisoning (other species of *Salmonella*).

Shigella—gram negative non-motile rods; cause dysentery.

Escherichia and other allied organisms often called collectively *coliforms*—gram negative rods normally present in the gastro-intestinal tract of man and animals; can cause wound and other infections (see Fig. 1f).

Haemophilus—delicate non-motile gram negative rods requiring special growth factors; can cause respiratory infections; the related organism *Bordetella pertussis* causes whooping cough.

Brucella—delicate slowly-growing gram negative rods; cause the chronic pyrexial illness brucellosis, also known as abortus or undulant fever and malta fever according to which species of *Brucella* is involved.

Chapter IV

INFECTION

Only a minority of bacteria are able to cause human disease; the great majority live either independently of man or in amicable association with him. Bacteria which live in association with living things, dependent to some extent on them for nutrients and a suitable environment are known as PARASITES; those fending for themselves are known as SAPROPHYTES. Only a proportion of parasitic bacteria cause harm to the host; these are known as PATHOGENIC i.e. disease-causing bacteria. It should be noted that the division into pathogenic and non-pathogenic bacteria is not absolute: under some specially favourable conditions strains usually considered to be non-pathogenic may cause disease.

Man normally carries with him a large number of bacteria. These are known as the NORMAL FLORA of the body. Far from causing harm, disease may sometimes arise if they are deliberately removed. Their presence may make it difficult for a pathogenic organism to gain a foothold and in some cases they produce substances which are of use to man. Thus destruction of the normal flora of the mouth by treatment of the patient with broad spectrum antibiotics may enable fungi such as *Candida albicans* to grow almost unrestrained, producing oral thrush. Overgrowth of antibiotic resistant *Staphylococcus aureus* may take place in the intestine when broad spectrum antibiotics largely destroy the bacterial flora; staphylococcal enterocolitis may develop and may endanger life. Bacteria are to be found on the skin, in the mouth and respiratory tract, in the gastro-intestinal tract and in the vagina. The type of bacterial flora differs in these various situations. Thus the

nose, mouth, pharynx, larynx and upper trachea contain Streptococci, non-pathogenic *Neisseria* and *Corynebacteria*, Staphylococci and Pneumococci; the bronchi and the lungs are normally sterile. The skin has mainly Staphylococci and *Corynebacteria* but may harbour other organisms at times. The intestines contain very large numbers of bacteria. These include coliforms, *Proteus*, *Pseudomonas*, *Bacillus*, *Clostridium* and *Streptococcus*. The vagina normally contains organisms which are able to live in the acid conditions prevailing there (Lactobacilli). The tissues and the body spaces which are remote from the outside are normally sterile. These include the nasal air sinuses, the middle ear cavity and the cavity of the uterus as well as the true interior of the body.

Infection is the result of the reaction between an invading bacterium and the body tissues. The body tissues may suffer severely or only slightly, depending on several factors. These are the local and general resistance of the body which are discussed in Chapter V, the number or DOSE of bacteria gaining access to the body and the capacity the organisms have to multiply in the body and produce damage. The ability of bacteria to produce severe damage is known as VIRULENCE. Thus a large dose of a highly virulent organism in a person with low resistance will produce a very severe infection and probably death whereas a small dose of an organism of low virulence in a normal subject may produce only a mild, possibly unrecognised, SUBCLINICAL infection. There are many grades of infection between these two extremes.

BACTERIAL VIRULENCE varies considerably, not only from species to species but even in different strains of the same species. The factors which determine virulence in a strain of bacterium are not completely known but several are of importance. The possession of weapons of attack and the ability to resist the body defences both play important parts in determining the virulence of bacteria. Some bacteria having a capsule are less easily destroyed than non-

capsulated strains. Perhaps the most important bacterial weapon of attack is the ability to produce substances which damage the tissues. These are known as TOXINS. Toxins may act either locally or be absorbed into the circulation and produce their damaging effects on tissues at a distance. The general effect of the production of large amounts of toxin by an infecting organism is known as TOXAEMIA. The local effects of toxin may be death or severe damage to the tissues around the area of infection and may seriously handicap the body defences. General effects include a raised temperature, general aches and pains, skin rashes and in some cases damage to "target" organs. These are organs which are specially damaged by a particular toxin; thus the toxin of diphtheria damages the heart whilst the toxin of tetanus affects the central nervous system.

TRANSMISSION OF INFECTION

Any infection is derived either directly or indirectly from a case. The case may be an obvious one or may be a person without symptoms carrying the particular organism—a CARRIER. In addition animals may be infected with human pathogens and hence serve as a source of infection. Carriers of a microbial disease are particularly important as sources of infection. They may be difficult to detect. A carrier may harbour and excrete the organism for long periods of time after recovery from clinical disease. For example, individuals have been known to excrete *Salmonella typhi* in faeces or urine for several decades after recovery from typhoid. On the other hand, excretion of a micro-organism may only occur for a few days after recovery from an infection. This still will constitute a hazard to susceptible persons who come into contact with the carrier during this period of time. Other carriers may not be aware of having suffered infection. They may be partially immune (see Chapter V) and suffer from SUBCLINICAL INFECTION. Nonetheless, they may pass on the infection to others, who

may develop the full clinical picture of the disease. Carriers of *Staphylococcus aureus* are particularly important in hospital cross infection (p. 29).

In cases of infectious disease or in carriers, micro-organisms will be present either in the urine, the faeces, the sputum or in discharges (e.g. nasal) produced as a result of the disease. The transfer of these materials spreads infection from a case to a susceptible individual. The methods of transfer may be subdivided thus:

1. by direct contact
2. by indirect contact
3. by air-borne transmission
4. by ingestion
5. by the agency of living creatures, e.g. insects.

The common modes of transfer of infection are illustrated in Fig. 9.

1. In the transmission of infection by direct contact pathogenic organisms are either placed on the skin or mucus membranes of the recipient or in some cases are directly implanted into the tissues as by a bite. Important examples of transmission by this means are the venereal diseases and in the case of direct implantation, rabies which is transmitted by the bite of an infected animal.

2. Spread of infection by indirect contact involves the contamination of some inanimate object by the sufferer; this then serves to pass the infection to another individual. Examples of this method are the spread of infection by contaminated surgical instruments, glassware and crockery, blankets, clothing and many other objects.

3. Organisms are sprayed into the air from the upper respiratory tract during speaking, coughing and sneezing and others are shed from both normal and infected body surfaces. Bacteria are usually found attached to particles of textile, dried up secretion, etc., and the smallest of the particles can remain suspended in the air for long periods. In this form bacteria can be transported on air currents for

considerable distances. They may be inhaled by a susceptible subject and induce disease or may fall on to a suitable site for growth, as on to a wound or a burn, and there cause infection. This type of transmission of infection is especially important in hospitals where many patients may be shedding

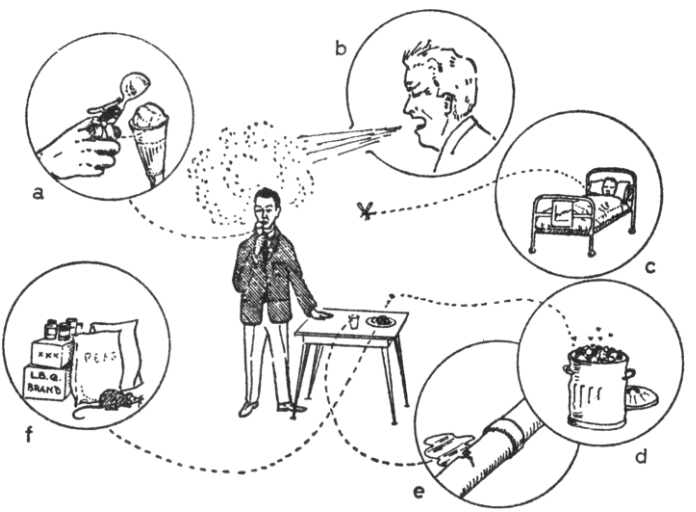

FIG. 9. The figure illustrates the different ways in which infectious disease may be spread.

(*a*) spread due to food contamination by handling (*e.g.* food poisoning) (*b*) air-borne infection (*e.g.* upper respiratory tract infections) (*c*) insect-borne infection (*e.g.* malaria), (*d*) fly-borne infection (*e.g.* dysentery), (*e*) spread by contaminated water supply (*e.g.* enteric fever), (*f*) spread by animal contamination of food (*e.g.* food poisoning).

pathogenic organisms and many others will have wounds able to become infected. This type of spread is usually referred to as hospital cross-infection (see p. 29).

4. The transmission of infection by ingestion of pathogenic bacteria is the prime mode of spread of the infectious diseases of the gastro-intestinal tract. The vehicle of transfer may be water, milk, or food. The bacteria present in the

food or drink have been placed there directly or indirectly either by a sufferer or a carrier of the disease or by an animal. Important diseases carried by this means include food poisoning, enteric fever and cholera.

5. In some diseases infection is transferred by the agency of some other living animal, perhaps the most important of which are the biting insects. The insects, by biting a sufferer from the disease and then biting a susceptible person, carry pathogenic organisms over considerable distances. Human diseases carried by this means include plague, yellow fever and typhus. In addition the protozoal disease malaria is transmitted by certain mosquitos. Animals larger than insects can transmit infection. Rabies is a virus disease which infects dogs, cats, fowl and occasionally other animals. A bite from such a rabid animal can cause disease in man.

THE PREVENTION OF INFECTION

The prevention or PROPHYLAXIS of infection is an important part of medicine as it is clearly better to prevent disease rather than to cure it once established. The methods used in the prevention of infection aim to interrupt the methods of spread discussed already under transmission of infection.

The most obvious way to prevent spread of infection by direct contact is to avoid such contact. Clearly this is usually impractical as someone must inevitably nurse an ill patient. In serious infectious diseases spread is limited by restricting contact to only those persons, nursing and medical, who are essential for the patient's recovery. Such isolation is usually carried out in a special isolation hospital. The method used in general hospitals is barrier nursing where the patient comes into contact with as few people as possible, who wear outer clothing which is not allowed outside the patient's immediate vicinity. In addition, crockery, cutlery and instruments, etc. which come into contact with the patient are restricted to the use of the one patient. Excreta and

soiled dressings are treated with the greatest care to avoid possible contact with susceptible persons. Barrier nursing if carried out conscientiously is a valuable method of preventing the spread of infection, both by direct and indirect contact.

In any case of infection, even a mild one in which barrier nursing or isolation are not considered necessary, it is essential that all contaminated material should either be destroyed or rendered safe by sterilisation. In addition all instruments, dressings, etc. used in the treatment of any patient should clearly be sterile and hence safe.

The prevention of infection by airborne spread is difficult. Particles carrying pathogenic bacteria can travel for long distances. Two main methods of attack are commonly used. Attempts can be made to diminish the amount of dust and to restrict its passage into the air, or the dust may be removed from the air as efficiently as possible. Methods to restrict the amount of dust include the use of cotton and synthetic fibre materials for blankets. These shed far less fibrous dust than the more common woollen ones. In addition cleaning and bed making are not carried out before any treatment procedure which carries a risk of infection. Vacuum cleaners should be of the type in which some of the dust does not spray out of the machine after it has been sucked in. One older method which is not used to any extent now was to apply oily substances to the floor in order to prevent dust from rising.

Ventilation is the most important method of removing dust from the air of a room. It is however important that the dust is removed to the outside air and not transported to some other room. Ideally, positive pressure ventilation is used. In this method filtered air is pumped into the room and escapes from ventilators. As the air pressure is always slightly higher in the room than outside it, all air flow is outwards and infected dust is not allowed to enter. This method is in use in some modern operating theatres. On a simpler scale ventilation by extractor fans or merely open

windows will aid in the removal of bacteria-containing dust. It is important to remember that the air leaving the room will be replaced from some other source which should not draw dust along with it. For example air should not be drawn into a ward from a surgical dressing room or from a heavily contaminated site. The prevention of such occurrences is largely a matter of good hospital design.

No one would knowingly eat or drink foods known to be contaminated with pathogenic bacteria and yet without bacteriological examination it is impossible to detect such contamination. It is therefore of great importance that food on sale to the public should be as safe as possible. In order to ensure safe food there are regulations governing its storage, sale, and quality. These are administered by the Public Health Service but depend in addition very much on the hygiene of the shop-keeper. The housewife is not without responsibility in the care of food. The way in which it is stored in the home is of prime importance.

Food may be contaminated directly from the animal which provided it, i.e. milk contaminated with tubercle bacilli from a tuberculous cow, or poultry contaminated with *Salmonella*. Control of animal health with the curing or more usually destruction of sick animals provides a means of stopping this type of contamination. It cannot be avoided completely as inevitably some animal carriers of infection are not detected. During processing or storage, food may become contaminated with bacteria from the air or from direct contact with man or animals such as mice, rats, or insects. Animal and aerial contamination can be avoided by suitable containers and food handlers should avoid contact with the hands. Moreover, food handlers should be healthy and should be medically examined at regular intervals. Any bacteria present in food will be killed by efficient heating as in an oven, and many will be killed merely by boiling. The food at this stage is safe, but if left at room temperature may become contaminated and dangerous. To minimise this risk, cooked food, if it is to

be stored, should be placed in a refrigerator. At refrigerator temperature most bacteria, though not killed, will not multiply.

Uncontaminated water is often taken for granted in many countries, but water-borne epidemics have occurred in the past and still are to found in some parts of the world. Water is normally treated by filtration in order to remove most of the bacteria. If the degree of contamination is high, chlorine may be added which chemically destroys bacteria. It is contamination after treatment which can cause trouble. A fractured water pipe in relation to a drain can pass bacteria directly into the drinking water. Control is achieved by repeatedly checking the bacteriological quality of water.

Transfer of infection by animals is usually controlled by attempting to remove the animals. In most cases this is not easy to accomplish. Thus although insecticides will reduce the population of insects, it is impossible to remove them all. If the disease in question is one which is confined to man, by denying the insects access to cases of disease the chain of infection will be broken. Both these approaches are usually employed together in preventing insect-borne disease. Rabies is an example of an animal-transmitted disease which has been controlled in this country. The compulsory muzzling of dogs, now no longer enforced, and the quarantine laws, which prevent the entrance into the country of infected animals, have completely eradicated rabies from Great Britain. Other countries have not been able to carry out these measures because of land frontiers and because of a wild animal reservoir of the disease.

HOSPITAL CROSS-INFECTION

The transmission of infection from patient to patient in hospital is obviously deserving of special consideration. Such transmission of infection is most likely to occur in a surgical ward in which many of the patients

have wounds which may easily become infected if contaminated with pathogenic bacteria. The typical story of an outbreak of serious hospital cross-infection is that it is first noticed that the number of post-operative infections in a surgical ward is increasing. Bacteriological examination will show that many of the infections are caused by the same species of organism. In the case of some organisms, notably *Staphylococcus aureus*, which is the commonest organism involved in hospital cross-infection, it is possible to divide the species into types or strains. Typing is carried out by determining the susceptibility of the strain of staphylococcus to a range of bacterial viruses known as *bacteriophages*. These viruses are able to attack and destroy bacteria in much the same way as the viruses of human disease attack human cells. By using a large range of different bacteriophages (or simply phages) a PHAGE TYPE is defined which is characteristic of the strain of *Staphylococcus*. In the typical outbreak many of the organisms will be of the same type, and will often be found to be particularly virulent. At this stage of the outbreak of infection the problem is to attempt to discover the source of infection and the major method of spread. The organism may have been introduced into the ward by a patient who was already suffering from an infection, or was carrying the organism on admission, or by a member of the medical or nursing staff. The history of the outbreak may sometimes suggest which of these possibilities is the most likely. If a patient has introduced the organism it is sometimes found that the first cases of infection occur in patients whose beds are in the immediate vicinity of the offending patient. If a member of staff is the source of infection, cases of infection may be traceable to a particular procedure carried out by that member of staff. It will often prove necessary in outbreaks of staphylococcal infection to examine nasal and possibly skin swabs from both patients and staff to discover carriers of the offending type of organism.

The mode of spread of infection may be by the air, or by direct or indirect contact. The history of the outbreak will

again sometimes help in deciding which is the major route of transfer. Bacteriological examination of air samples may be useful in detecting air-borne spread, and a thorough critical examination of all techniques in use in the ward will sometimes reveal a careless practice which is spreading infection.

Once the source and mode of spread are known, attempts are made to remove the source by medical treatment or by isolation, and to prevent cross-infection by correcting techniques, improving ventilation, reducing or removing dust, etc., as already discussed under the heading "the prevention of infection". It may sometimes prove impossible to discover both the source and mode of spread of the infection in a particular outbreak. In this case the best method of control is to attack all possible modes of spread and so produce conditions in the ward in which further cross-infection is less likely to occur.

Chapter V

BODY DEFENCES AGAINST INFECTION

The human body is by no means defenceless in the face of bacterial attack. Most commonly the attack is overcome and a state of health returns. Again, though man may come into close contact with a person suffering from an infectious disease, he may not contract it. For example only a small proportion of persons who come into contact with the highly infectious disease measles will contract the disease; the others will remain healthy. They are said to be IMMUNE to the disease. The term "immune" is not necessarily as absolute as in the example given, and also includes the ability to defend against bacterial attack even though an organism succeeds in establishing itself in the body and produces symptoms and signs of disease. Immunity to infection can be conveniently divided into the resistance to infection which is inherent in everyone and that which is acquired by previous experience of the organisms or its products. Inherent immunity is known as NATIVE (or INNATE) IMMUNITY in contradistinction to ACQUIRED IMMUNITY.

NATIVE IMMUNITY

Many pathogenic organisms will only attack a limited number of host species. Man does not suffer from many of the diseases which affect other animals and *vice versa.* Although not very well understood, the mechanism of resistance to infection with some animal pathogens is probably that human tissues do not provide appropriate conditions for growth. This prevents us from suffering, for example, from canine distemper. This type of native immunity is known as SPECIES IMMUNITY.

The intact skin provides a barrier through which most

bacteria cannot pass. In this respect it provides a good defence against invasion. Most bacteria entering the body via the skin must do so through a breach in the surface or through skin which has been in some way damaged perhaps by prolonged pressure or friction. Some micro-organisms, for example the causative organism of syphilis, can probably pass into the body by the intact healthy skin. The body tissues may also actively kill bacteria. The skin secretes substances which will very rapidly destroy some species of micro-organisms. If such organisms are applied to the surface of the normal skin none will be found after a short period of exposure to the secretions. There are, however, many species which are unaffected by contact with the skin. The hydrochloric acid secreted in the stomach is also capable of destroying micro-organisms and will therefore prevent entry of many organisms into the intestinal tract. A substance known as lysozyme is present in many body fluids including tears, and respiratory and gastro-intestinal mucus which will kill some species of bacteria by dissolving away their cell walls. A most important general means of defence is the inflammatory response. This is a general reaction of body tissues to a noxious agent, be it bacterial, chemical or physical in nature.

Following the entry into the tissues of an organism a series of changes take place. The small blood vessels increase in diameter and the rate of blood flow increases; the area becomes redder and warmer than its surroundings. The walls of the blood vessels allow plasma to escape into the tissue spaces and the white cells of the blood migrate into the tissue. This causes a swelling of the part. The white cells of the blood, together with certain tissue cells, move towards the bacteria and attempt to ingest them by a process known as PHAGOCYTOSIS (Fig. 10). In some instances phagocytosis may kill the bacterium, in others the white blood cell (phagocyte) may itself be killed. By surrounding the area of infection with plasma which often clots, and with phagocytes, the infection may be prevented from spreading. The flow of

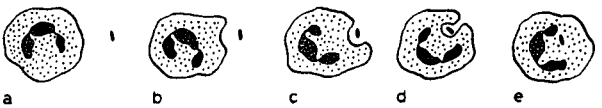

FIG. 10. Phagocytosis. The stages of ingestion of a bacillus by a polymorphonuclear leucocycte are illustrated in *a–e*.

fluid away from the area of inflammation is largely by means of the lymph vessels. Bacteria escaping from the area will usually enter the lymph and will be arrested at the nearest lymph node. Here a secondary inflammatory reaction may take place (lymphadenitis) but in many cases the infection will not become generalised. Thus the inflammatory response of the tissues tends to restrict the spread of infection within the body and in many cases to overcome it at the cost of a minor area of damage. If for some reason the inflammatory response is deficient, the infection will tend to become general and much more serious. The patient can be said to be less resistant to infection, to have less inherent native (or innate) immunity to infection.

ACQUIRED IMMUNITY

It has been known for very many years that second attacks of some diseases are very uncommon. This is especially obvious in cases of the common childhood diseases. Two attacks of measles, mumps, whooping cough, chickenpox, etc. are most rare. The person is said to have acquired immunity by virtue of his previous infection. It has been found that following infection substances can be detected in the blood which are able to react with the infecting agent in question. The reaction is quite particular to the agent and no reaction occurs with others; it is said to be SPECIFIC in its activity. These active substances are known as ANTIBODIES. They are protein in nature and are produced in response to the entry of many substances foreign to the body. Not only the micro-organisms them-

selves but their products, including toxins, induce antibody formation. Substances which induce antibody formation are named ANTIGENS. Reactions between antigens and antibodies can be demonstrated in the laboratory by several methods. If a suspension of bacteria is mixed with the appropriate antibody, the bacteria will stick together in clumps—AGGLUTINATION. If the antigen is one in solution, the addition of the specific antibody will result in a combination of the two reactants, which under suitable conditions will precipitate out of solution—PRECIPITATION. In this instance if the soluble antigen is a toxin the resultant toxin-antibody combination will no longer cause the damage which characterised the toxin before the reaction took place. The antibody here is known as an ANTI-TOXIN. In some instances the mixing of a micro-organism with the appropriate antibody will render it unable to cause infection; the antibody is a NEUTRALISING ANTIBODY. In the immune animal antibodies can carry out other functions. Their presence can encourage the phagocytes to ingest bacteria and they also take part in the dissolving or LYSIS of organisms. Immunity to a disease may depend on antibodies which destroy or which aid in the destruction of micro-organisms or on antibodies which neutralise a toxic product of the bacterium. The former is known as ANTI-BACTERIAL immunity and the latter as ANTI-TOXIC immunity. Which one or the other is the most important depends on whether the major damage caused by the disease is due to bacterial invasion or to the effect of toxins.

Acquired immunity can be conveniently divided into several types. The immunity may be ACTIVE, i.e. the antibodies are produced by the immune person, or it may be PASSIVE in which the antibodies are produced elsewhere and are then given to the subject.

Active Immunity depends on previous contact with the micro-organism or its products. Contact may be by virtue of a previous infection, overt or subclinical, or may be brought about artificially. Natural acquired immunity is of

great importance in the infectious diseases of children. The child becomes immune to such diseases as measles, mumps and chickenpox after natural infection and such immunity normally lasts for the whole of life. Artificial immunity of an active type is used in medicine as a means of preventing disease. The body is presented with either the organism or its toxin in such a way that disease does not occur but antibodies are produced and some degree of immunity is achieved. The bacterium or virus may be given as a suspension of dead organisms or it may be treated in such a way that although still alive it can no longer cause disease. Preparations such as these are known as KILLED VACCINES and ATTENUATED VACCINES respectively. It is possible to protect against some diseases by giving the patient a very mild subclinical infection which does no harm but confers a high degree of immunity against a subsequent natural infection. Vaccination for smallpox and live oral poliomyelitis vaccine are examples of this. If antitoxic immunity is considered to be the most suitable method of defence, the toxin is rendered non-toxic by various means and then given by injection. Toxins so treated are known as TOXOIDS and although they no longer produce damage on injection, they do induce the formation of antibody which will react with and neutralise the unaltered toxin. A single dose of an antigen induces the formation of only a small amount of antibody which in a short time disappears (primary response); further injections give rise to much more antibody and this continues to be produced, often for years (secondary response). Because of this a course, consisting of several immunising injections, is usually given. Preparations used to induce artificial active immunity are known as VACCINES. Artificial active immunity is available in the prevention of diphtheria, whooping cough, tetanus, smallpox, poliomyelitis, yellow fever, cholera, enteric fever and others. The infectious diseases in which artificial active immunity is commonly used and the types of vaccine available are shown in Table 1.

TABLE 1

DISEASE	TYPE OF VACCINE	PREPARATIONS USED
Diphtheria	Detoxified toxin—toxoid	Diphtheria toxoid—various preparations available, including ones precipitated with alum.
Tetanus		Tetanus toxoid.
Whooping cough (pertussis)	Killed bacteria	Suspension of killed *Bordetella pertussis*.
Enteric fever (typhoid and paratyphoid)		Mixture of killed suspensions of *Salmonella typhi* and *paratyphi A* and *B* (T.A.B.).
Cholera		Suspension of killed *Vibrio cholerae*.
Tuberculosis	Living attenuated bacteria (non-virulent)	Living suspension of the attenuated strain of *Mycobacterium tuberculosis*—Bacille Calmette-Guerin (BCG).
Poliomyelitis	Killed virus	Suspension of the three strains of poliovirus killed by formalin—Salk vaccine.
Poliomyelitis	Living attenuated (non-virulent) viruses	Mixture of living attenuated strains of the three types of poliovirus—Sabin vaccine.
Yellow fever		Suspension of a non-virulent strain of yellow fever virus (17D).
Measles		Suspension of attenuated measles virus.
Smallpox		Living virus of cowpox (vaccinia virus).

Passive immunity may be acquired in two different ways—naturally and artificially. In natural passive immunity antibody is obtained by the young from the mother either across the placenta or in breast milk. The human placenta

allows maternal antibody to pass into the foetal circulation. The baby is then born having maternal antibodies against the diseases to which the mother is immune. This provides the baby with defence at a time when it is very vulnerable, i.e. immediately after birth. The antibodies do not persist, and after a few months will have disappeared. New born cattle, and to a much less extent, humans, also obtain antibody in the breast milk. This is absorbed from the intestine and enters the circulation. In cattle this is a most important contribution to survival, but the amount of antibody obtained by the infant from human breast milk is negligible.

In artificial passive immunity the antibody is obtained from some individual or animal and is then injected into the recipient. Antibodies to bacterial toxins may be produced in animals, usually in horses. After repeated injections of the toxoid, large volumes of serum may be obtained from the horse which contains a high concentration of antibody. If this is injected into man a temporary immunity will be produced. As a foreign protein the horse antibody will be removed in a matter of weeks, but as a means of combating the toxin of diphtheria, tetanus or gas gangrene it provides immediate protection whereas active immunity would take weeks to induce. Horse antibody to tetanus toxin is commonly used in casualty departments to prevent tetanus in injured patients. Human antibodies are sometimes used to induce artificial passive immunity. If serum antibody is collected from a group in normal adults it will contain some antibody against most of the common infective diseases of childhood. The antibody preparation is known as *gamma globulin*. This is used to produce temporary protection against the common diseases of childhood in delicate children, in protection against infective hepatitis in adults at great risk and in preventing german measles (rubella) in pregnant women. Rubella infection during the early stages of pregnancy carries a considerable risk of damage to the foetus.

HYPERSENSITIVITY

So far the interaction between invading organisms and antibodies has been considered; the consequence to the host of an antigen-antibody reaction has been ignored. Most of the reactions between antigens and antibodies take place without causing any damage whatsoever to the host, but in some instances a state arises in which an abnormally great reaction occurs on presentation of the antigen. This is a state of hypersensitivity (sometimes referred to as ALLERGY). Hypersensitivity may manifest itself in several ways according to the type and to the way in which the antigen is presented. Two main types of reaction are found—the IMMEDIATE type where a reaction occurs within a matter of minutes, and a DELAYED type in which the reaction takes one or two days to reach its peak. Reactions in the skin to the injection of extracts of bacteria are used in the diagnosis of some diseases. The delayed skin reaction to tuberculin, a protein of the tubercle bacillus, is used in the diagnosis of tuberculosis, and a similar type of reaction is used in the diagnosis of Brucella infections. Not only bacterial antigens can give rise to hypersensitivity, indeed more important in medicine is hypersensitivity to pollens, foods, and other substances with which we frequently come into contact. The reaction which takes place between the antigen and antibody previously formed to it can give rise to such conditions as asthma, hay fever and urticaria. The antibody formed here is somewhat different from that so far discussed, and it tends to localise in tissue, such as the skin, the nasal mucosa and the lungs. When antigen is presented, the reaction occurs at the site of antibody attachment, release of active substances takes place, and these produce local damage to the tissues which is manifest in the symptoms of asthma, hay fever, etc. Tests for hypersensitivity to substances such as pollens and foods are carried out in the diagnosis of these conditions. By injecting small amounts of solution of the antigens into the skin, a wheal will occur if the patient is hypersensitive. A full

study of hypersensitivity is a subject in itself and is beyond the scope of this work.

DIAGNOSTIC SEROLOGY

As we have seen, the reaction between an antibody and its appropriate antigen is highly specific. This specificity is used in the diagnosis of infectious diseases of man by *serology* which is a study of antigen-antibody reactions. When an individual is infected with a particular micro-organism he will usually develop antibodies to the antigens present on the surface of the organism. Tests of the patients serum may be carried out in the laboratory to detect these antibodies, and so infer if they are present, that the patient has indeed suffered from such an infection. Antibody studies are commonly used in the diagnosis of enteric fever, brucellosis, streptococcal infections and in many virus infections. The specificity of antibodies may also be used in the opposite sense. Specific antibodies, usually prepared by repeated injections of antigen into rabbits, may be used for the final identification of micro-organisms once they have been isolated in the bacteriology laboratory. Such specific antibodies will of course only react with the micro-organism which was used to induce the antibody in the rabbit. This technique gives a very precise means of identification which supplements the usual cultural studies carried out on micro-organisms.

Chapter VI

THE DESTRUCTION OF BACTERIA

The ability to kill bacteria is useful both in the curing of infections and in their prevention. If infection is to be avoided, objects such as syringes, needles, surgical instruments and substances which are to be injected, must not carry bacteria into the patient. Wound dressings and other materials which come into contact with vulnerable tissues must be safe and free from living bacteria. To this end such objects are treated so as to STERILISE them. When bacteria must be killed we must not only consider the effect of the killing agent on the bacteria but also its effect on the object to be sterilised. Clearly, methods which may kill bacteria on a glass surface without damaging the glass may destroy a rubber or plastic object, or ruin a drug. From the patient's point of view, methods which may be suitable for the sterilisation of surgical instruments would damage human tissues if used to kill the bacteria causing an infection. In the treatment of infections, substances known as antibiotics and antibacterial agents are used. These are considered under the heading antibacterial therapy. The methods used to sterilise inanimate objects are conveniently divided into chemical and physical types, and they are discussed under these headings.

CHEMICAL STERILISATION

Very many different substances have been used as chemical sterilising agents. This was especially so in the days before antibiotics, when considerable effort was directed to try to obtain substances which would destroy bacteria in infective processes without damaging the tissues. Chemical agents have been divided into disinfectants which

kill bacteria and antiseptics which only prevent growth; this division has now lost its original meaning and the terms are usually used loosely. Disinfectants and antiseptics are often standardised by the Rideal-Walker or the Chick-Martin technique. These techniques compare in the laboratory the efficiency of a test agent with that of phenol. The laboratory test methods are sufficiently unlike the uses to which chemical agents are applied in clinical practice to make the results virtually valueless. In general, chemical methods of sterilisation are unreliable. The degree of contamination of the material to be sterilised and the presence of proteins such as serum or pus, both tend to make the efficiency most variable. Chemical sterilisation should only be used in situations where physical methods are unsatisfactory, such as when physical methods would damage the object to be sterilised. The chemical agents discussed in this section include only those most commonly used at the present time.

IODINE and CHLORINE both actively kill bacteria, but they tend to lose activity rapidly in solution and in contact with organic substances. Chlorine, usually used as a hypochlorite which liberates chlorine in solution, is used to sterilise water where adequate filtration methods are not available. Iodine, as an alcoholic solution, is widely used to sterilise skin. It is reasonably effective, reducing the bacterial population considerably, but rarely achieving complete sterility. Application of iodine to the skin of some persons may give rise to a severe reaction.

ALCOHOL, usually ethyl alcohol, is also sometimes used in an attempt to sterilise skin. It is most active when used as a 70% solution in water, but even at this concentration it is not very effective. It should be thought of as a skin cleaning agent rather than as a means of sterilisation.

FORMALDEHYDE is often used as a vapour released from "formalin tablets". In this form, with or without gentle heating, it is used to sterilise objects which will not stand high temperatures such as catheters or cystoscopes, etc.

Its efficacy is variable, depending largely on the degree of bacterial and protein contamination. If sterility is to be ensured 24 hours application of formalin vapour is required.

COAL TAR PRODUCTS such as phenols and cresols are very efficient in killing bacteria. They are used in laboratories and for general disinfecting purposes. Most are caustic, producing burns if they come into contact with the skin. Derivatives of this group of compounds such as chlorxylenol (Dettol), although, non-irritant have relatively poor disinfecting properties in practice.

DETERGENTS of some types have anti-bacterial properties. Centrimide (CTAB) is one such substance which has moderate activity. It is used in cleaning wounds but cannot be relied on as a sterilising agent.

CHLORHEXIDINE (hibitane) has considerable antibacterial activity, and is an excellent alternative to alcoholic iodine as a skin disinfectant. For this purpose it is used as a 0·5% alcoholic solution. It is also of value as an aqueous solution and has been used both to sterilise non-boilable instruments and as a store solution for already sterilised instruments.

ETHYLENE OXIDE is a fairly new sterilising agent in medical practice. It is used as a gas in sealed containers, and providing the conditions under which sterilisation is carried out are carefully standardised, it is very efficient. It has been used in the sterilisation of pharmaceutical products and plastic disposable medical equipment, but not to any great extent in small scale hospital sterilisation.

PHYSICAL STERILISATION

The physical methods of sterilisation include the use of heat, light and of the ionising radiations X-rays and gamma rays. Physical methods of sterilisation are more easily standardised than the chemical methods and are much more reliable. Unless the object to be sterilised is likely to be damaged by physical methods they are to be preferred to the more difficult to control chemical methods.

HEAT may be used either as dry or as moist heat, i.e. either with or without the presence of water or water vapour. Dry heat is the less efficient of the two types as bacteria are less easily killed if they are first dried than if they are hydrated throughout the sterilising process. Dry heat sterilisation may be achieved by heating an object to redness in a flame. This method can only be used if the object will stand this extreme treatment, but it is used to sterilise the platinum wires used in bacteriological culture methods. More useful is heating in a hot air oven. The usual type of oven is heated either by gas or better by electricity and can be set to give a desired temperature. It is essential that the set temperature is attained in all parts of the oven, and the best types have a circulator fan to ensure even heating throughout.

For sterilisation, high temperatures are required; 160°C for one hour is satisfactory. Lower temperatures may leave the much more resistant bacterial spore still alive. At a temperature of 160°C many objects such as dressings, medicaments, plastic equipment, etc. are damaged and to sterilise such objects other methods must be used.

Moist heat sterilisation may be carried out in several ways. The simplest method is boiling. Boiling water at 100°C kills bacteria very quickly but does not kill all bacterial spores even if boiling is continued for several hours. It cannot therefore be said to be a reliable sterilising method. It is however commonly used because it requires only simple inexpensive apparatus and it is quick. It should be realised that boiling an object does not sterilise it and that the method should only be used if alternative sterilising methods are not available. The use of the "sterilised" object should not result in harm even if spores are present. The time usually recommended for boiling is 5–10 minutes. Another method employing relatively low temperatures is used to "sterilise" objects such as non-boilable cystoscopes. This is sometimes known as "pasteurisation". This method uses water at only 70°C for 20 minutes. This treatment will kill the majority of bacterial cells but of course will not harm spores.

Using this method a calculated risk is taken; the risk that spores, if present, might cause infection in the urinary tract. Infections of the urinary tract with spore-bearing organisms are very uncommon and so the risk is generally considered to be justified.

Sterilisation by moist heat at temperatures greater than 100°C is carried out in an *autoclave* (Fig. 11). This is a device in which objects may be heated in the presence of saturated steam at pressures higher than atmospheric. Temperatures

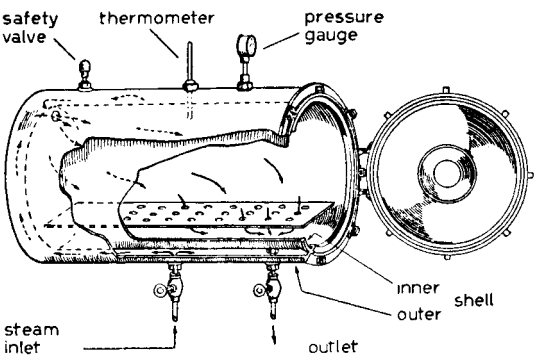

FIG. 11. Illustrates the appearances of a simple autoclave. The cut-away section shows the double shell construction, and the arrows show the path of the pressurised steam.

higher than that of unpressurised steam, i.e. greater than 100°C, are thus obtained. The temperature at which water boils, i.e. is converted into steam, depends on the pressure. Thus, although we are familiar with water boiling at 100°C (212°F), the temperature of boiling water will be less than this at the top of a mountain where the atmospheric pressure is lower than at sea level, and conversely it will be higher than 100°C if the water is boiled at the bottom of a deep mine. We use this principal in the pressure cooker in which foodstuffs are very quickly cooked because a high pressure is built up inside the cooker with a consequent increase in

the boiling point of water. The autoclave works on the same principal. It is important that the autoclave should contain steam without air because this both prevents the steam from entering porous objects such as dressings, and reduces its effectiveness as a killing agent. It is important that the steam supply does not contain free water as this also reduces the efficiency. Again, in order to kill micro-organisms the steam must actually reach them. If a dressing drum is packed very tightly, steam may not be able to reach the centre of the drum and the result will be unsterile dressings. If assembled glass syringes are treated by autoclaving, the steam will not penetrate into the thin space between the barrel and the plunger. The syringe will not be sterilised. If syringes and other similar pieces of equipment are to be sterilised by autoclaving, they must first be disassembled. Oil and grease on surfaces will prevent steam from penetrating. Equipment which requires greasing can only be sterilised satisfactorily by hot air treatment (160° for 60 minutes). Unfortunately hot air treatment may detemper steel and so damage surgical equipment. There is as yet no satisfactory solution to this problem.

When working at full efficiency, without either air or "wet" steam, if the pressure in the autoclave is 15 lb. per sq. in. the temperature will be 121°C, at 20 lb./sq. in. it is 127°C and at 30 lb./sq. in. it is 134°C. It is, however, wise to have a means of measuring the temperature at the coolest part of the autoclave (the bottom), and not to rely entirely on the pressure recorder. The time required for sterilisation depends on the temperature achieved, and hence on the steam pressure. It also depends on the time it takes the contents to reach the desired temperature. Thus a large object takes longer to heat up than a smaller one, and hence should be given a greater time for sterilisation. An average time for sterilisation is 20 minutes at 127°C (20 lb./sq. in.) with shorter times at higher temperatures and *vice versa.* The temperature and corresponding time selected depend mainly on the temperature which the object to be sterilised

will stand without sustaining damage. Thus relatively robust objects such as dressings and most surgical instruments will tolerate high temperatures without sustaining damage; these may be sterilised at higher temperatures—127°C (20 lb./sq. in.) for 20 minutes or 134°C (30 lb./sq. in.) for 10 minutes. Other commonly used articles such as rubber gloves will perish rapidly if exposed to such high temperatures and may be sterilised by using a lower temperature for a longer time.

It is desirable to control the efficiency of any autoclave by testing its sterilising ability from time to time. Probably the most satisfactory method is to insert into the middle of a typical load a "spore strip". This is a paper strip impregnated with particularly heat-resistant bacterial spores (*Bacillus stearothermophilus*). After autoclaving, the spore strip is cultured and if sterile indicates that the autoclave is working correctly. An alternative, but not as satisfactory a method, is to place Browne's tubes in the middle of the load. These are glass tubes, the contents of which change colour if they have been exposed to a particular temperature for a certain time. Tubes are available for the common times and temperatures used in routine work. Browne's tubes have the advantage of simplicity but will not always detect autoclave failure because of wet steam or steam containing air.

The most advanced types of autoclave carry out an automatic sterilising cycle. The autoclave is loaded and sealed, the air is then evacuated until the pressure is well below atmospheric pressure and steam is then admitted until the working pressure is reached. Because of the initial partial vacuum the steam penetrates into porous or hollow objects much better than in the simpler non-vacuum type autoclave. The autoclave is now held at the appropriate pressure for sufficient time and the steam is then removed to produce another partial vacuum. Dry, sterile air is now admitted which dries the contents of the autoclave. A continuous recording of the temperature and pressure changes is

usually made on a paper chart. Examination of such charts will enable a faulty cycle to be detected and the material treated by that cycle to be re-sterilised.

LIGHT, though bactericidal, is not a very useful sterilising agent. It has been found that direct sunlight will kill bacteria and that the portion of light responsible for this activity is the ultra-violet part of the spectrum. The disadvantages of ultra-violet sterilisation are its lack of penetration and the ease with which it is absorbed by such materials as glass. Ultra-violet light is sometimes used to sterilise the air of chambers in which materials are handled which must not be contaminated. It has also been used in attempts to sterilise delicate objects but is not very successful and is not commonly used for this purpose.

IONISING RADIATION such as X-rays or gamma-rays are active killers of bacteria but a very large dose of radiation is necessary to ensure sterility of an irradiated object. They penetrate through objects fairly well and for instance will sterilise the contents of a sealed glass ampoule. Some substances are damaged by irradiation so this method of sterilisation is not universally applicable. Because of the dangers to the health of persons exposed to radiation and because the equipment for safe irradiation is both large and expensive this method of sterilisation is not suitable for routine hospital practice. It is however used by pharmaceutical companies and by the manufacturers of some types of medical equipment.

FILTRATION is a physical method of sterilisation which may be used only with liquids. By passing a liquid through a very fine filter, bacteria are retained by the filter pad and the filtrate will be bacteriologically sterile. It should be noted that viruses are able to pass through the filters in common use. Filtration may be carried out in a Seitz filter which uses a thick pad of compressed asbestos to retain the bacteria, or in more modern filters which use thin porous sheets of a cellulose ester. Older methods, now rarely used, include the Berkefeld filter in which the liquid is

passed through a column of the fine earth kieselguhr, and the Chamberland filter which filters through fine unglazed porcelain. Filtration methods of sterilisation are used when a liquid to be sterilised will not tolerate other methods.

DISPOSAL OF CONTAMINATED MATERIALS

Problems sometimes arise in hospital practice concerning safe means of disposing of contaminated materials. For this purpose the materials must be classified first into whether they are disposable, e.g. a pus-soaked dressing, or non-disposable, e.g. a contaminated surgical instrument or a hospital sheet contaminated with pus. Disposable materials are either combustible or non-combustible. Those which may be burnt, e.g. dressings, should be placed in a polythene bag, sealed, and then burnt in an incinerator. Those which cannot be burnt should be placed in a suitable container, autoclaved to render handling safe, and then be handed over to the local authority refuse disposal service. Disposable plastic syringes have become a large problem in many hospitals. Although they may be burnt with difficulty, the smell produced is offensive and the melting plastic tends to impare the efficiency of the incinerator. They should be treated as non-combustible disposable objects. Some hospitals first autoclave them and then grind them to a coarse powder which the local authority will find easier to deal with.

Objects and materials which are required for further use are usually either metallic, e.g. instruments, or textiles, e.g. sheets, tray covers, etc. In dealing with contaminated re-usable objects, it is important to decide whether handling them is likely to constitute a hazard. A useful classification of contaminated objects divides them into:

(*a*) *Dirty*—no hazard to handlers, as for example a used bed sheet from the bed of a non-infectious patient.

(*b*) *Foul*—grossly dirty, as for example bed linen soiled with faeces from a non-infectious patient. Though no

hazard is involved in handling foul linen, most persons would find it offensive.

(*c*) *Infectious* — contaminated with micro-organisms which may well cause infection in a handler. Objects, bed linen, instruments, etc., used in connection with patients suffering from infectious disease should be included in this group. The treatment of bed linen illustrates well the use of this grouping. *Dirty* linen is sent straight to the laundry for routine washing; *foul* linen should never be mixed with dirty linen and should be given a preliminary separate wash followed by normal laundry washing. *Infectious* linen should first be autoclaved and then be passed into the normal laundry routine.

ANTIBACTERIAL THERAPY

The aim of antibacterial therapy is to treat a patient with a substance which will kill the bacteria causing an infection without at the same time damaging the patient's own tissues. This is not easy to achieve and it was not until recent years that satisfactory substances were discovered. Such substances fall into two groups; those originally made in the research laboratory by strictly chemical means—known usually as CHEMOTHERAPEUTIC AGENTS, and those which are made by living micro-organisms—the ANTIBIOTICS. The distinction is somewhat artificial, but chemotherapeutic agents are usually much simpler substances than antibiotics. No chemotherapeutic agent or antibiotic is available which will be effective against all types of bacteria. The type or types of bacteria against which a material has activity is known as its ANTIBACTERIAL SPECTRUM. Even if an antibacterial agent is found to be effective against a number of strains of a particular species of organism it does not follow that it will be equally effective against all strains of that organism. It is the rule rather than the exception that some strains of a usually sensitive species will be found to be resistant. In addition it is possible for a sensitive strain to become resistant

either spontaneously or after exposure to non-lethal amounts of an antibacterial agent. Most commonly the change from the sensitive to the resistant state occurs spontaneously by MUTATION. In order to understand the importance of such mutational change to resistance it is useful to consider an infection in which a change to resistance to antibiotic X has taken place in one bacterium. If a sample of pus is cultured at this stage and tested for sensitivity to antibiotic X the bacteria will be reported as "sensitive to X" because, of necessity, only a relatively small sample of the total population of bacteria are in fact tested. If the patient is now treated with antibiotic X the majority of the bacteria, being sensitive to X, will be killed. The resistant bacterium and its daughter cells will not be affected by X and will continue to grow. A sample taken at this stage will now show that the organisms isolated are resistant to X, and the infection will not have responded as well as was hoped. Such an observation is common during the treatment of bacterial infections with antibiotics and chemotherapeutic agents. If the surviving bacteria from the patient treated with antibiotic X was passed on to some other individual and there initiated a new infection they will be resistant to antibiotic X from the start. The use of antibiotic Y in this patient may select a strain resistant to both X and Y, and in this way multiple resistant strains are produced. Such strains are common in hospital practice because antibiotics are used in large quantities and the opportunity for transfer of organisms from patient to patient is high (see hospital cross-infection, p. 29). In order to minimise the development of resistant strains of bacteria, antibiotics are sometimes administered in pairs on the basis that the chances of simultaneous mutation to resistance to two antibiotics at once is very much less than the chances of mutation to resistance to one only. In addition, limitation of the use of antibiotics to only those cases who really require such treatment, and the use in these individuals of full dosage courses will also reduce the incidence of multiple

resistant strains of bacteria. Because bacterial resistance to antibiotics is common, it is important that the sensitivity of an organism isolated from a patient is tested in the laboratory to decide the most suitable agent to use.

Laboratory testing of the sensitivity of bacteria to antibacterial agents may be carried out by several methods. The one most commonly used is the "disc" method and this only is here considered. The organism to be tested is cultivated on a suitable solid medium on to which discs of blotting paper impregnated with antibacterial agent are applied. The agent diffuses outwards into the medium thus stopping the growth of sensitive bacteria. The end result is that around a disc containing an agent to which the organism is sensitive growth will not occur, whilst a resistant bacterium will grow up to the edge of the disc (Fig. 12). Although this is a somewhat crude method the results obtained provide a satisfactory guide to therapy.

Antibacterial agents can be roughly divided into two groups according to whether they are able to kill organisms or only to stop their multiplication. The former type is said to have BACTERICIDAL activity and the latter BACTERIOSTATIC activity. The body's own defence mechanisms are usually able to deal satisfactorily with the non-dividing bacteria resulting from treatment with a bacteriostatic agent. If it is known that the patient's own defences are deficient it is preferable to use a bactericidal agent.

Antibacterial agents act by upsetting some important part of the physiology of the micro-organism. It is not therefore surprising that they do on occasions result in upsetting the patient's physiology. This results in a TOXIC REACTION. Toxic reactions to antibacterial agents vary considerably in type and severity, the mildest being nausea and vomiting, diarrhoea, and skin rashes, and the most severe being damage to the blood-forming elements of the body, with perhaps death.

Antibacterial agents may be administered in several ways. Most commonly they are given by mouth and are then

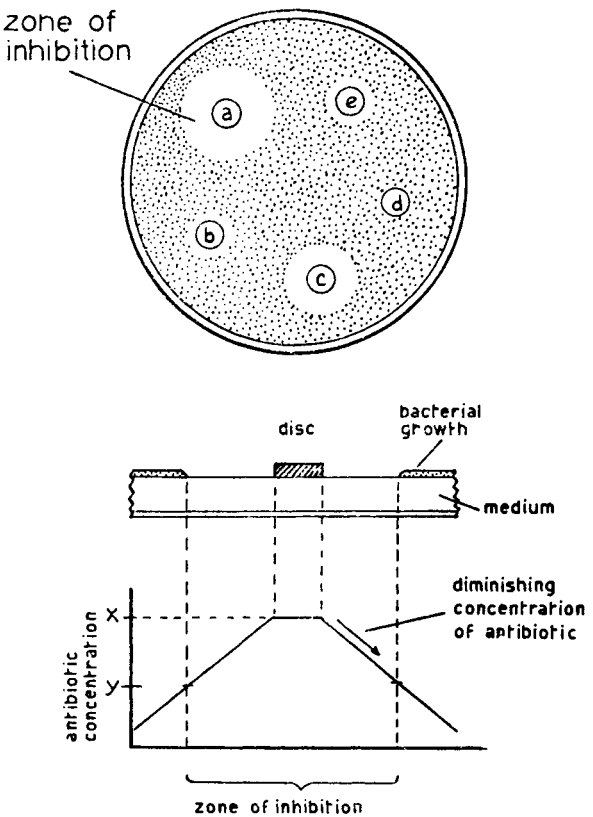

FIG. 12. The upper figure shows the appearances of the disc method for the determination of the antibiotic sensitivity of bacteria. The antibiotics are contained in the discs labelled *a*—*e*. Antibiotics contained in discs labelled *a* and *c* have produced large zones of inhibition of growth indicating bacterial sensitivity. Antibiotics *b* and *e* are surrounded by very small zones and antibiotic *d* is without a zone. The bacterium is resistant to antibiotics *b*, *d* and *e*. The lower figure illustrates the principles involved in the disc sensitivity method. Concentration *x* is the concentration of antibiotic incorporated into the disc; concentration *y* is the minimum concentration which will inhibit growth.

absorbed into the circulation from the intestine. In the case of some antibiotics absorption from the intestine is poor and they may then be given by injection either into a vein or into a muscle. In the treatment of some infections where a high concentration of antibiotic is required in the tissues as quickly as possible, administration by injection is often preferred. Antibiotics are sometimes applied directly to an infective process using either a powder or some form of ointment. This is known as topical application. In most situations this method of administration is not to be recommended as it is usually relatively inefficient and it tends to lead to the development of resistant strains of bacteria.

The following are brief notes on the more commonly used antibacterial drugs.

SULPHONAMIDES are a group of synthetic substances, i.e. are chemotherapeutic agents which act by competing with a substance necessary for bacterial growth. They are bacteriostatic and though usually given by mouth may be given by the intravenous route if speed and a high level of activity is indicated. Streptococci, pneumococci, *Neisseria* and coliforms may be sensitive although resistant strains are fairly common. Modern developments in the sulphonamides have resulted in substances which are only rarely toxic and which need not be taken as frequently as was necessary with the earlier compounds.

PARA-AMINO SALICYLIC ACID (P.A.S.) is another synthetic chemotherapeutic agent which is used in the treatment of tuberculosis. It is bacteriostatic and is usually given in combination with either streptomycin or isoniazid. It is given orally and may produce gastro-intestinal upsets.

ISONIAZID (I.N.H.) is also a synthetic compound with activity against *Mycobacterium tuberculosis*. It is given by mouth and as with P.A.S. is used in combination to reduce the incidence of resistant strains of the tubercle bacillus.

NALIDIXIC ACID and NITROFURANTOIN are both chemotherapeutic agents used in the treatment of urinary

tract infections. Both are given by mouth and are concentrated in the urine. Both have antibacterial activity against many of the bacteria which commonly cause urinary tract infections.

PENICILLIN was the first satisfactory antibiotic. It is produced during the growth of a fungus and is hence an antibiotic. There are several types of penicillin produced either naturally by fungi or more recently by chemical alteration of a preformed molecule. The first type of penicillin to be used was BENZYL PENICILLIN, known also as penicillin G and as crystalline penicillin. This is given by intramuscular injection because it is destroyed by the hydrochloric acid of the stomach if given by mouth. It has activity against the Gram positive cocci—the streptococci, pneumococci, and the staphylococci, but has little if any destructive action on Gram negative organisms other than the *Neisseria*, which are very sensitive. Benzyl penicillin given by injection is rapidly absorbed from the muscle and very rapidly excreted by the kidneys in the urine, hence the time during which it is available to attack bacteria is very limited. It must be given every three or four hours. DEPÔT PREPARATIONS whereby the absorption from the muscular site of injection is much slower require to be given less often. PROCAINE PENICILLIN is a popular depôt preparation consisting of benzyl penicillin and the local anaesthetic procaine.

A variety of penicillin which may be given by mouth is PHENOXYMETHYL PENICILLIN or PENICILLIN V. This has a similar range of antibacterial activity to benzyl penicillin but is not destroyed by gastric hydrochloric acid when taken by mouth. It is consequently used in medical practice where injections are inconvenient or undesirable.

Chemical alteration of the molecule of penicillin has yielded several useful penicillins. Only the more commonly used types will be considered. These are METHICILLIN, CLOXACILLIN, and AMPICILLIN. Many strains of *Staphy-*

lococcus are resistant to benzyl penicillin. The resistance is brought about by the organism producing a substance—an enzyme—known as PENICILLINASE which is able to break down penicillin and render it inactive. Methicillin is not inactivated by staphylococcal penicillinase and is able to attack benzyl penicillin resistant strains. It must be given by injection because it is broken down by gastric hydrochloric acid if given by mouth, and should only be used if indicated by laboratory tests. Cloxacillin has a similar range of activity to methicillin, again being resistant to staphylococcal penicillinase. It has the advantage of being active when given by mouth.

Ampicillin, the last SEMI-SYNTHETIC penicillin to be considered, has a much wider spectrum of activity than other penicillins. In addition to Gram positive and negative cocci it will also attack many strains of Gram negative bacilli, notably the coliform group and to a less extent *Proteus* species. The main use of this antibiotic is to treat infections caused by coliforms which are resistant to the more commonly used antibiotics.

STREPTOMYCIN is an antibiotic which has activity against a wide range of organisms. Resistant strains of a "normally" sensitive species are common, thus limiting its value. It is given by intramuscular injection, usually two to four times per day. Streptomycin has considerable activity against *Mycobacterium tuberculosis* and is often used in combination with either P.A.S. or I.N.H. in the treatment of tuberculosis. It is also used by mouth to reduce the bacterial flora of the intestine prior to surgery and sometimes in the treatment of gastro-intestinal infections.

Toxic effects produced by streptomycin are not common if only short courses are used, but prolonged treatment results in damage to the eighth cranial nerve with resulting deafness and dizziness, which may be permanent.

CHLORAMPHENICOL is an antibiotic most usually given orally. It is a "broad spectrum" antibiotic and is the antibiotic of choice in the treatment of enteric fever. It is

one of the few antibiotics with a definite effect on pertussis (whooping cough). It occasionally produces very serious toxic effects, with the damage falling mainly on the bone marrow, with not infrequently death as the final result. Because of the known toxic effects of chloramphenicol many physicians only use the antibiotic where others are known to be valueless, and where without antibacterial therapy the patient is likely to be seriously ill or to die.

THE TETRACYCLINES form a group of closely related antibiotics all having virtually identical activity. The three most important members of the group are OXYTETRACYCLINE ("terramycin"), CHLORTETRACYCLINE ("aureomycin") and TETRACYCLINE ("achromycin"). They are broad spectrum antibiotics taken most usually by mouth. Resistant strains of bacteria are not uncommon and may develop during the treatment of an infection caused by what was originally a sensitive strain. Toxic effects are not serious—mild gastro-intestinal disturbances being the most common.

ERYTHROMYCIN is an oral antibiotic with a similar spectrum of activity to that of benzyl penicillin, i.e. it attacks the Gram positive cocci, streptococci and staphylococci. It has been useful in the treatment of penicillin resistant infections but resistant strains of staphylococci are not uncommon and easily develop during treatment. It has no important toxic effects.

Chapter VII

RICKETTSIAE AND VIRUSES

Not all micro-organisms of medical importance can be classified as bacteria. There are in addition the fungi and the protozoa, the latter being discussed in Chapter XV, and the Rickettsia and Viruses which are the subject of this chapter. The Rickettsia and Viruses are parasitic to an even greater degree than the bacteria so far considered. Whereas parasitic bacteria depend for habitat and for food materials on their host, but can often exist independently of him, the Rickettsia and Viruses are so dependent on the host that they live within the cells of his body and cannot remain alive for long in other situations.

Rickettsia can be considered as the ultimate in bacterial parasitism. In appearance they are small gram negative bacilli which cannot be grown on bacteriological media. They can be studied by producing experimental infections in either laboratory animals, of which the guinea pig is commonly used, or by infecting living, fertile hens eggs. In these ways they may be isolated from sufferers from the diseases which they cause. Such work is however attended with a considerable risk that the laboratory worker will himself become infected. Much more commonly the diagnosis of rickettsial infection is confirmed by the demonstration of the development of specific antibody in the patient's serum.

Rickettsia cause a variety of human diseases including typhus, scrub typhus, rocky mountain spotted fever and Q fever. In most cases the rickettsial infection is transmitted to man by an insect. The insect either obtains the infection itself from a human case of the disease or from an animal carrying the disease. Thus epidemic typhus is spread by the

bite of the louse, endemic typhus by the rat flea, scrub typhus by a particular type of mite. Q fever is in all probability not insect-spread, indeed the organism of this disease differs in other ways from the remainder of the *Rickettsia* and is often classified as a separate genus—*Coxiella.*

As already mentioned the rickettsial diseases are usually diagnosed by the demonstration of the specific antibody response. This may be carried out as a complement fixation test against *Rickettsia* grown in the hen's egg, but a simpler, though not so satisfactory a method, is also available. It was found that certain strains of the Gram negative bacillus *Proteus* were agglutinated by the serum of patients recovering from typhus. This is because they happen to contain antigens very similar to those possessed by the typhus-Rickettsia. Agglutination of three strains of *Proteus* by serum from patients with Rickettsial diseases is known as the WEIL-FELIX REACTION. It is not of value in all diseases caused by *Rickettsia,* but is very useful in the diagnosis of typhus and scrub typhus.

The viruses are even smaller than the *Rickettsia.* They are so small that they cannot be seen satisfactorily with the light microscope. They require the greater magnification provided by the electron microscope to be seen. The size varies from approximately $\frac{1}{4}$ to 1/100th that of the bacterium *Staphylococcus.* Originally their presence was detected by using very fine filters. Material obtained from an infection if passed through such a filter was rendered bacteria-free; in some diseases such filtrates were still infective. The filterable agent was at first known as a "filterable virus" and later this has been contracted to—virus.

Although viruses cause a great variety of human diseases they behave basically in a similar manner. Living virus enters a living human (or animal, plant or bacterial) cell; the type of cell favoured depends on the type of virus. Once inside the cell it has the ability to instruct the cell to produce, not cellular products useful to the cell itself, but

more virus components. These are built up into more virus particles which then leave the now damaged cell to infect further living cells. The virus itself has no ability to reproduce without the use of the host cell's manufacturing processes. It is an absolute parasite.

The methods used in the diagnosis of virus diseases fall into three main classes. Simple light microscopy will in some diseases demonstrate changes in the cells which indicate infection. The individual virus particles are not themselves seen, but the changes they produce are visible. The classical example of the use of this method is in the diagnosis of rabies in the dog, in which objects known as NEGRI BODIES may be found in the brain.

Secondly, the virus can be induced to infect living cells in the laboratory. This may be by the production of an experimental infection in a laboratory animal or a fertile hen's egg or by infecting living isolated animal or human cells growing in special solutions in tubes or bottles. This latter method is known as tissue culture and is probably the most important of the three. When isolated animal or human cells are grown in suitable media they multiply and form a sheet of cells known as a MONOLAYER. If the monolayer is infected with a virus, visible changes will often take place, including the degeneration and death of cells. Such appearances are known as CYTOPATHIC CHANGES and will indicate to the virologist the type of virus likely to be causing them. Final identification of the virus is carried out using specific antibodies. The process of isolating and identifying a virus is both time-consuming and difficult, and may often take several weeks to complete.

The third method of diagnosis is to examine the serum for the development of antibody to the virus in question. Because some virus diseases such as influenza are fairly common, the presence of antibody does not necessarily indicate current infection, but may be the result of infection months or years previously. It is therefore important to prove an increase in the serum content of specific antibody

which indicates active antibody production and hence infers current infection. The other problem is that there may be many viruses capable of producing very similar symptoms and signs. Under these conditions a large number of serological tests using different virus preparations will need to be carried out.

Virus diseases spread from subject to subject by methods similar to those already outlined for bacteria in Chapter IV. Many of the virus diseases involving the respiratory tract—the common cold, influenza etc.—are spread in the air by droplets expelled by a sufferer. A large group of viruses, which for a portion of their life history live in the cells of the intestine, spread by means of faeces in the same way that bacterial dysentery spreads from case to case. This group includes poliomyelitis. A large and interesting group of viruses are spread by the bite of an insect. These include yellow fever, dengue fever, and very many others. As yet there is not a completely satisfactory classification scheme for the viruses and they are usually known by the name of the disease which they cause, i.e. the polio virus, the influenza virus, the yellow fever virus.

Chapter VIII

THE COLLECTION OF BACTERIOLOGICAL SPECIMENS

Bacteriological diagnosis is made either by identifying a disease-causing micro-organism in specimens obtained from the patient or by examining serum for specific antibody. Both methods of diagnosis are of course complementary. In either case it is of great importance that the specimens are collected correctly otherwise the results obtained may not be reliable.

General factors to be considered in the collection of specimens are:—

(a) That the sample is from the actual disease process; it is, for example, pointless to take a specimen of saliva if sputum is required and yet this is a very common mistake.

(b) The specimen must be examined in the laboratory within a fairly short time. This is important for two reasons. Firstly more delicate organisms may die rapidly at room temperature, and secondly some organisms may grow quite rapidly at room temperature thus "swamping" slow growers and giving a false impression of the total number of bacteria in the specimen.

(c) The specimen should not be contaminated accidentally. This could take place during the collection, be present in the specimen container or be added during transport to the laboratory.

(d) Specimens of blood for examination for antibodies are usually required as clotted blood. Venous blood is collected and allowed to clot in a sterile container; the clot shrinks, expressing clear serum which is used for the tests. It is important that the specimen is removed from the patient using a *dry* sterile syringe and is later handled with

care in order to minimise damage to the red cells with the release of haemoglobin (lysis). Lysed specimens can make certain types of antibody test difficult or impossible to perform.

(e) Specimens should always be labelled carefully so that there is no possibility of confusion as to the source, type, and date of collection of the material.

The following notes give important points with respect to different types of bacteriological specimens.

PUS

Material from pus producing infections may be collected in a sterile bottle or tube if it is present in large quantities as is sometimes the case with an abscess. Care should be taken not to contaminate the outside of the container and if a cotton-wool plug is used to stopper the container it also should not be allowed to touch the pus. This is because

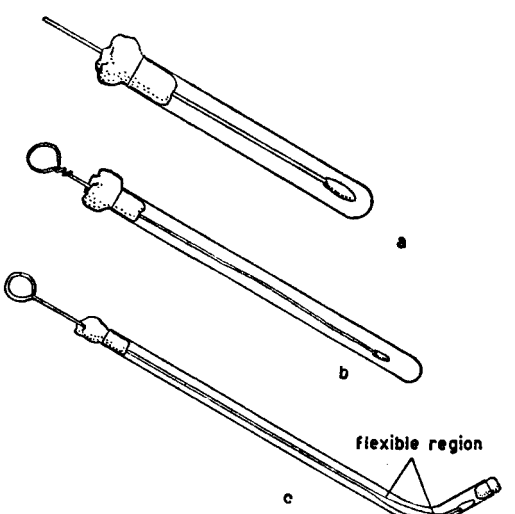

FIG. 13. (*a*) A general purpose swab, (*b*) a per-nasal swab, (*c*) a post-nasal swab (West's).

although dry cotton wool acts as a very efficient bacterial filter, once wetted, it will allow bacteria to pass through. In addition, removal of a pus-soaked cotton wool plug will constitute a serious infection hazard to the laboratory worker.

Smaller quantities of pus such as may be obtained from an ulcer or from an infected wound are best transported to the laboratory on a swab (Fig. 13). This consists of either a stick or a wire with a small amount of cotton-wool firmly wound on to one end. The whole swab is supplied inside a

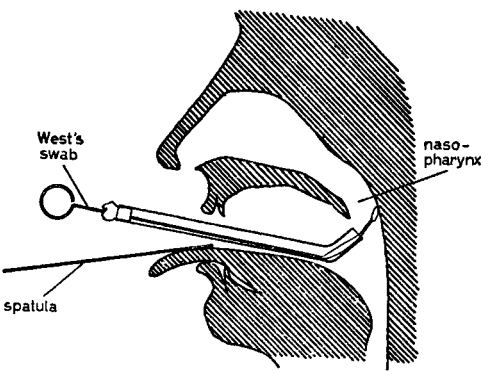

FIG. 14. Illustrates the method of taking a specimen using a post-nasal swab.

suitable container to avoid contamination. As much pus as possible should be soaked into the cotton-wool end of the swab; a rolling motion is often the best way to coat all surfaces of the swab. The swab should be returned to its container without touching the sides of the glass and the specimen labelled. Swabs may dry out quickly and should reach the laboratory without delay.

Special types of swab are sometimes used. A PER-NASAL swab is longer and more slender than the common swab and is passed through the nostrils backwards to the post-nasal space to obtain material from this site. It is sometimes used to obtain bacteriological specimens in whooping

cough. Another method of approach to this site is the use of a POST-NASAL SWAB (West's). This is illustrated in Fig. 14. The glass tube serves to prevent contamination of the swab as it passes through the mouth. Once in the post-nasal space the tip is pushed out and the curve on the glass tube directs it upwards. The tip should be retracted into the tube as it passes out through the mouth.

URINE

Passed in the usual way urine is invariably contaminated by organisms present on the external genitalia. In order to obtain a specimen of urine suitable for bacteriological examination this contamination must be avoided or minimised. A specimen obtained by means of a urethral catheter is entirely suitable, but the catheterisation procedure suffers from the risk of introducing infection into the urinary tract. The most common safe method is to collect a MID-STREAM SPECIMEN OF URINE (M.S.S.U.). This is obtained using either a STERILE funnel and a narrow-necked container or using a wide-mouthed container. The first part of the stream of urine is passed away, the next 50 ml. or so is collected, and the remainder of the urine is passed to waste. The first part of the urine washes away many of the organisms from the urethral orifice and so the M.S.S.U., although containing a few bacteria, is not heavily contaminated. Because of the slight contamination almost invariably present in the urine specimen it should be cultured without delay to prevent those organisms present from multiplying and so giving a false idea of the total microbial population. Mid-stream specimens taken from female patients are not as satisfactory as those from males, but if taken with care and if preceded by cleansing of the vulva with a mild antiseptic do give adequate results.

FAECES

These are normally collected in a non-sterile container as they already contain a vast bacterial population and the

organisms sought in faecal specimens are most unlikely to reach the specimen by contamination. The container should only be partially filled, and should be tightly capped to avoid spillage. Faeces may require to be examined for the presence of intestinal parasites; a similar type of specimen is used for this purpose except in certain instances. In the diagnosis of amoebic dysentery it is essential that the specimen reaches the laboratory within MINUTES of passing otherwise the typical movement of the amoeba will be difficult to find. After treatment of a tape worm infestation it is desirable to search the faeces for the tape worm head, so confirming the cure. In this case all the faeces which the patient passes must be examined.

BLOOD

Culture of the blood obtained from a vein is an important bacteriological examination carried out in infections of the heart valves, in septicaemia and in typhoid, etc. The blood must be obtained without contamination otherwise the result is valueless. A "no touch" aseptic technique is used to collect the blood, and the skin over the vein should be carefully cleaned with either hibitane in alcohol or tincture of iodine.

SPUTUM

This is usually collected in a wide-mouthed container; a sterile Petri dish is used in some hospitals. It is important that the specimen provided is sputum, i.e. is mucoid, mucopurulent or purulent, and is not saliva. Some of the organisms isolated from sputum are rather delicate and the specimen should be cultured without delay and not allowed to dry up.

CEREBRO-SPINAL FLUID (C.S.F.)

This is required to be cultured in cases of meningitis. It is collected in a sterile container and should be examined as soon as possible. In meningitis caused by the *meningococcus* some bacteriologists prefer to culture the specimen

at the bedside as the organism dies very quickly at room temperature.

OTHER BODY FLUIDS such as those obtained from the pleural, peritoneal, pericardial and joint cavities are collected in sterile containers. The only points to note are that the containers should not be overfilled and that a small ADDITIONAL sample should be treated with citrate or some other anticoagulant to prevent the clotting, which sometimes occurs, from interfering with the microscopic examination of the cells present in the fluid.

SPECIMENS FOR VIRUS ISOLATION are collected in very much the same way as those for bacterial culture. Specimens which may be examined include faeces, throat swabs, blood, skin scrapings, etc. It is advisable to enquire of the laboratory concerned which type of specimen they require. At any event the specimens should reach the laboratory speedily as many viruses die quickly at room temperature.

Chapter IX

THE PYOGENIC INFECTIONS

The response of the body to invasion by a wide variety of bacteria is very similar. It responds by an increased blood supply to the area and by an outpouring of serous fluid and white blood cells. This is the typical inflammatory response already briefly discussed in Chapter V. The white cells which pass out from the blood into the infected tissues attempt to ingest the bacteria (phagocytosis), many cells die and the resultant material consisting of both living and dead white cells (pus cells) and bacteria, together with damaged local tissues and blood proteins, constitutes PUS. Infections in which pus is produced are known as pyogenic, i.e. pus-producing infections. Pus may be present as a localised collection deep in the tissues—an ABSCESS, it may be produced on a surface, e.g. the mucosa of the pharynx, the mucosa of the bladder, the meninges, indeed any body surface, it is then known as a PURULENT EXUDATE, or it may spread evenly through the tissues—a CELLULITIS. The type of pus production will depend on the organism causing the infection, on the tissue in which the infective process is taking place, and also on the body resistance to the infection.

Although the pyogenic infections have very similar appearances whatever the causative organism, different sites of the body have a tendency to be infected with particular species of bacteria. This is best illustrated by considering the more common bacteria associated with infection in different parts of the body.

WOUND INFECTIONS

A wound, whether surgical or accidental, has a tendency to become infected. The bacterial barrier provided by the

skin has been breached and micro-organisms can pass directly into the tissues. This need not necessarily result in pus formation if the local and general body defences deal rapidly with the invaders. This means that potentially harmful bacteria may be cultured from a wound which is not purulent and which, even in the absence of treatment, never becomes purulent. However in most wounds the local defences are handicapped by the presence of severely damaged and possibly dead tissue and by blood clot. Here bacterial invasion is not resisted speedily and efficiently, and pus is produced.

The commonest bacterium isolated from infected wounds is *Staphylococcus aureus.* This is a coccus which is to be found in the noses and on the skin of a high proportion of normal people. They are healthy carriers of the organism. Unfortunately they may spread the organisms to sites in themselves and in other persons in which staphylococci multiply and produce an infection. Wounds, with their reduced resistance to bacterial invasion, provide very suitable sites for staphylococcal invasion. The organism may also spread from patient to patient during surgical dressing procedures in the ward. Staphylococci are also to be found in dust and may infect wound by dust-borne spread.

Strains of *Staphylococcus aureus* which are resistant to many of the available antibiotics are not uncommon in hospitals. These are sometimes known as "hospital staphylococci". Infection with such organisms can prove very difficult to treat although the more recently developed penicillins have eased the problem.

Other organisms commonly found in infected wounds are those which are normal inhabitants of the faeces. These include the "coliforms" (*Escherichia coli* and others), *Proteus* species, *Pseudomonas* and *Streptococcus faecalis.* These organisms are to be found on the skin of the buttocks, thighs, lower abdomen and sometimes elsewhere. It is not therefore surprising that wounds, particularly those of the lower abdomen, may become infected with these bacteria.

Two important types of wound infection are caused by bacteria of the genus *Clostridium*. These are large sporing rod-shaped bacteria which will not grow in the presence of oxygen, i.e. they are ANAEROBIC. They cause GAS GANGRENE and TETANUS. The Clostridia are to be found in soil and in dust; infection is always possible in a wound contaminated with such materials. In gas gangrene, infection with the particular species of *Clostridium* only usually takes place if there is extensive tissue damage, especially to muscle. The organisms produce much gas in their breakdown of the sugars in the tissues. The tissues become blown up with bubbles of gas which further damages them by interfering with the blood supply, in addition the bacteria also produce tissue-damaging toxins. The result of this infection is the widespread death of tissue—gangrene, with bubbles of gas.

Tetanus is caused by *Cl. tetani* which is able to produce one of the most potent bacterial toxins known. The actual area of infection is usually very small, indeed it may be insignificant. The wound is often a deep one but need not be large. The toxin produces severe damage to the nervous system, often resulting in death.

In both types of Clostridial wound infection actual pus formation is not marked, and may be completely absent in some cases of tetanus. They are included in this chapter because they are infections mainly of wounds, and on occasions the causative organisms are isolated from pus obtained from a wound also infected with pyogenic organisms. Antisera prepared in horses are used both to protect against or to treat gas gangrene and tetanus.

SKIN INFECTIONS

Two important types of pyogenic skin infection will be discussed which illustrate the different way in which the skin and deeper tissues respond to infection with two types of bacterium. The organisms are the *Staphylococcus aureus* and *Streptococcus pyogenes*. The two types of inflammation

are the localised boil caused by *Staph. aureus* and the spreading infection ERYSIPELAS caused by *Strept. pyogenes.*

The boil is a common infection which almost always remains localised to a small area of skin. The infection starts in a hair follicle or a sweat gland duct; a pyogenic inflammatory reaction takes place and pus is produced. This distends the tissues locally but remains localised by the toughness of the surrounding tissues and by the very efficient inflammatory reaction. It is in fact a small abscess which usually bursts through to the surface and then heals. Sometimes there is some spread away from the original abscess which enlarges and then reaches the surface in several nearby points; this is a CARBUNCLE.

A completely different type of reaction occurs in erysipelas. Here there is no tendency for the infection to localise and to form an abscess. A typical pyogenic reaction occurs but obvious pus is rarely to be seen. Instead the infection spreads rapidly through the skin and subcutaneous tissues, and is seen as a diffuse spreading redness. The causative bacterium—*Strept. pyogenes*—had the ability to break down the tissue barriers which limit the staphylococcal infection just described and consequently spread continues until the infection is either treated or until the body defences gain the upper hand.

MENINGITIS

The coverings of the brain and spinal cord (MENINGES, see Fig. 16, p. 103) may become infected with a variety of micro-organisms when the result is meningitis. If the bacterium is in the pyogenic group it is known as PYOGENIC MENINGITIS. There is no basic difference in pus production in the meninges from that produced anywhere else, but because of its location the infection will sometimes produce very serious effects. Meningitis is an example of a pyogenic infection producing a purulent exudate; pus mainly is to be found on the surface of the meninges. Separating the brain and spinal cord from the meninges is a space con-

taining a clear fluid known as CEREBRO-SPINAL FLUID or c.s.f. Into this fluid the pus cells and bacteria escape, rendering it turbid. Examination of the c.s.f. as obtained by lumbar puncture is the best way to confirm the diagnosis of meningitis. In pyogenic meningitis large numbers of pus cells will be found whereas normal c.s.f. contains only very occasional cells. Also bacteria can often be seen in stained films. The important species of bacteria causing pyogenic meningitis are *Meningococcus* (*Neisseria meningitidis*), *Pneumococcus* (*Strept. pneumoniae*), *Haemophilus influenzae*, and in children *Escherichia coli*. As these organisms have quite different appearances in stained films it may be possible to obtain a reasonably accurate preliminary identification within a very short time. Culture is necessary to confirm the diagnosis and to carry out sensitivity testing. Meningococcus is killed by quite short exposures to room temperature and c.s.f. should therefore be cultured within minutes of leaving the patient in any suspected case of pyogenic meningitis.

URINARY TRACT INFECTIONS

The urinary tract comprises the two kidneys, the ureters, the bladder and the urethra. Commonly the two important sites of bacterial infection are the pelvis of the kidney and the bladder. These infections are known as PYELITIS (or pyelonephritis as the kidney itself is usually infected as well as the renal pelvis) and CYSTITIS respectively. Sometimes an ascending infection occurs which starts as a cystitis and moves up the renal tract to involve the kidney, in other cases the infection remains localised in one site or the other.

The bacteria commonly causing urinary tract infections are *Escherichia coli* and other related organisms—the "coliforms", *Proteus*, *Pseudomonas pyocyanea* and *Streptococcus faecalis*. These are the bacteria commonly found in faeces, and already seen to be the cause of many wound infections, especially of surgical wounds of the abdomen. It is very unusual for the normal urinary tract to become infected spontaneously, but if other diseases such as

tumours, congenital malformations, injuries, etc. are present infection often occurs as a complication. The infection may be introduced by surgical procedures such as catheterisation, or may occur without intervention, either by upward passage of bacteria from the outside, or spread to the urinary tract from the intestine by the blood or lymph vessels. One type of urinary tract infection worthy of note is PYELITIS OF PREGNANCY. In pregnancy the urinary tract cannot be considered normal; the obstruction to urine flow provided by the enlarged uterus, and the stretching of pelvic structures both increase the susceptibility to infection. The commonest offending organism in this type of urinary infection is *Esch. coli.*

Bacteriological confirmation of the diagnosis of acute urinary tract infections is relatively straightforward. Microscopic examination of a mid-stream specimen of urine will show the presence of many pus cells, and culture will yield a growth of the causative organism. Urinary tract infections may often recur in spite of efficient treatment and may ultimately become chronic. Diagnosis is then not quite so easy, as pus cells may be scanty and only be present in the urine intermittently. Cylindrical masses of cells known as CASTS may be found in chronic urinary infections. Chronic urinary tract infections almost invariably involve the kidneys, and may eventually result in failure of kidney function.

PERITONITIS AND PLEURISY

In infection of the peritoneum and the pleura, both serous membranes, the inflammation takes the form of a purulent exudate. In more severe infections free pus is formed. This is known as an EMPYEMA in the case of pus in the pleural cavity. Peritonitis is usually caused by organisms derived from the gastro-intestinal tract. They reach the peritoneum often by rupture of the intestine as by perforation of a gastric ulcer, of an inflamed appendix, by wounds, either surgical or otherwise. The organisms

involved include those already mentioned under urinary infections. In addition anaerobic organisms will sometimes be isolated from peritoneal pus. These include the anaerobic Streptococci and bacilli of the genus *Bacteroides*. The organisms causing infection of the pleura reach this site by way of the lungs, secondary to pulmonary infection, i.e. pneumonia. The common organisms isolated include *Pneumococcus* (*Strept. pneumoniae*), *Staphylococcus aureus* and *Klebsiella pneumoniae*. Serious infection of the pleural cavity is no longer very common due to the treatment of pneumonia with antibiotics.

Infections of both the pleura and the peritoneum are commonly followed by healing with the formation of bands or sheets of fibrous tissue which join adjacent portions of the membranes together. These are known as adhesions. In the peritoneal cavity they may cause intestinal obstruction by being stretched tightly across a loop of intestine.

MISCELLANEOUS PYOGENIC INFECTIONS

GONORRHOEA is an acute pyogenic infection involving mainly the urethra in the male, and in the female also the cervix of the uterus. It is caused by the coccus *Neisseria gonorrhoeae*. Infection is spread from a sufferer from the disease to others by means of sexual contact. In the female there may be a vaginal discharge and pain or irritation on passing urine. The symptoms are more definite in the male in whom a purulent discharge occurs from the urethra. The Neisseria may be seen as pink oval cocci within pus cells when stained by the Gram technique. The infection usually responds well to treatment with penicillin, but if left untreated becomes chronic and may produce more serious damage to both male and female reproductive systems.

ARTHRITIS

Inflammation of a joint may be infective or non-infective, the latter type being by far the most common. Types of non-infective arthritis include osteo-arthritis, rheumatoid

arthritis and the arthritis of rheumatic fever. Purulent arthritis, which is quite rare, may occur as a result of accidental or surgical wounds of a joint when the bacteria isolated are those already discussed in the section on wound infection. Bacteria may reach a joint by way of the blood stream when the arthritis produced will appear as a complication of another bacterial disease or as a sudden unexpected happening. In pyogenic arthritis there is an outpouring of fluid into the joint space which will contain many pus cells. Quite commonly there is considerable destruction of the structure of the joint, particularly of the joint cartilages. Bacteria which may cause pyogenic arthritis include the gonococcus, *Staphylococcus aureus*, and *Streptococcus pyogenes*.

Chapter X

CHRONIC BACTERIAL INFECTIONS

The inflammation resulting from bacterial infection may be either ACUTE or CHRONIC. A major difference between the two types is the pace of the inflammatory response. We have seen in Chapter IX that the pyogenic response occurs speedily; the disease process rapidly reaches a peak, and usually the patient recovers either with or without treatment or sometimes dies. The essence of acute inflammation is its speed. In chronic bacterial inflammation events occur much more slowly, the disease may continue at a low level of activity, slowly destroying surrounding tissues for months and years. An intermediate type known as SUBACUTE inflammation is also sometimes described, but there is considerable difficulty in deciding where its boundaries lie; it is perhaps best considered as prolonged acute inflammation.

By no means all chronic inflammation is caused by bacteria. Inflammation of a chronic type occurs as a result of repeated frequent damage to a part of the body, as for example a joint, also it may result from chemical damage to tissues. It is found in many well-recognised diseases, the cause of which is still unknown, but in which there is considerable evidence available to suggest that bacteria are not the cause.

The chronic inflammatory diseases selected for consideration here are syphilis and tuberculosis. There are certain similarities in these diseases; they result in the formation of a CHRONIC GRANULOMA at some stage of their natural history. A chronic granuloma is an inflammatory process in which there is destruction of the host tissues with replacement by inflammatory cells and fibrous tissue. The inflam-

matory cell characteristic of the chronic granuloma is not the pus cell of acute inflammation but the large scavenging cell—the MACROPHAGE. In addition the LYMPHOCYTE, a cell found in lymph nodes, the spleen and in normal blood, is also seen in the chronic granuloma.

TUBERCULOSIS

The micro-organism causing tuberculosis is *Mycobacterium tuberculosis.* It is a rod-shaped, often slightly curved, organism and it may have a beaded appearance when stained. Gram's method fails to stain *M. tuberculosis*, and the ZIEHL-NEELSEN method is used (p. 7). The organism will grow on specialised artificial media, but is much slower to produce a visible colony than most bacteria already considered, about four weeks being required. Two main strains of *M. tuberculosis* can be distinguished—the human and the bovine strains. Both can cause human disease. The human strain of tuberculosis is spread from man to man most often by means of infected sputum—i.e. mainly by airborne spread. The bovine strain reaches man in milk derived from a tuberculous cow. The latter type has now been successfully controlled in many countries by the pasteurisation of milk and the testing of cattle for tuberculosis (tuberculin tested—T.T. herds). The two strains of *M. tuberculosis* tend to cause tuberculosis of different sites in the body mainly because of the difference in the route of infection. Human strain tuberculosis is most often of the lungs, whereas bovine tuberculosis usually involves the intestine and the lymph nodes of the neck.

In a population in which tuberculosis is common most persons contract the disease in childhood, so that by adolescence almost every person will show evidence of past or of active infection. In the vast majority of persons the infection is rapidly overcome and a measure of resistance to the disease develops. In such a primary infection a small area of inflammation occurs, most commonly in the lung, and the local lymph nodes and lymph vessels also share in the

inflammation. This is known as a PRIMARY COMPLEX. The characteristic cells of chronic inflammation are found arranged in small roughly spherical groups known as TUBERCLES (Fig. 15). Healing takes place with only minimal

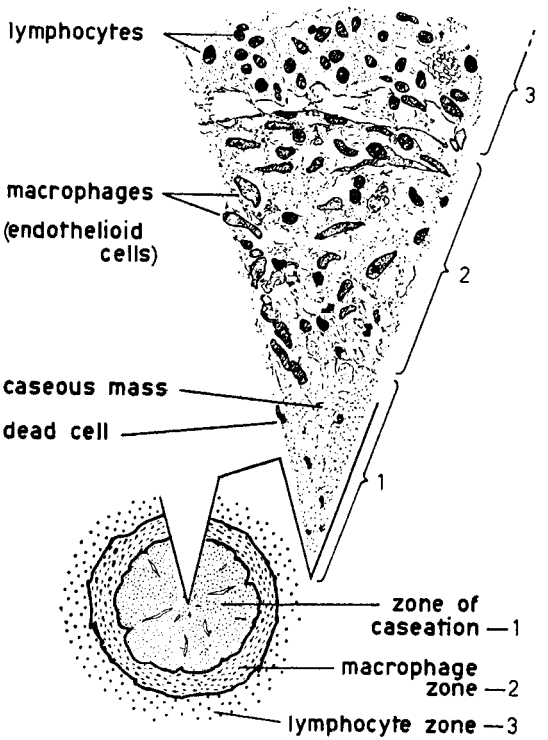

FIG. 15. Illustrates the microscopic appearances of a tubercle. Note the concentric arrangement of the caseation, large macrophage-like cells (endotheloid cells) and lymphocytes.

destruction of tissue and all that remains is a tiny scar which may later become calcified. Because of the primary infection the person develops an increased sensitivity to an extract of the tubercle bacillus (TUBERCULIN). If this

material is injected into the skin an area of temporary inflammation occurs, whereas it produces no reaction at all in a person who has never been infected with tuberculosis. This test is known as the MANTOUX test and is used to determine whether or not a person has had tuberculosis in the past. There are other variations of the test; the most modern being the HEAF test in which a "gun" is used to prick the tuberculin into the skin.

Occasionally the primary complex does not heal and spread may take place. The reason for the spread may be that the sufferer has a very low resistance to infection, or that the tubercle bacillus was a specially virulent strain, or that the dose of bacteria received was large. Spread may take place locally with more destruction of neighbouring tissue, or the bacteria may enter the blood stream with the result that tuberculosis of many parts of the body occurs. Blood-stream spread tuberculosis is known as MILIARY TUBERCULOSIS. Many organs will develop tiny MILIARY TUBERCLES, the patient will become very ill and may die. One very important site of miliary spread is the meninges when tuberculous meningitis results.

It has been said that the primary complex confers a measure of resistance to further infection, but this is by no means absolute and second infections do occur not uncommonly. The response to second infection is somewhat different to the primary infection. The inflammation induced is of a greater degree and there is much more damage to the host tissues. The result is that there is a slowly expanding area of inflammation with death of the tissue in the centre. In tuberculosis the dead tissue has a characteristic "cheesy" appearance and is described as being CASEOUS; the process is known as CASEATION. Surrounding the area of caseation is the characteristic inflammatory tissue of tuberculosis made up of many tubercles. This is the chronic granuloma of tuberculosis. There are often some areas in the inflammation which partially heal with the production of fibrous tissue. Tuberculosis at this

stage is often known as FIBRO-CASEOUS tuberculosis. At this stage of the disease involving the lungs, tuberculous material may be coughed up; the patient then spreading the disease to other people. He is known as an "open" case of pulmonary tuberculosis because the tubercle bacillus can be detected in his sputum. A "closed" case of tuberculosis does not have the bacillus in the sputum; the disease process is not in direct contact with the air passages, and he cannot pass on his infection.

Secondary tuberculosis may involve organs other than the lungs. The kidneys may be the site of tuberculous inflammation when there will be a progressive destruction of these organs. The tubercle bacillus may be detected in the urine. Bones and joints are also not uncommonly involved.

Three main drugs are currently used in the treatment of tuberculosis. These are streptomycin by injection, isoniazid (I.N.H.) and para-amino salicylic acid (P.A.S.) by mouth. Most commonly two of these substances are given simultaneously as this has been found to reduce the rate at which the tubercle bacilli develop resistance to the drugs (see p. 51).

SYPHILIS

The causative organism of syphilis is the spirochaete *Treponema pallidum*. The disease is one of the venereal diseases, that is it is transferred from case to case by sexual contact. The spirochaete of syphilis is a very delicate organism, it dies quickly on removal from the body and on drying; it cannot be cultured in the laboratory. It is also difficult to stain, and is seen and identified by the use of a special type of microscopy known as DARK GROUND MICROSCOPY.

Syphilis is usually described as having three stages. After infection by contact with a sufferer from the disease there is a period of about three weeks during which nothing appears to happen. A red raised area then develops at the site of infection and later ulcerates. This is known as the PRIMARY CHANCRE. The most common site for a primary

chancre is on the genitalia, but they may occur on the lips, tongue and rarely on the fingers. *T. pallidum* can be easily seen in the discharge from the ulcerated chancre using dark ground microscopy. The primary chancre is highly infectious, and contact with it is likely to result in transmission of the disease. Even if not treated the chancre will slowly heal and the patient may believe himself to be cured.

The SECONDARY STAGE of the disease usually starts a month or so after the appearance of the primary chancre. The patient is generally ill with headaches, chills and often vague aches and pains. He develops skin rashes, and ulcers occur in the mouth and on the genitals. The spirochaete has spread widely throughout the body and can be found easily in the discharges from the ulcers. These are again highly infectious to others. The secondary stage clears up spontaneously within a few weeks.

The TERTIARY STAGE does not usually start for several years. Chronic granulomata occur in various sites in the body. These differ from the inflammation of fibro-caseous tuberculosis in that there is very much more fibrous tissue and that although the centre of the inflammatory reaction dies, it does not become as soft and cheesy as tuberculous caseation. This inflammatory reaction is known as a GUMMA. Gummas are found in the liver, bones, genitalia, indeed they may occur anywhere. In some organs, notably the central nervous system and the cardiovascular system, the typical gumma is not seen and the inflammatory process is found diffusely through the tissue. Syphilis of the nervous system may produce a wide variety of clinical pictures. The commonest are tabes dorsalis, where the main damage is to the spinal cord, and general paralysis of the insane (G.P.I.), where there is considerable brain damage. In the cardiovascular system the aorta and aortic valves are commonly affected, resulting in aortic incompetance and sometimes aneurism (dilatation) of the aorta.

In tertiary syphilis the spirochaetes are very scanty and difficult to find. The diagnosis is made on the clinical

findings and confirmed by the use of antibody tests. Tests commonly used include the Wassermann reaction and the Kahn test or some variation of it. These tests become positive about the time of the secondary stage and are of great value in the diagnosis of the unusual skin rashes which occur in this stage.

Penicillin in adequate dosage will kill *T. pallidum* and is successful in curing both the primary and secondary stages of the disease. If the disease has reached the tertiary stage the damage produced will still remain although the organisms will be destroyed.

Chapter XI

GENERALISED INFECTIONS

In some bacterial infections micro-organisms are to be found not only in one area of infection, but can be isolated from specimens taken from several or many sites in the body. Such infections are known as generalised infections. Spread of infection throughout the body may be the result of failure of the local body defences to contain an infection, or may invariably occur as a distinct phase in a specific infective disease. Micro-organisms spread in the body by means of two main routes—the blood and the lymph. Lymphatic spread is often arrested by an intervening lymph node, but if this fails, micro-organisms will pass eventually into the blood stream. Blood spread of infection is then ultimately the most important method and is usually divided into three types. These are SEPTICAEMIA, PYAEMIA and BACTERAEMIA.

Septicaemia can be viewed as a failure of the local body defences to contain the bacterial attack. Micro-organisms and their toxins reach the blood stream and are distributed around the body. They may settle in any organ in the body and here produce further inflammation. The body suffers generally from a severe toxaemia. Septicaemia may arise from a localised pyogenic infection such as an abscess or may be a phase of an infectious disease such as enteric fever or brucellosis (see p. 85). In such diseases, in which septicaemia is a normal part of the infectious process, the invading micro-organisms invariably overcome the local body defences at their portal of entry and spread throughout the body. In septicaemia the offending micro-organism may be isolated from the blood; this usually provides a very useful diagnostic test.

Pyaemia is a complication of a pyogenic infection. The name means literally "pus in the blood". The most important difference between pyaemia and septicaemia is in the size of the masses of bacteria entering the blood stream. In pyaemia these are relatively large clumps of bacteria and pus cells, whereas in septicaemia solitary bacteria are more usual. The effect of the large clumps of bacteria in pyaemia is to block small blood vessels, shutting off the blood supply to a small piece of tissue, thus reducing the local resistance to infection. The bacteria in the clump find themselves in an ideal site for multiplication, and an abscess results. Multiple PYAEMIC ABSCESSES in various organs are the usual and characteristic finding in pyaemia.

Bacteraemia means "bacteria in the blood" and is a surprisingly common occurrence in normal individuals. There is no general reaction to a few bacteria entering the blood stream; they are usually rapidly killed and the episode goes unnoticed. Bacteraemia certainly occurs after tooth extraction and after wounding and may occur without any obvious precipitating cause. As already mentioned, bacteraemia usually does not result in disease, but on occasions the bacteria may settle in a suitable site for multiplication and an infection results. It is in this way that bacteria reach the heart valves to cause infection there (sub-acute bacterial endocarditis), and may be the means whereby bacteria reach an internal structure, there to cause an infection. Diseases such as osteomyelitis (infection of a bone) may arise in this way. Spread is by means of the blood stream in many diseases caused by viruses. In virus infections the condition is known as VIRAEMIA. In the common diseases of childhood, measles and chickenpox, the generalised nature of the disease is due to blood spread after the virus has entered and established itself in the body. In order to illustrate the spread of micro-organisms in generalised infections several different diseases will be considered. These are enteric fever, brucellosis, subacute bacterial endocarditis, plague and measles.

ENTERIC FEVER is the name given to a group of diseases caused by several bacteria of the genus *Salmonella.* These are *Salm. typhi, Salm. paratyphi A, Salm. paratyphi B* and *Salm. paratyphi C.* Alternatively enteric fever may be named TYPHOID or PARATYPHOID. The causative organism of enteric fever enters the body by the mouth, carried there in food or water which has been contaminated by a case or carrier of the disease. The bacteria pass through the wall of the intestine and settle to multiply in various organs. The liver, the spleen and lymphoid tissue are the main sites of multiplication. This process takes about two weeks and is followed by passage of the bacteria and toxins into the blood with general symptoms of septicaemia. This is the clinical onset of the disease; the initial multiplication having taken place without serious upset to the patient. Bacteria may be isolated from the blood during this stage of the disease, and also usually from the urine, which they reach after being filtered from the blood by the kidneys. At this stage of the disease the patient presents with a temperature (pyrexia) and general toxaemia, but with little else to indicate the nature of the disease. It is an important cause of PYREXIA OF UNKNOWN ORIGIN (P.U.O.). Later the bacteria invade and multiply in the lymphoid tissue of the intestine and now may be isolated from the faeces. Ulceration, haemorrhage and perforation may result from this attack on the intestine. The antibiotic of choice for the treatment of enteric fever is chloramphenicol.

BRUCELLOSIS is a subacute or chronic disease caused by bacteria of the genus *Brucella.* The disease presents as an intermittent pyrexia which continues for months and is associated with a general feeling of ill-health. The disease reaches man in milk from diseased cattle, and in areas in which goat's milk is used, from infected goats. After entry into the body the bacteria multiply mainly in the lymphoid tissue. They appear to be able to survive and to multiply inside the larger cells of the lymphoid tissue. *Brucella* may also enter the blood and can be isolated from this site.

The septicaemia of brucellosis is intermittent and the number of bacteria in the blood is less than in most other septicaemic conditions, both factors making the isolation of the organism difficult. Diagnosis is confirmed by culture of the blood on repeated occasions, and by antibody and skin hypersensitivity tests.

SUBACUTE BACTERIAL ENDOCARDITIS (S.A.B.E.) is an infection involving the lining of the heart (endocardium), mostly commonly that covering the heart valves. The most common causative organism is *Streptococcus viridans* which is a normal inhabitant of the upper respiratory tract. Other bacteria may occasionally cause the disease. The infection starts on a valve previously damaged by rheumatic heart disease, but may also occur on a part of the endocardium which is abnormal because of a congenital malformation. *Strept. viridans* reaches the damaged valve during the transient bacteraemia which not uncommonly occurs in normal individuals, and which certainly takes place during dental manipulations. A small plug of fibrin develops on the infected endocardium, and this is known as a VEGETATION. Small vegetations may break off the endocardium and pass via the blood stream to other organs, there producing further tissue damage. *Strept. viridans* may be isolated by blood culture. Treatment is difficult because the body defences are hampered by the lack of an efficient inflammatory response. Penicillin in high dosage for a long period of time is the usual method of treatment. Prophylactic treatment with penicillin is often given before dental operations in individuals with rheumatic or congenital heart disease, to prevent the occurrence of S.A.B.E.

PLAGUE is a disease of considerable historical importance. Vast epidemics of the disease have killed millions of people. The disease is now fortunately rare in civilised communities, but is still to be found in under-developed countries. The causative organism is the Gram negative bacillus *Pasteurella pestis.* The disease occurs in rats and is spread amongst the rat population by the rat flea. When a

rat dies of plague the fleas search for a new host and if a further rat is not available will attack man. The flea implants the plague bacilli into the skin of man either directly during the biting or indirectly by contaminating the skin with faeces containing the micro-organism which, because of the itching produced, are scratched into the skin. After an incubation period of about a week during which multiplication of the bacteria takes place, the local lymph nodes become painful and swollen. The enlarged, inflamed lymph nodes are known as "buboes" and the disease is often called BUBONIC PLAGUE for this reason. This localised inflammation may be followed by septicaemia with sometimes coma. The organism may be isolated from the blood and from any tissue during this stage. Bleeding into the skin often occurs, producing discoloured areas which gave the disease its old name of "the black death". Once septicaemia has occurred the death rate even with treatment is high. The disease may spread from man to man by droplet infection during an epidemic; the portal of entry is now the lungs and an even more severe form of the disease is found—PNEUMONIC PLAGUE.

MEASLES is a common disease of childhood characterised by fever, cough, a skin rash, nasal discharge and inflammation of the conjunctiva of the eye. It is caused by a virus, and probably spread by droplet infection from child to child. Although usually in itself a mild disease, it lowers the body resistance to other infections which often occur as a complication of measles. When measles is introduced into a population in which it does not normally occur, i.e. an isolated group of people, the disease itself can be of considerable severity. The incubation period of the disease is about 14 days, during which it is presumed that the virus multiplies in the body, possibly in lymphoid tissue, without producing symptoms. The virus then spreads throughout the body by way of the blood, and may be isolated from the blood by special techniques. The characteristic symptoms of measles occur at this time. The disease is rapidly

overcome by the body defences without the necessity for treatment although any complications occurring must be detected and treated.

It will be seen that there is a general pattern of behaviour in the diseases in which general spread of infection is the rule. The relationship of the invader to the host is such that initially the body defences are easily overcome; multiplication takes place and is then followed by spread throughout the body. After this the body wins the battle, possibly requiring assistance in the form of medical treatment, or the patient dies. The type of micro-organism which produces this type of disease is very well adapted to the pathogenic existence; it either has very good weapons of attack which overcome the initial attempts to remove it or is not initially susceptible to the body defences, as in the case of measles virus and *Brucella*, by being able to live and multiply inside the cells of the body.

Chapter XII

INFECTIONS OF THE RESPIRATORY TRACT

The respiratory tract may be divided for the purpose of this chapter into the UPPER RESPIRATORY TRACT comprising the nose and nasal passages, the mouth, the pharynx and the larynx, and the LOWER RESPIRATORY TRACT being the trachea, the bronchi and the lungs. The airway has thus been divided into two above and below the larynx. Acute infections of the two areas are considered separately.

UPPER RESPIRATORY TRACT INFECTIONS

To be considered under this heading are the two very important infections of the fauces and pharynx caused by *Corynebacterium diphtheriae* and by *Streptococcus pyogenes*, together with the less important infections, Vincent's angina and the virus infections of the upper respiratory tract.

DIPHTHERIA is a disease in which there is a local infection, usually in the pharynx, but which may also extend further into the respiratory tract or occur in the nose. This is associated with the production of a toxin which can cause very serious damage to other organs. The causative organism is *Corynebacterium diphtheriae* and the toxin is known as diphtheria toxin. Of recent years the disease has been uncommon in communities with efficient medical services because of prophylactic immunisation, but it still occurs from time to time and is also a not inconsiderable problem in countries in which an immunisation programme has not been carried out.

The local infection in the nose or throat will be noticed as a nasal discharge or as a severe "sore throat". There is a pyogenic reaction in the infected tissue, but in addition the effect of the diphtheria toxin is to kill the tissue cells locally, producing a grey, dead-looking area of tissue. This is

described as a MEMBRANE. The inflammation may spread down the respiratory tract where it may cause obstruction of the airway, particularly if it involves the larynx. Diphtheria toxin is absorbed from the local infection and is distributed throughout the body. It produces severe damage to the heart muscle and to nervous tissue. The effects of the toxin may cause death of the patient. Treatment is directed towards neutralising the toxin by the use of injections of diphtheria antitoxin prepared in horses. If given early in the course of the disease this method of treatment is effective, but once the diphtheria toxin has combined with the target tissues the tissue damage is not reversible. Although treatment with antitoxin is of paramount importance in diphtheria, the local lesion should not be ignored. Penicillin is effective in killing *C. diphtheriae.*

STREPTOCOCCUS PYOGENES INFECTIONS of the upper respiratory tract usually involve the tonsils but may spread to nearby tissues in the pharynx. The organism is a Gram positive coccus which occurs in chains. Streptococci are divided up into large groups according to the type of lysis which they produce when grown on media containing red cells (blood agar). The streptococci of most importance in medicine are those which produce an area of complete clearing of the red cells around a colony. This is known as BETA-HAEMOLYSIS, and such streptococci are known as beta-haemolytic streptococci. Other streptococci produce a green colour in the area of haemolysis around a colony—ALPHA-HAEMOLYSIS; these are known as *Strept. viridans.* Many streptococci produce no haemolysis—non-haemolytic streptococci. *Strept. pyogenes* is a beta-haemolytic streptococcus of a type known as Lancefield group A. The Lancefield group of a streptococcus is determined by a serological technique, and group A are by far the most important human pathogens.

Streptococcal tonsilitis is a common infection which presents as a sore throat and fever with often considerable general aches and pains in the limbs. The patient is often

considerably more ill than the local infection in the throat would suggest he should be. There is a pyogenic reaction in the infected area with redness and swelling and often pus is visible on the surface of the tonsil. Some strains of *Strept. pyogenes* produce a toxin which damages the skin, giving rise to a rash. This is the ERYTHROGENIC TOXIN, and the disease is known as SCARLATINA—scarlet fever if the rash occurs. Apart from the skin rash, which is of minor inconvenience only, there is no difference between a *Strept. pyogenes* tonsilitis and scarlatina. Antibody is formed against the erythrogenic toxin and so even though one may have many attacks of streptococcal tonsilitis the rash of scarlet fever usually only occurs during the first attack. The infection will often resolve with only the minimum of treatment, but it is preferable to cure the condition rapidly with penicillin, to which antibiotic the organism is very sensitive.

Two important complications may occur after infection with *Strept. pyogenes.* These are rheumatic fever and nephritis. About two weeks after recovery from a *Strept. pyogenes* infection the patient develops either evidence of damage to the kidneys (nephritis) or to the joints and heart (rheumatic fever). Although it is believed that the previous streptococcal infection in some way initiates these diseases, the mechanism whereby this is brought about is still unknown. Actual infection of the kidneys, heart and joints with the streptococci is not the mechanism, and a form of hypersensitivity reaction to the infecting streptococci is a more likely explanation.

VINCENT'S ANGINA is a disease which causes ulceration in the mouth and sometimes in the pharynx. It is caused by two micro-organisms which are found together in the inflammatory exudate. These are a long thin spirochaete—*Borrelia vincenti,* and a gram positive bacillus—*Fusiformis fusiformis.* The ulcers formed are shallow and the condition is often associated with a poor standard of dental hygiene. The diagnosis is made entirely on the examination of a stained smear of the exudate when a mixture of the two

organisms are seen in large numbers in a typical case. Treatment consists of correcting the dental condition and the application of gentian violet.

VIRUS INFECTIONS OF THE UPPER RESPIRATORY TRACT are very common indeed. We all suffer from time to time from conditions usually called the common cold. In fact quite a large variety of viruses produce the symptoms which we associate with the common cold—pyrexia, nasal discharge, headaches, sore throat. The true cold viruses have recently been isolated, but in addition the *adeno-viruses*, the *coxsackie viruses*, and *parainfluenza viruses*, the *echo viruses* and others are isolated from conditions which often would be described as "a cold". Other symptoms may sometimes suggest which virus is involved. Thus adeno-virus infections may commonly have a sore throat, coxsackie infections may result in ulceration of the pharynx, whilst parainfluenza infections may have croup as the main symptom. It is however impossible to make an accurate clinical diagnosis of the virus involved, and as the amount of work and time required to isolate and identify these viruses is considerable we are likely to continue to describe a mild virus infection of the upper respiratory tract as—a cold.

LOWER RESPIRATORY TRACT INFECTIONS

Infections of the lower respiratory tract include acute and chronic bronchitis, pneumonia, which will be considered under the headings lobar pneumonia, bronchopneumonia and atypical pneumonia, and whooping cough.

CHRONIC BRONCHITIS is a very common disease in this country. The disease is characterised by a chronic cough which produces thick viscid sputum. The primary cause is almost certainly not bacterial and atmospheric pollution, smoking, and in some cases allergy to environmental antigens, are more likely causative factors. Bacteria however play a part in maintaining and causing deterioration of the condition. Sufferers from chronic bronchitis tend to develop episodes of acute infection which occur most

commonly in the winter months, and are often preceded by a virus upper respiratory tract infection. Repeated episodes of acute infection tend to damage still further the already diseased bronchi and lungs, and heart failure may eventually occur.

The organism most commonly isolated from the sputum during acute episodes in sufferers from chronic bronchitis is *Haemophilus influenzae;* others include pneumococcus, staphylococci and coliforms. The avoidance of acute episodes is of such importance that many physicians treat the patient with antibiotics for the whole of the winter months in the hope of preventing acute bacterial infections. Another method is to give the patient a supply of antibiotic with the suggestion that he take it if he develops a cold or the weather is foggy. The usual antibiotic for such uses is one of the tetracyclines.

ACUTE BRONCHITIS usually occurs in normal individuals as a complication of an upper respiratory tract infection. Instead of the expected rapid recovery, the patient develops a cough with purulent sputum. The illness is not so severe as that found in acute infection in chronic bronchitis and responds well to treatment with antibiotics. The same types of bacteria are found in the sputum as those described as occurring in acute episodes of chronic bronchitis.

BRONCHOPNEUMONIA is an infection of the lungs. It is best considered as an extension of acute bronchitis. The inflammatory process has spread beyond the bronchi to involve the bronchioles and the alveoli of the lung. The disease is much more serious and may be fatal. The normal individual rarely develops bronchopneumonia as a complication of acute bronchitis, but this may occur in the young child, in an old person, and in persons of all ages who for some reason have a decreased resistance to infection. This is often found after anaesthesia, and many of the patients with "a post-operative chest" have mild bronchopneumonia, often associated with small areas of pulmonary collapse. In addition, the damage caused in the respiratory

tract by virus infections such as influenza will predispose to bronchopneumonia. Because of the route by which infection reaches the lung, i.e. via the bronchi, the inflammation in the lung is patchy. Areas of pyogenic inflammatory exudate are found around small bronchi and bronchioles. Inflammatory exudate in the alveoli of the lung gives the tissue a solid feel, known as CONSOLIDATION. Thus bronchopneumonia results in patchy areas of consolidation in relation to bronchi and bronchioles. The organisms which cause bronchopneumonia include the pneumococcus, *Haemophilus influenzae*, *Staphylococcus aureus*, coliforms and others. Antibiotic treatment of choice is determined by laboratory testing of the organism isolated from sputum.

LOBAR PNEUMONIA is so named because the inflammation is often of a whole lobe of the lung. This is unlike bronchopneumonia where the inflammation is patchy. Lobar pneumonia is an acute disease which affects all age groups and is not limited to the young and the old. The causative organism is the pneumococcus. The reason why so large a volume of lung is involved is not known with certainty, but is probably related to the relatively poor "first line" body defences against the pneumococcus. The pneumococcus has a slippery capsule which prevents the ingestion of the organism by phagocytes; in the first stages of infection the organism is therefore not restricted. Spread is also encouraged by the outpouring of fluid into the alveoli. The lobe of the lung becomes firm and airless as a result of the cellular and fluid exudate; it is consolidated. Spread to other lobes may occur but is not common because the fibrous tissue between the lobes acts as a barrier. If the patient does not die of overwhelming infection and toxaemia in the earlier stages of the disease, antibody is eventually formed. The most important antibody is that directed against the antigens in the bacterial capsule. Once antibody has stuck onto the capsule of the pneumococcus, phagocytosis may proceed normally as the surface is now sticky. With the body defences now able to cope efficiently with the

invader the disease process is rapidly brought under control. Clinically this rapid improvement in the situation is seen as a fall in temperature with recovery of the patient. This is known as resolution by "crisis". Some cases of pneumonia may recover more slowly —resolution by "lysis".

The pneumococcus is very sensitive to penicillin, and as this antibiotic is usually given to the patient in the early stages of the disease, the inflammation subsides without reaching the stage of extensive consolidation and without a "crisis". Indeed, the typical established clinical picture of lobar pneumonia is now rarely seen.

ATYPICAL PNEUMONIA is a disease which does not fit in with the descriptions of either lobar or broncho-pneumonia. The patient has a cough, possibly with chest pain, but does not often produce very much sputum. The chest X-ray findings aid in the diagnosis. The causative agents include *Coxiella burneti*, the Rickettsia-like organism which causes Q fever and at least one other organism called *Mycoplasma pneumoniae* (Eaton's agent). The diagnosis is usually confirmed in the laboratory by the use of antibody tests. There are almost certainly other agents able to cause a similar clinical picture yet to be discovered.

WHOOPING COUGH (pertussis) is a common disease of childhood caused by *Bordetella pertussis*. Clinically the child often suffers initially from symptoms of an upper respiratory tract infection, but later develops a persistent cough. In typical cases the "whoop" is heard. This is a noisy, high pitched inspiration during a series of coughs, which is due to the patient's difficulty in coughing up thick sputum. Often a typical "whoop" does not occur or is missed. Vomiting after coughing is a symptom which occurs in whooping cough, particularly in small children. The organism is not easy to isolate although the disease involves both the upper and the lower respiratory tracts. The post-nasal space is the best site from which to isolate *Bord. pertussis*. Specimens are obtained either using an approach through the mouth with a West's swab or through

the nose using a per-nasal swab. The organism dies rapidly if not placed on suitable media. An alternative method is to take a COUGH PLATE. A petri dish of suitable medium is placed a few inches in front of the child's mouth as it coughs. This is then incubated. Patience may be required in waiting for a suitably explosive cough. The disease will recover spontaneously in the majority of patients, but in some cases it results in permanent lung damage, and death can occur. In severe cases chloramphenicol is of value.

Chapter XIII

INFECTIONS OF THE GASTRO-INTESTINAL TRACT

Infections of the gastro-intestinal tract are very common. They vary in severity from mild diarrhoea to severe and sometimes fatal cholera. Gastro-intestinal infections are most common and tend to be most severe in tropical countries. In this country gastro-intestinal infections are most common during the summer months. Diarrhoea and vomiting are the two important symptoms of gastro-intestinal infection, but only one or other of the two symptoms may be present in a particular case. Infections of the gastro-intestinal tract are spread by means of contaminated food or drink. The contamination reaches the food from infected cases or animals directly, or may be transferred from infected excreta by insects, e.g. flies. Any case of food-borne infection indicates a failure in food hygiene, and as such requires correction if more persons are not to become infected. Having isolated a pathogenic organism from a case of gastro-intestinal infection we must attempt to discover the source of infection and remove it. Most of this "detective" work is carried out by the Public Health Authorities, who will be notified of cases of infection by the medical practitioner attending the patient. Often it is not possible to discover the source of infection in a single case, but when several or many persons are infected the chances of finding the source increase.

The diseases which are considered in this chapter are dysentery, "food poisoning", gastro-enteritis of children, and cholera.

DYSENTERY is an infection of the gastro-intestinal tract with bacilli of the genus *Shigella*. The principal symptom of

this disease is diarrhoea. The faeces are liquid and contain mucus and often blood. The patient will have a raised temperature and will have general symptoms of toxaemia. There are several species of *Shigella* which cause dysentery of different types. The commonest in this country is *Sh. sonnei* which causes a relatively mild form of the disease. Others are *Sh. flexneri* and *Sh. shigae;* the latter producing a much more severe illness in tropical countries. Diagnosis is confirmed by isolating the organism from the faeces. Selective media are used which suppress the growth of many of the faecal organisms but which allow *Shigella* and other pathogens to grow. Treatment is directed towards control of the diarrhoea with simple mixtures such as Mist. Kaolin. et Morph. B.P.C., and antibiotics are used to cure the infection. Sulphonamides and tetracyclines are useful, but often the organisms can still be isolated from the faeces after a full course of treatment. It is usual to insist on three negative faecal cultures before cure is considered complete.

FOOD POISONING is a name for the gastro-intestinal upsets which are associated with eating contaminated food. It is not a single condition and there are several possible causes for an outbreak of food poisoning. The typical story of an outbreak of food poisoning is that a group of persons become ill with evidence of gastro-intestinal irritation after eating a meal together. The cause may not be bacterial, excessive eating and drinking can in itself cause diarrhoea and vomiting. Again, irritant substances might have found their way into the food by accident. The causes of bacterial food poisoning are of two types. The first is due to the presence in the food of pre-formed bacterial toxin and the second type is due to bacterial infection with organisms of the genus *Salmonella.*

Toxin may be produced in food if it is first contaminated with bacteria and then stored under unsuitable conditions for some time. During the storage period the bacteria grow and produce the toxin. The two micro-organisms which are most commonly implicated in pre-formed toxin

food poisoning are *Staphylococcus aureus* and *Clostridium welchii.* The type of food often involved is cooked meat which is either served cold or is "warmed up" without thorough heating, i.e. at too low a temperature to destroy the toxin. Food which is thoroughly cooked and served hot without storage is safe. Storage of cooked foods must be carried out under conditions in which bacterial growth cannot take place. Refrigeration is a suitable method. Contamination of the food can sometimes be traced directly to one of the food handlers. Staphylococcal infection of the skin such as infected cuts or boils is a common source of *Staph. aureus* contamination of food. Ideally, food handlers with such infections should be given another job until the infection has cleared. Failing this the infected area should be covered with an occlusive dressing. The symptoms of pre-formed toxin food poisoning start very soon after eating the contaminated food. Vomiting and abdominal pains are very common and the patient may suffer from general toxaemia sometimes associated with considerable shock. The course of the illness is short and recovery is usually complete within a day.

Salmonella may reach food from several sources. They may be placed there by a food handler who is suffering from the infection himself, or who has recently recovered from infection and is still excreting *Salmonella.* The food may be contaminated with animal excreta containing *Salmonella;* rats and mice are probably the worst offenders. The animal providing the source of food may have been infected at the time it was killed. This is especially the case in poultry, eggs, shell-fish, and some imported meats. If the food is thoroughly cooked and served immediately there is no risk of infection because the organisms will be killed. Uncooked foods, and foods which are stored provide the usual source of infection.

There are very many species in the genus *Salmonella;* these are identified by the use of specific antibodies. The ones most commonly involved in food poisoning in this

country are *Salm. typhi-murium*, which is a natural pathogen of mice, and *Salm. enteritidis*. It should be noted that the organisms of enteric fever belong to the genus *Salmonella*, but that the species which cause Salmonella food poisoning do not cause enteric fever and *vice versa*. The two diseases are quite distinct from each other even though the causative organisms belong to the same genus.

The symptoms of Salmonella food poisoning include diarrhoea, abdominal discomfort, pyrexia and sometimes vomiting. The symptoms do not start as soon after eating the contaminated food as do those of pre-formed toxin food poisoning, there being an interval of about 24 hours between infection and symptoms. The symptoms subside in a few days, even without antibiotic treatment, but the organisms may persist in the faeces for weeks or even longer. There is no septicaemic phase as in enteric fever. Diagnosis is confirmed by isolating the organism from the faeces and if available from vomitus and from suspect food.

GASTRO-ENTERITIS OF CHILDREN is an important disease of early life which carries a not inconsiderable mortality. The child, usually a few months old, suffers from severe vomiting and diarrhoea and may die of dehydration if not treated rapidly. Some cases are due to *Salmonella* infection, but the most important group of cases are caused by several strains of *Escherichia coli*. This organism is a normal inhabitant of the intestine, but some strains—ENTERO-PATHOGENIC STRAINS, are able to cause infection in the very young. These are in many respects very similar to the common inhabitants of the intestine and they can only be identified by antibody typing. Infection is spread by poor hygiene, particularly failure to sterilise feeding utensils. The source of infection is probably symptom-free adults or other children. Diagnosis is confirmed by isolating the organism from the faeces. The organism may be sensitive to sulphonamides, tetracyclines, neomycin and chloramphenicol which have all

been used in the treatment. Of paramount importance in the treatment is the correction of dehydration by means of intravenous fluids.

CHOLERA is a tropical disease caused by the organism *Vibrio cholera.* It is most common in the Far East, where large epidemics have occurred in the past, and still occur from time to time. The infection is usually spread by means of unsatisfactory drinking water which is contaminated by a human sufferer from the disease. Adequately purified, i.e. filtered or chlorinated, water is safe. The symptoms of cholera start about one or two days after drinking contaminated water. Profuse diarrhoea—"rice water" stools, pyrexia, abdominal pain and general toxaemia are found in this disease. The patient may die of dehydration and the mortality rate may be as high as 80%. The organism may be isolated in the faeces although sometimes this is only achieved with difficulty. Vaccines are available for protection against cholera, but repeat doses should be given at about six monthly intervals to maintain immunity. Treatment is by antibiotics; sulphonamides, streptomycin, tetracycline, and chloramphenicol have all given promising results, and by general medical and nursing care.

Chapter XIV

INFECTIONS OF THE NERVOUS SYSTEM

Bacterial infections of the central nervous system (C.N.S.) are pyogenic in nature, and usually take the form of abscesses. Bacteria may reach the C.N.S. in the blood stream as part of a septicaemia or pyaemia or may extend inwards from an infection outside the C.N.S. The commonest example of the latter type of spread is extension of a middle ear infection through the skull into the temporal lobe of the brain. Apart from the serious results of damage to a part of the nervous system, such abscesses are very similar to those already described in Chapter IX, and they will not be discussed further.

Virus infections of the nervous system are of considerable interest and importance. The major damage may fall on one particular part of the C.N.S. as in POLIOMYELITIS where the damage is to the motor cells of the spinal cord, and in HERPES ZOSTER where the ganglia of sensory nerves are involved, or may involve large parts of the brain and spinal cord. Virus infections of the brain are known as ENCEPHALITIS, infections of the spinal cord as MYELITIS, and if both are involved in the infection, as ENCEPHALOMYELITIS.

POLIOMYELITIS is an acute virus disease in which the major damage is to the motor cells in the anterior horns of the spinal cord (Fig. 16). This results in an interruption in the pathway of the nervous control of muscle movement. The result is muscle weakness and paralysis. The degree of paralysis produced depends on the number and distribution of motor cells destroyed and damaged, and varies from weakness of one limb to complete paralysis of all four limbs, paralysis of the respiratory muscles, and often death. The

disease attacks all age groups, but is usually most severe in adults.

For part of the life history of the virus, the cells lining the alimentary tract are infected and the virus may be detected in the faeces. In addition it may be isolated from the pharynx on occasions. The faeces and possibly the saliva are the vehicles by which the virus passes from case to case. Having infected the cells of the intestine, often without producing any symptoms, the disease process may cease and the person suffers no ill-effects. This type of subclinical

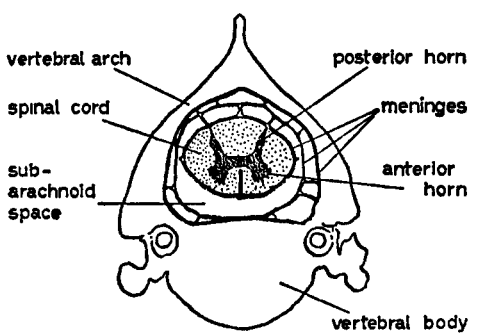

FIG. 16. Transverse section of a vertebra to show the structure of the spinal cord and meninges.

infection is relatively common, especially in a community in which the virus is widespread and the standards of hygiene are low. Under these circumstances many persons are infected, but few suffer from symptoms of the disease because they become infected in childhood when the nervous system seems to be more resistant to infection, or as a baby whilst still having a measure of passive immunity derived from the mother (see p. 37). If the infection does not remain subclinical viraemia occurs. The virus may be detected in the blood, and the patient suffers from a vague general illness with a raised temperature. The virus soon settles in the anterior horn cells of the spinal

cord, and symptoms of muscle weakness and paralysis are produced. No antibiotics will attack the polio virus, and treatment is directed towards preventing pyogenic infection and pneumonia, reducing the effects of paralysis by complete rest, and preventing the development of muscle contractions by maintaining the paralysed limbs in a suitable position. If the respiratory muscles are involved a respirator is necessary to carry out breathing movements for the patient. If the patient survives the acute phase of the disease, some degree of recovery of muscle power can be expected. The amount of recovery varies from patient to patient.

Vaccines are available which give a considerable degree of protection against poliomyelitis. These are of two types—the SALK VACCINE which consists of killed polio virus of the three main strains, and SABIN VACCINE which consists of live virus which has been attenuated, i.e. is unable to cause damage to the C.N.S. The Salk vaccine is given by injection and at least three doses are required, whereas the Sabin vaccine is given by mouth, when a subclinical infection with safe virus takes place.

HERPES ZOSTER is a disease of adults which is caused by the same virus which causes chicken pox in children. The usual source of infection in herpes zoster is a case of chicken pox, and not another case of the same disease. The fact that the adult may have himself suffered from chicken pox in childhood does not seem to provide complete protection against the development of herpes zoster. The disease presents as a painful and irritating rash on the skin in the distribution of one or more sensory nerves. The commonest site is in the distribution of the cutaneous nerves derived from the thoracic spinal cord. The rash passes obliquely around one side of the chest, being higher at the back than the front. The rash is made up of small blisters with surrounding redness. The virus can be isolated from the blisters, but the major damage is in the sensory ganglion on the posterior root of the spinal cord. The disease may involve cranial sensory nerves in addition to spinal nerves. Recovery is

usually completed without any treatment, but secondary infection of the skin rash may occur, and in some patients the pain may persist for long periods and prove difficult to relieve. It is not known why the same virus produces such apparently different diseases in adults and children. It may be that residual immunity present in an adult from chicken pox contracted as a child prevents the virus from multiplying anywhere in the body except in the nerve cells of the sensory ganglia.

ENCEPHALITIS may be caused by several different viruses. The disease presents many forms, but the usual symptoms are headache, raised temperature, drowsiness, possibly progressing to coma and death, and other evidence of damage to the brain such as convulsions, tremor, abnormalities of eye co-ordination, facial palsy, etc. If the infection also involves the spinal cord (encephalo-myelitis) there will be paralysis and/or sensory loss involving the limbs. Viruses have been identified in some types of encephalitis, but there are many cases which it is assumed are caused by viruses from which so far no virus has been isolated. It is assumed that this is due to the technical difficulty of growing some viruses. Viruses have been isolated and shown to be the cause of rabies, St. Louis encephalitis, Japanese B encephalitis, equine encephalitis, Australian X disease and Russian spring–summer encephalitis. In some cases it has been shown that the virus is transmitted to man by the bite of insects such as mosquitos and ticks, and that the virus causes a natural disease of animals which provides a reservoir of infection. Rabies is usually transmitted by the bite of an infected animal such as a dog, the vampire bat, and others. All types of encephalitis have a high mortality. There is no specific form of treatment available. Survivors from encephalitis may show evidence of permanent damage to the brain. This may take the form of POST-ENCEPHALITIC PARKINSONISM in which tremor and inco-ordination of movement are the principal signs of residual damage.

Chapter XV

ELEMENTARY PARASITOLOGY

Parasitology is a study of animals which live inside or on the surface of other animals, and which derive benefit from this habitat at the expense of the host animal. It is usual to exclude bacteria from a study of parasitology though they do in fact fit the definition. In this chapter we are only concerned with human parasites, although in the case of some parasites of man another animal host is involved in the life history. Parasites often have very complicated life histories, and may spend a part of their life in several different animals. The animal in which the parasite reaches the adult stage is known as the DEFINITIVE HOST, whilst hosts which sustain the earlier (larval) stages of parasite development are known as SECONDARY HOSTS. Parasites are sometimes divided into those which live on the surface of the host—ECTOPARASITES, and those which live inside the host body—ENDOPARASITES.

ECTOPARASITES OF MAN belong to the large group of jointed limbed animals, the *Arthropoda*. This group includes the crabs, lobsters, centipedes, spiders, insects, etc. Parasites of man within this group are the mites, ticks and insects. Ectoparasites are usually biting animals which require blood as a food. In some cases the blood feed is required only once in the life of the parasite, in others several or many feeds are usual. The ectoparasites of man are important for several reasons. Firstly they may act as agents in the transmission of infection. Some of the infections which are transmitted by ectoparasites are shown in Table 2. Secondly ectoparasites may also cause harm to man by invading the skin. The itch mite which causes scabies is an example of this type of damage. In addition, the itching

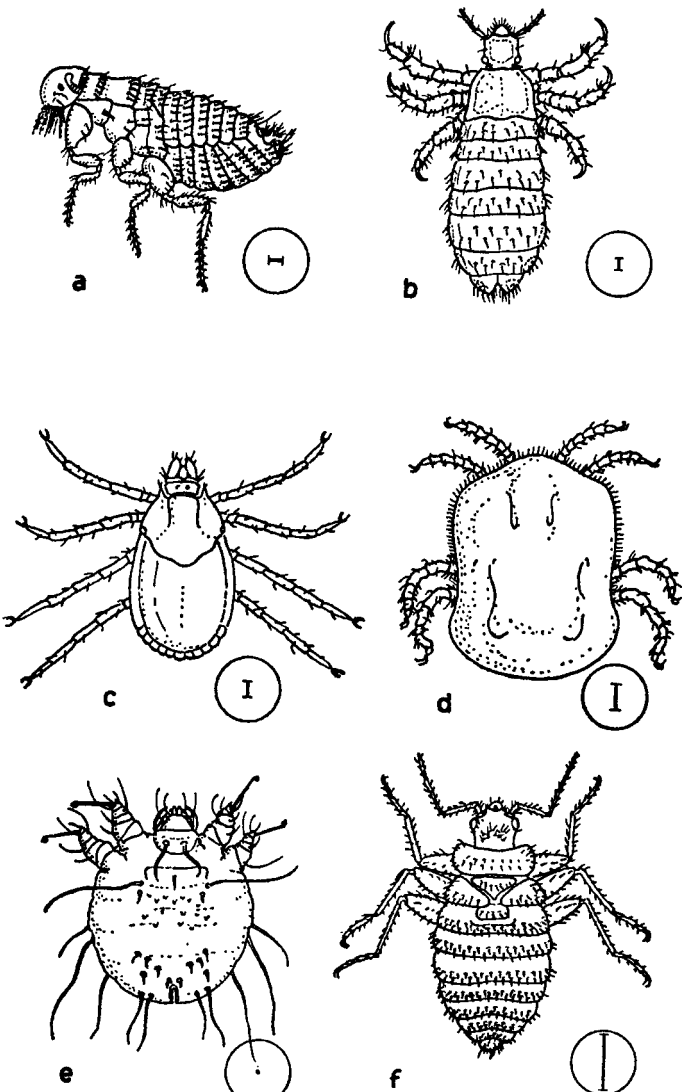

FIG. 17. Ectoparasites of man.

(*a*) Flea, (*b*) Louse, (*c*) Hard tick, (*d*) Soft tick, (*e*) Mite (scabies), (*f*) Bug. The small line enclosed in the circle next to each parasite indicates its approximate life size.

produced by frequent biting by mosquitos, flies, etc., in itself constitutes a considerable nuisance. Figure 17 illustrates the appearance of several important ectoparasites of man.

Table 2

DISEASES TRANSMITTED BY ECTOPARASITES

PARASITE	DISEASES
Flea	Plague, endemic typhus
Louse	Epidemic typhus
Tick	Many rickettsial infections
Mite	Scrub typhus
Mosquito	Malaria, yellow fever, encephalitis, other virus diseases
Biting flies	Sleeping sickness, kala-azar, sand fly fever.

ENDOPARASITES may live in various situations in man. They may exist in the blood, in the tissues, in the lymph vessels and in the gastro-intestinal tract. Most human ectoparasites are either single-celled animals—*Protozoa*, or various types of worms. The worms may be divided into FLAT WORMS (*Platyhelminthes*) and ROUND WORMS (*Nemathelminthes*). The flat worms include the flukes and the tape worms. We will first consider examples of parasitic protozoa and then discuss some of the more important parasitic worms.

PARASITIC PROTOZOA

The examples of parasitic protozoa selected for discussion are *Plasmodium*, the causative agent of malaria which is a blood parasite, *Entamoeba histolytica*, a parasite of the intestine which causes amoebic dysentery, and *Trichomonas vaginalis* which causes infections of the female genital tract.

MALARIA is a disease which occurs in tropical and sub-tropical countries. The protozoa which cause malaria

belong to the genus *Plasmodium*, and there are several species—*P. vivax*, *P. falciparum*, *P. ovale*, and *P. malariae*—which can be identified and which cause different types of the disease. Malaria is transmitted to man by the female ANOPHELES MOSQUITO. This genus includes many different species. The mosquito becomes infected by the *Plasmodium*, which undergoes part of its life history in the tissues of the mosquito. The rest of the life history is carried out in human tissues, notably in the red cells of the blood. The life cycle of *Plasmodium* then requires two hosts—man and the mosquito, in order that it may be complete. The link between the two hosts is the bite of the mosquito. If man is bitten by a mosquito infected with *Plasmodium* there is an incubation period of about two weeks before symptoms occur, during which the injected parasites live inside tissue cells in the liver. They leave the liver and enter the red cells of the blood where they develop from tiny objects (*trophozoites*) into much larger ones which almost fill the red cell (*Schizonts*). The large form divides into many smaller forms (*merozoites*) which break out of the cell. This coincides with the clinical attack of malaria in which the patient's temperature rises, he alternately feels cold and shivers and hot, and sweats profusely. The merozoites released from the red cell infect other cells and the cycle continues again. It will be noted that reproduction of the *Plasmodium* is asexual during this cycle, and as the time taken to carry out this cycle is constant the attacks of malaria occur at regular intervals, each time related to the bursting out of the merozoites. The time for the cycle is 48 hours in *P. vivax* infections, 72 hours in *P. malariae* infections, and slightly less than 48 hours in *P. falciparum* infections. *P. vivax* infections are for this reason called TERTIAN MALARIA—attacks on the first and THIRD days; *P. malariae* infections with attacks on the first and FOURTH days are known as QUARTAN MALARIA, and *P. falciparum* infections with attacks at just less than 48 hour intervals are known as SUBTERTIAN MALARIA, or more commonly as

MALIGNANT TERTIAN MALARIA because it tends to be more severe than *P. vivax* BENIGN TERTIAN malaria.

Some time after the asexual cycle has become established in man some of the parasites develop into male and female cells. These have no part to play in the human infection but are necessary for the continuation of the life cycle in the mosquito. If the male and female cells are taken up by the mosquito in a blood meal, fertilisation of the female cells takes place and further development occurs in the mosquito tissues. The fertilised cell penetrates the stomach wall of the mosquito where it enlarges and multiplies to form a cyst

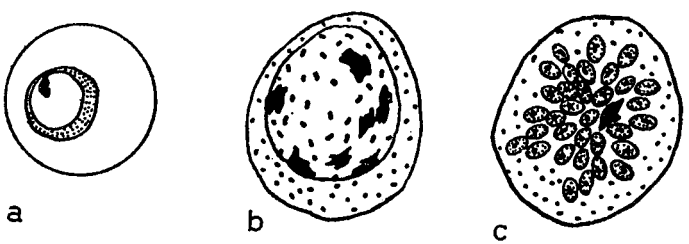

FIG. 18. Malaria parasites.

(*a*) Ring form within a red blood corpuscle (trophozoite), (*b*) A later stage within the red cell (schizont), (*c*) Division of the schizont to produce many merozoites which will now burst out of the cell.

containing numerous small structures—*sporozoites*. The sporozoites leave the cyst in the stomach wall and migrate to the mosquito's salivary glands. If the mosquito bites man at this stage the sporozoites are injected into the human tissues and the cycle is completed.

The diagnosis of malaria is confirmed by finding the parasite in stained films of blood. The species may also be determined by this means. Because the number of parasites may be small it is usual to examine a thick film of blood prepared by spreading several drops of blood over an area of a microscope slide about $\frac{1}{2}$ in. in diameter. This is allowed to dry and then examined by a special method

using Field's stain. Figure 18 shows the appearance of some stages of the malaria parasite whilst in the human red cell.

Treatment of malaria is now very satisfactory using modern drugs such as chloroquin. Control and prevention of malaria are important public health duties in malarious areas of the world. The chain of infection may be attacked at several points. Adult mosquitos are destroyed by the use of insecticides, and the larval stages of the mosquito are killed by treating the water in which they live with oil. In addition, wherever possible the mosquitos are denied the water they require for breeding by drainage schemes. Mosquitos are prevented from biting man by the use of fine mesh screens at doors and windows and by the use of mosquito netting over beds. The drug paludrine if taken daily will prevent the development of the malaria parasite in man even in an area in which malaria-infected mosquitos abound. By the use of such methods some areas of the world in which malaria was common are now completely free of the disease.

AMOEBIC DYSENTERY is an infection of the large intestine with the protozoal parasite *Entamoeba histolytica.* The disease is common in tropical and subtropical countries, but may be found almost anywhere in the world. The parasite does not require a secondary host, and infection is transmitted by food and water contaminated with the faeces of sufferers or carriers. Particularly important are salads, which in some countries are grown in soil fertilized with human faeces. Cooked foods are safe. The parasite lives in the mucous membrane of the large intestine in which it produces ulceration. The symptoms are chronic intermittent diarrhoea, often with some abdominal pain. Occasionally the parasite spreads from the large intestine to produce abscesses elsewhere in the body. The most common site is in the liver, but other sites are sometimes involved. Diagnosis of amoebic dysentery is confirmed by identifying the parasite in the faeces. This may prove difficult

particularly in the very chronic case. The parasite may be present in the faeces as the active *vegetative form* or as a *cyst.* The appearance of these forms is illustrated diagrammatically in Fig. 19. The typical appearances of the vegetative forms of *E. histolytica* disappear when the temperature of the faeces falls after passing. For this reason the specimen should be examined in the laboratory within minutes of being passed. As there are other species of amoeba which may be found in the faeces, and which appear to cause no harm, considerable

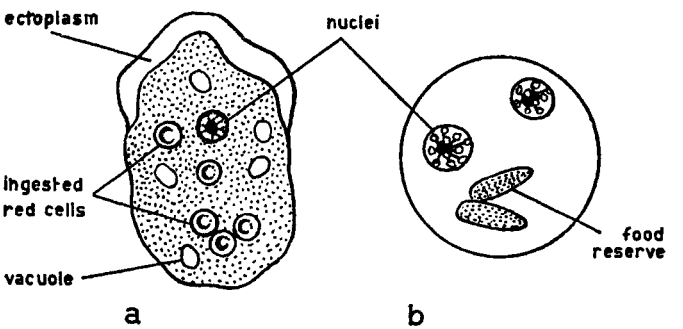

FIG. 19. *Entamoeba histolytica.*
(*a*) Vegetative stage, (*b*) Cyst stage.

skill is required in identifying *E. histolytica.* The tetracyclines and emitine bismuth iodide are used in the treatment of amoebic dysentery.

The third protozoan parasite to be considered is *Trichomonas vaginalis.* This produces an infection of the vagina which results in an offensive vaginal discharge. The disease is fairly common and in some cases, though not necessarily all, is transmitted by sexual contact. The same organism may be isolated from the urethra of the male, where it produces either no symptoms at all or a mild urethritis. Diagnosis of *T. vaginalis* infection is made by finding the typical parasite in the discharge. It is a large protozoan which moves by means of flagella. The parasite is illustrated

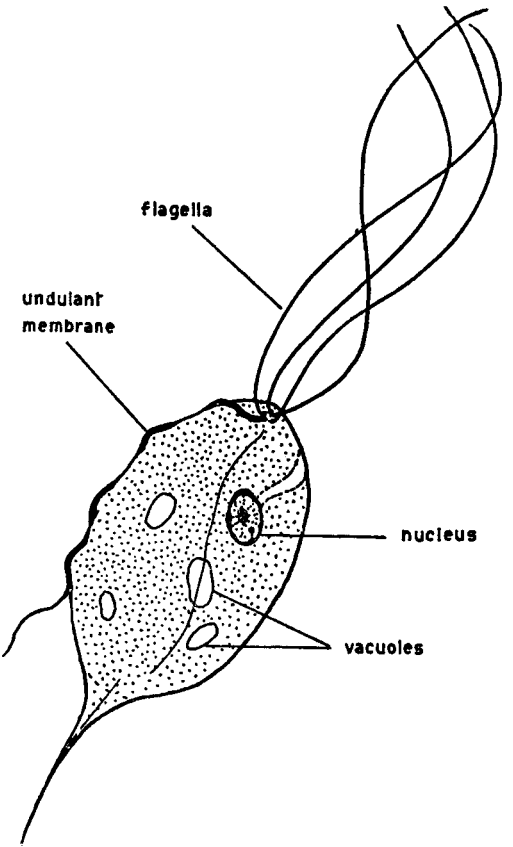

FIG. 20. *Trichomonas vaginalis.*

in Fig. 20. Culture methods are available to detect the parasite when so few are present that visual detection is difficult. This method is of value in isolating the parasite from the male urethra. Treatment has been improved recently by the introduction of a substance—metronidazole, which destroys the parasite when administered orally.

PARASITIC WORMS

There are very many different species of "worm" which may parasitise man. They may be found in the gastro-intestinal tract, in the urinary tract, in the lymphatics, in the subcutaneous tissues and in the liver. Only four common species will be considered, all of which are found in this country. These are the tape worms *Taenia* and *Echinococcus*, the round worm *Ascaris* and the thread worm *Enterobius*.

Taenia is a genus of tape worms which has two species able to infect man. These are *T. solium* and *T. saginata*. They are very similar in appearance, but may be differentiated on detailed examination. The worms have a head, which in the case of *T. solium* has small hooks, and in both worms suckers, a neck, and below this a series of *proglottids* (see Fig. 21). Each proglottid is a reproductive unit in itself. The proglottids are formed continuously at the neck of the worm and are pushed towards the rear end by the development of more new ones. The proglottids in the middle of the worm are larger and sexually mature. They contain both male and female sex apparatus. Fertilisation of the female cells takes place, and the proglottid becomes filled with fertilized ova. At the rear end of the worm the proglottids are largest, and consist almost entirely of a uterus filled with ova. The whole worm will consist of several hundred proglottids often resulting in a total length of several feet. The rearmost proglottids are shed in the faeces.

Both *T. saginata* and *T. solium* live in the human intestine where quite often they remain undetected. Symptoms which may be produced if the number of worms is large are anaemia and loss of weight. The mature proglottids and free ova are shed in the faeces, and the patient's complaint is more likely to be the finding of a proglottid, than actual illness. Diagnosis is confirmed by identifying a proglottid, or by finding ova of Taenia on microscopic examination of the faeces. The second stage of the life history takes place in either the pig (*T. solium*) or in cattle (*T. saginata*). If fertile

ova are eaten by these animals, they hatch and larvae emerge which penetrate the wall of the intestine and migrate by way of the blood and the lymph to the muscles, where they encyst. The cysts remain in the muscle until the meat is eaten in an uncooked or partially cooked state when

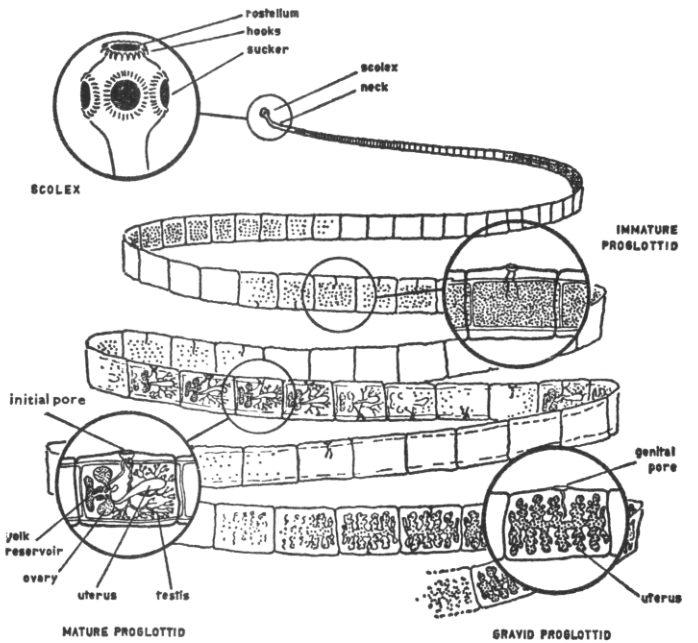

FIG. 21. The tape worm *Taenia solium*.
The inset figures show the detailed structure of the parasite.

they develop into the adult worm and attach themselves by means of the hooks and/or suckers to the intestinal wall. The encysted stage of *T. solium*, which normally is found in pig muscle, may occasionally occur in man. This is brought about by the ingestion of fertile eggs by man. The stages of the life cycle which normally takes place in the

pig now occur in man. The disease is known as *cysticercosis.* Cysts may be found in many organs, but are most serious when present in the brain or the eye.

Treatment of tape worm infection is directed towards damaging the worm so that it may be passed in the faeces. Mepacrine, a drug originally used in the treatment of malaria, usually gives satisfactory results. It is most important to ensure that the head is passed otherwise a cure cannot be guaranteed. All the faeces passed should be carefully examined for the presence of the head by carefully washing them through a fine mesh sieve.

Echinococcus granulosus is the dog tape worm and although the natural secondary host is the sheep, man may sometimes act as accidental secondary host. The ova are shed from the mature tape worm into the intestine of the dog and pass out with the faeces. If taken in by mouth either by man or the sheep, the fertilised ovum develops into a cystic stage known as a bladder worm. In man this is usually known as a *hydatid cyst* and occurs most commonly in the liver, but also sometimes in the lung. Dogs become infected by eating infected sheep tissues. The infection occurs particularly in sheep-farming communities where there is an intimate association of man, the dog, and sheep. Skin tests (Casoni test) and tests for antibodies are used to confirm the diagnosis of hydatid cyst. No drugs have an effect on hydatid disease, and the treatment is surgical.

Ascaris is a large round worm which usually measures approximately 6 in. long by $\frac{1}{4}$ in. in diameter. It is pointed at both ends, and is yellowish-grey in colour. Males and females may be recognised by detailed examination; the female being larger than the male. *Ascaris* infections are common throughout the world, particularly in children. Symptoms are not common, but may include anaemia. The commonest presentation is the passage of the adult worm in the faeces, or the vomiting of a worm. The adult worm lives in the small intestine, on occasions in large numbers. Mating takes place, and large numbers of ova are shed into

the intestinal contents which are easily seen on microscopic examination of the faeces. There is no secondary host in the life history of *Ascaris*. The ova, if shed on to moist warm earth, pass through a stage of maturation which lasts about a month. The ova are now infective to man if eaten. Transference to man is brought about by soil contamination of vegetables, and in children by dirty fingers. After ingestion, a larva emerges from the ovum, passes through the intestinal wall, invades a blood vessel and so reaches the liver. It next migrates to the lungs, enters a bronchus and passes by way of the trachea into the oesophagus and thence into the intestine where it develops into the adult stage. During the passage of the larvae through the lungs there may be transient cough, sometimes with blood-stained sputum. There are several substances available for the treatment of *Ascaris* infections. A very satisfactory drug is piperazine which is taken by mouth as a syrup.

Enterobius is a small round worm measuring less than 1 in. in length. Its common name is the THREAD WORM or pin worm. Infection with this worm is very common especially in children. The worm is found attached to the mucosa of the intestine where mating takes place. The fertilised female worm now migrates to the rectum and anal canal and deposits the ova on the peri-anal skin. This causes intense itching, especially at night, which is the predominant symptom of thread worm infection. The ova when deposited contain a coiled larva, and unlike *Ascaris* require only a short time before they become infective. Commonly the ova are transferred to the person's fingers during scratching, and from thence to the mouth. Thus there is a tendency for the infection to be perpetuated once established. There is no complex migration of the larva as in some other round worm life histories, and the *Enterobius* larva merely becomes adult on the way down the small intestine and attaches to the mucosa. It is unusual to find the ova in the faeces, but they may be seen in scrapings from the peri-anal skin. A useful method is to apply a strip

of Sellotape to the peri-anal skin, sticky side innermost. When peeled off and examined microscopically the ova are usually easy to see.

If self re-infection can be stopped the worms die within a few months, and the infection is thus cured. It is unfortunately almost impossible to prevent a child from scratching, especially at night. Methods which are adopted include the use of gloves and one-piece night clothing. The use of ammoniated mercury ointment around the anus is also valuable. Piperazine is a valuable specific form of treatment.

GLOSSARY

Abscess	A localised collection of pus within the body tissues.
Acid-fast bacillus	A member of the genus *Mycobacteria* which, when once stained, will resist decolorisation with acid.
Agglutination	The sticking together of particles (bacteria, etc.) by specific antibody which reacts with antigen present on the surface of the particles.
Alpha haemolysis	The green discoloration of the medium produced by some bacteria when grown on blood agar (*see* beta haemolysis).
Anaerobe	A micro-organism which will grow in the absence of oxygen.
Active immunity	Specific resistance to infection induced by previous contact with the infective agent or its products.
Antibiotic	A substance produced by a bacterium or a fungus which has a destructive activity against other micro-organisms.
Antibody	A type of protein, found in the blood, which will combine specifically with the antigen which induced its formation.
Antigen	A substance, most commonly either a protein or a polysaccharide, which will induce antibody formation in an animal if suitably presented (usually injected).
Anti-toxic immunity	Immunity to infection which depends on the presence of circulating antibody (anti-toxin) which can neutralize the toxin of the infecting agent.
Anti-toxin	An antibody which can specifically neutralise a particular toxin.

Acquired immunity	Specific immunity to infection which may be acquired during life, either naturally or artificially (*see* innate immunity).
Arthropoda	The large group of animals characterised by having a hard outer skeleton (exoskeleton) and jointed limbs. The group includes crabs, lobsters, insects, spiders, etc., and is of interest to bacteriologists because some members of the group transmit human disease.
Attenuated strain	A strain of micro-organism which has diminished virulence as a result of various laboratory procedures.
Autoclave	A device in which objects are sterilised by steam under pressure.
Bacillus	A general term for a rod-shaped bacterium. Also the name of a genus of aerobic spore-bearing rod-shaped bacteria, e.g. *Bacillus anthracis*, the causative agent of anthrax.
Bacteriophage (*phage*)	A special type of virus which is able to infect and destroy bacteria. Phages are very host-specific and will often only attack certain strains of a particular bacterial species. Because of this phages are used to type bacteria.
Beta haemolysis	The complete clearing of the red cells in a blood-agar plate around a colony of certain bacteria, notably some types of *Streptococcus* (*see* alpha haemolysis).
Binary fission	Multiplication of micro-organisms by division to form two daughter cells.
Broth	Simple liquid medium used to grow bacteria in the laboratory.
Capsule	The outer mucoid layer of some bacteria. The capsule is outside the cell wall.

Carrier	A person, who, though not suffering obviously from a particular disease, continues to harbour and to excrete the causative organisms which he may pass on to others.
Caseation	The soft cheesy material which is found in tissues destroyed by tuberculous inflammation.
Cellulitis	A diffuse inflammation of a tissue in which the inflammatory exudate does not usually localise to form pus, but which is spread evenly in the tissue spaces.
Cell wall	The firm outer layer of a bacterial cell which gives the organism its shape. (N.B. if the organism possesses a capsule this will be outside the cell wall.)
Chemotherapeutic agent	A synthetic substance which has a destructive action against micro-organisms, and which is used to treat infection.
Coccus	A spherical bacterial cell.
Colony	A visible group of bacterial cells growing together on a solid bacteriological medium. They are usually assumed to have developed from a single cell by multiplication.
Conjugation	A para-sexual method of exchange of genetic material in bacteria.
Consolidation	The firmness found in the lung in pneumonia due to the air spaces being filled with inflammatory exudate.
Cystitis	Inflammation of the bladder.
Dark ground microscopy	A method of microscopy which allows unstained micro-organisms to be seen.
Dry heat sterilisation	A method of sterilisation by heating in an oven, usually to a temperature of 160°C for 1 hour.

Ectoparasite	A parasite which lives on the surface of its host, e.g. a flea.
Encephalitis	Inflammation of the brain tissue.
Encephalomyelitis	Inflammation of the brain and spinal cord.
Endoparasite	A parasite which lives inside its host, e.g. malaria parasite.
Erythrogenic toxin	A toxin produced by *Streptococcus pyogenes* which is responsible for the skin rash of scarlet fever.
Erysipelas	A spreading inflammation of the skin caused by *Streptococcus pyogenes.*
Facultative anaerobe	A micro-organism which can grow under both anaerobic and aerobic conditions.
Fermentation	The incomplete splitting of sugars by micro-organisms to provide energy for their growth and which yields alcohols, acids and gases. Oxygen is not necessary for the reaction.
Flagellum	A whip-like structure which projects from the cell wall of certain bacteria. The bacterium is able to move by waving the flagella (plural).
Gamma-globulin	The portion of serum proteins which contains the antibody activity. Human pooled gamma-globulin is used to produce passive immunity to some diseases.
Gas gangrene	An infection, usually of muscle, which is characterised by death of tissue and the production of a large amount of gas which distends the infected part. The causative organisms are members of the genus *Clostridium.*
Genus	A group of animals or plants (or bacteria) which, though not identical, have many characters in common.

Gram stain — A method of bacteriological staining which divides bacteria into Gram-positive and Gram-negative types. The Gram reaction depends on the nature of the bacterial cell wall.

Growth factor — A substance which needs to be present in small amounts in order to grow certain species of bacteria in artificial media. May be considered as bacterial vitamins.

Heaf test — A skin test for the detection of past or present tuberculous infection. A Heaf gun is used to inject tuberculin into the skin.

Hypersensitivity — A state in which a person or an animal responds in an unexpectedly vigorous and damaging way to a substance which would not be expected to cause such a reaction.

Innate immunity — The resistance to infection which is inborn in the animal and is not acquired either naturally or artificially.

Kahn test — A serological test used in the diagnosis of syphilis.

Lymphadenitis — Inflammation of a lymph node.

Lymphocyte — A small cell found in the blood and in lymphoid tissue (lymph nodes, the spleen, etc.); found also in chronic inflammation.

Macrophage — A large cell which has the ability to ingest (phagocytose) bacteria and other particles; found in chronic inflammation.

Mantoux test — A test for the detection of past or present tuberculous infection by the injection of tuberculin into the skin using a very fine needle and syringe (*see* Heaf test).

Medium	The mixture of substances in or on which bacteria are cultivated in the laboratory.
Meninges	The membranes which surround the brain and spinal cord.
Meningitis	Inflammation of the meninges.
Microaerophilic	Bacteria which grow best in the presence of a low concentration of oxygen, i.e. less than that found in air.
Micron	A unit of measurement of length; equals 1/1,000th of a millimetre.
Moist heat sterilisation	Sterilisation in the presence of water, or steam. Boiling, steaming, and the use of pressurised steam in an autoclave are examples of this type of sterilisation.
Motile	Able to move under its own power.
Mutation	The spontaneous, random change which sometimes occurs in the genetic constitution of an organism. The change, having taken place, may be inherited by the progeny.
Myelitis	Inflammation of the spinal cord.
Native immunity	Resistance to infection which is not acquired during life, but is inherent in that species of animal.
Negri body	Small granules found in the brain of animals suffering from rabies. They are detected by examination of stained sections or smears of brain tissue.
Non-motile	Unable to move by its own power.
Normal flora	The micro-organisms which are found on the skin, in the respiratory tract, in the intestines, etc., of the normal healthy animal (including man).
Parasite	An animal (or plant or micro-organism) which depends on some other living animal (or plant) to

provide some or all the necessities for its life processes.

Passive immunity Immunity which does not depend on the active participation of the animal so immune. The transfer of antibody from mother to foetus with the result that the newborn is immune to some diseases to which its mother is immune is an example of passive immunity.

Pathogenic Disease-producing.

Peritonitis Inflammation of the membrane lining the abdominal cavity and covering the viscera.

Petri dish A shallow dish with a lid into which solid bacteriological media is placed for the cultivation of bacteria.

Phagocyte A cell which can ingest particles including bacteria. Macrophages and polymorphonuclear leucoytes are examples of phagocytes.

Phagocytosis The process of ingestion of particles by phagocytes.

Pleurisy Inflammation of the pleura (the membranes which line the thorax, and which cover the lungs).

Polymorph Abbreviation in common use for polymorphonuclear leucocyte. A cell found in the blood which is a phagocyte and is very important as a first-line defence against bacterial invasion.

Primary chancre The first stage of syphilis; a painless ulcer with thickened edges.

Primary complex The tissue changes of the first stage of tuberculous infection in a person who has never experienced the disease before. The complex includes the area of primary inflammation together with the inflamed lymph vessels and local lymph nodes.

Prophylaxis	Prevention; usually used as in prophylaxis of disease—prevention of disease.
Protozoa	Single-celled animals. Does not include bacteria and viruses which are nearer to the plant than the animal kingdom.
Purulent exudate	The products of acute inflammation. The exudate is made up of blood proteins and inflammatory cells.
Pyaemia	Literally—"pus in the blood"; the presence of aggregates of bacteria and inflammatory cells in the blood.
Pyelitis	Inflammation of the pelvis of the kidney.
Pyelonephritis	Inflammation of the pelvis of the kidney with spread to the kidney substance.
Pyogenic	Literally—"pus producing"; usually applied to an infection in which pus is produced.
Respiration	The process whereby complex chemical substances are broken down to simpler ones with the liberation of energy which may be used by the organism. The breakdown may or may not require the presence of oxygen.
Saprophyte	A micro-organism which is able to live without parasitising an animal or a plant. It is not directly dependent on some other life form for the provision of the necessities of life.
Sensitivity test	A laboratory test to determine to which antibiotics an organism is sensitive, i.e. which antibiotics will either kill it or inhibit its growth.
Septicaemia	The result of failure of the body defences to contain a bacterial invasion with the result that bacteria and their products (including toxins)

	are distributed about the body by the blood stream.
Species	A group of micro-organisms (or plants, or animals) which have very many characters in common; they are identical or near identical. There may be minor variations in some characters which are known as intra-species variation or strain differences.
Species immunity	Resistance to infection by a particular micro-organism which is an inherited character of a species of animal.
Spirillum	A spiral shaped organism with a rigid cell wall which is motile by means of flagella.
Spirochaete	Slender spiral organisms which are flexible, and which are motile without possessing flagella.
Spore	A structure produced by some species of bacteria which is very resistant to adverse conditions, e.g. heating or drying, which would kill the average bacterium. The spore is able to survive the adverse conditions and to germinate once conditions are favourable and so re-establish a bacterial population.
Stain	A dye used in bacteriology to colour micro-organisms and so make them more easily visible when examined microscopically.
Sterilisation	A process whereby the living micro-organisms present on an object or in a liquid are destroyed or removed.
Sub-clinical infection	An infection with a pathogenic micro-organism which fails to produce the expected symptoms and so is not normally detected by the sufferer.

Synthesise	To make; to build up complex substances from simpler ones.
Toxaemia	The presence of toxins in the circulation, producing general symptoms and, in the case of some toxins, producing damage to certain target tissues.
Toxin	A substance produced by a micro-organism which has a damaging action on the tissues of a susceptible animal.
Toxoid	A toxin which has been treated to render it no longer toxic, but still able to induce anti-toxin formation if injected into an animal.
Vaccine	A preparation of living or dead micro-organisms or of toxoids which when injected or in some other way presented to an animal or to man result in specific antibody formation and some measure of resistance to the appropriate infection develops.
Vibrio	A bacterium shaped as a curved rod, rather like a comma.
Virulence	An expression of the efficiency of a pathogenic micro-organism in causing disease. Virulence is very difficult to measure, but an estimate may be obtained by determining the minimum number of organisms which will cause the death of an animal into which they are injected.
Virus	A minute, microscopically invisible parasite which can only multiply within the substance of the body cells of its host.
Wasserman reaction	A serological test used in the diagnosis of syphilis.

Weil-Felix reaction	A serological test used in the diagnosis of some Rickettsial diseases, notably in typhus and scrub typhus.
Ziehl-Neelsen stain	A stain used to demonstrate acid-fast bacteria such as *Mycobacterium tuberculosis.*

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