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Neonatology

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Contents

PART TWO. NEONATAL CONDITIONS AND DISEASES

Preface

Neonatology is intended to be a practical bedside reference – not a comprehensive textbook – for problems likely to be encountered in the Newborn Nursery or Newborn Intensive Care Unit by residents, neonatal nurse practitioners, Neonatal-Perinatal Medicine Fellows, family physicians, pediatricians, and neonatologists. In addition to covering neonatal conditions, supportive care of the newborn, and neonatal procedures, sections on maternal conditions that have implications for the newborn, as well as a section on the differential diagnosis of presenting signs in the newborn are included. Material is presented in outline format as bullets with short statements. Information is provided under headings that are common to all the topics in that section to facilitate navigating among the information presented under each topic. For example, information in the sections on conditions is presented under the headings History & Physical, Tests, Differential Diagnosis, Management, Specific Therapy, Follow-Up, and Complications and Prognosis, while that in procedures is presented under the headings Indications, Contraindications, Special Considerations, and Complications.

We hope you find our book useful in your day-to-day encounters with sick newborn infants and their families.

Richard A. Polin, MD, and John M. Lorenz, MD

PART ONE

Maternal Conditions and Diseases

CIGARETTE SMOKING, MATERNAL

J.M. LORENZ, MD

HISTORY & PHYSICAL

Neonatal and fetal effects

- Spontaneous abortion
- Premature labor
- IUGR (avg wt reduction of 200 g per pack per day)
- Placental abruption
- 2-fold increase in cleft lip/palate

TESTS

- Nonspecific
  - ➢ As indicated for prematurity, IUGR
- Specific
  - ➢ Exposure can be quantitated by serum cotinine concentration; not clinically indicated

DIFFERENTIAL DIAGNOSIS

N/A

MANAGEMENT

- Supportive for prematurity, IUGR (see **INTRAUTERINE GROWTH RETARDATION**)
- Avoid passive smoking exposure postnatally.

SPECIFIC THERAPY

- None

FOLLOW-UP

- Usual well child

COMPLICATIONS AND PROGNOSIS

- Complications
  - ➢ Related to prematurity, IUGR
- Prognosis
  - ➢ 2-fold increased risk of SIDS
  - ➢ Increased prevalence of asthma w/ passive smoke exposure

COCAINE ABUSE, MATERNAL

J.M. LORENZ, MD
REVISED BY TOVE S. ROSEN, MD

EFFECTS OF COCAINE

- Vasoconstriction
- Decreased cholinesterase activity
- Increased nor-epi, serotonin & dopamine levels

HISTORY & PHYSICAL

- Prevalence: 1–15% pregnant women
- Maternal risk factors
  - H/o of prior drug abuse
  - Tobacco, ethanol, other illicit substance use
  - <3 prenatal care visits
  - Low socioeconomic status
  - Greater number of pregnancies & abortions
  - Poor nutrition
  - H/o STD; HIV
  - H/o prostitution
  - H/o dysfunctional family life
  - H/o domestic abuse
  - H/o psychiatric illness
  - Unemployment
  - H/o freq relocation, homelessness, living in shelters, encounters w/law enforcement
- Maternal hx
  - Sensitivity of ***routine*** prenatal interview for h/o substance abuse is as low as 25%.
  - ***Structured*** interviews (impractical for clinical use), ***repeated*** throughout pregnancy, for h/o cocaine use detect ~65% of cases.

Fetal/Neonatal Effects

- Effects related to dose, time, length of exposure
- Tobacco, alcohol, other illicit drug use & poor prenatal care contribute to effects
- Spontaneous abortion (25–40%)
- Stillbirth (5–10× increase)
- Premature rupture of membranes (2–5× increase)

- Chorioamnionitis
- Placental abruption
- Pre-eclampsia/eclampsia
- Fetal distress, asphyxia
- Meconium-stained amniotic fluid (2× increase)
- Premature birth (20–25%); on avg, assoc w/ 2-wk decrease in GA)
- IUGR (2–5× increase; mean decrease in wt 400 g, length 2 cm, OFC 2 cm)
- Other uncommon, anecdotal findings described:
  - ➢ Vascular disruption syndrome: limb reduction defects, intestinal atresias
  - ➢ CNS abnormalities: infarcts, cysts, hemorrhages due to perinatal cerebrovascular accidents
  - ➢ Congenital anomalies: GU (hypospadias), cardiac, ocular

Signs in newborn/fetus

- None distinctive
- Prematurity
- Low birth wt
- Microcephaly
- Low Apgar scores due to asphyxia
- Signs [due to pharmacologic effect on developing fetus, neonate (cocaine intoxication) or withdrawal?]
  - ➢ Irritability, tremors, hypertonia, posture & movement abnormalities (25%)
  - ➢ Lethargy
  - ➢ On NBAS: Poor state regulation, increased stress response & hyperactivity
- Tachycardia, hypertension
- Apnea, seizures, lethargy, hypotonia w/ cerebrovascular accident
- Bilious emesis, abd distention w/ intestinal atresia

TESTS

- Nonspecific
  - ➢ Screen for STDs, if not prev performed
  - ➢ Screen for other illicit drug use
  - ➢ As indicated for prematurity, IUGR, asphyxia
  - ➢ As necessary to r/o other etiologies for above signs: neonatal narcotic withdrawal, maternal amphetamine use, CNS hemorrhage, hyperthyroidism

- ➢ Head US/MRI
- ➢ Abnl EEG: CNS irritability w/ bursts of sharp waves, spikes for as long as 6–12 mo
- ➢ Abnl BAER: increased interwave intervals
- ➢ Abnl visual evoked potentials
- ➢ Renal US as indicated
- ➢ Echocardiogram, EKG as indicated
- ➢ GI contrast studies as indicated

■ Specific – Drug screening for cocaine metabolites – screening (lower specificity/higher sensitivity, e.g. immunoassay) AND different confirmatory testing (high sensitivity/higher specificity, e.g. gas chromatography/mass spectroscopy) recommended

- ➢ Maternal urine
  - Window of detection ~24–72 hr (depends on dose); high false-negative rate
  - **Skilled maternal interview & maternal urine toxicology increase detection over either alone.**
- ➢ Neonatal
  - Urine (specimen collected ASAP after birth) – detects only recent exposure; high false-negative rate
  - Meconium (collected in first 2 days of life)
    - Preferred screening method
    - Sensitivity ~90%, specificity 100% for maternal 2nd- or 3rd-trimester use compared to repeated, structured maternal interview; allowing sample to stand at room temp >12–24 hr decreases sensitivity

DIFFERENTIAL DIAGNOSIS

■ Other causes of IUGR (see **INTRAUTERINE GROWTH RESTRICTION**)
■ Other causes of irritability (e.g., neonatal narcotic withdrawal, CNS anomalies, hyperthyroidism)
■ Other causes of stroke (see **STROKE, ISCHEMIC, PERINATAL AND NEONATAL**)
■ Other causes of microcephaly
■ Other causes of hypertension (see **HYPERTENSION**)

MANAGEMENT

■ Careful interview re h/o tobacco, alcohol, other illicit drug use
■ Supportive care for complications assoc w/ prematurity, growth restriction, asphyxia, other complications

- Breastfeeding contraindicated unless cessation of use documented
- Social service consultation

SPECIFIC THERAPY

- None

FOLLOW-UP

- Neurodevelopmental

COMPLICATIONS AND PROGNOSIS

- Complications
  - Related to dose & length of exposure & other drug use
  - Boys seem to be more vulnerable.
  - Related to prematurity, IUGR, asphyxia
  - Related to cerebrovascular accident
  - Intestinal atresia
  - Transmission of associated STD, HIV to fetus/neonate
- Prognosis – related to interaction of the pharmacologic effects of the drug & the high-risk environment associated with the drug culture & poverty, including disorganization, dysfunctional families, poor maternal-infant interaction & nurturing
  - Catch-up growth within 1–2 mo
  - ? increased risk of SIDS
  - Hypertension as long as 18 mo
  - Hypertonicity as long as 18 mo
  - Persistence of primitive reflexes & tremors up to 24 mo
  - Persistence of abnormal arousal response; greater reactivity & state changes
  - Deficits in gross & fine motor development: balance, hand-eye coordination
  - Delayed speech & language development
  - No significant differences in mean scores of cognitive performance, but greater prevalence of scores <75
  - Behavioral problems: attention deficit, distractibility, aggressiveness (especially in boys), learning problems
  - Increased prevalence of child abuse/neglect

DIABETES MELLITUS (GESTATIONAL, TYPE I, AND TYPE II), MATERNAL

CHRISTIANA FARKOUH, MD

CLASSIFICATIONS

- American Diabetes Association
  - Type I: juvenile onset, insulin dependant
  - Type II: adult onset, insulin dependant
  - Type III: gestational diabetes mellitus (GDM)
- White's
  - A – any, w/o vascular disease, dx'd before pregnancy
  - B – onset ≥ age 20 yr or duration <10 yr, w/o vascular disease
  - C – onset age 10–19 yr or duration 10–19 yr, w/o vascular disease
  - D – onset < age 10 yr or duration ≥ 20 yr, w/o vascular disease
  - F – nephropathy
  - H – atherosclerotic heart disease
  - R – proliferative retinopathy or vitreous hemorrhage
  - T – after renal transplantation

HISTORY & PHYSICAL

- Maternal classification of DM & degree of glycemic control (more complications w/ poor control) associated w/ the degree of complications in IDMs:
- Fetal/Neonatal
  - Embryopathy/Congenital anomalies (4–8× risk w/overt DM prior to pregnancy)
    - CNS (16× risk) – e.g., anencephaly, holoprosencephaly, meningomyelocele
    - Congenital heart disease (18× risk) – ventricular septal defect & transposition of great arteries most common, but risk of double outlet left ventricle & truncus arteriosus specifically increased
    - Renal
    - Musculoskeletal
      - Caudal regression sequence
      - Limb anomalies
  - Abnormal growth
    - Macrosomia (birth wt >90th percentile for gestational age or birth weight >4 kg)

- 15–50% of diabetic pregnancies (vs. 10–14% of nl pregnancies)
- Function of 2nd- & 3rd-trimester glycemic control
- Contributes to the higher frequency of intrapartum/birth injury
- IUGR: w/ maternal disease >10 years & coexisting nephropathy or retinal or cardiac disease

➢ Diabetic cardiomyopathy
- Predominantly septal hypertrophy (30%)
- May obstruct LV output
- Typically resolves by age 1 yr

➢ 2× increase in perinatal mortality rate

■ Neonatal

➢ Metabolic disorders
- Hypoglycemia
  - Peak occurrence: 30–90 min of age
  - Usually asymptomatic, but may be protracted & difficult to resolve
  - Related to the maternal glycemic control 6–12 wk before birth & maternal serum glucose at birth
  - Tight glucose control has not decreased prevalence of hypoglycemia.
- Hypocalcemia
  - Up to 50% of IDMs have serum calcium level <7 mg/100 mL
  - Peak occurrence: 24 h
  - Usually asymptomatic
  - If correction indicated, correction of associated hypomagnesemia may be necessary to do so
- Hypomagnesemia – related to maternal hypomagnesemia & severity of maternal diabetes

➢ Cardio/respiratory disorders
- Congestive cardiomyopathy (w/o hypertrophy) due to hypoglycemia, hypocalcemia &/or polycythemia – rare
- Respiratory distress syndrome (RDS)
  - 5–6× increased risk of RDS, adjusted for confounders
  - Risk persists to 38.5 wk completed gestational age

➢ Hematologic disorders
- Polycythemia/hyperviscosity
- Hyperbilirubinemia – due primarily to prematurity & polycythemia

- ➢ Birth injury (see **BIRTH TRAUMA**) – increased risk of shoulder dystocia w/macrosomia; fractures of humerus or clavicle, Erb's palsy, and/or phrenic nerve palsy
- ➢ Perinatal asphyxia
- ➢ Other
  - Small left colon syndrome
  - Renal vein thrombosis – rare

TESTS

- Hct at 2–4 h; repeat at 12 h w/ borderline elevation
- Serum glucose level q1–2h for first 6 h by bedside method until WNL & stable – values <40–50 mg/dL should be confirmed in lab, esp if persistent
- Serum Ca 12 and/or 24; serum Mg w/hypocalcemia
- Serum bilirubin indicated by physical exam or nursery protocol
- ECG, echocardiogram as indicated

DIFFERENTIAL DIAGNOSIS

N/A

MANAGEMENT

- Prevention
  - ➢ Maternal screening
    - 1st trimester 50-g glucose challenge test for high-risk pregnancies [maternal age >25 yr; h/o previous infant >4 kg, unexplained fetal demise, gestational DM; strong immediate family hx type 2 or GDM; obesity (>90 kg)]
  - ➢ Universal screening
    - 50-g glucose challenge test at 26–28 weeks gestation
    - If >135 mg/dL, either 2-h or 3-h glucose challenge test
      - Tight maternal glycemic control periconceptionally (w/ established DM) & during pregnancy
- Neonatal Rx
  - ➢ See **HYPOXIC ISCHEMIC ENCEPHALOPATHY; BIRTH TRAUMA; HYPERGLYCEMIA; HYPOCALCEMIA; HYPOMAGNESEMIA; HYPERBILIRUBUNEMIA, UNCONJUGATED; HYPERTROPHIC CARDIOMYOPATHY; CONGESTIVE HEART FAILURE**
  - ➢ Polycythemia/hyperviscosity – partial exchange transfusion
  - ➢ As indicated for congenital anomalies

SPECIFIC THERAPY
None

FOLLOW-UP
- Neurodevelopmental as indicated for neonatal complications
- As indicated for congenital anomalies

COMPLICATIONS AND PROGNOSIS
- Increased risk of childhood obesity w/macrosomia
- Increased risk of glucose intolerance in later childhood & adulthood
- Other long-term problems depend on neonatal complications

ETHANOL USE/ABUSE, MATERNAL

See **FETAL ALCOHOL SPECTRUM DISORDERS** in the "Neonatal Conditions" section.

FACTORS FOR NEONATAL GBS INFECTION, MATERNAL: GBS COLONIZATION/PREVIOUS INFANT WITH INVASIVE GBS DISEASE/ROM >18 H/MATERNAL INTRAPARTUM TEMPERATURE ≥100.4°F

RAKESH SAHNI, MD

Early-onset group B streptococcal (GBS) disease (sepsis, pneumonia, meningitis)
- Onset: birth-7 d (mean 20 h)
- Incidence
  - 0.5 in 1,000 live births
  - 1–2% of infants of GBS-colonized mothers
- 15–40% mothers colonized
- 50% infants of GBS + mothers colonized
- Maternal risk factors
  - Colonization w/ GBS
  - High genital GBS inoculum
  - Urinary tract infection
  - Asymptomatic bacteriuria
  - Previous infant with invasive GBS disease
  - Age <20 y
  - Black race

- ➢ Hispanic ethnicity
- ➢ Malnutrition
- ➢ Low socioeconomic status
- ➢ Recently acquired STD

■ Intrapartum risk factors
- ➢ ROM >18 h
- ➢ Chorioamnionitis
  - Unexplained maternal fever ≥100.4°F
  - Uterine tenderness
  - Purulent, foul-smelling amniotic fluid
  - WBC shift to left
  - Sustained fetal tachycardia
  - Fetal distress: late decelerations
- ➢ Use of fetal scalp electrode
- ➢ Prolonged labor
- ➢ Multiple vaginal exams
- ➢ Instrumentation
- ➢ Difficult delivery
- ➢ Neonatal depression (5-min Apgar < 5)

■ Neonatal risk factors
- ➢ Prematurity
- ➢ Male gender
- ➢ Twin gestation
- ➢ Low birth wt

HISTORY & PHYSICAL

■ See **EARLY-ONSET NEONATAL SEPSIS/PNEUMONIA**

TESTS

Nonspecific

■ No single lab test diagnostic of infection
■ Individual lab tests have at best ~30–35% positive predictive value
■ Sepsis screens = combination of lab tests (WBC/differential, C-reactive protein)
- ➢ Positive sepsis screen defined as 2 or more abnl lab values obtained CONCURRENTLY
- ➢ If only single value is abnl, sepsis screen negative
- ➢ Negative sepsis screen excludes infection w/ 99% negative predictive value
- ➢ Abnl values
  - Absolute neutrophil (PMN) count ≤ 1,750/mm^3

- Immature/total PMN ratio ≥ 0.2
- Absolute band count ≥2,000/mm^3
- C-reactive protein ≥1 mg/dL

■ CXR – Indistinguishable from that with RDS (see RESPIRATORY DISTRESS SYNDROME)
■ Lumbar puncture: indications
➢ + blood culture
➢ Sepsis screen strongly suggestive of bacteremia
➢ Abnl neurol signs (seizures, persistent lethargy, etc.)

Specific
■ + culture result from normally sterile body fluid (e.g., blood, urine, CSF, abscess, etc.)

DIFFERENTIAL DIAGNOSIS
N/A

MANAGEMENT
■ Maternal intrapartum antimicrobial prophylaxis (IAP), either strategy:
➢ 1) Screen all pregnant women at 35–37 wk for anogenital GBS colonization, offer if
- GBS + (unless a planned cesarean delivery is performed in the absence of labor or membrane rupture)

or
- GBS unknown w/ risk factors present (<37 wk gestation, fever ≥100.4°F, ROM >18 h) OR

➢ 2) No screening cultures; offer IAP if
- GA < 37 wk
- Maternal fever ≥100.4°F or
- ROM > 18 h

➢ Regardless of strategy used
- Treat symptomatic or asymptomatic GBS bacteriuria during pregnancy at time of Dx; offer IAP
  - IAP: h/o previous infant w/ GBS disease (no screening culture required)
    - IV penicillin (5 million U initially, then 2.5 million U q4h until delivery) drug of choice for IAP Alternatives
  - Ampicillin IV, 2 g initially, then 1 g q4h until delivery
  - For penicillin-allergic women: cefazolin IV, 2 g initially, then 1 g q8h until delivery

■ Guidelines for mgt of infants born to mothers who receive IAP
➢ 1) For GBS

- Asymptomatic infants
  - If <35 wk or IAP duration <4 h before delivery: blood culture (optimal vol 0.5–1 mL), sepsis screen at birth & & 12 h, observation for ≥48 h
  - If ≥35 wk + IAP duration >4 h before delivery: observation for ≥48 h +/− sepsis screen at 12 h
- Symptomatic infants: blood culture, sepsis screen at birth & & 12 h, CXR, empiric therapy

➢ 2) For suspected chorioamnionitis
- Blood culture, sepsis screen at birth & 12 h, CXR, empiric therapy

➢ Empiric therapy: ampicillin, gentamicin
- Relative contraindications to use of gentamicin: suspected birth asphyxia w/ renal compromise, hypermagnesemia
- Ampicillin & cefotaxime an alternative empiric therapy

SPECIFIC THERAPY

■ See **SEPSIS/PNEUMONIA, EARLY-ONSET** and **MENINGITIS**

FOLLOW-UP

■ Guidelines for beginning empiric therapy in asymptomatic infants
  ➢ Positive sepsis screen: positive for 1st time at 12 hr, repeat blood culture before beginning Rx
  ➢ Signs c/w GBS disease develop
  ➢ + blood culture: perform LP before beginning Rx
■ Guidelines for discontinuation of empiric antibiotic therapy
  ➢ Asymptomatic infants w/ + sepsis screen, but negative blood culture: D/C after 48 h
  ➢ Cultures negative but infant symptomatic: consider treatment for 7–10, esp w/ + sepsis screen

COMPLICATIONS AND PROGNOSIS

■ Complications: See **SEPSIS/PNEUMONIA, EARLY-ONSET** and **MENINGITIS**
■ Prognosis
  ➢ Excellent w/o GBS disease
  ➢ 5–10% mortality w/GBS disease
  ➢ Major neurodevelopmental sequelae in 15% w/ meningitis
■ Implications for future pregnancies
  ➢ GBS colonization: none
  ➢ Infant w/ GBS disease: intrapartum antibiotic prophylaxis indicated for subsequent pregnancies

GRAVES DISEASE, MATERNAL (PRESENT OR PAST; +/− ANTITHYROID MEDICATION)

J.M. LORENZ, MD

May cause fetal &/or neonatal

- Thyrotoxicosis due to thyroid stimulating hormone receptor (TSHR)-stimulating antibody (Ab) – 1–12.5% risk of overt hyperthyroidism

OR

- Even less commonly, hypothyroidism, due to
  - ➢ Maternal Rx for Graves disease

  or
  - ➢ TSH receptor-blocking Ab [See **HASHIMOTO'S (AKA CHRONIC LYMPHOCYTIC OR AUTOIMMUNE) THYROIDITIS, MATERNAL**]

HISTORY & PHYSICAL

Neonatal/fetal effects

- Fetal/neonatal thyrotoxicosis (1–12.5%)
- Fetal/neonatal disease related to maternal level of TSHR-stimulating Ab in third trimester, NOT maternal thyroid status
  - ➢ May occur with Graves disease during pregnancy or past h/o Graves disease
  - ➢ If maternal TSHR Ab >5× upper limit of normal, then fetus/neonate at risk

Signs

- Fetal thyrotoxicosis (after 20–24 wk)
  - ➢ Fetal tachycardia (>160 bpm)
  - ➢ Growth retardation
  - ➢ Goiter
  - ➢ Advanced bone age
  - ➢ Craniosynostosis
  - ➢ Hydrops fetalis
  - ➢ Fetal death w/ fetal thyrotoxicosis (24% w/o maternal Rx, 5–7% w/ maternal Rx)
  - ➢ Premature delivery due to maternal thyrotoxicosis (53% w/o maternal, 4–11% w/ maternal Rx)
- Neonatal thyrotoxicosis

- ➢ See **HYPERTHYROIDISM, CONGENITAL** in the "Neonatal Conditions and Diseases" section.
- ➢ Onset may be delayed until age 5–10 days by transplacental transfer of maternal anti-thyroid Rx or coexisting TSHR-blocking Ab

TESTS

- Nonspecific: none
- Specific: neonatal T4, free T4, TSH
  - ➢ On cord blood (will reflect fetal thyroid status); also measure neonatal functional TSHR Ab (if available)
  - ➢ At 2–7 days if h/o fetal thyrotoxicosis, high maternal TSHR-stimulating Ab, or maternal antithyroid Rx at delivery
  - ➢ At 10–14 d

DIFFERENTIAL DIAGNOSIS

N/A

MANAGEMENT

- Ensure adequate caloric intake for growth.
- Cardiac signs
  - ➢ Tachycardia: propranolol
    - PO: 0.25 mg/kg q6h; increase prn to maximum of 3.5 mg/kg q6h
    - IV: 0.01 mg/kg over 10 min q6h; increase prn to maximum of 0.15 mg/kg q6h
    - Side effects: hypoglycemia, bradycardia, hypotension
  - ➢ Severe CHF
    - Digoxin
    - Prednisone 2 mg/kg/day
- Sedation prn
- Maternal PTU, carbimazole

SPECIFIC THERAPY

- Fetal
  - ➢ If mother euthyroid: maternal PTU & T4 (latter to maintain mother euthyroid)
  - ➢ If mother hyperthyroid: maternal PTU
- Neonatal
  - ➢ Rx depends on neonatal TFTs
    - Normal: no Rx

- Hyperthyroid: see **HYPERTHYROIDISM, CONGENITAL** in the "Neonatal Conditions and Diseases" section
- Hypothyroid: repeat TFTs; Rx w/ thyroxine if confirmed (see **HYPOTHYROIDISM, CONGENITAL** in the "Neonatal Conditions and Diseases" section)

➢ If Rx required: pediatric endocrinology consultation
➢ Rarely, surgical division of isthmus for tracheal obstruction due to large goiter
➢ Sedation prn

FOLLOW-UP

■ See **HYPERTHYROIDISM, CONGENITAL** or **HYPOTHYROIDISM, CONGENITAL** in the "Neonatal Conditions and Diseases" section.

COMPLICATIONS AND PROGNOSIS

■ Fetal hyperthyroidism
  ➢ Fetal effects (see "History and Physical")
  ➢ No evidence of intellectual or growth defects of neonates exposed to antithyroid medication in utero
■ Neonatal
  ➢ Spontaneous resolution usually by 8–20 wk, but as long as 48 wk
  ➢ Withdrawal syndrome (irritability, tachycardia, sweating, hypertension) w/ abrupt discontinuation of propranolol
  ➢ Possible craniosynostosis
■ Possible neurologic impairment, esp. hyperactivity; degree correlated w/ severity of intrauterine hyperthyroidism, presence of craniosynostosis

HASHIMOTO'S (AKA CHRONIC LYMPHOCYTIC OR AUTOIMMUNE) THYROIDITIS, MATERNAL

J.M. LORENZ, MD

■ Maternal autoimmune thyroiditis in early pregnancy associated w/ miscarriage
■ May cause neonatal &/or fetal
  ➢ Hypothyroidism (uncommonly) due to transplacental passage of TSH receptor-inhibiting antibody

  OR

  ➢ Even less commonly, thyrotoxicosis (see **GRAVES DISEASE, MATERNAL**)

HISTORY & PHYSICAL

Neonatal/fetal effects
- Neonatal hypothyroidism (5%)

Signs in neonate/fetus
- See **HYPOTHYROIDISM, CONGENITAL** in the "Neonatal Conditions and Diseases" section.

TESTS
- Nonspecific: none
- Specific
  - ➢ Normal or decreased free T4, increased TSH
  - ➢ TSH receptor blocking activity >3 SD above the mean

  Note: not clear whether maternal Rx is protective for fetal CNS effects

DIFFERENTIAL DIAGNOSIS
N/A

MANAGEMENT
- Pediatric endocrinology consultation if fetal/neonatal hypothyroidism suspected

SPECIFIC THERAPY
- Prevention
  - ➢ TSH screening before or early in pregnancy
  - ➢ Maternal levothyroxine Rx as appropriate
- Rx for neonatal hypothyroidism – levothyroxine (see **HYPOTHYROIDISM, CONGENITAL** in the "Neonatal Conditions and Diseases" section)

FOLLOW-UP
Free T4, TSH, TSH-receptor blocking activity (see **HYPOTHYROIDISM, CONGENITAL** in the "Neonatal Conditions and Diseases" section)

COMPLICATIONS AND PROGNOSIS
- Spontaneous resolution over months
- Cognitive impairment reported w/ maternal free T4 <10th percentile in the 1st trimester & circulating maternal anti-thyroid peroxidase antibodies in 3rd trimester

HEPATITIS A, ACUTE DISEASE IN MOTHER DURING PREGNANCY

J.M. LORENZ, MD

HISTORY & PHYSICAL

Neonatal and fetal effects

- Premature delivery
- Vertical transmission
  - ➢ Due to fecal-oral transmission (intrapartum or postpartum; however, 1 case of intrauterine transmission reported)
  - ➢ Risk probably highest w/ onset of maternal symptoms within 2 wk before or 1 wk after delivery
  - ➢ Transmission rate unknown, but rare
- Does not cause spontaneous abortion, congenital anomalies, or IUGR

Signs in newborn and fetus

- Mild constitutional signs 2–7 wk after exposure
- Clinical jaundice uncommon
- Other routes of transmission: postnatal from transfusion, other infants, or healthcare workers

TESTS

- Nonspecific
  - ➢ Abnl LFTs 2–7 wk after exposure
- Specific
  - ➢ + anti-HAV (anti-hepatitis A virus) IgG due to passive transplacental Ab transmission
  - ➢ Dx of neonatal infection requires either:
    - + anti-HAV IgM (almost always present at the first sign of clinical disease; persists for 4–6 mo)
    - Persistence of anti-HAV IgG >6 mo

DIFFERENTIAL DIAGNOSIS

N/A

MANAGEMENT

- Infection control
  - ➢ Nursery: none beyond universal precautions in 1st 2 wk of life, then contact isolation if infant remains hospitalized
  - ➢ Isolation from mother not indicated; careful handwashing

- ➢ No case of transmission via breast milk reported; breastfeeding not contraindicated

SPECIFIC THERAPY
- Prevention: 0.02 mL/kg serum immune globulin after birth w/ onset of maternal symptoms within 2 wk before or 1 wk after delivery
- Neonatal Rx: none

FOLLOW-UP
- Anti-HAV IgG >age 6 mo to confirm or exclude infection

COMPLICATIONS AND PROGNOSIS
- Fulminant hepatitis rare

HEPATITIS B, ACUTE MATERNAL HEPATITIS DURING SECOND TRIMESTER W/ NEGATIVE MATERNAL HEPATITIS B SURFACE ANTIGEN IN THIRD TRIMESTER

J.M. LORENZ, MD

HISTORY & PHYSICAL
- Does not cause spontaneous abortions, congenital anomalies, or IUGR
- Transplacental transmission (6%)
  - ➢ Little information re: outcome
- No PE signs in fetus or newborn

TESTS
- Neonatal HBsAg (hepatitis B surface ANTIGEN) & HBsAb (hepatitis B surface ANTIBODY) at birth
- Note: Neonatal HBsAb will be positive due to passive transplacental transmission.

DIFFERENTIAL DIAGNOSIS
N/A

MANAGEMENT
- Infection control
  - ➢ Nursery: universal precautions
  - ➢ Isolation from mother not indicated
  - ➢ Breastfeeding not contraindicated

SPECIFIC THERAPY
- If neonatal HbsAg +: evaluate & f/u for chronic liver disease
- If neonatal HBsAg negative: none; hepatitis B vaccine as for all newborns

FOLLOW-UP
- If neonatal HbsAg +: evaluate & f/u for chronic liver disease
- If neonatal HBsAg negative: complete course of hepatitis B immunization

COMPLICATIONS AND PROGNOSIS
- If neonatal HbsAg +: little information re: outcome of transplacental transmission
- If neonatal HBsAg negative: none

HEPATITIS B, ACUTE MATERNAL HEPATITIS IN THIRD TRIMESTER OR WITHIN 2 MONTHS OF DELIVERY OR MOTHER CHRONIC CARRIER (PERSISTENTLY HEPATITIS B SURFACE ANTIGEN POSITIVE)

J.M. LORENZ, MD

HISTORY & PHYSICAL

Neonatal and fetal effects
- Premature delivery
- In utero transmission in <2% of cases
- Intrapartum transmission
  - ➢ 75% if mother has acute hepatitis
  - ➢ 70–90% if mother HBeAg (hepatitis B e antigen) positive chronic carrier
  - ➢ 5–25% if mother HBeAg negative chronic carrier
  - ➢ Does not cause spontaneous abortions, congenital anomalies, or IUGR

Signs in neonate and fetus
- None

TESTS
- Nonspecific: none
- Specific

- ➢ HBsAg
  - Negative in neonatal period (may be transiently + after vaccination)
  - Becomes + within first few wk to several mo of life
- ➢ Dx of intrapartum infection requires either
  - HBsAg (hepatitis B surface ANTIGEN) positive within 1st 6 mo of life OR
  - Persistence of HBsAb (hepatitis B surface ANTIBODY) >6 mo

DIFFERENTIAL DIAGNOSIS

N/A

MANAGEMENT

- Infection control
  - ➢ Nursery: universal precautions
  - ➢ Isolation from mother not indicated
  - ➢ Breastfeeding not contraindicated

SPECIFIC THERAPY

- Prevention
  - ➢ Maternal: antiviral Rx during last mo of pregnancy not routinely recommended
  - ➢ Neonatal:
    - HBIG 0.5 mL (250 IU) IM ASAP & within 12 h of delivery
    - HB single antigen vaccine IM concomitant w/ HBIG, but at different site

    and
    - Birth wt

      ≥2 kg: complete vaccine series at recommended schedule (second dose at age 1–2 mo)

      <2 kg: complete vaccine series at recommended schedule (not counting dose at birth) with next dose at age 1–2 mo
- Neonatal Rx: none

FOLLOW-UP

- HBsAg & HBsAb at 9–18 mo of age, after completion of vaccine series
  - ➢ If HBsAb ≥ 10 mIU/mL: no further prophylaxis or f/u required
  - ➢ If HBsAb < 10 mIU/mL: reimmunize w/ 3 doses HB vaccine at 2-mo intervals, then retest
  - ➢ If HBsAg +: evaluate & f/u for chronic liver disease

COMPLICATIONS AND PROGNOSIS

- None w/ effective prophylaxis
- With intrapartum acquired HBV infection
  - ➢ Chronic infection w/ persistent or periodic increase in transaminases after age 6–12 wk & persistently positive HBsAg (90% of infected neonates)
  - ➢ Neonatal hepatitis syndrome at age 3–4 mo (uncommon); may be fulminant, progressing to cirrhosis or death
  - ➢ Primary liver cancer (40% of chronically infected neonates)
- Implications for future pregnancies: vertical transmission possible

HEPATITIS B, MATERNAL HEPATITIS B STATUS UNKNOWN

J.M. LORENZ, MD

HISTORY & PHYSICAL

Neonatal/fetal effects

- Possibility of intrapartum transmission cannot be excluded

Signs in newborn/fetus

- None

TESTS

HBsAb (hepatitis B surface antibody) may be + due to passive transplacental transmission of maternal Ab if mother HBsAb + (testing not indicated)

DIFFERENTIAL DIAGNOSIS

N/A

MANAGEMENT

- Infection control
  - ➢ Nursery: universal precautions
  - ➢ Isolation from mother not indicated
  - ➢ Breastfeeding not contraindicated

SPECIFIC THERAPY

- Prevention
  - ➢ Maternal: universal prenatal screening for HBsAg (hepatitis B surface antigen)
  - ➢ Neonatal
    - Birth wt ≥2 kg
      - Determine maternal HBsAg status
      - While awaiting results, HB vaccine IM within 12 h of birth
      - If maternal HBsAg +: HBIG 0.5 mL IM, preferably within 48 hr, but before age 1 wk
      - Complete vaccine series at recommended schedule (second dose at age 1–2 mo)
    - Birth weight <2 kg & preterm
      - Determine maternal HBsAg status
      - If maternal HBsAg + or cannot be obtained within 12 hr:
      - HB vaccine IM AND HBIG 0.5 mL IM (at different site) within 12 hr of birth
      - Complete vaccine series at recommended schedule (not counting dose at birth) with next dose at age 1–2 mo
- Neonatal Rx: none

FOLLOW-UP

- None if maternal HBsAg negative
- If maternal HBsAg +: HBsAg & HBsAb at 9–18 mo of age, after completion of vaccine series
  - ➢ If HBsAb ≥ 10 mIU/mL: no further prophylaxis or f/u required
  - ➢ If HBsAb < 10 mIU/mL: reimmunize w/ 3 doses HB vaccine at 2-mo intervals, then retest
  - ➢ If HBsAg +: evaluate & f/u for chronic liver disease

COMPLICATIONS AND PROGNOSIS

- None w/ effective prophylaxis
- With intrapartum acquired HBV infection
  - ➢ Chronic infection w/ persistent or periodic increase in transaminases after age 6–12 wk & persistently positive HBsAg (90% of infected neonates)
  - ➢ Neonatal hepatitis syndrome at age 3–4 mo (uncommon); may be fulminant, progressing to cirrhosis or death
  - ➢ Primary liver cancer (40% of chronically infected neonates)
- Implications for future pregnancies: vertical transmission possible

HEPATITIS B, MATERNAL HEPATITIS B SURFACE ANTIBODY (HBSAB) POSITIVE

J.M. LORENZ, MD

Mother immune – no risk of vertical transmission

HISTORY & PHYSICAL

Neonatal/fetal effects
- None

Signs in newborn/fetus
- None

TESTS

Neonatal HBsAb + due to passive transplacental transmission (testing not indicated)

DIFFERENTIAL DIAGNOSIS

N/A

MANAGEMENT

- Infection control
  - Nursery: universal precautions
  - Isolation from mother not indicated
  - Breastfeeding not contraindicated

SPECIFIC THERAPY

- None necessary
- Hepatitis B vaccine as recommended

FOLLOW-UP

None

COMPLICATIONS AND PROGNOSIS

None

HEPATITIS C, MATERNAL ANTI-HEPATITIS C VIRUS (HCV) POSITIVE IGG, BUT HCV-RNA NEGATIVE

J.M. LORENZ, MD

- Seroprevalence 1–2% in pregnant women in USA

HISTORY & PHYSICAL

Neonatal/fetal effects

- Very low risk of vertical transmission, even w/ concomitant HIV infection

Signs in newborn/fetus

- None

TESTS

- Positive anti-HCV IgG due to passive transplacental Ab transmission (testing not indicated)

DIFFERENTIAL DIAGNOSIS

N/A

MANAGEMENT

- None required

SPECIFIC THERAPY

- None required

FOLLOW-UP

- None required

COMPLICATIONS AND PROGNOSIS

- No complications or prognostic significance

HEPATITIS C, MATERNAL HCV-RNA POSITIVE, REGARDLESS OF ANTI-HCV IGG STATUS

J.M. LORENZ, MD

- Transmitted by blood exposure
- Risk factors:
  - HBV or HIV infection
  - IV drug use
  - Transfusion or transplantation before 1992
  - Repeated direct percutaneous exposure to blood products
  - Sexual partner w/ chronic HCV/HBV/HIV infection
  - Chronic dialysis
  - Body piercing
- Signs & symptoms indistinguishable from hepatitis A or B
- Asymptomatic to mild & insidious onset; jaundice in <20%

- Chronic hepatitis develops in 60–70% of infected adults.
- Positive anti-HCV IgG with positive HCV-RNA does NOT indicate recovery from infection or lack of contagiousness.

HISTORY & PHYSICAL

Neonatal/fetal effects

- Transplacental & intrapartum transmission
  - ➢ Transient: 15–20% of infants
    - Transiently positive (i.e., at ages <12 mo) HCV-RNA & anti-HCV IgG (ie, "spontaneous clearance")
    - Single positive HCV-RNA may represent false-positive result.
    - Single negative result is inconclusive.
  - ➢ Persistent: 3–7% of infants
    - Risk related to maternal viral load ($>10^6$ genomic equiv/mL has greater risk of vertical transmission)
    - Risk increased 4–5× w/ concomitant maternal HIV infection
    - Dx: persistently positive HCV-RNA or persistently positive anti-HCV IgG > age 18 mo
- Does not cause spontaneous abortions, congenital anomalies, or IUGR
- Other transmission: blood products (risk 1:1 million transfused units)

Signs in newborn/fetus

- None

TESTS

- Nonspecific: none
- Specific
  - ➢ Positive anti-HCV IgG due to passive transplacental transmission; proportion of infants ultimately NOT infected w/ positive anti-HCV IgG:
    - 94–98% at age 3 mo
    - 69–82% at age 6 mo
    - 32–47% at age 9 mo
    - 6–18% at age 12 mo
    - 0–4% at age 15 mo
    - 0–1% at age 18 mo
  - ➢ HCV-RNA may/may not be positive in newborn period.

DIFFERENTIAL DIAGNOSIS

N/A

MANAGEMENT

- Infection control
  - ➢ Nursery: contact isolation
  - ➢ Isolation from mother not indicated
  - ➢ Breastfeeding not contraindicated – emphasize handwashing (consider abstaining if nipple cracked or bleeding)

SPECIFIC THERAPY

- Prevention: cesarean section delivery, no consensus re: indication
- Neonatal Rx: generally not necessary in infancy

FOLLOW-UP

- Anti-HCV IgG & HCV-RNA at > age 18 mo:
  - ➢ Anti-HCV IgG & HCV-RNA negative indicate no infection.
  - ➢ HCV-RNA + confirms infection.
  - ➢ If anti-HCV IgG + but HCV-RNA negative, then repeat testing q 6 mo until both are negative or positive
- Transaminases if infant HCV-RNA +
- Overt symptoms unlikely

COMPLICATIONS AND PROGNOSIS

- Chronic infection in 80%
  - ➢ Asymptomatic chronic hepatitis in 60–80% w/ chronic infection
  - ➢ 20% will clear infection in childhood
- Chronic active cirrhosis (15–20%) & hepatocellular carcinoma (1–4% per yr w/ cirrhosis) in adulthood w/ chronic infection
- Implications for future pregnancies: h/o vertical transmission does not change risk of transmission in subsequent pregnancies

HEPATITIS D, MATERNAL

J.M. LORENZ, MD

HISTORY & PHYSICAL

- Risk factors:
  - ➢ Acute or chronic maternal hepatitis B infection is prerequisite.
  - ➢ Maternal IV drug use
  - ➢ Maternal immigration from endemic area (southern Italy, parts of eastern Europe, South America, Africa, Far East)

- Vertical transmission of hepatitis D virus (HDV) requires high level hepatitis B viral replication (i.e., + hepatitis B e antigen) in mother
- Does not cause spontaneous abortions, congenital anomalies, or IUGR
- Incidence: rare
- Consequences of HDV infection alone in infant are unknown.
- Neonatal immunoprophylaxis for hepatitis B is EFFECTIVE against HDV.

TESTS

- Anti-HDV IgG
  - ➢ May be + due to transplacental transmission of maternal antibody
  - ➢ Diagnostic of neonatal HDV infection only if persistently positive >6 mo
- For hepatitis B only [see **HEPATITIS B, ACUTE MATERNAL HEPATITIS IN THIRD TRIMESTER OR WITHIN 2 MO OF DELIVERY OR MOTHER CHRONIC CARRIER (PERSISTENTLY HEPATITIS B SURFACE ANTIGEN POSITIVE)**]

DIFFERENTIAL DIAGNOSIS

N/A

MANAGEMENT

- Infection control
  - ➢ Nursery: universal precautions
  - ➢ Isolation from mother not indicated
  - ➢ Breastfeeding not contraindicated

SPECIFIC THERAPY

- None for hepatitis D
- For prevention of hepatitis B [see **HEPATITIS B, ACUTE MATERNAL HEPATITIS IN THIRD TRIMESTER OR WITHIN 2 MO OF DELIVERY OR MOTHER CHRONIC CARRIER (PERSISTENTLY HEPATITIS B SURFACE ANTIGEN POSITIVE)**]

FOLLOW-UP

- For hepatitis B virus [see **HEPATITIS B, ACUTE MATERNAL HEPATITIS IN THIRD TRIMESTER OR WITHIN 2 MO OF DELIVERY OR MOTHER CHRONIC CARRIER (PERSISTENTLY HEPATITIS B SURFACE ANTIGEN POSITIVE)**]
- Anti-HDV IgG only if infected w/ hepatitis B virus

COMPLICATIONS AND PROGNOSIS

- As for hepatitis B [see **HEPATITIS B, ACUTE MATERNAL HEPATITIS IN THIRD TRIMESTER OR WITHIN 2 MO OF DELIVERY OR MOTHER CHRONIC CARRIER (PERSISTENTLY HEPATITIS B SURFACE ANTIGEN POSITIVE)**]
- In adults infected w/ hepatitis B & D, fulminant hepatitis is more likely than with perinatally acquired hepatitis B alone.

HEPATITIS E, ACUTE MATERNAL INFECTION DURING THIRD TRIMESTER OR IN PERINATAL PERIOD

J.M. LORENZ, MD

- Fecal-oral transmission from infected humans or animals
- Person-to-person transmission less efficient than for hepatitis A virus
- Uncommon in USA
- Maternal risk factors: immigration from or h/o travel to endemic areas
- More severe in pregnant women – 10% mortality due to fulminant hepatitis

HISTORY & PHYSICAL

Neonatal/fetal effects

- Intrauterine death or premature delivery w/ fulminant maternal hepatitis
- Vertical transmission:
  - ➢ Third-trimester maternal infection: transplacental (~50%?)
  - ➢ Perinatal maternal infection: intrapartum or postpartum fecal-oral transmission

Signs in newborn/fetus

- Transplacental:
  - ➢ Ranges from asymptomatic to IUGR to death due to hepatic necrosis
- Intrapartum/postpartum
  - ➢ None in newborn period
  - ➢ Clinical hepatitis by 6–8 wk

TESTS

- Performance of anti-HEV assays not well characterized; interpret results w/ caution

- Transplacental
  - ➢ Nonspecific: elevated transaminases
  - ➢ Specific
    - Positive anti-HEV (anti-hepatitis E virus) IgG due to passive transplacental transmission
    - Dx of transplacental infection requires either:
      - PCR + for HEV (available only in research labs) OR
      - Anti-HEV IgM
- Intrapartum/postpartum
  - ➢ Nonspecific: none in newborn period
  - ➢ Specific
    - Positive anti-HEV IgG due to passive transplacental transmission
    - Dx of neonatal infection requires either:
      - PCR + for HEV
      - Anti-HEV IgM

      or
      - Persistence of anti-HEV IgG >6 mo

DIFFERENTIAL DIAGNOSIS

N/A

MANAGEMENT

- Infection control
  - ➢ Nursery: contact isolation of newborn
  - ➢ Isolation from mother not indicated; emphasize careful handwashing
  - ➢ Breastfeeding not contraindicated

SPECIFIC THERAPY

- Prevention: none
- Neonatal Rx: none

FOLLOW-UP

If negative PCR for HEV & anti-HEV IgM, anti-HEV IgG > age 6 mo to confirm/exclude intrapartum, postpartum infection

COMPLICATIONS AND PROGNOSIS

- Transplacental
  - ➢ IUGR
  - ➢ Death due to hepatic necrosis
- Intrapartum/postpartum
  - ➢ None in newborn period

➢ Not implicated in chronic or fulminant hepatitis, but data limited

HEPATITIS E, MATERNAL ANTI-HEV IGG POSITIVE DUE TO REMOTE INFECTION

J.M. LORENZ, MD

Mother immune – no risk of transmission

HISTORY & PHYSICAL

Neonatal and fetal effects
- None

Signs in neonate and fetus
- None

TESTS
Neonate anti-HEV IgG + due to passive transplacental transmission (testing not indicated)

DIFFERENTIAL DIAGNOSIS
N/A

MANAGEMENT
None

SPECIFIC THERAPY
None necessary

FOLLOW-UP
None

COMPLICATIONS AND PROGNOSIS
None

HEPATITIS GBV-C/HGV, MATERNAL ANTI-GBV-C/HGV IGG POSITIVE

J.M. LORENZ, MD

HISTORY & PHYSICAL

Neonatal/fetal effects
- Mother immune – no risk of vertical transmission

Signs in newborn/fetus
- None

TESTS
Neonate GBV-C/HGV anti-E2 IgG + due to passive transplacental transmission (testing not indicated)

DIFFERENTIAL DIAGNOSIS
N/A

MANAGEMENT
- Infection control
  - ➢ Nursery: universal precautions
  - ➢ Isolation from mother not indicated
  - ➢ Breastfeeding not contraindicated

SPECIFIC THERAPY
- None necessary

FOLLOW-UP
None

COMPLICATIONS AND PROGNOSIS
None

HEPATITIS GBV-CHGV, MOTHER GBV-CHGV RNA POSITIVE

J.M. LORENZ, MD

- More common than hepatitis C virus (HCV) infection
- Maternal risk factors
  - ➢ IV drug use
  - ➢ Hepatitis C virus infection

HISTORY & PHYSICAL

Neonatal/fetal effects
- Vertical transmission: 45–80%
- Transmission related to high maternal GBV-C/HGV RNA titer, but not concomitant maternal HCV viremia or vertical transmission
- Other route of transmission: transfusion

Signs in newborn/fetus
- None

TESTS
- Nonspecific: none
- Specific: GBV-C/HGV RNA may be + in neonatal period, but may not be + until age 3–6 mo

DIFFERENTIAL DIAGNOSIS
N/A

MANAGEMENT
- Infection control
  - ➢ Nursery: none beyond universal precautions
  - ➢ Isolation from mother not indicated
  - ➢ Breastfeeding not contraindicated

SPECIFIC THERAPY
- Prevention: possibly cesarean section, but not recommended
- Neonatal Rx: none

FOLLOW-UP
- Retest for GBV-C/HGV RNA at 3 & 6 mo if initially negative
- GBV-C/HGV RNA, GBV-C/HGV anti-E2 IgG, & transaminases q1–2 yr if GBV-C/HGC RNA + initially or at 3 or 6 mo

COMPLICATIONS AND PROGNOSIS
- Persistent infection common (80–95%); seroconversion to GBV-C/HGV anti-E2 uncommon
- No clinical or biochemical signs of hepatitis reported in absence of co-infection w/ HCV or HIV
- Implications for future pregnancies: vertical transmission possible

HERPES SIMPLEX, MATERNAL GENITAL LESIONS, INTRAPARTUM

J.M. LORENZ, MD

HISTORY & PHYSICAL

Neonatal effects
- Neonatal herpes infection (see **HERPES SIMPLEX INFECTION, INTRAUTERINE/NEONATAL INFECTION**, in the "Neonatal Conditions and Diseases" section)
- Transmission rates w/ vaginal delivery

- ➢ 50% w/ 1st episode, PRIMARY genital herpes (1st infection w/ either HSV 1 or 2)
- ➢ 30% w/ 1st episode, NON-PRIMARY genital infection (1st infection w/ an HSV type after prior infection w/ alternate type)
- ➢ <2% w/ recurrent genital herpes

NOTE: ABSENCE OF CLINICAL HX DOES NOT RULE OUT 1ST EPISODE INFECTION

TESTS

- Nonspecific
  - ➢ W/o signs c/w neonatal infection or positive neonatal screening culture for herpes simplex (see "Specific Tests" below): none
  - ➢ W/ signs c/w neonatal infection or positive neonatal screening culture: see **HERPES SIMPLEX INFECTION, INTRAUTERINE/NEONATAL INFECTION**, in the "Neonatal Conditions and Diseases" section

DIFFERENTIAL DIAGNOSIS

N/A

MANAGEMENT

- Prevention: See **HERPES SIMPLEX INFECTION, INTRAUTERINE/NEONATAL INFECTION** in the "Neonatal Conditions and Diseases" section
- Infection control
  - ➢ Contact isolation in separate room
  - ➢ Isolation from mother not indicated

SPECIFIC THERAPY

- Prophylactic (w/o signs of neonatal infection or positive neonatal screening culture) acyclovir not indicated
- Presumptive Rx (w/ signs c/w neonatal herpes or w/ positive screening cx at 24–48 h (see **HERPES SIMPLEX INFECTION, INTRAUTERINE/NEONATAL INFECTION**, in the "Neonatal Conditions and Diseases" section)

FOLLOW-UP

- During incubation period
  - ➢ Vigilance for signs c/w neonatal infection; may present 2nd DOL to 4 wk
  - ➢ Consider weekly eye, nasopharyngeal, mouth, skin cultures × 4 wk

- Long-term: none in absence of disease; subclinical infection does not occur

COMPLICATIONS AND PROGNOSIS
- No complications or sequelae w/o disease
- Implication for subsequent pregnancies: risk of neonatal infection ~1:2,000

HERPES SIMPLEX, MATERNAL OROLABIAL HERPES LESION

J.M. LORENZ, MD

HISTORY & PHYSICAL
- Vertical transmission/neonatal infection (in 1st mo of life) possible (see **HERPES SIMPLEX, INTRAUTERINE AND NEONATAL INFECTION,** in the "Neonatal Conditions and Diseases" section)
- HSV type 1 as virulent for neonate as type 2, but rare
- Isolation of infant from mother not indicated if mother advised of risk
- Advise:
  - ➢ Scrupulous handwashing before handling infant
  - ➢ Strictly avoid hand contact w/ lesion when handling infant and direct contact of the infant w/ lesion (ie, kissing) until the lesion crusted
- Breastfeeding not contraindicated in the absence of breast lesions

TESTS
N/A

DIFFERENTIAL DIAGNOSIS
N/A

MANAGEMENT
N/A

SPECIFIC THERAPY
N/A

FOLLOW-UP
N/A

COMPLICATIONS AND PROGNOSIS
N/A

HERPES SIMPLEX, MATERNAL PRENATAL INFECTION

J.M. LORENZ, MD

HISTORY & PHYSICAL
- Transplacental transmission extremely rare (see **HERPES SIMPLEX, INTRAUTERINE AND NEONATAL INFECTION,** in the "Neonatal Conditions and Diseases" section)
- No assoc w/ spontaneous abortion or preterm delivery w/o transplacental transmission
- No isolation or eval of infant w/o signs compatible w/ transplacental transmission

TESTS
N/A

DIFFERENTIAL DIAGNOSIS
N/A

MANAGEMENT
N/A

SPECIFIC THERAPY
N/A

FOLLOW-UP
N/A

COMPLICATIONS AND PROGNOSIS
N/A

HERPES ZOSTER, MATERNAL, POSTNATAL ONSET

J.M. LORENZ, MD

See **VARICELLA (CHICKENPOX), POSTNATAL EXPOSURE**

HERPES ZOSTER, MATERNAL, PRENATAL

J.M. LORENZ, MD

No pregnancy or fetal effects

HUMAN IMMUNODEFICIENCY VIRUS (HIV) INFECTION, MATERNAL

J.M. LORENZ, MD

- Intrauterine (probably 3rd trimester, 25–40%) or intrapartum (60–75%) infection; also may be transmitted postpartum via breastfeeding infection
  - ➢ Risk factors for fetal/neonatal infection
    - Maternal p24 antigenemia
    - Maternal CD4 counts <400 cells/mm^3
    - High maternal HIV RNA level
    - Maternal IV drug abuse
    - Maternal hepatitis C co-infection
    - Symptomatic (CDC class IV) mother
    - Rupture of membranes >4 h
    - Birth wt <2,500 g
    - Prematurity
  - ➢ Transmission rates (in absence of breastfeeding)
    - 16–25% w/o prophylaxis; ~ doubled by breastfeeding
    - 10% w/ neonatal prophylaxis alone
    - 10% w/ intrapartum & neonatal
    - <2% w/ antepartum, intrapartum, & neonatal prophylaxis

HISTORY & PHYSICAL

Neonatal and fetal effects

- Spontaneous abortion
- Prematurity (19%)

Signs

- None in newborn/fetus

TESTS

- Nonspecific – tests for other STDs
- Specific

- ➢ No role for serologic testing in infancy
- ➢ HIV DNA PCR; of infants who acquire HIV vertically:
  - 20–30% will be positive w/in 48 h of birth (implies in utero transmission); DNA PCR should NOT be performed on cord blood
  - 95% will be positive by 1 mo
  - 100% will be positive by 6 mo

  Note: 2 or more negative HIV DNA PCRs, the first at >= 1 mo, the last at >= 4 mo, excludes vertical transmission in the non-breastfed infant.

DIFFERENTIAL DIAGNOSIS

N/A

MANAGEMENT

- Infection control
  - ➢ Universal precautions
  - ➢ Breastfeeding: contraindicated

SPECIFIC THERAPY

Prevention

- Maternal screening for HIV infection
  - ➢ Universal screening of all pregnant women at 1st prenatal visit
  - ➢ Expedited maternal HIV screening of all mothers who present in labor w/o previous screening
- Prophylaxis w/ confirmed maternal HIV infection
  - ➢ Antepartum: appropriate therapy for mother plus zidovudine during 2nd, 3rd trimesters (if not included in former)
  - ➢ Intrapartum
    - Zidovudine 2 mg/kg over 1 h then 1 mg/kg/h IV until delivery
    - Cesarean section delivery before ROM depending on maternal viral load
  - ➢ Neonatal
    - <34 weeks
      - Zidovudine 2 mg/kg PO (or 1.5 mg/kg IV) w/in 8–12 h of birth then q12h from birth to 2 wk
      - 2–6 wk: Zidovudine 2 mg/kg PO (or 1.5 mg/kg IV) q6h from 2–6 wk
      - 6 wk-4 mo: Trimethoprim (TMP) 75 mg/m2 BID & sulfamethoxazole (SMX) 375 mg/m2 BID for 3 consecutive d/wk
    - >34 wk

- Zidovudine 2 mg/kg PO (or 1.5 mg/kg IV) w/in 8–12 h of birth then q6h from birth to 6 wk
- 6 wk-4 mo: TMP 75 mg/m2 BID & SMX 375 mg/m2 BID for 3 consecutive days/wk

FOLLOW-UP

- HIV DNA PCR at birth & 1, 4, 6 mo; any + test should be repeated for confirmation; if confirmed, follow RNA PCR thereafter
- CBC at birth: 4 & 6 wk; 2, 3, 4, 6 mo
- Serum BUN, creatinine, LFTs at birth, 6 wk, & 3, 4, 6 mo
- Serum immunoglobulins at 4, 6 mo
- Lymphocyte subsets at 1, 3, 6 mo
- Urine cx for CMV at birth & 2 mo
- Growth & development

COMPLICATIONS AND PROGNOSIS

- None w/o vertical transmission
- W/ vertical transmission:
  - Growth delay
  - *Pneumocystis carinii* pneumonitis, usually at 3–6 mo (40% w/o appropriate prophylaxis)
  - Lymphocytic interstitial pneumonitis (50%)
  - Recurrent bacterial infection
  - Wasting syndrome (wt loss, anoxia, +/ − diarrhea)
  - Encephalopathy
  - Candida esophagitis or pneumonia
  - CMV infection
  - *Mycobacterium avium* infection (20% w/advanced disease)
  - Severe *Herpes simplex* infection
  - Severe varicella infection
  - Cryptosporosis
  - Cancer, most commonly non-Hodgkin's lymphoma (2% during childhood)
  - Death (20% by age 12)

HYPERTENSION (HTN), MATERNAL

J.M. LORENZ, MD

- Prevalence: 4% in USA
- Classification

- ➢ Chronic HTN: BP >/= 140/90 prev to preg, <20 wk GA w/o proteinuria, persisting >84 d postpartum
- ➢ Gestational HTN: onset HTN >20 GA w/o proteinuria
- ➢ Preeclampsia, mild
  - BP >/= 140/90
  - >0.3 g/d albuminuria
  - GA > 20 wk
- ➢ Severe preeclampsia: >/= 1 of following
  - BP >/= 160/110
  - >2 g/d albuminuria
  - IUGR, oligohydramnious
  - Increased maternal serum creatinine
  - Maternal symptoms (e.g., headache, visual disturbance, epigastric pain, pulmonary edema)
  - HELLP syndrome (hemolysis, elevated liver enzymes, low platelet ct)
- ➢ Preeclampsia superimposed on chronic HTN: chronic HTN w/ new-onset proteinuria
- ➢ Eclampsia: preeclampsia + seizure(s) w/o other cause

HISTORY & PHYSICAL

Neonatal/fetal effects

- Fetal/neonatal effects: Eclampsia > severe preeclampsia > preeclampsia superimposed on chronic HTN > chronic HTN > mild preeclampsia & gestational HTN
- Placental insufficiency
- Placental abruption (2× increase)
- Meconium-stained amniotic fluid
- Non-reassuring/abnl fetal heart rate pattern
- Stillbirth
- Prematurity due to delivery for maternal or fetal indications

Signs in newborn/fetus

- Oligohydramnios
- Neonatal depression
- IUGR, usually asymmetric
- Decreased subcutaneous fat
- Apnea/hypotonia/decreased GI motility due to maternal MgSO4 Rx
- Disseminated intravascular coagulation

TESTS

- Nonspecific

- ➢ Fetal/neonatal metabolic acidosis
- ➢ Increased nucleated RBC count
- ➢ Hypermagnesemia due to maternal MgSO4 Rx
- ➢ Hypoglycemia
- ➢ Polycythemia
- ➢ Neutropenia
- ➢ Thrombocytopenia (4× increase)

■ Specific
- ➢ None

DIFFERENTIAL DIAGNOSIS
N/A

MANAGEMENT
■ Supportive

SPECIFIC THERAPY
■ None

FOLLOW-UP
■ Growth & development

COMPLICATIONS AND PROGNOSIS
■ Complications
- ➢ Fetal/neonatal asphyxia
- ➢ Fetal/neonatal blood loss w/ placental abruption
- ➢ Apnea/hypotonia/decreased GI motility due to maternal MgSO4 Rx
- ➢ Meconium aspiration syndrome
- ➢ Sepsis due to neutropenia
- ➢ Disseminated intravascular coagulation

■ Prognosis
- ➢ 2–4× increase in perinatal mortality
- ➢ Catch-up growth the rule
- ➢ Increased risk of neurodevelopmental sequelae w/ prematurity, asphyxia, IUGR, hypoglycemia, polycythemia, sepsis

MARIJUANA (MARIHUANA, CANNABIS) USE, MATERNAL

TOVE S. ROSEN, MD

Most commonly used illicit drug among women of reproductive age & in pregnancy (2.9% in 1996)

HISTORY AND PHYSICAL

- Maternal hx
  - Sensitivity of ***routine*** prenatal interview for h/o substance abuse is as low as 25%.
  - ***Structured*** interviews (impractical for clinical use), ***repeated*** throughout pregnancy, for h/o marijuana use detect ~60% of cases.
- Fetal Effects
  - No increase in perinatal mortality or morbidity
  - Shortens gestation by 1 week in daily users; higher incidence of premature births & LBW in heavy users only
  - Precipitous labor more common
  - No effect on Apgar score
- Neonatal Effects
  - No effect or small dose-related effect on birth weight, length, & head circumference (negative correlation with dose & frequency of use), which disappears by age 8–12 mo
  - No major physical abnormalities
  - Minor anomalies (e.g., hypertelorism, severe epicanthus) reported in heavy users
- Behavioral abnormalities
  - Tremulousness, exaggerated & prolonged startles (spontaneous & in response to stimulation) may persist >1 mo.
  - Altered autonomic arousal
  - High-pitched cry
  - Less quiet sleep
  - Impaired habituation to visual stimuli poorer (Brazelton)

TESTS

Nonspecific

- Screen for other illicit drug use
- Serum glucose, electrolytes, cranial ultrasound for DDx

Specific

- Drug screening for primary metabolite, 11-nor-delta-9 tetrahydrocannabinol-9-carboxylic acid (TCH-COOH) – screening (lower specificity/higher sensitivity, e.g. ELISA) AND different confirmatory testing (high sensitivity/higher specificity, e.g. liquid chromatography/mass spectroscopy) recommended
- Maternal
  - Urine or stool; 70% excreted within 72 hr; w/heavy use, half-life as long as 10 days; window of detection is 1–30 days

- ➢ **Skilled maternal interview & maternal urine/stool toxicology increase detection over either alone.**
- Neonatal
  - ➢ Urine (collect specimen ASAP after birth) – detects only recent exposure; high false-negative rate
  - ➢ Meconium (collect specimen in first 2 days of life)
    - Preferred screening method
    - Sensitivity ~20% for maternal 2nd or 3rd trimester use compared to repeated, structured maternal interview; false-negatives more likely w/sparse, episodic use or when sample allowed to stand at room temp >12–24 hr

DIFFERENTIAL DIAGNOSIS

Other causes of tremulousness/high-pitched cry (e.g., hypoglycemia, hypercalcemia, neonatal narcotic withdrawal, CNS abnormalities)

MANAGEMENT

- Careful interview re: h/o tobacco, alcohol, other illicit drug use
- Breastfeeding contraindicated unless cessation of use documented
- Social service consultation

SPECIFIC THERAPY

- None

COMPLICATIONS AND PROGNOSIS

- Delay in visual developmental milestones
- Delay in gross motor developmental milestones
- Impaired short-term memory
- Attention deficit, hyperactivity, poor impulse control
- Impaired executive functioning
- Delinquency, aggressive behavior, conduct disorders

METHAMPHETAMINE ABUSE, MATERNAL

TOVE S. ROSEN, MD

- Most common in the Midwest, in both urban & rural areas
- Highly addictive CNS stimulant
- Cheap, long-lasting, easy to make
- Potent sympathomimetic agent – acutely decreases uterine BF & placental perfusion

HISTORY AND PHYSICAL

Maternal signs

- Euphoria, increased alertness, increased confidence
- Hostility, violent behavior, hallucinations, paranoid psychosis
- Anorexia

Fetal and neonatal effects

- Data limited
- IUGR (decreased birthweight & head circumference) due to uterine vessel vasoconstriction &/or anorexia; growth effects related to dose & duration of use in pregnancy
- Growth deficiency exacerbated by cigarette smoking
- Increased incidence of obstetric complications & premature labor
- Many infants quiet & withdrawn (due to neurotoxicity)
- Withdrawal symptoms of irritability (49%; 4% requiring Rx)

TESTS

Nonspecific

- Screening tests for STDs, if not prev performed
- For DDx
  - ➢ Of IUGR as indicated
  - ➢ Urine/meconium screening for other illicit drugs
  - ➢ Head US/MRI as indicated

Specific

- Drug screening for amphetamine/methamphetamine & metabolites – screening (lower specificity/higher sensitivity, e.g. immunoassay) AND different confirmatory testing (high sensitivity/higher specificity, e.g. liquid chromatography/mass spectroscopy) are recommended
  - ➢ Maternal urine – window of detection
    - Window of detection ~1–4 days (depends on dose & administration route); high false-negative rate
    - False-positive for illicit amphetamines may be due to legal amphetamines, but these rarely prescribed in pregnancy
    - **Skilled maternal interview & maternal urine toxicology increase detection > either alone.**
  - ➢ Neonatal
    - Urine (specimen collected ASAP after birth)
      - Window of detection longer than maternal due to slower elimination by fetus

- However, still detects only recent exposure; high false-negative rate
- Meconium (collected in first 2 days of life)
  - Preferred screening method
  - Little data re: sensitivity & specificity relative to maternal hx

DIFFERENTIAL DIAGNOSIS
- Other causes of IUGR
- Other causes of irritability, e.g. neonatal narcotic withdrawal, maternal cocaine use, CNS abnormalities, hyperthyroidism

MANAGEMENT
- Careful interview re: h/o tobacco, alcohol, other illicit drug use
- Breastfeeding contraindicated unless cessation of use documented
- Social service consultation

SPECIFIC THERAPY
None

FOLLOW-UP
Neurodevelopmental

COMPLICATIONS AND PROGNOSIS
- High risk of developmental & behavioral problems
- Smaller subcortical brain volumes (putamen, globus pallidus, hippocampus MRI studies at school age)
- Neurocognitive deficits in attention & memory domains, visuomotor integration
- Aggressive behavior & social maladjustment
- Lower scores in achievement in mathematics, language & motor function

NARCOTIC (HEROIN/PRESCRIPTION OPIATES/METHADONE) USE/ABUSE, MATERNAL

J.M. LORENZ, MD
REVISED BY TOVE S. ROSEN, MD

HISTORY & PHYSICAL
- Risk factors
  - <3 prenatal care visits
  - H/o substance abuse

- H/o STD
- H/o HIV
- H/o psychiatric illness
- H/o prostitution
- H/o freq relocation, encounters w/ law enforcement
- H/o dysfunctional family

- Maternal hx
  - Sensitivity of ***routine*** prenatal interview for h/o substance abuse is as low as 10–25%.
  - ***Structured*** interviews (impractical for clinical use) for h/o opiate use, ***repeated*** throughout pregnancy detects, detect ~70% of cases.
- Fetal Effects
  - Abruptio placentae
  - Preeclampsia/eclampsia
  - Chorioamnionitis
  - Stillbirth
  - Premature birth
  - IUGR
  - Intrauterine asphyxia
  - Meconium-stained amniotic fluid
- Neonatal Effects
  - Prematurity
  - Low birth wt
  - Small head circumference
  - Decrease in length
  - Neonatal depression
  - Thrombocytosis (only described in methadone exposure; rare)
  - Direct pharmacologic effects
    - Neonatal narcotic abstinence syndrome (NAS)
      - 55–94% incidence among exposed neonates (risk related to duration of drug use, maternal dose in late pregnancy, time of last dose, maternal & neonatal metabolism & elimination of drug; severity less w/ prematurity)
      - Natural hx: onset usually w/in 48–72 h, peaks by age 3–7 d, ameliorates by end of 1–2 wk, usually resolves by 8–16 wk; more protracted w/methadone: may start at a few weeks of age; may last for several months
    - Signs and Symptoms
      - CNS: Hyperactivity, irritability, high-pitched cry, coarse tremors, jitteriness, myoclonic jerks, hypertonia, hyperreflexia

- Facial scratches; pressure point abrasions (elbows, knees)
- Fist sucking, sneezing, hiccupping, yawning
- Nasal stuffiness
- Flushing, sweating, hyperthermia
- Mottling, hypothermia
- Tachypnea
- Disorganized, uncoordinated sucking; drooling; feeding difficulties
- Hyperphagia
- Vomiting
- Diarrhea
- Poor weight gain
- Seizures (rare)

TESTS

- Nonspecific
  - ➢ Screen for STDs, if not prev performed
  - ➢ Screen for other illicit drug use
  - ➢ As indicated for prematurity, IUGR (see **INTRAUTERINE GROWTH RESTRICTION**), asphyxia (see **HYPOXIC ISCHEMIC ENCEPHALOPATHY**)
  - ➢ As necessary to r/o other etiologies for above signs: maternal cocaine or amphetamine use, CNS hemorrhage, hyperthyroidism
- Specific: Drug screening for opiates & opiate metabolites – screening (lower specificity/higher sensitivity, e.g. radioimmunoassay) AND different confirmatory testing (high sensitivity/higher specificity, e.g. gas chromatography/mass spectroscopy) recommended
  - ➢ Maternal urine
    - Window of detection depends on specific opiate, dose, & pattern of use
      - For most opiates ~24–72 hr; high false-negative rate
      - W/chronic, high-dose use, may be as long as 10 days
      - Methadone: increased window of detection
    - **Skilled maternal interview & maternal urine toxicology increase detection over either alone.**
  - ➢ Neonatal
    - Urine (specimen collected ASAP after birth): detects only recent exposure (except w/methadone); high false-negative rate
    - Meconium (collected in first 2 days of life)
      - Preferred screening method

- Sensitivity ~80%, specificity ~80% for maternal 2nd- or 3rd-trimester use compared to repeated, structured maternal interview
- False-positive for illicit narcotic use may be due to prescribed narcotic; hx and ID of narcotic important

DIFFERENTIAL DIAGNOSIS

- IUGR (see **INTRAUTERINE GROWTH RESTRICTION)**
- Asphyxia (see **HYPOXIC ISCHEMIC ENCEPHALOPATHY**)
- Other etiologies for irritability: maternal cocaine or amphetamine use, CNS hemorrhage, hyperthyroidism

MANAGEMENT

Nonspecific

- Supportive care for complications assoc w/ prematurity, IUGR, asphyxia
- Social service consultation & follow-up
- NAS: swaddle, cuddle; facilitate hand-to-mouth activity (pacifier); darkened quiet environment (low stimulation)

Specific therapy for NAS

- Indications for pharmacologic Rx
  - ➢ Severe irritability & tremors interfering w/ feeding & sleep
  - ➢ Poor feeding, diarrhea, vomiting resulting in excessive wt loss or dehydration
  - ➢ Moderate to severe tachypnea interfering w/ feedings
  - ➢ Fever
  - ➢ Seizures
- Treatment does not alter long-term prognosis.
- Appropriate withdrawal scoring tool (e.g., Finnegan NAS Scoring System) allows dosing to be semi-quantitatively titrated.
- Preferred drug: tincture of opium, 10 mg/mL
  - ➢ Use 25-fold dilution (0.4 mg/mL morphine equivalent)
  - ➢ Start at 0.1 mL/kg or 2 qtts q4h before feeds
  - ➢ Increase 0.1 mL/kg q4h as necessary to control signs
- Alternatively: PO morphine
  - ➢ Start at 0.2 mg/kg/dose
  - ➢ Taper dose w/o decreasing freq after withdrawal signs have stabilized for 3–5 d
  - ➢ Once low doses have been reached, decrease frequency
- Other drugs:
  - ➢ Methadone (esp. if prolonged Rx is required)

- ➢ Paregoric (suboptimal because of other chemicals in preparation)
- ➢ Phenobarbital (not specific Rx)

FOLLOW-UP

- During Rx
  - ➢ Physical exam, weight gain, daily withdrawal scoring
- Long-term
  - ➢ Neurodevelopmental

COMPLICATIONS AND PROGNOSIS

- Early complications:
  - ➢ Most infants do well
  - ➢ Increased risk of transient tachypnea of newborn, respiratory distress syndrome w/prematurity, persistent pulmonary hypertension of the newborn, aspiration pneumonia
  - ➢ Dehydration, poor wt gain, poor feeding
  - ➢ Transmission of assoc STDs, hepatitis B, C, D & HIV to neonate
  - ➢ NBAS less alert, poor performance on orientation items, poor habituation & less consolable
- Prognosis
  - ➢ Increased incidence of SIDS
  - ➢ Growth deficiencies, esp. head growth
  - ➢ Strabismus/nystagmus
  - ➢ Higher frequency of impaired cognitive performance
  - ➢ Tone discrepancies
  - ➢ Poor fine motor coordination
  - ➢ Hyperactivity w/ poor attention span
  - ➢ Delay in acquisition of language skills
  - ➢ Disturbed mother-infant interactions
  - ➢ Increased prevalence of child abuse/neglect

PHENYLKETONURIA, MATERNAL

WENDY K. CHUNG, MD, PHD

Pregnant women w/ phenylketonuria must strictly adhere to phenylalanine-restricted diet to prevent mental retardation & congenital heart disease in the fetus.

Measure quantitative amino acids in serum: Goal = phenylalanine < 300 mcmol/L.

SYPHILIS/REACTIVE SEROLOGIC SYPHILIS TEST, MATERNAL, ACTIVE MATERNAL SYPHILIS LIKELY OR CANNOT BE EXCLUDED

J.M. LORENZ, MD

HISTORY & PHYSICAL

- Risk of maternal syphilis & fetal/neonatal consequences depend on maternal history, serologic status, h/o treatment
- MATERNAL SYPHILIS CANNOT BE RULED OUT W/ SEROLOGIC TESTING ALONE
- Active maternal syphilis likely (or cannot be excluded) if

1. Maternal rapid plasma reagin (RPR) OR Venereal Disease Research Laboratory (VDRL) reactive

AND

Maternal fluorescent treponemal Ab, absorbed w/ nonpallidum Ab (FTA-ABS) OR Treponema pallidum particle agglutination test (TP-PA) reactive

AND

No or inadequate treatment

NOTE: Rx INADEQUATE if

- Rx not DOCUMENTED
- Non-penicillin Rx
- Inappropriate penicillin regimen for stage of syphilis
- <4× fall in RPR or VDRL titer or decrease in titer cannot be DOCUMENTED
- Rx <30 days before delivery

OR

2. High or increasing maternal quantitative RPR OR VDRL titer, regardless of past Hx of adequate treatment

OR

3. Early syphilis during pregnancy w/ no or inadequate treatment, EVEN W/ negative maternal serologic syphilis tests

OR

4. Recent maternal sexual partner w/ active syphilis & no or inadequate maternal treatment, EVEN W/ negative maternal serologic syphilis test

Neonatal/fetal effects

If mother has syphilis & receives no or inadequate treatment

- Syphilitic fetal death
  - 3% w/ primary syphilis
  - 20% w/ secondary (disseminated) syphilis
  - 17% w/ "early-latent" infection
  - 5% w/ "late-latent" infection
- Congenital infection +/− premature birth
  - 26% w/ primary syphilis
  - 39% w/ secondary syphilis
  - 33% w/ "early-latent" infection
  - 8% w/ "late-latent" infection

Signs in neonate/fetus

- Syphilitic stillbirth
  - Polyhydramnios/hydrops
  - Paler, thicker, larger-than-nl placenta
  - Maceration
  - Vesicles or bullae
- Congenital syphilis
  - None, expression may be delayed mos to yrs; most common
  - Polyhydramnios/hydrops
  - Paler, thicker, larger placenta
  - Possibly IUGR
  - Hepatomegaly +/− splenomegaly (50%)
  - Generalized lymphadenopathy (30–50%)
  - Mucocutaneous manifestations (15–60%)
    - Persistent rhinitis (snuffles)
    - Laryngitis w/ aphonia
    - White mucosal patches
    - Maculopapular rash (usually oval, pink/red, involving palms, soles progressing to coppery brown w/ superficial desquamation)
    - Pemphigus syphiliticus (widespread vesicles/bullae)
  - Interstitial keratitis
  - Chorioretinitis, salt-and-pepper fundus, glaucoma, uveitis, cataract (all rare)
  - Syphilitic pneumonia w/ resp distress/failure (rare)
  - Pseudoparalysis (rare at birth; infrequent after a few wks)

TESTS

- Nonspecific
  - Coombs neg hemolytic anemia; leukocytosis or leukopenia; lymphocytosis or monocytosis; thrombocytopenia

- ➢ Indirect &/or direct hyperbilirubinemia (33%); abnl LFTs
- ➢ Increased CSF cell count or protein; reactive CSF VDRL
- ➢ Osteochondritis, periostitis, or osteomyelitis of long-bone or ribs (60–90%)

■ Specific (infants blood should be tested in preference to cord blood)

- ➢ Reactive RPR OR VDRL (non-treponemal tests; high false positive rate w/ maternal malignancy, autoimmune conditions, EBV infection and hepatitis; sensitivity 60–90% with primary syphilis, higher with secondary syphilis)

AND

Reactive FTA-ABS OR TP-PA (treponemal tests; more specific than non-treponemal tests, but false positive w/ Lyme disease, yaws, pinta; become reactive earlier and remain positive regardless of Rx)

Note: do not alone = congenital infection; may be reactive in neonate secondary to placental transmission

- ➢ T. pallidum in amniotic fluid, placental tissue, or fetal/neonatal body fluid or tissue by dark-field microscopy, fluorescent antibody, special stains, or PCR.
- ➢ Certainty of Dx classified as
  - CONFIRMED
    - congenital syphilis: microscopic identification of T. pallidum in amniotic fluid, placental tissue, or fetal/neonatal body fluid or tissue
    - Quantitative RPR or VDRL titer >= 4× mother's (at the same time, using same test) or >= 4× rise in infant's titer over time
  - PRESUMED congenital syphilis:
    - neonate whose mother has untreated or inadequate Rx at delivery
    - neonate w/ reactive FTA-ABS or TP-PA & any of following
      - Evidence of congenital syphilis on physical exam
      - Evidence of congenital syphilis on skeletal survey
      - CSF cell count >25 WBC/mm3 or protein >150 mg/dL in full terms (>170 mg/dL in preterms) w/o other cause
      - Reactive CSF VDRL
      - Reactive FTA-ABS or TP-PA at 15 mo of age
  - POSSIBLE congenital syphilis: asymptomatic neonate w/ single RPR or VDRL titer <4× mother's & normal LFTs, CSF, skeletal survey

DIFFERENTIAL DIAGNOSIS
N/A

MANAGEMENT
- General measures: supportive
- Infection control
  - ➢ Nursery
    - Strict adherence to universal precautions
    - Contact isolation w/ infectious lesions (mucosal patches, rhinitis, pemphigus syphiliticus, condylomata lata) until after 24 h of treatment
  - ➢ Isolation from mother not indicated w/ good handwashing, prevention of contact w/ infectious lesions
  - ➢ Breastfeeding contraindicated only w/ infectious breast lesions until after first 24 h of Rx

SPECIFIC THERAPY
- PREVENTION of fetal/neonatal infection
  - ➢ Appropriate MATERNAL surveillance (Hx, PE, serology) & treatment:
    - Primary, secondary, or early latent maternal syphilis: DOCUMENTED maternal Rx w/ PCN G benzathine 2.4 million units IM >30 days before delivery, sometimes repeated in 1 wk (repeated weekly × 2 wk w/ concomitant maternal HIV infection) W/ DOCUMENTED 4× FALL IN TITER (if initially high)
    - Latent (>1 y) maternal syphilis – DOCUMENTED maternal RX w/ PCN G benzathine 2.4 million units IM, weekly × 3, >30 days before delivery
  - ➢ Neurosyphilis: DOCUMENTED maternal Rx w/ aqueous crystalline PCN 3–4 million units IV q4h × 10–14 days or DOCUMENTED maternal Rx w/ procaine PCN 2.4 million units IM qd PLUS probenecid 500 mg PO qid × 10–14 days – 14% failure rate for prevention of fetal infection; higher w/ secondary syphilis
- Neonatal Rx
  - ➢ RPR (sensitivity > VDRL) & LP w/ CSF VDRL before Rx
  - ➢ Aqueous crystalline PCN 50,000 units/kg IV × 10–14 days
    - q12h at age <=1 wk
    - q8h at age 1–4 wk
    - q6h at age >4 wk

    OR

    Procaine PCN 50,000 units/kg IM qd × 10–14 days

- ➢ Indications for retreatment
  - Signs persist or recur
  - $<4\times$ fall in titer within 1 y (if initially high) or any rise in quantitative RPR or VDRL
- ➢ Side effects: Jarisch-Herxheimer reaction uncommon in newborn; more common w/ later Rx

FOLLOW-UP

- During/after Rx:
  - ➢ RPR at 1, 2, 3, 6 mo
    - If RPR initially negative, until persistently negative at 6 mo
    - If RPR initially positive, until RPR becomes nonreactive if initially reactive or $4\times$ fall in RPR titer on 2 consecutive tests
  - ➢ Repeat LP at 6 mo if initially abnl
  - ➢ RPR at 15 mo: confirms congenital infection if reactive, but may be nonreactive in 30–50% of cases of congenital infection
- Long-term: neurol w/ CNS involvement, ophthal w/ eye involvement, dental w/ dental involvement

COMPLICATIONS AND PROGNOSIS

- All avoidable w/ Rx within 1st 3 mo of life
  - ➢ Chorioretinitis
  - ➢ Perioral/perianal condylomata lata after age 2–3 mo
  - ➢ Nephrotic syndrome after age 2–3 mo
  - ➢ Acute syphilitic leptomeningitis at age 3–6 mo
  - ➢ Late congenital syphilis after age 2 yr
    - Hutchinson's triad [peg-shaped, notched central incisors; interstitial keratitis at 5–20 yrs of age, 8th nerve deafness (3%)]
    - Mulberry first lower molars
    - High-arched palate w/ protruding mandible
    - Saddle nose
    - Rhagades at mouth, nose, anus
    - Frontal bossing
    - Saber shin
    - Clutton's joints
    - Higouménakis' sign
    - Chronic meningovascular syphilis(arrested hydrocephalus, cranial nerve palsies, developmental deterioration, cerebral infarction with hemiplegia, seizures) – uncommon
- Implications for future pregnancies: recurrence possible w/ no or inadequate Rx or w/ reinfection

SYPHILIS/REACTIVE SEROLOGIC SYPHILIS TEST, MATERNAL, ACTIVE MATERNAL SYPHILIS UNLIKELY

J.M. LORENZ, MD

HISTORY & PHYSICAL

- Risk of maternal syphilis, fetal/neonatal consequences depend on maternal Hx, serologic status, h/o Rx
- MATERNAL SYPHILIS CANNOT BE RULED OUT W/ SEROLOGIC TESTING ALONE
- Active maternal syphilis is unlikely if:
  1. Reactive maternal fluorescent treponemal Ab, absorbed w/ nonpallidum Ab (FTA-ABS) or Treponema pallidum particle agglutination test (TP-PA) WITH ADEQUATE RX IN ABSENCE OF HIGH OR RISING RAPID PLASMA RAGIN (RPR) OR VENEREAL DISEASE RESEARCH LABORATORY (VDRL)

  OR

  2. Reactive maternal RPR or RPR at low titer with negative FTA-ABS; i.e., NOT believed to be secondary to past or present maternal syphilis
- Risk of congenital syphilis increased w/
  - ➢ Unmarried or teenage mothers
  - ➢ Inadequate prenatal care
  - ➢ Disadvantaged minorities
  - ➢ Residence in southeastern USA
  - ➢ H/o sexual promiscuity
  - ➢ H/o drug use by mother or sexual partner
  - ➢ H/o STD in mother or sexual partner
- NOTE: Possibility of congenital syphilis can be EXCLUDED ONLY by nonreactive maternal RPR titer >1 mo postpartum, or persistently nonreactive neonatal RPR or >4× fall in neonatal RPR titer

Neonatal/fetal effects

- Syphilitic fetal death, congenital infection (see **SYPHILIS/REACTIVE SEROLOGIC SYPHILIS TEST; ACTIVE MATERNAL SYPHILIS LIKELY OR CANNOT BE EXCLUDED** for signs of same) less likely, but possible, w/o maternal Rx

TESTS

- RPR (& VDRL if latter was done in mother)
- CBC

- Lumbar puncture, long-bone films if CBC is abnl or Rx w/ one dose of benzathine PCN planned

DIFFERENTIAL DIAGNOSIS
N/A

MANAGEMENT
- General measures: supportive

SPECIFIC THERAPY
- PE, CSF, skeletal survey normal, RPR or VDRL <= 4× mother's, AND ADEQUATE INFANT F/U IS ASCERTAINED: None – close F/U
- PE, CSF, skeletal survey normal AND RPR or VDRL <= 4× mother's, BUT ADEQUATE INFANT F/U NOT ASCERTAINED: Benzathine PCN 50,000 units/kg IM x 1
- Signs c/w congenital infection or RPR or VDRL >= 4× mother's: See **SYPHILIS/REACTIVE SEROLOGIC SYPHILIS TEST; ACTIVE MATERNAL SYPHILIS LIKELY OR CANNOT BE EXCLUDED.**

FOLLOW-UP
- RPR q2–3 mo
  - ➢ If RPR nonreactive at birth, until persistently negative at 6 mo
  - ➢ If RPR reactive at birth, until it becomes nonreactive or >4× fall titer on 2 consecutive tests

COMPLICATIONS AND PROGNOSIS
- None w/o congenital syphilis
- With untreated congenital syphilis: See SYPHILIS/REACTIVE SEROLOGIC SYPHILIS TEST; ACTIVE MATERNAL SYPHILIS LIKELY OR CANNOT BE EXCLUDED

TUBERCULOSIS, MATERNAL

J.M. LORENZ, MD

Risk factors: foreign birth, travel to high-prevalence country, migrant workers, exposure to contagious individual, illicit drug use, incarceration, homelessness, HIV infection

HISTORY & PHYSICAL

Maternal effects

- Signs of disease: weight loss, fever, malaise, fatigue, night sweats, hemoptysis; menstrual irregularity, menorrhagia, lower abdominal pain w/GU TB
- Tuberculous mastitis – single mass w/ or w/o draining sinus, very rare; transmission to infant exceedingly rare, if occurs at all

Neonatal/fetal effects

- Spontaneous abortion/premature delivery w/ untreated active maternal disease
- Congenital infection (see **TUBERCULOSIS, CONGENITAL**)
- Neonatal infection via inhalation or ingestion of infected droplets

Signs in newborn/fetus

- None in newborn period in absence of congenital infection

TESTS

Depend upon maternal condition

- Mother well w/ normal CXR
  - ➢ Isolation from mother not indicated
  - ➢ Tuberculin skin test for all household contacts
  - ➢ No eval of infant indicated if household contacts are negative
  - ➢ No Rx of infant indicated
- Mother asymptomatic w/ abnl CXR
  - ➢ Isolation from mother until confirmed to be non-contagious
  - ➢ Tuberculin skin test for all household contacts
  - ➢ Tuberculin skin test for infant at 4 mo, then on usual schedule
  - ➢ No Rx of infant indicated if household contacts are negative
- Mother w/ active disease
  - ➢ Isolation from mother until infant receiving INH
  - ➢ Report to Department of Health
  - ➢ Breastfeeding not contraindicated once infant receiving INH
  - ➢ Tuberculin skin test for all household contacts
  - ➢ Eval infant for congenital TB (see **TUBERCULOSIS, CONGENITAL)**
    - If no disease, Rx infant w/INH until mother culture-negative for 3 mo, then skin test infant
      - If skin test negative, d/c INH; repeat skin test at ages 6 & 12 mo
      - If skin test +, eval for disease (see **TUBERCULOSIS, CONGENITAL**)

- If no disease, continue INH until age 9 mo
- If disease confirmed, see **TUBERCULOSIS, CONGENITAL**

DIFFERENTIAL DIAGNOSIS
N/A

MANAGEMENT
See "Tests"

SPECIFIC THERAPY
See **TUBERCULOSIS, CONGENITAL**

FOLLOW-UP
- Serial liver enzymes if treated w/INH
- Wt gain; skin/sclera for jaundice; liver, spleen, lymph node size

COMPLICATIONS AND PROGNOSIS
- 40% of infants infected postnally develop disease w/o Rx
- Risk of severe disease markedly increased

VARICELLA (CHICKENPOX), MATERNAL, FIRST OR SECOND TRIMESTER (USUALLY <20 WK)

J.M. LORENZ, MD

HISTORY & PHYSICAL

Neonatal & fetal effects
- Fetal death secondary to congenital infection rare
- Severe maternal illness may cause fetal death or premature delivery
- Fetal varicella-zoster syndrome (1–2%; range 0–9%)

Signs in newborn and fetus
- Fetal varicella-zoster syndrome
  - ➢ Skin lesions (60–70%): usually cicatricial, depressed pigmented, often in a Z-configuration; uncommonly scattered bullae or depressed white scars
  - ➢ Eye abnormalities (60%): chorioretinitis, microphthalmia, Horner's syndrome, cataract, nystagmus
  - ➢ Neurologic abnormalities (60%): cortical atrophy, mental retardation, microcephaly, seizures, dysphagia or vocal cord paralysis due to bulbar palsy (25%), absent DTRs, limb paresis

- ➢ Limb hypoplasia (poor prognostic sign) +/− absent digits, talipes equinovarus or calcaneovalgus deformity (50%)
- ➢ Prematurity or IUGR (30–50%)
- ➢ GI abnormalities (33%): gastroesophageal reflux, duodenal stenosis, jejunal dilatation, microcolon, atresia of the sigmoid colon, poor anal tone
- ➢ Urinary tract anomalies (30%): poor vesicular sphincter tone

TESTS

- Total IgM may be increased, but specific IgM to VZV may not
- Viral isolation not expected
- Persistence of IgG to VZV > age 7 mo or early onset of zoster diagnostic
- PCR & in situ hybridization will be tests of choice in the future

DIFFERENTIAL DIAGNOSIS

N/A

MANAGEMENT

- Infection control: transmission of varicella not possible unless herpes zoster not present

SPECIFIC THERAPY

- Prevention
  - ➢ Immunization of susceptible women of reproductive age w/ varicella vaccine
  - ➢ Elective termination of pregnancy not routinely recommended for gestational varicella w/o evidence of fetal abnormalities on prenatal ultrasound (sensitivity unknown)
  - ➢ Role for maternal VZIG or acyclovir not determined

FOLLOW-UP

Neurol, ophthal, orthopedics, urology, surgery as indicated

COMPLICATIONS AND PROGNOSIS

- Prognosis
  - ➢ Death (25% overall; 40% w/ hypoplastic limb), usually secondary to pneumonia
  - ➢ Mental retardation
    - 40% with hypoplastic limb
    - No effect of gestational varicella on IQ in infants w/o fetal varicella syndrome

- ➢ Visual impairment
- ➢ Orthopedic problems secondary to limb abnormalities
- ➢ Urinary & fecal incontinence
- ➢ Dysphagia/aspiration
- ➢ Early-onset (< age 2 yr) zoster (20%): vesicular skin lesions in dermatome distribution, usually unilaterally, as result of reactivation of latent VZV

■ Implications for future pregnancies: no recurrence

VARICELLA (CHICKENPOX), MATERNAL, ONSET OF MATERNAL ILLNESS <5 D PRIOR TO OR <48 HR AFTER DELIVERY

J.M. LORENZ, MD

HISTORY & PHYSICAL

Neonatal & fetal effects
Congenital chickenpox (25–50%)

Signs in newborn and fetus
- ■ Incubation period: 9–15 d after onset of rash in mother
- ■ Clinical signs may range from mild infection (a few skin vesicles) to fulminant disease & death w/:
  - ➢ Fever
  - ➢ Recurrent crops of skin lesions over prolonged time: progresses from maculopapular to vesicular rash to pustular or hemorrhagic rash
  - ➢ Pneumonia (usually the cause of death)
  - ➢ Encephalitis, aseptic meningitis, myelitis
  - ➢ Hepatitis, generalized visceral involvement
- ■ Increased severity due to:
  - ➢ Lack of sufficient time for transplacental transfer of maternal anti-VZV IgG
  - ➢ Immaturity of cell-mediated immunity
  - ➢ Large inoculum as result of maternal viremia

TESTS
- ■ Presence of VZV antigen, VZV DNA isolation, or VZV from vesicular fluid

DIFFERENTIAL DIAGNOSIS
N/A

MANAGEMENT
- Infection control
  - ➢ Nursery
    - No staff susceptible to VZV should care for infant
    - Exclude seronegative hospital personnel from patient care activities days 8–21 after exposure
    - Contact isolation of infant in separate room w/ door closed, preferably w/ negative air pressure compared to that in the corridor
      - Exposure w/o signs of varicella infection: 21 days if VZIG not given (28 days if it is) or until discharge home
      - Non-disseminated varicella disease: minimum of 5 days, until all lesions crusted, or discharged home
      - Disseminated disease: for duration of illness
  - ➢ Isolation from mother
    - Until after neonate receives VZIG
    - After VZIG, expert recommendations contradictory
    - If isolation elected, until no new lesions for 72 hr & all vesicles dry (usually for 5–7 d after onset of maternal rash)
    - Isolation from mother not indicated if infant infected

SPECIFIC THERAPY
- Prevention: Varicella zoster immune globulin, 125 U (1.25 mL) IM ASAP & before 48 h of age/within 48 h of exposure
  - ➢ 50% attack rate even after VZIG, but disease severity decreased
- Treatment of neonatal infection
  - ➢ Rapid evolution of large # of vesicles, hemorrhagic manifestations, respiratory involvement, CNS involvement, disseminated disease:
    - Acyclovir 20 mg/kg q8h IV over 1 h × 7–10 days
      - Ensure adequate hydration to minimize nephrotoxicity
      - Increase dose interval w/ renal impairment, GA <34 wk
      - Side effects: phlebitis (dilute solution), transient elevation of serum creatinine, crystalluria
  - ➢ Milder disease than above: acyclovir not recommended

FOLLOW-UP
- During Rx: monitor IV site, renal & hepatic function

- Long-term: neurol w/ CNS involvement, ophthal, orthopedics, urology, surgery as indicated

COMPLICATIONS AND PROGNOSIS

- Complication: secondary bacterial infection (streptococcal or staphylococcal)
- Prognosis
  - ➢ Death (20–30%)
  - ➢ Increased risk of childhood zoster (relative risk of 3–21)
  - ➢ Mental retardation/cerebral palsy
- Implications for future pregnancies: no recurrence

VARICELLA (CHICKENPOX), MATERNAL, ONSET OF MATERNAL ILLNESS 6–21 DAYS PRIOR TO DELIVERY OR >48 H AFTER DELIVERY

J.M. LORENZ, MD

HISTORY & PHYSICAL

Neonatal & fetal effects

Depends on gestational age

- >=28 wk gestation: chickenpox (25–50%)
- <28 wk gestation:
  - ➢ 6–12 days prior to delivery: congenital chickenpox [see **VARICELLA (CHICKENPOX), MATERNAL, ONSET OF MATERNAL ILLNESS <5 D PRIOR TO OR <48 HR AFTER DELIVERY**]
  - ➢ 48 hr after delivery: disseminated varicella disease (indistinguishable from congenital chickenpox)

Signs in newborn and fetus

- >=28 wk gestation: same signs as w/ childhood disease, except incubation period is shorter (6–16 days) if acquired prior to delivery
- <28 wk gestation: congenital chickenpox

TESTS

- Presence of VZV antigen, VZV DNA isolation, or VZV from vesicular fluid

DIFFERENTIAL DIAGNOSIS

N/A

MANAGEMENT
- >=28 wk gestation
  - ➢ Same mgt as for childhood disease
  - ➢ VZIG not indicated
- <28 wk gestation: same mgt as for congenital chickenpox [see **VARICELLA (CHICKENPOX), MATERNAL, ONSET OF MATERNAL ILLNESS <5 D PRIOR TO OR <48 HR AFTER DELIVERY**]

SPECIFIC THERAPY
- >=28 wk gestation: same treatment as for childhood disease
- <28 wk gestation: same treatment as for congenital chickenpox >=2 (see **VARICELLA (CHICKENPOX), MATERNAL, ONSET OF MATERNAL ILLNESS < 5 D PRIOR TO OR < 48 HR AFTER DELIVERY**)

FOLLOW-UP
- >=28 wk gestation: same follow-up as after childhood disease
- <28 wk gestation: same follow-up as after congenital chickenpox (see **VARICELLA (CHICKENPOX), MATERNAL, ONSET OF MATERNAL ILLNESS < 5 D PRIOR TO OR < 48 HR AFTER DELIVERY**)

COMPLICATIONS AND PROGNOSIS
- >=28 wk gestation: same complications & prognosis as childhood disease
- <28 wk gestation: same complications & prognosis as congenital chickenpox [see **VARICELLA (CHICKENPOX), MATERNAL, ONSET OF MATERNAL ILLNESS <5 D PRIOR TO OR <48 HR AFTER DELIVERY**]

VARICELLA (CHICKENPOX), MATERNAL, THIRD TRIMESTER AND >21 DAYS PRIOR TO DELIVERY

J.M. LORENZ, MD

HISTORY & PHYSICAL

Neonatal/fetal effects
- Transmission possible

Signs in newborn/fetus
- None in newborn period

TESTS

Persistently positive anti-VZG IgG >8 mo indicates fetal infection.

DIFFERENTIAL DIAGNOSIS
N/A

MANAGEMENT
None required

SPECIFIC THERAPY
None required

FOLLOW-UP
None required

COMPLICATIONS AND PROGNOSIS
- Early-onset zoster w/fetal infection
- Implications for future pregnancies: no recurrence

PART TWO

Neonatal Conditions and Diseases

4P-SYNDROME (WOLF-HIRSCHHORN SYNDROME)

KWAME ANYANE-YEBOA, MD

HISTORY & PHYSICAL

- Severe IUGR w/ mean birth wt of 2,000 g
- Microcephaly
- Frontal bossing w/ a high frontal hairline
- Hemangioma over forehead, glabella or elsewhere
- Proptosis due to hypoplasia of orbital ridges
- Widely spaced eyes w/ upslanted palpebral fissures
- Ptosis, exotropia & ectopic pupils
- Stenosis or atresia of lacrimal ducts
- Short upper lip w/ downslanted corners of mouth
- Beaked nose w/ large, prominent bridge
- Small mandible
- Large, floppy or misshapen ears
- Narrow external ear canal
- Long, narrow chest
- Hypoplastic, wide-spaced nipples
- Diastasis recti
- Large clitoris in females
- Hypoplastic external genitalia w/ small scrotum in males; cryptorchidism & hypospadias (>66%)
- Sacral sinus
- Hip dysplasia
- Talipes or other foot problems
- Slender fingers
- Congenital heart defects, incl valvar defects & complex types
- Renal anomalies, incl hypoplasia, cystic dysplasia, unilateral agenesis & hydronephrosis
- Hypoplasia, aplasia or corpus callosum
- Ocular abnormalities, incl coloboma of iris (25%)
- Microphthalmia (5%)
- Cleft palate (33%)
- Cleft lip & palate (15%)
- Preauricular pits & tags
- Uterine hypoplasia, unicornis, or bicornis
- Scalp defects
- Umbilical hernia

- Inguinal hernia
- Diaphragmatic hernia
- Hypoplasia or duplication of thumbs
- Duplication of big toes
- Cleft vertebrae
- Severe delay in bone maturation
- Hypotonia

TESTS
- Chromosome studies, FISH for WHS

DIFFERENTIAL DIAGNOSIS
- Other chromosomal syndromes

MANAGEMENT
- Management of early feeding difficulties by tube feeding
- Monitor for seizures
- Physical & occupational therapies
- Genetic counseling

SPECIFIC THERAPY
None

FOLLOW-UP
- Monitor for infections
- Monitor for seizures
- Physical & occupational therapy
- Psychosocial support

COMPLICATIONS AND PROGNOSIS
- At least 30% of pts die in the 1st year
- Failure to thrive due to feeding difficulties
- Severe muscle hypotonia & neurologic deficits
- Delayed eruption of teeth
- Kyphoscoliosis
- High susceptibility to infection
- Profound developmental delay
- Overall prognosis poor

5P-SYNDROME

See **CRI-DU-CHAT SYNDROME**

ADRENAL INSUFFICIENCY

THOMAS WILSON, MD

HISTORY & PHYSICAL

History

- Maternal exposure to glucocorticoids
  - ➢ Dexamethasone/betamethasone cross placenta
  - ➢ Prednisone/hydrocortisone do not cross placenta
- Acute clinical deterioration
- Asphyxia
- Difficult labor
- Sepsis
- Family Hx of:
  - ➢ Adrenal disease
  - ➢ Early neonatal demise
  - ➢ Genital ambiguity

Signs

- Dehydration
- Hypotension, shock
- Pigmented genitalia
- Pigmented areolae
- Ambiguous genitalia
- Hypoglycemia
- Hyponatremia
- Hyperkalemia

TESTS

- Serum & urine electrolytes
- Serum glucose
- Serum creatinine
- Urinalysis
- Cortisol
- Aldosterone
- ACTH
- Plasma renin activity
- 17-OH-progesterone
- Sepsis workup
- Cortisol response to Cortrosyn
  - ➢ Baseline serum cortisol

- ➢ Give Cortrosyn 250 mcg/m^2 IV
- ➢ Obtain serum cortisol at 60 min
- ➢ Normal: peak cortisol > 18 mcg/dL

- Karyotype
  - ➢ W/ ambiguous genitalia
  - ➢ If adrenal hyperplasia is suspected, see **CONGENITAL ADRENAL HYPERPLASIA**
- If adrenal hypoplasia is suspected: cholesterol & triglycerides [triglycerides elevated in glycerol kinase deficiency (closely linked to the adrenal hypoplasia gene (DAX1) on X chromosome)]
- If adrenaleukodystrophy is suspected
  - ➢ Long-chain fatty acids
  - ➢ CT or US of abdomen & pelvis
    - Adrenal hemorrhage
    - Adrenal calcifications
      - Wolman disease
      - Old adrenal hemorrhage

DIFFERENTIAL DIAGNOSIS

- DDx of signs
  - ➢ Sepsis
  - ➢ Other causes of hypoglycemia (see HYPOGLYCEMIA)
  - ➢ Acute renal failure
  - ➢ Acute UTI
  - ➢ Obstructive uropathy
  - ➢ Gastroenteritis
  - ➢ Na-losing nephropathy
  - ➢ Hypoaldosteronism
  - ➢ Pseudohypoaldosteronism
- DDx of etiology of adrenal insufficiency
  - ➢ Congenital adrenal hypoplasia
    - X-linked form
      - Partial X deletion
      - Deletion/mutation of DAX1
    - Autosomal recessive form
      - Deletion/mutation of SF1
  - ➢ Congenital adrenal hyperplasia (see **CONGENITAL ADRENAL HYPERPLASIA**): many forms, all autosomal recessive
  - ➢ Adrenal hemorrhage (w/ difficult delivery/asphyxia)
  - ➢ Wolman syndrome
    - Liposomal storage disease

- Acid lipase deficiency
- Hepatomegaly
- Autosomal recessive

➢ Adrenaleukodystrophy
- Usually later in childhood
- Often w/ neurological symptoms
- X-linked

MANAGEMENT

- Dextrose to correct hypoglycemia
  - ➢ D10W 2–4 cc/kg IV push
  - ➢ Then dextrose at 4–6 mg/kg/min
  - ➢ Maintain serum glucose > 50 mg/dL
- Fluid, electrolytes to correct shock
  - ➢ If hypotensive, 10–20 mL/kg D5W NS or D5W 0.5% NS, then 100–200 cc/kg/d
  - ➢ If hyperkalemic, withhold K; see **HYPERKALEMIA** for treatment to lower serum K
- Obtain baseline serum cortisol, aldosterone, 17-OH progesterone, ACTH & 1st urine electrolytes BEFORE BEGINNING STEROID Rx

SPECIFIC THERAPY

- Hydrocortisone
  - ➢ Acute
    - 2 mg/kg IV push, then 2 mg/kg/day divided q6h
    - If salt wasting, 5–10 mg/kg IV push, then 5–10 mg/kg/d q6h
  - ➢ Chronic: 0.5–1 mg/kg/day or 10–25 mg/m^2/day
- If mineralocorticoid deficient
  - ➢ Fludrocortisone 0.1 – 0.2 mg/day
  - ➢ Na supplements of 2–5 g NaCl/day PO (necessary until old enough to forage for salt)
- Stress management
  - ➢ Increase glucorticoids 3-fold
  - ➢ Counsel & train parents
  - ➢ For NPO/vomiting patient: hydrocortisone 50–100 mg/m^2/day IV/IM div q6–8h
- Steroid potencies
  - ➢ Relative glucorticoid effect
    - Hydrocortisone 1
    - Prednisone 4
    - Methylprednisone 5

- Dexamethasone 50
- Fludrocortisone 12

- Relative mineralocorticoid effect
  - ➢ Hydrocortisone 1
  - ➢ Prednisone 0.75
  - ➢ Methylprednisone 0.5
  - ➢ Dexamethasone 0
  - ➢ Fludrocortisone 125

FOLLOW-UP

- Monitor:
  - ➢ Growth
  - ➢ Blood pressure
  - ➢ Serum glucose
  - ➢ Electrolytes
  - ➢ Plasma renin activity
  - ➢ ACTH
- Counseling
  - ➢ See ambiguous genitalia
    - Issues of rearing
    - Sex assignment
    - Issues/need for surgery (extent & timing controversial)
  - ➢ Recurrence risk if genetic
  - ➢ Mgt of illnesses
  - ➢ Stress doses of steroid
  - ➢ Patient counseling for associated disorders
    - Adrenal hypoplasia
      - Glycerol kinase deficiency
        - Increased serum glycerol
        - Increased triglycerides
      - Muscular dystrophy (contiguous gene deletion on X chromosome)
      - Gonadotropin deficiency
    - Wolman disease: neurologic deterioration
    - Adrenal leukodystrophy: neurologic deterioration

COMPLICATIONS AND PROGNOSIS

Complications of Rx

- Excessive glucocorticoid: poor growth
- Excessive fludrocortisone
  - ➢ Hypertension
  - ➢ Hypokalemia

Prognosis

- Death if:
  - ➢ Adrenal insufficiency untreated
  - ➢ Stress not covered w/ steroids
  - ➢ Recurring shock, dehydration & hypoglycemia
  - ➢ Hyperkalemia inadequately treated
- Prognosis good if adequately treated; exceptions:
  - ➢ Adrenaleukodystrophy
  - ➢ Wolman disease
  - ➢ Neurolologic dysfunction

AMBIGUOUS GENITALIA

ALAN M. GOLDSTEIN, MD AND TERRY HENSLE, MD
REVISED BY TERRY HENSLE, MD, AND GRACE HYUN, MD

- Intersex disorders: discordance between gender genotype and phenotype
- Intersex disorders: medical & psychosocial emergencies
- External genitalia will develop along female lines unless systemic androgens (dihyrotestosterone [DHT]) induce male differentiation
- Male differentiation requires:
  - ➢ Sex determining region of Y (SRY) gene
  - ➢ Bilateral testes producing Mullerian inhibiting substance (MIS) & testosterone
  - ➢ 5-alpha reductase enzyme (external genitalia)
  - ➢ Functional testosterone & DHT receptor (internal & external genitalia)

HISTORY & PHYSICAL

History

- Family Hx – Many intersex states are genetic, therefore family history is important:
  - ➢ Infertility
  - ➢ Consanguinity
  - ➢ Prior infant demise
  - ➢ Hirsutism
  - ➢ Acne
  - ➢ Oligo- or amenorrhea
  - ➢ Hypospadias

- Maternal conditions
  - ➢ Use of birth control pills after conception
  - ➢ Maternal virilization (androgen-secreting tumors)
  - ➢ Maternal exposure to androgens, progestins or other meds (seizure meds)
- Assoc conditions
  - ➢ Turner syndrome: female phenotype w/ streak gonads
  - ➢ Klinefelter syndrome: micropenis w/ small testes
  - ➢ Camptomelic dwarfism (XY gonadal dysgenesis)
  - ➢ Denys-Drash syndrome
    - Nephropathy, genital abnormalities & Wilms' tumor
  - ➢ Congenital adrenal hyperplasia (CAH; see **CONGENITAL ADRENAL HYPERPLASIA**)

Signs

- If gonad descended & palpable, most likely testis or, rarely, ovotestis
- If gonads not palpable in scrotum, check inguinal canal
- Rectal exam: uterus palpable in females during 1st 48 h of life due to maternal estrogen
- Intersex problem should be suspected in apparent males w/:
  - ➢ Micropenis (<2.0 cm in term infant)
  - ➢ Bilateral cryptorchidism, especially impalpable testes
  - ➢ Bifid scrotum
  - ➢ Severe hypospadias
  - ➢ Any hypospadias with undescended testicle
- Intersex problem should be suspected in apparent females w/:
  - ➢ Enlarged, rugated labioscrotal folds
  - ➢ Clitoromegaly (>1 cm)
  - ➢ Posterior labial fusion (same differential as clitoromegaly)
  - ➢ Labial or inguinal mass
- Hyperpigmentation of areola or scrotum w/ CAH (see **CONGENITAL ADRENAL HYPERPLASIA**)
- Dehydration, hypotension w/:
  - ➢ 21-hydroxylase deficiency (CAH), virilization of females
  - ➢ 3-beta-hydroxysteroid dehydrogenase deficiency (CAH), mild virilization in females, severe hypospadias in males
  - ➢ Congenital lipoid hyperplasia, incomplete masculinization
- Hypertension w/:
  - ➢ 11-beta-hydroxylase deficiency (CAH), virilization of females
  - ➢ 17-alpha-hydroxylase deficiency (CAH), incomplete masculinization

TESTS

- Serum electrolytes
- Expedited karyotype
- Abd US for presence/absence of uterus
  - ➢ Presence of uterus indicates bilateral ovaries or dysgenetic gonads that failed to produce Mullerian inhibiting substance
- 17-hydroxyprogesterone, androstenedione & serum testosterone (T) (obtained between 24–48 h)
  - ➢ Decreased levels of testosterone
    - Leydig cells deficient
    - Luteinizing hormone (LH) activity impaired
    - Testosterone biosynthetic defect
  - ➢ Markedly elevated 17-hydroxyprogesterone, androstenedione, & testosterone w/ 21-hydroxylase deficiency (CAH)
- Genitography
  - ➢ To determine anatomy of urethra, vagina
  - ➢ To assess presence/absence of urogenital sinus
- HCG stimulation test
  - ➢ Useful to assess for presence/absence of testicular tissue or to diagnose testosterone biosynthetic defect
- Additional studies
  - ➢ XX infant w/ Mullerian ducts
    - 17-hydroxyprogesterone
    - 11-deoxycortisol
    - Cortisol
    - Renin
    - 17-hydroxypregnenolone
    - Testosterone
  - ➢ XX infant w/o Mullerian ducts
    - Testosterone
    - Estradiol (E2)
    - Luteinizing hormone
    - Follicle-stimulating hormone (FSH)
    - SRY
  - ➢ XY infant w/ Mullerian ducts
    - Testosterone
    - Estradiol
    - Luteinizing hormone
    - Follicle-stimulating hormone
  - ➢ XY infant w/o Mullerian ducts

- Testosterone & dihydrotestosterone (DHT)
  - If testosterone/DHT increased, consider HCG stimulation test
  - If testosterone normal/low, obtain:
    - Androstenedione
    - Dihydro-epiandrosterone
    - 17-hydroxy-pregnenolone
    - 17-hydroxy-progesterone
    - Deoxycorticosterone (DOC)
    - Cortisol
    - Consider ACTH stimulation test
  - Luteinizing hormone
  - Follicle-stimulating hormone

DIFFERENTIAL DIAGNOSIS

- Genetic male w/ severe hypospadias or undescended testes
- Female pseudohermaphroditism
  - ➢ CAH (most common)
    - Karyotype 46 XX
    - Androgenized females
    - Autosomal recessive inborn error of steroidogenesis 90% due to 21-hydroxylase deficiency, leading to impaired cortisol synthesis resulting in elevation of serum 17-hydroxyprogesterone, androstenedione & testosterone
    - Can have severe, life-threatening salt wasting from reduced aldosterone production
    - Acute adrenal insufficiency as early as day 5 of life
    - Increased melanocyte-stimulating hormone darkens areola, scrotum
    - Internal organs female
    - Phenotype typically incl single urogenital opening along ventral shaft of enlarged clitoris, absence of palpable gonads, rugated & enlarged labioscrotal folds
  - ➢ Maternal androgens
    - Exogenous (i.e., medication)
    - Endogenous (i.e., androgen-secreting tumors)
- Male pseudohermaphroditism
  - ➢ Karyotype 46 XY
  - ➢ Defective virilization
  - ➢ No Mullerian organs (MIS intact)
  - ➢ Etiologies

- Complete androgen insensitivity syndrome
  - Androgen receptor abnormal
  - Unable to respond to circulating testosterone
  - Presentation: bilateral inguinal hernias
  - Phenotypically normal female w/ Blind-ending vagina, no Mullerian structures secondary to MIS secretion from normal Sertoli cells
  - Testis in inguinal canal or intra-abdominal
- Partial androgen insensitivity syndrome – phenotype varies from apparently normal female w/ clitoral hypertrophy to apparently normal male w/ hypospadias
- Decreased testosterone synthesis – severe hypospadias, small penis, cryptorchidism
- 5-alpha-hydroxylase deficiency
  - Inability to convert testosterone to DHT, which promotes virilization of external genitalia
  - Autosomal recessive
  - Severe hypospadias, bifid scrotum, cryptorchidism
  - Can be phenotypically female at birth
- Anorchia (vanishing testis syndrome) – results in loss of testosterone after 14 wk gestation
- Persistent Mullerian duct syndrome
  - MIS receptor abnormal or no secretion of MIS
  - Presents w/ undescended testis, which can be impalpable, or hernia
  - Mullerian structures (uterus, fallopian tubes) remain

■ Chromosomal anomalies

➢ Pure gonadal dysgenesis
- Karyotype usually 46 XY, but may be XO (Turner syndrome) or XX
- MIS & testosterone both absent because of failed gonadal differentiation
- Phenotypically normal females
- Increased risk of malignancy

➢ Turner's syndrome
- 45 XO or 46 XX/45 XO mosaic
- Female phenotype w/ streak gonads
- Somatic abnormalities: short stature, webbed neck, shield chest,
- coarctation of aorta, horseshoe kidney
- Sexual infantilism: amenorrhea, sparse hair, no pubertal development

- ➢ Mixed gonadal dysgenesis
  - Karyotype 46 XY or 45 XO/46XY mosaic
  - Asymmetric gonads, one streak gonad or one dysgenetic testis
  - Streak gonad: 25% risk of malignancy (gonadoblastoma); must remove
  - Usually incompletely virilized males w/ microphallus, hypospadias, partial labioscrotal fusion, only one palpable gonad
- ➢ True hermaphroditism
  - Karyotype usually 46 XX, but can be 46 XY or 46 XX/46 XY mosaic
  - Asymmetric gonads: testis on 1 side/ovarian tissue on other or combined ovotestis on 1 or both sides
  - Varies from female phenotype w/ clitoromegaly to male w/ hypospadias & asymmetrically descended testes

MANAGEMENT

- What to do first
  - ➢ Salt-wasting CAH requires aggressive treatment (see **CONGENITAL ADRENAL HYPERPLASIA**)
    - Correction of hypovolemia (normal saline w/ 5% glucose)
    - Glucocorticoid replacement w/ hydrocortisone at 3–6× maintenance
    - Mineralocorticoid replacement (Florinef)
- General measures
  - ➢ Expeditious & appropriate sex assignment
  - ➢ Interdisciplinary team approach: neonatology, endocrine, psychiatry, genetics & urology should all be involved early
  - ➢ Surgical Rx
    - Isolated hypospadias usually repaired at 9 mo
    - Female pseudohermaphrodite usually assigned female sex, treated w/ clitoral reduction, vaginoplasty by age 6 mo
    - Male pseudohermaphrodite: sex assignment varies depending on external phenotype & Dx
    - Gonadal dysgenesis usually assigned female sex; gonadectomy for high risk of malignancy

SPECIFIC THERAPY

- Depends on underlying etiology

FOLLOW-UP

- Depends on underlying etiology

COMPLICATIONS AND PROGNOSIS
- Depends on underlying etiology

APERT SYNDROME

KWAME ANYANE-YEBOA, MD

- Autosomal dominant w/ mutations in FGFR2 gene
- Majority due to fresh mutations assoc w/ advanced paternal age

HISTORY & PHYSICAL
- Acrocephaly due to craniosynostosis
- Mitten syndactyly of hands
- Syndactyly of toes 2–5
- High forehead
- Flat occiput
- Hypertelorism
- Strabismus
- Down-slanted palpebral fissures
- Small nose
- Large anterior fontanel
- Cleft palate
- Bifid uvula
- Delayed dental eruption
- Malocclusion
- Normal birth length
- Genesis of corpus callosum
- Ventriculomegaly
- Gyral malformations
- Hydrocephalus
- Fusion of cervical vertebrae at C5–C6
- Joint hypermobility
- Genu valgum
- Ectopic anus
- Moderate to severe acne

NOTE: Facial features & pattern of syndactyly in Apert syndrome are distinctive.

TESTS
- Imaging studies to assess craniosynostosis & brain
- FGFR2 mutational analysis

DIFFERENTIAL DIAGNOSIS
- Cruzon, Pfeiffer, Saethre-Chozen & Jackson-Weiss syndromes

MANAGEMENT
- Neurosurgical correction of premature suture closure
- Cosmetic surgery of face
- Correction of syndactyly
- Genetic evaluation & parental counseling
- Psychosocial support

SPECIFIC THERAPY
None

FOLLOW-UP
- Multispecialty team approach

COMPLICATIONS AND PROGNOSIS
- Hydrocephalus
- Ventriculomegaly
- Mental retardation in 50% (early surgery of craniosynostosis does not prevent)
- Short stature in childhood

APNEA OF PREMATURITY

MEENA LACORTE, MD
REVISED BY FRANCIS AKITA, MD

HISTORY & PHYSICAL
- Cessation of breathing for >20 sec or any duration associated w/ pallor, cyanosis or bradycardia
- Diagnosis of exclusion of other causes of recurrent apnea
- Incidence of apnea correlates inversely w/ gestational age
- Onset evident on 1st or 2nd day after birth in spontaneously breathing infant – w/ ventilatory support, onset is delayed
- Most episodes occur during active sleep
- Types of apnea
  - ➢ Central apnea: Lack of respiratory effort; ≈40%
  - ➢ Obstructive apnea: Inspiratory efforts occur but airway is obstructed; ≈10%
  - ➢ Mixed apnea: Combination of airway obstruction & central apnea; ≈50%

- May occur after general anesthesia in premature infants until 50–60 wks postconceptional age

TESTS

- Impedance-based cardiorespiratory monitoring & pulse oximetry
- Correlation w/ visual observation of infant
- To r/o other causes as indicated
  - ➢ CBC, serum glucose, serum electrolytes (including Ca & Mg)
  - ➢ Blood culture, lumbar puncture
  - ➢ Arterial blood gas
  - ➢ Cranial imaging studies, usually head ultrasound

DIFFERENTIAL DIAGNOSIS

- Sepsis/pneumonia/meningitis/UTI
- Hypoglycemia
- Hypocalcemia?
- Hypoxemia
- Overheating
- Intracranial hemorrhage
- Intrapartum administration of magnesium sulfate to mother if in the immediate postnatal period
- Administration of opiates, sedatives, prostaglandin E_1 to infant
- Gastroesophageal reflux
- Metabolic disorders

MANAGEMENT

General measures

- Cardiopulmonary & pulse oximetry monitoring of all infants until infant is at least 34 wks postconceptional age or free of associated cyanosis & bradycardia without intervention for 4–7 days
- Appropriate thermal environment (see **THERMAL MANAGEMENT** in the "Supportive Care" section)
- Positioning to avoid compromise of upper airway from flexion
- Monitoring oxygenation w/ desired saturation of 88–95%
- PRBC if hematocrit <25%
- Oscillating water bed
- Tactile stimulation
- Nasal continuous positive airway pressure – reduces incidence of mixed & obstructive apnea; side effects include:
  - ➢ Nasal trauma
  - ➢ Gastric distention
  - ➢ Feeding intolerance

- Mechanical ventilation – low peak inspiratory pressure and rate if apnea is only indication

SPECIFIC THERAPY

- Other cause of apnea excluded
- Relative indications for treatment
  - ➢ Frequent episodes of apnea, prolonged associated w/ significant bradycardia or hypoxia
  - ➢ Positive pressure ventilation required for recovery
- Methylxanthines – to reduce incidence of central apnea
  - ➢ Caffeine citrate
    - Dose: 10–20 mg/kg (caffeine BASE) loading dose followed by 2.5–4 mg/kg (caffeine BASE) q24h
    - Route: IV or PO
    - Therapeutic level: 5–25 mcg/mL
    - Wider therapeutic index w/ fewer side effects than theophylline
    - Less need to check blood levels
    - Once-daily administration
    - Toxicity: tachycardia, tachypnea, jitteriness, tremors
    - Monitor drug levels in infants w/ hepatic dysfunction
  - ➢ Theophylline
    - Dose: 4–6 mg/kg loading dose followed by 1.5–3 mg/kg q8–12h
    - Route: IV or PO
    - Therapeutic level: 8–12 mcg/dL
    - May exacerbate gastroesophageal reflux
    - Toxicity: tachycardia, tachypnea, jitteriness, tremors, unexplained seizures
  - ➢ Doxapram (rarely indicated)

    Indications: failure of optimal methylxanthine & CPAP to resolve apnea of prematurity otherwise requiring mechanical ventilation
    - Dose: 1 mg/kg loading dose followed by 0.5 mg/kg/h
    - Route: IV (not well absorbed PO)
    - Contraindicated in the 1st week of life or if bilirubin is high (associated w/ IVH, kernicterus)
    - Preparation available in USA contains benzyl alcohol but the dose required results in only 5.4 mg/kg/day of benzyl alcohol, far below amount assoc w/ toxicity in preterms
    - Side effects: abdominal distention, increased gastric residuals, irritability, hyperglycemia, mild hypertension

FOLLOW-UP

- Cardiopulmonary & pulse oximetry monitoring of all infants until infant is at least 34 wks postconceptional age or free of associated cyanosis & bradycardia without intervention off methylxanthines for 4–7 days
- Cardiorespiratory monitoring until 43–44 wks postconceptional age may be an alternative to a prolonged hospital stay

COMPLICATIONS AND PROGNOSIS

- Separating the consequences of preterm birth from the effects of apnea of prematurity is difficult.
- Cerebral ischemia accompanies severe bradycardia w/ a heart rate <80 beats/minute.
- Precisely measured predischarge apnea has been reported to be predictive of lower developmental indices at 2 years of age.

ATRIAL SEPTAL DEFECT

KALYANI R. TRIVEDI, MBBS, MD
AND LEE N. BENSON, MD
REVISED BY GANGA KRISHNAMURTHY, MD

Any opening in the atrial septum, other than a competent foramen ovale, is an atrial septal defect (ASD).

ASDs are classified into the following based on location relative to the fossa ovalis (FO):

1. Secundum ASD: Defect in the region of the FO
2. Primum ASD: Defect caudal to FO, also assoc w/ cleft in mitral valve
3. Sinus venosus defect: Defect posterior to FO, assoc w/ anomalous connection of the right pulmonary veins

HISTORY & PHYSICAL

History

Most infants w/ ASD are asymptomatic, often undetected

- Older children w/ large defects are symptomatic w/ dyspnea & fatigue. Rarely, recurrent lower respiratory tract infection, growth failure
- +/− antenatal diagnosis possible by fetal echocardiogram

Physical

- Asymptomatic in newborn period

- ASD usually diagnosed on routine physical exam due to murmur at 1–2 years of age; typical exam in the older child w/ moderate to large ASD:
  - ➢ Prominent apical impulse
  - ➢ Wide, fixed splitting of S2
  - ➢ Soft systolic murmur in upper left intercostal space
  - ➢ Mid-diastolic murmur in lower left sternal border
  - ➢ With development of pulmonary hypertension, left-to-right shunt decreases or ceases. Wide splitting of S2 disappears, P2 is louder, systolic murmur is shorter, diastolic murmur disappears.

TESTS

- CXR: normal in newborn period; later mild to moderate cardiomegaly, increased pulmonary vascular marking. If pulmonary vascular disease develops, lung fields become oligemic.
- 12-lead ECG: rightward QRS axis, rSR′ pattern in right-sided precordial leads, right ventricular hypertrophy
- Echocardiogram
  - ➢ Secundum ASD of variable size
  - ➢ Doppler evidence of left-to-right atrial shunting
  - ➢ Right ventricular dilatation, right ventricular volume overload (rare in newborn period)
  - ➢ Main pulmonary artery dilatation
  - ➢ Increased flow across the pulmonary valve w/ Doppler

DIFFERENTIAL DIAGNOSIS

Other lesions that cause can right heart dilatation (see **TOTAL ANOMALOUS PULMONARY VENOUS CONNECTION** and **PARTIAL ANOMALOUS PULMONARY VENOUS CONNECTION**)

MANAGEMENT

For major ASD (Qp:Qs > 1.5:1), elective surgical closure usually between 2–4 years of age to prevent pulmonary vascular disease

- Surgical closure either primary or w/ patch if defect large
- Transcatheter closure w/ device placement is an alternative to surgical closure

FOLLOW-UP

- Spontaneous closure unlikely after age 1 yr
- Before repair: follow growth & cardiopulmonary status
- After repair: SBE prophylaxis required for 6 mo after device closure or after patch closure of ASD

COMPLICATIONS AND PROGNOSIS

Untreated ASD is usually asymptomatic in the first decades of life

- Risk for pulmonary vascular disease
- Risk of atrial arrhythmia increases w/ age & right ventricular dilatation
- Congestive cardiac failure may occur after 40 years

Repair: Low-risk procedure: mortality <1%

BILIARY ATRESIA

CHARLES J.H. STOLAR, MD

HISTORY & PHYSICAL

- Mixed hyperbilirubinemia usually noted at >= 4th wk of age
- Total bilirubin usually <10 mg/dL
- Term pregnancy

TESTS

- Bilirubin, total & direct
- Liver function panel
- Hepatitis screen
- Alpha-1-antitrypsin level
- Thyroid hormone level
- Cystic fibrosis screen
- Liver/spleen ultrasound
- Liver biopsy
- HIDA scan

DIFFERENTIAL DIAGNOSIS

- See **HYPERBILIRUBINEMIA, CONJUGATED**

MANAGEMENT

- Exploratory laparotomy w/ Kasai procedure (biliary portoenterosotomy) before age 8 wk; bile drainage unlikely after that
- Consider primary liver transplant for delayed Dx

SPECIFIC THERAPY

- Liver transplant

FOLLOW-UP

- Surgery & GI
- Growth & development
- LFTs

COMPLICATIONS AND PROGNOSIS

W/ Kasai procedure before age 8 wk

- 1/3 drain bile; liver function normal
- 1/3 drain bile; liver function abnl
- 1/3 drain no bile

BIOTINIDASE DEFICIENCY

WENDY K. CHUNG, MD, PhD

HISTORY & PHYSICAL

- Lethargy, change in mental status
- Vomiting
- Seizure
- Ataxia in older children
- Hypotonia
- Alopecia & erythematous rash
- Abnormal newborn screen result

TESTS

- Arterial blood gas: metabolic acidosis
- Urine analysis: ketosis
- Lactic acidosis
- Hyperammonemia
- Urine organic acids: 3-methylcrotonylglycine, 3-hydroxyisovaleric acid, 3-hydroxypropionic acid & 2-methylcitric acid
- Serum biotinidase activity

DIFFERENTIAL DIAGNOSIS

- Organic aciduria (see **METABOLIC ACIDOSIS**)/other metabolic conditions
- Sepsis
- Hypoxia

MANAGEMENT

- Airway, breathing, circulation
- IV fluids w/ D10 at 1.5× maintenance
- NPO until diagnosis is established
- Carefully monitor glucose levels

SPECIFIC THERAPY

- Biotin 10 mg q day PO

FOLLOW-UP

- For biotinidase activity <10%, follow lactate, ammonia, & urine organic acids to ensure sufficient biotin dose
- For biotinidase activity 10–25%, determine whether continued treatment is necessary after the 1st year of life

COMPLICATIONS AND PROGNOSIS

- Excellent prognosis for most children if medically compliant

BIRTH TRAUMA, INTRODUCTION

DAVID BATEMAN, MD AND
CATHERINE A. HANSEN, MD

- Caused by mechanical trauma to fetus during labor &/or delivery
- Incidence estimated 5–8/1,000 births
- Risk factors for injury
  - ➢ Prolonged labor
  - ➢ Precipitous delivery
  - ➢ Abnormal fetal presentation (e.g., face, breech)
  - ➢ Difficult fetal extraction (e.g., w/ shoulder dystocia)
  - ➢ Use of forceps or vacuum
  - ➢ Nuchal cord
  - ➢ Fetal size (very large or very small)
  - ➢ Fetal anomalies predisposing to injury (e.g., osteogenesis imperfecta, hepatosplenomegaly)

BIRTH TRAUMA: BRACHIAL PLEXUS INJURY

DAVID BATEMAN, MD AND
CATHERINE A. HANSEN, MD

- Involves traction injury to cervical-thoracic nerve roots C5-T1
- Incidence 0.4–2.6/1,000 live births

HISTORY & PHYSICAL

History

- Breech or abnormal cephalic presentation (56% of brachial plexus injuries)

- Shoulder dystocia (50% of brachial plexus injuries)
- Oxytocin during labor (50% of brachial plexus injuries)
- Large fetal size (>3,500 g in 50–75% of brachial plexus injuries)
- Low Apgar score (<4 at 1 min in 39% of brachial plexus injuries)

Physical

- Typical pattern: progressive, downward involvement; cephalic to caudal
- Weak, hypotonic, hyperextended upper extremity; asymmetric Moro reflex
- Erb's palsy: C5, C6, C7; shoulder internally rotated; elbow extended; wrist flexed; hand pronated
- Erb-Klumpke's palsy: C5-T1; Erb's palsy findings + weak hand movement; absent grasp
- Assoc findings
  - ➢ Diaphragmatic palsy (~5%): involves C4, C5; paradoxical breathing pattern
  - ➢ Horner's syndrome (30% in Klumpke's palsy): involves T1; ptosis, miosis on affected side
  - ➢ Facial palsy, fractured clavicle, fractured humerus, subluxation of shoulder, cervical spine injury (5–20%)
- Extent, progress of lesion defined mainly by physical exam; persistent lesions should be monitored for recovery using standardized tool (e.g., British Muscle Movement Scale)

TESTS

- X-ray to r/o associated clavicular or humeral fracture, humeral-epiphyseal separation
- EMG, nerve conduction velocity, MRI, myelography not helpful in early mgt
- Fluoroscopy or US to confirm presence of diaphragmatic paralysis

DIFFERENTIAL DIAGNOSIS

- Physical findings of brachial plexus injury distinctive
- Asymmetric Moro reflex
  - ➢ Fracture of clavicle
    - May be assoc w/ brachial plexus palsy
    - Incidence 5/1,000 live births
    - Risk factors similar to those for brachial plexus injury, but half w/ normal labor/delivery
    - More common on right due to LOA fetal position

- Normal muscle tone; abnl Moro reflex; pain on motion; local swelling, crepitus

➢ Positive x-ray findings
➢ Fractured humerus, shoulder subluxation – distinguished by physical signs, x-ray
➢ Septic arthritis; osteomyelitis of humerus

■ Fractured humerus, subluxed shoulder

MANAGEMENT

■ Gentle immobilization of arm in 1st wk
■ Physical therapy, wrist splints after 1–2 wk to prevent contractures if persistent

SPECIFIC THERAPY

■ After partial recovery, tendon transfers can further improve shoulder external rotation & abduction
■ Microsurgery (nerve transfer or nerve grafts) has successfully restored some function in selected pts w/ persistent paralysis (see "Complications and Prognosis")

FOLLOW-UP

■ Careful neurol exams to follow progress of recovery
■ EMG, nerve conduction, myelography, CT-MRI may help define lesion at 1–4 mo of age, but physical exam remains the ultimate guide to assess recovery & decide on surgical interventions
■ Physical therapy

COMPLICATIONS AND PROGNOSIS

■ Full, spontaneous recovery in >90% of infants by 4–12 mo of age
■ Usually some improvement noted by 2 wk
■ Patterns of damage & recovery
➢ Neurapraxia: hemorrhage; edema between nerve sheath, axon: recovery
➢ Neurotmesis: axon ruptures w/in intact nerve sheath: regeneration along sheath, partial recovery
➢ Complete avulsion, rupture at nerve or nerve root: poor recovery
■ Non-recoverers
➢ Nerve root avulsion will not recover spontaneously; in these cases nerve transfer before 3 mo of age may limit motor endplate loss & maximize recovery
➢ Ruptures have varying degrees of recovery; indications & timing of microsurgery controversial; most centers recommend

transection of the neuroma & sural nerve grafting in extraforaminal ruptures btwn 3–9 mo of age
- ➢ Long-term prognosis: significant psychosocial disability

BIRTH TRAUMA: CEPHALOHEMATOMA, SUBGALEAL HEMATOMA

DAVID BATEMAN, MD AND
CATHERINE A. HANSEN, MD

HISTORY & PHYSICAL

History
- Vertex presentation, sometimes w/ forceps or vacuum assistance
- Prolonged, difficult labor; primigravidity
- Subgaleal hematoma assoc w/ vacuum extraction, coagulopathy

Physical
- Cephalohematoma
  - ➢ Fluctuant, subperiosteal hemorrhage (does not cross suture lines)
  - ➢ Slow accumulation, hours-days
  - ➢ Lateralized to one or both parietal bones
  - ➢ Transillumination negative
- Subgaleal hematoma
  - ➢ Dependent, fluctuant mass
  - ➢ May expand rapidly, leading to tachycardia, poor peripheral perfusion, pallor, oliguria
  - ➢ Crosses suture lines
  - ➢ Transillumination negative
  - ➢ Cranial molding
  - ➢ Subconjunctival hemorrhage
  - ➢ Jaundice

TESTS
- Transillumination may help differentiate an edema (caput succedaneum) from a hemorrhagic fluctuance
- Skull x-rays not usually indicated
- Hemoglobin, bilirubin w/ large-volume bleeds, clinical jaundice
- Platelet count, coagulation studies w/ subgaleal hemorrhage

DIFFERENTIAL DIAGNOSIS
- Caput succedaneum

- ➢ Edema, usually pitting not fluctuant
- ➢ Present at delivery
- ➢ Crosses suture lines
- ➢ Transillumination usually +
- ➢ Resolves quickly

MANAGEMENT
- Supportive for jaundice, anemia, hypovolemia

SPECIFIC THERAPY
- None

FOLLOW-UP
N/A

COMPLICATIONS AND PROGNOSIS
- Cephalohematoma
  - ➢ Resolves slowly (wks) w/o treatment
  - ➢ Linear skull fracture (incidence <5% if cephalohematoma is unilateral, 18% if bilateral)
  - ➢ Jaundice, anemia, thrombocytopenia, infection (rare)
  - ➢ Parental reassurance, documentation important
- Subgaleal hematoma
  - ➢ Jaundice, anemia, thrombocytopenia, hypovolemia, infection (rare)
  - ➢ Hypovolemia, shock
  - ➢ Resolves spontaneously w/ visible dependent ecchymosis

BIRTH TRAUMA, INTRAABDOMINAL INJURIES

DAVID BATEMAN, MD AND
CATHERINE A. HANSEN, MD

- Liver, spleen, adrenals: highly vascular organs susceptible to traumatic injury

HISTORY & PHYSICAL

History
- Predisposing factors
  - ➢ Breech presentation
  - ➢ Organ enlargement
  - ➢ Coagulopathy

- ➢ Asphyxia
- ➢ Storage diseases

Physical
- Enlarging RUQ or LUQ mass
- Enlarging flank mass
- Signs of hypovolemic shock (see **SHOCK**)

TESTS
- Abdominal US or CT scan
- Serial hematocrit/hemoglobin
- Serum electrolytes, glucose for adrenal hemorrhage (see **ADRENAL INSUFFICIENCY**)
- Urinalysis for hematuria

DIFFERENTIAL DIAGNOSIS
- Organomegaly w/ deteriorating clinical status may occur in:
  - ➢ Overwhelming bacterial or viral infection (e.g., congenital infection)
  - ➢ Acute congestive cardiac failure
  - ➢ Rh hemolytic disease
  - ➢ Inborn error of metabolism
- Hematuria: renal vein thrombosis – usually related to hypovolemia, hyperviscosity
- Calcifications after adrenal hemorrhage may be confused w/ neuroblastoma

MANAGEMENT
- Replace blood vol, clotting factors (see **SHOCK** in the "Supportive Care" section)
- Emergency imaging to determine cause of organ enlargement, site of hemorrhage
- Pediatric surgical consultation

SPECIFIC THERAPY
- Surgical intervention usually reserved for rupture of hematoma
- Partial preferable to complete splenectomy

FOLLOW-UP
- Neurodevelopmental w/ shock

COMPLICATIONS AND PROGNOSIS
- Prognosis for full recovery excellent for infants who receive timely supportive measures &/or surgery

- Antibacterial prophylaxis/pneumococcal vaccine after total splenectomy required
- Bilateral adrenal hemorrhage rarely results in adrenal insufficiency

BIRTH TRAUMA: INTRACRANIAL HEMORRHAGE, SKULL FRACTURES

DAVID BATEMAN, MD AND
CATHERINE A. HANSEN, MD

HISTORY & PHYSICAL

History

- Same general risk factors as other birth injuries; in particular:
  - ➢ Difficult, traumatic cephalic delivery
  - ➢ Birth asphyxia
  - ➢ Forceps delivery
  - ➢ Premature birth, lethargy, hypotonia

Physical exam

- Signs of trauma
  - ➢ Facial bruising, forceps marks
  - ➢ Caput, cephalohematoma
  - ➢ Extreme molding of skull
  - ➢ Facial nerve palsy, asymmetric crying face
- Bulging fontanels
- Altered in alertness, responsiveness, muscle tone (often dynamic, not static)
  - ➢ Hyperalertness may progress to coma
  - ➢ Hyperreflexia, clonus may progress to hypotonia
- Abnl pupillary responses, abnl eye movements, depressed suck/swallowing
- Seizures (usually multifocal)
- Apnea, bradycardia, obtundation, shock
- Skull fractures
  - ➢ Linear fractures: +/− molding, superficial scalp trauma, or cephalohematoma
  - ➢ Depressed skull fracture: palpable “ping-pong ball” depression

TESTS

- Brain imaging

- ➢ Head CT or MRI useful for depressed skull fractures, subdural, subarachnoid, infratentorial hemorrhage, edema/infarction, structural malformations
  NOTE: In the presence of head trauma, altered or deteriorating neurol condition, CT/MR scan is the only reliable way to determine presence, location of bleed that may need immediate neurosurgical attn
- ➢ Cranial US useful to detect intraventricular hemorrhage, ventricular dilatation

- LP to r/o infectious etiology for abnl neurol status (defer w/ cardioresp instability or signs of increased intracranial pressure)
- Acid-base status, electrolytes, Ca, Mg, glucose, NH3 to eval for metabolic etiology for abnl neurol status (Note: These are screening tests, not diagnostic tests.)

DIFFERENTIAL DIAGNOSIS

DDx of signs

- Intracranial hemorrhage, asphyxia may coexist; signs, symptoms may overlap
- Metabolic diseases (e.g., urea cycle defects, branched-chain amino-acidopathies, cytochrome C oxidase deficiency)
- Sepsis/meningitis
- Inherited neuromuscular disorder (e.g., congenital myasthenia or myotonic dystrophy)
- Drug withdrawal (e.g., from opiates, methadone)

DDx of intracranial hemorrhage

- Epidural hemorrhage
  - ➢ Usually assoc w/ linear skull fracture
  - ➢ Usually silent but may cause neurol deterioration if large
- Subdural hemorrhage
  - ➢ Severe cranial distortion may lacerate internal dura (tentorium, falx) & rupture adjacent venous structures (eg venous sinuses, vein of Galen, infratentorial vein)
  - ➢ Acute neurol deterioration w/ seizures, coma if hemorrhage large
  - ➢ Posterior fossa bleeds: Danger! Possible brain stem compression, rapid deterioration & death
  - ➢ Subdural hemorrhage over convexity of brain may have silent or chronic presentation
- Intraventricular, periventricular, subarachnoid hemorrhage

- ➢ VLBW infants: germinal matrix hemorrhage due to hypoxic-ischemic event
- ➢ Term infants: choroid plexus hemorrhage due to hypoxic-ischemic-traumatic event

MANAGEMENT

- Serial brain imaging
- Serial neurologic exams to detect changes in status
- Cardiorespir stabilization, supportive care (mechanical ventilation, treatment of shock, electrolyte abnormalities, hypoglycemia, etc.)
- Anticonvulsants for seizures
- Fluid restriction for CNS edema
- Antibiotics for possible sepsis/meningitis
  - ➢ Treat immediately but defer LP in presence of cardiorespir instability or signs of increased intracranial pressure
- Neurosurgical consultation for:
  - ➢ Posterior fossa hemorrhage
  - ➢ Any significant subdural or epidural hemorrhage assoc w/ altered/deteriorating neurologic status
  - ➢ Depressed skull fracture

SPECIFIC THERAPY

N/A

FOLLOW-UP

- Neurodevelopmental

COMPLICATIONS AND PROGNOSIS

- Epidural hemorrhages: good prognosis for survivors cortical injury
- Subdural hemorrhages
  - ➢ Large hemorrhage due to laceration of tentorium or falx – few survivors
  - ➢ Smaller subtentorial hemorrhage
    - Hydrocephalus, 15%
    - Major sequelae, 5–10%
  - ➢ May evolve into chronic subdural effusion (w/ lethargy, vomiting, failure to thrive) when over convexity of brain & require drainage
- Intraventricular, periventricular hemorrhage
  - ➢ Term infants
    - Most require VP shunt for hydrocephalus

- 50% have major neurol deficit; most needing VP shunt

➢ Preterm infants (see **INTRAVENTRICULAR HEMORRHAGE**)

- Skull fractures
  - ➢ Linear fractures usually heal w/o treatment; exception: "growing" skull fracture caused by arachnoid ("leptomeningeal") cyst protruding through tear in dura into fracture line, requires repair
- Depressed fracture
  - ➢ May elevate spontaneously
  - ➢ Persistent depressions & those w/ bone fragments require neurosurgical attn
  - ➢ Prognosis excellent w/o damage of underlying cortex

BLADDER EXSTROPHY

See **EPISPADIAS/BLADDER EXSTROPHY**

BROCHOGENIC CYST

See **LUNG BUD MALFORMATIONS**

BRONCHOPULMONARY DYSPLASIA (BPD)

RICHARD A. POLIN, MD

HISTORY & PHYSICAL

History

- Definition:
  - ➢ Persistent need for supplemental O_2 &/or CPAP at or after 36 wk postmenstrual age
  - ➢ Physiological definition: Inability to maintain a saturation value $\geq$90% when challenged w/ 21% oxygen
- Clinical setting
  - ➢ Classic/old BPD: infants w/ RDS, pneumonia or meconium aspiration syndrome aggressively ventilated w/ high positive airway pressure, O_2 for extended period
  - ➢ New BPD: milder disease; ELBW infants requiring only moderate concentrations of O_2 or positive-pressure ventilation

- Etiologic/associated factors
  - Pulmonary immaturity
  - Positive-pressure ventilation
  - Prolonged exposure to high FiO_2
  - Increased administration of colloid or crystalloid
  - Patent ductus arteriosus
  - Pulmonary infections
  - Poor nutrition
  - Vitamin A deficiency
  - Family Hx of asthma or reactive airway disease
  - Colonization w/ Ureaplasma
  - Chorioamnionitis (often subclinical)
- Signs and Symptoms
  - Need for supplemental O_2
  - Retractions
  - Tachypnea
  - Prolonged expiratory time
  - Expiratory wheezing
  - Rales & rhonchi

TESTS

- CXR
  - Classic/old BPD: overinflation, cystic emphysema & fibrosis
  - New BPD: diffuse haziness that progresses to fine lacy pattern
- Arterial blood gas
  - Respiratory acidosis w/ metabolic compensation
  - Need for supplemental O_2 to maintain PO_2 in normal range
- Pulmonary function testing
  - Reduced compliance
  - Maldistribution of ventilation
  - Increased physiologic dead space
- Infants receiving diuretics should have electrolytes monitored at least weekly
- Echocardiogram every 4–6 wk in infants w/severe BPD to detect cor pulmonale

DIFFERENTIAL DIAGNOSIS

Clinical setting usually diagnostic, but must consider complications:

- Congestive heart failure (see **CONGESTIVE HEART FAILURE**)
- Cor pulmonale (see below)

- Chronic aspiration/GER (see **GASTROESOPHAGEAL REFLUX**)
- Viral or bacterial pneumonia
- Tracheomalacia (see below)

MANAGEMENT

What to do first

- ABCs (airway, breathing, circulation)

General measures

- Maintain:
  - ➢ Arterial PO_2 60–80 mmHg
  - ➢ Pulse O_2 saturation >89–92%
  - ➢ pH >= 7.25
  - ➢ PCO_2 < 70 mmHg
- Aggressive nutritional support: caloric need often ranges from 125–150 cal/kg/day
- Gradual weaning of O_2 & resp support

SPECIFIC THERAPY

- Maintain Hct >=30% if infant O_2 dependent
- Antimicrobial therapy for intercurrent infections
- Fluid restriction
  - ➢ Note: Fluid intake should be minimized, but never at expense of adequate nutrition
- Patent ductus arteriosus (PDA)
  - ➢ All infants <1,000 g should have echocardiogram on day 3 of life; IF
    - Ductus arteriosus patent

    and
    - Infant requires ventilation or >0.30 FiO_2 by continuous positive airway pressure (CPAP),

    Indomethacin or ibuprofen warranted if no contraindications
  - ➢ Infants w/evolving chronic lung disease & PDA should have medical & or surgical closure of PDA
- Bronchodilators
  - ➢ Albuterol indicated for acute bronchospastic episodes
  - ➢ Inhaled albuterol &/or theophylline indicated for chronic wheezing
- Diuretics
  - ➢ Indications

- 3- to 5-day trial if IV furosemide for chronic BPD w/o improvement
  - W/ no improvement, discontinue furosemide
  - W/ improvement, change to PO diuretic
- Infants w/stable BPD who suddenly deteriorate due to excess fluid intake
- Infants who must receive increased volume to meet caloric needs

➢ Acutely improve lung function
➢ Do not facilitate extubation or shorten hospitalization
➢ Chlorothiazide & furosemide both effective
- Furosemide
  - Initial dosing should be every other day & increased to daily dose if necessary
  - Assoc w/ disturbances in acid-base balance and K+ leading to hypokalemic-hypochloremic metabolic alkalosis
  - May cause nephrocalcinosis

■ Corticosteroids
➢ Prophylactic steroids
- Not recommended
- Numerous side effects (intestinal perforation, ulceration, cerebral palsy)

➢ Therapeutic steroids for established BPD
- Not recommended except in unusual clinical circumstances or research studies
- Side effects
  - Adrenal suppression
  - Increased risk of infection
  - Hypertension
  - Hyperglycemia
  - Hypertrophic cardiomyopathy
  - Increased risk for cerebral palsy

➢ When used, should be used at the lowest effective dose & for very short duration

■ BPD spells
➢ Bronchospasm
- Infants exhibit hypercapnia & variable degrees of hypoxemia
- Spells usually brief (min to h)
- Respond to bronchodilators (see above)

■ Tracheomalacia
➢ CO_2 retention out of proportion to hypoxemia

- ➢ Spells usually brief (min)
- ➢ Good response to increased CPAP levels
- ➢ Fluoroscopy or pulmonary function testing can help determine amount of CPAP needed to stent open trachea

- Pulmonary hypertension
  - ➢ Spells may last for days
  - ➢ Hypoxemia usually out of proportion to CO_2 retention
  - ➢ Generally responds to ventilation w/ high concentrations of O_2
  - ➢ Data on nitric oxide are insufficient to recommend
- Gastroesophageal reflux (see **GASTROESOPHAGEAL REFLUX**)

FOLLOW-UP
- Developmental, neurologic
- Hearing screen after ototoxic drugs (furosemide, aminoglycosides)
- Echocardiography w/cor pulmonale
- Growth

COMPLICATIONS AND PROGNOSIS
- Uncertain whether BPD as independent variable increases risk of neurological handicaps, but is associated
- Infants w/severe BPD at increased risk for cor pulmonale, increasing risk of death
- After hospital discharge mortality rate in infants w/BPD is ~10%
- Exercise tolerance good in survivors, but pulm function abnormalities persist

CANDIDIASIS, CONGENITAL

J.M. LORENZ, MD

- Transmission: intrauterine (hematogenous or ascending w/ROM?) or intrapartum due to massive maternal vaginal colonization
- *C. albicans* most common etiologic species
- Uncommon

HISTORY & PHYSICAL
- Risk factors: prolonged ROM, uterine foreign body
- Presents w/in first 24 h of life as:
  - ➢ Widespread erythematous maculopapular rash evolving to vesicles/pustules
  - ➢ Pneumonia, esp preterm infants

TESTS
- Nonspecific
  - ➢ Nodular or alveolar infiltrates on CXR w/pneumonia
  - ➢ W/ dissemination: see **CANDIDIASIS, SYSTEMIC**
- Specific
  - ➢ Positive Gram stain of vesicle/pustule content, KOH prep of skin scrapings, culture of skin fold or vesicle/pustule content
  - ➢ W/ dissemination: see **CANDIDIASIS, SYSTEMIC**

DIFFERENTIAL DIAGNOSIS
See **SEPSIS/PNEUMONIA, EARLY-ONSET**

MANAGEMENT
- Supportive therapy
- Infection control: none beyond universal precautions

SPECIFIC THERAPY
- Prevention: appropriate Dx & Rx of maternal vaginosis & UTI during pregnancy
- Treatment
  - ➢ Cutaneous infection: topical anti-candidal agents (e.g., clotrimazole, ketoconazole, nystatin)
  - ➢ In preterm infant or w/ pneumonia: systemic antifungal therapy (see **CANDIDIASIS, SYSTEMIC**)

FOLLOW-UP
- Infection limited to cutaneous involvement: close surveillance for systemic infection
- W/ pneumonia, disseminated disease
  - ➢ Serial blood/urine/CSF cultures
  - ➢ Indirect ophthalmoscopy, echocardiogram, renal US, head US
  - ➢ Serial CBC, serum electrolytes, Mg, creatinine, urine output, liver function tests for drug toxicity
- Long-term w/ recovery w/o dissemination: none

COMPLICATIONS AND PROGNOSIS
- Complications
  - ➢ Extensive skin desquamation in the preterm infant may lead to fluid & electrolyte disturbances, secondary bacterial infection
  - ➢ Hematogenous dissemination (see **CANDIDIASIS, SYSTEMIC**) uncommon; more likely w/ prematurity, widespread cutaneous involvement, central venous catheters

- Prognosis
  - ➢ Good if limited to cutaneous involvement
  - ➢ W/ disseminated disease (see **CANDIDIASIS, SYSTEMIC**)

CANDIDIASIS, SYSTEMIC AND CATHETER-RELATED CANDIDEMIA

J.M. LORENZ, MD

- *Candida albicans* colonizes the skin, GI tract, or female genital tracts of 5% of NICU admissions, 50% of pts after 1 wk in NICU, 75% after 1 mo
- *C. albicans, C. parapsilosis* most common etiologic species
- Transmission is vertically from mother at vaginal birth (primary rout for *C. albicans*), via breast feeding, & via health care workers (primary route for *C. parapsilosis*)
- Prevalence of systemic disease
  - ➢ Birth wt < 1,500 g: 2–10%
  - ➢ Birth wt > 2,500 g in NICUs: <1% (usually assoc w/ major congenital anomalies, complex surgery)
- Risk factors for systemic disease
  - ➢ Prematurity (esp <28 wk, <1,500 g)
  - ➢ Broad-spectrum antibiotic Rx
  - ➢ Corticosteroid Rx
  - ➢ Intravascular catheters, esp central venous catheters
  - ➢ Administration of parenteral nutrition, esp high-dextrose conc solutions
  - ➢ Administration of IV lipid emulsions
  - ➢ Neutropenia
  - ➢ Hyperglycemia
  - ➢ Abdominal surgery, cardiac surgery
  - ➢ Necrotizing enterocolitis, spontaneous intestinal perforation
  - ➢ Malnutrition
  - ➢ Urethral, intraventricular catheters
  - ➢ Prolonged intubation
  - ➢ Candida diaper dermatitis in preterm infants

HISTORY & PHYSICAL

- See **SEPSIS**, **NOSOCOMIAL** and **MENINGITIS**
  - ➢ Mean age at dx: 20–40 days

TESTS

- Nonspecific
  - ➢ Thrombocytopenia & hyperglycemia are common presenting signs
  - ➢ Neutrophilia, neutropenia, increased I:T
  - ➢ Increased C-reactive protein
  - ➢ W/ pneumonia: infiltrates on CXR
  - ➢ W/ meningitis: CSF pleocytosis, hypoglycorrhachia, increased protein; Gram stain usually negative (nl CSF & negative CSF culture do not exclude CNS involvement)
  - ➢ W/ renal involvement: hematuria, proteinuria, pyuria
- Specific
  - ➢ + blood (peripheral & indwelling catheters if present), urine, CSF culture, or other usually sterile body site
    Note: + blood from intravascular catheter or urine from indwelling urethral catheter catheter-related *candidemia*/*candiduria*, i.e., w/o tissue invasion
  - ➢ Serial cultures increase the likelihood of confirming candidemia, but persistently negative blood cultures do not exclude disseminated disease (specificity 100%, but sensitivity for disseminated disease ranges from 30% with 1 involved organ to 80% with 4)
  - ➢ Any growth from urine obtained by SPA specimen or $>10^4$ col/mL by sterile urethral catheter = + urine culture
  - ➢ Budding yeast/hyphae in urine obtained by suprapubic aspiration or by sterile urethral catheter
  - ➢ Std bacteriologic culture medium is adequate; separate fungal cultures not necessary
  - ➢ 90% of + cultures will be positive by 72 hr, before & immediately after the initiation of antifungal Rx
  - ➢ Gram stain of buffy coat
  - ➢ Pleural, peritoneal, joint fluid culture as indicated
  - ➢ Molecular assays for *Candida sp* proteins & DNA have not been evaluated in newborns
  - ➢ Positive Gram stain or culture of endotracheal tube aspirates NOT diagnostic of pneumonia; may represent colonization
  - ➢ Positive mouth, nasopharyngeal, skin, stool culture NOT diagnostic of disseminated infection
  - ➢ W/ candiduria or documented or suspected candidemia
    - Cranial imaging (head US at a minimum)
    - Renal US

- Echocardiography
- Dilated ophthalmologic exam by pediatric ophthalmologist

DIFFERENTIAL DIAGNOSIS

See **SEPSIS, NOSOCOMIAL** and **MENINGITIS**

MANAGEMENT

- Supportive therapy
- Remove intravascular/urethral/intraventricular catheters
- Infection control: none beyond universal precautions

SPECIFIC THERAPY

- Prevention
  - ➢ Strict aseptic technique in preparation of parenteral nutrition fluid, manipulation of indwelling catheters
  - ➢ Limit use of broad-spectrum antibiotics, indwelling catheters to extent possible
  - ➢ No data supporting efficacy of prophylactic oral nystatin
  - ➢ Fluconazole prophylaxis not recommended
    - Dose, duration, indication not defined
    - Safety not established
    - Emergence of resistance reported
- Treatment
  - ➢ Systemic *candidiasis*: evidence of focal infection or persistently + blood or urine culture after removal of indwelling catheters
    - First line: Amphotericin B deoxycholate
      Dose: initially 00.5 mg/kg IV over 2–6 h, then 1 mg/kg q24-48h; test dose is not indicated
      Duration: minimum of 14 days after negative cultures, resolution of clinical signs (incl fungal abscesses, renal lesion, intracranial lesions, right atrial fungal balls)
      Side effects: phlebitis, hypokalemia, hyponatremia, hypomagnesemia, renal tubular acidosis, azotemia, oliguria, anemia, thrombocytopenia
    - Second line (w/ renal impairment or inadequate response to Amphotericin B): Amphotericin B liposome
      Dose: 1 mg/kg IV over 2 h first day; increase dose 1 mg/kg qd to 5 mg/kg q day (use higher dose w/ meningitis, osteomyelitis)
      Duration: minimum of 14 days after negative cultures, resolution of clinical signs (incl fungal abscesses, renal lesion, intracranial lesions, right atrial fungal balls)

Side effects (less nephrotoxic than Amphotericin B): anemia, thrombocytopenia, hypokalemia, increased transaminases, direct bilirubin

- Third line (recommended only after *Candida sp* is identified & susceptibility is confirmed): Fluconazole

  Loading dose: 12 mg/kg; maintenance dose: 6 mg/kg; route: IV over 30 min initially; completion of course w/ oral Rx acceptable

  Dose interval: depends on postmenstrual age (PMA) & postnatal age (PNA)

  PMA, PNA, interval:
  <= 29 wk, 0–14 days, q72h
  <= 29 wk, >14 days, q48h
  30–36 wk, 0–14 days, q48h
  30–36 wk , >14 days, q24h
  37–44 wk, 0–7 days, q48h
  37–44 wk, > 7 days, q24 h
  >= 45 wk, any, q24h

  Duration: 4–6 wk

  Duration: minimum of 14 days after negative cultures, resolution of clinical signs (incl fungal abscesses, renal lesion, intracranial lesions, right atrial fungal balls)

  Side effects: eosinophilia, transient thrombocytopenia, increased creatinine, mild hyperbilirubinemia, transient increases in transaminases

  Primary concern: potential for development of resistance

- NOTE: Monotherapy w/ 5-flocytocone is contraindicated because of rapid development of resistance

➢ CNS infection: consider adding fluconazole or 5-flucytocine, which have excellent CSF penetration, to Amphotericin B

➢ *Catheter-related candidemia*: + catheter blood culture w/ NEGATIVE peripheral blood culture, no focal signs, negative CSF, negative CNS imaging, negative indirect ophthalmoscopy, negative echocardiogram, & negative renal US w/o persistently positive blood or urine cultures after catheter removal

- Remove catheter as soon as possible
- Same drugs & doses as for disseminated disease
- Duration: 7–10 days

➢ *Urethral catheter-related candiduria*: same as for catheter-related candidemia

- Remove catheter

- Same drugs, doses as for disseminated disease; however, fluconazole (6 mg/kg qd) is an excellent alternative to Amphotericin B for susceptible *Candida sp* because it is excreted unaltered in the urine
- Duration: 7–10 days

FOLLOW-UP

- During systemic Rx
  - ➢ Serial blood/urine/CSF cultures
  - ➢ Indirect ophthalmoscopy, echocardiogram, renal US, head US
  - ➢ Serial CBC, serum electrolytes, creatinine, urine output, liver function tests for drug toxicity
- Long-term
  - ➢ Developmental, neurologic
  - ➢ Ophthal w/ endophthalmitis or if preterm

COMPLICATIONS AND PROGNOSIS

- Complications
  - ➢ Endocarditis, right atrial fungal ball
  - ➢ Renal pelvic fungal mass, parenchymal infiltration, acute renal failure, hypertension
  - ➢ Deep organ microabscesses
  - ➢ Endophthalmitis (6% of VLBW infants w/systemic disease)
  - ➢ Meningitis, ventriculitis, parenchymal abscesses (as many as 50% of VLBW infants w/ systemic disease)
  - ➢ Septic arthritis/osteomyelitis
  - ➢ Peritonitis
  - ➢ Empyema
  - ➢ Skin abscesses
- Prognosis
  - ➢ Assoc w/ increased risk of chronic lung disease, periventricular leukomalacia, threshold retinopathy of prematurity
  - ➢ 10–15% mortality; increased w/ delayed Dx, persistently + blood cultures >24 h after initiation of Rx; prematurity
  - ➢ 2- to 3-fold increase in developmental disability

CARDIAC ARRHYTHMIAS

ZVI S. MARANS, MD

HISTORY & PHYSICAL

History

- Irritability, poor feeding, listlessness
- Elevated, slow, or irregular fetal heart rate (HR)

Signs

- Abnormality in HR
  - ➢ Regular & rapid
  - ➢ Irregular HR: rapid, normal or slow
  - ➢ Slow HR
- Color change
  - ➢ Pallor due to decreased cardiac output
  - ➢ Cyanosis
    - Central cyanosis due to associated CHD
    - Peripheral cyanosis due to decreased cardiac output
- Respiratory distress
- Poor perfusion
  - ➢ Decreased pulses
  - ➢ Prolonged capillary refill
  - ➢ Cool extremities
- Auscultation
  - ➢ Murmur
  - ➢ Gallop rhythm
- Hepatomegaly

TESTS

- 12-lead ECG essential, rhythm strip from monitor not adequate
- No need for further testing to commence urgent treatment

Other tests

- CXR
- Echocardiogram
- Arterial blood gas
- Serum electrolytes, ionized Ca, Mg

DIFFERENTIAL DIAGNOSIS

- Narrow complex tachycardia
  - ➢ Supraventricular tachycardia (SVT)
  - ➢ Atrial flutter (AF)

- Wide complex tachycardia
  - SVT w/ aberrancy
  - Ventricular tachycardia (VT): might have narrower QRS complex, esp in newborns
- Bradycardia
  - Complete heart block (CHB): maternal antibodies (e.g., systemic erythematous lupus)
  - Sinus bradycardia
- Irregular HR
  - Atrial premature beats
  - Ventricular premature beats
  - Chaotic rhythms

MANAGEMENT

- DOCUMENT ARRHYTHMIA WITH 12-LEAD ECG!
- Maintain ABCs (airway, breathing, circulation)

SPECIFIC THERAPY

Tachyarrhythmia

- Acute Rx
  - In hemodynamically unstable neonate w/ tachycardia, DC cardioversion immediately indicated, even before intubation/IV access
  - Adenosine will terminate SVT; it is diagnostic in AF, temporarily blocks conduction through the atrioventricular node, unmasking flutter waves
  - If adenosine not effective, first-line drug therapy to terminate most common tachyarrhythmias (SVT, AF): digoxin, total digitalizing dose of 20–30 mcg/kg IV, divided in 3 doses over 8–24 h (less in premature infants)
  - SVT resistant to digoxin: procainamide may be added; beta-blocker, sotalol, flecainide or amiodarone sometimes used
  - 12-lead ECG following resolution of arrhythmia; look for pre-excitation (Wolff-Parkinson-White [WPW] syndrome)
- Maintenance Rx
  - SVT/AF prevention: digoxin maintenance dose of 6–8 mcg/kg/day IV divided BID or 8–10 mcg/kg/day (or higher) PO divided BID (less in premature infants); in context of pre-excitation, beta-blocker is preferable for maintenance
  - VT: lidocaine
  - Rx underlying problem, if identified: electrolyte abnormality, CHD, cardiac tumor, etc.

Bradyarrhythmia

- Long-standing bradycardia due to congenital complete heart block usually very well tolerated, no urgent intervention necessary
- Sinus bradycardia in distressed newborn often preterminal
- Atropine, isoproterenol, temporary intracardiac pacing can be used in emergency setting

Irregular HR

- Single premature supraventricular, ventricular beats, even if frequent, rarely need to be treated
- In stable neonates, can monitor chaotic rhythms initially w/o treatment

FOLLOW-UP

- During hospitalization
  - ➢ Frequent ECGs
  - ➢ Cardiac monitor
- Outpatient
  - ➢ Early office follow-up
  - ➢ ECG, Holter monitor, event recorder
  - ➢ Careful attn & rapid medical response to generalized symptoms, e.g., irritability
  - ➢ Electrophysiologic testing for difficult/complex cases
- Duration of therapy
  - ➢ Depends on underlying arrhythmia
  - ➢ Most tachyarrhythmias treated for 3–12 mo; meds discontinued if there are no breakthrough episodes

COMPLICATIONS AND PROGNOSIS

- Neonatal AF: excellent prognosis, most do not recur after newborn period
- SVT: good prognosis
  - ➢ Most cases come under excellent control
  - ➢ Some "burn out"
  - ➢ Others, esp WPW, may persist
  - ➢ Radiofrequency ablation (when child is older) curative in 80–95% of patients w/ SVT
- Bradycardia due to congenital CHB never resolves, ultimately requires elective pacemaker placement
- Sudden death: rare complication in pediatric arrhythmias, but can occur, esp in association w/ CHB, VT

CEREBELLAR HEMORRHAGE

HELEN M. TOWERS, MD

HISTORY & PHYSICAL

History

- Difficult breech delivery in term infants
- Cranial deformations, occipital diastasis
- Hypoxic ischemic encephalopathy
- Severe respiratory distress in premature infants

Signs

- Appear w/in 1st 3 wks of life, most w/in 1st 2 days
- Catastrophic clinical deterioration w/ apnea, bradycardia, drop in Hct
- Stupor or coma
- Cranial nerve abnormalities
- Opisthotonos

TESTS

- CBC, platelets
- Coagulation studies
- CT
- MRI
- Occasionally cranial US demonstrates cerebellar hemorrhage

DIFFERENTIAL DIAGNOSIS

Other forms of intracranial hemorrhage (see: **INTRAVENTRICULAR HEMORRHAGE, SUBARACHNOID HEMORRHAGE, SUBDURAL HEMORRHAGE**)

MANAGEMENT

- Conservative mgt vs. surgical intervention depending on size of hemorrhage & clinical state of infant
- Supportive care w/ fluids, ventilation
- PRBC transfusion prn
- Correct coagulopathy prn

SPECIFIC THERAPY

N/A

FOLLOW-UP
- Neurologic, neurodevelopmental
- Repeat cranial US or CT imaging

COMPLICATIONS AND PROGNOSIS
- Preterm infants w/ severe intracerebellar hemorrhage: poor prognosis
  - ➢ Significant motor, cognitive impairment result
  - ➢ Hydrocephalus
- Term infants: intention tremor, dysmetria, truncal ataxia, hypotonia

CHARGE SYNDROME

KWAME ANYANE-YEBOA, MD

- Etiology: majority due to autosomal dominant mutations in Chromodomain helicase DNA-binding protein-7 gene (CHD7) gene, but mutations also identified in the Semaphorin-3E (SEMA3E) gene

HISTORY & PHYSICAL

Frequent
- **C**oloboma, most often of retina (80%)
- **H**eart defect: tetralogy of Fallot, PDA, ASD, AV canal, double outlet RV, right-sided aortic arch (85%)
- **C**hoanal atresia (57%)
- **R**etardation of postnatal growth (87%) & mild to profound mental retardation (95%)
- **G**enital hypoplasia in males (75%)
- **E**ar malformation 91% &
- Deafness: sensorineural or mixed (60–88%)

Less frequent
- Micrognathia
- Cleft palate
- DiGeorge sequence
- Feeding difficulties
- Ptosis
- Anal atresia
- Renal malformations
- Microcephaly
- Hypogonadotrophic hypogonadism

- Growth hormone deficiency
- Omphalocele
- Tracheo-esophageal fistula
- Congenital facial palsy
- Antimongoloid slant of palpebral fissures

TESTS
- CHD7 gene mutation screen (for a list of labs offering test go to www.genetests.com)
- Chromosome studies to exclude translocations & deletions
- BAER to assess auditory pathway

DIFFERENTIAL DIAGNOSIS
N/A

MANAGEMENT
- Genetic evaluation & counseling
- Cardiac, ENT, audiology, GI, neurodevelopmental
- Other consultations as appropriate
- Nasogastric feeds & gastrostomy tube feeds if indicated
- Correction of choanal atresia
- Physical, occupational & speech therapies

SPECIFIC THERAPY
- None

FOLLOW-UP
- Cardiac, ENT, GI & other consultations as appropriate

COMPLICATIONS AND PROGNOSIS
- Overall prognosis poor w/ significant growth & developmental delay
- Poor vision, when colobomas involve optic nerve head

CHOANAL ATRESIA, BILATERAL

J.M. LORENZ, MD

- Prevalence 1:7,000 live births
- Male:female = 1:2
- Obstruction predominantly bony in 90%
- 0–50% of newborns may not initiate oral breathing w/ nasal occlusion

HISTORY & PHYSICAL

- History
  - ➢ Severe respiratory distress immediately after delivery
  - ➢ Cyclic respiratory distress relived by crying
  - ➢ Cyanosis w/ sucking
- Physical signs
  - ➢ Cyanosis, severe retractions, absent breath sounds
  - ➢ Inability to pass 6-Fr suction catheter into oropharynx via nares
  - ➢ Assoc congenital anomalies in 20–50%
    - Most commonly, CHARGE association (colobomas, heart defects, atresia choanae, genital hypoplasia in males, ear anomalies/deafness)
    - Congenital heart disease
    - Brachial arch defects
    - Ear anomalies
    - Microcephaly
    - Micrognathia
    - Palatal defects
    - Nasopharyngeal defects
    - Mandibulofacial dysostosis

TESTS

- Flexible nasopharyngoscopy
- Axial CT scan (after thorough suctioning of nares & topical decongestant)
- Echocardiogram
- W/ assoc anomalies, chromosome studies to exclude translocations & deletions

DIFFERENTIAL DIAGNOSIS

- Airway obstruction due to amniotic fluid debris, meconium, improper mask ventilation technique, hypotonia much more common
- Severely decreased lung compliance due to pulm hypoplasia, pneumonia
- Anterior nasal obstruction due to severe nasal pyriform aperture stenosis
- Nasopharyngeal obstruction
  - ➢ Encephalocele
  - ➢ Tumor
- Laryngeal obstruction: atresia, web

MANAGEMENT

What to do first

- Establish airway: oral airway, McGovern nipple, or orotracheal intubation

General Measures

- Resuscitate as required
- Gavage feeding
- Genetic consultation w/ assoc anomalies

SPECIFIC THERAPY

- ENT consultation for elective surgical resection

FOLLOW-UP

- ENT (incl hearing test)

COMPLICATIONS AND PROGNOSIS

- Complications
  - ➢ Asphyxia
  - ➢ Postoperative infection
  - ➢ Postoperative stenosis
- Prognosis
  - ➢ Good: w/ prompt resuscitation, depending on assoc anomalies
  - ➢ Poor: postnatal growth & mental retardation w/ CHARGE association
  - ➢ Surgical revision commonly required

CLOACAL EXSTROPHY

See **EPISPADIAS/BLADDER EXSTROPHY**

COAGULOPATHY

See **HEMORRHAGIC DISORDERS**

COARCTATION OF THE AORTA (COA)

KALYANI R. TRIVEDI, MD, AND LEE N. BENSON, MD
REVISED BY GANGA KRISHNAMURTHY, MD

- CoA is typically a discrete stenosis of the juxtaductal region of the proximal thoracic aorta
- Incidence 6–8% of pts w/ CHD
- May be isolated (simple) or associated w/ other defects (complex, e.g., bicuspid aortic valve, arch hypoplasia, VSD, PDA, aortic or mitral stenosis, subaortic stenosis, Shone's complex, TGA)
- 35% of pts w/ Turner's syndrome can be affected w/ CoA

HISTORY & PHYSICAL

History

- Presentation in the newborn period in CHF or shock (w/ closure of ductus arteriosus)

Signs

- "Shocky" state in neonates presenting in CHF
- Tachypnea, tachycardia, UE BP > LE BP (if CO is low there may not be a BP differential), +/− hypotension, O_2 saturation lower in LE than UE
- Retractions, +/− rales
- Active precordium, RV heave, normal S1; S2 can be loud w/ pulmonary hypertension; gallop rhythm in CHF; +/− ejection click (indicates bicuspid aortic valve); +/− systolic murmur in left upper sternal border & left interscapular area (CoA murmur), other murmurs based on assoc defects; poorly felt LE pulses, poor perfusion
- Hepatomegaly in CHF

TESTS

- Arterial blood gases for metabolic acidosis
- Serum arterial lactate
- BUN/Creatinine
- LFTs
- CXR: cardiomegaly, pulmonary venous congestion/pulmonary edema
- ECG: usually normal in newborn period; LVH in older children
- Echocardiogram
  - ➢ Posterior shelf in the juxtaductal region

- ➢ Diminished systolic peak on abdominal descending aortic Doppler profile
- ➢ Diastolic runoff on Doppler flow profile across coarctation
- ➢ High flow velocity across coarctation
- ➢ Doppler evidence of elevated RVP by TR jet
- ➢ Associated cardiac defects

DIFFERENTIAL DIAGNOSIS
- Critical aortic stenosis
- Hypoplastic left heart syndrome
- Sepsis
- Non-cardiogenic causes for shock (see **SHOCK**)

MANAGEMENT

General measures
- ABC (airway, breathing, circulation)
- Fluid resuscitation
- Correction of metabolic acidosis
- PGE1 for ductal patency
- Inotropic support
- Monitor cardiac output/post-coarctation perfusion w/ serial arterial blood gases & lactates

SPECIFIC THERAPY
- Via a lateral thoracotomy: surgical resection of coarctation & end-to-end anastomosis
- Via median sternotomy for long-segment stenosis, arch hypoplasia & other associated cardiac defects that need repair
- Other surgical techniques: extended end-to-end anastomosis, patch aortoplasty, subclavian flap aortoplasty

FOLLOW-UP
- Check for UE to LE BP differential due to re-coarctation in 10%; may be managed w/ transcatheter balloon angioplasty
- Follow BP due to risk for persistent hypertension

COMPLICATIONS AND PROGNOSIS
- Surgical mortality for simple CoA ~0%
- Surgical mortality for complex CoA 5–15%
- Postoperative complications: re-coarctation, postoperative paradoxical hypertension (seen in older children), recurrent laryngeal nerve paralysis, phrenic nerve paralysis, chylothorax

- Persistent systemic hypertension w/ corrective surgery delayed beyond 5 yr of age

CONGENITAL ADRENAL HYPERPLASIA

THOMAS WILSON, MD

HISTORY & PHYSICAL

History

- Family Hx of:
  - Adrenal disease
  - Early neonatal demise
  - Shock
  - Genital ambiguity
  - Hyponatremia
  - Hyperkalemia
- Signs
  - Ambiguous genitalia
  - Dehydration
  - Vomiting
  - Hypotension, shock
  - Pigmented genitalia
  - Pigmented areolae
  - Hyponatremia
  - Hyperkalemia

TESTS

- Serum & urine electrolytes
- Serum glucose
- Serum creatinine
- Urinalysis
- 17-OH-progesterone, androstenedione
- Testosterone
- Cortisol
- Aldosterone
- ACTH
- Plasma renin activity
- Karyotype w/ ambiguous genitalia
- Sepsis workup
- Other steroidogenic precursors if 17-OHylase deficiency not present

- ➢ 11-desoxycortisol
- ➢ 17-OH-pregnenolone
- ➢ DHEA, DHEAS

- With ambiguous genitalia
  - ➢ Pelvic ultrasound to determine presence of uterus
- Optional
  - ➢ Cortisol & 17-OH-progesterone response to Cortrosyn:
    - Baseline serum cortisol
    - Give Cortrosyn 250 mcg/m^2 IV
    - Obtain serum cortisol & 17 OH-progesterone at 60 min
    - Normal: peak cortisol > 18 mcg/dL
    - See nomogram in Pediatric Endocrinology text for normative 17-OH progesterone response
- If adrenal hypoplasia suspected – cholesterol & triglycerides [triglycerides elevated in glycerol kinase deficiency (closely linked to the adrenal hypoplasia gene (DAX1) on X chromosome)]
- If adrenaleukodystrophy suspected
  - ➢ Long-chain fatty acids
  - ➢ CT or US of abdomen & pelvis
    - Adrenal hemorrhage
    - Adrenal calcifications
      - Wolman disease
      - Old adrenal hemorrhage
- If 5-alpha-reductase suspected: dihydrotestosterone/testosterone
- If androgen insensitivity syndrome suspected: androgen receptor gene analysis

DIFFERENTIAL DIAGNOSIS

- DDx of signs
  - ➢ Sepsis
  - ➢ Other causes of hypoglycemia (see **HYPOGLYCEMIA**)
  - ➢ Acute renal failure
  - ➢ Acute UTI
  - ➢ Obstructive uropathy
  - ➢ Gastroenteritis
  - ➢ Pyloric stenosis
  - ➢ Na-losing nephropathy
  - ➢ Hypoaldosteronism
  - ➢ Pseudohypoaldosteronism
  - ➢ Other disorders of sexual differentiation
    - Disorders of testosterone or dihydrotestosterone synthesis

- Androgen insensitivity syndrome
- Chromosome abnormalities
- Syndromes w/ ambiguous genitalia

■ DDX of etiology of adrenal insufficiency (see ADRENAL INSUFFICIENCY)
  ➢ Congenital adrenal hypoplasia
    - X-linked form
      - Partial X deletion
      - Deletion/mutation of DAX1
    - Autosomal recessive form
      - Deletion/mutation of SF1
  ➢ Adrenal hemorrhage (w/difficult delivery/asphyxia)
  ➢ Wolman syndrome
    - Liposomal storage disease
    - Acid lipase deficiency
    - Hepatomegaly
    - Autosomal recessive
  ➢ Adrenoleukodystrophy
    - Usually later in childhood
    - Often with neurological symptoms
    - X-linked

MANAGEMENT

■ Dextrose to correct hypoglycemia
  ➢ D10W 2–4 cc/kg IV push
  ➢ Then dextrose at 4–6 mg/kg/min
  ➢ Maintain serum glucose > 50 mg/dL
■ Fluid, electrolytes to correct shock
  ➢ If hypotensive, 10–20 mL/kg D5W NS or D5W 0.5% NS, then 100–200 cc/kg/d
  ➢ If hyperkalemic: (withhold K; see **HYPERKALEMIA** for treatment to lower serum K)
■ Obtain baseline serum cortisol, aldosterone, 17-OH progesterone, ACTH and 1st urine electrolytes BEFORE BEGINNING STEROID Rx

SPECIFIC THERAPY

■ Hydrocortisone
  ➢ Acute
    - 2 mg/kg IV push, then 2 mg/kg/day divided q6h
    - If salt wasting, 5–10 mg/kg IV push, then 5–10 mg/kg/d q6h
  ➢ Chronic: 0.5–1 mg/kg/day or 10–25 mg/m^2/day

- If mineralocorticoid deficient
  - ➢ Fludrocortisone 0.1–0.2 mg/day
  - ➢ Na supplements of 2–5 g NaCl/day PO (necessary until old enough to forage for salt)
- Stress management
  - ➢ Increase glucorticoids 3-fold
  - ➢ Counsel & train parents
  - ➢ For NPO/vomiting patient: hydrocortisone 50–100 mg/m^2/day IV/IM div q6–8h
- Steroid potencies
  - ➢ Relative glucorticoid effect
    - Hydrocortisone 1
    - Prednisone 4
    - Methylprednisone 5
    - Dexamethasone 50
    - Fludrocortisone 12
  - ➢ Relative mineralocorticoid effect
    - Hydrocortisone 1
    - Prednisone 0.75
    - Methylprednisone 0.5
    - Dexamethasone 0
    - Fludrocortisone 125

FOLLOW-UP

- Monitor:
  - ➢ Growth
  - ➢ Blood pressure
  - ➢ Serum glucose
  - ➢ Electrolytes
  - ➢ Plasma renin activity
  - ➢ ACTH
  - ➢ 17-OH-progesterone w/ adrenal hyperplasia
- Counseling
  - ➢ For ambiguous genitalia
    - Issues of rearing
    - Sex assignment
    - Need for surgery (extent & timing controversial)
  - ➢ Management of illnesses
  - ➢ Stress doses of steroid
  - ➢ Recurrence risk
  - ➢ Prenatal treatment & diagnosis

- ➢ Genetic counseling for future pregnancies
- ➢ Counseling for associated disorders

COMPLICATIONS AND PROGNOSIS

Complications of Rx

- Excessive glucocorticoid: poor growth
- Excessive fludrocortisone
  - ➢ Hypertension
  - ➢ Hypokalemia

Prognosis

- Death if:
  - ➢ Adrenal insufficiency untreated
  - ➢ Stress not covered w/ steroids
  - ➢ Recurring shock, dehydration & hypoglycemia
  - ➢ Hyperkalemia inadequately treated
- Prognosis good if adequately treated

CONGENITAL DIAPHRAGMATIC HERNIA

CHARLES J.H. STOLAR, MD

HISTORY & PHYSICAL

- Usually diagnosed antenatally: heart & stomach in same plane on US; polyhydramnios
- Diagnosed postnatally in term newborn w/ significant resp distress, asymmetric breathing, scaphoid abd
- May be assoc w/ congenital heart disease
- No pattern of inheritance

TESTS

- CXR
- Echocardiogram

DIFFERENTIAL DIAGNOSIS

- Cystic adenomatoid malformation, congenital, pulmonary (see **LIMB BUD MALFORMATIONS**)
- Diaphragm eventration

MANAGEMENT

- Intubation ASAP after birth, do not suppress spontaneous respiration, permissive hypercapnea, minimize baro/volutrauma

- Base treatment decisions on ***preductal*** SaO_2
- Experience w/ nitric oxide, surfactant, oscillating ventilators largely anecdotal
- ECMO only w/:
  - ➢ Evidence of sufficient lung development based on preductal SaO_2

  and
  - ➢ Expected mortality >90% despite best conventional care
- Elective operation when stable & weaned from most resp support
- Reduce hernia, build diaphragm, close abd at operation
- Continue above resp strategy postop

SPECIFIC THERAPY
N/A

FOLLOW-UP
Coordinated multidisciplinary (Surg, Pulm, Cardiol, Developmental, GI) follow-up optimal

COMPLICATIONS AND PROGNOSIS
- Chronic lung disease
- Pulm hypertension
- Most pts survive w/ normal heart/lung function, but should be followed as needed
- Foregut dysmotility most persistent problem; usually managed by prokinetic agents/H2 blockers; surgery seldom needed except when stomach will not empty

CONJUNCTIVITIS (OPHTHALMIA NEONATORUM)

J.M. LORENZ, MD

HISTORY & PHYSICAL
- Prevalence: ~2% of live births
- History
  - ➢ Type of gonococcal eye prophylaxis
  - ➢ Maternal STDs
  - ➢ Maternal genital herpes
  - ➢ Positive maternal culture for *Chlamydia trachomatis*
  - ➢ Maternal rubella status
  - ➢ Forceps delivery

- Physical
  - ➢ Injected, edematous conjunctiva
  - ➢ Watery discharge to purulent exudate
  - ➢ Swollen palpebrae
  - ➢ Preauricular lymphadenopathy
  - ➢ Corneal clouding w/ assoc keratitis
  - ➢ Cough, rhinorrhea, rash w/ viral conjunctivitis
  - ➢ Signs c/w sepsis, meningitis w/ *Staphylococcus aureus*, *Neisseria gonorrhoeae*, *Pseudomonas aeruginosa* conjunctivitis
  - ➢ Red, swollen, tender joints w/ gonococcal septic arthritis
  - ➢ +/− signs c/w congenital rubella
  - ➢ +/− signs c/w congenital syphilis
  - ➢ +/− signs c/w herpes simplex infection

TESTS

- Gram stain of exudate
- Fluorescent staining of cornea
- Giemsa &/or direct immunofluorescent staining of scrapings taken from lower palpebral conjunctiva after exudate removal (sensitivity 22–95% for chlamydiae depending on collection technique & examiner's skill)
- Enzyme immunoassay or direct fluorescent staining or enzyme immunoassay of scrapings taken from lower palpebral conjunctiva after exudate removal (sensitivity > 90%, specificity >/= 95% for chlamydiae)
- Cultures
  - ➢ Routine bacterial
  - ➢ Thiocyanate broth culture for *N. gonorrhoeae*
  - ➢ Chlamydial tissue culture of conjunctival scrapings
  - ➢ Viral (optional unless herpes simplex possible)
- Ophthalmologic consultation for exam as indicated

DIFFERENTIAL DIAGNOSIS

- Non-infectious (Gram stain of exudate usually negative for bacteria, though not excluded by bacteria on Gram stain; latter may be commensal)
  - ➢ Chemical conjunctivitis
    - Due to topical Ag nitrate when used for gonococcal prophylaxis; most common cause of neonatal conjunctivitis
    - Much less common w/ erythromycin prophylaxis
    - Usually presents 6–24 h after birth, spontaneously resolves in 24–48 h
  - ➢ Congenital glaucoma

- Enlarged (>9.5 mm diameter at term), cloudy cornea w/ photosensitivity & tearing
- Increased intraocular pressure

➢ Birth trauma (usually secondary to forceps delivery): presents soon after birth w/ unilateral corneal clouding w/o purulent exudates; usually associated w/ swollen, ecchymotic palpebrae & conjunctival hemorrhage

■ Infectious

➢ Conjunctivitis

- *C. trachomatis* (0.3–0.8% of live births)
  - Most common cause of infectious neonatal conjunctivitis w/o Ag nitrate gonococcal prophylaxis
  - Risk: 60–70% w/ maternal cervical infection
  - Usually presents in 5–14 days (may present earlier w/ PROM)
  - Hyperemic & thickened conjunctiva w/ marked palpebral edema & purulent exudate; lymphoid follicles rare
  - Preauricular adenopathy unusual
  - Gram stain & bacterial culture negative (unless concomitant gonococcal conjunctivitis)
  - Large, purple intracytoplasmic inclusion bodies in epithelial cells on Giemsa-stained conjunctival scrapings (after 24 h)
  - + direct immunofluorescent staining conjunctival scrapings
  - + chlamydial tissue culture (after 24 h)
- *N. gonorrhoeae* (0.02–0.3% of live births)
  - MUST BE RULED OUT IN EVERY CASE OF CONJUNCTIVITIS WITHIN 1ST WK OF LIFE OR PERSISTENCE OF PRESUMPTIVE CHEMICAL CONJUNCTIVITIS > 24–28 H
  - Usually presents at 2–5 days (may be earlier w/PROM or later w/ failed prophylaxis)
  - Usually bilateral; clear watery discharge progressing to tense palpebral edema, conjunctival hyperemia & chemosis w/ copious, thick purulent exudate
  - Gram-negative diplococci w/in WBC on Gram stain
  - + culture
- *S. aureus*
  - Usual presents at 5 days to 2 wk
  - Gram-positive cocci in clusters on Gram stain
  - + culture
- *P. aeruginosa* (rare)

- Presents at 5–18 d
- Assume Dx if gram-negative rods on Gram stain (can't wait for culture to start treatment)

- Other bacteria: *Staphylococcus sp*, *Streptococcus sp*, *E. coli*, *Enterococcus sp*, *Haemophilus sp*, *M. hominis*, *Corynebacterium diphtheriae*, *Moraxella catarrhalis*: same as w/ *S. aureus*, except for Gram stain findings if not *Staphylococcus sp*.
- Herpes simplex
  - Localized disease presents at 2–3 days; presents at 1–5 wk of age when secondary to disseminated infection
  - Usually unilateral
  - Red, swollen palpebrae; watery discharge; conjunctival membrane or small hemorrhages; +/− corneal involvement (epithelial dendritic, geographic fluorescent staining, or central stromal opacifications)
  - May/may not be assoc herpetic cutaneous vesicles
  - Multinucleated giant cells on Giemsa staining of conjunctival scrapping c/w, but not diagnostic
  - + viral culture
- Other viruses (adenovirus, enterovirus, coxsackievirus): unusual in 1st mo of life
  - Present end of first wk of life or later
  - Red, edematous palpebrae; conjunctival hyperemia, chemosis, hemorrhage; watery discharge
  - Gram stain for bacteria & bacterial culture negative
  - Often assoc w/ cough, rhinorrhea, rash

➢ Keratitis w/o conjunctivitis: corneal clouding w/o prominent conjunctival involvement

- Rubella
  - Corneal involvement rare
  - Presents at birth
  - Transient
- Syphilis: bilateral interstitial keratitis, corneal vascularization, stromal opacities, ridges of Descemet's membrane

MANAGEMENT

- Ophthalmologic consultation except for chemical, bacterial (other than *N. gonorrhoeae*, *P. aeruginosa*), & viral (other than herpes simplex) conjunctivitis
- Conjunctivitis

- ➢ Non-infectious
  - Chemical conjunctivitis: none
  - Congenital glaucoma
    - Ophthalmologic consult
    - Topical beta-blockers
    - Acetazolamide 5 mg/kg/dose q6h
    - Surgery
  - Birth trauma: none
- ➢ Infectious
  - *C. trachomatis*
    - Prophylaxis
      - Screen & Rx all pregnant women prior to delivery
      - Neonatal prophylaxis not effective, not indicated
    - Treatment: Erythromycin 40 mg/kg/day PO divided into 4 doses × 14 days
      - ~20% treatment failure rate; may require 2nd, 3rd course
      - Consider concomitant infection w/ *N. gonorrhoeae*
    - Infection control: universal precautions
  - *N. gonorrhoeae*
    - Prophylaxis
      - Maternal Dx & Rx prior to delivery
      - Topical neonatal w/ 1% Ag nitrate or 0.5% erythromycin ophthalmic ointment w/in 1 hr of birth
        NOTE: Prophylaxis failure does occur
      - W/ known exposure: ceftriaxone, 50 mg/kg (max 125 mg) IM or IV × 1
    - Treatment
      - Blood & CSF culture for disseminated disease
      - W/o DISSEMINATED DISEASE: ceftriaxone, 50 mg/kg (max 125 mg) IM or IV × 1
      - W/ DISSEMINATED DISEASE: cefotaxime, 25 mg/kg IM or IV over 30 min q6-12h, depending on postmenstrual & postnatal ages) × 7 d (10–14 days w/ meningitis; 14 days w/septic arthritis)
      - Irrigate both eyes w/ buffered NS to remove exudate
      - Consider concomitant infection w/ *C. trachomatis* if response to Rx not satisfactory
    - Infection control: contact isolation
  - *S. aureus*
    - Blood/CSF culture as indicated
    - Topical antibiotic ointment in both eyes 2–3×/day

- *P. aeruginosa*
  - Blood/CSF culture as indicated
  - Appropriate systemic antibiotic treatment (initially aminoglycoside +/− anti-pseudomonal PCN or ceftazidine, depending on sensitivities of prevalent *Pseudomonas* isolates; then as indicated by sensitivities) until local signs of infection resolve
  - Topical gentamicin ophthalmic ointment 2–3×/day
- Other bacteria: same as for *S. aureus*
- Herpes simplex: see **HERPES SIMPLEX, INTRAUTERINE, NEONATAL INFECTION**
- Other viral: none; resolves spontaneously in 2–4 wk

➢ Keratitis
- Rubella: none; transient
- Syphilis: see **SYPHILIS** in the "Maternal Conditions and Diseases" section

SPECIFIC THERAPY

N/A

FOLLOW-UP

■ During Rx
➢ PE w/ special attention to cornea

■ Long-term
➢ Ophthal for *N. gonorrhoeae*, *P. aeruginosa* or herpes simplex conjunctivitis; glaucoma; keratitis

COMPLICATIONS AND PROGNOSIS

■ Non-infectious
➢ Chemical conjunctivitis: none, resolves spontaneously
➢ Congenital glaucoma: optic nerve atrophy, blindness w/o treatment
➢ Birth trauma: usually resolves spontaneously; may result in visual impairment due to scarring in visual axis or refractive error

■ Infectious
➢ Conjunctivitis
- *C. trachomatis*
  - None w/ early Rx
  - Resolves w/o Rx in few mo; usually resolves spontaneously but may produce pannus formation, sheet scarring, & blindness w/ delayed (>2 wk) or no treatment

- Possibly chlamydial pneumonia at age 2 wk to 3 mo w/o systemic treatment (30% of infants w/ nasopharyngeal infection)
- *N. gonorrhoeae*
  - Gonococcal septic arthritis, sepsis, meningitis
  - No ocular sequelae w/ early treatment
  - Corneal ulceration, scarring, visual impairment
  - Corneal perforation, anterior staphloma, rarely panophthalmitis w/ loss of eye
- *S. aureus*
  - Sepsis/meningitis
  - Usually no ocular sequelae w/ early treatment, but corneal involvement w/ scarring & visual impairment possible
- *P. aeruginosa*
  - Corneal infiltration, perforation
  - Rapidly progressive virulent necrotizing endophthalmitis
  - Sepsis, meningitis, brain abscess, shock, death
  - Blindness
- Other bacteria: same as *S. aureus*
- Herpes simplex
  - Ocular: corneal scaring, visual impairment w/ corneal involvement
  - Other: see **HERPES SIMPLEX, INTRAUTERINE, NEONATAL INFECTION**
- Other viral: keratitis, usually transient, w/o scarring

■ Keratitis

➢ Rubella
- Ocular: none related to keratitis; but microphthalmia, cataract, glaucoma, anterior uveal disease, pigmentary retinopathy may be assoc or develop w/o keratitis
- Others related to CNS involvement (deafness, mental retardation) & CHD

➢ Syphilis
- Ocular: usually none due to keratitis, but chorioretinitis may be assoc or develop
- Others: see **SYPHILIS/REACTIVE SEROLOGIC SYPHILIS TEST, MATERNAL, ACTIVE MATERNAL SYPHILIS LIKELY OR CANNOT BE EXCLUDED** in the "Maternal Conditions and Diseases" section.

CORNELIA DE LANGE SYNDROME

KWAME ANYANE-YEBOA, MD

- Autosomal dominant form, most sporadic, w/ mutations in NIPBL gene in ~50% of all Cornelia de Lange syndrome cases
- Milder X-linked dominant form w/ mutations in SMCIA gene – 5%

HISTORY & PHYSICAL

- IUGR
- Generalized hirsutism
- Microcephaly
- Bushy eyebrows & synophrys
- Long, curly eyelashes
- Microphthalmia
- Small/short nose
- Anteverted nares
- Depressed nasal bridge
- Long philtrum
- Thin upper lip
- High-arched palate
- Cleft palate
- Small mandible
- Congenital diaphragmatic hernia
- Low-pitched voice
- Hypoplastic inverted nipples
- Feeding problems in infants
- Poor postnatal growth
- Dysphagia
- Inguinal hernia
- Umbilical hernia
- Intestinal malrotation
- Pyloric stenosis
- Small penis/hypospadias
- Cryptorchidism
- Multiple renal cysts
- Small hands
- Small feet
- Phocomelia
- Hypoplastic or absent ulna
- Radial hypoplasia
- Absent fingers

- Cleft hands/oligodactyly
- Proximally placed thumbs
- Cutis marmorata
- Thrombocytopenia
- Malrotation of gut
- Myopia
- Nystagmus
- Hearing loss
- Syndactyly of toes
- VSD
- Choanal atresia

TESTS
- Screening for mutations in NIPBL & SMCIA genes (for labs offering tests go to www.genetests.com)
- Chromosome studies to exclude 3q26.3 duplication & trisomy 18
- BAER to assess auditory pathway
- Abdominal US

DIFFERENTIAL DIAGNOSIS
- Children w/ chromosome 3q26.3 duplication have some features of de Lange syndrome
- Trisomy 18

MANAGEMENT
- May require nasogastric feeds
- May require high-calorie feedings
- Physical, occupational & speech therapies

SPECIFIC THERAPY
- None

FOLLOW-UP
- Ensure adequate caloric intake
- Monitor growth & development

COMPLICATIONS AND PROGNOSIS
- Poor feeding
- Severe growth delay
- Severe mental retardation
- Thrombocytopenia
- Autistic, self-destructive behavior

CRI-DU-CHAT SYNDROME (5P-SYNDROME)

KWAME ANYANE-YEBOA, MD

HISTORY & PHYSICAL

Frequent

- Mean birth wt 2,600 g
- Mewing cry; disappears w/ age
- Microcephaly
- Full cheeks
- Depressed nasal bridge
- Inner canthal folds
- Downslanted palpebral fissures
- Hypotonia
- Clinodactyly of 5th fingers

Less frequent

- Club foot
- Congenital heart disease
- Cleft palate
- Preauricular pits
- Hypospadias
- Cryptorchidism
- Syndactyly of 2nd & 3rd toes or fingers
- Intestinal malrotation
- Thymic dysplasia

TESTS

- Chromosome studies
- CXR to evaluate thymus
- T-cell subsets if thymic aplasia suspected

DIFFERENTIAL DIAGNOSIS

- Other chromosomal syndromes

MANAGEMENT

- Genetic evaluation, parental counseling
- Cardiac evaluation
- Physical, occupational & speech therapies
- Psychosocial support

SPECIFIC THERAPY
- None

FOLLOW-UP
- Neurodevelopmental
- Cardiol, Ortho, Hematol, Urol as indicated
- Physical, occupational & speech therapies

COMPLICATIONS AND PROGNOSIS
- 10% of pts die by end of 1st postnatal yr, most commonly due to heart defects, infections or asphyxia
- Most short & underweight
- Malocclusion
- Scoliosis
- Early graying of hair
- Muscle tone normal or increased
- Severe speech & developmental delay w/ IQ <20
- Some pts able to feed themselves, achieve sphincter control & achieve some verbal skills
- Many pts never walk
- Many pts survive to adulthood & may need to be institutionalized

CRITICAL PULMONARY STENOSIS

KALYANI R. TRIVEDI, MD, AND LEE N. BENSON, MD
REVISED BY GANGA KRISHNAMURTHY, MD

- Congenital obstruction to RV outflow
- Usually at valvular level

HISTORY & PHYSICAL

History
- Antenatal diagnosis can be made by fetal echocardiogram
- Cyanosis at birth

Physical signs
- Cyanosis
- Ejection click, single S2
- Ejection systolic murmur: more severe the obstruction, the softer the murmur due to decreased flow across the pulmonic valve in the presence of right-to-left atrial shunt

TESTS
- Arterial blood gas
- CXR
  - ➢ Normal to mild cardiomegaly unless RV failure
  - ➢ Decreased pulmonary vascular markings in severe stenosis
  - ➢ Prominent main pulm artery segment due to post-stenotic dilatation (may be absent in infants)
  - ➢ Rounded cardiac apex
- ECG: RA & RV hypertrophy, right axis deviation
- ECHO
  - ➢ Thickened pulmonary valve leaflets, doming w/ post-stenotic dilatation of pulm artery
  - ➢ Pulmonic valve is dysplastic, thickened & immobile, pulmonic valve annulus hypoplastic, supra-annular narrowing of proximal main pulm artery; no post-stenotic dilatation in these cases
  - ➢ Antegrade flow across pulmonic valve
  - ➢ RV hypertrophy
  - ➢ +/− infundibular obstruction, Doppler gradient

DIFFERENTIAL DIAGNOSIS
All causes of central cyanosis in the newborn period (see **CYANOSIS** in the "Neonatal Presenting Signs" section)

MANAGEMENT
- PGE1 to maintain ductal patency

SPECIFIC THERAPY
- Transcatheter pulmonary balloon valvuloplasty (success rate high)
- Discontinue PGE1 after valvuloplasty
- If saturations decline after discontinuing PGE1, another trial of withdrawing PGE1 should be tried in 2–3 wks
- If PGE1 wean fails 2nd time, systemic-pulm artery shunt indicated

FOLLOW-UP
- Monitor growth, saturations
- SBE prophylaxis

COMPLICATIONS AND PROGNOSIS
- W/ non-dysplastic (typical) pulmonic valve morphology, good outcome (i.e., Doppler gradient <36 mm Hg & no further interventions) in 85%
- W/ dysplastic pulm valve, good outcome in 65%

CRUZON SYNDROME

KWAME ANYANE-YEBOA, MD

- Autosomal dominant disorder; 25% representing fresh mutations
- >90% due to mutations in fibroblast growth factor receptor 2 gene; rest of cases represent Cruzon syndrome w/ acanthosis nigricans w/ mutation in FGFR3 gene

HISTORY & PHYSICAL

- Frequent findings
  - Proptosis
  - Hypertelorism
  - Optic atrophy
  - Beaked nose
  - Craniosynostosis of coronal, lambdoid & sagittal sutures
  - Acanthosis nigricans develops during childhood in some
- Less frequent findings
  - Hydrocephalus
  - Seizures
  - Agenesis of corpus callosum
  - Keratoconus
  - Bifid uvula
  - Coloboma of iris
  - Subluxation of radial heads
  - Acanthosis nigricans

TESTS

- Chromosome studies to r/o chromosome syndromes
- Imaging studies of skull to assess sutures
- Fibroblast growth factor 2 (FGFR2) & FGFR3 mutation analysis (for labs offering tests go to www.genetests.com)

DIFFERENTIAL DIAGNOSIS

- Saethre-Chozen, Jackson-Weiss, Pfeiffer, Apert syndromes
- Differentiated by variable degree of limb involvement & syndactyly

MANAGEMENT

- Genetic evaluation, testing & counseling
- Avoidance of corneal ulcers by frequent irrigation w/ artificial tears & partial suturing of eyelids
- Neurosurgical & ophthalmologic evaluation

SPECIFIC THERAPY
- Surgical procedures to maintain patency of sutures
- Cosmetic reconstruction of face

FOLLOW-UP
- Multispecialty craniofacial team of neurosurgeons, plastic & reconstructive surgeons, dental orthodontia, ENT, geneticist & other specialists

COMPLICATIONS AND PROGNOSIS
- Poor visual acuity
- Conductive hearing loss
- Seizures
- Occasional mental retardation

CYSTIC ADENOMATOID MALFORMATION (CCAM), CONGENITAL, PULMONARY

See **LUNG BUD MALFORMATIONS**

CYTOMEGALOVIRUS (CMV) INFECTION, PERINATAL/NOSOCOMIAL

J.M. LORENZ, MD

- Perinatal (vertical) via:
  - ➢ Breast milk: transmission rate 30–70%
  - ➢ Maternal genital secretions: transmission rate 30–50%
- Nosocomial
  - ➢ Blood transfusion from CMV seropositive donor (risk w/ increased # seropositive donors, lack of maternal Ab, VLBW)
  - ➢ Infected nursery personnel; fomites (rare)

HISTORY & PHYSICAL
- Perinatal infection
  - ➢ Vast majority asymptomatic
  - ➢ Pneumonitis: tachypnea, cough, apnea, coryza, nasal congestion, retractions (incubation period 2–4 wk); CXR: prominent pulmonary makings, air-trapping, atelectasis
  - ➢ Leukocytosis, eosinophlia

- ➢ VLBW infants often also develop hepatosplenomegaly, neutropenia, lymphocytosis, thrombocytopenia
- Transfusion-acquired postnatal infection
  - ➢ Asymptomatic or mild in term infants of seropositive mothers
  - ➢ Septic appearance, hepatosplenomegaly, atypical & absolute lymphocytosis, thrombocytosis in infants of seronegative mothers or VLBW infants
  - ➢ VLBW infants often develop hepatosplenomegaly, neutropenia, lymphocytosis, thrombocytopenia

TESTS
- Positive urine or saliva culture or PCR (sensitivity 89%, specificity 96%) 3–12 wk after exposure
- Anti-CMV IgM is inadequately sensitive & specific
- Positive neonatal anti-CMV IgG w/ seronegative mother suggests nosocomial infection

DIFFERENTIAL DIAGNOSIS
- Vertical: *Chlamydia trachomatis* pneumonia, RSV
- Transfusion-acquired: bacterial/viral infection

MANAGEMENT
- Prevention
  - ➢ Vertical: hand washing to prevent acquisition from genital shedding
  - ➢ Nosocomial
    - Transfusion-acquired: transfuse w/ CMV seronegative; deglycerolized, frozen; or leukocyte-filtered RBC
    - From nursery personnel: universal precautions
- Infection control: contact isolation of infected infant
- Supportive therapy

SPECIFIC THERAPY
None

FOLLOW-UP
Long-term: serial audiol & ophthal testing; developmental, dental

COMPLICATIONS AND PROGNOSIS
- Chronic viral excretion in urine (as long as 6 yr) & saliva (as long as 2–4 yr)

Prognosis

- Vertical: none in asymptomatic, healthy term infants; data limited in preterms, but risk of sequelae probably low
- Transfusion-acquired: limited data

CYTOMEGALOVIRUS INFECTION (CMV), CONGENITAL (TRANSPLACENTAL)

J.M. LORENZ, MD

- Primary infection in susceptible women during pregnancy 2%
- Prevalence of neonatal infection: ranges from 0.2% w/ higher socioeconomic status (SES) to 2.2% w/ lower SES
- Transmission
  - 40% w/ primary maternal infection
  - 0.15% (higher SES) to 1% (lower SES) w/ reactivation of infection

HISTORY & PHYSICAL

- Maternal
  - <5% symptomatic w/ primary infection
  - None symptomatic w/ recurrent infection
- Congenital infection
  - Prevalence of neonatal signs
    - 10–15% w/ primary maternal infection
    - 1% have disease or sequelae w/ recurrent maternal infection
  - Petechiae* (76% of infants symptomatic in 1st wk)
  - Neurologic abnormalities (68% of symptomatic infants)
    - Microcephaly (53% of symptomatic infants)
    - Lethargy/hypotonia (27% of symptomatic infants)
    - Poor suck (19% of symptomatic infants)
    - Seizures (7% of symptomatic infants)
    - Hydrocephalus
    - Intracranial calcifications (70% of symptomatic infants by CT)
  - Jaundice (67% of symptomatic infants); may be present on DOL 1; initially unconjugated, then conjugated, hyperbilirubinemia
  - Hepatosplenomegaly* (60% of symptomatic infants)
  - IUGR (50% of symptomatic infants)
  - Prematurity (34% of symptomatic infants)
  - Purpura (13% of symptomatic infants)

- ➢ Chorioretinitis (14% of symptomatic infants), strabismus, optic atrophy (cataract, colobomas, microphthalmos)
- ➢ Pneumonitis (<1% of symptomatic infants)
  - * May be the only signs

TESTS

- Nonspecific (# in parentheses indicates % of symptomatic infants w/ the sign in 1st wk)
  - ➢ ALT > 80 U/L (83%)
  - ➢ Plt ct < 100 K/mm^3 (77%) w/ or w/o DIC
  - ➢ Direct bili > 4 mg/dL (69%)
  - ➢ Hemolytic anemia (51%)
  - ➢ CSF protein > 120 mg/dL (46%)
  - ➢ Intracranial calcifications on skull films
- Specific

  PRENATAL
  - ➢ Positive amniotic fluid PCR
    - Delay testing until 7 wk after onset of maternal infection
    - Sensitivity
      - <21 wk GA: 30%
      - >21 wk GA: ~100%
    - ? Usefulness in the absence of fetal US findings since there will be non-CNS sequelae in 80–90%

  POSTNATAL
  - ➢ + urine or saliva culture or PCR (sensitivity 89%, specificity 96%) diagnostic of *congenital* infection if specimen obtained w/in 2 wk of birth)
  - ➢ Isolation by culture from CSF rare
  - ➢ Placental pathology: inclusion bearing cells, focal necrosis w/ plasma cell infiltration; usual w/ symptomatic, unusual w/ asymptomatic infection
  - ➢ Negative anti-CMV IgG in mother & neonate excludes congenital infection (neonate may be + due to transplacental maternal Ab as long as 4–9 mo)

DIFFERENTIAL DIAGNOSIS

- DDx of:
  - ➢ IUGR (see **INTRAUTERINE GROWTH RESTRICTION** in the "Neonatal Presenting Signs" section)
  - ➢ Microcephaly

- ➢ Hepatomegaly (see **HEPATOMEGALY** in the "Neonatal Presenting Signs" section)
- ➢ Thrombocytopenia (see **THROMBOCYTOPENIA** in the "Neonatal Presenting Signs" section)
- ➢ Direct hyperbilirubinemia (see **HYPERBILIRUBINEMIA, CONJUGATED** in the "Neonatal Presenting Signs" section)

- Bacterial/viral sepsis
- Other TORCH infections: congenital syphilis (see **SYPHILIS/REACTIVE SEROLOGIC SYPHILIS TEST, ACTIVE MATERNAL SYPHILIS LIKELY OR CANNOT BE EXCLUDED** in the "Maternal Conditions and Diseases" section, toxoplasmosis (see **TOXOPLASMOSIS, CONGENITAL**), rubella, HSV (see **HUMAN IMMUNODEFICIENCY VIRUS INFECTION, MATERNAL** in the "Maternal Conditions and Diseases" section)

MANAGEMENT

- Supportive therapy
- Infection control
  - ➢ Contact isolation
  - ➢ Isolation from mother not indicated
  - ➢ OK to breastfeed

SPECIFIC THERAPY

- Prevention: none
- Treatment
  - ➢ Asymptomatic infection: none
  - ➢ Symptomatic infection: ganciclovir, 6 mg/kg q12h × 42 d
    - Shown to reduce risk of hearing loss
    - Neutropenia most significant toxicity

FOLLOW-UP

- During Rx: weekly CBC w/ differential
- Long-term: serial audiol & ophthal testing, developmental, dental, REGARDLESS of presentation, Rx

COMPLICATIONS AND PROGNOSIS

- Complications
  - ➢ Chronic viral excretion in urine (as long as 6 yr) & saliva (as long as 2–4 yr)
- Prognosis
  - ➢ Symptomatic: 90–95% of survivors w/ mild to severe handicap

- ➢ Asymptomatic: 10–15% handicapped, usually apparent within 2 yr
- ➢ Deafness most common (58% sympt, 7% asympt; progressive in half, bilateral in half of sympt infants and 2/3rds of asympt infants of cases of deafness)
- ➢ Note: Universal hearing screening in nursery detects only half of cases of deafness due to congenital CMV)
- ➢ Mental retardation (40–50% sympt, 4% asympt)
- ➢ Seizures (23% sympt, 1% asympt)
- ➢ Paresis/paralysis (12% sympt, 0% asympt)
- ➢ Abnl dental enamel w/ caries (27% sympt, 4% asympt)
- ➢ 6% mortality among sympt (30% mortality in most severely affected)
- ➢ Learning disabilities even w/o MR or deafness
- ➢ Late-onset chorioretinitis (20% sympt, 2% asympt)

■ Implications for subsequent pregnancies: 4% risk of congenital infection, <1% of infected infants symptomatic

DIGEORGE SYNDROME (VELO-CARDIO-FACIAL SYNDROME)

KWAME ANYANE-YEBOA, MD

■ Most cases due to microdeletion of chromosome 22q11 or mutation of TBX1 gene; small number due to microdeletion of chromosome 10p13–14

HISTORY & PHYSICAL

■ Cardiac defects in 80%
- ➢ Truncus arteriosus (17.5–22.5% of infants w/ conotruncal heart anomalies have DiGeorge syndrome)
- ➢ Interrupted aortic arch
- ➢ Tetralogy of Fallot (32% of tetralogy of Fallot w/ pulmonary aplasia or VSD w/ pulmonary atresia associated w/ DiGeorge syndrome)
- ➢ Double outlet RV
- ➢ Right aortic arch
- ➢ VSD

- Other associated cardiovascular lesions: cervical aorta, vascular ring, aberrant left subclavian, retroesophageal arch, Komnerell's diverticulum
- Broad nasal root
- Bulbous tip of nose
- Small rounded ears
- Hypocalcemia
- Abnormal T-cell function
- Thymic aplasia or hypoplasia
- Cleft palate
- Cleft uvula
- Cleft upper lip
- Cleft lip/palate
- Tracheal or laryngeal abnormalities
- Extra ribs
- Preaxial polydactyly
- Postaxial polydactyly
- Bifid thumb
- Bifid hallux
- Microcephaly
- Holoprosencephaly
- Lissencephaly
- Hemivertebrae
- Meningomyelocele
- Congenital diaphragmatic hernia
- Hypertelorism
- Iris coloboma
- Asymmetric crying face
- Microstomia
- Velopharyngeal insufficiency
- Imperforate anus
- Choanal atresia
- Esophageal atresia
- Feeding difficulties

TESTS

- Karyotype
- Fluorescence in situ hybridization (FISH) w/ 22q11 probe (>90% have 22q11 deletion)
- DNA analysis for small deletions & point mutations in TBX1 gene
- FISH test for 10p13–14 deletion

- Total, ionized serum Ca; P
- Parathyroid hormone levels
- T-cell subsets
- Immunoglobulins

DIFFERENTIAL DIAGNOSIS
- CHARGE association (see **CHARGE SYNDROME**)
- Noonan syndrome (see **NOONAN SYNDROME**)
- VATER (VACTERL) association
- Fetal alcohol syndrome (see **FETAL ALCOHOL SPECTRUM DISORDERS**)
- Retinoic acid embryopathy

MANAGEMENT
- Cardiac evaluation & treatment
- Assessment of future risk for infection by Infectious Disease
- Endocrine evaluation
- Genetic evaluation, parental counseling
- Gavage feed if poor suck
- Ca supplements if indicated

SPECIFIC THERAPY
- Surgery for CHD
- Transplant of thymic tissue in cases of severe immune deficiency restores immune function

FOLLOW-UP
- Nasogastric or gastrostomy tube feeds if poor suck persists
- Monitor for infections even if T-cell function adequate
- Check serum levels during periods of stress
- Refer for "early intervention"
- Physical, occupational, speech, language therapies
- Monitor for attention-deficit/hyperactivity disorder (ADHD)
- Formal evaluation by developmental pediatrician in preschool children
- Monitor growth, development

COMPLICATIONS AND PROGNOSIS
- Advances in cardiac surgery have significantly reduced mortality assoc w/ cardiac defects
- Growth, developmental delay in infants
- Risk for recurrent sinopulmonary infections high in those w/ poor T-cell function

- Death from overwhelming sepsis in those w/ severe immune deficiency w/o thymic transplant
- Autoimmune disease in small fraction
- ADHD in most children
- Learning disabilities in 80–100%
- IQ < 70 in 45%
- Schizophrenia in 25%

EBSTEIN'S ANOMALY OF THE TRICUSPID VALVE

KALYANI R. TRIVEDI, MD, AND LEE N. BENSON, MD
REVISED BY GANGA KRISHNAMURTHY, MD

- Abnormality of the tricuspid valve (TV) w/ displacement of the septal & posterior leaflets into the right ventricle (RV)
- Rare defect (<1% of all CHD)

HISTORY & PHYSICAL

History

- Fetal diagnosis by echocardiography
- Symptoms depend on severity of defect, degree of tricuspid regurgitation (TR) & associated lesions (VSD, pulmonary stenosis [PS] or atresia [PA])
- Infants w/ mild defects may be asymptomatic

Physical signs

- Infants may present with:
  - ➢ Cyanosis of varying degree
    - Due to right-to-left shunting across patent foramen ovale (PFO)/atrial septal defect (ASD) or decreased antegrade flow across RV outflow tract
    - Diminishes as pulmonary vascular resistance (PVR) drops after birth
- Heart failure (see **CONGESTIVE HEART FAILURE** in the "Neonatal Presenting Signs" section)
- Incidental murmur: systolic murmur at left lower sternal border, varying grades depending on severity of TR
- Arrhythmia: episodic tachycardia in 20–30%, due to manifest or occult accessory pathways, Wolff-Parkinson-White
- Other signs
  - ➢ Quadruple rhythm: split S1 & split S2, prominent S3, S4

➢ ± Mid-diastolic rumble may be present at left lower sternal border

TESTS

- ABG if severely cyanotic
- Serum arterial lactate to assess adequacy of cardiac output
- CXR
  - ➢ Mild Ebstein's: normal CT ratio w/ normal pulmonary vascular markings
  - ➢ Moderate to severe Ebstein's:
    - Marked cardiomegaly due to dilated right atrium (consider Ebstein's anomaly in cyanotic newborn w/ massive cardiomegaly)
    - Reduced pulmonary vascularity
- ECG: right atrial enlargement, right bundle branch block, preexcitation, supraventricular tachycardia
- Echocardiogram
  - ➢ Dilated right atrium
  - ➢ TR of varying severity
  - ➢ Apical displacement of septal & posterior leaflets of TV
  - ➢ Redundant, elongated sail-like anterior leaflet of TV
  - ➢ Atrialized RV, +/− hypoplasia of body of RV
  - ➢ ± pulmonary stenosis/atresia or functional pulmonary atresia
  - ➢ ± ASD
- Holter monitoring for arrhythmia

DIFFERENTIAL DIAGNOSIS

- Other causes of cyanosis in the newborn period (see **CYANOSIS** in the "Neonatal Presenting Signs" section)

MANAGEMENT

General measures

- Close follow-up in mild cases: monitor for increasing cyanosis, CHF, supraventricular tachycardia
- Moderate to severe cases w/ significant cyanosis in the newborn period
  - ➢ Distinguish btwn functional & anatomic PA
    - With anatomic PA/PS: PGE1 for ductal patency to provide PBF
    - With functional PA: iNO to reduce PVR. As PVR decreases, iNO is weaned; saturations should be maintained in at least 70's off iNO; saturations generally improve over several wks

- ➢ Balloon atrial septostomy for restrictive ASD to maintain LV preload
- Anti-congestive therapy w/ CHF (see **CONGESTIVE HEART FAILURE** in the "Neonatal Presenting Signs" section)
- Antiarrhythmic meds for SVT (see **CARDIAC ARRHTHYMIAS**)

SPECIFIC THERAPY

- W/ anatomic restriction to pulmonary blood flow (PS/PA), initial palliation w/ systemic-pulmonary artery shunt is required
- Severely ill newborns w/ severe TR may require:
  - ➢ Definitive therapy: repair of TV & plication of atrialized RV
  - ➢ Alternatively, Starnes operation: closure of TV, creation of ASD, modified Blalock-Taussig shunt, & staging towards a univentricular circulation
  - ➢ Severe cases may be candidates for cardiac transplantation
- Surgical/transcatheter-based ablation of accessory (bypass) tracts

FOLLOW-UP

- Close follow-up when unrepaired in newborn period, monitoring for cyanosis, exercise intolerance, CHF

COMPLICATIONS AND PROGNOSIS

- Predictors of poor outcome: severe displacement of TV or TR
- Without surgical intervention, 10–20% mortality in 1st yr of life
- Actuarial survival: 67% survival at 1 yr and 59% at 10 yrs
- In pts who require & survive TV replacement or valvuloplasty, 83–92% 10- to 18-yr survival rate
- Freedom from reoperation is approximately 80% at 15 yrs

EPIDERMOLYSIS BULLOSA (EB)

RICHARD A. POLIN, MD
REVISED BY KIMBERLY D. MOREL, MD

HISTORY & PHYSICAL

History

- EB simplex
  - ➢ EB simplex, Köbner subtype
    - Autosomal dominant
    - Mild form of EB w/ cutaneous blistering
    - Onset in neonatal period or infancy

- Nail dystrophy in 50%
- Focal callosities of palms & soles
- Extracutaneous manifestations can occur

➢ EB simplex, Weber-Cockayne subtype
- Autosomal dominant or autosomal recessive
- Most common form of EB
- Blisters develop later in infancy or childhood on hands, feet
- Nail dystrophy in 10–25%
- Focal callosities on palms & soles

➢ EB simplex, Dowling-Meara subtype
- Autosomal dominant
- Blistering at birth or soon thereafter
- May be severe or life-threatening
- Grouped blisters (herpetiform)
- Severity decreases over time?

■ Junctional EB
➢ Autosomal recessive
➢ Severe blistering

■ Dystrophic EB
➢ Dominant form: mild
➢ Recessive form: severe
- Severe blistering at birth
- Recessive dystrophic EB, Hallopeau-Siemens subtype
- Recessive dystrophic EB, non-Hallopeau-Siemens subtype

Signs

■ Friction induces skin blistering (positive Nikolsky's sign)
■ Vaginal delivery may lead to blisters on face & scalp
■ Superficial blisters rupture easily, leading to erosions
■ Erosions can become crusted, infected
■ Deeper blisters tense or hemorrhagic
■ Blistering can lead to scarring, milia or pigmentary abnormalities
■ EB simplex
➢ EB simplex (Koebner)
- Mild to moderate blistering, often generalized
- Occasional mucosal involvement
- No scarring

➢ EB simplex (Weber-Cockayne)
- Mild blistering, often localized
- Rare mucosal involvement
- Usually involves hands, feet

- ➢ Dowling Meara EB simplex herpetiformis
  - Moderate to severe blistering
  - Begins generalized, becomes grouped
  - Lesions common in periungual area
  - Hyperkeratotic palms, soles, ages 1–3 yr
- Junctional EB
  - ➢ Junctional EB, Herlitz type
    - Moderate to severe blistering
    - Large erosions
    - Dystrophic or absent nails
    - Granulation tissue
    - Severe mucosal involvement
    - Extracutaneous involvement (erosions of respiratory, GI & urinary tracts)
    - Corneal erosions
    - Dental abnormalities, caries
  - ➢ Junctional EB, non-Herlitz type
    - As above plus anemia, failure to thrive
  - ➢ Junctional EB w/ pyloric atresia, subtype associated w/ pyloric atresia
- EB dystrophica
  - ➢ Dominant form
    - Mild to moderate blistering
    - More severe in neonatal period
    - Nail dystrophy
  - ➢ Recessive form
    - Severe blistering
    - Scarring
    - Joint contractures
    - Pseudosyndactyly, mitten deformities of hands & feet
    - GI involvement (esophageal strictures)
    - Microstomia, dental caries
    - Failure to thrive
    - Anemia
    - Eye involvement
    - Urinary tract involvement

TESTS

- Gram stain & bacterial/viral culture of blister fluid to r/o infectious causes or if secondary infection suspected

- Skin biopsy for routine histology as well as immunofluorescence mapping; consider electron microscopy
- Blood for mutation analysis

EB subtype	*Protein/gene systems*
EB simplex	Keratin 5, Keratin 14
EB simplex assoc w/muscular dystrophy	Plectin
Junctional EB	Laminin 5
Junctional EB assoc w/ pyloric atresia	$\alpha 6\beta 4$ Integrin
Dystrophic EB	Type VII collagen

DIFFERENTIAL DIAGNOSIS

- Bullous impetigo
- Herpes simplex infection
- Sucking blisters
- Mastocytosis
- Maternal autoimmune blistering diseases
  - ➢ Herpes gestationis (pemphigoid gestationis)
  - ➢ Pemphigus vulgaris
  - ➢ Pemphigus foliaceus
- Chronic bullous dermatosis of childhood
- Neonatal lupus erythematosus
- Staphylococcal scalded skin syndrome
- Toxic epidermal necrolysis
- Congenital erosive & vesicular dermatosis
- Incontinentia pigmenti
- Acrodermatitis enteropathica
- Methylmalonic acidemia
- Purpura fulminans
- Epidermolytic hyperkeratosis
- Ectodermal dysplasias
- Aplasia cutis congenita
- Traumatic skin injury

MANAGEMENT

General measures

- Careful attention to fluid, electrolyte balance
- Prevention of trauma to skin
- Avoidance of tape
- Drain tense vesicles w/ sterile needle

- Wound care
  - ➢ Cover erosions w/ emollients containing topical antibiotics
  - ➢ Non-adherent dressings
- Monitor closely for infections
- Aggressive nutritional support
- Monitor for extracutaneous involvement
- Psychosocial support
- Genetic counseling

SPECIFIC THERAPY

- None available

FOLLOW-UP

- Lifetime care & follow-up required

COMPLICATIONS AND PROGNOSIS

- Complications
  - ➢ Secondary infection
  - ➢ Scarring; pigmentary alteration
  - ➢ Squamous cell carcinoma, especially within chronic wounds
- Prognosis
  - ➢ Variable even within known genotypes & phenotypes
  - ➢ Guarded prognosis w/ the most severe forms
    - May be lethal in infancy in severe forms of junctional EB, Herlitz subtype
    - High risk of infection, esp in younger children
    - High risk of squamous cell carcinoma in severe forms in young adulthood
- Mildest forms may have an excellent prognosis

EPISPADIAS/BLADDER EXSTROPHY

DEBRA L. FROMER, MD, AND TERRY HENSLE, MD
REVISED BY TERRY HENSLE, MD AND GRACE HYUN, MD

- Exstrophy-epispadias spectrum
  - ➢ Classic bladder exstrophy: 80%
    - Bladder mucosa exposed on lower abdomen
    - Inguinal hernia
    - Absent umbilicus
  - ➢ Isolated epispadias: 10%
  - ➢ Cloacal exstrophy, variants: 10%

- As w/ classic bladder exstrophy plus
- Omphalocele
- Prolapsed hindgut
- Bifid bladder

HISTORY & PHYSICAL

Prenatal diagnosis possible
- No urine in bladder on fetal US
- Bladder visualized extra-abdominally
- Abdominal wall defect

Postnatal physical exam
- Classic bladder exstrophy: 80%
  - ➢ Bladder mucosa open on lower abdominal wall
  - ➢ Inguinal hernia
  - ➢ Absent umbilicus
- Cloacal exstrophy
  - ➢ Bifid bladder, mucosa exposed open on the lower abdomen
  - ➢ Omphalocele
  - ➢ Male genital defects
    - Epispadias w/ splayed corporal bodies
    - Dorsal chordee
    - Sex assignment may be questionable in cloacal exstrophy
  - ➢ Female genital defects
    - Short urethra, vagina
    - Anteriorly placed, stenotic vagina
    - Bifid clitoris
    - Divergent labia, mons pubis, clitoris
    - Vaginal septum
  - ➢ Anorectal defects
    - Anteriorly placed anus
    - Rectal prolapse
  - ➢ Musculoskeletal defects: widening of symphysis pubis w/ outward rotation of pelvis
  - ➢ Cloacal exstrophy is assoc w/ myelomeningocele/neurogenic bladder

TESTS
- Renal US for renal anatomy
- Abdominal x-ray: widening of symphysis pubis, spina bifida

DIFFERENTIAL DIAGNOSIS
- Isolated epispadias
- Classic exstrophy
- Cloacal exstrophy

MANAGEMENT
N/A

SPECIFIC THERAPY
- Urology consultation in the prenatal period if diagnosed; otherwise in the immediate postnatal period
- Surgical correction
  - ➢ Early total (single-stage) repair: w/in 48 h at center of excellence
  - ➢ Staged repair
    - Bladder closure in the newborn period
    - Repair epispadias at 6 mo
    - Bladder neck reconstruction at 4 yr

FOLLOW-UP

Long-term follow-up
- Renal/bladder US
- Video urodynamics
- Other depending on presence of associated anomalies

COMPLICATIONS AND PROGNOSIS
- Vesicoureteral reflux (all)
- Urinary continence
  - ➢ Dependent on bladder size, associated anomalies
  - ➢ May require bladder augmentation, bladder neck reconstruction, continence mechanisms
- Development of "waddling" gate
- Preserved sexual function in both males & females
- Female fertility should be normal
- Pregnancy: cervical, uterine prolapse before/after delivery

FATTY ACID OXIDATION DISORDERS

WENDY K. CHUNG, MD, PhD

HISTORY & PHYSICAL
May present at any age
Specific symptoms will vary depending on the exact metabolic defect

- Lethargy, change in mental status, coma (often w/ fasting/intercurrent illness)
- Vomiting
- Seizure
- Hypotonia, muscle weakness
- Cardiac failure
- Failure to thrive
- SIDS or family Hx of SIDS
- Consanguineous parents
- Altered mental status
- Hepatomegaly
- Heart murmur or irregular heartbeat
- Pigmentary retinopathy (w/ long-chain 3-hydroxyacyl CoA dehydrogenase deficiency only)

TESTS

Results will depend on exact metabolic defect

- Hypoglycemia, acidosis
- Urine analysis: hypoketosis
- LFTs may be elevated
- CPK may be elevated
- Ammonia mildly elevated
- Uric acid may be elevated
- CXR: cardiomegaly
- ECG: LV hypertrophy
- Echo: cardiomyopathy or pericardial effusion
- Urine organic acids: dicarboxylic aciduria (can be an artifact of certain diets high in medium-chain triglycerides) or ethylmalonic aciduria in short-chain acyl-CoA dehydrogenase deficiency
- Free carnitine
  - ➢ Extremely low w/ carnitine transporter deficiency
  - ➢ Secondarily low levels w/ many other fatty acid oxidation disorders
  - ➢ High in carnitine w/ palmitoyl transferase deficiency
- Acylcarnitine profile: abnl increases in specific chain lengths of acyl carnitines will indicate specific metabolic defect
- Urine acylglycines
- Provocative fasting will show urine dicarboxylic acids >> 3-hydroxybutyrate
- Fibroblast culture w/ radiolabeled palmitate or other fatty acid interrogation for definitive Dx

- Medium-chain acyl-dehydrogenase deficiency can be diagnosed genetically; included in newborn screen in some states
- Prenatal Dx available

DIFFERENTIAL DIAGNOSIS
- Reye syndrome
- SIDS

MANAGEMENT
- Airway, breathing, circulation
- IV fluids w/ D10 at 1.5× maintenance (maintain serum glucose >100 mg/dL)
- Carefully monitor glucose levels

SPECIFIC THERAPY
- Carnitine 100 mg/kg q day. Go up to 300 mg/kg IV during metabolic crisis.
- Specific dietary treatments can be made only after type of disorder identified
- Medium-chain acyl-dehydrogenase should NEVER be treated w/ high concentrations of medium-chain triglycerides
- Long-chain fatty acid oxidation disorders: maintain diet w/ majority of fat derived from medium-chain triglycerides
- Avoid fasting in all conditions, especially >12 h; if necessary provide cornstarch 1 g/kg qHS
- Immediately treat metabolic crisis w/ IV glucose

FOLLOW-UP
- Normalize free carnitine levels

COMPLICATIONS AND PROGNOSIS
- Depends on type of disorder & severity of attacks
- Better metabolic control = better prognosis
- Normal intellect, life expectancy possible w/ some conditions if metabolic crisis has not resulted in hypoxemic damage
- Myopathy, cardiomyopathy potentially reversible
- Potentially fatal w/ each metabolic crisis

FETAL ALCOHOL SPECTRUM DISORDERS (FASD)

J.M. LORENZ, MD

- Umbrella term describing a continuum of effects that can occur w/ gestational alcohol exposure ranging from:
  - ➢ No discernable effect

  to
  - ➢ Alcohol-related neurodevelopmental disorder (ARND): CNS anomalies/neurodevelopmental deficits w/o growth restriction & w/o all 3 facial features necessary for dx of fetal alcohol syndrome (FAS) (see "Tests")

  to
  - ➢ Alcohol-related birth defects (ARBD): major anomalies of other organs w/o growth restriction & w/o all 3 facial features necessary for dx of FAS

  to
  - ➢ Partial FAS: 2 of the 3 facial features necessary for dx of FAS plus either (1) prenatal &/or postnatal growth restriction or (2) structural &/or functional CNS abnormalities

  to
  - ➢ FAS: characteristic facial dysmorphia plus prenatal &/or postnatal growth restriction plus structural &/or functional CNS abnormalities

HISTORY & PHYSICAL

- Maternal risk factors
  - ➢ Chronic, daily heavy alcohol use: ≥6 drinks/day
    or
    Heavy intermittent alcohol use: ≥5 drinks per occasion and ≥45 drinks/mo
    → 30–50% risk of FAS
    Note: 1 drink = 4 oz wine, 12 oz beer, or 1 oz 80-proof liquor
  - ➢ Age ≥ 30 yr: 3–5× increased risk
  - ➢ Low socioeconomic status
  - ➢ Previous child w/ FASD: >75% risk
- No safe threshold for alcohol intake during pregnancy established Neonatal/Fetal Effects
- Expression highly variable
- Dx difficult in newborn period; often not diagnosed until after age 2 yr

Signs

Any of the following (see "Tests" for diagnostic criteria for FAS)

- Facial abnormalities
  - Short palpebral fissures
  - Elongated, smooth philtrum
  - Thin, smooth upper lip
  - Retrognathia
  - Short, upturned nose
  - Maxillary hypoplasia
  - Ptosis, epicanthal folds
  - Facial hirsutism in infancy
  - Microphthalmia
  - Cleft lip/palate
  - Protruding ears, hearing impairment
  - High-arched palate
  - Mildly webbed or short neck
- IUGR
- CNS abnormalities
  - Tremulousness, irritability
  - Microcephaly (<10th percentile w/ nl ht & wt; <3rd percentile w/growth restriction)
  - Hydrancephaly
  - Hydrocephalus
  - Cortical atrophy
  - Abnormal/absent corpus callosum
  - Reduced cerebellar volume, esp anterior vermis
  - Reduced basal ganglia volume, esp caudate
  - Meningomyelocele
- Other abnomalities
  - Pectus excavatum
  - Hypoplastic labia minora
  - Atrial septal defect
  - Ventricular septal defect, tetralogy of Fallot, great vessel anomalies
  - Congenital diaphragmatic hernia
  - Umbilical hernia
  - Inguinal hernia
  - Renal agenesis or hypoplasia
  - Hypospadias
  - Small distal phalanges, hypoplastic nails
  - Cervical vertebral anomalies
  - Rib anomalies

- ➢ Camptodactyly, clinodactyly
- ➢ Developmental dysplasia of hip

TESTS

- No test to confirm dx's
- No sign(s) diagnostic
- Dx's of exclusion, esp w/ unknown h/o of maternal alcohol intake during pregnancy; in this case, dx should be qualified by "w/ unknown prenatal alcohol exposure"
- Prenatal alcohol exposure alone does not warrant these dx's
- Confirmed abstinence from alcohol during entire pregnancy precludes these dx's
- MRI for structural CNS abnormalities
- Echocardiogram, abdominal US, ophthalmologic exam as indicated
- CDC diagnostic criteria
  - ➢ FAS
    - Growth retardation: prenatal &/or postnatal weight or length/height <10th percentile

    and
    - Facial dysmorphism
      - Smooth philtrum: University of Washington Lip-Philtrum Guide rank of 4 or 5 (http://depts.washington.edu/fasdpn/htmls/lip-philtrum-guides.htm)
      - Thin vermillion border: University of Washington Lip-Philtrum Guide rank of 4 or 5

      and
      - Short palpebral fissures: length <10th percentile for GA/age

    and
    - CNS abnormalities
      - Microcephaly
      - Structural brain anomalies
      - Delayed motor development or fine motor dysfunction
      - Functional CNS deficits (see "Complications and Prognosis"); >1 SD below the mean on standardized testing)
  - ➢ No diagnostic criteria exist for effects of fetal alcohol exposure that do not meet the criteria for FAS

DIFFERENTIAL DIAGNOSIS

See **WILLIAMS SYNDROME, CORNELIA DE LANGE SYNDROME, DIGEORGE (VELO-CARDIO-FACIAL) SYNDROME.**

Fetal hydantoin syndrome
Dubowitz syndrome
Functional neurologic impairment due to abuse/neglect, disruptive home environment, lack of opportunities

MANAGEMENT
Early dx & stable, nurturing home environment are strong protective factors for neurodevelopmental impairment

SPECIFIC THERAPY
Prevention: US Surgeon General recommends that pregnant women & women who may become pregnant abstain from alcohol consumption

FOLLOW-UP
Developmental; ophthal, cardiol, dental, ENT as indicated

COMPLICATIONS AND PROGNOSIS
- Characteristic facies become less prominent after puberty
- Growth deficiency
- Cognitive impairment
  - Performance >2 SD below the mean on standardized tests (25%)
  - Performance >1 SD below the mean in 3 functional domains on standardized tests
- Other functional CNS deficits
  - Executive functioning deficits
  - Gross & fine motor impairment
  - Attention deficits, poor impulse control
  - Poor adaptive & social skills
  - Tactile defensiveness, oral sensitivity
  - Impaired memory
  - Pragmatic language deficits
  - Poor coordination
- Others
  - Strabismus
  - Myopia
  - Small teeth w/abnl enamel
  - Eustachian tube dysfunction
  - Dental malocclusion

GALACTOSEMIA

WENDY K. CHUNG, MD, PhD

HISTORY & PHYSICAL

History

- Normal pregnancy/delivery; symptom onset 1st few days of life or after initiating milk feeding
- Jaundice
- Failure to thrive or wt loss
- Vomiting
- Developmental delay
- Positive newborn screen
- Sepsis w/ *E. coli*

Physical signs

- Hepatomegaly
- Jaundice
- Edema
- Bleeding
- Cataracts

TESTS

- Prenatal Dx possible
- Increased bilirubin, LFTs, coagulation tests
- Urinary reducing substance (e.g., Clinitest®) + (but only if receiving lactose)
- Newborn state metabolic screen
- Direct measurement of erythrocyte galactose-1-phosphate uridyl transferase activity

DIFFERENTIAL DIAGNOSIS

(See HYPERBILIRUBINEMIA, CONJUGATED and HYPERBILIRUBINEMIA, UNCONJUGATED in the "Neonatal Presenting Signs" section)

- Neonatal hepatitis
- Sepsis
- See HYPOTHYROIDISM, CONGENITAL
- Metabolic abnormalities

MANAGEMENT

- Airway, breathing, circulation
- NPO w/ IV D10W

SPECIFIC THERAPY
- Galactose-free diet lifelong: substitute soy for milk/milk products

FOLLOW-UP
- Monitor galactose-1-phosphate level (should be <4 mg/dL)
- At 12 months of age, trial of full lactose diet for 2 wks & monitor galactose-1-phosphate to determine if continued dietary mgt is required

COMPLICATIONS AND PROGNOSIS
- Earlier the metabolic control, better the outcome
- Normal IQ possible if detected early & compliant, but higher prevalence of developmental & speech delay
- Mental retardation if untreated w/in 1st few months of life
- Hyperactivity, learning disabilities even in compliant pts
- Cataracts reversible if treated w/in 1st 3 months of life
- Hypergonadotrophic hypogonadism & ovarian failure in treated females, though some have delivered children

GASTROESOPHAGEAL REFLUX (GER)

JOSEPH LEVY, MD

- Regurgitation of stomach contents up the esophagus, w/ or w/o overt vomiting

HISTORY & PHYSICAL
- Important to distinguish physiological GER from pathological GER disease, i.e. GER associated w/:
  - ➢ Pulmonary complications
  - ➢ Apnea & bradycardia
  - ➢ Esophagitis
  - ➢ Feeding difficulties
  - ➢ Blood loss
- Important to quantify vol, composition, forcefulness, accompanying signs
- Inquire re: feeding difficulties, arching, pulling away from nipple after few sucks
- Never assume bilious vomiting is physiologic
- Auscultate for discoordinated swallowing & gulping, stridor, wheezing

- Consider possibility of underlying anatomical abnormality: T-E fistula, pyloric stenosis, small bowel obstruction, or malrotation

TESTS

- Barium swallow/videofluoroscopy
  - ➢ Neither sensitive nor specific, but useful to identify structural anomalies
  - ➢ Presence of reflux does not correlate w/ pathologic GER
- Prolonged pH monitoring
  - ➢ The gold standard
  - ➢ Useful in determining timing of episodes, symptom correlation, esophageal acid clearance
  - ➢ Does not detect neutral, alkali reflux
  - ➢ Significant parameters of pH study
    - # of episodes w/ pH < 4.0
    - Duration of longest episode
    - # of episodes longer than 5 min
    - Reflux index: % time pH < 4.0
- Endoscopy
  - ➢ Required to document esophagitis
  - ➢ Useful in identifying eosinophilic infiltration, marker of reflux
  - ➢ Marked tissue eosinophilia reflects eosinophilic esophagitis/enteropathy
- Scintigraphy
  - ➢ Allows quantification of gastric emptying, identifies non-acid reflux
  - ➢ May document pulmonary aspiration

DIFFERENTIAL DIAGNOSIS

- Nonspecific irritability
- Chest pain
- Esophageal compression
- T-E fistula
- Hyperreactive airway disease
- Cystic fibrosis
- RSV, pertussis

MANAGEMENT

- Upright positioning
- Prone positioning w/ caution
- Decrease vol of feeds
- Avoid infant seats w/ full stomach

- Thicken formula, 1 Tbsp dry cereal/oz
- Cross-cut nipple

SPECIFIC THERAPY

- Antacids
  - ➢ Calcium carbonate
  - ➢ Aluminum or magnesium hydroxide, 0.5–2 mL/kg 3–5×/day
- Acid suppression
  - ➢ Ranitidine 2–4 mg/kg/dose BID or TID

  or
  - ➢ Famotidine 1.0–1.2 mg/kg/day divided BID or TID

  or
  - ➢ Cimetidine 10 mg/kg QID
- Proton pump inhibitors (not approved for use in infants younger than 1 yr)
  - ➢ Lansoprazole, 15- & 30-mg SoluTab available 0.6–1.2 mg/kg/day; in practice: <30 kg: 15 mg qd, >30 kg: 30 mg qd

  or
  - ➢ Omeprazole, 0.7–3.3 mg/kg/day; in practice, <30 kg: 10 mg qd, >30 kg: 20 mg qd
- Prokinetics
  - ➢ Not available in U.S. market at present
  - ➢ Metoclopramide poor choice: weak promotility action, potential for neurological side effects
- Surgery
  - ➢ Fundoplication
    - Full wrap: Nissen
    - Partial wrap: Thal
  - ➢ Complications
    - Herniation of wrap into chest cavity
    - Gas bloating
    - Difficulties burping, vomiting
    - Retching
    - Dysphagia
    - Dumping syndrome

FOLLOW-UP

- Ensure adequate wt gain
- Confirm lack of respiratory sx
- Monitor Hgb & stool guaiac if esophagitis suspected
- Investigate dysphagia to assess esophageal anatomy, function

- W/ severe chronic GERD, endoscope periodically to diagnose Barrett's esophagus (columnar metaplastic changes w/ malignant potential)

COMPLICATIONS AND PROGNOSIS

Complications

- Esophagitis
- Dysphagia
- Strictures
  - ➢ W/ T-E fistula, esophageal atresia & congenital diaphragmatic hernia, risk for chronic reflux & peptic strictures
  - ➢ Long-term use of PPI considered safe & might help prevent complications
- Aspiration, chronic airway disease
- Apnea/stridor/hoarseness/cough
- Barrett's esophagus

Prognosis

- Physiologic GER resolves spontaneously in >50% by 2 mo, 80–90% by 18 mo

GASTROSCHISIS/OMPHALOCELE

CHARLES J.H. STOLAR, MD

Gastroschisis is due to a vascular disruption

- Omphalocele is a malformation

HISTORY & PHYSICAL

- Dx often antenatal made on fetal US
- Omphalocele
  - ➢ Always covered by umbilical membrane (sometimes ruptured) & contained w/in umbilicus
  - ➢ Sometimes assoc w/ other defects, e.g. CHD (usually A-V canal defect), Hirschsprung disease, imperforate anus, cloacal exstrophy, trisomy 21
  - ➢ "Giant" omphalocele containing liver assoc w/ resp distress
  - ➢ Upper abd omphalocele assoc w/ resp insufficiency
- Gastroschisis
  - ➢ Abd viscera herniated to right of umbilicus; NOT covered by umbilical membrane

- ➢ Exposure of bowel to amniotic fluid causes serositis; can be severe; assoc w/ foreshortening of gut
- ➢ Seldom assoc w/ other anomalies except occasional intestinal atresia

TESTS
Chromosome analysis
Echocardiogram for omphalocele

DIFFERENTIAL DIAGNOSIS
N/A

MANAGEMENT
- Cover exposed bowel w/ warm saline-soaked gauze & waterproof covering
- Maintain nl body temperature
- Keep covered bowel upright or turn baby on side to avoid kinking vena cava
- Intubate electively
- Prophylactic antibiotic coverage
- Surgery for omphalocele can be delayed if membrane intact; if omphalocele large, covering w/ stretch gauze can begin reduction
- Surgery for gastroschisis cannot be delayed
- Goal of surgery: to reduce abd organs into abdomen, close abd w/o undue pressure; primary closure preferred if safe
- Delayed closure uses prosthetic materials to temporarily augment abd wall, followed by serial reductions & final fascial closure
- Atresias w/ gastroschisis reduced, repaired subsequently
- Both defects must have access for parenteral nutrition
- Assoc defects managed as needed

SPECIFIC THERAPY
N/A

FOLLOW-UP
- Contrast studies w/ gastroschisis for atresias
- Growth & nutrition
- Pulm/cardiac follow-up as needed

COMPLICATIONS AND PROGNOSIS

Immediate
- Primarily fluid, electrolyte, nutritional

Later
- Poor growth due to feeding intolerance
- May develop gastroesophageal reflux
- May develop abdominal wall hernia or inguinal hernia

GLYCOGEN STORAGE DISEASE TYPE 1A (VON GIERKE'S DISEASE)

WENDY K. CHUNG, MD, PhD

HISTORY & PHYSICAL

History
- Failure to thrive
- Bleeding
- Neonatal hypoglycemia, lethargy/seizures, decreased nighttime feeds
- Vomiting
- Protuberant abdomen

Signs
- Hepatomegaly
- Short stature
- Cutaneous xanthomas later in course
- Gouty nodules later in course

TESTS
- Hypoglycemia & metabolic acidosis
- Appropriately suppressed serum insulin
- Urine analysis: ketosis
- LFTs elevated
- Coagulation tests elevated
- Lactic acidosis
- Hyperlipidemia
- Hyperuricemia
- Subnormal glycemic response to glucagon challenge
- Liver biopsy w/ lipid & glycogen accumulation; direct enzyme analysis for definitive Dx
- Direct genetic testing for definitive Dx
- Prenatal Dx is available

DIFFERENTIAL DIAGNOSIS
- See **FATTY ACID OXIDATION DISORDERS**
- Disorders of gluconeogenesis
- Hyperinsulinemia
- Electrolyte abnormalities
- Other metabolic disorders

MANAGEMENT
- Airway, breathing, circulation
- Push IV glucose & repeat D-sticks (see **HYPOGLYCEMIA** in the "Neonatal Presenting Signs" section)
- Maintain plasma glucose >80 mg/dL

SPECIFIC THERAPY
- Frequent feeds w/ 65–70% carbohydrate meals; fasting contraindicated
- Uncooked cornstarch (1.6 g/kg q4h in infants, ~2 g/kg q6h in older children); mix w/ formula in infants
- NG or G-tube feeds may be necessary at night for infants
- Restrict galactose & fructose ingestion
- Allopurinol to lower urate levels
- Liver transplant: curative

No contraindications to treatment

FOLLOW-UP
- Monitor D-sticks w/ intercurrent illness
- Monitor lactate, triglycerides, uric acid, liver size to assess metabolic control
- Monitor for hepatic adenomas by CT or US
- Monitor for oral ulcers & inflammatory bowel disease in type IB

COMPLICATIONS AND PROGNOSIS
- Earlier the treatment & better the metabolic control, better the outcome
- Metabolic improvement w/ age, w/ less frequent hypoglycemia
- Cognitive development declines w/ increasing freq of hypoglycemic seizures
- Short stature possible
- In adulthood, may develop hepatic adenomas that can transform into malignant hepatocellular carcinoma

GLYCOGEN STORAGE DISEASE TYPE II (POMPE'S DISEASE)

RICHARD A. POLIN, MD
REVISED BY WENDY K. CHUNG, MD, PhD

HISTORY & PHYSICAL

- Symptoms generally not evident for several wks, but may present in 1st days of life
- Hypotonia (usually w/ preservation of deep tendon reflexes initially), weakness, failure to thrive, poor feeding, CHF most common symptoms
- Macroglossia
- Difficulty sucking, crying, swallowing
- Skeletal muscles develop a characteristic rubbery feel
- Hepatomegaly secondary to CHF

TESTS

- Prenatal Dx possible
- CXR: cardiomegaly, signs of CHF
- ECG: short P-R interval, giant QRS complexes, inverted T waves
- Echocardiogram: severe concentric hypertrophy; LV may be small; LV outflow obstruction in 20%
- CPK & SGOT may be elevated
- Muscle biopsy: large amounts of PAS-positive material
- EMG: fibrillation, pseudomyotonic bursts, small polyphasic potentials
- Assay for acid maltase (alpha-glucosidase) in leukocytes, fibroblasts or muscle; can be assayed from blood spots on filter paper

DIFFERENTIAL DIAGNOSIS

- See **HYPOTONIA, CONGESTIVE HEART FAILURE & HEPATOMEGALY** in the "Neonatal Presenting Signs" section.

MANAGEMENT

- Cardiorespiratory support while initiating enzyme replacement

SPECIFIC THERAPY

- Enzyme replacement therapy w/ biweekly infusions of alpha-glucosidase

FOLLOW-UP

- Monitor cardiac status w/ serial echocardiograms

COMPLICATIONS AND PROGNOSIS

- Excellent improvement in cardiac hypertrophy & function w/ enzyme replacement therapy
- If initiated early, enzyme replacement therapy may greatly slow myopathy, although there may be a residual neuropathy

HEMORRHAGIC DISORDERS IN THE NEWBORN, CONGENITAL AND ACQUIRED

HELEN M. TOWERS, MD

HISTORY AND PHYSICAL

History

- Family Hx of consanguinity
- H/o previous infant w/ coagulopathy
- Maternal h/o anticonvulsant Rx during pregnancy
- Maternal idiopathic thrombocytopenia (ITP) or Hx thereof
- Vitamin K administered postnatally?
- Liver disease

Physical

- Bleeding from umbilical cord, puncture site; GI, GU, pulmonary, IVH; after circumcision
- Ecchymosis
- Petechiae
- Hepatosplenomegaly, flank mass
- Associated congenital anomalies, e.g., absent radii

TESTS

- CBC w/ platelet count
- Coagulation studies of intrinsic system (aPTT), extrinsic system (PT), thrombin time, bleeding time, fibrinogen, D-dimers
- LFTs
- Specific coagulation factor assays (NOTE: reference ranges specific to plasma concentrations, gestational & postnatal age)
- Interpretation of coagulation studies
  - ➢ Prolonged PT & PTT
    - Uncorrected w/ 1:1 mixing w/ normal plasma suggests heparin effect

- Corrected w/ 1:1 mixing w/ normal plasma suggests vitamin K deficiency, disseminated intravascular coagulation (esp w/low fibrinogen, elevated D-dimers, thrombocytopenia), or impaired liver synthetic function

➢ Prolonged PTT: corrected w/ 1:1 mixing w/ normal plasma suggests hemophilia A or B, or contact factor abnormalities (factors XI, XIII, prekallikrein, high-molecular-weight kininogen)

➢ Thrombocytopenia (see **THROMBOCYTOPENIA** in the "Neonatal Presenting Signs" section)

➢ All coagulation tests nl: consider Factor XIII deficiency, alpha-2-antiplasmin, or plasminogen activator inhibitor-1 deficiency, platelet dysfunction (e.g., after indomethacin), von Willebrand disease

- Platelet antibody studies in parents w/ platelet count $<50{,}000/mm^3$ at birth
- Blood & viral cultures, TORCH studies
- Cranial US, CT

DIFFERENTIAL DIAGNOSIS

- Congenital disorders of coagulation factors
  - ➢ Autosomally inherited
    - Deficiencies of factors II, V, VII, XI
    - Von Willebrand disease
  - ➢ X-linked recessive
    - Deficiencies of factors VIII, IX
    - Wiskott-Aldrich syndrome
  - ➢ Congenital liver disease
- Congenital disorders of fibrinogen: homozygous
  - ➢ Afibrinogenemia
  - ➢ Hypofibrinogenemia
  - ➢ Dysfibrinogenemia
- Congenital platelet disorders
  - ➢ Neonatal alloimmune thrombocytopenia (NAIT)
  - ➢ Autoimmune thrombocytopenia (due to maternal ITP)
  - ➢ Associated w/ chromosomal disorders, e.g. Noonan's syndrome, trisomy 13, 18, 21
  - ➢ Thrombocytopenia w/ absent radii syndrome
  - ➢ Fanconi's anemia
  - ➢ Congenital amegakaryocytic thrombocytopenia
  - ➢ Kasabach-Merritt syndrome
- Acquired bleeding disorders

- ➢ Vitamin K deficiency: 3 types
  - Early, due to maternal intake of meds that inhibit vitamin K (e.g., anticonvulsants)
  - Classic, due to inadequate intake, onset day 2–7
  - Late onset, due to inadequate intake or liver disease, from 2 wks to 6 mo
- ➢ Heparin overdose
- ➢ Disseminated intravascular coagulation
- ➢ Liver disease (e.g., due to hypoxic damage, viral infections, shock, hydrops, complications of parenteral nutrition)
- ➢ ECMO
- ➢ Drug-induced thrombocytopenia

MANAGEMENT

- What to do first: ABCs
- RBC transfusion for bleeding w/ >20–25% loss of circulating blood volume
- Platelet transfusions for platelet count
  - ➢ <80,000–100,000/mm^3 w/ bleeding
  - ➢ <50,000/mm^3 if invasive procedure req (e.g., LP)
  - ➢ <20,000/mm^3
- Treat associated underlying conditions
- Coagulation products
  - ➢ Fresh frozen plasma (FFP)
  - ➢ Cryoprecipitate: contains fibrinogen & factors VIII & XIII
  - ➢ Stored plasma: lacks factor V

Note: Factor IX concentrates not recommended except for proven severe factor IX deficiency due of risk of thrombosis.

- Vitamin K: IV or subQ to avoid hematomas

SPECIFIC THERAPY

- Coagulation factor deficiencies
  - ➢ Factor VII, VIII, IX as appropriate
  - ➢ Prenatal Dx possible for most coagulation factor deficiencies, in-utero factor replacement possible
- Alloimmune thrombocytopenia
  - ➢ Compatible (i.e., antigen-negative) platelets, from mother or phenotyped donor
  - ➢ IgG, 1 g/kg over 6–8 hrs on 2 successive days
  - ➢ May require exchange transfusion to remove antibody
- Autoimmune thrombocytopenia
  - ➢ Corticosteroid Rx
  - ➢ IgG 1 g/kg over 6–8 hrs on 2 successive days

- ➢ May require exchange transfusion to remove antibody
- ➢ Splenectomy only for life-threatening & no effective alternatives

- Disseminated intravascular coagulation
  - ➢ Rx of underlying condition critical
  - ➢ FFP or platelet concentrates
  - ➢ Low-dose heparin may be helpful in controlling consumption of platelets & fibrinogen
- Liver disease: exchange transfusion w/ FFP followed by platelet concentrate may improve hemostasis to allow liver biopsy

FOLLOW-UP

- Inherited coagulation defects require close follow-up
  - ➢ Infusion of stored plasma, FFP or specific factor concentrates prior to surgical or invasive procedures
  - ➢ Reevaluation of factor levels at age 3–6 mo recommended
- Neurodevelopmental w/ CNS hemorrhage

COMPLICATIONS AND PROGNOSIS

- Inherited coagulation deficiencies: factor II, V, VII, VIII, IX, X, XI & XIII deficiencies may cause neonatal intracranial hemorrhage
  - ➢ Factor II assoc w/ bleeding in adulthood following venipuncture
  - ➢ Factor V deficiency assoc w/ pre- & postnatal intracranial hemorrhage, umbilical & soft tissue bleeding; thrombotic complications occur in adults, not reported in neonates
  - ➢ Factor VII deficiency: plasma concentration
    - <1%, severe hemorrhage
    - >5%, milder hemorrhagic complications
  - ➢ Factor VIII deficiency (severe) assoc w/ 10% incidence of hemorrhage in neonatal period, 70% incidence of a severe hemorrhagic event by age 18 mo
- Immune thrombocytopenia: resolves w/ clearance of maternal antibody over months
- Others depend on underlying conditions

HEPATITIS, IDIOPATHIC NEONATAL GIANT CELL

J.M. LORENZ, MD

HISTORY & PHYSICAL

- Prolonged conjugated hyperbilirubinemia w/o biliary atresia, stigmata of systemic viral infection, or specific etiology
- Prevalence: 1:5,000–9,000 live births

- Etiology unknown, probably multiple; may be pathophysiologically related to biliary atresia
- 10–15% recurrence in siblings
- History
  - ➢ Low birth wt
  - ➢ More common in males
  - ➢ Poor feeding, vomiting
  - ➢ Conjugated hyperbilirubinemia in sibling
- Physical
  - ➢ Jaundice may be present at birth, but more typically presents at days to 6 wk of age
  - ➢ Initially abdominal distention w/ hepatomegaly, progressing to small hard liver w/ splenomegaly, ascites
  - ➢ Acholic stools
  - ➢ Dark urine (+ for bilirubin, urobilinogen)

TESTS

- For known infectious & metabolic causes of conjugated hyperbilirubinemia (see **HYPERBILIRUBINEMIA, CONGUGATED** in the "Neonatal Presenting Signs" section)
- Serum alpha-fetoprotein MAY be elevated w/ idiopathic neonatal hepatitis, but not biliary atresia
- Liver US: enlarged liver; normal gallbladder; patent, non-dilated bile ducts
- Hepatobiliary scintigraphy (HIDA scan) after 5 days of phenobarbital: sluggish or absent uptake of isotope; some appears in stool w/ uptake
- Percutaneous liver biopsy (w/ above workup, establishes Dx in >90% of cases): hepatocellular necrosis; prominent multinucleated giant cell transformation foamy cytoplasm w/ acidophilic bodies, bile pigment; canalicular cholestasis; Kupffer cells swollen, contain bile pigment hemosiderin, lipofuscin; modest lymphocyte portal inflammatory infiltrates; extramedullary hematopoiesis; ductular proliferation; bile thrombi rare
- Laparotomy w/ cholangiography, wedge biopsy if biliary atresia cannot be excluded w/ above evaluation by age 2–3 mo

DIFFERENTIAL DIAGNOSIS

- Dx of exclusion: biliary atresia, known infectious & metabolic causes of hepatitis (see **BILIARY ATRESIA**; see **HEPATOMEGALY** and **HYPERBILIRUBINEMIA, CONGUGATED** in the "Neonatal Presenting Signs" section)

MANAGEMENT

- Dietary: 120–150 kcal/kg/day; consider MCT formula
- Ursodiol, 10–15 mg/kg PO q day
- Cholestyramine, 0.25–0.5 g/kg/day in 3 divided doses
  - Vitamins, trace mineral supplementation
  - Vitamin A, 5,000–25,000 IU/day PO
  - Vitamin D, 1,200–5,000 IU/day PO
  - Vitamin E, 15–25 IU/kg/day PO
  - Vitamin K1, 2.5 mg PO 2x/wk
  - Se, 1–2 mcg/kg/day PO
  - Zn, 1.0 mg/kg/day PO
- Liver transplant w/end-stage liver disease

SPECIFIC THERAPY

- None

FOLLOW-UP

- Total & direct serum bilirubin, liver enzymes, albumin, prothrombin time, ammonia, cholesterol, vitamin A, vitamin E:total serum lipids, 25-hydroxy vitamin D, Ca, Mg, P
- Repeat liver US, HIDA scan, percutaneous liver biopsy if pale or acholic stools persist >1 mo w/o significant decrease in direct bilirubin

COMPLICATIONS AND PROGNOSIS

- Complications
  - Malabsorption
    - Poor growth
    - Steatorrhea
    - Fat-soluble vitamin deficiencies
    - Mineral, trace element deficiencies
  - Portal hypertension, variceal bleeding
  - Bleeding diathesis
  - Ascites
- Prognosis
  - Recovery (50%)
  - Death w/in 1 y (25%)
  - Progression to cirrhosis or biliary atresia (25%)

HERPES SIMPLEX INFECTION, INTRAUTERINE/NEONATAL INFECTION

J.M. LORENZ, MD

- HSV types 1 & 2 responsible for 25% & 75% of neonatal infections, respectively, but are similarly virulent
- Types of fetal/neonatal infection
  - ➢ IN UTERO (transplacental, ascending): 1:200,000 live births
  - ➢ NEONATAL: 1:2,000–5,000
    - INTRAPARTUM (85–90% of neonatal infections): transmission risk w/ vaginal delivery is related to type of maternal genital infection & genital shedding (regardless of clinical signs)
      - W/ 1st episode maternal PRIMARY genital herpes (first infection w/ either HSV 1 or 2)
        Risk 50%
        Prevalence 1:1,900 live births
      - W/ 1st episode maternal NON-PRIMARY genital infection (1st infection w/HSV type subsequent to prior infection w/ alternate type)
        Risk 30%
      - W/ recurrent maternal genital herpes
        Risk: symptomatic 1–5%, asymptomatic 0.01%
        Prevalence 1:8,000 live births
      - Rare regardless of category of maternal infection w/ cesarean section delivery w/in 6 h of ROM
    - POSTPARTUM (until ~ age 1 mo) acquisition from maternal or non-maternal, non-genital source (10–15% of neonatal infections)

HISTORY & PHYSICAL

- MATERNAL: usually none
  - ➢ Prevalence of viral shedding at delivery is 0.01–0.39% regardless of past medical history of genital herpes
  - ➢ 60–80% OF WOMEN WHOSE INFANTS ACQUIRE INFECTION VERTICALLY HAVE NO H/O GENITAL HERPES & ARE ASYMPTOMATIC DURING PREGNANCY AND DELIVERY. CONSIDER DX IN ANY INFANT W/ COMPATIBLE SIGN REGARDLESS OF MATERNAL HX.
- NEONATAL: Infection is invariably symptomatic CLASSIFICATION
  - ➢ IN UTERO INFECTION (presents at birth; 3% of infected infants)

- Spontaneous abortion
- Placental pathology: necrosis, inclusions in trophoblasts
- Skin vesicles or scarring
- Keratoconjunctivitis, chorioretinitis, microphthalmia, retinal dysplasia
- Microcephaly, hydrancephaly

➢ NEONATAL (INTRAPARTUM, POSTPARTUM)

- LOCALIZED TO SKIN, EYES, OR MOUTH (40% intrapartum & postnatally acquired infections)
  - ***Localized keratoconjunctivitis*** presents at 2–3 days w/ red swollen palpebrae, purulent exudate, conjunctival membrane, corneal epithelial dendritic or geographic fluorescent staining or central stromal opacifications
  - ***Localized skin/oral mucosal involvement*** (90% of localized infection) presents at 7–14 days after exposure w/ small vesicle on erythematous base on skin (90%) or oral mucosa, progressing to clusters that may coalesce
- ENCEPHALITIS +/− SKIN, EYE, MUCOSAL INVOLVEMENT (35% of intrapartum & postnatally acquired infections)
  - Presents 1–4 days, but as late as 6 wk after exposure
  - Skin/oral mucosal involvement (63%)
  - Focal/generalized seizures
  - Lethargy, irritability, tremors
  - Poor feeding
  - Temp instability
  - Budging fontanel
  - Pyramidal tract signs
  - Hx or development of mucocutaneous vesicles (60%)
  - CSF: pleocytosis, mild to moderate decrease in glucose; progressive increase in protein to >/= 1,000 mg/dL (increased in >90% at onset); PCR useful; culture usually negative
- DISSEMINATED INFECTION (25% of intrapartum & postnatally acquired infections)
  - More common w/o maternal HSV 1 & HSV 2 Ab
  - Presents 1–7 d after birth (may be present at birth w/ PROM) or 2–14 days after postpartum exposure
  - Irritability, seizures
  - Respiratory distress
  - Fulminant hepatitis w/ jaundice, coagulopathy
  - Shock

- Skin vesicles develop in 80% w/o Rx, but usually not present at onset
- Meningoencepahlitis w/CSF pleocytosis, mild to moderate decreased glucose; progressive increase in protein (60–75%); culture may be +

TESTS

- Nonspecific: CBC, LFTs; LP (***always*** indicated even in the absence of CNS signs); fluorescent corneal staining; EEG, head CT regardless of presentation; coagulation studies, CXR (diffuse interstitial pattern +/− pleural effusion w/pneumonia), AXR as indicated
- Specific (must be interpreted in light of clinical & nonspecific laboratory signs)
  - ➢ GOLD STANDARD: Positive culture base of skin vesicle, blood, urine or CSF
  - ➢ Positive culture of conjunctival, nasopharyngeal or resp secretions, rectal swab (Note: Viral isolation from superficial sites in absence of lesions may represent colonization, esp if infant is <24 h)
  - ➢ Positive PCR on CSF – w/CNS involvement: sensitivity 75–100% & specificity 71–100%, w/considerable intralaboratory variability)
  - ➢ Direct immunofluorescence staining of scrapings from base of skin vesicle (sensitivity 60–70%; specificity 65%)
  - ➢ Histologic methods insensitive, nonspecific
  - ➢ Serologic tests of little value

DIFFERENTIAL DIAGNOSIS

- TRANSPLACENTAL INFECTION
  - ➢ Fetal varicella zoster (VZ) syndrome
- INFECTION LOCALIZED TO SKIN, EYES, OR MUCOSA
  - ➢ Erythema toxicum
  - ➢ Transient pustular melanosis of the newborn
  - ➢ Varicella
  - ➢ Enteroviral disease
  - ➢ Syphilis
  - ➢ Acrodermatitis enteropathica
  - ➢ Incontinentia pigmentosa
- ENCEPHALITIS +/− SKIN, EYE, MUCOSAL INVOLVEMENT
  - ➢ Bacterial/viral meningitis or encephalitis
  - ➢ Intracranial hemorrhage/infarct
  - ➢ Metabolic disease
  - ➢ See **SEIZURES** in the "Neonatal Presenting Signs" section

- DISSEMINATED INFECTION
  - Bacterial sepsis
  - Enteroviral disease
  - Congenital VZ
  - Congenital cytomegalovirus infection
  - Congenital syphilis

MANAGEMENT

- Supportive therapy
- Infection control
  - Contact isolation in separate room
  - Isolation from mother w/ genital infection not indicated

SPECIFIC THERAPY

- PREVENTION
  - TRANSPLACENTAL INFECTION – none
  - INTRAPARTUM INFECTION
    - Maternal suppressive Rx w/acyclovir for primary infection at >/= 36 wk GA
    - Risk:benefit of maternal suppressive Rx with h/o primary infection prior to or during early pregnancy not defined – not recommended
    - Careful vaginal exam on presentation for delivery; if lesions present, cesarean section delivery, esp if ROM <6 h
    - Avoid fetal scalp monitoring/sampling in women with h/o genital herpes
    - Neonatal acyclovir prophylaxis (as opposed to presumptive Rx) NOT recommended
  - POSTPARTUM INFECTION
    - Neonatal acyclovir prophylaxis (as opposed to presumptive Rx) NOT recommended
    - Mothers (& household contacts) w/ herpes labialis should cover & not touch their lesion, avoid kissing/nuzzling the infant, & be scrupulous about hand washing [Postnatal acquisition (after term delivery) from seropositve mother w/ herpes labialis does not often result in disease; seronegative mother w/ herpes labialis may pose a more significant risk]
    - Exclusion of staff w/ herpes labialis from direct patient contact is controversial; at a minimum, staff should cover & not touch their lesion & comply w/ hygiene policy
    - Staff w/ herpetic whitlow SHOULD be excluded from direct patient contact
- TREATMENT

- ➢ TRANSPLACENTAL INFECTION
  - None effective w/ CNS manifested by microcephaly, hydrancephaly
  - With acute disease due to ascending infection w/ prolonged ROM: same as for intrapartum/postpartum infection
- ➢ INTRAPARTUM/POSTPARTUM INFECTION: Acyclovir 20 mg/kg/dose q8h IV over 1 h × 14 days (localized disease) or 21 days (encephalitis/disseminated disease)
  - Ensure adequate hydration to minimize nephrotoxicity
  - Increase dose interval w/renal impairment, GA <34 wk
  - Side effects: phlebitis (make solution more dilute), transient elevation of serum creatinine, crystalluria

■ Plus

- ➢ WITH EYE INVOLVEMENT: trifluridine ophthal soln 1%, 1 gtt in affected eye q2h while awake to max of 9 gtts/day until cornea is reepithelialized (usually w/in 2–7 days), then 1 gtt q4h × 7 days; do not exceed 21 days of Rx

FOLLOW-UP

■ W/ known neonatal exposure at birth but no signs of disease: consider eye & nasopharyngeal (& skin lesion should any develop) cultures at 12 & 48 h after birth +/− weekly culture for the first 4 wk of life

■ During Rx

- ➢ Serial CBCs, LFTs, serum creatinine
- ➢ Ophthal exam including corneal staining w/ fluorescein as indicated
- ➢ EEG & head CT before discharge
- ➢ Long-term: developmental, neurol, ophthal, audiol

COMPLICATIONS AND PROGNOSIS

■ TRANSPLACENTAL INFECTION

- ➢ Mortality 30%
- ➢ Neurodevelopmental sequelae in almost all survivors

■ ASCENDING/INTRAPARTUM/POSTPARTUM INFECTION

- ➢ Recurrent skin & mouth lesions for mos to yrs w/ or w/o Rx
- ➢ Chorioretinitis, cataracts, retinal detachment w/eye involvement w/ or w/o Rx
- ➢ Mortality & neurologic impairment depend on presentation & promptness of Rx
  - INFECTION LOCALIZED TO SKIN, EYES, OR MUCOSA

- 70% progress to encephalitis or disseminated disease w/o Rx
- Non-fatal w/o progression
- Neurologic impairment (CP, microcephaly, blindness) in the absence of progression in 40% w/o Rx , ~0% w/ Rx

- ENCEPHALITIS ± SKIN, EYE, MUCOSAL INVOLVEMENT
  - 50% mortality w/o Rx, 4% w/ Rx
  - Neurologic impairment (psychomotor retardation, microcephaly, hydrancephaly, porencephalic cysts, spasticity, blindness, chorioretinitis, learning disability) in 80% w/o Rx, 70% w/ Rx
- DISSEMINATED INFECTION
  - 80% mortality w/o Rx, 30% w/ Rx
  - Neurologic impairment in 50% w/o Rx, 20% w/ Rx

HIP, DEVELOPMENTAL DYSPLASIA (CONGENITAL DISLOCATION)

J.M. LORENZ, MD

- Incidence
  - ➢ Transiently dislocatable hip, 1:1,000
  - ➢ Transiently subluxatable hip, 10:1,000
  - ➢ 60–80% identified by PE in the newborn resolve spontaneously
- Risk factors
  - ➢ Female gender (80% of those w/ DDH are female)
  - ➢ Family hx (12–33% of those w/ DDH); risk is 6% w/ 1 affected sibling, 12% w/ 1 affected parent, 36% w/ affected parent & sibling
  - ➢ Breech presentation
  - ➢ First-born status (2× the risk of subsequent siblings)
  - ➢ Oligohydramnios
  - ➢ In utero postural deformities
- More common on left [60%; may be bilateral (20%)]

HISTORY & PHYSICAL

- Usually, but not always, present in first few days of life
  - ➢ Each hip must be examined separately while stabilizing the pelvis by holding the contralateral hip w/ diaper removed & infant relaxed

- ➢ + Barlow maneuver: "clunk" as femoral head slips OUT of the acetabulum w/ adduction of hip in flexion & posterolateral pressure over anterior proximal thigh
- ➢ + Ortolani maneuver: "clunk" as femoral head slips INTO the acetabulum w/ adduction of hip in flexion & anterior pressure over posterior proximal thigh

- May be assoc w/ congenital muscular torticollis or metatarsus adductus
- Limited hip abduction is an insensitive marker until after age 3–6 mo

TESTS

- Nonspecific: none
- Specific
  - ➢ Plain radiographs: of limited use until age 4–6 mo when femoral heads are ossified
  - ➢ Hip US
    - Overly sensitive in first 6 wk of life; 90% so identified
    - Not recommended for routine screening

DIFFERENTIAL DIAGNOSIS

- "Clicks" w/ Barlow & Ortolani maneuvers
- "Teratology" hip dislocation (fixed in utero dislocation, usually due to genetic or neuromuscular disorders)

MANAGEMENT

- Subluxation may be observed for resolution for 2 weeks w/o Rx
  - ➢ Dislocation or persistent subluxation
  - ➢ Goal is to maintain reduction of femoral head in the true acetabulum; the earlier Rx is instituted, the more likely it is to be successful
  - ➢ Pavlik harness splinting of the hip in flexion & mid-abduction as soon as Dx confirmed until hip is clinically stable & acetabular development normal (usually 3–4 mo)
  - ➢ Closed surgical reduction w/ skin traction & hip spica casting if splinting unsuccessful
  - ➢ Open surgical reduction if closed reduction unsuccessful

FOLLOW-UP

- During Rx
  - ➢ Serial exams for hip stability
  - ➢ Confirm reduction, follow acetabular development by sonography

- Long-term: radiologic until skeletal maturity

COMPLICATIONS AND PROGNOSIS

- Complications
  - ➢ W/o reduction
    - Progressive acetabular dysplasia & maldirection, excessive femoral anteversion & hip muscle contractures
    - Avascular necrosis of the hip
    - Degenerative changes in the hip in second decade
    - Arthritis in the third decade
    - Chronic pain
  - ➢ W/ reduction
    - Avascular necrosis of femoral head
    - Femoral nerve palsy, usually self-limited
- Prognosis w/ Pavlik harness splinting
  - ➢ 95% successful w/ subluxatable or dislocatable hip
  - ➢ 80% successful w/ frankly dislocated hip

HIRSCHSPRUNG DISEASE

CHARLES J.H. STOLAR, MD

HISTORY & PHYSICAL

- Failure to pass meconium in 1st 48 h of life
- Usually term white male, but not always
- Abd distention
- Acute abdomen from enterocolitis
- Seen w/ trisomy 21 & Ondine's curse
- Normal-appearing anus

TESTS

- Most important: full-thickness rectal biopsy just proximal to dentate line to look for ganglion cells in submucosal & intramuscular planes
- Transition zone usually in the sigmoid, but not always
- Suction biopsy excludes Dx only if ganglion cells seen in submucosa
- Contrast enema only suggests Dx
- Abd plain films can suggest Dx of enterocolitis

DIFFERENTIAL DIAGNOSIS

- Enterocolitis of other etiologies

- Hypothyroidism
- Small colon syndromes
- Meconium ileus (cystic fibrosis)
- Meconium plug (may occur w/ Hirschsprung disease as well)

MANAGEMENT
- Gentle rectal dilatation
- Rectal irrigation w/ 15–20 mL/kg warm saline
- Plan for primary pull-through if no enterocolitis in 1st wk of life
- Leveling colostomy if unable to do primary pull-through safely
- Goal of definitive surgery: bring ganglionated bowel to dentate line
- Enterocolitis: treated w/ bowel rest & decompression, rectal irrigations, broad-spectrum antibiotics

SPECIFIC THERAPY
N/A

FOLLOW-UP
- Ped Surg

COMPLICATIONS AND PROGNOSIS
- Bacterial translocation may lead to recurrent episodes of sepsis
- Postop enterocolitis not uncommon; treat like preop
- Pelvic abscess in early postop period
- Possible anastomotic stricture in late postop period
- Most children eventually well

HYDRONEPHROSIS, PRENATAL

DIX PHILLIP POPPAS, MD

- Definition: in utero sonographic detection of fetal renal pelvic dilatation, pelviectasis, &/or hydronephrosis
- May be a normal developmental variant or severe obstructive uropathy
- Prevalence: 1:100 to 1:500 pregnancies
- Hydronephrosis may be detected from the 15th wk of gestation
- No racial predilection

HISTORY & PHYSICAL
- Earlier identification suggests more severe condition

- Criteria for fetal hydronephrosis
  - ➢ Renal pelvic diameter
    - >8 mm by 25 wk gestation
    - 10 mm by 32 wk
    - 15 mm at term
  - ➢ Presence of calycectasis
  - ➢ Renal cortical thinning or cysts
- Unilateral or bilateral
- Bladder distention suggests posterior urethral valves in male
- Change in degree of dilation relative to bladder dilation suggests ureterovesicular reflux
- Oligohydramnios
  - ➢ Indicates compromised renal function
  - ➢ Assoc w/ severe obstructive uropathy
    - Posterior urethral valves
    - Urethral atresia
  - ➢ Increase risk for pulm hypoplasia when severe before 20–22 wk gestation
- Polyhydramnios may occur w/ unilateral hydronephrosis assoc w/ intestinal compression
- Physical exam
  - ➢ Prenatal: Maternal physical exam for fundal height, oligohydramnios
  - ➢ Postnatal
    - Palpable kidney(s)
    - Distended bladder
    - Genital anomalies
    - Urinary stream (if weak in male, suggests posterior urethral valves)

TESTS

- Prenatal
  - ➢ Amniotic fluid volume
    - 90% composed of fetal urine after the 16th wk of gestation
    - Correlates w/ fetal renal function
  - ➢ Serial fetal sonography
  - ➢ Assessment of fetal urinary Na & Cl concentration, osmolality
    - Indication: bilateral hydronephrosis assoc w/ oligohydramnios IF none of the following are present:
      - Pulm hypoplasia

- Assoc life-threatening anomalies
- Signs indicative of poor prognosis for recovery of renal function w/ intervention: renal cortical cysts, diffuse renal parenchymal echogenicity
- Urine [Na] < 100 mmol/L, urine [Cl] < 90 mmol/L, urine Osm <210 mOsm/L c/w preservation of renal function

■ Postnatal
  ➢ Serum electrolytes
  ➢ Serial serum creatinine and/or serum creatinine after 5 days when it reflects neonatal renal function
  ➢ Serum total CO_2 for acidosis
  ➢ Urinalysis, urine culture
■ Postnatal assessment
  ➢ Unilateral hydronephrosis in male or bilateral hydronephrosis in female
    - Delay initial renal/bladder US for 7 days (avoids false-neg result due to low urine flow rate in immediate neonatal period)
    - Repeat renal/bladder US at 1 mo
    - Voiding cystourethrogram (VCUG) at 1 mo
    - Diuretic nuclear renal scan at 4–6 wk
  ➢ Bilateral hydronephrosis in male – early postnatal assessment w/ sonogram VCUG to exclude posterior urethral valves

DIFFERENTIAL DIAGNOSIS

Of etiology

■ Renal
  ➢ Ureteropelvic junction obstruction
  ➢ Duplication anomalies
■ Vesicoureteral
  ➢ Reflux
  ➢ Ureterovesical junction obstruction
    - Prune-belly syndrome
    - Megacystis-megaureter microcolon syndrome
■ Multicystic dysplastic kidney
■ Autosomal recessive polycystic kidney disease
■ Intestinal disorders
  ➢ Intestinal duplication
  ➢ Mesenteric cysts
  ➢ Imperforate anus
  ➢ Persistent cloaca
  ➢ Cloacal exstrophy

- Ovarian cysts
- Tumors
  - ➢ Neuroblastoma
  - ➢ Congenital mesoblastic nephroma

MANAGEMENT

- Prenatal
  - ➢ Assessment of hydronephrosis, oligohydramnios
  - ➢ Unilateral
    - Serial fetal sonography q4 wk; delivery at term
    - Severe progressive hydronephrosis: consider intrauterine drainage if abd circumference may make vaginal delivery difficult
  - ➢ Bilateral cases w/ oligohydramnios
    - Termination

    versus
    - Observation: consider fetal intervention* for severe oligohydramnios before 32–34 wk or early delivery to allow neonatal intervention after 32–34 wk IF NONE OF THE FOLLOWING EXIST:
      - Pulmonary hypoplasia
      - Assoc life-threatening congenital anomalies
      - Signs indicative of poor prognosis for recovery of renal function – i.e., renal cortical cysts, diffuse renal parenchymal echogenicity, abnormal fetal urine composition (urine [Na] > 100 mmol/L, urine [Cl] > 90 mmol/L, urine Osm > 210 mOsm/L)
    - Fetal intervention
      - Percutaneous aspiration of fetal urine from the bladder
      - Percutaneous urinary bladder to amniotic fluid shunting
- Postnatal
  - ➢ IV line for fluids & antibiotics
  - ➢ Pulmonary support for respiratory deficiency as necessary
  - ➢ UTI prophylaxis: amoxicillin, 12 mg/kg q day PO
  - ➢ Imaging studies (timing based on whether hydronephrosis is unilateral or bilateral; see "Tests")
  - ➢ Indications for early pyeloplasty for ureteropelvic junction obstruction
    - Differential function <35% in the affected kidney
    - Grade IV hydronephrosis in the affected kidney
    - Grade II, or worse, hydronephrosis in a solitary kidney

SPECIFIC THERAPY
N/A

FOLLOW-UP
- Prenatal: sonogram q 4 wks
- Postnatal: based on initial evaluation

COMPLICATIONS AND PROGNOSIS
- Prognosis good if renal function preserved at delivery
- W/ bilateral hydronephrosis & polyhydramnios at GA <20–22 wk
  - ➢ Chronic renal failure

HYPERTHYROIDISM, CONGENITAL

JENNIFER J. BELL, MD

HISTORY & PHYSICAL

History
- Maternal hyperthyroidism, Hx of or during pregnancy
- Fetal tachycardia
- Prematurity (early labor, PROM)
- IUGR

Signs and symptoms
- Mild disease
  - ➢ Irritability, hyperkinesis
  - ➢ Tachycardia, arrhythmias
  - ➢ Hyperphagia
  - ➢ Poor weight gain
  - ➢ Poor growth
- Severe disease
  - ➢ Goiter +/− tracheal compression
  - ➢ Proptosis/exophthalmos
  - ➢ Diarrhea
  - ➢ High-output CHF
  - ➢ Hypertension
  - ➢ Hyperthermia
  - ➢ Jaundice
  - ➢ Lymphadenopathy
  - ➢ Thrombocytopenia
  - ➢ Polycythemia
  - ➢ Hepatosplenomegaly

TESTS
- TFTs: total T4, free T4 (equilibrium dialysis preferable), total T3, TSH
- Thyroid-stimulating hormone-receptor antibody
- Skull x-ray (R/O intrauterine craniosynostosis)
- Bone age (often advanced)

DIFFERENTIAL DIAGNOSIS
- Transient, due to maternal antibodies, majority of cases (see **GRAVES DISEASE, MATERNAL**)
- Familial autosomal dominant hyperthyroidism – permanent neonatal thyrotoxicosis, due to gain of function mutation that leads to constitutively activated TSH receptor
  - ➢ Familial autosomal dominant hyperthyroidism
  - ➢ Sporadic mutation
- Elevated T4 w/ nl free T4 & nl TSH – thyroxine-binding globulin excess = familial X-linked increase in serum carrier protein; euthyroid

MANAGEMENT
- Ensure adequate caloric intake for growth
- Cardiac signs
  - ➢ Tachycardia: propranolol
    - PO: 0.25 mg/kg q6h; increase prn to maximum of 3.5 mg/kg q6h
    - IV: 0.01 mg/kg over 10 min q6h; increase prn to maximum of 0.15 mg/kg q6h
    - Side effects: hypoglycemia, bradycardia, hypotension
  - ➢ Severe CHF
    - Digoxin
    - Prednisone 2 mg/kg/day
- Sedation prn

NOTE: Almost always transient, will subside in ~3 mo, as maternal Ab metabolized

SPECIFIC THERAPY

If infant is symptomatic
- Acute therapy
  - ➢ Lugol's solution, 1 drop PO q8h × 3 days
- Maintenance therapy
  - ➢ Long-acting iodine-containing agents
    - Sodium ipodate 100 mg/day PO alone or w/ antithyroid med

OR

- Iopanoic acid (Telepaque) 500 mg PO q3 day

OR

➢ Antithyroid meds

- Methimazole 0.5–1.0 mg/kg/d in 3 doses q8h

OR

- PTU 5–10 mg/kg/d in 3 doses q8h

- In permanent neonatal thyrotoxicosis, partial thyroidectomy necessary

FOLLOW-UP

- Keep serum T4 in range of 10–14 mcg/dL
- Monitor TFTs weekly to avoid hypothyroidism (LACK OF INCREASE IN TSH DOES NOT EXCLUDE POSSIBILITY)
- Discontinue propranolol when T4 normalized
- Start taper of antithyroid therapy when TFTs low normal or after 2 mo
- Follow-up skull x-rays to R/O craniosynostosis

COMPLICATIONS AND PROGNOSIS

- Spontaneous resolution usually by 8–20 wk, but as long as 48 wk
- Withdrawal syndrome (irritability, tachycardia, sweating, hypertension) w/ abrupt discontinuation of propranolol
- Possible craniosynostosis (4–6%)
- Limited data, but possible neurological impairment, esp hyperactivity; degree correlated with severity of intrauterine hyperthyroidism, presence of craniosynostosis

HYPOPLASTIC LEFT HEART SYNDROME (HLHS)

KALYANI R. TRIVEDI, MD, AND LEE N. BENSON, MD
REVISED BY GANGA KRISHNAMURTHY, MD

- Underdevelopment of the left-sided structures of the heart
- 7% of all CHD

HISTORY & PHYSICAL

History

- Antenatal Dx possible by fetal echocardiography
- Dx of HLHS can be missed in newborn nursery

- Undiagnosed HLHS present usually by 10 days of life (as ductus closes) w/ Hx of poor feeding, irritability, poor urine output, pallor & rapid progression to shock-like state

Physical
- "Shocky," lethargic
- Vital signs: tachypnea, tachycardia, ± hypotension
- Resp: tachypnea, retractions, rales
- Cardiovascular: normal S1, single S2, soft systolic ejection murmur, ± mid-diastolic murmur, weak or absent distal pulses, poor perfusion
- Other: hepatomegaly

TESTS
- ABG for metabolic acidosis
- Serum arterial lactate to assess adequacy of cardiac output
- Bun/Creat, LFTs
- CXR: ± cardiomegaly, ± pulmonary edema, increased pulmonary vascular markings
- ECG: right ventricular hypertrophy, absence of left-sided forces
- Echo
  - ➢ Hypoplastic LV, mitral valve stenosis/atresia, aortic valve stenosis or atresia, severe hypoplasia of the ascending aorta & arch, coarctation
  - ➢ Atrial communication may be restrictive or atrial septum may be intact
  - ➢ Large RA, RV, PA
  - ➢ Patent ductus arteriosus w/ right-to-left flow across ± retrograde perfusion of arch

DIFFERENTIAL DIAGNOSIS
- See **COARCTATION OF THE AORTA** and **CRITICAL PULMONARY STENOSIS**
- Other causes of shock (see **SHOCK**)

MANAGEMENT
What to do first: ABCs (airway, breathing, circulation)

General
- Start PGE1, 0.05 mcg/kg/minute
- Fluid resuscitation, correction of metabolic acidosis
- Inotropic support w/ dopamine or dobutamine

- If atrial septum is intact or restrictive, emergent transcatheter creation of atrial communication
- Prior to surgery
  - ➢ Balance Qp (pulmonary blood flow) & Qs (systemic blood flow)
  - ➢ Elective intubation & mechanical ventilation may be required to raise PVR

SPECIFIC THERAPY

- Palliation: Staged palliation towards a single-ventricle circulation
  - ➢ Stage 1: Norwood operation
    - Performed after Dx & stabilization
    - Atrial septectomy
    - Arch reconstruction
    - Modified Blalock-Taussig shunt or RV-PA conduit (Sano modification)
  - ➢ Stage 2: Bidirectional Glen
  - ➢ Stage 3: Lateral tunnel fenestrated Fontan, extracardiac conduit
- Cardiac transplantation
- Comfort care (becoming a more controversial option)

FOLLOW-UP

- Monitor O_2 saturation, feeding & growth
- Close cardiology follow-up w/ regular ECG & ECHO to assess RV function, shunt patency, AV & systemic valves, arch, recurrence of coarctation, etc.
- Meds: diuretics, digoxin, ACE inhibitors
- SBE prophylaxis
- Synagis in RSV season
- Cardiac catheterization for hemodynamic evaluation prior to 2nd & 3rd stages
- Neurodevelopmental assessment

COMPLICATIONS AND PROGNOSIS

- Postop complications after stage 1 palliation
  - ➢ Shunt occlusion
  - ➢ Impaired RV function
  - ➢ AV valve regurgitation
  - ➢ Residual coarctation
- Poor feeding, oral aversion, poor growth, rehospitalization
- Survival (at high-volume centers)
  - ➢ After Stage 1 palliation
    - 90% w/o risk factors

- 50% w/ birth wt <2.5 kg, obstructed pulmonary venous return, other congenital anomalies, Norwood operation after age 2–4 wk

➢ After Stage 2: 98%
➢ After Stage 3: 98%
➢ If cardiac transplantation is planned
- 30–50% mortality awaiting donor heart
- 5-yr survival similar to staged palliation

■ Neurodevelopmental outcome
➢ IQ < 70 (18%)
➢ One third require special ed
➢ Cerebral palsy (17%)
➢ Fine & gross motor deficits in 50%
➢ Attention problems (30–50%)
■ Cardiac transplantation likely required in late 2nd to early 3rd decade of life

HYPOTHYROIDISM, CONGENITAL

JENNIFER J. BELL, MD

HISTORY & PHYSICAL

■ Usually diagnosed by newborn screening; signs rare in neonatal period
■ History
➢ Maternal Hashimoto's thyroiditis (see **HASHIMOTO'S THYROIDITIS, MATERNAL**)
➢ Family hx of hypothyroidism
➢ Maternal iodine-containing meds or skin preps
➢ Fetal goiter on ultrasound
➢ Recurrent goiter in siblings
➢ Trisomy syndrome (esp trisomy 21)
➢ Midline facial defect
➢ Septo-optic dysplasia
➢ MRI showing ectopic posterior pituitary; interrupted pituitary stalk
■ Signs and Symptoms
➢ Fetal: signs suggesting significant intrauterine hypothyroidism:
- Hoarse cry
- Distended abdomen

- Macroglossia

➢ Neonatal: signs <5% of hypothyroid newborns, <15% at 1 mo of age
- Lethargy
- Slow feeding
- Hypotonia
- Temp instability/cutis marmorata
- Respiratory distress: nasal stuffiness, not RDS
- Infrequent stooling (<1/day)
- Sinus bradycardia
- Large posterior fontanel (>1 cm)
- Prolonged jaundice (>3 wk of age)
- Goiter

TESTS

- State-mandated newborn screening, usually done on day 2 or 3 in full term, ~ age 1 wk in preterm
- NOTE: If signs c/w hypothyroidism or goiter present, do stat thyroid function tests (TFTs) IN ADDITION TO state-mandated screen
- If newborn screen abnormal: TFTs: Serum T4, TSH, free T4 (equilibrium dialysis preferred), T3, to diagnose, classify primary vs. secondary vs. tertiary hypothyroidism
- If T4 low: thyroxine-binding globulin (TBG), to r/o decreased T4 due to familial X-linked decrease in serum carrier protein
- If hypothyroid
  - ➢ Thyroglobulin (Tg) for presence, function of gland
  - ➢ Thyroid technetium scan &/or ultrasound: location, size of gland
  - ➢ X-ray of knee, foot: extent of fetal hypothyroidism
  - ➢ RAI uptake scan if goiter present: size, function of gland

DIFFERENTIAL DIAGNOSIS

Usually no physical signs

DDx of etiology depends on results of TFTs

- LOW T4, INCREASED TSH
  - ➢ Permanent primary hypothyroidism
    - Sporadic congenital hypothyroidism (CH), 80–90% of CH; due to dysgenesis
      - Athyreosis
      - Hypoplasia
      - Ectopia

- Familial (goitrous) hypothyroidism, 10–20% of CH; due to dyshormonogenesis

➢ Transient primary hypothyroidism, due to intrauterine factors:
- Maternal iodine deficiency
- Maternal TSH-receptor blocking Abs (see **HASHIMOTO'S THYROIDITIS, MATERNAL**)
- Maternal exposure to iodine-containing meds, skin prep

■ LOW T4, NORMAL TSH
➢ Permanent
- Pituitary (secondary) or hypothalamic (tertiary) hypothyroidism
- Euthyroid w/thyroxine-binding globulin (TBG) deficiency

➢ Transient
- Transient hypothyroxinemia in preterm: due to immature hypothalamic-pituitary axis; T4 normally low (<6.5 mcg/dL); may be reported "abnormal" on neonatal screening
- "Sick euthyroid" syndrome in ill premature exaggerates transient hypothyroxinemia

■ NORMAL T4, INCREASED TSH
➢ Impending permanent hypothyroidism
➢ Transient idiopathic hyperthyrotropinemia

■ INCREASED T4, NORMAL OR INCREASED TSH
➢ Thyroid hormone resistance: mutation in thyroid hormone nuclear receptor, or post-receptor

MANAGEMENT

■ PEDIATRIC ENDOCRINOLOGY CONSULTATION
■ PRINCIPLE: if in doubt, institute Rx & re-evaluate at 3 y of age
■ GOAL: early adequate thyroid hormone replacement to normalize levels as rapidly as possible; maintain T4 in high normal range
■ General measures
➢ TSH > 20 mU/mL, T4 < 6.5 mcg/dL
- Draw TFTs, start Rx immediately; rest of w/u in next few days while TSH still elevated
- Exception: if transient hypothyroidism suspected, repeat tests; no treatment pending results

➢ TSH > 20 mU/mL, T4 normal: TFTs, thyroid scan
- If scan abnormal, Rx immediately
- If scan & TFTs normal, repeat TFTs in 1 wk

■ TSH normal, T4 < 6.5 mcg/dL
➢ In full term

- TBG
- Brain MRI to r/o structural lesions
- Evaluate other pituitary hormones

➢ In preterm, repeat TFTs weekly
- If TSH increased, Rx
- If TSH normal, Rx controversial

SPECIFIC THERAPY

■ L-thyroxine tablets
➢ Initial dose: 10–15 mcg/kg/day PO, 1× d
➢ Repeat TFT in 1 wk; if T4 normal, reduce dose to 8–10 mcg/kg/day PO
➢ Aim to normalize T4 within 2 wks
➢ TSH should normalize in 14–28 days, but may take longer

NOTE: Crush tablets in breast milk or water. Avoid mixing tablets with soy formula or Fe- or Ca-containing preparations.

FOLLOW-UP

■ Maintain T4 between 10–14 mcg/dL, free T4 in upper normal range, for first 12 mo
■ Repeat TFT q1 wk × 1 mo, then q1 mo × 6 mo, then q3 mo × 2 y, then yearly to puberty

COMPLICATIONS AND PROGNOSIS

■ Neurological impairment highly dependent on extent of fetal hypothyroidism, speed of normalization of thyroxine levels, continual maintenance of normal thyroxine levels
■ W/ Rx, physical growth, development normal

HYPOXIC-ISCHEMIC ENCEPHALOPATHY (HIE)

RAKESH SAHNI, MD

■ Incidence 1.0–1.5% (9% in <36 wks gestation, 0.5% >36 wks gestation)

HISTORY AND PHYSICAL

History

■ Antepartum
➢ Maternal diabetes
➢ Pregnancy-induced hypertension
➢ Placental insufficiency

- IUGR
- Maternal hypotension
- Prematurity
- Fetal malformation

- Intrapartum
  - Maternal bleeding (placenta previa, abruptio placentae)
  - Maternal hypotension-shock
  - Cord prolapse
  - Dystocia
  - Traumatic delivery
  - Prolonged expulsive period
  - Infection
- Postpartum
  - Severe pulmonary disease
  - Cyanotic congenital heart disease
  - Sepsis
  - Cardiovascular collapse

Physical

- Majority of intrauterine hypoxic-ischemic insults do not exhibit overt signs or subsequent neurological injury
- Neurologic signs shortly after birth c/w recent intrapartum insult
- Spectrum of clinical manifestations from mild to severe; severity correlates w/ duration & severity of the hypoxic-ischemic insult
- Moderately to severely affected infants show:
  - Generalized hypotonia
  - Paucity of spontaneous movements
  - Depressed reflexes
  - Cranial nerve palsies
  - Seizures
    - Onset w/in 12–24 h of birth c/w intrapartum insult
    - May be secondary to hypoglycemia
    - 5-min Apgar score $\leq$5, need for intubation in the delivery room & umbilical cord arterial pH $\leq$ 7.0 significantly associated w/ seizures
  - Lethargy, obtundation, or coma
- Hypoxic-ischemic injury of $\geq$1 organs in $\geq$80% w/ HIE
  - Cardiovascular
    - Tricuspid insufficiency
    - Hypotension
    - Ventricular dysfunction

- Congestive heart failure
- Myocardial necrosis

➢ Renal
- Acute renal failure
- Syndrome of inappropriate antidiuretic hormone (SIADH)
- Acute tubular or cortical necrosis

➢ Hepatic
- Elevated liver enzymes
- Elevated ammonia
- Elevated indirect, direct bilirubin
- Decreased clotting factors

➢ GI: necrotizing enterocolitis

➢ Pulmonary
- Respiratory distress syndrome
- Persistent pulmonary hypertension
- Meconium aspiration syndrome

➢ Hematologic
- Thrombocytopenia
- Disseminated intravascular coagulopathy
- Anemia if HIE due to hemorrhage

➢ Metabolic
- Lactic acidosis
- Hypoglycemia
- Hypocalcemia
- Hypomagnesemia
- Hyponatremia w/ acute renal failure, SIADH

TESTS

■ Lab studies

➢ Arterial blood gas

➢ Arterial lactate

➢ Serum electrolytes, creatinine, LFTs

➢ Aspartate-aminotransferase

➢ Brain-specific creatine kinase isoenzyme BB (CK-BB)

➢ Hypoxanthine

➢ Erythropoietin beta-endorphin

➢ CSF
- Lactate, lactate dehydrogenase
- Hydroxybutyrate dehydrogenase
- Neuron-specific enolase
- Fibrinogen degradation products
- Ascorbic acid

- Imaging studies
  - ➢ Head US
    - Useful for intraventricular hemorrhage & periventricular leukomalacia (PVL)
    - Poor for differentiating ischemic & hemorrhagic lesions
    - Insensitive for cortical lesions; may be missed
  - ➢ CT scan
    - Normal CT predictive of normal outcome or mild disability
    - Generalized, diffuse hypoattenuation predictive of neonatal death & severe long-term disability
    - Focal, multifocal, & generalized ischemic lesions
    - Diffuse cortical injury not be apparent until several wks after insult
    - Intraparenchymal, intraventricular, subarachnoid, cerebellar hemorrhages
    - Basal ganglia–thalamic lesions & selective neuronal injury more reliably visualized by MRI
  - ➢ MRI: imaging modality of choice
    - Sensitive for focal & multifocal ischemic lesions
    - Diffusion-weighted imaging (DWI) is the most sensitive for detecting ischemia
    - Lesions in parasagittal zone w/ mild to moderate insult
    - Bilateral abnormalities, primarily in lateral thalami, posterior putamina, hippocampi, & perirolandic cortices, w/ severe insult
    - Diffuse cortical abnormalities w/ even more severe insult
    - In premature infants, MRI more sensitive than sonography in demonstrating PVL lesion, esp noncystic PVL
  - ➢ Magnetic resonance spectroscopy (MRS)
    - Decreased ratio of N-acetylaspartate (NAA) to choline & elevated lactate peaks & lactate-to-NAA ratio indirect evidence of ischemia
    - High lactate-to-choline ratios w/ basal ganglial & thalamic abnormalities predictive of poor neurologic outcome
    - Increased inorganic phosphorus (31P): occurs in 1st 24–72 hr, returns to normal over subsequent days
  - ➢ Timing of MRI & MRS changes
    - 1st 24 hr: increased lactate peak
    - 24–72 hr: decreased NAA-to-choline ratio & DWI signal intensity
    - 72 hr: increased T2-weighted signal intensity
    - 1–3 wks: generalized atrophy, cystic changes

- ➢ EEG
  - For Dx neonatal seizures
    - Low-voltage (5–15 μV) activity, electrocerebral inactivity (voltage, <5 μV), & burst-suppression predictive of a poor outcome
    - Early EEG abnormalities helpful in selecting infants for possible neuroprotective therapies
- Sarnat & Sarnat staging: to monitor & assess severity
  - ➢ Stage 1
    - Hyperalert, excessive reaction to stimuli
    - Normal tone
    - Hyperreflexia
    - Weak suck
    - Eyes wide open, decreased blinking, mydriasis
    - Normal EEG
    - Duration <24 h
    - Good prognosis; no long-term neurologic sequelae
  - ➢ Stage 2
    - Lethargy or obtundation
    - Mild hypotonia
    - Cortical thumbs
    - Suppressed primitive reflexes
    - Seizures
    - Miosis, heart rate <120 bpm, increased peristalsis, copious secretions
    - EEG
      - W/in 24 hrs of insult: relatively low voltage (<25 μV), slow theta & delta
      - >24 hrs after insult: bursting pattern & multifocal low-frequency (1–1.5 Hz) electrographic seizures
    - Good prognosis w/clinical & EEG recovery w/in 5 days
    - Poor prognosis w/ periodic EEG with isoelectric interburst intervals, bursting frequency <6 sec, bursting pattern (every 3–6 sec) >7 days
  - ➢ Stage 3
    - Stupor w/ only withdrawal response or decerebrate posturing w/ strong stimuli; rarely coma
    - Severe hypotonia
    - Decreased deep tendon & primitive (i.e., Moro, tonic neck oculocephalic, suck) reflexes
    - Decreased corneal & gag reflexes

- Clinical apparent seizures less frequent than w/ stage 2
- Deep, periodic EEG pattern w/ high amplitude & bursts less than every 6–12 sec; very-low-voltage or isoelectric EEG
- Invariably major neurologic sequelae: microcephaly, mental retardation, cerebral palsy, seizures

■ Other tests

➢ Amplitude-integrated EEG (aEEG)
- Less sensitive for detecting seizures but easier to interpret than EEG
- Normal: Upper voltage margin >10 μV, lower margin > 5 μV
- Moderately abnormal: Upper voltage margin >10 μV but lower margin <5 μV
- Severely abnormal: Upper voltage margin <10 μV, lower margin <5 μV; usually indicative burst-suppression pattern

➢ Evoked electrical potential [somatosensory (SSEP), visual (VEP), or auditory]
- Normal SSEPs & VEPs are strong predictors of a normal outcome
- Bilaterally, persistently (≥1 wk after insult) absent SSEP cortical potentials associated w/ adverse neurologic sequelae
- Abnormal VEPs ≥1 wk after insult assoc w/ high risk of neonatal mortality or severe neurologic deficits
- Brain stem auditory evoked potentials (BAEPs) useful in brain stem injury but lack predictability of SSEPs & VEPs

➢ Near-infrared spectroscopy (NIRS): monitors cerebral oxyhemoglobin; increased cerebral venous oxygen saturation despite increased cerebral oxygen delivery c/w decreased postasphyxial oxygen utilization

MANAGEMENT

■ Optimal mgt is prevention by identifying & monitoring at-risk fetus

■ Supportive treatment

➢ Se **RESUSCITATION** in the "Procedures" section
- Optimize ventilation & oxygenation
- Maintain normal BP, optimize cardiac output
- Correct metabolic acidosis
- Maintain serum glucose of 75–100 mg/dL
- Avoid hyperviscosity
- Rx seizures (see **SEIZURES** in the "Neonatal Presenting Signs" section)

- Fluid restriction (glucocorticoids & osmotic agents ***not*** recommended)

- Neuroprotective treatment
  - ➢ Hypothermia started within 6 hr of insult & continued for 72 hr
    - Selective head cooling & mild systemic hypothermia (rectal temp 34–35°C) with cool-cap
      - Whole-body hypothermia (esophageal temperature 33–34°C) w/ cooling blanket
      - Both safe & effective in reducing combined outcome of death or neurologic disability at 18 mo
  - ➢ Other neuroprotective strategies not proven to be effective

SPECIFIC THERAPY

N/A

COMPLICATIONS AND PROGNOSIS

- Most survivors of hypoxic-ischemic insults do not have major sequelae
- Normalization of neurologic exam in 1–2 wks is a good prognostic sign
- Overall risk
  - ➢ Death 12.5%
  - ➢ Neurologic handicap 14%
  - ➢ Death or neurologic handicap 25%
- Risk for neurologic sequelae increased w/:
  - ➢ Apgar score 0–3 at 20 min of age
  - ➢ Multiorgan failure, particularly oliguria >36 h
  - ➢ Severity & neurologic signs (also see Sarnat & Sarnat staging under "Tests")
    - Mild: good prognosis
    - Moderate: prognosis difficult to predict (poor if >5 days); delayed arithmetic, reading, &/or spelling skills, difficulties w/ attention & short-term memory in nondisabled survivors
    - Severe: high mortality (~80%) or multiple disabilities (profound mental, spastic CP retardation, cortical blindness, or seizure disorder; hearing usually normal)
  - ➢ Seizures, esp within first 12 h of insult or difficult to treat
  - ➢ Abnormal MRI in 1st 24–72 h after insult
  - ➢ MRS findings of:
    - Elevated lactate levels & elevated ratio of lactate to NAA
    - Elevated 31P

- ➢ Severity & duration of EEG abnormalities
  - Normal or mildly abnormal EEG pattern w/in 1st days after insult: most likely normal outcomes
  - Recovery to normal EEG background activity by day 7 assoc w/ normal outcome
    - Moderate to severely abnormal EEG patterns assoc w/ abnormal outcome
    - Burst-suppression or isoelectric pattern on any day & prolonged EEG depression >12 days after insult associated with poor outcome
- ➢ Persistent abnormalities of brain stem function incompatible w/long-term survival
- ➢ Abnormal SSEPs, VEPs & BAEPs persisting beyond 7 days of life
- ➢ Increased cerebral blood flow on Doppler sonography w/in 1st 3 days of insult
- ➢ Decreased cerebral resistive index on fetal Doppler sonography
- ➢ Microcephaly at age 3 mo predictive of poor neurodevelopmental outcome
- ➢ Optic atrophy indicates poor visual outcome

IMPERFORATE ANUS

CHARLES J.H. STOLAR, MD

HISTORY & PHYSICAL
- No anus present on newborn physical exam
- Fourchette fistula in girls w/ low anomalies
- Meconium stripe in median raphe in boys w/ low anomalies
- Assoc w/ other midline defects such as cardiac, spinal cord, renal

TESTS
- Plain film of abdomen
- CT scan of spinal cord
- Renal/cardiac US

DIFFERENTIAL DIAGNOSIS
- Difficult to confuse w/ other conditions
- Perineal or fourchette fistula may be hard to identify at first

MANAGEMENT
- Always wait at least 24 h before doing anything to a male

- Perineal anoplasty for clearly low anomalies
- Dilatation of fourchette fistula as temporizing measure for females
- Colostomy for all intermediate & high anomalies w/ reconstruction after 6 mo

SPECIFIC THERAPY
N/A

FOLLOW-UP
Ped Surg

COMPLICATIONS AND PROGNOSIS
- Hyperchloremic metabolic acidosis from urine reflux into colon in males
- Prognosis for continence
- Excellent for low anomalies
- Unclear for all others, but most will require aggressive bowel training program for many years

INFARCT, CEREBRAL

See **STROKE, ISCHEMIC, PERINATAL AND NEONATAL**

INTESTINAL ATRESIA

CHARLES J.H. STOLAR, MD

HISTORY & PHYSICAL
- Duodenal atresia assoc w/ polyhydramnios & double bubble on prenatal US & other anomalies (cardiac, anorectal, trisomy 21)
- More distal atresias are usually isolated anomalies secondary to vascular event prior to birth
- The more proximal the atresia, the earlier vomiting & abd distention

TESTS
- Supine, prone, & R/L lateral decubitus abd films: double bubble w/ duodenal atresia
- Karyotype
- Contrast enema for distal atresia
- Upper GI for proximal atresia, but usually diagnosed by plain films
- Cystic fibrosis work-up if suspected

- Echocardiogram, renal US w/ duodenal atresia

DIFFERENTIAL DIAGNOSIS
- Cystic fibrosis vs. ileal atresia
- Small colon syndromes w/ maternal diabetes or maternal magnesium Rx
- Hirschsprung disease
- Hypothyroidism

MANAGEMENT
- Pediatric surgery consultation
- For duodenal atresia: duodeno-duodenostomy or duodeno-jejeunostomy + gastrostomy w/ trans-anastomotic feeding tube
- For all other atresias, limited resection of proximal bowel, end-to-end anastomosis +/− gastrostomy
- Parenteral nutrition until enteral feeds established
- NG decompression until ileus resolved
- Feeding therapist may be needed
- Use gastrostomy for weaning from continuous to bolus feeds

SPECIFIC THERAPY
N/A

FOLLOW-UP
- Ped Surg
- Gastrostomy removal once GI function is established

COMPLICATIONS AND PROGNOSIS
- Excellent outcome once GI function is established

INTRAVENTRICULAR HEMORRHAGE (IVH)

HELEN M. TOWERS, MD

- Grades
  - Grade I: germinal matrix hemorrhage (GMH)
  - Grade II: IVH
  - Grade III: IVH w/ ventricular dilatation
  - Grade IV: intraparenchymal hemorrhage (hemorrhagic infarct)

HISTORY & PHYSICAL

History

- Term infant
  - ➢ Hypoxia-ischemia
  - ➢ 25% w/o discernable pathogenesis
  - ➢ Small minority: hemorrhagic infarction, ruptured vascular lesion, tumor or coagulopathy
- Preterm infant
  - ➢ Incidence of hemorrhage directly correlated w/ degree of prematurity
  - ➢ Incidence of germinal matrix bleed/intraventricular hemorrhage 20–40%
  - ➢ 50% of GM/IVH originate on 1st day of life
  - ➢ 90% of GM/IVH, before 4 days of life
  - ➢ Periventricular hemorrhagic cerebral infarction in ~15%

Signs

- Term infant
  - ➢ Seizures, focal or multifocal, 65%
  - ➢ Irritability, stupor
  - ➢ Apnea, fever
  - ➢ Full fontanel, vomiting w/ increased intracranial pressure
- Preterm infant (multiple presentations)
  - ➢ Asymptomatic, most common
  - ➢ Neurologic deterioration over days
  - ➢ Catastrophic presentation w/ coma, apnea, extensor posturing, brain stem dysfunction, flaccid quadriparesis

TESTS

- Cranial US (first US on day 4, if + repeat on day 7)
- CT scan
- CBC
- Coagulation studies in term infants or w/ other excessive bleeding

DIFFERENTIAL DIAGNOSIS

- Other types of intracranial hemorrhages (see **SUBARACHNOID HEMORRHAGE**, **SUBDURAL HEMORRHAGE**, **CEREBELLAR HEMORRHAGE**)

MANAGEMENT

- Prevention
  - ➢ Prevention of preterm delivery
  - ➢ Prophylactic indomethacin (if prevalence of severe IVH >10%)

- Supportive Rx: ABCs

SPECIFIC THERAPY
N/A

FOLLOW-UP
- Short-term: repeated cranial US at 1- to 2-wk intervals if hemorrhage is present on day 4 or 7 US for extension of hemorrhage, hydrocephalus
- Long-term: neurodevelopmental

COMPLICATIONS AND PROGNOSIS
- 20–40% of grade I/II hemorrhages extend in 1st wk of life
- Term infant
  - ➢ Normal >50%
  - ➢ Major neurologic deficit ~40%
  - ➢ Hydrocephalus requiring shunting ~50%
  - ➢ Mortality ~5%
- Preterm infant
  - ➢ Acute increased intracranial pressure w/ major intraventricular hemorrhage
  - ➢ Ventriculomegaly in ~35% of infants; may be static or spontaneously resolve in ~65%
  - ➢ Posthemorrhagic hydrocephalus
  - ➢ Major neurologic deficit
    - No increased risk w/ grades I/II
    - W/ grades III/IV 65–80%
- Periventricular leukomalacia, highly predictive of CP
- Mortality ~10%

LACTIC ACIDEMIAS

WENDY K. CHUNG, MD, PhD

A family of disorders

HISTORY & PHYSICAL

History
- Failure to thrive
- Vomiting
- Developmental delay/regression

- Hypotonia
- Seizures
- Ataxia, clumsiness
- Acute decompensation precipitated by intercurrent illness
- Physical Signs
- Failure to thrive
- Hypotonia
- Hypoventilation/apnea
- May have alopecia/dermatitis (pyruvate carboxylase)
- Nystagmus
- Cortical blindness

TESTS

- Arterial lactate repeatedly elevated (no tourniquet, calm child, on ice, run immediately)
- Elevated arterial pyruvate
- Increased lactate:pyruvate ratio >25 suggests mitochondrial respiratory chain defect
- Elevated alanine on serum amino acid analysis
- Elevated CSF lactate
- Elevated brain lactate by MRS
- Echocardiogram: cardiomyopathy (variable)
- MRI: absence of corpus callosum, hypodensity in caudate, putamen
- (Leigh syndrome)
- Serum biotinidase to exclude biotinidase deficiency
- Acylcarnitine profile to evaluate for fatty acid oxidation disorders
- Urine organic acid analysis: organic acidemias will be diagnostic
- Provocative fasting w/ glucagon administration; if hypoglycemia develops, it suggests disorder in gluconeogenesis (pyruvate carboxylase, fructose 1,6-biphosphatase deficiency). If no response to initial glucagon, it suggests glycogen storage disorder I.
- Muscle biopsy: ragged red fibers, biochemical analysis of mitochondrial complexes & mitochondrial DNA
- Mitochondrial DNA analysis for definitive diagnosis of some disorders of lactic acid metabolism (MELAS, MERRF, NARP)
- Fibroblast biochemical analysis for pyruvate carboxylase & pyruvate dehydrogenase

DIFFERENTIAL DIAGNOSIS

- Hypoxia
- Hypoventilation

- Shock (see **SHOCK**)
- Sepsis
- Organic acidemias (see **METABOLIC ACIDOSIS** in the "Neonatal Presenting Signs" section)
- See **FATTY ACID OXIDATION DISORDERS**

MANAGEMENT
- Airway, breathing, circulation
- IV fluid w/ D10W

SPECIFIC THERAPY
- Treat severe metabolic acidosis w/ sodium bicarbonate
- Biotin for biotinidase deficiency
- High-carbohydrate diet
- Avoidance of fasting for pyruvate carboxylase deficiency
- Ketogenic diet or diet w/ 50% cal as fat for pyruvate dehydrogenase complex deficiencies
- Dichloroacetic acid (DCA): an experimental agent for lactic acidosis to increase activity of pyruvate dehydrogenase. *Should not be used for gluconeogenic defects.*
- NOTE: KETOGENIC DIET ABSOLUTELY CONTRAINDICATED IN PYRUVATE CARBOXYLASE DEFICIENCY.

FOLLOW-UP
- Monitor serum lactate, pyruvate, pH
- G-tube may be necessary to feed during intercurrent illness or for inability to feed by mouth

COMPLICATIONS AND PROGNOSIS
- Variable depending on exact condition
- Many children w/ severe lactic acidosis will have poor neurological outcome
- Some disorders will be lethal in infancy

LOBAR EMPHYSEMA

See **LUNG BUD MALFORMATIONS**

LUNG BUD MALFORMATIONS (CONGENITAL CYSTIC ADENOMATOID MALFORMATION, BRONCHOGENIC CYST, LOBAR EMPHYSEMA, PULMONARY SEQUESTRATION)

CHARLES J.H. STOLAR, MD

- Include:
  - ➢ Congenital cystic adenomatoid malformation
  - ➢ Bronchogenic cyst
  - ➢ Lobar emphysema
  - ➢ Pulmonary sequestration

HISTORY & PHYSICAL

- Abnormality often identified on prenatal US, but exact nature of malformation may not be clear until birth
- Suspected postpartum because of:
  - ➢ Resp distress
  - ➢ Asymmetric breathing, but normal contour to abdomen
  - ➢ High-output cardiac failure
  - ➢ Pulm infection (rare in newborn)

TESTS

- CXR
- CT scan w/ IV contrast
- MRI/A
- Angiography (rarely required)

DIFFERENTIAL DIAGNOSIS

- Congenital cystic adenomatoid malformation
  - ➢ Hamartoma of lung w/ cystic, solid components
  - ➢ Can involve single lobe or whole lung
  - ➢ May have same physiology as congenital diaphragmatic hernia
- Bronchogenic cyst
  - ➢ Cystic dilatation of non-communicating airspace
  - ➢ Usually upper lobes or behind carina
- Lobar emphysema
  - ➢ Paucity of bronchial cartilage w/ air trapping
  - ➢ Usually in upper lobes
- Pulm sequestration
  - ➢ Persistence of systemic arterial vessel from aorta to "sequestered" lobe
  - ➢ Always lower lobe

MANAGEMENT
- Usually resection or enucleation (bronchogenic cyst only)
- Sometimes lobectomy
- Limited observation only if asymptomatic, very small & resolving

SPECIFIC THERAPY
N/A

FOLLOW-UP
Pulmonary

COMPLICATIONS AND PROGNOSIS
N/A

LYSOSOMAL STORAGE DISORDERS

WENDY K. CHUNG, MD, PhD

HISTORY & PHYSICAL

History
- Chronic progressive symptoms, not acute decompensation
- Failure to thrive
- Short stature
- Developmental delay
- Loss of developmental milestones & progressive neurological deterioration
- Nonimmune hydrops
- Seizures (w/ oligosaccharidoses & sphingolipidoses)
- Consanguineous parents
- Ashkenazi Jewish heritage for some

Signs
- Short trunk
- Gingival hypertrophy
- Macroglossia
- Doughy skin
- Coarse facial features
- Corneal clouding
- Macular cherry red spot
- Optic atrophy

- Retinal degeneration
- Hepatosplenomegaly
- Hypotonia
- Heart failure/cardiomyopathy
- Limitation of joint movement

TESTS

- Prenatal testing available for most
- X-rays show dystosis multiplex in mucopolysaccharidoses & adrenal calcifications in Wolman disease
- Urine for oligosaccharides or mucopolysaccharides
- Vacuolated lymphocytes on smear or bone marrow biopsy
- Skin or conjunctival biopsy for lysosomal inclusions
- Direct enzymatic assay from leukocytes or fibroblasts
- Direct DNA testing for some disorders

DIFFERENTIAL DIAGNOSIS

- Highly dependent upon presentation

MANAGEMENT

- Supportive care
- Referral to biochemical geneticist for definitive Dx

SPECIFIC THERAPY

- For a limited # of disorders, specific enzyme replacement therapy available
- Bone marrow transplant for some disorders; efficacy depends on timing of transplant
- Contraindication for enzyme replacement therapy: severe CNS involvement

FOLLOW-UP

- Measure enzyme levels in pts w/ bone marrow transplant to monitor efficacy

COMPLICATIONS AND PROGNOSIS

- Highly dependent on specific disorder; many neurologically devastated, may have shortened life span

MALROTATION

CHARLES J.H. STOLAR, MD

HISTORY & PHYSICAL
- Usually term newborn, 2nd-4th wk of life, but not exclusively
- Bilious or bile-stained vomitus of any kind
- Abd exam can be normal
- Blood in stool w/ acute abdomen only in advanced stages
- Malrotation can exist w/ or w/o volvulus & be equally dangerous

TESTS
- Plain films of abdomen
- EMERGENCY upper GI series to identify location of ligament of Treitz
- Contrast enema not helpful, only misleading
- Pass NG tube yourself if nature of vomitus in question
- Always err on side of doing upper GI

DIFFERENTIAL DIAGNOSIS
- Other causes of neonatal intestinal obstruction (see **INTESTINAL OBSTRUCTION** in the "Neonatal Presenting Signs" section)
- Intercurrent medical illness

MANAGEMENT
- Emergency pediatric surgery consult
- IV fluid resuscitation, antibiotics
- Emergency operation: Ladd's procedure
- Repeat laparotomy if bowel viability in question
- May need parenteral nutrition

SPECIFIC THERAPY
N/A

FOLLOW-UP
N/A

COMPLICATIONS AND PROGNOSIS
- Outcome excellent if bowel viability preserved
- Main complication infarction of entire midgut if Dx delayed
- Has potential for short-bowel syndrome if gut compromised
- Recurrent volvulus rare, but adhesive bowel obstruction possible

MAPLE SYRUP URINE DISEASE

WENDY K. CHUNG, MD, PhD

HISTORY & PHYSICAL

History

- Child appears normal at birth
- W/in 1st 2 wk of life poor feeding or vomiting, wt loss
- Lethargy progressing to coma
- Opisthotonos, convulsions
- + newborn metabolic screen for leucine elevation

Signs

- Hypotonia alternating w/ hypertonia
- Comatose w/ opisthotonic posture
- Bulging fontanel
- Apnea
- Urine, sweat, cerumen smells of maple syrup or burnt sugar

TESTS

- Basic test: newborn screen for leucine (>4 mg/dL abnormal)
- Specific diagnostic test: serum amino acid analysis w/ elevated leucine, > isoleucine & valine w/ alloisoleucine (pathognomonic)
- Urine organic acid: oxoisocaproic acid, 2-oxo 3-methylvaleric acid, 2-oxoisovaleric acid
- Addition of 2,4-dinitrophenylhydrazine to urine results in yellow precipitate
- CT or MRI shows cerebral edema or decreased attenuation of white matter
- EEG shows a comb-like rhythm of sharp waves

DIFFERENTIAL DIAGNOSIS

- Sepsis
- Electrolyte abnormalities
- Hypoglycemia
- Metabolic disorders

MANAGEMENT

- Admit pt to ICU
- General measures for fluid resuscitation, respiratory support
- Load w/ phenobarbital if evidence of seizures

SPECIFIC THERAPY
- NPO
- Thiamine (100 mg/day IV) trial for all pts for 3 wks; not all will respond. Pt can be switched to PO thiamine after acute crisis.
- Hemodialysis/continuous venovenous extracorporeal hemodiafiltration
- Maintain anabolic w/ 10–15% glucose infusion, intralipid, TPN (initially w/o branch-chain amino acids); may also use insulin 0.1 units/kg/hour) while monitoring glucose to maximize anabolic state
- If not vomiting, may place NG tube & use metabolic formula (Complex MSUD Amino Acid Blend® from Applied Nutrition Corp.) instead of IV nutrition; give 2.6–5.2 g/kg of formula QD via continuous feeds.
- Liver transplant can be curative

No contraindications to treatment

FOLLOW-UP
- Pt must be maintained on lifelong dietary treatment w/ restriction of branch-chain amino acids to minimum for growth (MSUD formulas available from Ross & Mead-Johnson)
- Frequent monitoring of dietary efficacy w/ amino acid analysis
- Metabolic crises likely to recur w/ anabolic states, including intercurrent illness
- Pregnancy in pts especially difficult to manage
- Prenatal Dx possible

COMPLICATIONS AND PROGNOSIS
- Earlier the treatment, better the prognosis
- Better the metabolic control, better the prognosis
- Normal IQ theoretically possible if treated before 10 days of age
- All children have some learning disabilities
- Possibility of death or severe brain injury w/ metabolic crisis

MECKEL'S DIVERTICULUM

CHARLES J.H. STOLAR, MD

HISTORY & PHYSICAL
- Seldom a neonatal problem
- Painless gross blood in 2-y-old

- Abd pain or acute abdomen at any age
- Intestinal obstruction due to:
  - Diverticulum, or
  - Assoc omphalomesenteric remnant
- May present as intussusception
- May be incidental finding at surgery

TESTS
- High index of suspicion required for Dx
- Meckel's scan may help if ectopic gastric mucosa present
- Bleeding scan may help if active bleeding (always distal to ectopic gastric mucosa)
- Plain films for acute abdomen
- Contrast studies not helpful

DIFFERENTIAL DIAGNOSIS
- All causes of acute abdomen
- Acute appendicitis
- All causes of GI bleeding (see **GASTROINTESTINAL BLEEDING** in the "Neonatal Presenting Signs" section)

MANAGEMENT
- Laparoscopic or open operation
- Resection, anastomosis
- Make sure all ectopic gastric mucosa is removed to prevent recurrent bleeding

SPECIFIC THERAPY
N/A

FOLLOW-UP
- Once GI function restored, no specific follow-up needed

COMPLICATIONS AND PROGNOSIS
- Prognosis excellent

MECONIUM ASPIRATION SYNDROME (MAS)

THOMAS A. WISWELL, MD

HISTORY & PHYSICAL

History

- Meconium-stained amniotic fluid (MSAF)
- Thick-consistency MSAF increases risk markedly (at least 5- to 20-fold compared w/ thin-consistency MSAF)
- Fetal distress: abnormal fetal heart race tracings, abnormal biophysical profile
- More common when GA >=42 wk
- Oligohydramnios
- Neonatal depression
- Resuscitation often required in delivery room

Signs

- Respiratory distress soon after birth
- Post-dates signs: peeling skin, dystrophic umbilical cord, wasted appearance
- Meconium-stained nails, skin, umbilical cord, hair
- Meconium-stained amniotic fluid suctioned from trachea
- Increased anterior-posterior chest diameter ("barrel chest")

TESTS

- CXR (variable findings)
  - ➢ Diffuse, patchy infiltrates (classic description)
  - ➢ Hyperinflation
  - ➢ Consolidation
  - ➢ Pneumothorax
  - ➢ Hypovascularity
  - ➢ Atelectasis
  - ➢ "Wet-lung" appearance
- Arterial blood gases
  - ➢ Hypoxemia
  - ➢ Hypercapnia
  - ➢ Mixed metabolic/respiratory acidosis
- Oxygen saturations (pulse oximetry)
  - ➢ Frequently low
  - ➢ Often pre- and postductal difference >10%, c/w **PERSISTENT PULMONARY HYPERTENSION OF NEWBORN** (PPHN)

- CBC/differential
  - ➢ Frequent leukocytosis w/ left shift
  - ➢ Increased nucleated RBCs
- Other
  - ➢ Evaluation for perinatal asphyxia, PPHN if history, physical exam, clinical course consistent

DIFFERENTIAL DIAGNOSIS

- Congenital pneumonia
- Sepsis w/ pulmonary edema
- See **TRANSIENT TACHYPNEA OF NEWBORN, PERSISTENT PULMONARY HYPERTENSION OF NEWBORN**
- Difficult transition between intrauterine, extrauterine life
- See **RESPIRATORY DISTRESS SYNDROME**
- Aspiration of amniotic fluid/blood
- Congenital cyanotic heart disease
- Acute respiratory distress syndrome (ARDS)

MANAGEMENT

- Oxygen
  - ➢ Use sufficient to maintain O_2 saturation >=95% & PaO_2 50–80 mmHg
  - ➢ O_2 up to FiO_2 of 1.00 often used (w/o positive pressure) because of air leak risk w/ continuous positive airway pressure (CPAP), positive-pressure ventilation
  - ➢ Follow oxygenation index (OI) to determine effect of mgt & when to escalate to other therapies:
    $OI = (\text{mean airway pressure})(FiO_2)(100)/PaO_2$
- Continuous positive airway pressure
  - ➢ Some consider a trial of CPAP before positive-pressure ventilation is started
  - ➢ Others believe CPAP may predispose to air leaks
- Mechanical ventilation
  - ➢ Patient-triggered ventilation: Assist/Control & synchronized intermittent mandatory ventilation (SIMV) may be considered
  - ➢ Volume targeted ventilation an option
  - ➢ Many employ hyperventilation/alkalosis (see **PERSISTENT PULMONARY HYPERTENSION OF NEWBORN**)
  - ➢ Many advocate "gentle" ventilation (lower PaO_2 & higher $PaCO_2$ levels than typically accepted) to minimize ventilator peak inspiratory pressure to prevent "volutrauma"

- ➢ No randomized, controlled trials demonstrate any method to be superior
- Sedation
  - ➢ Consider if infant requires mechanical ventilation
- Surfactant
  - ➢ In trials, bolus surfactant given when OI >=15–20
  - ➢ Standard (or 1.5x standard) doses
  - ➢ Response commonly not seen until after at least 2–3 doses
  - ➢ Dilute surfactant lavage has been described, but insufficient data to currently support therapy
- High-frequency ventilation (HFV)
  - ➢ No prospective, randomized controlled trials of HFV for MAS
  - ➢ Consider if air leaks occur
  - ➢ Consider if OI >=10–15 can be maintained w/ conventional mechanical ventilation
- Systemic steroids
  - ➢ Insufficient data to support generalized use of therapy
- Inhaled nitric oxide (iNO)
  - ➢ See **PERSISTENT PULMONARY HYPERTENSION OF NEWBORN**
- Extracorporeal membrane oxygenation (ECMO)
  - ➢ Cardiopulmonary bypass to allow lung "rest and healing"
  - ➢ See **PERSISTENT PULMONARY HYPERTENSION OF NEWBORN**
- Other as appropriate for organ (other than pulmonary) damage/dysfunction

SPECIFIC THERAPY

None

FOLLOW-UP

- Neurodevelopmental, esp w/ associated perinatal asphyxia
- For pulmonary complications (chronic lung disease, altered pulmonary mechanics)
- See **PERSISTENT PULMONARY HYPERTENSION OF NEWBORN**

COMPLICATIONS AND PROGNOSIS

- Mortality <5%
- Chronic lung disease in 5–10% of those requiring mechanical ventilation
- Many have long-term (>/=8–10 yr) alteration in pulmonary mechanics (increased resistance, decreased compliance)

- Reactive airway disease, pneumonia during 1st several years of life not uncommon among those needing mechanical ventilation for MAS
- At increased risk for cerebral palsy, seizures, cognitive delays, autism

MECONIUM ILEUS

CHARLES J.H. STOLAR, MD

HISTORY & PHYSICAL

- Family Hx of cystic fibrosis
- Prenatal genetic testing indicating cystic fibrosis
- Prenatal US indicating "thickened bowel"
- Resp distress at birth
- Soft, "doughy" abd distention
- No meconium passage
- Positive newborn screen

TESTS

- Abd x-ray: "soap bubbles" in area of terminal ileum, calcifications
- Usually no air-fluid levels; meconium too thick
- Buccal smear for "CF" DNA probe

DIFFERENTIAL DIAGNOSIS

- See **HIRSCHSPRUNG DISEASE** and **HYPOTHYROIDISM, CONGENITAL**
- Small colon syndrome

MANAGEMENT

- Contrast enema w/ H_2O-soluble agent containing Tween-80
- Try to reflux agent past inspissated meconium in terminal ileum
- Repeat enema in 24 h & more often as long as progress being made
- Aggressive IV hydration, antibiotic coverage
- Direct surgical evacuation of meconium if enemas unsuccessful; may need fecal diversion

SPECIFIC THERAPY

None

FOLLOW-UP

- Parenteral nutrition support while ileus resolves
- Pancreatic enzymes required when enteral feeds instituted

- Referral to Cystic Fibrosis Center

COMPLICATIONS AND PROGNOSIS
- Related largely to cystic fibrosis

MEDIUM-CHAIN ACYL COA DEHYDROGENASE DEFICIENCY (MCAD)

WENDY K. CHUNG, MD, PhD

HISTORY & PHYSICAL
May present at any age, often w/ intercurrent illness
- Lethargy, change in mental status
- Vomiting
- Seizure
- SIDS or family Hx of SIDS
- Abnormal newborn screen result

TESTS
- Hypoglycemia
- Urine analysis: hypoketosis
- Hyperammonemia
- Hyperuricemia
- Increased CPK
- Urine organic acids: medium-chain dicarboxylic aciduria
- Free carnitine secondarily low
- Acylcarnitine profile: increased octanoyl & hexanoylcarnitine
- Urine acylglycines: hexanoic acid & suberic acid glycine conjugates
- Provocative fasting will show urine dicarboxylic acids $\gg$ 3-hydroxybutyrate
- DNA-based test (A985G is most common mutation in Caucasians)

DIFFERENTIAL DIAGNOSIS
- Other causes of hypoglycemia
- Reye syndrome
- SIDS

MANAGEMENT
- Airway, breathing, circulation
- IV fluids w/ D10 at 1.5$\times$ maintenance (maintain serum glucose $>$100 mg/dL)
- Carefully monitor glucose levels

SPECIFIC THERAPY
- Carnitine 100 mg/kg q day PO. Go up to 300 mg/kg IV during metabolic crisis.
- Avoidance of fasting in all conditions, especially >12 h; if necessary provide cornstarch 1 g/kg qHS
- Immediately treat metabolic crisis w/ IV glucose

FOLLOW-UP
- Normalize free carnitine levels

COMPLICATIONS AND PROGNOSIS
- Excellent prognosis: normal intellect, life expectancy if fasting & hypoglycemia are avoided
- Potentially fatal if allowed to fast w/ metabolic crisis

MENINGITIS

RICHARD A. POLIN, MD

HISTORY & PHYSICAL

History
- Risk factors for meningitis identical to those for sepsis (see **SEPSIS/PNEUMONIA, EARLY-ONSET**; **SEPSIS, NOSOCOMIAL**)
- Most cases of meningitis result from bacteremia during labor, delivery or postnatal life
- Risk of meningitis
  - W/ early-onset sepsis: 20–25%
  - W/ late-onset sepsis: ~10%
- Bacterial pathogens w/ a predisposition for CNS
  - Group B streptococcus
  - *Listeria monocytogenes*
  - *K1 E. coli*

Signs
- Signs of meningitis nearly identical to those of sepsis
- Nuchal rigidity in only 15%
- Signs referable to CNS (e.g., seizures) more common

TESTS
- Cultures (for suspected sepsis/meningitis)
  - <72 h of age: blood & CSF culture
  - >=72 h: blood, CSF, urine culture

➢ Lumbar puncture (see **LUMBAR PUNCTURE** in the "Procedures" section)
- Indications
  - + blood culture
  - Persistently abnl neurological signs (seizures, lethargy, etc.)
  - Infants w/ signs of sepsis who fail to respond quickly to antimicrobial therapy
- Should be repeated 48 h into treatment to confirm CSF is sterile
  NOTE: Cultures may be positive up to 72 h w/ gram-negative meningitis
- CAUTION: LUMBAR PUNCTURE SHOULD BE DEFERRED IN UNSTABLE INFANTS OR INFANTS W/ UNCORRECTED BLEEDING DIATHESIS

■ Lumbar puncture results w/ meningitis
➢ Positive CSF culture, immunoassay or Gram stain
➢ Other
- Traumatic tap w/ blood present: nearly impossible to interpret; calculating ratio of RBC/WBC highly inaccurate
- Pleocytosis
  - >15 leukocytes: suspect for meningitis
  - >20 leukocytes: confirmed meningitis
  - Neutrophil predominance usual w/ bacterial meningitis
- Protein concentration (w/o traumatic tap or intraventricular hemorrhage [IVH])
  - Term infant
    - >100 mg/dL: abnormal
  - Preterm infant
    - Correlates inversely w/ gestational age
    - 150–200 mg/dL may be seen in healthy infants <1,000 g
- Glucose concentration (in the absence of IVH): w/o hypoglycemia CSF glucose should be >50 mg/dL & ~2/3 the glucose
- NOTE: SEVERAL DAYS AFTER IVH, CSF FINDINGS MAY MIMIC THOSE OF MENINGITIS W/ PLEOCYTOSIS, INCREASED PROTEIN CONCENTRATIONS & LOW GLUCOSE CONCENTRATIONS)

■ Neuroimaging (CT/MRI) is indicated w/ persistently + cultures despite appropriate antibiotics

DIFFERENTIAL DIAGNOSIS

■ Metabolic disturbances (hypoglycemia, inborn errors of metabolism)

- CNS injury/anomaly
- Congenital infections (TORCH)
- Viral meningitis/meningoencephalitis

MANAGEMENT

What to do first

- ABCs (airway, breathing, circulation)

General measures

- Correct acid/base disturbances
- Establish IV access
- Remove central lines w/ bacteremia
  - ➢ Bacteremia w/ *Staphylococcus epidermidis* can often be treated by administering antibiotics through the central venous line.
  - ➢ Bacteremia w/ *Staphylococcus aureus, Candida* sp. & gram-negative bacteria can rarely be treated without central catheter removal.

SPECIFIC THERAPY

- Antimicrobial therapy
  - ➢ Choice of empiric therapy depends on sensitivities of organisms causing sepsis in given nursery
  - ➢ Most infants successfully treated w/parenteral therapy; intrathecal treatment generally not needed
  - ➢ Initial empiric therapy must be appropriate for gram-positive & gram-negative pathogens
    - Early-onset bacterial sepsis (meningitis unproven)
      - Ampicillin/aminoglycoside
    - Early-onset bacterial sepsis (meningitis suspected)
      - Ampicillin/cefotaxime

      NOTE: Rapid development of resistance may occur when cefotaxime is used as initial empiric therapy for all infants w/ suspected sepsis
    - Nosocomial sepsis
      - Vancomycin/aminoglycoside for empiric therapy
      - Amphotericin for fungal sepsis/meningitis
    - W/ vancomycin or aminoglycoside antibiotics: monitoring of serum drug levels necessary when treatment continues beyond 72 h
      - Vancomycin: trough < 10 mcg/mL
      - Gentamicin
        - Peak 5–10 mcg/mL

- Trough < 2 mcg/mL
- Recommendations for specific organisms based on ***common*** sensitivity patterns (CAUTION: SENSITIVITY PATTERNS MUST BE CONFIRMED)
  - *Streptococcus glaciate* (group B streptococcus)
    - Ampicillin or penicillin & gentamicin until CSF sterilized, then gentamicin may be discontinued
    - Continue ampicillin or penicillin alone for 14 days after 1st negative culture
  - *Escherichia coli*: cefotaxime × 21 days (or 14 days after 1st negative culture)
  - *Pseudomonas aeruginosa*: ceftazidime & gentamicin or carbenicillin & gentamicin × 21 days (or 14 days after 1st negative culture)
  - *Staphylococcus epidermidis*: vancomycin × 14 days; an aminoglycoside is sometimes added for synergism
  - *Listeria monocytogenes*: ampicillin & gentamicin × 14 days

FOLLOW-UP

- Neurodevelopmental
- Hearing screen

COMPLICATIONS AND PROGNOSIS

- Complications
  - ➢ SIADH
  - ➢ Hydrocephalus
  - ➢ Brain abscess
- Prognosis
  - ➢ Mortality, 13%
  - ➢ Moderate or severe disability, 17%

MUSCLE DISEASES CAUSING NEONATAL WEAKNESS AND HYPOTONIA

DAVID BATEMAN, MD
CATHERINE A. HANSEN, MD

Weakness & hypotonia are nonspecific symptoms that may result from disruptions of the efferent neuromuscular pathway, beginning in cerebral cortex, terminating in muscle, or from generalized systemic illness

HISTORY & PHYSICAL

History

- Birth asphyxia frequently associated due to respiratory muscle involvement – can complicate recognition of underlying disorder
- See **MYOTONIC DYSTROPHY, CONGENITAL**
  - ➢ Maternal myotonic dystrophy
    - Autosomal dominant transmission via affected mother: 25% of infants develop disease
    - Maternal disease may be unrecognized (shake mom's hand)
  - ➢ Decreased fetal movement, polyhydramnios, dysfunctional labor, birth depression/asphyxia
  - ➢ Stillbirth, premature labor in severely affected infant
- Congenital muscular dystrophies
  - ➢ Autosomal inheritance
  - ➢ Several types assoc w/ major structural CNS malformations
  - ➢ Structural eye abnormalities (e.g., Walker-Warburg syndrome)
- Congenital myopathies: usually autosomal inheritance, type varies w/ specific myopathy
- Metabolic myopathies
  - ➢ Autosomal recessive inheritance

Signs

- Congenital myotonic dystrophy
  - ➢ Severe hypotonia
  - ➢ No myotonia in neonatal period
  - ➢ Profound muscle weakness, central > peripheral
  - ➢ Mask-like myopathic face, tented upper lip
  - ➢ Poor suck/swallow, pooled secretions, feeding intolerance
  - ➢ Severe resp depression, apnea, cyanosis, asphyxia
  - ➢ Deep tendon reflexes depressed
  - ➢ Arthrogryposis, esp involving lower extremities; clubbed feet
- Congenital muscular dystrophies
  - ➢ Hypotonia, weakness, joint contractures, depressed reflexes
  - ➢ Hydrocephalus, seizures, microphthalmia, cataract, etc., depending on subtype
- Congenital myopathies
  - ➢ Hypotonia, weakness, joint contractures, depressed reflexes, abnormal suck/swallowing
  - ➢ High-arched palate, simian creases, clinodactyly, hip dislocation, arthrogryposis, abnormal arches of the feet
- Storage diseases – enlargements of heart, liver, spleen, or tongue consistent

TESTS

- CPK
  - ➢ Marked elevation in merosin-deficient congenital muscular dystrophies
  - ➢ Normal/moderately elevated in congenital myotonic dystrophy, myopathies, merosin-positive muscular dystrophies
  - ➢ Elevated in Pompe's disease
  - ➢ May be difficult to interpret because of normal rise after birth
- CNS imaging
  - ➢ Congenital myotonic dystrophy: 80% of cases have ventricular dilatation
  - ➢ Congenital muscular dystrophy
    - White matter abnormality: merosin-deficient subtype
    - Lissencephaly-pachygyria: Fukuyama, Walker-Warburg types
    - Hydrocephalus, cerebellar abnormality: Walker-Warburg
- EMG
  - ➢ Myotonic dystrophy: myotonic discharges on maternal (not usually neonatal) test
  - ➢ Myopathies: usually abnl, but not definitive
  - ➢ Fasciculations, fibrillations indicate nerve disorders, but rare w/ nemaline rod/myotubular myopathy
  - ➢ Pompe's disease has a characteristic myopathic EMG
- Muscle biopsy
  - ➢ Requires specialized histological, histochemical, immunohistochemical, electron microscopic, biochemical studies
  - ➢ Biopsy diagnostic in following:
    - Central core myopathy
    - Nemaline (rod body) myopathy
    - Myotubular myopathy
    - Congenital fiber type disproportion
    - Mitochondrial myopathies
    - Metabolic myopathies (abnl lipid/glycogen staining)
  - ➢ Biopsy abnl but not diagnostic in following:
    - Congenital myotonic dystrophy
    - Congenital muscular dystrophy
    - Immunohistochemical staining for merosin-positive in classic ("Occidental") muscular dystrophies (not involving CNS)
    - Prominent lymphocytic infiltration indicates polymyositis (rare, but steroid responsive)
- EKG is characteristic for Pompe's disease w/ short PR interval & biventricular hypertrophy
- Genetic studies

- ➢ Myotonic dystrophy gene (autosomal dominant through mother) – chromosome 19q13.3; codes for MD protein kinase; disease severity related to # of CTG trinucleotide repeats in untranslated gene segment (severely affected individuals may have hundreds of repeats)
- ➢ Specific genes identified for many other muscular dystrophies & myopathies (updated list avail in each issue of "Neuromuscular Disorders"; search www.sciencedirect.com) & metabolic disorders (>40 mutations have been identified in the gene for acid maltase, the enzyme lacking in Pompe's disease)

- Spinal muscle atrophy (SMA) & Prader-Willi syndrome can be ruled out by molecular studies
- Prenatal diagnosis of Pompe's disease is possible by measuring acid maltase activity in cultured amniocytes

DIFFERENTIAL DIAGNOSIS

- Many disorders of CNS, lower motor neuron, neuromuscular junction cause hypotonia, weakness, joint contractures (see HYPOTONIA in the "Neonatal Presenting Signs" section)
- Congenital myotonic dystrophy, transient myasthenia gravis
- (see **MYASTHENIA GRAVIS, TRANSIENT AND CONGENITAL**) have characteristic maternal history, physical findings, EMG pattern
- Congenital myasthenia syndromes (see **MYASTHENIA GRAVIS, TRANSIENT AND CONGENITAL**), muscular dystrophies, myopathies distinguished by physical findings, results of head MRI, EMG, nerve conduction, muscle biopsy, genetic tests
- Metabolic myopathies may be assoc w/ lactic acidosis, hypoglycemia, decreased carnitine levels
- Central core disease may be assoc w/ malignant hyperthermia

MANAGEMENT

- Close observation, monitoring at birth – profound weakness, hypotonia can lead to early death
- Supportive care (ventilatory support, frequent suctioning, tube feedings)
- Early specific diagnosis for genetic counseling, prognosis
- Physical, occupational, orthopedic therapy to minimize joint contractures

SPECIFIC THERAPY

- Enzyme replacement therapy started early has been shown to greatly improve symptoms of Pompe's disease

- No specific therapy yet available for the other muscle disorders

FOLLOW-UP

N/A

COMPLICATIONS AND PROGNOSIS

- Congenital myotonic dystrophy
  - ➢ Hypotonia evolves to myotonia
  - ➢ Muscle wasting apparent as edema resolves
  - ➢ 15–20% mortality in neonatal period
  - ➢ Psychomotor retardation, skeletal abnormalities, impaired nutrition, cardiac arrhythmias apparent in those who survive to childhood
- Congenital muscular dystrophies
  - ➢ Merosin-positive muscle biopsy defines milder clinical course
  - ➢ Early mortality in Fukuyama, Walker-Warburg dystrophies
- Congenital myopathies
  - ➢ Progressive deterioration or early death in nemaline, centronuclear/myotubular myopathies
  - ➢ Slowly progressive course in central core disease
- Most metabolic myopathies (cytochrome C oxidase deficiency or fatty acid oxidation deficiencies) are still generally fatal, but recent results of enzyme replacement therapy in Pompe's disease show better outcomes
- Benign infantile myopathy (transient COX deficiency) – good prognosis

MYASTHENIA GRAVIS, TRANSIENT AND CONGENITAL

DAVID BATEMAN, MD
CATHERINE A. HANSEN, MD

HISTORY & PHYSICAL

History

- **Maternal myasthenia gravis** (MG)
  - ➢ 10–20% of infants develop transient MG due to anti-acetylcholine (ACh) receptor antibodies
  - ➢ 75% recurrence rate w/ previously affected sibling
  - ➢ High anti-fetal to anti-adult ACh receptor antibody ratio assoc w/ symptoms in neonate

- **Congenital myasthenia syndromes** (MS): autosomal recessive more common than autosomal dominant inheritance
- Decreased fetal movement, polyhydramnios, birth depression/asphyxia w/ either neonatal MG or congenital MS
- **Maternal $MgSO_4$**
- **Infantile botulism** assoc w/ honey/corn syrup (15% of exposures)
- Time of onset
  - ➢ Transient MG: 80% w/in 24 h
  - ➢ Congenital MS: birth to 1 wk
  - ➢ Hypermagnesemia: at delivery
  - ➢ Infantile botulism: 2 wk to 6 mo

Physical exam

- Hypotonia, often profound
- Muscle weakness
  - ➢ Worse after exertion
  - ➢ Poor suck/swallow, pooled secretions, weak cry
  - ➢ Ptosis/ophthalmoplegia (congenital MS > transient neonatal MG)
  - ➢ Symptoms fluctuate in congenital MS
  - ➢ Mydriasis may occur w/ botulism
- Respiratory depression, often severe, sometimes w/ apnea, cyanosis
- Deep tendon reflexes usually normal
- Arthrogryposis not common with transient neonatal MG or congenital MS

TESTS

- Maternal tests: EMG, anti-ACh receptor antibodies
- Edrophonium (Tensilon) test
  - ➢ Positive response (improved symptoms) in transient MG, some congenital MS (familial infantile myasthenia, congenital ACh receptor deficiency)
  - ➢ Negative in some congenital MS (slow channel syndrome, endplate Ach-Esterase deficiency)
  - ➢ Test should be done using quantified response (e.g., ability to suck, swallow)
  - ➢ Neostigmine longer-acting
- EMG
  - ➢ Decremental response to repetitive stimulus in transient MG & congenital MS
  - ➢ Incremental response in infantile botulism

- Muscle biopsy: diagnostic for congenital MS, but requires detailed ultrastructural testing to establish type (i.e., presynaptic, postsynaptic, synaptic, or mixed)
- Metabolic studies such as lactate, pyruvate, carnitine, glucose, ketones, Mg; stool toxin assay for *Clostridium botulinum*
- LP, MRI, CPK generally normal

DIFFERENTIAL DIAGNOSIS

See **HYPOTONIA** in the "Neonatal Presenting Signs" section.

MANAGEMENT

- Close monitoring after birth; range of presentations variable including early, sudden deterioration
- Supportive care: prn ventilatory support, freq suctioning, tube feedings
- Early specific diagnosis for genetic counseling & prognosis
- Physical, occupational, & orthopedic therapy to minimize joint contractures
- Aminoglycosides may potentiate symptoms; use alternate drug when possible

SPECIFIC THERAPY

- Anticholinesterase drugs for transient neonatal MG, some congenital MS (see "Tests")
- Neostigmine, 0.04 mg/kg IM 20 min prior to feeding; enteral dose (via NG tube) 10× parenteral dose
- 3,4-Diaminopyridine may increase terminal ACh release in receptor deficiency syndrome
- Exchange transfusion, IVIG have been used for severe transient neonatal MG

FOLLOW-UP

- Physical, occupational, & orthopedic therapy to minimize joint contractures

COMPLICATIONS AND PROGNOSIS

- Transient neonatal MG: mean duration of symptoms 18 days (5 days-2 mo)
- Congenital MG syndromes
  - ➢ Generally good outcome but variable
  - ➢ Fluctuating course may result in delayed motor development
  - ➢ Episodic deteriorations may be severe
  - ➢ May require treatment into adulthood

- Infantile botulism self-limited but may require prolonged (wks-mos) supportive treatment
- Hypermagnesemia resolves quickly w/ postnatal urinary excretion of Mg

MYOTONIC DYSTROPHY, CONGENITAL

KWAME ANYANE-YEBOA, MD

- Almost always inherited from mildly affected or asymptomatic mother
  - ➢ Autosomal dominant transmission
- Congenital form assoc w/ CTG trinucleotide repeat size >2,000 in DMPK gene, compared to <=35 in unaffected individuals
  - ➢ 25% of infants born to affected mothers have congenital form.

HISTORY & PHYSICAL

- Diminished fetal movements
- Polyhydramnios
- Non-immune hydrops fetalis
- Premature delivery in 55%
- Forceps delivery or vacuum extractions in 21% because of poor uterine contractions in affected mother

Signs

- Striking facial diplegia
- Open, triangular, "tented" mouth
- Inability to close eyes fully
- Talipes equinovarus
- General hypotonia w/ areflexia
- Difficulty sucking
- Difficulty swallowing
- Respiratory insufficiency
- Elevation of diaphragm on chest radiograph due to hypoplasia
- Thin ribs on chest radiograph
- Absence of myotonia
- Absence of myotonic discharges on EMG

TESTS

- Careful exam of mother for weakness, myotonia
- DNA analysis of myotonic dystrophy gene (DMPK) for CTG trinucleotide expansion

- EMG, muscle biopsy ***not*** useful in neonates w/ muscular dystrophy

DIFFERENTIAL DIAGNOSIS

See **HYPOTONIA** in the "Neonatal Presenting Signs" section.

MANAGEMENT

- Supportive therapy for resp insufficiency
- Gavage feeding
- Frequent suctioning to avoid aspiration
- Pediatric neurology evaluation
- Genetic evaluation, parental counseling
- Orthopedic mgt of talipes

SPECIFIC THERAPY

- None

FOLLOW-UP

- Consider G-tube placement if feeding difficulties persist
- Suctioning, postural drainage to prevent aspiration & pneumonia
- Early intervention
- Psychosocial support
- Follow-up by pulmonary, neurol, GI, genetics

COMPLICATIONS AND PROGNOSIS

- Resp problems dominate neonatal period
- Infant mortality rate 25%, w/ most deaths occurring in neonatal period due to resp failure
- Improvement in resp distress in surviving infants
- Sucking/swallowing difficulty resolves in 8–12 wk in full-term infants but may persist longer in premature
- Gradual improvement in hypotonia
- Clinical, EMG signs of myotonia appear after age 2–3 yr
- Delayed motor development w/ walking after age 3 yr
- Multiple joint contractures
- Chronic constipation due to smooth muscle involvement
- Sensitive to muscle relaxants, sedation, analgesia in general; pts require close monitoring in postop period
- Mental retardation in up to 50%
- Cardiac conduction, rhythm abnormalities w/ occasional Adams-Stokes syncope in adults (ECG abnl in 70%)
- Cataracts in adults

NECROTIZING ENTEROCOLITIS (NEC)

JESUS C. JAILE-MARTI, MD

Overall incidence 1–5% of NICU admissions
60–90% of affected infants are premature (but can be seen in full-term infants)
Mortality rates 10–40% in infants weighing <1,500 g, 45–100% in infants weighing <1, 000 g
Etiology thought to be multifactorial & includes abnormal intestinal flora, intestinal ischemia, intestinal mucosal immaturity
Clinical staging system:

Stage 1: Suspected NEC
IA – Mild symptoms, nonspecific
IB – As above w/ grossly bloody stools
Stage 2: IIA Definite NEC, mildly ill
IIB Definite NEC, moderately ill
Stage 3: IIIA Advanced NEC, severely ill, no perforation
IIIB Advanced NEC, severely ill, w/ perforation

HISTORY & PHYSICAL

History

- Hypoxic and/or hypotensive event
- Hypothermia
- Umbilical vessel catheterization
- Enteral alimentation w/ formula, breastfeeding has been shown to be protective
- Sepsis
- Indomethacin administration
- Patent ductus arteriosus
- Cold stress

Signs and symptoms

- GI
  - ➢ Abd distention
  - ➢ Abd tenderness
  - ➢ Bloody stools (may be occult)
  - ➢ Vomiting or bilious gastric residuals
  - ➢ Abdominal wall erythema, edema, induration (c/w peritonitis)
  - ➢ Abdominal mass (c/w walled-off perforation)
- Nonspecific

- ➢ Hyper/hypoglycemia
- ➢ Increased resp distress or O_2 requirement
- ➢ Increased frequency of apnea
- ➢ Decreased activity, "septic-appearing"
- ➢ Shock/poor perfusion

TESTS

- Serum electrolytes including calcium (monitor q8–12h)
  - ➢ Hyponatremia, hyperkalemia & hypocalcemia common
  - ➢ Metabolic acidosis
- CBC w/ manual differential & platelet count (monitor q8–12h)
- Arterial blood gases/capillary gases/venous blood gases
  - ➢ Route dependent on access
  - ➢ Metabolic acidosis may signify ischemic or dead bowel
  - ➢ Frequency dictated by clinical status of infant
  - ➢ At least one blood gas should be obtained
- Coagulation profile w/ fibrinogen & fibrin split products if disseminated intravascular coagulation suspected
- Blood culture and, if clinically indicated, CSF culture
- Abdominal radiographs, initially AP & left lateral decubitus; left lateral decubitus after Dx is confirmed (initially q6–8h intervals, then q12–24h until normal)
  - ➢ Pneumatosis intestinalis
  - ➢ Portal venous gas
  - ➢ Free air in peritoneum

DIFFERENTIAL DIAGNOSIS

- Sepsis
- Feeding intolerance of prematurity
- Abdominal distention due to continuous positive airway pressure
- Colitis from milk protein allergy
- Rectal fissure
- Intussusception
- Intestinal obstruction (see **INTESTINAL OBSTRUCTION** in the "Neonatal Presenting Signs" section)

MANAGEMENT

- What to do first:
  - ➢ ABCs (airway, breathing, circulation)
  - ➢ NPO, suction abdominal contents & place Replogle to continuous suction
- General measures

- ➢ Fluid resuscitate as needed; provide maintenance fluids & electrolytes; place central line to provide TPN once electrolytes stable
- ➢ Transfuse PRBC, FFP & platelets as needed

SPECIFIC THERAPY

- Medical therapy
  - ➢ Vancomycin & cefotaxime or gentamicin; in presence of perforation and/or peritonitis, consider clindamycin or Flagyl
  - ➢ Maintain NPO w/ Replogle tube in stomach to continuous suction
- Surgical therapy
  - ➢ Indications
    - Pneumoperitoneum
    - Peritonitis
    - Failure to improve w/ medical therapy
  - ➢ Procedures
    - Laparotomy w/ resection of ischemic bowel & externalization most commonly performed; w/ extensive bowel ischemia, no resection may be performed; a "second-look" operation is then performed at a later date to evaluate intestinal viability
    - Peritoneal drain placement at the bedside may be considered in infants <1,500 g who are not stable enough for surgery. Once stabilized, may require to laparotomy.

FOLLOW-UP

- In convalescent, radiologic contrast study may be required to rule out strictures

COMPLICATIONS AND PROGNOSIS

- Most common cause of death in premature infants undergoing surgery
- Stricture formation is most common complication, occurring in as many as 30% of infants surviving NEC
- Long-term medical complications
  - ➢ Fistulas
  - ➢ Malabsorption
  - ➢ Short bowel syndrome
  - ➢ Malnutrition
  - ➢ TPN cholestasis
- Increased risk of neurodevelopmental problems

NEUROBLASTOMA

MICHAEL WEINER, MD

- Most common tumor in infancy, accounts for 7.5% of all childhood malignancies
- ~10 cases diagnosed in U.S./million live births
- Incidence increased in past 10 yr secondary to routine use of non-invasive diagnostic tests, e.g., prenatal ultrasound
- Primary tumors may arise from any site in sympathetic nervous system

HISTORY & PHYSICAL

- Depend on site, presence of metastases
- Nonspecific constitutional symptoms: lethargy, anorexia, pallor, weight loss, pain, weakness, irritability
  - ➢ Head/neck: palpable mass, Horner's syndrome (myosis, ptosis, enophthalmos, anhydrosis)
  - ➢ Orbits: periorbital hemorrhage (raccoon eyes), exophthalmos, ecchymosis, opsoclonus (dancing eye syndrome)
  - ➢ Thoracic tumors: dyspnea, dysphagia, Horner's syndrome
  - ➢ Abdominal/pelvic tumors: anorexia, vomiting, enlarging mass, pain, constipation, urinary retention
  - ➢ Paraspinal tumors (dumbbell-, hourglass-shaped mass): pain, tenderness, limpness, weakness, hypotonia, paralysis
- Symptoms related to metastatic disease site-dependent; common sites include bones, liver, lymph nodes, bone marrow

TESTS

- CBC
- Serum chemistries, BUN, creatinine, uric acid, AST, ALT, LDH, alkaline phosphatase
- Urinalysis
- Serum ferritin
- Urinary catecholamines (VMA [vanillylmandelic acid], HVA [homovanillic acid])
- CT scan or MRI
- MIBG scintigraphy &/or bone scan
- Bilateral bone marrow aspirates & biopsies

DIFFERENTIAL DIAGNOSIS

- Depends on presentation

MANAGEMENT

- DETERMINE STAGE
  - Stage 1: Localized tumor + complete gross excision
  - Stage 2A: Localized tumor + incomplete gross excision
  - Stage 2B: Localized tumor +/− gross excision w/ non-adherent lymph nodes positive
  - Stage 3: Unresectable unilateral tumor extending across midline +/− lymph node involvement
  - Stage 4: Primary tumor + metastatic spread to lymph nodes, bone, bone marrow, liver, skin, etc.
  - Stage 4S: Localized primary tumor as defined for stages 1, 2A, or 2B w/ dissemination limited to skin, liver, bone marrow in INFANTS <1 YR OF AGE
- DETERMINE PATHOLOGIC SUBTYPE
  - Favorable Shimada
    1. Stroma rich w/o nodular pattern, all ages
    2. Stroma poor, differentiated, mitotic-karyorrhectic index (MKI) <100
  - Unfavorable Shimada
    1. Stroma rich w/ nodular pattern, all ages
    2. Stroma poor >5 y of age
    3. Stroma poor, 1–5 y of age, undifferentiated
    4. Stroma poor, differentiated, 1–5 y of age, MKI >100
- DEFINE PROGNOSTIC VARIABLES: unfavorable factors associated w/ poor prognosis:
  - Advanced stage
  - Age >1 yr
  - Unfavorable Shimada pathologic classification
  - Elevated serum ferritin
  - Elevated serum LDH
  - VMA/HVA ratio < 1
  - Diploid tumors (DNA index = 1)
  - N-MYC amplification
  - Loss at chromosome 1p
  - Gain at chromosome 17q
  - Low expression of nerve growth factor TrkA
- ESTABLISH RISK GROUP ASSIGNMENT
  - Low risk

- Age < 1 yr
- Favorable histology
- Stage 1
- Stage 2A/2b, age < 1 yr, N-MYC non-amplified, hyperdiploid

➢ Intermediate risk
- Stage 3, age < 1 yr, N-MYC non-amplified, any ploidy, any histology
- Stage 3, age > 1 yr, N-MYC non-amplified, favorable histology
- Stage 4, age < 1 yr, N-MYC non-amplified, favorable histology

➢ High risk
- Stage 2A/2B, age > 1 yr, N-MYC amplified, unfavorable histology
- Stage 3, age < 1 yr, N-MYC amplified, any ploidy, any histology
- Stage 3, age > 1 yr, N-MYC non-amplified, unfavorable histology
- Stage 4, age < 1 yr, N-MYC amplified, any ploidy, any histology
- Stage 4, age > 1 yr, N-MYC amplified/non-amplified, any ploidy, any histology

SPECIFIC THERAPY

■ Special considerations for NEONATAL neuroblastoma
➢ May be identified on prenatal US
➢ Stage 4S most prevalent
➢ Frequently identify subcutaneous nodules, bone marrow disease, extensive liver involvement
➢ Massive adrenal hemorrhage often seen
➢ Specific management for neonates/infants
- Observation if asymptomatic
- Obtain urinary VMA, HVA
- Surgery may be necessary to confirm diagnosis

➢ Treat w/ chemotherapy if respiratory compromise secondary to massive hepatic involvement

■ Low risk
➢ Surgery, supportive care, observation
➢ Excellent prognosis, 5-yr survival >95%

■ Intermediate risk
➢ Surgery
➢ Moderately intensive chemotherapy (cisplatin, etoposide, Cytoxan, vincristine)
➢ Local radiation therapy for unresectable tumors
➢ Good prognosis, 5-yr survival 80%

- High risk
  - ➢ Induction: dose-intensive chemotherapy (Cytoxan, cisplatin, doxorubicin, vincristine, ifosfamide, etoposide)
  - ➢ Local control: surgery, radiation therapy
  - ➢ Consolidation: autologous bone marrow transplant (myeloablative therapy, melphalan/thiotepa +/− total body irradiation) -hematopoietic stem cell support
  - ➢ Therapy for minimal residual disease w/ cis-retinoic acid
  - ➢ Poor prognosis, 3-yr survival 25–30%
- Treatment of relapse: Relapse portends ominous prognosis that may be treated w/ experimental phase I & II novel therapies

FOLLOW-UP

N/A

COMPLICATIONS AND PROGNOSIS

Prognosis

- Low risk: excellent prognosis, 5-yr survival >95%
- Intermediate risk: good prognosis, 5-yr survival 80%
- High risk: poor prognosis, 3-yr survival 25–30%
- Treatment of relapse: ominous prognosis

NONKETOTIC HYPERGLYCINEMIA

WENDY K. CHUNG, MD, PhD

HISTORY & PHYSICAL

History

- Prenatal hiccups
- Normal at birth & during first 48 h
- Lethargy, decreased feeding w/ onset of formula/breast feeding
- Coma
- Seizures
- Flaccidity
- Apnea
- Family Hx: neonatal death of unknown etiology
- Family Hx: consanguineous parents

Signs

- Seizures
- Myoclonus

- Persistent hiccups
- Hypotonia progressing to spasticity

TESTS
- Diffusely abnormal EEG
- Serum amino acids: increased glycine
- Elevated CSF glycine:serum glycine ratio (0.10–0.20) w/ glycine elevation
- Serum carnitine may be low
- Normal urine organic acids
- Prenatal Dx available w/ chorionic villus sampling

DIFFERENTIAL DIAGNOSIS
- Sepsis
- Electrolyte abnormalities
- Metabolic disorders, incl organic acidemias
- Transient nonketotic hyperglycinemia, rare

MANAGEMENT
- Airway, breathing, circulation; intubate immediately

SPECIFIC THERAPY

NOTE: Parents may opt not to Rx an affected neonate as prognosis is not significantly improved w/ Rx
- Dialysis or exchange transfusion
- Sodium benzoate (500 mg/kg/day)
- Dextromethorphan (7.5 mg/kg/day)
- Carnitine if levels are low (100 mg/kg/day divided BID)
- Dietary restriction of glycine
- G-tube may be necessary for long-term feeding

FOLLOW-UP
- Follow serum glycine

COMPLICATIONS AND PROGNOSIS
- Extremely poor w/ classical disease, which accounts for the majority of cases: almost all die within 1st 12 mo of life even w/ Rx; continuous seizures in survivors w/ little cognitive development

NOONAN SYNDROME

KWAME ANYANE-YEBOA, MD

- Autosomal dominant inheritance w/ many cases representing mutations
- 50% have mutations in PTPN11 gene, 10% in SOS1 gene, <5% in KRAS gene, the rest in as yet unidentified gene(s)

HISTORY & PHYSICAL

- Epicanthal folds
- Ptosis of upper eyelids
- Hypertelorism
- Downslanted palpebral fissures
- Low nasal bridge
- Low-set abnormal ears
- Short &/or webbed neck
- Low posterior hairline
- Shield chest
- Pectus excavatum &/or carinatum
- Pulmonary valve stenosis, cardiomyopathy
- Pulmonary artery branch stenosis
- ASD, PDA, coarctation
- Small penis, hypospadias, cryptorchidism
- Bleeding diathesis due to partial factor XI, XII, VII deficiencies, von Willebrand disease, thrombocytopenia
- Large or asymmetric head
- Kyphoscoliosis
- Edema of dorsum of hands, feet
- Wooly, curly hair
- Chylothorax
- Transverse palmar crease
- Nerve deafness
- Hypoplastic nipples
- Skin nevi
- Keloids

TESTS

- Chromosome studies to exclude Turner syndrome, XO/XY mosaicism
- FISH test to exclude chromosome 22q11 deletion

- DNA testing for mutations in PTPN11, KRAS, SOS1 genes (see www.genetests.com for labs offering DNA tests)

DIFFERENTIAL DIAGNOSIS
- Principal DDx in females: Turner syndrome
- Features overlap those of Costello, cardio-facio-cutaneous, LEOPARD, Watson, & DiGeorge (velo-cardio-facial) syndromes [see **DIGEORGE (VELOCARDIOFACIAL) SYNDROME**]

MANAGEMENT
Appropriate mgt of cardiac disease, poor feeding, failure to thrive in infancy

SPECIFIC THERAPY
None

FOLLOW-UP
Genetic, cardiac, developmental, GI as indicated

COMPLICATIONS AND PROGNOSIS
- Poor feeding in newborn period
- Failure to thrive in infancy
- Mental retardation in 25%
- Rapidly progressive scoliosis may occur in older children, adolescents

OMPHALOCELE

See **GASTROSCHISIS/OMPHALOCELE**

ORNITHINE TRANSCARBAMYLASE DEFICIENCY/UREA CYCLE DISORDERS

WENDY K. CHUNG, MD, PhD

HISTORY & PHYSICAL

History
- Normal prenatal history, term delivery, normal birth
- Poor feeding, vomiting in 1st 48 hr
- Lethargy
- Grunting, apnea, seizures, coma

- Usually male w/ ornithine transcarbamylase (OTC) deficiency

Signs
- Bulging fontanel
- Apnea
- Deep coma w/ fixed, dilated pupils

TESTS
- Basic test: NH3 usually > 500 mcg/dL
- ABG: respiratory alkalosis unless apneic for long periods
- Serum electrolytes, glucose
- Urinalysis
- Specific diagnostic tests
  - ➢ Serum amino acid analysis (elevated citrulline >1,000 mcmol/L in citrullinemia; elevated arginine in argininemia; elevated glutamine in OTC)
  - ➢ Urine organic acids (elevated orotic acid in OTC deficiency)
- Genetic DNA testing/hepatic enzymatic testing
- Prenatal diagnosis possible if mutation can be identified in previously affected child

DIFFERENTIAL DIAGNOSIS
- Sepsis
- Intracranial hemorrhage
- Organic acidemia (anion gap elevated acidosis, ketosis)
- Fatty acid oxidation disorder (see FATTY ACID OXIDATION DISORDER) (no ketones, hypoglycemia)
- Transient hyperammonemia of newborn
- Liver failure

MANAGEMENT
- Maintain airway, breathing, circulation; intubate
- NPO; discontinue all protein/amino acid intake
- D10W IV
- Prepare for IMMEDIATE transport to metabolic center. Rapidly fatal if not correctly treated.

SPECIFIC THERAPY
- 10% arginine hydrochloride 2 mL/kg over 1 hr, then over 24 hr
- Sodium benzoate 0.25 g/kg & sodium phenylacetate 0.25 g/kg in 30 cc/kg 10% glucose IV over 90 min, then same amount over 24 hr. Note: These meds are usually available only in metabolic centers.
- Mannitol for increased ICP

- Dialysis, hemodialysis, or ECMO to remove ammonia
- Pyridoxine 5 mg IV q day & folic acid 0.1 mg IV q day
- Peritoneal dialysis or exchange transfusion inadequate in neonates but may temporize until hemodialysis possible
- Liver transplant curative & recommended
- No contraindications to treatment

FOLLOW-UP

- Follow NH3 levels
- Metabolic crises precipitated by any catabolic state, e.g. intercurrent infection
- Metabolic crises require Rx as above, usually starting w/ IV meds before dialysis; early Dx imperative
- Diet w/ restricted protein intake

COMPLICATIONS AND PROGNOSIS

- Earlier Rx instituted, better the outcome
- Often mental retardation of varying severity
- Many pts w/o liver transplant will die of metabolic crisis during infancy

OSTEOMYELITIS

RICHARD A. POLIN, MD

HISTORY & PHYSICAL

History

- Majority of cases are hematogenous in origin & assoc w/ + blood culture
- Most common site: metaphysis
- Direct spread to epiphysis & joint space not uncommon
- Multiple bone involvement not uncommon
- Responsible pathogens
  - ➢ *Staphylococcus aureus*
  - ➢ Groups A & B streptococci
  - ➢ Enteric organisms
  - ➢ *Candida sp*
- Risk factors for osteomyelitis incl those for acute bacterial sepsis & nosocomial sepsis (see **SEPSIS/PNEUMONIA, EARLY-ONSET; SEPSIS, NOSOCOMIAL**)

Signs

Physical

- Any of the signs, symptoms of sepsis can be present (see **SEPSIS/PNEUMONIA, EARLY-ONSET**; **SEPSIS, NOSOCOMIAL**; **PNEUMONIA, NOSOCOMIAL**)
- Limited spontaneous movement, pain on passive movement, pseudoparalysis most common presenting signs
- Localized tenderness, erythema, warmth, swelling

TESTS

- Blood culture is + in 60% of cases
- Early in course plain radiographs, bone scans usually normal
- Aspiration of bone yields + culture in 70% of cases
- If the infant appears ill, urine & CSF cultures indicated
- If bone aspiration not successful, plain radiographs indicated for:
  - ➢ Deep edema
  - ➢ Joint effusion
  - ➢ Bone destruction
- If radiographs, plain films not helpful, technetium bone scan indicated
- US of hip is a sensitive way to detect joint effusions & osteomyelitis of the hip

DIFFERENTIAL DIAGNOSIS

- Bacterial sepsis
- Fracture
- TORCH infection w/ bony involvement

MANAGEMENT

General measures (infants w/ suspected bacteremia)

- Correction of acid/base disturbances
- Establish IV access

SPECIFIC THERAPY

- Antimicrobial therapy
  - ➢ Choice of empiric therapy depends on sensitivities of organisms causing sepsis in given nursery
  - ➢ Initial empiric therapy must be appropriate for gram-positive AND gram-negative pathogens
    - Early-onset bacterial sepsis
      - Ampicillin/aminoglycoside
    - Nosocomial sepsis
      - Vancomycin/aminoglycoside for empiric therapy

- ➢ Final antibiotic selection based on sensitivities
- ➢ Duration of treatment 3–6 wk
- ➢ Mobilize affected limb w/ splints

■ Surgery
- ➢ If pus recovered, surgical drainage indicated
- ➢ If no pus recovered, treatment w/ broad-spectrum antibiotics sufficient unless infant remains clinically ill >48–72 h w/ therapy
  - Repeated needle aspiration attempts indicated if no clinical improvement w/in 48 h
  - Surgery indicated if infant remains ill, even if needle aspiration attempts are negative
- ➢ Osteomyelitis of flat bones (skull, vertebra) almost never needs aspiration
- ➢ Infants w/ joint involvement always require drainage
  - If hip involved, open drainage indicated
  - For all other joints, repeated needle aspiration may suffice

FOLLOW-UP

■ To detect discrepancies in growth &/or development of osteoarthritis

COMPLICATIONS AND PROGNOSIS

■ Complications
- ➢ Septic arthritis
- ➢ Necrosis of femoral head w/ hip involvement

■ Prognosis
- ➢ Recovery w/ residual deformities or growth disturbances is the rule

OSTEOPENIA OF PREMATURITY

WINSTON KOO, MD

HISTORY & PHYSICAL

History

■ Prematurity (usually extremely low birth weight, <1,000 g, complicated postnatal course w/ intestinal, hepatic, pancreatic or renal dysfunction)

■ Chronic diuretic therapy +/ − postnatal steroid therapy

■ Inadequate nutrient intake
- ➢ Prolonged volume restriction

- ➢ Parenteral nutrition: low mineral (calcium & phosphorus) content
- ➢ Enteral feeding
  - Delayed initiation & achieving full volume
  - Inappropriate milks/diet: unfortified human milk or milk formulas designed for term infants e.g., soy, protein hydrolysate or standard milk formulas
- Vigorous physical therapy results in fractures
- Often present as incidental finding on an x-ray (acute fractures or callus formation, rachitic changes)
- May be recently discharged from hospital

Physical examination

- Often <10th percentile for weight & length even after correction for prematurity; relatively higher percentile for head circumference
- Skull bones often soft & may have "ping-pong" feel
- Other typical features of classical rickets such as rachitic rosary (uncommon), bowing of legs & kyphoscoliosis (rare)
- Muscle tone is generally appropriate w/ the extent of prematurity
- Swelling +/ − immobility assoc w/ fractures +/ − callus formation
- May have features assoc w/ chronic illnesses such as bronchopulmonary dysplasia

TESTS

- Basic
  - ➢ Radiograph of affected limb(s) & skeletal survey to determine presence of osteopenia, rickets, fractures. Serial radiographs of affected region q 1–3 mo until complete healing.
  - ➢ Serum or plasma calcium (Ca), phosphorus (P), total alkaline phosphatase (AP), total protein & albumin, creatinine (Cr). Serial monitoring q 1–4 wks until normal × 2.
  - ➢ Urine Ca, P, Cr as baseline
- Specific: serum or plasma bone-specific AP, vitamin D metabolites [25 OH- and 1,25 (OH)2- vitamin D]. Serial monitoring q 1–3 mo until normal × 2.
- Other tests as appropriate
  - ➢ Liver function tests if cholestatic jaundice suspected
  - ➢ Blood gas, serum & urine amino acids, acid-base status if suspect renal tubular defect
  - ➢ Bone densitometry & serum bone turnover markers experimental

➢ Maternal & family screening if suspect metabolic/endocrine disorders of mineral metabolism

DIFFERENTIAL DIAGNOSIS

- Nutrient deficiency, particularly of calcium, phosphorus, copper, vitamin D
- Toxic contaminant in nutrients – e.g., aluminum
- Child abuse
- Metabolic/endocrine disorders of bone mineral metabolism

MANAGEMENT

- Pain relief if recent fracture: splint +/ − analgesic
- Adequate overall nutritional support, in particular high-mineral-containing parenteral nutrition or preterm infant formula. Fortification of milk (commercial fortifier mixed w/ small amount of human milk q4–6h w/ feed) if breast fed.
- Infants who tolerate adequate volumes of appropriate enteral feeding probably do not require additional vitamin supplement
- Vitamin D supplement at 400 IU daily if documented vitamin D deficiency (low serum 25 OHD)
- Minimize pharmacotherapy that may adversely affect bone mineralization
- Treat underlying disorder if possible – e.g., liver disease

FOLLOW-UP

- Serial anthropometric measurements until normal growth, resolution of deformity, appropriate dietary intake for age ensured

COMPLICATIONS AND PROGNOSIS

- Risk for permanently stunted growth
- Permanent deformities: uncommon

PATENT DUCTUS ARTERIOSUS (PDA)

ULANA M. SANOCKA, MD

- Postnatal closure
  - ➢ Term infants: functional closure occurs by age 24–72 hr
  - ➢ Preterm infants: functional closure commonly delayed
- Incidence of PDA inversely related to GA & birth wt – DA patency on DOL:
  - ➢ 79% of infants 24–25 wks

- ➢ 69% of infants 26–27 wks
- ➢ 38% of infants 30–31 wks
- ➢ 17% of infants 32–33 wks

- Ductal closure is delayed w/ respiratory distress syndrome (RDS)
  - ➢ PDA closes spontaneously in 90% of healthy preterm infants by DOL 4
  - ➢ PDA closes spontaneously in 40% of infants w/ RDS by DOL 4
- Antenatal corticosteroids reduce the prevalence of PDA

HISTORY & PHYSICAL

History

- Apnea, bradycardia
- Deterioration in respiratory status of infant recovering from RDS or lack of progress in weaning from ventilator

Signs

- Cardiac murmur: usually systolic murmur heard best in left infraclavicular region; not usually continuous in 1st wk of life – NO MURMUR IN 20–50% OF HEMODYNAMICALLY SIGNIFICANT PDAS IN FIRST WK OF LIFE ("silent ductus")
- Hyperdynamic precordium (most sensitive sign; not specific)
- Bounding pulses, palmar pulses
- CHF
- Signs of decreased systemic perfusion (e.g., metabolic acidosis, rising serum creatinine or oliguria)

TESTS

- 2-D echocardiogram w/ pulsed, continuous or color Doppler diagnostic
  - ➢ ALWAYS indicated to r/o right-to-left PDA shunting & ductal dependent CHD
- CXR neither sensitive nor specific
  - ➢ +/− cardiomegaly
  - ➢ Difficult to distinguish intrinsic lung disease from pulmonary congestion
- ECG of limited value

NOTE: RELIANCE ON CLINICAL OR RADIOGRAPHIC SIGNS FAILS TO IDENTIFY SUBSTANTIAL NUMBER OF PATIENTS W/ PDA!

All ventilated preterm infants w/ RDS should have cardiac echocardiogram by DOL 3–7

DIFFERENTIAL DIAGNOSIS

- Peripheral pulmonary flow murmur of prematurity
- PDA as part of complex CHD
- Any cause of heart murmur

MANAGEMENT

- Supportive respiratory care
- Avoid excessive fluid intake
- Correct anemia
- Rx congestive heart failure prn (see **CONGESTIVE HEART FAILURE** in the "Neonatal Presenting Signs" section)

SPECIFIC THERAPY

- No consensus re indication for closure of DA in infants <28 wk, but infants >=28 wks, not requiring assisted ventilation, rarely require closure (spontaneous closure likely by DOL 7 & risk of complications associated w/ PDA is low)

  NOTE: Right-to-left PDA shunting is contraindication to closure

  ➢ Close only symptomatic PDA (recommended)
  - Infants <28 wk or requiring assisted ventilation – echocardiogram on DOL 3–7
    - Close DA if patent & PDA symptomatic (i.e., failure to wean from assisted ventilation, deteriorating resp status, CHF, or signs of decreased systemic perfusion)
    - Observe if DA patent but not symptomatic; close if symptoms develop
  - Infants >28 wk not requiring assisted ventilation > DOL 2–3 days
  - echocardiogram only for signs c/w possible symptomatic PDA; then, close if DA patent

  ➢ Presymptomatic closure of documented PDA (not recommended) – echocardiogram in all infants <28 wk or requiring assisted ventilation on DOL 3–7; close if DA still patent
  - Reduces incidence of symptomatic PDA
  - Reduces duration of suppl O_2 requirement
  - NO EFFECT ON MORTALITY, PULMONARY MORBIDITY, NECROTIZING ENTEROCOLITIS, RETINOPATHY OF PREMATURITY, LONG-TERM NEURODEVELOPMENTAL OUTCOME c/w closing only symptomatic PDA

  ➢ Prophylactic closure (not recommended) – Rx all infants <28 wk, or requiring assisted ventilation, w/in 12 hr of life

- Reduces need for surgical ligation
- Reduces incidence of grade 3 & 4 intraventricular hemorrhage
- NO EFFECT ON MORTALITY, PULMONARY MORBIDITY, NECROTIZING ENTEROCOLITIS, RETINOPATHY OF PREMATURITY, LONG-TERM NEURODEVELOPMENTAL OUTCOME C/W closing only symptomatic PDA

■ Options to close PDA

➢ MEDICAL THERAPY

- Indomethacin
  - Contraindications
    - Serum creatinine >1.8 or urine output <0.5 mL/kg/h
    - Platelet count <50,000/mm^3 or active bleeding
    - Suspected/proven necrotizing enterocolitis
  - Dosing regimens
    - Standard (recommended)
      - Dose
        Age <48 hr, any birth wt: 1st dose, 0.2 mg/kg; 2nd dose, mg/kg; 3rd dose, 0.1 mg/kg
        Age 2–7 days, birth wt <1,250 g: 1st dose, 0.2 mg/kg; 2nd dose, 0.1 mg/kg; 3rd dose, 0.1 mg/kg
        Age 2–7 days, birth wt >1,250 g: 1st dose, 0.2 mg/kg; 2nd dose, 0.2 mg/kg; 3rd dose: 0.2 mg/kg
        Age >7 days, any birth wt: 1st dose, 0.2 mg/kg; 2nd dose, 0.2 mg/kg; 3rd dose: 0.2 mg/kg
      - Dosing interval – 2nd & 3rd doses at 12- to 24-hr intervals
      - Route: IV over 30 min
      - If oliguria develops, delay or cancel subsequent doses
      - 2nd course of indomethacin may be given if DA remains patent
      - If 2 courses of indomethacin fail & closure still indicated, ligate PDA
      - Efficacy
        Related to plasma conc achieved
        Decreased w/ larger PDA, lower birth weight, surfactant 35–75% close w/ 1st course; 60–90% close w/ 2nd course 10–25% reopen
    - Prophylactic (not recommended)
      - 1st dose, 0.2 mg/kg within 12 hr of life; then, 0.1 mg/kg, 24 & 48 hr after 1st dose
      - Reduces need for ligation

- Reduces prevalence of grade 3 & 4 intraventricular hemorrhage
- NO EFFECT ON MORTALITY, PULMONARY MORBIDITY, NECROTIZING ENTEROCOLITIS, RETINOPATHY OF PREMATURITY, LONG-TERM NEURODEVELOPMENTAL OUTCOME

- Prolonged low-dose indomethacin (not recommended) – 0.1 mg/kg q24h × 5–7 days
  - Efficacy ***not*** greater than w/ standard regimen
  - No reduction in morbidity or mortality compared w/ standard regimen
  - Borderline significant reduced risk of PDA re-opening compared w/ standard regimen in more mature infants
- Continuous, prolonged indomethacin – insufficient data
- Adverse effects
  - Transient renal impairment
    - Decreased urine output, increased serum creatinine; secondary hyponatremia; hyperkalemia w/ anuria
    - Usually resolves w/in 72 hr
    - Most common recognizable side effect
    - Narrow therapeutic window: plasma levels req to close DA likely to result in transient renal impairment
    - Not related to plasma conc
    - Prophylactic furosemide or dopamine to prevent ***not*** recommended
  - GI bleeding
  - Decreased mesenteric blood flow
  - Spontaneous intestinal perforation, esp w/ concurrent steroid Rx
  - Decreased cerebral blood flow, oxygenation, & reactivity to changes in pCO_2, but no difference in long-term neurodevelopmental outcome
  - Impaired platelet aggregation
  - Hypoglycemia
- Ibuprofen
  - Contraindications – Same as for indomethacin
  - Dosing regimens
    - Standard
      - Dose: 1st dose, 10 mg/kg; 2nd & 3rd doses, 5 mg/kg, at 24 & 48 hr
      - Route: IV over 15 min

- If oliguria occurs, delay or cancel subsequent doses
- If ductus fails to close a 2nd course of ibuprofen or rescue w/ indomethacin may be tried
- Similar efficacy to indomethacin
- Adverse effects
  - Less oliguria & less elevated serum creatinine than w/ indomethacin
  - No effect on mesenteric blood flow
  - No effect on cerebral blood flow, cerebral blood volume or tissue oxygenation index
- Prophylactic ibuprofen
  - Same dosing regimen as standard Rx
  - Reduces occurrence of PDA at age 3 days
  - Reduces need for rescue Rx w/ indomethacin/ibuprofen or surgical ligation
  - Less oliguria than w/ indomethacin
  - ***No reduction in intraventricular hemorrhage***
- Oral ibuprofen – insufficient data

- Adverse effects
  - Transient renal impairment – decreased urine output, increased serum creatinine; secondary hyponatremia
  - Pulmonary hypertension reported, responds to nitric oxide
  - Displaces bilirubin from albumin, may increase risk of bilirubin encephalopathy
  - Increased serum half-life of amikacin
- No long-term outcome date

➢ SURGICAL LIGATION

- Reserve for failed indomethacin or ibuprofen Rx or w/ contraindication to medical Rx
- Extrapleural approach preferred to avoid chest tube
- Adverse effects/risks, all uncommon in experienced centers
  - General anesthesia
  - Mistaken ligation of pulm artery or aorta
  - Hemorrhaging

FOLLOW-UP

- Urine output
- Serum electrolytes, creatinine
- Clinical signs of PDA

- Repeat echocardiogram 24–48 hr after last indomethacin/ibuprofen dose
  - 20% of infants have residual ductal flow w/o clinical signs after indomethacin Rx; comparable data not available for ibuprofen
  - W/ residual flow, DA re-opens clinically in 90% of infants
  - Even with no flow, least mature infants are at high risk of re-opening ductus
    - 24–25 wk, 26%
    - 26-27 wk, 14%

COMPLICATIONS AND PROGNOSIS

- Complications
  - Due to PDA
    - Exacerbation of respiratory distress syndrome
    - Pulmonary hemorrhage
    - Exacerbation of apnea/bradycardia
    - CHF
    - Decreased cerebral, mesenteric & renal perfusion
      - Metabolic acidosis
      - Impaired renal function
      - Intraventricular hemorrhage, periventricular leukomalacia
      - Necrotizing enterocolitis
  - Due to Rx – see "Specific Therapy"
- ***Associations*** w/ PDA – etiologic relation ***not*** proven
  - Chronic lung disease
  - Survival
- Prognosis
  - Eventual spontaneous closure
  - Long-term prognosis – depends on gestational age, associated complications

PERSISTENT PULMONARY HYPERTENSION OF THE NEWBORN (PPHN)

THOMAS A. WISWELL, MD

HISTORY & PHYSICAL

History

- Meconium-stained amniotic fluid

- Fetal distress: abnl fetal heart race tracings, abnl biophysical profile
- Perinatal asphyxia (hypoxia, hypercapnia, acidosis)
- Resuscitation req in delivery room
- IUGR
- Evidence of infection (e.g., chorioamnionitis)
- Polycythemia/hyperviscosity
- Postdates GA
- Maternal use of nonsteroidal anti-inflammatory drugs (e.g., aspirin, ibuprofen)
- Hydrops fetalis
- Congenital malformations
  - ➢ Congenital diaphragmatic hernia (CDH)
  - ➢ Congenital cystic adenomatoid malformation (CCAM)
  - ➢ Pulmonary hypoplasia
  - ➢ Congenital heart disease

Signs

- Respiratory distress soon after birth (tachypnea, grunting, flaring, retracting)
- Cyanosis
- Post-dates appearance: peeling skin, dystrophic umbilical cord, wasting
- Meconium-stained nails, skin, umbilical cord, hair
- Meconium-stained amniotic fluid suctioned from trachea
- Heart murmur (often due to tricuspid regurgitation); S2 often single due to increased pulm artery pressure
- Scaphoid abdomen w/ CDH
- Oligohydramnios sequence w/ pulmonary hypoplasia

TESTS

- CXR (findings vary w/ underlying etiology)
  - ➢ Hypovascularity (esp w/ primary PPHN)
  - ➢ Hyperinflation, diffuse, patchy infiltrates (meconium aspiration syndrome or congenital pneumonia)
  - ➢ Granular, ground-glass appearance w/ respiratory distress syndrome
  - ➢ Stomach/intestinal gas present in chest & chest shifted to opposite side w/ CDH
  - ➢ Pneumothorax or pneumomediastinum
  - ➢ Pleural effusions w/ hydrops fetalis
  - ➢ "Wet-lung" appearance
  - ➢ Cystic areas in lungs (w/ CCAM)

- Arterial blood gas
  - ➢ Hypoxemia
  - ➢ Hypercapnia
  - ➢ Metabolic acidosis
  - ➢ Preductal to postductal d PaO_2 >=20–25 mmHg difference w/ right-to-left shunting across patent ductus arteriosus; not seen if shunting only at level of foramen ovale
  - ➢ Marked lability in oxygenation (PaO_2 values may vary markedly from one moment to next on same or minimally different ventilator settings)
- O_2 saturations (pulse oximetry)
  - ➢ Frequently low
  - ➢ Preductal to postductal d PaO_2 >=20–25 mmHg difference w/ right-to-left shunting across patent ductus arteriosus; not seen if shunting only at level of foramen ovale
  - ➢ Marked lability in oxygenation (O_2 sats may vary markedly from one moment to next on same or minimally different ventilator settings)
- Hyperoxia test
  - ➢ Obtain arterial blood gas after 10–15 min in FiO_2 1.0 (some advise intubation & assisted ventilation for hyperoxia test)
    - W/ parenchymal lung disease, PaO_2 should be >100 mmHg, except w/ V/Q mismatching
    - If cyanotic heart disease, PaO_2 changes little
    - If PPHN, PaO_2 may either rise slightly or remain same; w/ hyperventilation w/ 100% O_2 for 10–15 min to decrease $PaCO_2$ to 25–30 mmHg & increase pH to >=7.50, a dramatic increase in PaO_2 suggests PPHN
      NOTE: Some believe even brief hyperventilation is contraindicated
- Echocardiography (mandatory)
  - ➢ R/o structural congenital heart disease (total anomalous pulmonary venous return is particularly difficult to exclude)
  - ➢ Assess direction of shunting across the foramen ovale, ductus arteriosus
  - ➢ Evaluate size of RA & RV
  - ➢ Estimate pulmonary artery pressure (by evaluating regurgitant tricuspid "jet")
  - ➢ Assess myocardial function
- CBC/differential
  - ➢ Check hemoglobin, hematocrit to r/o polycythemia

- ➢ Leukocytosis w/ left shift on WBC differential common in pneumonia, sepsis, meconium aspiration syndrome, w/ pneumothorax
- ➢ Increased nucleated RBC suggests in utero hypoxia
- ➢ Increased lymphocytes soon after birth w/ recent in utero hypoxia

- Other
  - ➢ Fatal cases should have autopsy performed to assess for histopathological findings (e.g., capillary-alveolar dysplasia)
  - ➢ Evaluation for asphyxia, meconium aspiration syndrome, pneumonia, other underlying etiology

DIFFERENTIAL DIAGNOSIS

- Severe pulmonary parenchymal disease (w/ or w/o associated PPHN)
  - ➢ See **MECONIUM ASPIRATION SYNDROME**
  - ➢ Congenital pneumonia (see **SEPSIS/PNEUMONIA, EARLY-ONSET**)
  - ➢ See **RESPIRATORY DISTRESS SYNDROME**
- Congenital cyanotic heart disease

MANAGEMENT

- Prenatal/intrapartum
  - ➢ Identify high-risk infants
    - Structural anomalies
    - Evidence of infection
    - Post-dates
    - Abnormal fetal heart rate tracings
- Delivery room
  - ➢ Optimize resuscitation
  - ➢ Avoid hypothermia, hypoglycemia, hypovolemia, acidosis
- Postnatal: general measures
  - ➢ Establish diagnosis
  - ➢ Treat underlying disorder
  - ➢ Correct mechanical problems
    - Pneumothorax
    - Pleural effusions
    - Other
  - ➢ Maintain adequate systemic BP, cardiac output:
    - Vol expansion
    - Inotropes as necessary (dobutamine, dopamine)
- Oxygen

- ➢ Use sufficient to maintain O_2 saturations >=95% or PaO_2 levels 50–80 mmHg (some clinicians prefer even higher levels, but no data support this as better approach)
- ➢ Follow oxygenation index (OI) to determine effect of mgt, when to escalate to other therapies:
  $OI = (\text{mean airway pressure})(FiO_2)(100)/PaO_2$

■ Mechanical ventilation
- ➢ Conventional mechanical ventilation – i.e., intermittent mandatory ventilation – typically the primary mode
- ➢ Patient-triggered ventilation (Assist/Control, SIMV) may be considered
- ➢ Vol-controlled ventilation an option
- ➢ Many employ hyperventilation/alkalosis
  - Take advantage of vasodilatory effect of alkalosis, hypocapnia on pulmonary vasculature
  - Decrease $PaCO_2$ to the "critical" value: below this, sharp rise in PaO_2 or O_2 saturation
  - ***Hypocapnia may be harmful to brain, lungs***; avoid $PaCO_2$ <25–30 mmHg
- ➢ Many advocate "gentle" ventilation (lower PaO_2s & higher $PaCO_2$s than above) to minimize ventilator support, prevent "volutrauma"
- ➢ No randomized, controlled trials demonstrate superiority of any mechanical ventilation method
- ➢ When weaning, make slow, small changes in ventilator settings (because of lability, infants may "flip-flop" w/ large changes)

■ Pharmacologic alkalosis: sodium bicarbonate to achieve alkalosis
- ➢ pH usually kept above 7.50
- ➢ No efficacy data

■ Consider sedation w/ mechanical ventilation, but avoid suppression of spontaneous ventilatory effort

■ Minimize stimulation
- ➢ Avoid loud noises, consider ear plugs
- ➢ Consider mask
- ➢ Minimize handling (needle punctures, suctioning, chest physiotherapy, etc.)

■ Surfactant
- ➢ Efficacious for respiratory distress syndrome
- ➢ May be of benefit w/ meconium aspiration syndrome, congenital pneumonia
  - Give w/ OI >= 15–20; some use at lower levels

- Use standard (or 1.5×) dose

- High-frequency ventilation (HFV)
  - ➢ No clear-cut advantages of HFV
  - ➢ Some consider high-freq oscillatory ventilation to "optimize" lung vol
  - ➢ Hyperventilation may be easier to achieve w/ HFV
  - ➢ Consider HFV w/ air leaks
  - ➢ Consider HFV w/ OI >=10–15 on conventional mechanical ventilation
- Inhaled nitric oxide (iNO)
  - ➢ Selective pulmonary vasodilator
  - ➢ Dose: 5–20 ppm
  - ➢ Some use iNO in combo w/ high-freq oscillatory ventilation
- Non-iNO pulmonary vasodilators
  - ➢ None specifically approved by FDA for PPHN pts
  - ➢ Sildenafil, enterally; case reports only
  - ➢ IV magnesium sulfate – effective in several small trials
  - ➢ Prostaglandins – little data to support efficacy
  - ➢ Adenosine infusion – minimal data
  - ➢ Nitroglycerine – no data to support
  - ➢ Arginine infusion – experimental
- Extracorporeal membrane oxygenation (ECMO)
  - ➢ Therapy of last resort
  - ➢ Generally, rescue modality when predicted mortality >=80% (typically at OI levels >=40)
  - ➢ Overall survival > 80%; best w/ meconium aspiration syndrome, worst w/ CDH
  - ➢ Systemic anticoagulation necessary; bleeding complications not uncommon
  - ➢ Venoarterial bypass results in loss of right carotid artery

SPECIFIC THERAPY

Depending on underlying etiology

FOLLOW-UP

- Follow for neurodevelopmental outcomes, pulmonary complications (chronic lung disease, altered pulmonary mechanics, reactive airway disease)
- Depending on underlying etiology

COMPLICATIONS AND PROGNOSIS

- 10–20% mortality

- Chronic lung disease (need for O_2/mechanical ventilation at age 28 days) in 5–10%
- Abnormal neurodevelopmental outcome in 20–40% of survivors: cerebral palsy, seizures, cognitive delays, deafness, autism

PHENYLKETONURIA, NEONATAL

WENDY K. CHUNG, MD, PhD

HISTORY & PHYSICAL

History
- Abnormal newborn screen most likely initial presentation
- Vomiting, irritability, unusual mousy odor (phenylacetic aciduria)

Physical signs
- Blue eyes, blond hair, fair skin, eczematous rash

TESTS
- Basic tests: newborn screen for increased phenylalanine by Guthrie test or tandem mass spectroscopy
- Specific diagnostic tests: quantitative amino acids in serum – phenylalanine >1,200 mcmol/L is diagnostic w/ normal or decreased tyrosine
- Carnitine
- Other tests as appropriate
  - ➢ Urine for phenylpyruvic acid, orthohydroxyphenylacetic acid in classic PKU
  - ➢ Genetic testing for phenylalanine hydroxylase deficiency (classic PKU)
  - ➢ Response to IV tetrahydrobiopterin to diagnose non-classic PKU caused by defective tetrahydrobiopterin metabolism (<2%)

DIFFERENTIAL DIAGNOSIS
- See TYROSINEMIA
- Transient tyrosinemia of newborn
- Hyperphenylalaninemia variant
- Full amino acid profile will differentiate

MANAGEMENT
- Admit pt for administration of low-phenylalanine diet at metabolic center ASAP

SPECIFIC THERAPY

- Indications for treatment: phenylalanine >10 mg/dL
- Treatment
  - Phenylalanine-restricted diet: Lofenalac® (Mead Johnson) or Analog XP® (Ross)
  - Low-protein diet w/ restricted phenylalanine until puberty to maximize IQ. Best to maintain diet lifelong.
  - Carnitine supplementation if levels are low (100 mg/kg divided BID)
  - Pregnant women must strictly adhere to diet to prevent mental retardation & congenital heart disease in the fetus

No contraindications to treatment

FOLLOW-UP

During treatment

- Measure quantitative amino acids in serum: Goal = phenylalanine <300 mcmol/L
- Long-term: neurodevelopmental

COMPLICATIONS AND PROGNOSIS

- Good long-term prognosis if compliant w/ diet
- May be assoc w/ hyperactivity, anxiety, decreased fertility in men

PNEUMOTHORAX, TENSION

RAKESH SAHNI, MD

HISTORY AND PHYSICAL

- Acute deterioration in pt's status
- Signs & symptoms
  - Cyanosis/hypoxia
  - Metabolic acidosis
  - Tachypnea
  - Sudden bradycardia/tachycardia
  - Sudden increase in systolic BP followed by narrowing pulse pressure & hypotension
  - Asymmetric chest (bulging on affected side)
  - Abdominal distention (due to downward displacement of diaphragm)

- ➢ Decreased breath sounds on affected side
- ➢ Shift of cardiac apical impulse away from affected side

TESTS

- Transillumination
- CXR
  - ➢ Confirmatory; given pt's condition, time may not allow
  - ➢ AP & lateral decubitus w/ side on which pneumothorax suspected up
  - ➢ AP view shows:
    - Mediastinal shift away from pneumothorax side
    - Diaphragmatic depression on affected side
    - Displacement of lung away from chest wall on affected side

DIFFERENTIAL DIAGNOSIS

- Obstructed/displaced ET tube
- Pneumopericardium
  - ➢ Acute onset
  - ➢ Drop in BP, weak/absent pulse
  - ➢ Distant/absent heart sounds
  - ➢ May transilluminate
  - ➢ CXR: halo around heart
  - ➢ Treatment: pericardiocentesis
- Pneumomediastinum
  - ➢ May be asymptomatic, unless accompanied by pneumothorax
  - ➢ May present w/ respiratory distress, but not w/ sudden deterioration
  - ➢ CXR: "wind-blown spinnaker sail" (thymus elevated off heart)
  - ➢ No Rx required; usually resolves spontaneously, but may progress to pneumothorax or pneumopericardium
- Congenital lobar emphysema (see **LUNG BUD MALFORMATIONS**)
  - ➢ Overdistention of one lobe (usually left upper) secondary to air trapping
  - ➢ Onset usually not acute
  - ➢ May transilluminate
  - ➢ Rx: surgical excision for symptomatic pts
- Atelectasis w/ compensatory hyperinflation
  - ➢ CXR: compensatory emphysema mimics pneumothorax
  - ➢ Onset usually not acute
  - ➢ May transilluminate

- ➢ Treatment – expansion of atelectatic lung w/ chest physiotherapy, positioning infant w/ hyperinflated side down

MANAGEMENT

- Supportive

SPECIFIC THERAPY

- Immediate thoracentesis followed by thoracotomy tube placement (see **THORACENTESIS** and **THORACOTOMY TUBE INSERTION** in the "Procedures" section)

FOLLOW-UP

- Follow-up CXR for resolution of pneumothorax

COMPLICATIONS AND PROGNOSIS

- Complications
  - ➢ Shock due to decreased venous return
  - ➢ Cardiopulm arrest & death
  - ➢ Related to Rx (see **THORACENTESIS** and **THORACOTOMY TUBE INSERTION** in the "Procedures" section)
- Prognosis: w/ rapid, effective Rx, long-term outcome depends on underlying etiology

POLYCYTHEMIA

MARY J. MARRON-CORWIN, MD

DEFINITION

- Free-flowing venous hematocrit ≥65% / venous hemoglobin ≥ 22 g/dL
- Hct peaks at 2 h of life w/ early cord clamping

HISTORY AND PHYSICAL

- History: risk factors
  - ➢ Delayed cord clamping (≥45 seconds)
  - ➢ Maternal diabetes
  - ➢ Twin-to-twin transfusion
  - ➢ Placental insufficiency
    - Small for gestational age
    - Preeclampsia
    - Postmaturity

- ➢ Maternal-to-fetal transfusion
- ➢ Maternal smoking
- ➢ Pregnancies at high altitudes
- ➢ Dehydration
- ➢ Chromosome abnormalities (e.g., trisomy 13, 18, 21)
- ➢ Neonatal hypo/hyperthyroidism
- ➢ Beckwith-Wiedemann syndrome
- ➢ Congenital adrenal hyperplasia

- Physical
  - ➢ Plethora
  - ➢ Acrocyanosis due to peripheral venous stasis
  - ➢ Tremors/jitteriness (esp w/ hypoglycemia or hypocalcemia)
  - ➢ Lethargy, hypotonia
  - ➢ Poor suck, feeding
  - ➢ Jaundice
  - ➢ Petechiae (w/ thrombocytopenia)
  - ➢ Signs of congestive heart failure
  - ➢ Seizures
  - ➢ NEC
  - ➢ Renal failure w/ renal vein thrombosis
  - ➢ Priapism

TESTS

- Serum glucose, bilirubin, calcium, electrolytes
- Further testing as indicated by history & physical exam

DIFFERENTIAL DIAGNOSIS

N/A

MANAGEMENT

- If asymptomatic w/ Hct < 70%:
  - ➢ Hydration & observation w/ follow-up Hct in 4–6 h
- If asymptomatic w/ venous Hct ≥ 70%:
  - ➢ Consider partial exchange transfusion
- If symptomatic w/ venous Hct ≥ 65%:
  - ➢ Partial exchange transfusion (see **EXCHANGE TRANSFUSION** in the "Procedures" section)

NOTE: Partial exchange transfusion lowers Hct & improves physiologic derangements due to hyperviscosity but may not affect long-term outcome.

SPECIFIC THERAPY
N/A

COMPLICATIONS & PROGNOSIS
- Complications
  - ➢ Hypoglycemia, hypocalcemia, hyperbilirubinemia
  - ➢ CHF, NEC, umbilical vein thrombosis, seizures
  - ➢ Those associated w/ umbilical vein catheterization (see **UMBILICAL VENOUS CATHETERIZATION** in the "Procedures" section)
  - ➢ Other related to underlying etiology
- Prognosis
  - ➢ Neurodevelopmental abnormalities (may be related to underlying etiology rather than to hyperviscosity)
  - ➢ Others related to complications or underlying etiology

POMPE'S DISEASE

See **GLYCOGEN STORAGE DISEASE TYPE II**

POSTERIOR URETHRAL VALVES

DIX PHILLIP POPPAS, MD

- Prevalence 1:5,000–8,000 live births; most common cause of lower urinary tract obstruction in males
- Males only
- No racial predilection
- Congenital only

HISTORY & PHYSICAL
- Prenatal sonography
  - ➢ Bilateral hydroureteronephrosis
  - ➢ Distended bladder
  - ➢ Distended posterior urethra: "keyhole" sign
  - ➢ Oligohydramnios
  - ➢ Urinary ascites
- Postnatal signs
  - ➢ Abdominal mass: bladder &/or kidneys
  - ➢ Failure to thrive

- ➢ Urosepsis
- ➢ Diminished or absent urinary stream
- ➢ Urinary ascites
- ➢ W/ oligohydramnios before 20–22 wk GA: Potter's facies, limb deformities, palpable bladder, resp failure

TESTS

- Urinalysis
- Urine culture
- Serum electrolytes
- CBC
- Blood culture/lumbar puncture w/ signs of sepsis
- Renal & bladder US
- Contrast (fluoroscopic) voiding cystourethrogram
- Radionuclide renal scan (MAG3 w/ furosemide)

DIFFERENTIAL DIAGNOSIS

- Antenatal & postnatal
  - ➢ Anterior urethral valves
  - ➢ Prune-belly syndrome
  - ➢ Severe bilateral vesicoureteral reflux
  - ➢ Congenital urethral stricture
  - ➢ Megacystis/microcolon syndrome
  - ➢ Neurogenic bladder
  - ➢ Bilateral ureteroceles
  - ➢ Bladder neck obstruction (rare)

MANAGEMENT

- What to do first
  - ➢ Insert 5Fr to 8Fr feeding tube into bladder to dependent drainage
  - ➢ Daily weights
  - ➢ Accurate input/output of fluid balance
  - ➢ Routine vital signs
  - ➢ IV line for fluids, antibiotics
- General measures
  - ➢ Medical
    - Correction of fluid, electrolyte imbalance
    - Broad-spectrum antibiotics
    - Supportive therapy for resp failure

SPECIFIC THERAPY

- Surgical
  - ➢ Transurethral removal of valve (>80% of cases)
  - ➢ Cutaneous vesicostomy – if urethral approach not poss (<20% of cases) w/ delayed valve resection, closure of vesicostomy at 2–6 mo
  - ➢ Bilateral cutaneous ureterostomies as immediate treatment; rarely required today
  - ➢ Nephrectomy of nonfunctioning kidney at later date
  - ➢ Reimplantation of persistently refluxing, functioning kidney may be required at later time
  - ➢ Bladder augmentation limited to rare situations

FOLLOW-UP

- Timing determined by severity of disease
- Urinalyses, culture
- Serum electrolytes, urea N, creatinine
- Renal, bladder US to follow dilation
- Voiding cystourethrograms to assess ablation of valve, bladder size, progress of ureteral reflux
- Radionuclide scans to assess differential renal function, drainage

COMPLICATIONS AND PROGNOSIS

- Complications
  - ➢ Early
    - Urinary infection
    - Fluid, electrolyte imbalance
    - Urinary ascites
    - Resp failure
  - ➢ Late
    - Poor renal function (33% of patients)
    - End-stage renal failure (15%)
    - Mortality due to renal dysfunction (~10%)
    - Persistence of vesicoureteral reflux
    - Unilateral nonfunctioning kidney assoc w/ ipsilateral reflux & renal dysplasia
    - Bladder dysfunction secondary to poor compliance, fibrosis
    - Possibility of retrograde ejaculation leading to sterility

PRADER-WILLI SYNDROME

KWAME ANYANE-YEBOA, MD

- ~70% paternally derived microdeletion of chromosome 15q11–q13
- ~20% maternal uniparental disomy
- 5–10% translocations & imprinting center mutations

HISTORY & PHYSICAL

History

- Delayed onset of or reduced fetal movements

Signs

- Profound hypotonia; often causes depression at birth
- Mean birth wt 2.8 kg
- Hyporeflexia
- Poor feeding due to diminished swallowing, sucking reflexes; most infants require gavage feeding for 3–5 mo
- Hypoplastic labia in girls
- Hands, feet normal size at birth

TESTS

- Karyotype
- FISH studies using SNRPN probe
- DNA methylation studies for disomy, imprinting center mutations

DIFFERENTIAL DIAGNOSIS

- See HYPOTONIA in the "Neonatal Presenting Signs" section.
- All neonates w/ central hypotonia should be tested for Prader-Willi

MANAGEMENT

- Primary problem in neonates: feeding
  - ➢ Gavage feeding almost always required
  - ➢ Gastrostomy may be necessary
- Neurol eval
- Endocrine eval
- Genetic eval, counseling
- Defer muscle biopsy until lab test results avail if Prader-Willi suspected
- Refer to pediatric gastroenterologist, nutritionist at discharge

SPECIFIC THERAPY
None

FOLLOW-UP
- Strict diet control: greatly reduces diabetes, cardiac failure
- Growth hormone treatment for short stature
- Emotional, psychological support
- PT, OT, speech therapies

COMPLICATIONS AND PROGNOSIS

Infancy and childhood
- Feeding difficulties improve by 6 mo
- Failure to thrive in all infants
- Hyperphagia ensues by age 12–18 mo
- Extreme obesity w/o strict dietary control
- Small hands, feet
- Narrow bifrontal diameter
- Abnl-shaped eyes
- Strabismus
- Full cheeks
- Muscular hypotonia
- Truncal obesity
- Scars from picking skin
- Abd striae
- Hypopigmentation of skin in 75%
- Strabismus, nystagmus
- Precocious puberty in girls
- Thick saliva
- Insensitivity to pain

Adolescence and adulthood
- Adults are small compared to family members
- Extreme obesity w/o strict dietary control
- Diabetes secondary to high caloric intake; onset at puberty
- Serious psychological, emotional problems re: efforts to reduce food intake
- Cardiac insufficiency requiring digitalization if wt not controlled
- Severe skin-picking behavior
- Atypical presentation in African-American patients: present w/ normal-sized hands, feet & less growth reduction
- <10% have average intelligence, most pts are mildly to moderately retarded

- Premature death btwn 25–30 y from diabetes, heart failure in poorly controlled pts

PROPIONIC ACIDEMIA

WENDY K. CHUNG, MD, PhD

HISTORY & PHYSICAL

History
- Normal birth
- Vomiting
- Dehydration
- Lethargy
- Coma
- Deterioration w/ protein intake and/or infection
- Family Hx of neonatal death of unknown etiology

Signs
- Hypotonia
- Coma
- Apnea
- May appear dysmorphic: frontal bossing, hypertelorism, inverted nipples

TESTS
- Prenatal Dx possible
- ABG, electrolytes: metabolic acidosis w/ increased anion gap
- Urinalysis: ketonuria
- Hyperammonemia
- CBC: neutropenia, thrombocytopenia variable
- Serum amino acids: hyperglycinemia, hyperglutaminemia
- Urine organic acids: 3-hydroxypropionic aciduria, methylcitraturia
- Confirmatory enzymatic testing of propionyl CoA carboxylase from fibroblasts or leukocytes

DIFFERENTIAL DIAGNOSIS
- Sepsis
- Intracerebral hemorrhage
- Nonketotic hyperglycinemia

MANAGEMENT
- Airway, breathing, circulation; intubation, aggressive fluid resuscitation, initially w/ 20 cc/kg NS, then 10% dextrose IV
- NPO
- Correction of metabolic acidosis w/ $NaHCO_3$
- Follow electrolytes, urinalysis q6h, continue treatment w/ bicarbonate until ketonuria is gone, serum bicarbonate is normal

SPECIFIC THERAPY
- Carnitine 300 mg/kg/day IV initially, then 100 mg/kg/day divided BID PO for maintenance
- Treat hyperammonemia w/ dialysis or sodium benzoate & phenylacetate, depending on severity
- Dietary restriction: leucine, isoleucine, valine, methionine to minimal amounts necessary for growth
- Sterilize GI tract w/ neomycin 50 mg/kg or metronidazole 20 mg/kg
- Avoid fasting
- Monitor for ketonuria

FOLLOW-UP
- Manage recurrent ketotic crises as above (usually recur w/ infections)
- Monitor efficacy w/ urine organic acids
- Monitor urine daily for ketones in infancy

COMPLICATIONS AND PROGNOSIS
- Earlier & better the metabolic control, better the prognosis
- Developmental delay common, though normal cognition theoretically possible w/ prenatal or early neonatal Dx
- Many are microcephalic, mentally retarded
- Seizures may persist despite good metabolic control

PULMONARY ATRESIA WITH INTACT VENTRICULAR SEPTUM (PA/IVS)

KALYANI R. TRIVEDI, MD, AND LEE N. BENSON, MD
REVISED BY GANGA KRISHNAMURTHY, MD

0.7% of all CHD

HISTORY & PHYSICAL

History
- Antenatal diagnosis by fetal echocardiography

- Undiagnosed PA/IVS presents w/ cyanosis, which worsens as the ductus arteriosus closes

Signs
- Usually full-term infants w/ central cyanosis
- Low O_2 sat
- +/ − tachypnea
- Single S2, systolic murmur (tricuspid regurgitation) over left lower sternal border, 1–2/6 continuous murmur over left upper sternal border (ductal murmur)
- Significant hepatomegaly w/ restrictive atrial communication

TESTS
- ABG
- Serum arterial lactate to follow cardiac output status
- CXR: mild to moderate cardiomegaly, decreased pulmonary vascular markings
- ECG: QRS axis of +30 to +90, decreased RV forces, LV dominance or LV hypertrophy, RA enlargement
- ECHO: imperforate pulmonary valve w/ no antegrade flow across it; branch pulmonary arteries are usually normal. RV may be hypoplastic & uni-, bi- or tri-partite. Varying degrees of tricuspid regurgitation. Tricuspid valve size may vary. RA is dilated. Usually atrial septal defect is present with right-to-left shunting of blood.
- Angiocardiography: to assess size of RV, r/o or demonstrate ventriculo-coronary communications & RV-dependent coronary circulation (RVDCC)

DIFFERENTIAL DIAGNOSIS
- All causes of cyanosis in the newborn (see **CYANOSIS** in the "Neonatal Presenting Signs" section)

MANAGEMENT
- ABC (airway, breathing, circulation)
- PGE1 to maintain ductal patency

SPECIFIC THERAPY

Depends on the presence or absence of RVDCC & size of RV
- No RVDCC (coronary circulation is not RV-dependent) & tripartite RV: RV decompression can be attempted:
  - ➢ Initial transcatheter perforation of atretic pulmonary valve, then balloon valvoplasty to establish antegrade pulmonary blood flow & to promote RV growth

- ➢ PGE1 is weaned off, O_2 sats are followed until patent ductus arteriosus closes
  - If saturations remain in 70's w/ duct closed, infant can be closely followed up as outpatient; over several weeks & months, saturations improve
  - If saturations decline once PGE1 is discontinued, PGE1 is restarted & weaned again after 2–3 wks. If saturations decline again:
    - Surgical decompression of RV w/ RV outflow tract augmentation w/ trans-annular patch & modified Blalock-Taussig shunt placement is performed
    - After several months, as saturations improve, transcatheter closure of the shunt
- ➢ Subsequent mgt depends on RV growth
  - If RV growth is demonstrated & if RV can handle entire cardiac output, then atrial septal defect is closed
  - If RV growth inadequate, 1–1/2 ventricle repair (superior vena cava connected directly to pulmonary arteries; inferior vena cava blood continues to return to the RA)

- If RVDCC present or extremely hypoplastic RV w/ no potential for growth:
  - ➢ RV decompression is contraindicated due to risk for coronary insufficiency
  - ➢ Initial surgery is Blalock-Taussig shunt, followed by staged cavopulmonary anastomoses
- Coronary artery stenosis/atresia: cardiac transplantation

FOLLOW-UP

- Monitor saturations, growth
- Monitor RV growth

PROGNOSIS AND COMPLICATIONS

- Complications of transcatheter approach (radiofrequency ablation of PV & balloon valvuloplasty)
  - ➢ Perforation of RV outflow tract, tamponade, arrhythmia
  - ➢ May be unsuccessful; sometimes surgical intervention required
- Complications after surgical approach (RV outflow tract augmentation w/ trans-annular patch & Blalock-Taussig shunt): circular shunt & low cardiac output syndrome
- Biventricular circulation is achieved in many
- Insufficiency of pulmonary valve is usually of no clinical significance

PULMONARY ATRESIA WITH VENTRICULAR SEPTAL DEFECT

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AND LEE N. BENSON, MD
REVISED BY GANGA KRISHNAMURTHY, MD

HISTORY & PHYSICAL

History

- +/− antenatal Dx by fetal echo
- Fully saturated or mild, moderate or severe cyanosis at birth
- Mild, moderate or severe respiratory distress
- +/− poor feeding

Signs

- Cyanosis: mild, moderate or severe
- Tachypnea +/− distress
- Active precordium
- RV heave
- Single S2, +/− gallop
- +/− soft systolic murmur left lower sternal border
- +/− soft continuous murmur left upper sternal border
- +/− soft continuous murmur over the back
- +/− hepatomegaly
- +/− CHF

TESTS

- CBC w/ indices
- Serum Na, K, Ca, serum urea N, creatinine
- Arterial blood gas
- CXR: normal heart size, moderate cardiomegaly w/ RV cardiac silhouette, absence of pulmonary artery shadow, +/− reduced pulmonary vascularity, clear lung fields, ± right aortic arch (30%)
- ECG: normal axis (range: +60 to +140) or right axis deviation, RV hypertrophy
- Echocardiogram
  - ➢ Diagnostic features
    - Valvular pulmonary atresia, no antegrade flow through pulmonary valve
    - +/− infundibular atresia
    - +/− hypoplastic or atretic main pulmonary artery

- Normal/hypoplastic/rudimentary/absent branch pulmonary arteries
- Perimembranous ventricular septal defect w/ aortic override
- Anterior malalignment of hypertrophied infundibular septum
- Hypertrophied RV

➢ Other features
- Patent ductus arteriosus/bilateral patent ductus arteriosus as single source of blood supply to ipsilateral pulmonary artery
- +/− major aortopulmonary collateral arteries (MAPCA)
- +/− right aortic arch
- Size, shunting through atrial septal defect

■ Cardiac catheterization, selective collateral angiography
➢ Elucidate source of blood flow to each pulmonary segment
- From pulm arteries?
- Systemic supply through major aortopulmonary collateral arteries (MAPCA)

or
- Dual supply?

Note: This is important diagnostic info for surgical planning: categorizes into 3 subtypes (see "Specific Therapy")

■ FISH for microdeletion of chromosome 22

DIFFERENTIAL DIAGNOSIS

■ all causes of blue neonate (see **CYANOSIS** in the "Neonatal Presenting Signs" section)
■ All causes of a neonate w/ CHF (see **CONGESTIVE HEART FAILURE** in the "Neonatal Presenting Signs" section)

MANAGEMENT

■ What to do first: ABCs (airway, breathing, circulation)
■ General measures
➢ PGE1 for ductal patency
➢ Maintenance fluid therapy
➢ Avoid overhydration
➢ Monitor urine output
➢ Avoid acidosis
➢ Maintain normokalemia
➢ Anti-CHF medication for control of heart failure (see **CONGESTIVE HEART FAILURE** in the "Neonatal Presenting Signs" section)

SPECIFIC THERAPY

- Surgery
  - ➢ Subtype A (native pulmonary arteries present, supplied by patent ductus arteriosus, no MAPCA): primary newborn intracardiac repair w/ RV to pulm artery conduit
  - ➢ Subtype B (native pulmonary arteries small, MAPCA present):
    - Multistage approach w/ MAPCA unifocalization, then intracardiac repair (ventricular septal defect closure)

    or
    - Single-stage approach: bilateral unifocalization w/ concomitant or delayed intracardiac repair
  - ➢ Subtype C (no native pulmonary arteries, MAPCA sole supply to pulm segments: creation of central pulmonary arteries by tissue-to-tissue anastomosis of MAPCA, connection to RV w/ a conduit, then later closure of ventricular septal defect
  - ➢ Surgical interventions at later stage: closure of ventricular septal defect, outgrown conduit replacement, pulmonary valve replacement
- Transcatheter interventions
  - ➢ At several junctures for all 3 subtypes to rehabilitate pulm circulation: pulmonary artery angioplasty, MAPCA angioplasty, stent implantation, stent dilations, coil occlusion of superfluous MAPCA if dual segmental supply
  - ➢ At later stage: RV to PA conduit balloon dilation, enlargement w/ stent placement, placement of valved stent in conduit

FOLLOW-UP

- Monitor growth, feeding
- Close cardiology follow-up during infancy after surgical repair
  - ➢ Identify progression of residual stenosis in pulmonary arteries/RV outflow tract
  - ➢ ECG
  - ➢ Echo
  - ➢ +/− cardiac catheterization to evaluate pulmonary artery pressure, timing of ventricular septal defect closure
- Neurodevelopmental
- SBE prophylaxis

COMPLICATIONS AND PROGNOSIS

- Complications: pulmonary artery stenoses at suture lines, RV outflow tract conduit outgrowth/stenosis, residual ventricular septal defect, RV hypertension, RV dilation, RV function impairment

- High rate of both transcatheter & surgical reinterventions: collaborative approach essential
- Overall 60–70% achieve biventricular repair w/ full rehabilitation of pulm arterial tree; lower rate in subtype C

PULMONARY SEQUESTRATION

See **LUNG BUD MALFORMATIONS**

PYELONEPHRITIS

See **URINARY TRACT INFECTION**

RENAL TUBULAR ACIDOSIS (RTA), ISOLATED PRIMARY

MARTIN A. NASH, MD

- Anion gap normal, hyperchloremic metabolic acidosis due to primary defect in renal HCO_3 reabsorption or H+ excretion (Note: Premature infants have a lower threshold for bicarbonaturia & limited capacity to secrete H+ due to renal immaturity)
- Primary RTA
  - ➢ Proximal RTA (type 2)
    - Reduced proximal tubular capacity to reabsorb HCO_3
    - May be transient or persistent
    - May be sporadic or inherited
  - ➢ Distal RTA (type 1)
    - Reduced distal collecting tubule capacity to secrete H+
    - Sometimes assoc w/ deafness
    - Unusual to present in newborn period

HISTORY & PHYSICAL

- History
  - ➢ Postnatal growth retardation
  - ➢ Vomiting
  - ➢ Polyuria
- Physical
  - ➢ None

TESTS

- Anion gap normal, hyperchloremic metabolic acidosis
- Hypokalemia
- Urine pH & fractional excretion (FE) HCO_3 (on specimen collected under mineral oil)
  - ➢ Proximal RTA
    - W/ plasma [HCO_3] >15–18 mmol/L
      - Urine pH >=6
      - $FEHCO_3$ >10–15%
    - W/ plasma [HCO_3] <15–18 mmol/L
      - Urine pH <=5.5
      - $FEHCO_3$ <5%
  - ➢ Distal RTA: urine pH >=6, $FEHCO_3$ <10%, regardless of plasma [HCO_3]
- To r/o secondary causes: plasma Ca, P, 25-OH-vit D, PTH; urine glucose, protein, amino acids, Ca; renal US

DIFFERENTIAL DIAGNOSIS

See METABOLIC ACIDOSIS in the "Neonatal Presenting Signs" section

More commonly, RTA occurs secondary to or as part of other conditions

- Proximal RTA
  - ➢ Fanconi syndrome (primary or secondary; most common cause of Fanconi syndrome presenting in 1st mos of life is cystinosis)
  - ➢ Mitochondrial myopathies (anion gap may be elevated due to lactate)
  - ➢ Vitamin D deficiency
  - ➢ Drugs
    - Carbonic anhydrase inhibitors
    - Valproic acid
- Distal RTA
  - ➢ Fetal alcohol syndrome
  - ➢ Drugs
    - Amphotericin B
    - Vitamin D toxicity
  - ➢ Hypergammaglobulinemia due to maternal Sjögren syndrome
  - ➢ Nephrocalcinosis (may be CAUSED BY primary distal RTA as well)
  - ➢ Hyperparathyroidism
- Hyperkalemic (aldosterone-sensitive or type 4) RTA (see also **HYPERKALEMIA** in the "Neonatal Presenting Signs" section)
  - ➢ Obstructive uropathy

- ➢ Renal vein thrombosis
- ➢ Hyperkalemia
- ➢ Drugs
  - K-sparing diuretics
- ➢ Mineralocorticoid deficiency
  - Congenital adrenal hyperplasia due to:
    - 21-hydroylase deficiency
    - 3-beta hydroxysteroid dehydrogenase deficiency
    - Congenital lipoid hyperplasia
  - Bilateral adrenal hemorrhage
  - Congenital isolated aldosterone deficiency (extremely rare)
- ➢ Pseudohypoaldosteronism type I (extremely rare)

MANAGEMENT

- Nephrology consultation
- Sodium citrate
  - ➢ Start w/ 5 mmol/kg/day w/ proximal RTA; increase until corrected; may require >=10 mmol/kg/day
  - ➢ Start w/ 2 mmol/kg/day w/ distal RTA
- Potassium citrate w/ hypokalemia

SPECIFIC THERAPY

- None

FOLLOW-UP

- During Rx
  - ➢ Plasma electrolytes, alkaline phosphatase, growth
  - ➢ Hearing screening w/ distal RTA
- Long-term
  - ➢ Same as during Rx
  - ➢ Renal US w/ distal RTA for nephrocalcinosis

COMPLICATIONS AND PROGNOSIS

Complications

- Growth retardation
- Proximal RTA: acidosis; may resolve over 1st few years of life
- Distal RTA: nephrocalcinosis, urolithiasis, renal failure, rickets

Prognosis

- Nl growth & renal function w/ Rx

RESPIRATORY DISTRESS SYNDROME (RDS)

J.M. LORENZ, MD

- Prevalence w/o antenatal steroids
  - ➢ <28 wk GA, 60%
  - ➢ 28–31 wk GA, 40%
  - ➢ 30–34 wk GA, 15%
  - ➢ >=34 wk GA, 5%
- Antenatal steroid therapy reduces prevalence ~50%

HISTORY & PHYSICAL

- Prematurity
- Resp distress from birth: tachypnea, cyanosis, nasal flaring, grunting, retractions, paradoxical respirations, decreased breath sounds

TESTS

- Nonspecific
  - ➢ Blood gas: hypoxemia +/− metabolic acidosis, resp acidosis
  - ➢ CXR: typically ground glass w/ air bronchograms, decreased lung volume
- Specific
  - ➢ None

DIFFERENTIAL DIAGNOSIS

See **RESPIRATORY DISTRESS** in the "Neonatal Presenting Signs" section

MANAGEMENT

- See **RESPIRATORY SUPPORT** in the "Supportive Care" section
- Optimize O_2 delivery
  - ➢ Maintain Hct >35%)
  - ➢ Support cardiac output as necessary (see **SHOCK**)
- Antibiotics pending evaluation for infection (see **SEPSIS/PNEUMONIA, EARLY-ONSET**)

SPECIFIC THERAPY

- Prevention: maternal antenatal steroid Rx
- Treatment: intratracheal artificial surfactant
  - ➢ More effective when given early
  - ➢ Indications
    - Prophylaxis: ASAP after birth in infants at high risk
      - Decreases incidence & severity of RDS, air leaks, mortality, but not bronchopulmonary dysplasia

- Disadvantages: requires intubation of all infants, w/ attendant risks (see **ENDOTRACHAL INTUBATION** in the "Procedures" section); some infants will receive surfactant w/o benefit
- Rescue: after Dx of RDS in infants req mechanical ventilation (see **RESPIRATORY SUPPORT** in the "Supportive Care" section for indications); decreases severity, air leaks, mortality, but not bronchopulmonary dysplasia

➢ Preparations: Curosurf®, Infrasurf®, Survanta®
- No major advantage of one over another
- See package insert for preparation, storage of suspension, & administration instructions

FOLLOW-UP

■ During Rx: Monitor very closely for improved ventilation, oxygenation in 1st 30 min after surfactant dosing, adjust ventilator appropriately, physical exam, pulse oximetry, blood gases; CXR prn
■ Long-term: none in the absence of chronic lung disease

COMPLICATIONS AND PROGNOSIS

■ Complications
➢ Air leak: pulm interstitial emphysema, pneumomediastinum, pneumothorax, pneumopericardium
➢ Pulmonary hemorrhage
➢ See **PERSISTENT PULMOMONARY HYPERTENSION OF NEWBORN, PATENT DUCTUS ARTERIOSIS,** and **INTRAVENTRICULAR HEMORRHAGE**
➢ Death
➢ See **BRONCHOPULMONARY DYSPLASIA**
■ Prognosis
➢ Natural Hx
- W/o surfactant: worsens first 24–48 h, then resolves by 5–7 days
- W/ surfactant: usually improvement, often abrupt, within 30 min after dose; then may worsen, requiring redosing

➢ Long-term: depends on degree of prematurity & assoc complications

RETINOPATHY OF PREMATURITY (ROP)

JOHN T. FLYNN, MD

HISTORY & PHYSICAL

- Risk factors
  - Birth wt <1,500 g
  - Gestational age <=28 wk
  - Respiratory distress syndrome, intraventricular hemorrhage, necrotizing enterocolitis, sepsis, shock
- Physical
  - No external signs
  - Indirect ophthalmoscopy: presence of ridge of tissue at junction of vascular & avascular retina is pathognomonic
- International Classification of ROP
  - LOCATION
    - Zone 1: imaginary circle w/ optic nerve at center & radius 2× distance from optic nerve to macula
    - Zone 2: edge of zone 1 to equator on nasal side of eye & ~1/2 distance to ora serrata on temporal side
    - Zone 3: outer crescent-shaped area from zone 2 to ora serrata temporally
  - SEVERITY
    - Stage 1: thin white line of demarcation separating normal retina from immature avascular retina
      NOTE: "aggressive posterior (AP) ROP" + dilatation & tortuosity of posterior pole retinal vessels in all 4 quadrants out of proportion to the peripheral retinopathy, and absence of stages of ROP described below
    - Stage 2: ridge of scar tissue extending inward from plane of retina replaces line of stage 1
    - Stage 3: abnormal blood vessels, fibrous tissue on edge of ridge, extending into vitreous
    - Stage 4
      - A: partial retinal detachment not involving macula
      - B: partial retinal detachment involving macula
    - Stage 5: complete retinal detachment
  - Tortuosity of retinal vessels

- PRE-PLUS DISEASE w/ AP ROP = more dilated & tortuous vessels than normal, but less than required for a diagnosis of Plus disease
- PLUS DISEASE = dilation & tortuosity of retinal arteries & veins >=that is the standard photograph in >=2 quadrants (usually >=6 clock hrs)

➢ EXTENT: circumferential location characterized by clock hr in relevant zone

TESTS

- Binocular indirect ophthalmoscopy after pupillary dilation w/ scleral depression at 32 wk postmenstrual age of all infants
  - ➢ All infants <=1,500 g OR <=28 wks gestation
  - ➢ Infants 1,500–2,000 g at risk because of severity of illness
- Follow-up examination q 2–3 wk [q wk if progression to threshold disease (see "Specific Therapy") likely]
  - ➢ Retinal vascularization complete

  and
  - ➢ Disease regresses (~95%) or threshold disease develops (~5%)

NOTE: ELBW infants may require an examination at an earlier age (30 wks) & more frequent intervals (at least twice/ wk) because of the possibility of AP ROP

DIFFERENTIAL DIAGNOSIS

- None

MANAGEMENT

N/A

SPECIFIC THERAPY

- Laser therapy to avascular retina for THRESHOLD DISEASE; i.e.:
  - ➢ Any stage ROP w/ Plus disease in Zone I
  - ➢ Stage 3 ROP +/ − Plus disease in Zone I
  - ➢ Stage 2 or 3 ROP w/ Plus disease in Zone II
- Cryotherapy to sclera overlying avascular retina if laser cannot reach
- Repeat if Plus disease does not regress w/ in 10–14 days
- If laser fails, scleral buckle or vitreous surgery advocated by some (not proven effective)
- Contraindications to laser or cryotherapy
  - ➢ Medical conditions precluding general anesthesia
  - ➢ No view of retina (vitreous hemorrhage, dense cataract or other media opacity must be treated first)

FOLLOW-UP

- Weekly after laser to determine adequacy of therapy × 4 wk
- Monthly thereafter to determine status of treated retina, macula (heterotopias or traction); development of fixation, refraction (particularly myopia & anisometropia); strabismus; normal visual development

COMPLICATIONS AND PROGNOSIS

- Long-term complications
  - ➢ Blindness or severe visual impairment (<20/200)
  - ➢ High myopia, other refractive errors
  - ➢ Strabismus, amblyopia
  - ➢ Astigmatism
  - ➢ Late retinal detachment
- Prognosis
  - ➢ Stage 1 & 2 usually regress without obvious sequelae
  - ➢ Threshold disease – risk of extreme vision loss is:
  - ➢ 1:2 w/o therapy
  - ➢ 1:6 w/ therapy
  - ➢ Stages 4B, 5: extreme vision loss highly likely even w/ therapy
  - ➢ AP ROP responds poorly to laser therapy & may progress rapidly to partial or total retinal detachment.
  - ➢ Laser therapy ineffective in 15–20% due to severity of disease
  - ➢ Long-term outcome after laser therapy unknown

RUBENSTEIN-TAYBI SYNDROME

KWAME ANYANE-YEBOA, MD

- Majority of cases sporadic
- 10% due to chromosome 16p13 microdeletions
- Point mutations in CREBBP (40–60%) & EP300 (3%) genes detected in others

HISTORY & PHYSICAL

- Broad thumbs w/ radial angulation
- Broad great toes
- Persistent fetal fingertip pads
- Microcephaly
- Dandy-Walker malformation
- Large anterior fontanel

- Low frontal hairline
- Frontal hair upsweep
- Frontal bossing
- Low-set ears
- Downslanted palpebral fissures
- Hypertelorism
- Epicanthal folds
- Arched or thick eyebrows
- Glaucoma/myopia/cataract
- Large, beaked nose
- Deviated nasal septum
- Columella below alae nasi
- Microstomia
- Micrognathia
- Thin upper lip
- Narrow palate
- Abnormally shaped teeth
- Congenital heart disease
- Scoliosis
- Spina bifida occulta
- Accessory nipples
- Megacolon or Hirschsprung disease
- Cryptorchidism
- Cutaneous syndactyly of fingers
- Hirsutism
- Preaxial polydactyly of toes or bifid hallux
- Absent thymus
- Keloids
- Large foramen magnum
- Agenesis of corpus callosum
- Stereotypic movements
- Seizures w/ abnormal EEG
- Hypotonia
- Hyperreflexia

TESTS

- Chromosome studies
- FISH studies to detect chromosome 16p13 microdeletions
- Sequencing of CREBBP & EP300 genes
- MRI for tethered spinal cord

DIFFERENTIAL DIAGNOSIS
All other syndromes w/ broad thumbs, toes

MANAGEMENT
- Ophthalmologic consultation
- Orchipexy for undescended testes
- Control seizures when present
- Ensure adequate caloric intake
- Monitor for respiratory infections
- Genetic counseling
- Surgical correction to alleviate problems w/ thumbs, toes
- Speech therapy
- Occupational & physical therapies
- Psychosocial support

SPECIFIC THERAPY
- None

FOLLOW-UP
N/A

COMPLICATIONS AND PROGNOSIS
- Respiratory infections, feeding difficulties
- Recurrent ear infections
- Unusual reaction to anesthesia, incl resp distress & cardiac arrhythmia
- IQ 30–79
- Stiff, unsteady gait

SEPSIS/PNEUMONIA, EARLY-ONSET

RICHARD A. POLIN, MD

- Definition: clinical illness w/ positive bacterial blood culture at <= age 5 days
- Prevalence: 1:2,000–1:5,000 live births
- Etiologic agent
  - 50% gram positive, most commonly group B streptococcus (GBS)
  - 50% gram negative, most commonly *E. coli*

HISTORY & PHYSICAL

- Risk factors for early-onset bacterial sepsis
  - ➢ Prematurity
  - ➢ Rupture of membranes (>18 h)
  - ➢ Maternal colonization w/ GBS
  - ➢ Maternal UTI
  - ➢ Signs or symptoms of chorioamnionitis
    - Maternal fever (>38.1 C)
    - Maternal leukocytosis (note: maternal WBC normally elevated in pregnancy, labor)
    - Maternal abdominal pain
    - Cloudy or foul-smelling amniotic fluid
  - ➢ Preterm, premature rupture of membranes
  - ➢ Low socioeconomic status
  - ➢ Male gender

Signs

- Hypothermia
- Hyperthermia
- Respiratory distress
- Apnea
- Cyanosis
- Jaundice
- Hepatomegaly
- Hypoglycemia
- Hyperglycemia
- Hyperbilirubinemia (total &/or direct)
- Lethargy
- Irritability
- Hypotonia
- Vomiting
- Abdominal distention
- Diarrhea
- Weak pulses, poor perfusion, hypotension w/ shock
- Petechiae/bleeding w/ thrombocytopenia, DIC

TESTS

- No single laboratory test diagnostic of infection, other than positive culture result from deep body site (blood, urine, CSF, abscess, etc.)
- Best screening lab tests have <=30–35% pos predictive value
- Sepsis screens – combined tests (WBC/differential count, C-reactive protein) most useful

- ➢ Positive sepsis screen defined as 2 or more abnormal lab values obtained concurrently
- ➢ If only a single value is abnormal it is considered a negative sepsis screen
- ➢ Negative sepsis screen can exclude infection w/ a high degree of accuracy (99%) if obtained 12–24 hrs following birth.
- ➢ Abnormal values
  - Absolute neutrophil (PMN) count <=1,750/mm^3
  - Immature/total PMN ratio >=0.2
  - Absolute band count >=2,000/mm^3
  - C-reactive protein >=1 mg/dL
- ➢ Recommended screening strategy
  - Asymptomatic infants w/ risk factors (PROM >=18 hr, maternal colonization w/ GBS, signs consistent w/ maternal chorioamnionitis)
    - Sepsis screen age 12 hr
  - Symptomatic infants
    - Sepsis screen at 12 hr (DO NOT DELAY cultures & empiric therapy)

- Cultures (Note: negative blood cultures do not exclude sepsis, pneumonia, meningitis, or UTI)
  - ➢ <72 hr old: blood culture (optimal volume 1 mL)
  - ➢ >=72 hr old: blood & urine cultures
  - ➢ Repeat blood culture should be obtained in all infants w/ bacteremia after Rx initiated to ensure blood has been cleared
  - ➢ Lumbar puncture indicated for:
    - Positive blood culture
    - Persistently abnormal clinical signs (apnea, seizures, persistent lethargy, etc.)
  - ➢ Diarrhea: stool culture
- CXR w/ resp distress
- Tests to narrow DDx or to detect complications
  - ➢ Plasma glucose, plasma [Ca]
  - ➢ Blood gas
  - ➢ Hct, platelet count
  - ➢ PT, PTT, fibrinogen, D-dimers w/ petechiae, bleeding
  - ➢ CNS imaging w/ CNS signs
  - ➢ Abdominal films (AP & left lateral decubitus w/ abd signs)

DIFFERENTIAL DIAGNOSIS

- Other infections

- ➢ See **URINARY TRACT INFECTION**
- ➢ See **HERPES SIMPLEX INFECTION**
- ➢ See **CYTOMEGALOVIRUS, CONGENITAL & CYTOMEGALOVIRUS, PERINATAL**
- ➢ See **TOXOPLASMOSIS, CONGENITAL**
- ➢ See **CANDIDIASIS, SYSTEMIC**

- Inborn errors of metabolism, metabolic disturbances (see **ADRENAL INSUFFICIENCY** and **CONGENITAL ADRENAL HYPERPLASIA**; see **HYPOCALCEMIA** and **HYPOGLYCEMIA** in the "Neonatal Presenting Signs" section)
- CNS signs: asphyxia, hemorrhage, seizures (see **INTRAVENTRICULAR HEMORRHAGE** and **STROKE, ISHEMIC, PERINATAL AND NEONATAL**; see **SEIZURES** and **HYPOTONIA** in the "Neonatal Presenting Signs" section)
- Primary or acquired coagulopathy (see **HEMORRHAGIC DISORDERS IN THE NEWBORN**)
- Disorders causing resp distress (see **RESPIRATORY DISTRESS SYNDROME**)
- Disorders causing unconjugated/conjugated hyperbilirubinemia (see **HYPERBILIRUBINEMIA, UNCONJUGATED** and **HYERBILIRUBINEMIA, CONJUGATED** in the "Neonatal Presenting Signs" section)
- Disorders causing hepatomegaly (see **HEPATOMEGALY** in the "Neonatal Presenting Signs" section)
- Disorders causing shock (see **SHOCK**)
- Disorders causing abdominal signs

MANAGEMENT

What to do first:

- ABCs (airway, breathing, circulation)

General measures

- Correct acid/base disturbances
- Establish IV access

SPECIFIC THERAPY

- Antimicrobial therapy
  - ➢ Indications for initiating treatment
    - Persistent signs c/w sepsis in absence of clear etiology
    - Positive sepsis screen w/ risk factors
    - GA <35 wk w/ risk factors
  - ➢ Choice of antibiotics depends on sensitivities of organisms causing sepsis in given nursery
    - CAUTION: sensitivities must always be confirmed

- Empiric therapy must be appropriate for gram-positive AND gram-negative pathogens
  - Ampicillin/aminoglycoside
  or
  - Ampicillin/cefotaxime (Note: rapid development of resistance may occur w/ use of cefotaxime as initial empiric therapy)
- Once infecting organism is identified, usually treated w/ single antibiotic (see exceptions below)
  - *Streptococcus agalactiae* (GBS): penicillin or ampicillin
  - *E. coli*
    - Ampicillin (for susceptible strains)
    - Kanamycin or gentamicin for resistant strains
  - *Listeria monocytogenes*
    - Ampicillin & gentamicin
  - Enterococcus
    - Ampicillin & gentamicin
    - Vancomycin for resistant strains
  - *Staphylococcus epidermidis* resistant to oxacillin
    - Vancomycin
  - *Staphylococcus aureus*
    - Methicillin-sensitive: methicillin, oxacillin, or nafcillin
    - Methicillin-resistant (MRSA): vancomycin

➢ When vancomycin or aminoglycoside continues >72 h, monitor serum level
- Vancomycin: trough <10 mcg/mL
- Gentamicin
  - Peak 5–10 mcg/mL
  - Trough <2 mcg/mL

➢ Duration of treatment
- Discontinue antibiotic if blood culture is negative after 48 hr w/o clinical signs/setting strongly suggestive of sepsis/pneumonia
- Consider treatment for 7–10 days in spite of negative blood culture w/ clinical setting strongly suggestive of sepsis/pneumonia
- Sepsis confirmed by blood culture w/o meningitis 7–10 days
- Meningitis: see **MENINGITIS**

FOLLOW-UP
- Hearing screen for all infants receiving aminoglycoside antibiotics
- Neurodevelopmental

COMPLICATIONS AND PROGNOSIS

- Complications
  - Meningitis (see **MENINGITIS**)
  - DIC (see **HEMORRHAGIC DISORDERS IN THE NEWBORN**)
  - Shock (see **SHOCK** in the "Supportive Care" section)
- Prognosis
  - Mortality <10% in term infants w/ appropriate early therapy
  - Mortality increases w/ decreasing gestational age
  - Even w/o meningitis, confirmed bacterial sepsis associated w/ increased risk of neurologic handicaps

SEPSIS/PNEUMONIA, NOSOCOMIAL

JOAN A. REGAN, MD
REVISED BY RICHARD A. POLIN, MD

HISTORY & PHYSICAL

History

- Presents >5 days of age (mean, 17 days)
- Risk factors
  - Prematurity, LBW (marked increase in incidence at <30 wk & <1,500 g)
  - Maternal Hx of pre-eclampsia w/ infant neutropenia in 1st wks of life
  - Infants w/ pediatric surgical GI anomalies (e.g., congenital diaphragmatic hernia, necrotizing enterocolitis)
  - Male gender
  - Indwelling central venous lines (UV, PCVL, Broviac); assoc w/ 88% of cases of coagulase-negative staphylococcal sepsis
  - CNS shunts
  - Parenteral hyperalimentation
  - IV lipids
  - Recurrent/prolonged antibiotic treatment
  - Prolonged mechanical ventilation
  - H_2 blockers for gastroesophageal reflux
  - Steroid Rx for bronchopulmonary dysplasia
  - Prolonged length of stay
  - Overcrowding, understaffing, use of multiple-dose med vials in NICUs

Signs

- Sudden onset, recurrence or increase in episodes of apnea, bradycardia, &/or O_2 desaturation
- Increasing req for resp support
- Feeding intolerance w/ emesis &/or increased volume of gastric aspirates
- Temp instability (hyperthermia > hypothermia)
- Decreased activity &/or tone
- Hypotension; poor perfusion

TESTS

Basic tests

- Blood cultures: simultaneous cultures from peripheral vein, all indwelling central lines
  - ➢ Most commonly isolated organisms responsible for nosocomial sepsis: coagulase-negative staphylococci, *Staphylococcus aureus*, *Enterococcus sp*, *Enterobacter sp*, *E. coli*
  - ➢ *Klebsiella sp, Pseudomonas sp, Candida sp* more frequently isolated in "epidemic" outbreaks
- CBC w/ differential (calculate absolute neutrophil count, immature:total neutrophil ratio)
- Lumbar puncture w/ CSF culture, cell count, Gram stain, protein, glucose (nosocomial sepsis assoc w/ meningitis in ~10% of cases)
- Urine culture (suprapubic tap procedure of choice; clean-catch urine if platelet count low)
- CXR w/ resp distress
- W/ feeding intolerance: AP & left lateral decubitus abd films

Other diagnostic tests

- C-reactive protein (CRP)
  - ➢ Serial CRPs >3 mg/dL at time of symptoms, 12–18 hr later, >24 hr later have increasing sensitivities for identifying infants w/ nosocomial sepsis (35%, 92%, 97%, respectively)
  - ➢ CRP of value to determine whether to discontinue antibiotics at 48–72 hr
  - ➢ Persistently elevated CRP suggests further work-up required

DIFFERENTIAL DIAGNOSIS

Symptom-specific

- Apnea, bradycardia, O_2 desaturations/increasing req for resp support

- ➢ DDx
  - Apnea of prematurity
  - Worsening of primary lung disease or chronic lung disease
  - Anemia of prematurity
- ➢ Evaluation: Consider, based on physical, lab findings:
  - Trial of caffeine
  - Initiating or augmenting mgt of chronic lung disease w/ diuretics, systemic or inhaled steroids, or bronchodilators
  - PRBC transfusion (unproven efficacy)

- Feeding intolerance/abdominal distention
  - ➢ DDx
    - Necrotizing enterocolitis
    - Intestinal obstruction due to stricture
    - Physiologic hypomotility
    - Volvulus, etc.
  - ➢ Evaluation
    - Pediatric surgery consult
    - Serial abdominal films
    - Contrast studies as indicated
- Temp instability
  - ➢ Assess environmental temp control (see **THERMAL MANAGEMENT** in the "Supportive Care" section)
  - ➢ Consider CNS etiologies or drug effects (e.g., prostaglandin E1) on temp control

MANAGEMENT

What to do first

- After completion of sepsis evaluation, initiate empiric therapy w/ vancomycin & gentamicin

  NOTE: Epidemics of nosocomial sepsis may require temporary changes in choice of agents for empiric therapy

General measures

- Provide cardiorespiratory support as needed, incl O_2, ventilation, pressors
- Transfuse platelets, FFP, PRBC as indicated
- Place NPO; continue TPN
- Repeat blood cultures daily until sterile
- Remove all non-critical central lines, use peripheral IVs until blood cultures negative for at least 48 hr

- ➢ On occasion, nosocomial bacteremia can be treated by administering antibiotics through central line w/o removing it
- ➢ Central lines should always be removed with fungal or *S. aureus* sepsis

■ Monitor vancomycin (trough levels) & gentamicin (trough levels) & adjust dose &/or administration interval as indicated

SPECIFIC THERAPY

■ Prevention: UNIVERSAL adherence to good handwashing practices prior to contact w/ ANY infant

■ Antibiotic therapy
- ➢ If blood cultures positive, review sensitivities & narrow Rx to LEAST TOXIC, EFFECTIVE antibiotic regimen [e.g., for coagulase-negative staphylococci sensitive to oxacillin, d/c vancomycin & gentamycin, complete 10-day course of IV antibiotic Rx (from 1st day of neg cultures) w/ oxacillin]
- ➢ Consider 7-day course for coagulase-negative staphylococci sepsis that clears immediately w/ Rx
- ➢ If blood cultures negative, infant clinically improved, d/c antibiotics at 48–72 hr
- ➢ Lumbar puncture in all bacteremic infants when clinically stable

■ Adjuvant therapy
- ➢ IVIG – benefit marginal
- ➢ WBC transfusions
  - Reduce mortality in infants w/ documented bone marrow depletion of WBCs
  - More beneficial w/ gram-negative sepsis
  - Should be used w/ caution in gram-positive infections due to increased incidence of WBC aggregation in lungs w/ deterioration in pulm status
- ➢ ECMO: reduces mortality in infants w/ septic shock, pneumonia, persistent pulmonary hypertension of the newborn; higher incidence of morbidity compared to nonseptic infants treated w/ ECMO
- ➢ G-CSF: Treatment w/ early-onset sepsis has no impact on mortality but reduces subsequent incidence of nosocomial sepsis
- ➢ Low-dose prophylactic vancomycin to reduce the incidence of catheter-related coagulase-negative staphylococci septicemia
  - Does not affect overall mortality or length of stay
  - Weigh against risk of development of vancomycin-resistant organisms
  - NOT CURRENTLY RECOMMENDED

FOLLOW-UP

During treatment

- Serial CRPs
- Repeat blood cultures until negative
- W/ persistent bacteremia (>=2 + serial blood cultures 24–48 hr apart) or failure of elevated CRP to decline:
  - ➢ Echocardiogram to r/o endocarditis or "fungus ball"
  - ➢ Serial limb exam for evidence of septic joints or osteomyelitis; radiographic studies as indicated
  - ➢ Ophthal exam for evidence of septic emboli
  - ➢ Renal US for fungal sepsis
  - ➢ Neurol eval, imaging studies if supported by physical findings
  - ➢ Serial CRP &/or ESR to monitor response to antibiotic treatment or follow bone infection if present

COMPLICATIONS AND PROGNOSIS

- Increased mortality
- Increased risk of recurrent bacterial infections, infections w/ resistant organisms, fungal systemic infections
- Prolonged length of stay
- Prolonged need for resp support
- Increased incidence of bronchopulmonary dysplasia
- Increased risk of neurodevelopmental abnormalities

SHOCK

ROGER G. FAIX, MD

HISTORY & PHYSICAL

- History
  - ➢ Placental or cord accident
  - ➢ Vaginal bleeding
  - ➢ Maternal analgesia, anesthesia, or vasoactive drugs
  - ➢ Maternal amnionitis
  - ➢ Antenatal evidence of hydrops, structural heart disease, arrhythmia
  - ➢ Oliguria (<1.0 mL/kg/h)
  - ➢ Metabolic acidosis
  - ➢ Apnea or increasing respiratory insufficiency

- Physical
  - ➢ Capillary refill >4 sec
  - ➢ Central mottling
  - ➢ Pallor
  - ➢ Low mean arterial pressure
  - ➢ Abnormally wide or narrow pulse pressure
  - ➢ Abnl heart rate (fast or slow)
  - ➢ Cardiomegaly
  - ➢ Hepatomegaly
  - ➢ Abnl 4-limb BPs
  - ➢ Bulging fontanelle
  - ➢ Expanding hematoma or sanguineous discoloration

TESTS

- Central Hct
- Maternal Kleihauer-Betke if Hct <30 & no obvious source of blood loss
- Glucose, Ca (ionized, if possible), P, Mg, electrolytes
- Blood culture; urine culture & LP as indicated
- Chest radiograph (also abdominal, if distention present)
- Arterial blood gas
- Arterial lactate
- Central venous pressure & mixed venous blood gas (if access available)
- ECG if HR >220 or <100
- Consider 2-D echo w/ Doppler for anatomy & function
- Consider cross-sectional echo w/ Doppler of superior vena cava and/or common carotid artery to assess flow to & from brain
- Consider brain near-infrared spectroscopy (niroscopy) to assess brain oxygen dynamics

DIFFERENTIAL DIAGNOSIS

- Intravascular volume depletion (pallor **w/o** enlarged heart or liver)
  - ➢ Actual
    - Hemorrhage, internal or external
    - Iatrogenic due to blood sampling
    - Insensible fluid loss
    - High-output renal failure
    - Excess diuresis
    - Adrenal insufficiency
    - "Third spacing"

- ➢ Functional, due to impairment of venous return
  - Intrathoracic air leak, uncontrolled
  - Excessive intrathoracic pressure: hyperexpansion, mass
  - Increased intra-abdominal pressure: abdominal distention; ascites
- Distributive (suspect w/ signs c/w infection, necrotizing enterocolitis [NEC])
  - ➢ Sepsis
  - ➢ NEC
- Cardiogenic (suggested by hepatomegaly, cardiomegaly &/or impaired myocardial function on echo)
  - ➢ Arrhythmia
  - ➢ Cardiomyopathy
  - ➢ Structural heart disease
  - ➢ Electrolyte abnormalities
  - ➢ Post-asphyxial
  - ➢ Sepsis
  - ➢ Storage disease
  - ➢ Inborn metabolic errors

MANAGEMENT

- Correct/treat underlying/assoc problems
  - ➢ Hypoglycemia
  - ➢ Electrolyte problems (incl Ca, P)
  - ➢ Hypothermia
  - ➢ Resp failure
  - ➢ Presumed infection
  - ➢ Arrhythmia
  - ➢ Bradycardia <60
  - ➢ Pneumothorax, other air leak
  - ➢ Increased abdominal pressure
  - ➢ Excess intrathoracic pressure
  - ➢ Polycythemia
- If hematocrit <40 or pallor and
  - ➢ Cardiogenic process unlikely, administer 10–20 mL/kg packed RBCs over 30–60 min
  - ➢ Cardiogenic process likely, partial exchange transfusion to increase Hct >=40
- If Hct >=40, no pallor, & cardiogenic process unlikely, expand intravascular volume w/ 20 mL/kg normal saline, Ringer's lactate, or other crystalloid over 30–60 min

- If cardiogenic process likely OR failure to respond adequately to volume expansion, strongly consider:
  - ➢ Arterial line
  - ➢ Urethral catheter to monitor urine flow rate
  - ➢ Central venous catheter (CVC) for central venous pressure (CVP) measurement
    - Ensure proper position of CVC tip/transducer & transiently remove from positive end-expiratory pressure (PEEP) for measurement
      - If CVP <=8 cm H_2O (10 mm Hg), repeat volume expansion
      - If CVP >8 cm H_2O, add inotropic/vasoactive agents (see below)
    - If infant unable to tolerate removal from PEEP or has refractory thoracic air leak or increased intra-abdominal pressure, give 10 mL/kg volume challenge
      - If CVP does not increase >=4 cm H_2O (5 mmHg), continue cautious volume challenge
      - If CVP increases >=4 cm H_2O, volume is replete; remove volume given & add inotropic/vasoactive agents (see below)
  - ➢ Inotropic/vasoactive agents & steroids
    - Dopamine, start at 2–5 mcg/kg/min; if response inadequate, may advance at 20-min intervals by 5 mcg/kg/min to maximum 20 mcg/kg/min
    - If cardiac dysfunction suspected, start/add dobutamine, at 5 mcg/kg/min: if response inadequate, increase in 5-mcg/kg/min increments to 20 mcg/kg/min
    - If response to dopamine/dobutamine inadequate, add hydrocortisone (2.5 mg/kg); usual response w/in 4–6 h; may repeat hydrocortisone q4–6h as needed for 48 hr
    - If response to steroids inadequate, consider:
      - Epinephrine drip
        - Start at 0.05 mcg/kg/min, advance as needed to maximum 1.0 mcg/kg/min
        - Watch for hyperglycemia & renal/mesenteric ischemia

      or
      - Vasopressin drip
        - Start at 0.002 units/kg/min, advance as needed to 0.008 units/kg/min
        - Watch for fluid retention

      or

- Milrinone infusion
  - Load with 0.75 mcg/kg over 3 h, then maintain at 0.2 mcg/kg/min
  - Watch for drop in BP of >=10%; if occurs, give volume challenge

SPECIFIC THERAPY

As indicated for underlying disorder

FOLLOW-UP

- During treatment
  - ➢ Assess indicators that prompted Rx, esp acidosis, lactate, urine output, BP
  - ➢ Monitor liver, heart size for evidence of cardiogenic impairment after recovery from shock
  - ➢ In preterm infants, be careful to avoid hypertension (mean arterial pressure >45) or rapid increase in mean arterial pressure (>15 mmHg/30 min) to decrease risk of intraventricular hemorrhage
  - ➢ Cranial sonogram
  - ➢ If excessive vasoconstriction w/ inotropes (e.g., further increase in capillary refill time, decrease in urine output, decrease in renal/mesenteric flow), then consider addition of afterload-reducing agents (e.g., nitroprusside, milrinone)
- Long-term
  - ➢ Neurodevelopmental

COMPLICATIONS AND PROGNOSIS

- Complications (frequency & severity depend on duration, severity of insult & regenerative potential of organ)
  - ➢ Heart failure
  - ➢ Pulmonary edema
  - ➢ DIC
  - ➢ Ischemia/infarct of organs
    - Acute tubular necrosis
    - NEC
    - Hepatopathy
    - Encephalopathy/seizures
    - Periventricular leukomalacia/CNS destructive changes
    - Tricuspid insufficiency/myocardiopathy
  - ➢ Reperfusion injury
    - CNS hemorrhage/destructive changes
    - Myocardiopathy

- Prognosis depends on cause of shock, severity, duration & regenerative potential of affected organs

STROKE, ISCHEMIC, PERINATAL AND NEONATAL

MARLYSE HAYWARD, MD
GEOFFREY L. HEYER, MD

HISTORY AND PHYSICAL

Depend on type

- Arterial ischemic stroke (AIS)
  - ➢ Focal, ischemic brain injury corresponding to single cerebral artery's distribution
  - ➢ Incidence as high as 93 per 100,000 live births
  - ➢ Most commonly thromboembolic etiology
  - ➢ Multiple risk factors often present

    Perinatal risk factors
    - Maternal infection/chorioamnionitis
    - Cord & placental abnormalities
    - Pregnancy complications (preeclampsia, oligohydramnios, twin-twin transfusion syndrome, in utero demise)
    - Delivery complications (PROM, placental abruption, birth asphyxia)
    - Birth trauma (arterial dissection, arterial compression)
    - Maternal and/or fetal coagulation disorder
    - Maternal cocaine use
    - Maternal autoimmune disorder
    - Fetal heart disease
    - History of infertility

    Neonatal risk factors
    - Congenital heart disease
    - Cardiac surgery/catheterization
    - Coagulation disorder
    - Fetal infection/meningitis
    - Polycythemia
    - Hyperosmotic dehydration
    - Indwelling arterial or venous catheters
    - Vascular pathology
    - Genetic/metabolic disorder
    - Extracorporeal membrane oxygenation (ECMO)
  - ➢ Physical findings

- Asymptomatic in ~40% of neonates
- Seizures (focal, multifocal): most common symptomatic presentation
- Apnea
- Lethargy
- Focal weakness (paresis, plegia)
- Feeding difficulties
- Low Apgar scores/fetal distress (perinatal stroke)

■ Cerebral sinovenous thrombosis (CSVT)
➢ Thrombosis of cerebral venous structures often assoc w/ ischemic and/or hemorrhagic brain injury
➢ Incidence as high as 41 per 100,000 live births
➢ Multiple risk factors often present
- Fetal infection (sepsis, meningitis)
- Maternal complications (infection, diabetes, hypertension)
- Coagulation disorders
- Disseminated intravascular coagulation (DIC)
- Polycythemia
- Dehydration
- Delivery complications
- Asphyxia
- Congenital heart disease
- ECMO

➢ Physical findings
- May be asymptomatic
- Seizures (focal, multifocal) presentation
- Apnea
- Lethargy
- Hypotonia
- Poor feeding
- Signs of increased intracranial pressure (w/ extensive thrombosis)

■ Watershed ischemic stroke
➢ Ischemic brain injury corresponding to shared cerebral-artery distributions (watershed territories)
➢ Due to systemic or large artery ischemia/hypoperfusion
➢ Physical findings
- As w/ AIS

TESTS

■ Diagnostic

- ➢ MRI w/ diffusion-weighted imaging (DWI)
  - High sensitivity & specificity for AIS
  - Gradient-echo sequence for blood products/hemorrhage
  - MR angiography (MRA) for arterial abnormalities/obstruction
  - MR venography (MRV) and/or gadolinium for CSVT
- ➢ CT
  - Less sensitive than MRI for detecting acute stroke
  - Contrast for sinus thrombosis
- ➢ Head US least sensitive acutely

- To evaluate for subclinical seizures
  - ➢ EEG
- To determine etiology (case-specific)
  - ➢ Prothrombotic work-up (see THROMBOTIC DISORDERS)
  - ➢ Placental/cord pathology
  - ➢ Infectious work-up
  - ➢ Echocardiography for embolic source w/ AIS
  - ➢ Genetic/metabolic evaluation

DIFFERENTIAL DIAGNOSIS

- Non-ischemic congenital brain abnormality
- Infection (sepsis, meningitis, abscess)
- See **SEIZURES** in the "Neonatal Presenting Signs" section.

MANAGEMENT

- Supportive therapy (ABCs, intensive care management)
- Seizure control (see **SEIZURES** in the "Neonatal Presenting Signs" section)

SPECIFIC THERAPY

- Role of anticoagulant therapy controversial; no prospective treatment trials
- Current recommendations (ACCP guidelines): neonatal AIS
  - ➢ Unfractionated heparin (UFH) or low-molecular-weight heparin (LMWH) × 3 months for *proven* cardioembolic stroke etiology
  - ➢ No aspirin, no anticoagulation for AIS of other/unknown etiologies
- Current recommendations (ACCP guidelines): neonatal CSVT
  - ➢ UFH or LMWH × 3 months in neonates *without* large ischemic infarctions or intracranial hemorrhage

- ➢ *With* large ischemic infarctions or intracranial hemorrhage, consider anticoagulation only w/ radiographic evidence of clot extension

FOLLOW-UP

- Ensure seizure control
- Recurrence risk depends on etiology
- Repeat imaging w/ neurological change or to monitor CSVT extension
- Long-term developmental & neurological evaluations

COMPLICATIONS AND PROGNOSIS

- Depend upon:
  - ➢ Size, location of stroke
  - ➢ Etiology of stroke
  - ➢ Associated intracranial hemorrhage
  - ➢ Comorbidities
- Outcomes
  - ➢ Seizure disorder
  - ➢ Hemiparesis or motor abnormality, often not apparent until development of voluntary movements (3–8 months)
  - ➢ Developmental and/or language delay
  - ➢ Cognitive impairment
  - ➢ Behavioral abnormalities

SUBARACHNOID HEMORRHAGE

HELEN M. TOWERS, MD

HISTORY & PHYSICAL

History

- Traumatic delivery, incl vacuum & forceps extraction
- Hypoxic-ischemic injury
- Ruptured vascular lesion: arteriovenous malformation

Signs: 3 presentations identified

- Minimal or no clinical features
- Seizures w/in 24 hr, esp in term; infants well during interictal period
- Rapid neurol deterioration w/ massive subarachnoid hemorrhage

TESTS
- CBC, platelets
- Coagulation studies
- Uniformly bloody CSF, elevated RBC, protein
- CT: blood in superior longitudinal fissure, sulci
- Cranial US relatively insensitive
- EEG w/ suspected seizures

DIFFERENTIAL DIAGNOSIS
- Other forms of intracranial hemorrhage producing abnl neurol signs: see **INTRAVENTRICULAR HEMORRHAGE, CEREBELLAR HEMORRHAGE, SUBDURAL HEMORRHAGE**
- CNS tumor

MANAGEMENT
- Treat seizures w/ anticonvulsant medication (see **SEIZURES** in the "Neonatal Presenting Signs" section)
- Correct coagulopathy prn

SPECIFIC THERAPY
None

FOLLOW-UP
- Neurologic acutely

COMPLICATIONS AND PROGNOSIS
- Subarachnoid bleeds generally of venous origin, self-limited: prognosis excellent in majority of infants – term infants w/ seizures have 90% normal outcome
- Hydrocephalus occurs rarely in severe cases secondary to adhesions at outflow of 4th ventricle or over cerebral convexities
- Death may follow massive subarachnoid hemorrhage

SUBDURAL HEMORRHAGE

J.M. LORENZ, MD
REVISED BY HELEN M. TOWERS, MD

HISTORY & PHYSICAL

History
- Traumatic delivery

- Term or preterm infant w/
  - ➢ Breech delivery
  - ➢ Face or brow presentation

Signs

- Excessive molding
- Occipital diastasis w/ breech delivery
- Neurologic signs vary w/ tentorial, posterior fossa or cerebral convexity & size of bleed
  - ➢ Tentorial laceration
    - More common in term infants
    - Acute neurological disturbance from birth
    - Decreased level of consciousness
    - Focal seizures
    - Asymmetric motor findings, hemiparesis
    - Deviation of eyes to side of lesion
    - Nuchal rigidity
    - Ataxic respirations, respiratory arrest as clot enlarges
  - ➢ Posterior fossa subdural
    - Initial signs appear from 24 hr to 3–4 days as hematoma slowly enlarges
    - Signs of increased intracranial pressure: full fontanel, irritability, or lethargy, as CSF flow blocked in through the posterior fossa
    - Brain stem signs: respiratory abnormalities, oculomotor abnormalities, facial paresis
    - Seizures
  - ➢ Cerebral convexity subdural: typically unilateral; 3 presentations
    - Minimal/no clinical signs; hyperalert
    - Focal cerebral disturbance at 24–48 hr (i.e., hemiparesis, contralateral deviation of eyes, seizures)
    - Chronic subdural effusion over months w/ enlarging head, positive transillumination

TESTS

- CBC, platelets
- Coagulation studies
- Lumbar puncture ***not*** recommended because of possibility of herniation

- CT
- MRI more effective in delineating posterior fossa hemorrhage
- Cranial US detection of subdural hemorrhage unreliable
- Skull radiographs to exclude fractures
- Subdural tap for diagnosis of cerebral convexity hemorrhage if CT unavailable

DIFFERENTIAL DIAGNOSIS

- Other forms of intracranial bleeding: see **INTRAVENTRICULAR HEMORRHAGE, CEREBELLAR HEMORRHAGE, SUBARACHNOID HEMORRHAGE**

MANAGEMENT

- Close surveillance for progression of neurological symptoms in absence of major neurological signs
- Treat seizures w/ anticonvulsant medication (see **SEIZURES** in the "Neonatal Presenting Signs" section)
- Attn to concomitant hypoxic ischemic cerebral injury (see **HYPOXIC ISCHEMIC ENCEPHALOPATHY**)
- Correct coagulopathy

SPECIFIC THERAPY

- In severe tears of tentorium, falx, overt occipital osteodiastasis, treatment almost impossible
- Surgical evacuation by subdural tap or craniotomy of convexity subdural hemorrhage, particularly if evidence of midline shift

FOLLOW-UP

- Reevaluation w/ CT or MRI required w/ changing neurological status
- EEG if seizures at presentation
- Long-term: neurodevelopmental

COMPLICATIONS AND PROGNOSIS

- Poor prognosis for major lacerations of tentorium or falx: mortality rate ~40%
- Hydrocephalus frequently develops in survivors
- Lesser degrees of hemorrhage associated w/ >50% normal outcome

SUBGALEAL HEMATOMA

J.M. LORENZ, MD
REVISED BY HELEN M. TOWERS, MD

- Bleeding beneath epicranial aponeurosis connecting frontal, occipital portions of occipito-frontalis muscle
- Rare

HISTORY & PHYSICAL

Signs

- Firm to fluctuant mass extending onto neck, forehead
- Borders ill defined, may be crepitant
- Progressively increases from birth
- May be massive

TESTS

- Nonspecific
  - ➢ Consider PT/PTT, fibrinogen, D-dimers, platelet count if very large or other bleeding
  - ➢ Skull film for basilar skull fracture w/ hemotympanum, serosanguinous otorrhea, postauricular ecchymosis
- Specific: head CT scan (rarely indicated)

DIFFERENTIAL DIAGNOSIS

- Caput succedaneum
- Cephalohematoma

MANAGEMENT

- Correction of hypovolemia & coagulopathy as indicated

SPECIFIC THERAPY

None; aspiration contraindicated

FOLLOW-UP

None w/o complications

COMPLICATIONS AND PROGNOSIS

- Complications
  - ➢ Hypovolemia
  - ➢ Prolonged hyperbilirubinemia
  - ➢ Anemia
  - ➢ Skull fracture
- Prognosis: resolves spontaneously in 2–3 wk

TESTICULAR TORSION

TERRY HENSLE, MD
GRACE HYUN, MD

HISTORY & PHYSICAL
- Discolored (dark) scrotal mass
- Asymptomatic, firm to hard gonad
- Scrotum dusky, swollen
- No transillumination

TESTS
- Doppler ultrasound
- Nuclear scan

DIFFERENTIAL DIAGNOSIS
- Incarcerated hernia
- Birth trauma (hematoma)
- Yolk sac tumor
- Hydrocele

MANAGEMENT
N/A

SPECIFIC THERAPY
- Observation unless bilateral (testis rarely salvageable) versus
- Orchiectomy +/− contralateral orchiopexy: increasingly common therapeutic approach

FOLLOW-UP
- +/− testicular prosthesis
- If bilateral
  - ➢ Endocrine follow-up for hormone replacement
  - ➢ Psychiatry follow-up

COMPLICATIONS AND PROGNOSIS
N/A

TETRALOGY OF FALLOT (TOF)

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REVISED BY GANGA KRISHNAMURTHY, MD

- "Tetralogy"
  - ➢ Large, malaligned ventricular septal defect
  - ➢ Overriding aorta
  - ➢ Right ventricular hypertrophy
  - ➢ Right ventricular outflow tract (RVOT) obstruction
- 6.8% of all CHD

HISTORY & PHYSICAL

History

- Antenatal diagnosis can be made by fetal echo
- Presentation in the newborn period/early infancy
  - ➢ W/ moderate to severe RVOT obstruction: cyanosis
  - ➢ W/ minimal RVOT obstruction, pulmonary overcirculation & symptoms of CHF (see **CONGESTIVE HEART FAILURE** in the "Neonatal Presenting Signs" section)
- Cyanotic spells (aka "Tet" spells): acute increase in desaturation due to increased obstruction across RVOT

Physical

- Cyanosis of varying degrees; severity depends on degree of RVOT obstruction
- Prominent right precordial activity
- Loud, single S2
- Systolic ejection murmur at left upper sternal border
  - ➢ Milder the obstruction, louder the murmur
  - ➢ Murmur disappears or diminishes during Tet spell
- W/ "pink TET": signs of CHF (see **CONGESTIVE HEART FAILURE** in the "Neonatal Presenting Signs" section) due to unrestricted pulmonary blood flow
- W/ onset of Tet spell:
  - ➢ Acute worsening cyanosis
  - ➢ Respiratory distress
  - ➢ Irritability
  - ➢ Murmur diminishes or disappears
  - ➢ May progress to seizure, stroke, or death

TESTS

- CBC w/ RBC indices: iron deficiency anemia or polycythemia may be present in infancy
- CXR
  - "Boot-shaped heart" – concavity of left heart border & upturned apex
  - W/ moderate to severe pulmonary stenosis: decreased pulmonary vascular markings
  - W/ mild pulmonary stenosis: increased pulmonary vascular markings & cardiomegaly
  - Rightward aortic arch (25%)
- ECG
  - W/ cyanotic TOF: right axis deviation, right ventricular hypertrophy
  - W/ acyanotic TOF: normal QRS axis, biventricular hypertrophy
- ECHO
  - Perimembranous ventricular septal defect
  - Anterior deviation of ventricular septum
  - Aortic override, infundibular stenosis
  - Pulmonary stenosis: pulmonary valve annulus size & continuity of branch pulmonary arteries
  - Coronary artery anatomy: course of any vessel across infundibulum
  - Sidedness of the aortic arch
  - Branching pattern of brachiocephalic artery (r/o aberrant right subclavian artery)
- Genetics: karyotype & FISH for 22q11 deletion

DIFFERENTIAL DIAGNOSIS

All causes of cyanosis in newborn period (see **CYANOSIS** in the "Neonatal Presenting Signs" section)

MANAGEMENT

- **General measures**
  - Monitor O_2 saturations; observe for hypercyanotic spells
  - Medical mgt of CHF: diuretics & digoxin
  - SBE prophylaxis
  - For "hypercyanotic" spell
    - Knee-chest position
    - Morphine sulfate
    - O_2 by face mask

- Correct metabolic acidosis
- Phenylephrine

■ **Specific Therapy**
  ➢ Depending on institutional preference, neonates w/ significant restriction to pulmonary blood flow may have:
    - Initial palliation w/ Blalock-Taussig shunt, then complete repair at age 4–6 mo
    - Single-stage complete repair in the neonatal period
  ➢ Complete repair =
    - Closure of ventricular septal defect
    - Infundibular muscle bundle resection
    - Transannular patch w/ hypoplasia of pulmonary valve annulus

FOLLOW-UP

■ Prior to repair: monitor O_2 saturation, growth
■ After repair
  ➢ Regular follow-up w/ ECG, ECHO
  ➢ Holter, exercise testing later
■ Neurologic, developmental

COMPLICATIONS AND PROGNOSIS

Complications

■ Onset of Tet spell may progress to seizure, stroke, or death
■ Immediately postop
  ➢ RV diastolic dysfunction, decreased compliance
  ➢ Tachyarrhythmia: junctional, ventricular
  ➢ Complete heart block
  ➢ Residual ventricular septal defect
  ➢ Residual RVOT obstruction
■ In later years
  ➢ Sudden death & arrhythmias
  ➢ Progressive pulmonary valve insufficiency w/ RV dilatation; pulmonary valve replacement required to prevent (no consensus re optimal timing)

Prognosis

■ Overall outcome good w/ neonatal repair
  ➢ Low perioperative mortality (<1%)
  ➢ Long-term survival into 5th & 6th decades

THROMBOTIC DISORDERS

HELEN M. TOWERS, MD

HISTORY AND PHYSICAL

- History: risk factors
  - ➢ Indwelling catheters
    - Excluding renal vein thromboses, 97% of thrombotic events are catheter-related
    - Prevalence of asymptomatic thromboses w/ indwelling vascular catheters is 20–30%
  - ➢ 80% of thrombotic events assoc w/ severe preceding illness
  - ➢ Perinatal asphyxia
  - ➢ Systemic infection
  - ➢ Congenital heart disease
  - ➢ Maternal diabetes
  - ➢ Polycythemia
  - ➢ Disseminated intravascular coagulation
- Physical
  - ➢ Arterial thrombosis
    - White, pulseless limb c/w recent occlusion
    - Necrosis c/w prolonged arterial occlusion
  - ➢ Venous thrombosis
    - Edema, reddish-purple discoloration
    - Catheter occlusion may be presenting sign
  - ➢ Cerebral infarction (see **STROKE, ISCHEMIC, PERINATAL AND NEONATAL**)
    - Seizures or hemiparesis
    - 42% of newborns w/ cerebral infarction had >1 non-catheter prothrombotic risk factor
  - ➢ Renal vein thrombosis – flank mass +/− hypertension, hematuria, thrombocytopenia
  - ➢ Superior vena cava thrombosis – facial & upper chest swelling, prominent collateral veins
  - ➢ Cardiac atrial thrombi – signs of sepsis, heart failure, decreased cardiac output
  - ➢ Portal vein thrombosis – hepatic failure
  - ➢ Embolic phenomena

TESTS

- Color Doppler ultrasound, MRI angiography, echocardiography
- CBC, platelets
- In absence of catheter
  - ➢ Antithrombin levels
  - ➢ Immunologic & functional assays of protein C
  - ➢ Immunologic assays of total & free protein S
  - ➢ PCR for factor V Leiden & prothrombin G20210A mutation
  - ➢ Homocysteine levels (homocystinuria)
  - ➢ Methylene tetrahydrofolate reductase mutation
  - ➢ Maternal testing for lupus anticoagulant & anticardiolipin Ab
  - ➢ Heparin cofactor II deficiency
  - ➢ Von Willebrand factor (high levels assoc w/ venous thrombosis)
  - ➢ Factor VIII (high levels assoc w/ venous thrombosis)
  - ➢ Blood viscosity
  - ➢ Immunochemical & functional assays for plasminogen, its inhibitors & activators

DIFFERENTIAL DIAGNOSIS

- Hereditary prothrombotic risk factors
  - ➢ Factor V Leiden (activated protein C resistance)
    - 5–15% in Caucasians; not described in those of African descent
    - Assoc w/ cerebral infarction, catheter-related thrombosis
    - Identified in 30% of childhood venous thromboses
  - ➢ Prothrombin G20210A mutation
  - ➢ Protein C or protein S deficiency
    - Homozygous – may present w/ purpura fulminans, large vessel thrombosis, cerebral or retinal vessel occlusion
    - Heterozygous – assoc w/ venous thrombosis
  - ➢ Antithrombin deficiencies – Heterozygous may present w/ myocardial infarction; aortic thrombosis; seizures; straight, sagittal sinus & other cerebrovascular thromboses
  - ➢ Elevated factor VIII
  - ➢ Von Willebrand factor levels (ADAMTS13 deficiency) – assoc w/ thrombocytopenic purpura
  - ➢ Lipoprotein (a)
  - ➢ Dysplasminogenemia & hypoplasminogenemias rare
- Acquired thromboses
  - ➢ See information on risk factors under “History and Physical”
  - ➢ Heparin-induced thrombocytopenia type 2

- Rare
- Primarily assoc w/ venous thrombosis

➢ Thrombophilia – rarely produces clinically apparent thrombi in neonates

MANAGEMENT

■ Prevention
- ➢ Limit use/duration of central catheters to extent possible
- ➢ Heparin no better than NS for maintaining peripheral IV catheter patency
- ➢ Continuous-infusion heparin prolongs indwelling arterial catheter patency but doesn't prevent thrombus formation

■ Treatment
- ➢ Removal of associated catheter, unless local infusion of streptokinase, plasminogen activator planned (see "Specific Therapy")
- ➢ Elevate affected limb for venous thrombosis
- ➢ Warm contralateral limb for arterial thrombosis
- ➢ No BPs, vessel punctures, IVs in affected limb

SPECIFIC THERAPY

■ Therapy for neonates controversial
- ➢ Unfractionated heparin
  - 5- to 14-day course
  - Req IV access
  - Monitor w/ PTT, anti-Xa activity assay
  - Antithrombin required for effect
  - Antithrombin concentrate, pooled human plasma-derived concentrate that increases heparin sensitivity, for resistance
  - Term infants may req higher doses because of increased clearance, increased vol of distribution, accelerated drug metabolism
  - Infants <25 wk gestation may have greatly reduced heparin requirements due to decreased clearance
- ➢ Low-molecular-wt heparin
  - 4- to 6-wk course
  - Administered subcutaneously, once/day
  - Monitor w/ anti-Xa activity assay
  - Predictable pharmacokinetics
- ➢ Recombinant tissue plasminogen activator (t-PA)
  - Optimal dose undetermined

- Administer locally into the thrombus or systemically
- Bleeding frequent complication – FFP, platelets should be available

➢ Protein C concentrate

➢ FFP for purpura fulminans (w/ homozygous protein S deficiency) or hereditary thrombocytopenic purpura (ADAMTS13 deficiency)

➢ Thrombolytic therapy for life-threatening or extensive thrombosis, either arterial or venous

- Streptokinase; urokinase no longer available
- Assoc w/ allergic, toxic side affects
- Cranial US must be performed prior to initiation of thrombolytic therapy to exclude hemorrhage
- Contraindications: stroke, recent surgery or severe hypoxia

■ Surgical thrombectomy rarely req

FOLLOW-UP

■ Doppler US useful for monitoring renal venous thrombosis, peripheral artery thrombosis
■ Echo useful for monitoring intracardiac, large vessel thromboses
■ Infants w/ inherited defects may require long-term anticoagulation
■ Neurodevelopmental w/cerebral thrombosis
■ Renal & BP f/u w/ renal vein thrombosis

COMPLICATIONS AND PROGNOSIS

Depends on etiology, site, extent of thrombosis

■ Cerebrovascular thromboses may result in neurodevelopmental sequelae
■ Aortic thrombosis may produce permanent disability or death
■ Intracardiac thrombosis
  ➢ Risk of bacterial endocarditis
  ➢ Right-side thrombi may embolize to lung (or systemic arterial circulation w/ right-to-left intracardiac shunt with CHD)
  ➢ Left-side thrombi may embolize to systemic arterial circulation
■ Peripheral arterial thrombosis may lead to loss or impaired growth of distal extremity
■ Renal vein thrombosis may lead to renal atrophy, hypertension
■ Portal vein thrombosis may lead to portal hypertension, esophageal varices

TOTAL ANOMALOUS PULMONARY VENOUS RETURN (TAPVR) WITH OBSTRUCTION

KALYANI R. TRIVEDI, MD, AND LEE N. BENSON, MD
REVISED BY GANGA KRISHNAMURTHY, MD

Anomalous drainage of all 4 pulmonary veins w/ obstruction

HISTORY & PHYSICAL

History

- Newborn w/ marked central cyanosis
- Respiratory distress
- Symptoms usually do not develop in the first 12 hours of life; once above symptoms appear, rapid progression to cardiorespiratory failure

Physical

- Severe central cyanosis
- Quiet precordium
- Split S2, w/ loud pulmonary component
- Murmur usually absent
- Rales in lung bases
- Hepatomegaly

TESTS

- ABG
- CBC, serum electrolytes, creatinine, LFTs
- CXR
  - ➢ Normal cardiac silhouette
  - ➢ Prominent pulmonary vascular markings, pulmonary venous congestion, pulmonary edema, Kerley B lines
- ECG: right ventricular hypertrophy
- Echocardiogram
  - ➢ RA enlargement
  - ➢ RV enlargement
  - ➢ Paradoxical septal motion
  - ➢ Dilated pulmonary arteries
  - ➢ Patent foramen ovale/atrial septal defect w/ right-to-left shunting
  - ➢ Doppler evidence of systemic RV pressure from tricuspid regurgitation jet

- Pulmonary veins
  - Pulmonary vein connection to LA cannot be documented
  - Pulmonary venous confluence seen behind LA
  - Flow acceleration & turbulence on Doppler at site of connection of vertical vein to systemic vein (superior vena cava, innominate, inferior vena cava, etc.)

DIFFERENTIAL DIAGNOSIS

- Persistent pulmonary hypertension of newborn
- Respiratory distress syndrome
- Sepsis
- Pneumonia

MANAGEMENT

Obstructed TAPVR is a surgical emergency; medical stabilization is difficult

- Follow ABCs (airway, breathing, circulation); intubation is always required
- Ventilation can be difficult
- Inotropic support
- Correct metabolic acidosis
- Follow serial ABG, lactate
- PGE1 contraindicated – may worsen pulmonary edema

SPECIFIC THERAPY

Emergent surgical correction

- Anastomosis of venous confluence to LA
- Closure of atrial septal defect

FOLLOW-UP

- Regular cardiac follow-up for re-obstruction
- Neurologic, developmental

COMPLICATIONS AND PROGNOSIS

- In current era, postop mortality <10%
- Postop complications: pulmonary hypertensive crisis, RV dysfunction
- Recurrence rate of pulmonary venous obstruction 10–20%
- Late complication: atrial arrhythmias

TOTAL ANOMALOUS PULMONARY VENOUS RETURN (TAPVR) WITHOUT OBSTRUCTION

KALYANI R. TRIVEDI, MD, AND LEE N. BENSON, MD
REVISED BY GANGA KRISHNAMURTHY, MD

HISTORY & PHYSICAL

History

- Usually asymptomatic at birth
- Symptoms usually develop during the 1st month of life
- Initial symptoms are tachypnea & poor feeding, progressing to failure to thrive, recurrent lower respiratory tract infections & cardiorespiratory failure by 6 months

Signs

- Poorly nourished
- Mildly cyanotic
- Tachypnea, tachycardia
- Prominent RV heave
- S1 is loud, S2 widely split w/ P2 accentuation, S3 & S4
- 2/6 blowing murmur in left upper sternal border, diastolic tricuspid flow murmur
- Hepatomegaly

TESTS

- ABG, CBC, liver & renal function tests
- CXR
  - ➢ Cardiomegaly
  - ➢ Increased pulmonary vascular markings
  - ➢ Prominent right heart border & pulm artery
  - ➢ "Figure 8" or "snowman" appearance when TAPVR to left innominate vein
- ECG: right atrial hypertrophy, right axis deviation, right ventricular hypertrophy
- ECHO
  - ➢ RA & RV enlargement
  - ➢ Right ventricular volume overload (RVVO)
  - ➢ Dilated pulm artery
  - ➢ Small, under-filled LA & LV
  - ➢ Abnormal connection to systemic vein or coronary sinus

or

Connection btwn pulmonary veins & LA cannot be demonstrated

DIFFERENTIAL DIAGNOSIS

Causing RVVO: large secundum atrial septal defect, sinus venosus type defect

MANAGEMENT

- General mgt: anticongestive therapy (see **CONGESTIVE HEART FAILUREF** in the "Neonatal Presenting Signs" section)
- Specific therapy: surgical correction of anomalous pulmonary venous drainage

FOLLOW-UP

- Monitor for re-obstruction of pulmonary veins

COMPLICATIONS AND PROGNOSIS

- Perioperative mortality is very low
- Pulmonary venous re-obstruction
- Late complication – atrial arrhythmias (see **CARDIAC ARRHYTHMIAS**)

TOXOPLASMOSIS, CONGENITAL (TRANSPLACENTAL)

JOHN R. "RICK" STAFFORD, JR., MD
REVISED BY J.M. LORENZ, MD

- Prevalence of congenital infection in US: 0.1%
- Infection of the placenta as the result of maternal parasitemia is required
- Only *primary* infection peri-conceptionally or during gestation can result in congenital infection
- Risk of transmission to fetus w/ documented acute maternal infection during pregnancy depends on:
  - ➢ Time of infection: Transmission risk directly related to GA
    - Peri-conceptionally: 0–1%
    - 2–15 wk GA: 2–10%
    - 15–31 wk GA: prevalence of transmission rises sharply
    - 31–34 wk GA: 60–70%
    - Close (few wk) to term: 75 to >80%

    Note: Above rates w/ most mothers w/ acute infection treated during pregnancy

- ➢ Fetal incubation period after acute maternal infection inversely related to GA
- ➢ Severity related to GA
  - Substantial CNS necrosis almost always assoc w/ 1st or 2nd trimester maternal infection (~60% <16 wk, ~25% 17–23 wk)
  - Usually subclinical or mild w/ 3rd trimester maternal infection (~97%)
  - Risk of severe disease highest at 10–24 wk

HISTORY & PHYSICAL

History and physical

- Maternal
  - ➢ 90% asymptomatic, undiagnosed
  - ➢ When symptoms occur, nonspecific: fatigue, malaise, lymphadenopathy – parasitemia occurs before the appearance of clinical signs
- Fetal
  - ➢ Hydrops fetalis
  - ➢ Stillbirth
  - ➢ Hydrocephalus
  - ➢ Intracranial calcifications
  - ➢ Organomegaly
- Neonatal
  - ➢ Most commonly, none (i.e., subclinical – 55% of infections are subclinical at birth & age 12 mo)
  - ➢ Clinical signs (onset may be delayed months to years)
    - Prematurity (25–50% even w/ otherwise subclinical infection)
    - IUGR
    - Postmaturity
    - Neonatal depression
    - Ocular chorioretinitis/chorioretinal scars (most common physical findings: 20% of those w/o other signs of infection at birth), microphthalmia, microcornea, cataract
    - CNS
      - Encephalitis, obstructive hydrocephalus*, intracranial calcifications* (may be identified prenatally), seizures, strabismus, nystagmus, hypotonia, opisthotonos, bulbar palsies, paralysis
      - Usually appear age 3–12 mo w/ subclinical or mild infection at birth
    - Hepatosplenomegaly, jaundice, ascites

- Hypothermia, hyperthermia
- Lymphadenopathy
- Petechiae, ecchymosis
- Myocarditis
- Vomiting, diarrhea
- Resp distress due to pneumonitis or CNS lesions
  * May be the sole signs

➢ Prevalence of clinical signs
- 70% subclinical (no clinical signs during infancy)
- 15% mild (intracranial calcifications or chorioretinitis w/o subsequent mental retardation/neurologic deficit)
- 10% severe (intracranial calcifications AND chorioretinitis or subsequent mental retardation/neurologic deficit)
- 5% stillbirth or perinatal death

TESTS

■ Nonspecific

➢ Fetal US: see "History and Physical" (absence does not r/o infection)

➢ Neonate
- Elevated liver enzymes
- Conjugated hyperbilirubinemia
- Thrombocytopenia
- Anemia
- Leukocytosis, leukopenia, lymphocytosis, monocytosis or eosinophilia
- CSF ABNORMALITIES IN AS MANY AS 80% OF CASES OF SUBCLINICAL CONGENITAL INFECTION (MOST COMMON CLINICAL SIGN): xanthochromia, lymphocytosis, protein 150 to >1,000 mg/dL; persist 2 wk to 4 mo
- Intracranial calcifications on skull films, head US, CT (sensitivity CT > head US > skull films)

■ Specific

➢ MATERNAL INFECTION: primarily serologic
- Diagnosing acute infection & differentiating it from chronic infection w/ *T. gondii*-specific serologic tests is complex
  - Antigenic structure of *T. gondii* is complex
  - Sensitivity & specificity of *T. gondii*-specific serologic tests vary btwn tests, test kits (not standardized in the USA), and time of testing in relation to time of acute infection; positive results should be confirmed in a reference lab

- *T. gondii*-specific IgM ELISA or *T. gondii*-specific ISAGA IgM may persist for many mos or yrs after acute infection
- Results of any serologic test must be interpreted in combination w/ other serologic tests
- **Because of false-positives, a positive IgM alone never establishes the dx of any type of toxoplasmosis infection in older children & adults.**

- 1st trimester
  - *T. gondii*-specific IgM test negative
    but
    T. gondii-specific IgG positive
    → Infection mo to yrs before pregnancy
    → No risk of congenital infection
  - *T. gondii*-specific IgM ELISA test positive
    or
    T. gondii-specific ISAGA IgM positive
    and
    T. gondii-specific IgG positive
    Perform differential agglutination (HC/AC) test (description & interpretation beyond scope of this summary)
  - 2 of following 3:
    1) Lymphadenopathy in areas compatible w/ acute infection
    2) *T. gondii*-specific IgG > /= 300 IU/mL
       or
       Sig rise in titer in repeat sample obtained in 2–3 wk
    3) *T. gondii*-specific IgM test positive
       → Acute infection likely

➢ Any time in pregnancy
- Conversion of a *T. gondii*-specific serologic test from negative to positive
  or
  Rise in titer from a low to a significantly higher titer on serial specimens
  → Confirms acute infection
- *T. gondii*-specific IgM positive
  but
  T. gondii-specific IgG negative
  - Consider false-positive IgM
  - Test for IgG by other methods

➢ In perinatal period

- Positive *T. gondii*-specific IgM test not useful
- Positive *T. gondii*-specific ISAGA IgA or IgE suggests recent infection
- Differential agglutination test may be helpful
- To exclude false negative, test should be repeated >30 days after birth

➢ FETAL INFECTION (test >4 wk after onset of acute infection established in mother)

- Inoculation of amniotic fluid into lab mice
  - Sensitivity 64%
  - Results may take 4–6 wk
- DNA PCR amplification of *T. gondii* B1 gene in amniotic fluid
  - Results vary w/ GA at infection & from lab to lab – in best ref labs:

	SENSITIVITY NEG	PREDICTIVE VALUE
17–21 wk	93% (95%CI 88–97%)	96% (95%CI 90–100%)
22–26 wk	62% (95%CI 37–86%)	77% (95%CI 61–93%)
27–31 wk	68% (95%CI 48–89%)	88% (95%CI 48–89%)
>31 wk	50% (95%CI 22–78%)	14% (95%CI 2–52%)

Reliability & validation data should be requested from lab to interpret

Note: Not all cases can be detected because transmission may occur after amniocentesis.

➢ NEONATAL INFECTION

- Documented fetal infection
- Positive *T. gondii*-specific IgG: does not confirm congenital infection – may be due to transplacental maternal Ab
- Positive *T. gondii* Ag-specific IgM ELISA
  OR
  Positive ISAGA for IgM, IgA (90% sensitive), or IgE
  → Strong evidence for infection, but contamination w/ maternal blood must be r/o
  - Test mother for *T. gondii* Ag-specific IgM (negative test excludes contamination of neonatal sample w/ maternal blood)
  - If maternal *T. gondii* Ag-specific IgM is positive, repeat test in newborn in 3–4 days – if negative, c/w contamination w/ maternal blood
  - Sensitivity & specificity of ISAGA > ELISA
  - Positive results should be confirmed in a reference lab

Note: *T. gondii* Ag-specific IgM ELISA negative in 25% of congenitally infected newborns
W/ early fetal therapy, *T. gondii*-specific antibody tests may be negative for the first 6–12 mo of life

- Positive PCR in blood or spinal fluid
- Blast transformation of lymphocytes in vitro in response to *T. gondii* lysate antigens; 50% of infected newborns at birth, 100% by age 1 yr (specificity 84%)
- Placental pathology: histopathology may be positive for *T. gondii* w/ severe but not usually w/ subclinical or mild, congenital infection
- Inoculation of fresh placental tissue into lab mice (results may take 4–6 wk)

DIFFERENTIAL DIAGNOSIS

- DDx of chorioretinitis, intracranial calcifications, hydrocephalus, microcephaly; see **HEPATOMEGALY**, **THROMBOCYTOPENIA**, and **HYPERBILIRUBINEMIA, CONJUGATED** in the "Neonatal Presenting Signs" section
- Bacterial/viral sepsis
- Other congenital infections: CMV, syphilis, rubella, HSV

MANAGEMENT

- Supportive; shunting for hydrocephalus
- Infection control
  - ➢ Nursery isolation not indicated
  - ➢ Isolation from mother not indicated
  - ➢ OK to breastfeed

SPECIFIC THERAPY

Prevention

- PREVENTION OF MATERNAL INFECTION
  - ➢ Most pregnant women are susceptible to infection
  - ➢ Avoid exposure to cat feces (i.e., changing litter boxes, gardening)
  - ➢ Avoid touching mucous membranes, eyes when handling raw meat; thorough hand washing afterwards
  - ➢ Avoid consumption of meat not well done
  - ➢ Wash all fruits, vegetables
- PREVENTION OF FETAL INFECTION W/ ACUTE MATERNAL INFECTION
  Termination of pregnancy may be considered in 1st or 2nd trimester

VERSUS

Maternal spiramycin until term unless fetal infection is diagnosed

➢ Reduces rate of fetal infection w/o therapy prior to fetal infection from 50–60% to 20–25%; reduction in risk > in 1st & 2nd than 3rd trimester

➢ May reduce severity by delaying transmission

Therapy

■ THERAPY FOR CONFIRMED OR HIGHLY PROBABLE FETAL INFECTION

Termination of pregnancy may be considered in 1st or 2nd trimester

VERSUS

Maternal therapy

➢ Fetal infection diagnosed <17 wk: sulfadiazine, then pyrimethamine + sulfadiazine + leucovorin calcium after 18 wk

➢ Fetal infection diagnosed >=18 wk: pyrimethamine + sulfadiazine + leucovorin calcium as soon infection proven

Note: Rx reduces clinical manifestations of & fetal Ab response to infection

■ THERAPY FOR NEONATAL INFECTION

➢ Recommended for EVERY CASE of congenital toxoplasmosis in conjunction w/ U.S. Nat'l Collaborative Treatment Trial (773–834–4152)

➢ Does not effectively eradicate encysted form

➢ Pyrimethamine

- 1 mg/kg q12h × 2 days; then 1 mg/kg/day × 2 OR 6 mo (regimens currently being compared in Nat'l Collaborative Rx Trial; max 25 mg/day); then 1 mg/kg q Mon, Wed, Fri until 1-yr course of pyrimethamine completed
- Side effects: most commonly neutropenia; thrombocytopenia, anemia; respond to increased dose of folinic acid or withholding pyrimethamine)
- Concomitant Rx w/ phenobarbital shortens half-life & decreases blood levels

PLUS

➢ Sulfadiazine

- 50 mg/kg q12h × 1 yr
- Side effects: crystalluria, hematuria, bone marrow depression

PLUS

➢ Leucovorin calcium

- 10–20 mg 3×/wk during & for 1 wk after pyrimethamine Rx

➢ Prednisone, 0.5 mg/kg q12h, FOR

- CSF protein >1,000 mg/dL
- Active chorioretinitis threatening vision

UNTIL CSF protein <1,000 mg/dL & resolution of active chorioretinitis

FOLLOW-UP

During Rx: CBC twice/wk

Long-term: serial audiologic, ophthalmologic, neurologic, developmental, REGARDLESS of fetal Rx, clinical status at birth, or neonatal Rx

COMPLICATIONS AND PROGNOSIS

- Prognosis
  - ➢ Fetal infection more severe the EARLIER in gestation transmission occurs
  - ➢ Fetal infection more likely the LATER in gestation maternal infection occurs
  - ➢ Timely fetal Rx reduces the # of biologic signs, likelihood of severe damage in newborn
  - ➢ W/o neonatal Rx (even if infection subclinical) or w/ substantial generalized or neurologic disease before treatment: 80–90% eventually develop adverse sequelae: chorioretinitis (most common; incidence increases w/ age), strabismus, cataract, glaucoma, retinal detachment, optic atrophy, blindness, hydrocephalus, microcephaly, psychomotor, mental retardation, seizures, or deafness (17% of those w/ subclinical infection at birth) can occur mo to years
  - ➢ W/ early neonatal Rx for 1 yr: more favorable compared to historical controls; does not prevent recrudescent chorioretinitis after Rx discontinued
- Implications for subsequent pregnancies: no recurrence

TRACHEOESOPHAGEAL FISTULA/ESOPHAGEAL ATRESIA

CHARLES J.H. STOLAR, MD

HISTORY & PHYSICAL

- Maternal polyhydramnios
- Excessive salivation
- Unable to pass nasogastric tube (w/ esophageal atresia)

- Assoc anomalies incl cardiac, anorectal, vertebral, renal, extremity
- Abd distention causing respiratory distress

TESTS
- Pass nasogastric tube yourself
- CXR
- Cardiac echo for anatomy, arch location
- Renal US
- Chromosome analysis/genetics consult

DIFFERENTIAL DIAGNOSIS
N/A

MANAGEMENT
- Pediatric surgery consultation
- Sump tube in proximal pouch to minimize aspiration
- Decubitus position to minimize aspiration
- Watch for abd distention from distal fistula
- Intubate rather than continuous positive airway pressure, if resp support req, to minimize abd distention
- Surgery: division of fistula & esophago-esophagostomy via thoracotomy
- Gastrostomy &/or transanastomotic feeding tube may be placed

SPECIFIC THERAPY
None

FOLLOW-UP
- Extubate postop when respiratory status adequate
- Esophagram on postop day 7 to confirm intact anastomosis; feed PO if no leak

COMPLICATIONS AND PROGNOSIS
- GER often a problem (see **GASTROESOPHAGEAL REFLUX**)
- Usual postop problem: stricture at anastomosis related to reflux; managed by dilatations, anti-reflux surgery
- Prognosis generally excellent

TRANSIENT TACHYPNEA OF THE NEWBORN (TTN)

JESUS C. JAILE-MARTI, MD

A benign self-limited respiratory disorder characterized by an obstructive pattern w/ normal functional residual & increased total lung capacity

HISTORY AND PHYSICAL

Mainly seen in full-term infants, but can play a role in lung disease of prematurity

History (suggestive but not diagnostic)

- Delivery mode
  - ➢ More common in c-section babies
  - ➢ More common in precipitous deliveries
  - ➢ Extramural delivery
- Maternal sedation
- Neonatal depression requiring intermittent positive-pressure ventilation
- More common in infants of diabetic mothers
- Cord compression syndrome of any type
- Fetal distress
- Delayed cord clamping
- Possible association w/ maternal asthma

Signs and symptoms

– In general babies w/ TTN appear well within the first few hours of life, with only respiratory distress

- Tachypnea
- Grunting, flaring
- Retractions, usually mild; if more marked, consider complication/other Dx
- Barrel chest
- Rhonchi, rales
- +/− cyanosis
- Oxygen requirement

TESTS

- Serum electrolytes including calcium, glucose
- CBC w/ manual differential & platelet count; monitor as needed if sepsis is considered (see **SEPSIS/PNEUMONIA, EARLY-ONSET**)

- Continuous oximetry
- Arterial blood gases/capillary gases/venous blood gases
  - ➢ At least one blood gas should be obtained; frequency dictated by clinical status of infant; in general, serial blood gases not warranted
  - ➢ Route dependent on access
  - ➢ Mild CO_2 retention & acidosis may occur
  - ➢ Hypoxemia
  - ➢ Pulse oximetry useful tool
- Blood cultures & if clinically indicated LP (in most cases the latter not required)
- Radiological studies
  - ➢ Chest radiographs; consider two views
  - ➢ Classic findings
    - Hyperinflation
    - Fluid in fissures
    - Perivascular cuffing
    - Increased interstitial markings
    - +/ − fluffy infiltrates
  - ➢ Rule out other pathology
    - Pneumothorax
    - Respiratory distress syndrome
    - Pneumonia
  - ➢ Repeat only if a significant change in clinical status has occurred

DIFFERENTIAL DIAGNOSIS

See **RESPIRATORY DISTRESS** in the "Neonatal Presenting Signs" section

MANAGEMENT

What to do first:

- ABCs (airway, breathing, circulation)
- Oximetry; supplemental O_2 as indicated to maintain O_2 saturation in 50–70% range
- Usually level of distress warrants NPO
- Send CBC, blood gas, blood cultures
- CXR

General measures

- Respiratory support: supplemental O_2; may be provided via head box or nasal cannula, but nasal continuous positive airway pressure is a more effective modality
  - ➢ Promotes clearance of retained fluid

➢ Stents airway, decreasing obstructive component
- Provide IV access for fluids & meds
- Start antibiotics if at risk for sepsis (see SEPSIS/PNEUMONIA, EARLY-ONSET)
- Provide maintenance fluids & electrolytes
- Maintain thermoregulation

SPECIFIC THERAPY
None

FOLLOW-UP
None

COMPLICATIONS AND PROGNOSIS
- Excellent prognosis
- Resolution within 24–72 hrs
- Rarely complicated by pneumothorax
- No long-term complications
- No association w/ childhood asthma

TRANSPOSITION OF THE GREAT ARTERIES (TGA)

KALYANI R. TRIVEDI, MD, AND LEE N. BENSON, MD
REVISED BY GANGA KRISHNAMURTHY, MD

The great arteries arising from the ventricles are transposed: the aorta arises from the RV & the pulmonary artery arises from the LV.

HISTORY & PHYSICAL

History
- Antenatal diagnosis is possible by fetal echocardiogram
- Hx of restrictive atrial communication on fetal ECHO may indicate the need for emergent balloon atrial septostomy (BAS) after birth. NOTE: BAS performed by interventional cardiology; these infants must be delivered in institutions where available.
- Usually minimal respiratory distress
- Varying degrees of cyanosis, usually out of proportion to respiratory distress; most severe cases, w/ intact ventricular septum & restrictive atrial communication, need emergent BAS after birth to improve mixing

- Unsuspected TGA may present at birth w/ slight cyanosis that may be missed; progressive increase in work of breathing develops as pulmonary blood flow increases w/ decreasing pulmonary vascular resistance (PVR)

Signs

- Cyanosis
- Lower limb O_2 saturations are greater than upper limb saturations in the setting of TGA w/ pulmonary hypertension or coarctation
- No significant murmur; ejection systolic murmur at left upper sternal border (if there is associated pulmonary stenosis)
- Signs of congestive cardiac failure in late-presenting infant

TESTS

- ABG: arterial hypoxemia despite 100% oxygen c/w, but not diagnostic of, cyanotic heart defect
- CXR: narrow superior mediastinum
- EKG: rightward QRS axis; not diagnostic
- ECHO: diagnostic
  - ➢ Great vessels are transposed & parallel
  - ➢ Bifurcating great vessel (pulmonary artery) arises from the LV
  - ➢ Important to note ventricular septal defect, atrial communication, pulmonary stenosis, subaortic obstruction, anatomy of the coronary arteries (intramural course should be identified if present)

DIFFERENTIAL DIAGNOSIS

All causes of a cyanotic newborn (see **CYANOSIS** in the "Neonatal Presenting Signs" section)

MANAGEMENT

- What to do first: ABCs (airway, breathing, circulation)
- PGE1 for ductal patency, to improve pulmonary blood flow & increase left atrial pressure to improve mixing
- Emergent balloon septostomy if infant is cyanotic w/ restrictive atrial communication
- NOTE: Some surgeons prefer BAS for all infants w/ TGA regardless of atrial communication.
- Discontinue PGE1 after BAS if there is no associated ductal dependent lesion (i.e., severe pulmonary stenosis or critical coarctation)

SPECIFIC THERAPY

- Uncomplicated TGS: arterial switch operation (ASO) in the newborn period
- TGA w/ pulmonary stenosis: initial Blalock-Taussig shunt, subsequent Rastelli operation (baffling LV to aorta & placement of an RV-to-pulm artery conduit)
- Damus-Kaye-Stansel operation w/ associated sub-AS: main pulm artery transected w/ proximal pulm artery from LV to ascending aorta; RV to pulm artery conduit
- Undiagnosed & late-presenting TGA may first need LV conditioning (pulm artery banding) prior to ASO

FOLLOW-UP

- Immediately postop: EKG, troponin to monitor for coronary artery insufficiency
- Long-term
  - ➢ Monitor growth, feeding; supplement nutrition as indicated
  - ➢ Cardiac & neurodevelopmental

COMPLICATIONS AND PROGNOSIS

Complications

- After ASO
  - ➢ Immediate: myocardial ischemia secondary to injury/transection to coronary artery
  - ➢ Late: dilatation of neo-aortic root, branch pulm artery stenosis, aortic valvar regurgitation, coronary artery stenosis, tricuspid insufficiency
- After Rastelli: subaortic obstruction, conduit obstruction

Prognosis

- Mortality
  - ➢ Operative mortality after ASO <5% in most institutions
  - ➢ 5-year survival >90%
  - ➢ 20-year survival ~60%; tricuspid insufficiency requiring tricuspid valve replacement & complete heart block are poor prognostic indicators
- Neurodevelopmental
  - ➢ IQ usually wnl
  - ➢ Neurologic impairments in ~25% (mostly mild)
  - ➢ Attention, speech, learning & behavioral problems more common (~50% w/ impairment in one or more domains; most likely w/ neurologic impairment)

➢ Poor prognostic indicators: severe preoperative hypoxemia & acidosis, prolonged duration of cardiopulmonary bypass

TREACHER COLLINS SYNDROME

KWAME ANYANE-YEBOA, MD

Autosomal dominant, w/ 60% representing fresh mutations in treacle gene

HISTORY & PHYSICAL
- Marked variability in phenotype
- Downslanted palpebral fissures
- Lower eyelid colobomata (bilateral)
- Partial to total absence of eyelashes medial to colobomata
- Malar hypoplasia
- Malformation of auricles, resulting in microtia
- External ear canal defect
- Upper lid colobomata
- Conductive hearing loss in 40–50%
- Mandibular hypoplasia
- Myopia, amblyopia
- Choanal atresia
- Pharyngeal hypoplasia
- Projection of scalp hair onto lateral cheek
- Congenital heart disease
- Macrostomia or microstomia
- Skin tags btwn tragus & angle of mouth
- Cryptorchidism occasionally

TESTS
DNA tests for mutations in treacle gene when indicated (for labs offering test see www.genetests.com)

DIFFERENTIAL DIAGNOSIS
Differentiated from Goldenhar syndrome by lack of epibulbar dermoids & bilaterality

MANAGEMENT
- Appropriate mgt of choanal atresia when present
- Assessment of auditory function
- Genetic counseling

SPECIFIC THERAPY
- Plastic surgery for auricular malformations, other facial defects
- Hearing aid as indicated

FOLLOW-UP
Long-term follow-up requires multispecialty craniofacial team

COMPLICATIONS AND PROGNOSIS
- Narrow airways may cause difficulty w/ intubation, early respiratory problems – may require tracheostomy
- Early recognition, appropriate therapy for deafness enhances speech, language development
- Visual loss if amblyopia diagnosed & treated
- >95% have normal cognitive function

TRICUSPID ATRESIA

KALYANI R. TRIVEDI, MD, AND LEE N. BENSON, MD
REVISED BY GANGA KRISHNAMURTHY, MD

HISTORY & PHYSICAL

History
- Antenatal diagnosis possible by fetal ECHO
- Cyanosis from birth – degree varies w/ degree of obstruction to pulmonary blood flow (PBF)

Signs
- Cyanosis
- Systolic murmur (ventricular septal defect)
- Ejection systolic murmur (w/ associated pulmonary stenosis)
- Progressive congestive heart failure if PBF is unrestricted
- Decreased lower extremity pulses & BP differential w/ associated coarctation of aorta (CoA)
- Hepatomegaly w/ restrictive atrial communication

TESTS
- CXR
  - ➢ Mild cardiomegaly or normal-sized heart
  - ➢ Prominent RA
  - ➢ Decreased pulmonary vascularity w/ associated pulmonary stenosis or pulmonary atresia; increased pulmonary vascularity when PBF is unrestricted

- ECG: left axis deviation, RA enlargement
- Echo
  - ➢ Tricuspid valvular atresia
  - ➢ Ventricular septal defect usually is present
  - ➢ Atrial septal defect, size & direction of shunting
  - ➢ +/− pulmonary stenosis or pulmonary atresia
  - ➢ +/− transposition of great arteries
  - ➢ +/− coarctation, subaortic stenosis

DIFFERENTIAL DIAGNOSIS

All causes of cyanosis (see **CYANOSIS** in the "Neonatal Presenting Signs" section)

MANAGEMENT

- ABCs
- PGE1 to maintain ductal patency w/ pulmonary stenosis/atresia or coarctation
- Balloon atrial septostomy w/ restrictive atrial shunt to improve right-to-left flow
- If PBF is unrestricted, anticongestive therapy may be required

SPECIFIC THERAPY

- Staged palliation towards a Fontan circulation
- If PBF is restrictive (due to pulmonary stenosis or atresia or restrictive ventricular septal defect)
  - ➢ 1st stage: aorto-pulmonary shunt
  - ➢ Bidirectional cavo-pulmonary anastomosis at 6 mo of age
  - ➢ Total cavo-pulmonary connection as final stage at 3–4 yrs of age
- If tricuspid atresia is assoc w/ subaortic stenosis: initial Damus-Kaye-Stansel operation is performed w/ main pulmonary artery-to-aorta connection
- If tricuspid atresia is assoc w/ CoA or interrupted aortic arch, arch repair is performed

FOLLOW-UP

- Monitor growth & development
- Cardiology
- Neurodevelopmental

COMPLICATIONS AND PROGNOSIS

- Survival
  - ➢ 5-yr: 70%
  - ➢ 10-yr: 65%

TRISOMY 13

KWAME ANYANE-YEBOA, MD

- Incidence of 1 in 15,000
- Associated w/ advanced maternal age

HISTORY & PHYSICAL

- Avg birth wt 2,600 g
- Microcephaly
- Trigonocephaly
- Microphthalmia
- Arrhinencephaly
- Bilateral cleft lip, palate
- Postaxial hexadactyly (80%)
- Colobomata, retinal dysplasia
- High-arched palate
- Abnormal ears w/ preauricular tags/pits
- Narrow chest
- Kyphoscoliosis
- Omphalocele
- Umbilical hernia
- Flexed finger
- Narrow, convex nails
- Holoprosencephaly
- Premaxillary agenesis
- Arnold-Chiari malformation
- Congenital heart malformations: ventricular septal defect, atrial septal defect, patent ductus arteriosus
- Scalp defects (cutis aplasia)
- Rocker-bottom feet
- Renal anomalies, incl congenital hydronephrosis, polycystic kidneys, duplication
- Malrotation or nonfixation of intestines
- Transverse palmar crease
- Abnormal lung lobation
- Abnormality of ribs, including absence, hypoplasia, or abnormal shape
- Increased levels of hemoglobin F

TESTS
- FISH for chromosome 13 for rapid diagnosis
- Chromosome studies
- Head US
- Renal US
- Echocardiogram

DIFFERENTIAL DIAGNOSIS
- See **TRISOMY 18**
- Smith-Lemli-Opitz syndrome
- Hydrolethalus syndrome
- Pallister-Hall syndrome

MANAGEMENT
- Comfort care
- Genetic counseling
- Psychosocial support of family

SPECIFIC THERAPY
None

FOLLOW-UP
N/A

COMPLICATIONS AND PROGNOSIS
- 50% mortality w/in 1 mo
- <10% survive past age 12 mo
- Survival > age 10 yr possible
- Profound developmental delay the rule

TRISOMY 18

KWAME ANYANE-YEBOA, MD

HISTORY & PHYSICAL

History
- Pregnancy may be complicated by polyhydramnios, fetal distress
- Poor feeding in neonatal period

Signs
- IUGR (mean birth wt 2,300 g)

- Microcephaly
- Broad forehead
- Narrow palpebral fissures
- Small nose
- Small mouth, which is difficult to open
- Receding chin
- Low-set, poorly formed ears
- Cleft palate
- Esophageal atresia
- Radial hypoplasia
- CHD (90%): ventricular septal defect, patent ductus arteriosus, atrial septal defect, pulmonary stenosis, valve anomalies
- Omphalocele, inguinal hernia
- Hypoplastic penis w/ cryptorchidism
- Sex reversal (XY female)
- Small labia majora, prominent clitoris
- Hands, feet flexed in ulnar deviation
- Hands clenched
- 2nd finger overlaps 3rd, 5th overlaps 4th
- Transverse palmar crease
- Rocker-bottom feet
- Hypoplastic nails
- Partial syndactyly of toes
- Club feet
- Diminished subcutaneous tissue
- Hirsutism
- Increased muscle tone w/ opisthotonos, crossed legs
- Single umbilical artery
- Arthrogryposis
- Renal malformation; usually horseshoe, cystic, or hypoplastic kidneys, hydronephrosis
- Underdeveloped brain assoc w/ migrational defects, agenesis of corpus callosum, holoprosencephaly, Arnold-Chiari malformation
- Myelomeningocele (10%)
- Radial &/or thumb aplasia (10%)
- Thumb duplications (5%)
- Postaxial hexadactyly, split-hand deformity
- Slender, curved ribs
- Hypoplastic sternum
- Delayed bone maturation

- Pyloric stenosis
- Exstrophy of cloaca
- Uterine malformations
- Choanal atresia
- Cataract, coloboma, cloudy cornea, microphthalmia

TESTS
- Chromosome studies – Chr 18 FISH probes for rapid diagnosis
- Echocardiogram
- Renal US

DIFFERENTIAL DIAGNOSIS
- See **TRISOMY 13**
- VATER association
- See **CORNELIA DE LANGE SYNDROME**

MANAGEMENT
- Comfort care
- Genetic counseling
- Permanent tube feeding may be required for long-term survivors
- Psychosocial support of family

SPECIFIC THERAPY
None

FOLLOW-UP
N/A

COMPLICATIONS AND PROGNOSIS
- 80–90% die w/in first 2 yr, usually due to cardiac failure
- Later causes of death incl aspiration pneumonia, seizures, cardiac, renal failure
- Survival beyond age 2 yr exceptional, but survival to age 15 & 18 yr reported
- Long-term survivors: profound motor, mental deficiencies

TRISOMY 21

KWAME ANYANE-YEBOA, MD

Risk increased w/ advanced maternal age

HISTORY & PHYSICAL

History

- Abnormal triple screening in 1st trimester
- Thickened nuchal fold on 1st-trimester sonogram
- Polyhydramnios w/ duodenal atresia

Signs

- Hypotonia
- Brachycephaly
- Epicanthic folds
- Upslanted palpebral fissures
- Brushfield spots
- CHD (40%): ventricular septal defect, atrioventricular canal defect, tetralogy of Fallot
- Duodenal stenosis or atresia
- Esophageal atresia
- Umbilical hernia
- Hirschsprung disease
- Anal atresia
- Transverse palmar creases
- Clinodactyly of 5th fingers
- Thin, silky hair
- Cutis marmorata
- Small low-set ears w/ folded upper borders
- Esotropia
- Nystagmus
- Cataracts

TESTS

- Karyotype
- CBC: polycythemia, transient myeloproliferative (leukemoid) reaction, thrombocytopenia, thrombocytosis
- ECG, echocardiogram
- Thyroid function tests

DIFFERENTIAL DIAGNOSIS
- Other chromosomal syndromes

MANAGEMENT
- Surgical mgt of duodenal, anal atresia, Hirschsprung disease
- Partial exchange transfusion for polycythemia
- Cardiac evaluation, management of CHD
- Genetic counseling

SPECIFIC THERAPY
None

FOLLOW-UP
- Physical, occupational, speech therapies
- Special education
- Periodic visual, auditory screens
- Repeat thyroid function tests at 12 mo

COMPLICATIONS AND PROGNOSIS
- Congenital hypothyroidism (2%); additional source of retardation if undetected, untreated
- Growth hormone deficiency
- Autoimmune disease
- Frequent upper respiratory infections
- More frequent pneumonias
- Hearing loss due to middle ear effusion
- Developmental delay
- Speech & language delay, esp expressive language
- Childhood leukemia

TRUNCUS ARTERIOSUS

KALYANI R. TRIVEDI, MD, AND LEE N. BENSON, MD
REVISED BY GANGA KRISHNAMURTHY, MD

HISTORY & PHYSICAL

History
- Antenatal diagnosis is possible by fetal echocardiogram
- Symptoms usually appear in neonatal period
  - ➢ Initial mild cyanosis

- ➢ As pulmonary vascular resistance decreases & pulmonary blood flow increases, cyanosis diminishes
- ➢ With increased pulm blood flow, increase in work of breathing & poor feeding & failure to thrive

Signs

- Initial cyanosis that diminishes in few days to weeks
- Development of CHF: tachycardia, tachypnea
- Bounding peripheral pulses
- Active precordium
- S1 normal; single S2 preceded by ejection click
- Pansystolic murmur at left lower sternal border
- Apical diastolic murmur (increased flow across mitral valve)
- Early diastolic murmur in left upper sternal border (truncal valve insufficiency)

TESTS

- ABG, liver and renal functions, CBC
- FISH for 22 q 11 deletion
- CXR: increased pulmonary vascular markings, cardiomegaly
- ECG: biventricular hypertrophy; ST segment changes w/ coronary steal
- ECHO
  - ➢ Single great vessel
  - ➢ Quadricuspid semilunar valve; truncal valve may be regurgitant
  - ➢ Origin of pulmonary arteries
    - Type 1 TA: main pulmonary artery from truncus branching into right & left pulm artery
    - Type 2 TA: main pulmonary artery absent, right & left pulm arteries arise from posterior aspect of truncus
    - Type 3 TA: Branch pulm arteries arise from lateral aspect of truncus
  - ➢ Abnormal tricuspid valve
  - ➢ Truncus overrides large ventricular septal defect

DIFFERENTIAL DIAGNOSIS

All causes of CHF in neonate (see **CONGESTIVE HEART FAILURE** in the "Neonatal Presenting Signs" section, but especially:

- Large ventricular septal defect
- Complete common AV canal
- Unobstructed total anomalous pulmonary venous return

MANAGEMENT

General

- ABCs
- Anticongestive therapy for CHF w/ digoxin & Lasix (see **CONGESTIVE HEART FAILURE** in the "Neonatal Presenting Signs" section)

Specific therapy

- Early primary surgical repair in neonatal period
  - ➢ Gore-tex patch closure of ventricular septal defect
  - ➢ Detachment of main pulm artery or branch pulm arteries from the truncus, oversewing of defects
  - ➢ Placement of right ventricle to pulm artery conduit to re-establish RV-to-PA continuity

FOLLOW-UP

- Monitor growth & development
- Monitor for truncal regurgitation & conduit obstruction

COMPLICATIONS AND PROGNOSIS

Complications

- Postop complications
  - ➢ RV dysfunction
  - ➢ Pulmonary hypertension
  - ➢ Truncal valve insufficiency
- Long term
  - ➢ Progressive truncal valve insufficiency
  - ➢ Conduit obstruction requiring replacement

Prognosis

- Natural history in unrepaired TA: death due to CHF by end of 1st year
- Operative mortality 5%
- Long-term survival is better:
  - ➢ If operated earlier (<2 months)

  and
  - ➢ W/ better truncal valve competence

TUBERCULOSIS, CONGENITAL

J.M. LORENZ, MD

- Rare
- Due to hematogenous dissemination via umbilical vein or aspiration or ingestion of infected amniotic fluid
- Requires maternal bloodstream dissemination – can occur during asymptomatic initial infection or during disease (risk is higher w/ the former) – or GU disease

HISTORY & PHYSICAL

- Maternal (see **TUBERCULOSIS, MATERNAL** in the "Maternal Presenting Signs" section)
- Neonatal: signs may be present at birth, but usually not until >2–3 wk
  - ➢ Hepatosplenomegaly (76%)
  - ➢ Resp distress (72%)
  - ➢ Fever (48%)
  - ➢ Lymphadenopathy (38%)
  - ➢ Abdominal distention (24%)
  - ➢ Lethargy or irritability (21%)
  - ➢ Ear discharge (17%)
  - ➢ Papular skin lesions (14%)
  - ➢ Vomiting (<10%)
  - ➢ Apnea (<10%)
  - ➢ Jaundice (<10%)
  - ➢ Seizures (<10%)
  - ➢ Petechiae (<10%)

TESTS

- Nonspecific
  - ➢ CXR: miliary pattern (50%), adenopathy w/ patchy infiltrates
  - ➢ Abnl CSF in 1/3rd of cases (*M. tuberculosis* isolated in <20%)
- Specific
  - ➢ Tuberculin skin test (usually neg)
  - ➢ Positive acid-fast bacilli smear or culture of placenta (does not confirm congenital infection)
  - ➢ Positive acid-fast bacilli smear or culture of body fluids (gastric, tracheal, middle ear fluid aspirates) or biopsy tissue

DIFFERENTIAL DIAGNOSIS
- Bacterial sepsis/pneumonia (see **SEPSIS, NOSOCOMIAL**)
- Congenital syphilis (see **SYPHILIS/REACTIVE SEROLOGIC SYPHILIS TEST, MATERNAL, ACTIVE MATERNAL SYPHILIS LIKELY OR CANNOT BE EXCLUDED** in the "Maternal Presenting Signs" section)
- CMV [see **CYTOMEGALOVIRUS INFECTION (CMV), CONGENITAL**]
- Toxoplasmosis (see **TOXOPLASMOSIS, CONGENITAL**)

MANAGEMENT
- Supportive care
- Isolation
  - ➢ Respiratory isolation of infant
  - ➢ Isolation from mother not indicated after infant Dx confirmed
  - ➢ Breast feeding not contraindicated

SPECIFIC THERAPY
- Pediatric ID consultation
- Initiate 4-drug Rx until susceptibility testing available
  1. Isoniazid (INH) 10 mg/kg q day PO or IM; max 300 mg/d (w/ pyridoxine 25–50 mg/day if breast-fed)
  2. Rifampin (RIF) 15–20 mg/kg q day PO or IV; max dose 600 mg/day
  3. Pyrazinamide (PZA) 20–40 mg/kg qd PO; max 2 g/day

  AND
  4. Ethambutol (EMB) 15–25 mg/kg q day PO; max 2.5 g/day

     OR

     Streptomycin (STM) 20–40 mg/kg q day IM; max 1 g/day
- Add prednisone 1–2 mg/kg/day (or equivalent) × 6–8 wk w/ meningeal involvement
- Adjust drugs when susceptibilities available
  - ➢ If sensitive,
    - Discontinue EMB (or STM)
    - Rx w/ INH, RIF, & PZA × 2 mo as above
    - Then INH 10 mg/kg q day or 20 mg/kg 2×/wk PO; max 300 mg/day, 900 mg/wk (w/ pyridoxine 25–50 mg/day if breast-fed)

      AND

      RIF 10–20 mg/kg PO q day or 2×/wk; max 600 mg/day

      For a total of 9–12 mo
  - ➢ If resistant, Rx daily w/ 4-drug regimen × 12–18 mo
- Treatment should be DIRECTLY OBSERVED

FOLLOW-UP

- During treatment
  - ➢ Wt gain; skin/sclera for jaundice; liver, spleen, lymph node size
  - ➢ Serial liver enzymes, uric acid (w/ PZA), CXRs
- Long-term
  - ➢ Neurol w/CNS involvement
  - ➢ ENT w/ middle ear involvement

COMPLICATIONS AND PROGNOSIS

- Mortality 50% (due to delayed Dx)
- Hydrocephalus, impaired development, precocious puberty w/ CNS involvement
- Hearing loss, facial nerve paralysis w/ middle ear involvement

TURNER SYNDROME

KWAME ANYANE-YEBOA, MD

- Due to aneuploidy of X or Y chromosome
- 50% 45X; the remainder due to isochromosome Xq, mosaicism (46, XX/45,X or 46,XY/45,X), and Xp deletions
- Incidence: 1 in 2,500 female live births

HISTORY & PHYSICAL

- Frequent
  - ➢ Small stature, usually of prenatal onset
  - ➢ Lymphedema of dorsum of hands and feet (>80%)
  - ➢ Short neck with low posterior hairline (80%)
  - ➢ Webbed neck (50%)
  - ➢ Broad chest with widely placed nipples that may be small or inverted (>80%)
  - ➢ Cardiac defects
    - Most commonly bicuspid aortic valves
    - Coarctation of aorta (30%)
    - Valvar aortic stenosis (10%)
  - ➢ Gonadal dysgenesis (>90%)
  - ➢ Renal anomalies, most commonly horseshoe kidneys (>60%)
  - ➢ Skeletal anomalies
    - Cubitus valgus (>70%)
    - Short fourth metacarpals (50%)
    - Medial tibial exostosis (60%)

- ➢ Skin abnormalities, especially pigmented nevi, excess nuchal folds in infancy
- ➢ Narrow, hyperconvex, or deep-set nails
- ➢ Abnormal external ears (80%)
- ➢ Perceptive hearing impairment (50%)

- Less frequent
  - ➢ Ptosis (16%), strabismus, cataracts
  - ➢ Hypoplastic left heart syndrome, anomalous pulmonary venous return, persistent left superior vena cava

TESTS

- Karyotype w/ FISH to detect X chromosomes
- Echocardiogram to detect congenital heart disease
- Renal ultrasound to detect renal anomalies

DIFFERENTIAL DIAGNOSIS

Noonan syndrome (see **NOONAN SYNDROME**)
Costello syndrome
Cardio-facio-cutaneous Syndrome
Multiple lentigenes syndrome
Noonan-neurofibromatosis syndrome
Klippel-Feil syndrome
DiGeorge syndrome (see **DIGEORGE SYNDROME (VELO-CARDIO-FACIAL) SYNDROME**)

MANAGEMENT

- Management of congenital heart disease as indicated
- Growth hormone treatment for short stature
- Monitor weight to avoid obesity
- Monitor for diabetes and hypothyroidism
- Monitor of blood pressure to detect hypertension
- Estrogen replacement therapy in hypogonadotropic adolescent girls
- Assisted reproduction with donor eggs feasible in the majority who cannot get pregnant
- Periodic echocardiography in adult to detect aortic dilatation
- Close monitoring of cardiovascular status in pregnancy to avoid complications of hypertension and sudden death from aortic dissection

SPECIFIC THERAPY

None

COMPLICATIONS AND PROGNOSIS

- Excellent prognosis with appropriate management
- Average IQ ~ 90, but performance is usually less than verbal; mental retardation less frequent
- Complications
  - ➢ Hypertension
  - ➢ Mitral valve prolapse, aortic dissection (8–42%) and sudden death in adults
  - ➢ Autoimmune disease
  - ➢ Hypothyroidism
  - ➢ Short stature
  - ➢ Infertility
  - ➢ Autoimmune disease: diabetes, Crohn's disease, ulcerative colitis

TYROSINEMIA TYPE I

WENDY K. CHUNG, MD, PhD

HISTORY & PHYSICAL

History

- Jaundice in early infancy
- Abdominal distention
- Failure to thrive
- Vomiting/diarrhea
- Bleeding/hematemesis
- Liver failure
- Coma
- Newborn screen positive for PKU
- Consanguineous parents
- French Canadian & Finnish ethnicity

Signs

- Hepatomegaly
- Peripheral neuropathy
- Ascites
- Cabbage-like odor

TESTS

- LFTs minimally elevated

- Coagulation tests abnl
- Alpha-fetoprotein elevated
- Serum amino acid analysis: elevated tyrosine & methionine
- Urine organic acids: succinylacetone
- Confirmatory enzymatic testing of fumarylacetoacetate hydrolase in fibroblasts or hepatocytes
- Prenatal diagnosis available

DIFFERENTIAL DIAGNOSIS

See **HYPERBILIRUBINEMIA, CONJUGATED; HYPERBILIRUBINEMIA, UNCONJUGATED**; and **HEPATOMEGALY** in the "Neonatal Presenting Signs" section.

MANAGEMENT

- Airway, breathing, circulation
- NPO w/ parenteral fluids w/o tyrosine, phenylalanine
- Treat bleeding w/ FFP
- Monitor electrolytes; correct hypokalemia & hypophosphatemia

SPECIFIC THERAPY

- Diet low in tyrosine, phenylalanine
- NTBC – 2(2-nitro-4-trifluoromethylbenzoyl)-1,3-cyclohezanedione – at 1 mg/kg q day divided BID
- Liver transplant for liver failure or hepatocellular carcinoma

FOLLOW-UP

- Follow urinary succinylacetone
- Follow alpha-fetoprotein & abdominal CT for development of hepatocellular carcinoma
- Monitor for rickets secondary to renal Fanconi syndrome
- Monitor for neural pain crises similar to porphyria attack

COMPLICATIONS AND PROGNOSIS

- Greatly improved w/ current Rx w/ NTBC
- Hepatic disease may progress despite Rx
- Hepatocellular carcinoma (as early as age 3 yr)
- Normal intellect

UNDESCENDED TESTIS

TERRY HENSLE, MD, AND KIMBERLY COOPER, MD
REVISED BY TERRY HENSLE, MD, AND GRACE HYUN, MD

HISTORY & PHYSICAL

- Risk factors
  - ➢ Prematurity
  - ➢ Low birth wt
  - ➢ Advanced maternal age
  - ➢ Maternal exposure to estrogens in 1st trimester
  - ➢ First-born children
  - ➢ Positive family Hx
- Abnormalities of hypothalamic-pituitary-testicular axis
  - ➢ Prune-belly syndrome
  - ➢ Kallman syndrome
- Etiology
  - ➢ Abnl testicular descent (XY male)
  - ➢ Intersex individual (XY/XO)
- Physical exam
  - ➢ Empty hemiscrotum or scrotum noted
  - ➢ Palpate scrotum, lower abdomen
    - Supine in warm room
    - Must exam on >1 occasion (have experienced examiner show you to not confuse gubernaculums w/ gonad)
    - Can apply gentle pressure from superior iliac crest toward scrotum to deliver testicle that is at first impalpable

TESTS

- Abdominal/pelvic US
  - ➢ Effective to identify large testicles
  - ➢ Not effective in localizing atrophic testes or those in small infants
- Abd/pelvic CT
  - ➢ Can be effective in identifying intra-abd testes
  - ➢ Signif radiation exposure
  - ➢ Not necessary
- Abd/pelvic MRI
  - ➢ Has shown promise in localizing testicles, delineating vessels, cord structures

- ➢ May require sedation
- ➢ Expensive
- ➢ More experience needed to justify this modality

- Laparoscopy
  - ➢ Can document absence of a testis
  - ➢ May identify impalpable, intra-abdominal testis
  - ➢ High retroperitoneal dissection possible to gain greatest length on spermatic cord

DIFFERENTIAL DIAGNOSIS

- Palpable testes (80%)
  - ➢ Retractile
    - Withdrawn to extrascrotal position due to overactive cremaster or failure of gubernaculum to attach to lower pole of testis to scrotum
    - Most commonly located in groin
    - Does not require intervention
  - ➢ Ectopic
    - Arrives at abnl location after emerging from inguinal canal
    - Secondary to abnormally positioned gubernaculum
    - Most commonly found in area btwn external oblique aponeurosis, subcutaneous tissue
    - Not found anywhere in thigh, groin, or suprapubic areas
- Nonpalpable testes (20%)
  - ➢ Truly undescended, intra-abdominal testis
  - ➢ Absent testicle (vanished)

MANAGEMENT

- Identify whether testicle palpable or nonpalpable
- Identify whether condition unilateral or bilateral
- Karyotype, endocrine evaluation
  - ➢ Bilateral nonpalpable testes: must r/o congenital adrenal hyperplasia (see **AMBIGUOUS GENITALIA**)
  - ➢ Unilateral nonpalpable testis with hypospadias: r/o mixed gonadal dysgenesis (see **AMBIGUOUS GENITALIA**)

SPECIFIC THERAPY

- Spontaneous descent can occur in first few mo; rare after 6 mo
- Rationale for Rx if testis remains undescended
  - ➢ Impaired fertility
  - ➢ Increased incidence of testicular neoplasm

- ➢ Psychological aspects (anatomical difference from peers may be emotionally harmful to young boys)
- Treatment options
  - ➢ Medical
    - hCG stimulation
      - Mixed results
      - Not nearly as efficacious as surgery
  - ➢ Surgical (orchiopexy)
    - Places undescended testis in normal anatomic position
    - Achieves psychological, cosmetic benefits
    - Optimal age: 10–18 mo
    - Surgical success based on achievement of adequate spermatic cord length, repair of hernia sac

FOLLOW-UP

- Scrotal US, self-exams on regular basis as surveillance for testicular cancer

COMPLICATIONS AND PROGNOSIS

Complications

- Impaired fertility, more likely with bilateral than unilateral
  - ➢ Decreased testicular vol
  - ➢ Scrotal environment confers advantage for spermatogenesis
  - ➢ Abnl hormonal milieu
    - Decreased LH, testosterone
    - Blunted hormonal response
  - ➢ By age 2 almost 40% of undescended testes devoid of germ cells
  - ➢ Orchiopexy may not restore normal fertility
- Increased incidence of testicular neoplasms
  - ➢ 5- to 35-fold increase in risk of testicular cancer in BOTH testes
  - ➢ 10% of all testicular tumors arise in undescended testis
  - ➢ Intra-abdominal testis has greatest risk
  - ➢ Seminoma is most common histological type
  - ➢ Orchiopexy does not decrease risk of malignancy, but allows easier exams of the testis
- Complications of orchiopexy
  - ➢ Testicular retraction
  - ➢ Injury to vas deferens
  - ➢ Testicular atrophy due to devascularization

Prognosis w/ orchiopexy – good except does not decrease risk of infertility, testicular cancer

URINARY TRACT INFECTION, PYELONEPHRITIS

RICHARD A. POLIN, MD

HISTORY & PHYSICAL

History

- UTIs are rare during the first 3 days of life
- During course of bacterial sepsis, urinary tract may be involved
  - ➢ Pyelonephritis is always present w/ this route of infection
  - ➢ Any pathogen causing bacterial/fungal sepsis can seed urinary tract; nosocomial pathogens causing UTI include *E. coli*, *Pseudomonas*, *Candida* & coagulase-negative staphylococci
- W/ indwelling urethral catheter & beyond immediate neonatal period, UTIs begin in bladder, then spread to kidney
  - ➢ *E. coli:* most common pathogen responsible for community-acquired UTIs
- Risk factors for UTI include:
  - ➢ Those related to the risk of sepsis in the neonate (see **SEPSIS/PNEUMONIA, EARLY-ONSET**; **SEPSIS, NOSOCOMIAL**)
  - ➢ Anomalies of the urinary tract & vesicoureteral reflux – infection is a common presenting sign
  - ➢ Male gender
- Congenital infections (TORCH agents) commonly involve urinary tract, viral excretion can occur for months

Signs

- May be asymptomatic
- Signs c/w sepsis (see **SEPSIS/PNEUMONIA, EARLY-ONSET; PNEUMONIA, NOSOCOMIAL**; and **SEPSIS, NOSOCOMIAL**)
- Other nonspecific signs include:
  - ➢ Poor wt gain
  - ➢ Temperature instability
  - ➢ Cyanosis or poor skin color
  - ➢ Conjugated or unconjugated hyperbilirubinemia
  - ➢ Abdominal distention/vomiting/diarrhea

TESTS

- Blood culture
- Urine culture
  - ➢ Bag specimens often unreliable, difficult to interpret unless sterile

- ➢ Suprapubic aspiration (SPA)
  - Most reliable method
  - Contraindicated w/ thrombocytopenia or coagulopathy
  - Any bacteria growth from SPA considered significant, but most have >10,000 CFU/mL
- ➢ Bladder catheterization
  - Next-best alternative if SPA unsuccessful or contraindicated
  - Colony counts >10,000 CFU/mL significant
- ➢ Positive urine cultures should be repeated 3 days into treatment

- Examination of urine
  - ➢ Clean-catch specimen
    - >10 WBC/mm^3 should raise suspicion of UTI
    - Neither presence nor absence of pyuria is completely reliable evidence for/against UTI
    - Gram stains of unspun specimens demonstrating bacteria: positive predictive accuracy of ~50%
    - Presence of WBCs & bacteria increases positive predictive accuracy to 80–85%
  - ➢ Gross hematuria: rare
- WBC & acute phase reactants
  - ➢ Neutrophil indices frequently abnormal in infants w/ UTI
  - ➢ Elevated C-reactive protein and erythrocyte sedimentation rate indicate pyelonephritis
- Serum creatinine at initiation of therapy, repeated if abnormal
- Lumbar puncture for suspected or proven bacteremia & positive urine culture
- Radiological studies
  - ➢ Renal US to r/o GU anomalies; incidence as high as 30%
    - Voiding cystourethography after Rx to r/o reflux

DIFFERENTIAL DIAGNOSIS

- See **SEPSIS/PNEUMONIA, EARLY-ONSET; PNEUMONIA, NOSOCOMIAL**; and **SEPSIS, NOSOCOMIAL**
- See **HYPERBILIRUBINEMIA, UNCONJUGATED** and **HYPERBILIRUBINEMIA, CONJUGATED** in the "Neonatal Presenting Signs" section

MANAGEMENT

General measures (for infants w/ suspected bacteremia)

- Correct acid/base disturbances
- Establish IV access

SPECIFIC THERAPY

- Antimicrobial therapy
  - ➢ Choice of empiric Rx depends on sensitivities of organisms causing sepsis in given nursery
  - ➢ Initial empiric therapy must be appropriate for gram-positive AND gram-negative pathogens
    - Early-onset bacterial sepsis – ampicillin/aminoglycoside
    - Nosocomial sepsis – vancomycin/aminoglycoside
  - ➢ Final antibiotic selection based on sensitivities
  - ➢ Duration of treatment, 7–14 days
  - ➢ Infants w/ malformations or reflux should receive uroprophylaxis w/ amoxicillin or trimethoprim-sulfamethoxazole (contraindicated w/ unconjugated hyperbilirubinemia)

FOLLOW-UP

- Renal US as described in "Tests"
- Voiding cystourethography as described in "Tests"
- Repeat urine culture 1 wk after treatment completed

COMPLICATIONS AND PROGNOSIS

- Complications
  - ➢ Urosepsis
  - ➢ Recurrent infection, chronic pyelonephritis, end-stage renal failure (esp w/ malformations/reflux)
- Prognosis
  - ➢ Excellent w/o anatomic malformations, reflux, or associated sepsis
  - ➢ W/ associated sepsis; see **SEPSIS, NOSOCOMIAL**

VARICELLA (CHICKENPOX), NEONATAL DUE TO NON-MATERNAL POSTNATAL EXPOSURE

J.M. LORENZ, MD

Infection rare in newborns born to mothers immune to varicella due to passive transplacental passive of anti-VZV IgG

HISTORY & PHYSICAL

- Onset 10–28 days after exposure
- Clinical generally mild infection
  - ➢ Fever

- ➢ Recurrent crops of skin lesions over prolonged time: progresses from maculopapular to vesicular rash to pustular or hemorrhagic rash

■ Disseminated varicella (rare in term infants; more likely infants <28 wk or birth wt 1,000 g) – indistinguishable from congenital chickenpox (see **VARICELLA (CHICKENPOX), MATERNAL, ONSET OF MATERNAL ILLNESS <5 D PRIOR TO OR <48 HR AFTER DELIVERY** in the "Maternal Conditions and Diseases" section)

TESTS

■ Presence of VZV antigen, VZV DNA isolation, or VZV from vesicular fluid

DIFFERENTIAL DIAGNOSIS

■ With few lesions or no h/o exposure
- ➢ Neonatal herpes simplex infection – lesions tend to cluster rather than more even distribution of varicella
- ➢ Contact dermatitis
- ➢ Impetigo – large bleb instead of vesicles
- ➢ Anything that causes vesiculobullous disease

MANAGEMENT

■ Infection control
- ➢ No staff susceptible to VZV should care for the infant 8–28 days after exposure
- ➢ Exposed seronegative hospital personnel should be excluded from pt care activities days 8–21 after exposure
- ➢ Contact isolation of infant in separate room w/ door closed, preferably w/ negative air pressure compared to that in the corridor
  - Exposure w/o signs of varicella infection: 8–21 days after exposure if VZIG not given (28 days if it is) or until discharge home
  - Non-disseminated varicella disease: minimum of 5 days, until all lesions are crusted, or discharged home
  - Disseminated disease: for the duration of the illness

SPECIFIC THERAPY

■ Prevention
- ➢ GA >/=28 wk
  - If reliable h/o maternal chickenpox or serologically confirmed immunity, VZIG not indicated

- If no reliable h/o maternal chickenpox or serologic testing indicates maternal susceptibility, VZIG 125 U (1.25 mL) IM ASAP within 48 hr of exposure

➢ GA <28 wk or birth wt <1,000 g:
- VZIG 125 U (1.25 mL) IM ASAP within 48 hr of exposure, regardless of maternal status

■ Treatment of neonatal infection
➢ Rapid evolution of large # of vesicles, hemorrhagic manifestations, respiratory involvement, CNS involvement, or disseminated disease OR GA <28 wk or birth wt <1,000 g:
- Acyclovir 20 mg/kg q8h IV over 1 h × 7–10 days
  - Ensure adequate hydration to minimize nephrotoxicity
  - Increase dose interval w/ renal impairment, GA <34 wk
  - Side effects: phlebitis (dilute solution), transient elevation of serum creatinine, crystalluria

➢ GA >/=28 wk w/ milder disease than above: acyclovir not recommended

FOLLOW-UP
■ None for mild disease
■ Severe disease
➢ During Rx: monitor IV site, renal & hepatic function
➢ Long-term: neurologic

COMPLICATIONS AND PROGNOSIS
■ Complication: secondary bacterial infection (streptococcal or staphylococcal)
■ Prognosis: same as childhood varicella if disease not severe

VATER ASSOCIATION (VACTERL ASSOCIATION)

KWAME ANYANE-YEBOA, MD

■ VATER is an acronym for:
➢ Vertebral anomalies
➢ Anal atresia
➢ Tracheo-esophageal fistula
➢ Radial and renal anomalies
■ VACTERL is used to emphasize the cardiac and limb components.
■ This heterogeneous disorder has an unknown etiology.
■ Incidence is 1.6 per 1,000 births.
■ Incidence is higher in infants of diabetic mothers.

HISTORY & PHYSICAL

- Frequent
  - ➢ Vertebral anomalies (70%)
  - ➢ Anal atresia (80%)
  - ➢ Cardiac malformations: ventricular septal defect & other defects (53%)
  - ➢ Tracheo-esophageal fistula (80%)
  - ➢ Radial ray malformations, including thumb or radial hypoplasia, preaxial polydactyly, and syndactyly (60%)
  - ➢ Renal anomalies (53%)
  - ➢ Single umbilical artery (35%)
- Less frequent
  - ➢ Prenatal and postnatal growth deficiency
  - ➢ Ear anomaly, lower limb defects
  - ➢ Genital anomalies
  - ➢ Meningomyelocele
  - ➢ Spinal dysraphism with tethered cord
  - ➢ Laryngeal stenosis
  - ➢ Rib anomalies
  - ➢ Large fontanels
  - ➢ Torticollis
  - ➢ Scoliosis
  - ➢ Congenital hip dislocation
  - ➢ Neurogenic bladder

TESTS

- Karyotype to exclude 18 trisomy
- Chromosome breakage studies to exclude Fanconi anemia
- MRI if indicated to exclude VATER-hydrocephalus syndrome
- DNA analysis if indicated to exclude Townes-Brock syndrome
- Echocardiogram to detect congenital heart disease
- Renal ultrasound to detect renal anomalies
- X-ray of spine to detect vertebral anomalies
- Ultrasound or MRI of spine to rule out spinal dysraphism with tethered cord

DIFFERENTIAL DIAGNOSIS

- VATER-hydrocephalus syndrome: X-linked or autosomal dominant disorder with features of VATER associated with hydrocephalus, frequently aqueductal stenosis; one patient reported with mutation in PTEN gene
- Trisomy 18 (see **TRISOMY 18**)

- Holt-Oram syndrome
- Fanconi anemia
- Oculo-auriculo-vertebral spectrum defects, including Goldenhar syndrome
- Townes-Brock syndrome
- MURCS association

MANAGEMENT
- Genetic evaluation and counseling
- Surgical correction of tracheo-esophageal fistula, heart defects, anal atresia and other defects as indicated
- Monitor growth and development
- Physical, occupational and speech therapies as indicated

SPECIFIC THERAPY
None

COMPLICATIONS AND PROGNOSIS
- Failure to thrive may occur in early infancy
- Undetected spinal dysraphism may cause poor ambulation, asymmetric leg musculature and strength, enuresis and poor bladder control
- Majority have normal cognitive development

VELO-CARDIO-FACIAL SYNDROME

See **DIGEORGE SYNDROME**

VENTRICULAR SEPTAL DEFECT

KALYANI R. TRIVEDI, MBBS, MD, AND LEE N. BENSON, MD
REVISED BY GANGA KRISHNAMURTHY, MD

HISTORY & PHYSICAL

History
- +/− antenatal Dx by fetal echocardiogram
- Usually presents clinically at age 4–6 wk
  - ➢ Infant tires w/ feeding, diaphoretic
  - ➢ Resp distress w/ feeding
  - ➢ Failure to thrive

Signs

- Poor wt gain, not maintaining centiles
- Tachypnea +/ − resp distress
- Equal pulses, no 4-limb BP differential
- Active precordium ± precordial bulge
- +/ − gallop
- +/ − loud S2 (indicates pulm hypertension)
- 2–3/6 pansystolic murmur left lower sternal border
- +/ − 1–2/6 apical diastolic rumble
- CHF: tachycardia, rales, hepatomegaly

TESTS

- CBC w/ indices
- Serum Na, K, Ca, serum urea nitrogen, creatinine, arterial blood gas
- CXR: mild to moderate cardiomegaly, prominent LA, increased pulm markings
- ECG
  - ➢ LV or biventricular hypertrophy, +/ − LA enlargement
  - ➢ RV hypertrophy indicates pulm hypertension
- Echocardiogram diagnostic
  - ➢ Identifies size, location, # of ventricular septal defect
  - ➢ Identifies other assoc defects
  - ➢ Estimates pulm artery pressure
- Cardiac catheterization rarely indicated to determine operability

DIFFERENTIAL DIAGNOSIS

All causes of CHF (see **CONGESTIVE HEART FAILURE** in the "Neonatal Presenting Signs" section)

MANAGEMENT

- What to do first: ABCs (airway, breathing, circulation)
- General measures
  - ➢ Avoid overhydration; monitor urine output
  - ➢ Anticongestive Rx w/:
    - Diuretics & digoxin; maximize anticongestive doses to control CHF
    - Afterload reduction (captopril)
  - ➢ Full nutritional support: supplements, +/ − tube feeds, monitor growth
  - ➢ Avoid acidosis; maintain normokalemia
  - ➢ Avoid anemia
  - ➢ SBE prophylaxis

SPECIFIC THERAPY

- Surgical closure of ventricular septal defect; indications:
  - ➢ Large defects w/ failure of anti-CHF medical therapy
  - ➢ Signs of developing pulmonary hypertension
- Surgical palliation by pulm artery banding to control pulm blood flow limited to complex defects

FOLLOW-UP

- Before surgical closure
  - ➢ Monitor growth, feeding: nutritional supplementation, tube feeds
  - ➢ Symptomatic control of CHF
  - ➢ ECG: increasing RV forces mandate further evaluation by echocardiogram &/or cardiac catheterization for developing pulm hypertension
  - ➢ Echocardiogram
    - For size of ventricular septal defect: may get smaller, close spontaneously
    - Development of double-chamber RV w/ RV outflow obstruction
    - Aortic cusp prolapse, aortic regurgitation, subaortic ridge
- Long-term
  - ➢ Neurodevelopmental assessment

COMPLICATIONS AND PROGNOSIS

Complications

- Before surgical closure
  - ➢ Pulmonary hypertension
  - ➢ Development of double-chamber RV w/ RV outflow obstruction
  - ➢ Aortic cusp prolapse, aortic regurgitation, subaortic ridge
- Postop
  - ➢ Transient complete heart block indicates risk of late-occurring complete heart block
  - ➢ Residual shunts may require re-intervention if large

Prognosis

- Perioperative mortality 1–2%
- 10-y survival 93–95%

VON GIERKE'S DISEASE

See **GLYCOGEN STORAGE DISEASE TYPE 1A**

WAARDENBURG SYNDROME (WS)

KWAME ANYANE-YEBOA, MD

- Autosomal dominant mutations cause types I, II, III WS
- WSIV is autosomal recessive – caused by mutations in EDNRB, EDN3, Sox10 genes
- Mutations in paired box homeotic gene 3 (PAX 3) cause type I & III WS
- Mutations in microphthalmia-associated transcription factor gene (MITF) & PAX 3, encoding transcription factors cause type II WS
- Sox10 & Endothelin-3 genes are mutated in type IV WS

HISTORY & PHYSICAL

- Frequent findings
  - White forelock
  - Premature graying
  - Heterochromia irides
  - Hypopigmented ocular fundus
  - Hypopigmented skin lesion
  - Lateral displacement of inner canthi w/ short fissures in type I WS but not type II WS
  - Medial flare of bushy eyebrows, may merge over bridge of nose
  - Broad, high nasal bridge
  - Upper limb defects in type II WS
- Less frequent findings
  - Hirschsprung aganglionosis
  - Anal atresia
  - Esophageal atresia
  - Cardiac anomaly
  - Accessory ribs
  - Neural tube closure defect
  - Scoliosis
  - Absent vagina
  - Cleft lip/palate

TESTS

- BAER
- PAX 3 gene mutational analysis for type 1, III WS
- MITF gene analysis for type II WS (20% mutation detection rate)
- Clinical testing unavailable for type IV WS

DIFFERENTIAL DIAGNOSIS
- Lateral displacement of inner canthi also seen in oro-facial-digital syndrome type I

MANAGEMENT
- Genetic evaluation, pedigree analysis
- ENT evaluation, management of deafness
- Surgery w/ Hirschsprung disease

SPECIFIC THERAPY
None

FOLLOW-UP
- Genetic, ENT follow-up
- Assess other at-risk family members

COMPLICATIONS AND PROGNOSIS
- Excellent prognosis
- Normal cognitive development
- Deafness in 25% type I, 50% type II

WILLIAMS SYNDROME

KWAME ANYANE-YEBOA, MD

- Microdeletion of LIMK1 & elastin genes on chromosome 7q11
- Negligible recurrence risk in subsequent siblings

HISTORY & PHYSICAL

History
- May have persistent hypercalcemia in neonatal period

Signs
- Coarse face
- Characteristic heart defect: supravalvular aortic stenosis or peripheral pulm artery stenosis; ventricular septal defect, atrial septal defect & truncus arteriosus less common
- Stenosis of renal, carotid, cerebral, coronary arteries may be present
- Medial eyebrow flare
- Short palpebral fissures
- Periorbital fullness
- Blue eyes w/ stellate pattern in iris
- Depressed nasal bridge

- Anteverted nares
- Long philtrum
- Full cheeks
- Open mouth appearance
- Arnold-Chiari type 1 malformation
- Hyperacusis
- Radioulnar synostosis
- Hoarse voice
- Small teeth
- Umbilical hernia
- Ectopic, supernumerary, small kidneys
- Hypercalcemia, nephrocalcinosis
- Muscle weaknesses
- Joint contractures
- Bladder diverticula
- Dilated ureters

TESTS
- Karyotype
- FISH studies using chromosome 7q11 probe
- Echocardiogram
- Renal US
- Urinalysis
- Total & ionized serum Ca
- Spot urine [Ca]/[creatinine] ratio
- Thyroid function tests
- Ophthal eval
- Multidisciplinary developmental eval; incl assessment of motor, speech, language, personal, social, general cognitive, vocational skills

DIFFERENTIAL DIAGNOSIS
- See **TRISOMY 21**
- Mucopolysaccharidosis, other storage disorders

MANAGEMENT
- Genetic counseling
- Treatment for associated abnormalities

SPECIFIC THERAPY
None

FOLLOW-UP
- Monitor serum [Ca] carefully
- Monitor urine Ca excretion
- Avoid all multivitamin preparations w/ vitamin D
- Formal dietary assessment of Ca, vitamin D intake by trained nutritionist if hypercalcemia or nephrocalcinosis develops
- Monitor cardiovascular system for arterial narrowing
- Monitor BP
- Institute dietary regimen to prevent constipation
- Monitor wt carefully to prevent obesity
- Monitor for kyphoscoliosis
- Physical, occupational, speech therapies

COMPLICATIONS AND PROGNOSIS
- Sudden death reported in ~10% due to coronary artery stenosis, severe biventricular outflow tract obstruction
- Anesthesia-related deaths due to malignant hyperthermia reported
- Early infancy marked by irritability, frequent vomiting, colic, constipation
- Speech, language delay
- Demonstrate hyperactivity, negative moods, diminished attention span at & after age 3 yr
- Outgoing personality
- Mental retardation (75%)
- Obesity
- Frequent UTIs
- Recurrent otitis media
- Chronic constipation
- Rectal prolapse (15%)
- Diverticulosis
- Cholelithiasis
- Scoliosis, kyphosis, lordosis
- Progressive hypertension in adults

WILMS' TUMOR

MICHAEL WEINER, MD

- 500–600 cases/yr Dx in USA
- 6% of all childhood malignancies

- Males/females equally affected
- 80% in children <5 yr of age
- Three clinical scenarios
  - ➢ Sporadic: 90–92%
  - ➢ Assoc congenital anomalies or syndromes: 7–8%
  - ➢ Familial: 1–2%

HISTORY & PHYSICAL

History

- Obstipation &/or diarrhea
- Wt loss
- UTI
- Nausea, vomiting

Signs

- Abdominal mass +/− abdominal pain
- Hypertension
- Hematuria

Associated congenital anomalies and syndromes

- WAGR syndrome: Wilms' tumor, aniridia, genitourinary malformations, mental retardation
- Beckwith-Wiedemann syndrome: visceromegaly, macroglossia, omphalocele, hyperinsulinemia w/ hypoglycemia, hemihypertrophy, mental retardation
- 11p13 deletion: WT1 tumor suppressor gene, homozygous loss required for Wilms' tumor development
- Associated anomalies
  - ➢ Ocular (78%)
  - ➢ CNS (70%)
  - ➢ Ear (30%)
  - ➢ Growth retardation (25%)
  - ➢ Reproductive system (25%)
  - ➢ Genitourinary tract (20%)

TESTS

- CBC
- Urinalysis
- Serum urea N, creatinine, uric acid, AST, ALT, LDH, alkaline phosphatase
- Abd US
- Chest radiograph

- CT scan or MRI of abdomen to assess:
  - Presence, function of contralateral kidney
  - +/− bilateral disease
  - Vascular, lymph node involvement w/ tumor
  - Liver involvement
- CT scan of chest to determine pulmonary metastasis
- Skeletal survey, bone scan: determine bone metastasis in pts w/ clear cell sarcoma subtype
- MRI &/or CT scan of brain in pts w/ clear cell sarcoma or rhabdoid cell subtype

DIFFERENTIAL DIAGNOSIS

- Neuroblastoma
- Hepatic tumors
- Intra-abdominal lymphoma involving kidneys
- Sarcomas, primitive neuroectodermal tumor (PNET), desmoplastic round cell tumors
- Nephroblastomatosis: premalignant lesion represents persistent embryonal tissue
- Congenital mesoblastic nephroma: usually benign, but may have perirenal extension
- Renal cell carcinoma

MANAGEMENT

Nephrectomy, lymph node sampling

DETERMINE STAGE

- Stage I: Tumor limited to kidney, completely excised
- Stage II: Tumor grossly excised but extends beyond kidney through capsule to perirenal tissues
- Stage III: Residual tumor confined to abdomen: lymph nodes +, peritoneal seeding, tumor spillage
- Stage IV: Hematogenous metastases: lung, liver, bone, brain
- Stage V: Bilateral tumor involvement

DETERMINE PATHOLOGIC SUBTYPE

- Favorable histology: classic triphasic coexistence of epithelial, blastemal, stromal cells
- Unfavorable histology: anaplasia, focal or diffuse
- Clear cell sarcoma
- Rhabdoid tumor of kidney

SPECIFIC THERAPY

Postoperative chemotherapy +/− radiation therapy (RT) depending on stage, histology per National Wilms' Tumor Study Group guidelines:

- Stage I & II favorable histology: vincristine, actinomycin-D (18 wk); no RT
- Stage III & IV favorable histology; stage II-IV focal anaplasia: vincristine, actinomycin-D, doxorubicin (24 wk) + RT to abdomen, lungs (stage IV only)
- Stage II-IV diffuse anaplasia; stage I-IV clear cell sarcoma: vincristine, actinomycin-D, doxorubicin, cyclophosphamide, etoposide (24 wk) + RT to abdomen, lungs (stage IV only)
- Stage I-IV rhabdoid tumor of kidney: carboplatin, cyclophosphamide, etoposide (24 wk) + RT to abdomen, lung (stage IV only)
- Treatment of relapse: dose-intensive chemotherapy +/− RT, then autologous stem cell transplant

FOLLOW-UP

During therapy

- CBC, serum chemistries prior to each chemotherapy cycle
- Periodic CXR, abd US
- CT of abdomen, chest at completion of therapy

Off therapy

- Monthly physical exam
- CT of abdomen, chest at 6-mo intervals for 2 y then yearly for 5 y

COMPLICATIONS AND PROGNOSIS

Complications of therapy

- Chemotherapy (general): nausea, vomiting, alopecia, wt loss, bone marrow suppression, infection
- Chemotherapy (specific)
  - ➢ Doxorubicin: cardiac
  - ➢ Cyclophosphamide: infertility
  - ➢ Etoposide: allergic reactions, hypotension
  - ➢ Carboplatin: hearing loss
- RT: growth failure, veno-occlusive disease

Prognosis: 5-yr event-free survival

- Stage I-III, favorable histology: 90%
- Stage IV, favorable histology: 80%
- Stage V (bilateral disease): 83%
- Stage I, anaplasia (focal or diffuse): 88%

- Stage II-IV, anaplasia (focal): 92%
- Stage II-IV, anaplasia (diffuse): 55%
- Stage I-IV, clear cell sarcoma: 70%
- Stage I-IV, rhabdoid tumor of kidney: 27%

WOLF-HIRSCHHORN SYNDROME

See 4P-SYNDROME

PART THREE

Neonatal Presenting Signs

ABDOMINAL MASSES

RICHARD A. POLIN, MD

HISTORY & PHYSICAL

- Abdominal masses may be palpable/non-palpable
- Non-palpable masses may be discovered by prenatal ultrasound
- >50% of abdominal masses originate in GU tract

History

- Time of presentation:
  - ➢ Identified during fetal life by routine US
  - ➢ Palpable masses usually identified in 1st few days of life
- Maternal conditions
  - ➢ Oligohydramnios: obstructive uropathy or diminished fetal urine output
  - ➢ Perinatal asphyxia or traumatic delivery: adrenal hemorrhage
- Associated findings
  - ➢ Von Hippel-Lindau syndrome: pancreatic cysts
  - ➢ Blue-tinged subcutaneous nodules: neuroblastoma
  - ➢ Oligohydramnios sequence: obstructive uropathy
  - ➢ Cutaneous hemangiomata: vascular tumors
  - ➢ Neurol deficits: anterior myelomeningocele
  - ➢ Jaundice: choledochal cysts, pancreatic cysts
  - ➢ Polycythemia: renal vein thrombosis
  - ➢ Kaufman syndrome: vaginal atresia assoc w/ imperforate anus, renal anomalies, postaxial polydactyly
  - ➢ Intestinal obstruction: intestinal duplications & hydrometrocolpos
  - ➢ Urinary tract obstruction: hydrometrocolpos
  - ➢ Hemihypertrophy: hepatoblastoma

Signs

- Palpation should determine location of mass, if it is discrete or ill defined, fixed or movable, unilateral or bilateral

TESTS

- CBC w/ differential, platelet count
- Creatinine & blood urea N2
- Plain abdominal films
  - ➢ Useful for identifying soft tissue mass, intestinal obstruction, calcifications, vertebral anomalies

- Calcifications
  - Adrenal hemorrhage
  - Neuroblastoma
  - Teratoma

■ Abdominal ultrasound
■ If solid tumor suspected
➢ Alpha-fetoprotein
➢ Human chorionic gonadotropin
➢ Urine vanillylmandelic acid (VMA) & homovanillic acid (HVA)

DIFFERENTIAL DIAGNOSIS

■ Retroperitoneal
➢ Urinary tract
- Hydronephrosis
  - Bilateral
    - Urethral valves
    - Ureteroceles
    - Prune-belly syndrome
    - Polycystic renal disease
  - Unilateral
    - Ureteropelvic obstruction
    - Uterovesical obstruction
- Multicystic/dysplastic kidneys
- Mesoblastic nephromas (most common intrarenal tumor)
- Wilms' tumor (very rare) (see **WILMS' TUMOR** in the "Neonatal Conditions and Diseases" section)
- Renal vein thrombosis

➢ Adrenal
- Hemorrhage
  - Right side most commonly involved, 8–10% bilateral
  - Must be distinguished from hemorrhagic neuroblastoma
- Neuroblastoma: most common malignancy in neonates
- Cyst
- Pseudocyst

➢ Teratomas
- Most are sacrococcygeal, only a small percent present as abdominal mass
- 10% contain malignant components

➢ Pancreatic cysts
- Von-Hippel-Lindau syndrome: pancreatic & renal cysts w/ angiomata of retina & cerebellum

- Intraperitoneal
  - Liver
    - Hepatic tumors
      - Vascular tumors most common (hemangioendothelioma/hemangioma)
      - Mesenchymal hamartoma (usually cystic)
      - Cysts (rare)
      - Hepatoblastoma
      - Hepatomegaly (see **HEPATOMEGALY**)
  - Spleen
    - Cysts (simple & epidermoid)
  - Biliary tree
    - Choledochal cyst
    - Hydrops of gallbladder
  - Uterus
    - Hydrometrocolpos: due to imperforate hymen or transverse vaginal septum w/ accumulation of vaginal & cervical secretions
  - Ovary
    - Most discovered as asymptomatic abdominal masses, but 25% undergo torsion, rupture
    - Follicular & thecalutein cysts (benign)
    - Teratomas
    - Corpus luteum & germinal inclusion cysts (less common)
  - Mesentery/omentum
  - Intestinal duplications
  - Anterior myelomeningocele

MANAGEMENT

- What to do first
  - If resp compromise: begin w/ ABCs (airway, breathing, circulation)
  - Most masses require operative intervention

SPECIFIC THERAPY

Depends on specific cause

FOLLOW-UP

Depends on specific cause

COMPLICATIONS AND PROGNOSIS

Depend on specific cause

ACUTE SCROTUM

J.M. LORENZ, MD

HISTORY & PHYSICAL
- Scrotal erythema, edema, pain/tenderness

TESTS
- Transillumination
- Radionuclide scan or Doppler ultrasound of testes to evaluate blood flow if torsion not suspected but cannot be otherwise ruled out; IF TESTICULAR TORSION LIKELY, IMMEDIATE SURGICAL EXPLORATION INDICATED W/O CONFIRMATION SCAN

DIFFERENTIAL DIAGNOSIS
- Acute testicular torsion
  - ➢ Transillumination negative
  - ➢ Flow absent on radionuclide scan/Doppler ultrasound indicates testicular torsion
  - ➢ If torsion occurred in utero, may present at birth as non-tender, non-inflamed, firm scrotal mass
- Incarcerated inguinal hernia
  - ➢ More likely to present in inguinal canal or high in scrotum
  - ➢ Transillumination may be positive or negative
  - ➢ Normal or increased blood flow
- Sudden enlargement of existing hydrocele
  - ➢ H/o hydrocele
  - ➢ Transillumination positive
  - ➢ Normal or increased blood flow
- Torsion of appendix testis
  - ➢ Uncommon in newborns, but difficult to distinguish from torsion of testis
  - ➢ Normal or increased blood flow
  - ➢ Transillumination negative
- Acute bacterial epididymitis/orchitis
  - ➢ Fever & pyuria
  - ➢ Usually associated w/ neurogenic bladder or urinary fistula w/ imperforate anus, but may be hematogenous in origin
  - ➢ Transillumination negative
  - ➢ Normal or increased blood flow
- Peritonitis w/ extension into the scrotum via the processus vaginalis

- ➢ Clinical picture usually dominated by the peritonitis
- ➢ Transillumination negative
- ➢ Normal or increased blood flow

MANAGEMENT

- Surgical consultation

SPECIFIC THERAPY

- Testicular torsion – orchiectomy (the testis is rarely salvageable) w/ or w/o contralateral orchiopexy
- Incarcerated inguinal hernia – non-surgical reduction if possible
- Sudden enlargement of an existing hydrocele – surgery
- Torsion of appendix testis – symptomatic; some surgeons advocate excision of infarcted appendix testis
- Acute bacterial epididymitis/orchitis – broad-spectrum antibiotics
- Peritonitis – dictated by the underlying etiology

FOLLOW-UP

- None

COMPLICATIONS AND PROGNOSIS

- Testicular torsion – loss of ipsilateral testis likely; may recur in contralateral testis
- Incarcerated inguinal hernia – ischemic bowel injury
- Sudden enlargement of an existing hydrocele – none
- Torsion of appendix testis – none
- Acute bacterial epididymitis/orchitis – urosepsis, pyelonephritis
- Peritonitis – depends on underlying cause

ANEMIA

RICHARD A. POLIN, MD
REVISED BY SUJIT SHETH, MD

HISTORY & PHYSICAL

- Defined as hemoglobin level 2 standard deviations below mean for age (Hgb <13 g/dL at term)
- Physiologic anemia
  - ➢ All infants exhibit a postnatal drop in hemoglobin (physiologic anemia)
  - ➢ Term infants reach their physiological nadir at 8–10 weeks, preterm infants at 6–8 weeks

- ➢ Nadir is lower for preterm infants
- Anemia is pathologic when the tissues do not receive enough oxygen delivery to meet demands
  - ➢ 3 basic pathophysiologic causes
    - Hemorrhage (internal/external – including excessive phlebotomy)
    - Increased destruction (hemolysis)
    - Decreased production
- Time of cord clamping (early vs late) & position of infant relative to placenta have major effects on circulating blood vol & hemoglobin concentration
  - ➢ Normally infants receive half placental blood vol (30–50 mL) in 1 min
  - ➢ Infants held above placenta (e.g., during cesarean section) lose 20–30 mL/min back into placenta

History

- Perinatal Hx
  - ➢ Fetomaternal hemorrhage: trauma
  - ➢ Twin-to-twin transfusion: monochorionic twins
  - ➢ Placental abruption
  - ➢ Placenta previa
  - ➢ Cord rupture
    - Short cord
    - Funisitis
    - Precipitous delivery
  - ➢ Subgaleal hemorrhage
    - Difficult deliveries req instrument assistance
    - Vacuum extraction
  - ➢ Internal hemorrhage: trauma
  - ➢ Intracranial hemorrhage
    - Prematurity
    - Prolonged labor
    - Fetal thrombocytopenia (alloimmune thrombocytopenia)
  - ➢ Blood group incompatibility: isoimmune hemolytic anemia
  - ➢ Drugs taken by the mother causing hemolysis in G6PD-deficient infants
    - Sulfonamides
    - Anti-malarials
  - ➢ Hyperbilirubinemia

Signs

- Assess degree of pallor, cardiovascular stability
  - ➢ Acute hemorrhage of moderate/severe nature often results in cardiovascular instability (hypotension, tachycardia)
  - ➢ Chronic blood loss in utero: infants generally asymptomatic
- Hydrops always assoc w/ some degree of resp distress & congestive heart failure (indicates fetal origin of anemia)
- Look for signs of extramedullary hematopoiesis (hepatosplenomegaly; indicates fetal origin of anemia)
  - ➢ Hepatosplenomegaly may also indicate congenital infection
- Hyperbilirubinemia observed w/ internal hemorrhage, hemolysis
- Assoc findings (some may not be present in the neonatal period)
  - ➢ Fanconi's anemia
    - IUGR
    - Radial, thumb abnormalities
    - Microcephaly
    - Café-au-lait spots
    - Genitourinary abnormalities
    - Microphthalmia
  - ➢ Congenital hypoplastic anemia (Diamond-Blackfan syndrome)
    - Triphalangeal thumbs
    - Flattening of thenar eminences
    - Facial dysmorphism
  - ➢ Osteopetrosis
    - Hepatosplenomegaly
    - Bony sclerosis
    - Cranial nerve abnormalities
  - ➢ TORCH infections
    - Microcephaly/hydrocephaly
    - Organomegaly
    - Chorioretinitis
  - ➢ Congenital dyserythropoietic anemia
    - Hepatosplenomegaly
    - Bony abnormalities, syndactyly
  - ➢ Aase syndrome: abnormally digitalized thumbs
  - ➢ Pearson's syndrome
    - Metabolic acidosis
    - Pancreatic dysfunction

TESTS

- CBC w/ RBC indices

- ➢ Hgb may be normal immediately after acute hemorrhage
- ➢ Hemolysis +/− marked neutrophilia
- ➢ Thrombocytopenia suggests DIC, congenital infection or marrow aplasia

- Reticulocyte count
- Peripheral blood smear
- Other tests guided by Hx, physical exam [coagulation tests, maternal & neonatal blood types, Coombs test, hepatic & renal function studies, bone marrow aspirate, osmotic fragility test (spherocytosis), testing for G6PD deficiency]
- Diagnostic scheme
  - ➢ If reticulocyte count low consider causes of decreased red cell production: Diamond-Blackfan anemia, transient erythroblastopenia of the newborn, congenital dyserythropoietic anemia, congenital aplastic or hypoplastic anemia (Aase syndrome), acquired aplastic anemia (e.g., intrauterine parvovirus infection), transcobalamin II deficiency, Pearson's syndrome or bone marrow infiltration & replacement
  - ➢ If reticulocyte count normal or high (>5–10%), consider a hemolytic process, order direct & indirect antiglobulin test
    - A + test indicates immune hemolytic anemia
    - If antiglobulin test negative, review peripheral smear
      - Hypochromic microcytic anemia suggests alpha-thalassemia, gamma-thalassemia or iron deficiency secondary to chronic fetal maternal bleed or twin-twin transfusion
      - If RBC morphology abnl
        - Disturbances of red cell morphology
          - Spherocytosis
          - Elliptocytosis
          - Stomatocytosis
          - Pyropoikilocytosis
          - Fragmentation (suggestive of microangiopathic hemolytic anemia)
      - If RBC morphology normal
        - No jaundice
          - Acute blood loss
        - Rapid onset of jaundice
          - Congenital red cell enzyme defects (e.g., G6PD deficiency)
          - Infections
          - Other

- Drugs
- Galactosemia, etc.

➢ Note increased nucleated RBC observed w/:
- In utero onset of anemia
- Blood loss w/ shock
- Perinatal asphyxia
- Sepsis w/ cytokine release

DIFFERENTIAL DIAGNOSIS

■ Hemorrhage

➢ May be acute or chronic
- Antepartum
  - Fetomaternal hemorrhage
    - 50–75% of pregnancies have some degree of fetal maternal hemorrhage (mostly small vol)
    - Severe hemorrhage occurs in 1/1000 pregnancies
  - Twin-twin transfusion
    - Twins must be monochorionic (5–30% of monochorionic pregnancies)
    - Hemoglobin concentration difference btwn twins >5 g/100 mL
  - Hemorrhage after obstetric procedures
    - Amniocentesis
    - Percutaneous umbilical blood sampling (PUBS)
- Intrapartum
  - Placental abruption
  - Placenta previa
  - Vasa previa
  - Cord rupture, hematoma of cord, velamentous insertion of cord
- Postnatally: bleeding almost always secondary to 1) traumatic delivery, 2) anatomic malformation, or 3) disturbance of coagulation
  - Intraventricular hemorrhage (usually 1st few days of life: see **INTRAVENTRICULAR HEMORRHAGE** in the "Neonatal Conditions and Diseases" section)
  - Subgaleal bleed (begins intrapartum: see **SUBGALEAL HEMORRHAGE** in the "Neonatal Conditions and Diseases" section)

- Cephalohematoma (begins intrapartum: see **SUBGALEAL HEMORRHAGE** in the "Neonatal Conditions and Diseases" section)
- Pulm hemorrhage (acute phase of resp illness)
- Organ injury (liver, spleen, adrenal, kidney; usually in immediate postnatal period)
- Iatrogenic blood loss (phlebotomy)
- Gastrointestinal blood loss (multiple etiologies: see **GASTROINTESTINAL BLEEDING**)
- Disturbed coagulation (concurrent w/ coagulopathy)

■ Hemolysis

➢ Isoimmune hemolytic disease (hemolysis begins in utero, producing variable degrees of anemia)
- ABO or Rh incompatibility most common
- Others incl anti-E, anti-c, anti-C, anti-Kell, anti-MNS, anti-Duffy & anti-jka

➢ Congenital red cell defects
- Morphologic abnormalities
  - Hereditary spherocytosis (anemia & jaundice in the neonatal period)
    - Rare infant will have severe hemolysis in utero leading to hydrops
    - Some infants asymptomatic
  - Other red cell morphologic abnormalities (elliptocytosis, pyropoikilocytosis) produce varying degrees of anemia
    - Elliptocytosis: anemia rare in neonatal period
    - Pyropoikilocytosis: severe hemolysis in infancy
    - Stomatocytosis: variable severity
- Enzyme deficiencies
  - G6PD: risk of hemolysis when exposed to oxidizing agents
  - Pyruvate kinase deficiency: severe anemia in early infancy (occasional onset in utero)
  - Hexokinase deficiency: variable severity, +/− anemia in infancy
  - Glucose phosphate isomerase deficiency: severe anemia in early infancy (occasional onset in utero)

➢ Alpha-, gamma-thalassemia: variable severity from asymptomatic to hydrops fetalis, death depending on # of gene deletions

➢ Infections

- TORCH infections
- Bacterial sepsis
- Parvovirus B19: may cause severe anemia, hydrops in neonatal period
- Congenital malaria

➢ Microangiopathic hemolytic anemia: DIC

➢ Misc causes
- Galactosemia
- Drug-induced hemolysis: valproic acid
- Transfusion reactions

■ Decreased red cell production

➢ Anemia of prematurity: 3–12 wk of life

➢ Fanconi's anemia: rarely presents under 1 y of life (syndrome detected because of constellation of congenital anomalies)

➢ Congenital hypoplastic anemia (Diamond-Blackfan syndrome)
- Progressive anemia in 1st few mo of life

➢ Osteopetrosis: progressive anemia beginning in neonatal period

➢ Congenital dyserythropoietic anemia: presents in newborn period w/ megaloblastic anemia

➢ Aase syndrome: congenital hypoplastic anemia

➢ Pearson's syndrome: hypoplastic, sideroblastic anemia

MANAGEMENT

■ What to do first

➢ Fluid resuscitation w/ normal saline or 5% albumin for hypovolemia

➢ Check acid/base status

■ General measures

➢ Obtain blood for Dx studies before transfusion

➢ If severely anemic & in CHF, RBC should be given as partial exchange transfusion

➢ Asymptomatic infants w/o need for O_2 & no ongoing losses rarely need transfusion if Hgb is >7 g/dL (Hct ~20)

➢ Minimize phlebotomy, use micromethods for all testing if possible

➢ Suggested guidelines for transfusion in preterm infant
- Critically ill infants requiring mechanical ventilation (FiO_2 >50%): maintain Hct >35%
- Less critically ill infants requiring mechanical ventilation or CPAP (FiO_2 <50%): maintain Hct >30%

- Infants requiring supplemental O_2 w/o additional resp support: maintain Hct >25%
- Asymptomatic preterm infants w/ absolute reticulocyte count <100,000/mm^3: maintain Hct >20%

➢ Controversial indications to maintain the Hct >= 30%
- Poor growth
- Increased freq of apnea & bradycardia in infant receiving methylxanthines
- Increased lactate concentrations
- Signs, symptoms consistent w/ anemia
  - Tachycardia at rest (>180)
  - Tachypnea (>60)

Erythropoietin may be used in situations where the anemia is likely to be long-standing in order to reduce transfusion requirements. However, its use remains somewhat controversial.

SPECIFIC THERAPY

In many instances, when the anemia is secondary, as in sepsis, intrauterine infection, drug-induced hemolysis, etc., the underlying condition must be treated before the anemia can be ameliorated.

FOLLOW-UP

N/A

COMPLICATIONS & PROGNOSIS

N/A

ARTHROGRYPOSIS MULTIPLEX CONGENITA (AMC)

RICHARD A. POLIN, MD

HISTORY & PHYSICAL

- Disorder characterized by fixed position of multiple joints w/ limitation of movement
- Distal joints more affected than proximal joints
- Most common manifestations: talipes equinovarus, flexion deformities of wrist
- Affected joints may be webbed
- Muscles usually atrophic
- Congenital hip dislocation common
- Syndrome caused by multiple disorders

- ➢ Major intrauterine disorders of cerebrum or brain stem
- ➢ Diseases of anterior horn cell (most common)
- ➢ Disorders of peripheral nerve (rare)
- ➢ Disorders of neuromuscular junction (rare)
- ➢ Disorders of muscle (may represent 25–40% of cases)
- ➢ Primary disorder of joint or connective tissue
- ➢ Intrauterine mechanical compression

History

- Time of presentation: birth
- Maternal Hx
  - ➢ Reduced fetal movements
  - ➢ Polyhydramnios: indicative of decreased swallowing
  - ➢ Hx of myasthenia gravis
  - ➢ Uterine abnormality
  - ➢ Oligohydramnios
  - ➢ Hx of consanguinity suggestive of autosomal recessive disorder

Signs

- Assoc findings (other than joint contractures)
  - ➢ >Half of patients exhibit congenital anomalies of other organs, craniofacial structures, musculoskeletal system or CNS
  - ➢ >150 syndromes in which AMC is prominent sign

TESTS

- Lumbar puncture
  - ➢ Elevated protein concentration w/o other findings suggests polyneuropathy
- Serum enzymes
  - ➢ CPK specific isoenzymes
    - Levels elevated for several days after vaginal delivery
    - Levels normal in diseases of the anterior horn, neuromuscular junction
    - Best indicator of muscle disease, but not always elevated (e.g., values usually normal in myotonic dystrophy & many congenital myopathies)
- Nerve conduction velocity
  - ➢ Best study for disorder of peripheral nerve
  - ➢ Velocities normal in diseases of anterior horn (except late in the disease), neuromuscular junction & muscle

- ➢ Values normally lower in newborns
- ➢ Most abnormal in disorders of demyelination or failure of myelination
- ➢ Less severely depressed in axonal disorders

■ Electromyography
- ➢ Anterior horn cell disorders
  - Fibrillations (short-duration, low-amplitude potentials), fasciculations (high-amplitude, long-duration potentials)
  - Polyphasic potentials
  - Reduced number of motor unit potentials w/ contraction, increased in amplitude, duration
- ➢ Peripheral nerve disorders
  - Spontaneous fibrillations at rest
  - No fasciculations
  - # of motor unit potentials decreased w/ contraction, but not altered in amplitude or duration until late in disease
- ➢ Muscle disorders
  - Fasciculations, fibrillations not generally seen
  - W/ contraction motor unit potentials decreased in size, amplitude, but # of motor unit potentials relatively spared
  - Polyphasic potentials abundant
- ➢ Myotonia
  - Characteristic of myotonic dystrophy, but difficult to elicit in young infant
- ➢ Myasthenia
  - Decreased size of motor unit potential w/ repetitive stimulation

■ Muscle biopsy
- ➢ Most definitive test for evaluation of motor unit
- ➢ Normal in diseases above lower motor neuron or at neuromuscular junction

■ Ultrasound/CT/MRI scan of brain or spinal cord

■ Other tests indicated for specific disorders

DIFFERENTIAL DIAGNOSIS

■ Major causes
- ➢ Cerebrum, brain stem: microcephaly, migrational disorders, fetal alcohol syndrome, CMV infection, pontocerebellar hypoplasia, leptomeningeal angiomatosis, destructive processes (e.g., porencephalies), hydrocephalus

- ➢ Anterior horn cell disease: agenesis, destruction, Möbius syndrome, cervical spinal atrophy, lumbar spinal atrophy, meningomyelocele, sacral agenesis
- ➢ Peripheral nerve or root: hypomyelinative polyneuropathy, axonal polyneuropathy, neurofibromatosis
- ➢ Neuromuscular junction: transient or permanent myasthenia gravis
- ➢ Muscle: congenital muscle dystrophy, congenital myotonic dystrophy, myotubular myopathy, central core disease, nemaline myopathy, congenital polymyositis, congenital fiber type disproportion, glycogen storage myopathy, mitochondrial myopathy
- ➢ Primary disorder of joint or connective tissue: Marfan syndrome
- ➢ Intrauterine mechanical obstruction: uterine abnormality, amniotic bands, oligohydramnios, twin pregnancy, extrauterine pregnancy

MANAGEMENT

- What to do first
  - ➢ ABCs (airway, breathing, circulation)
- General measures
  - ➢ Initiate the diagnostic eval after stabilization
  - ➢ Passive stretching
  - ➢ Serial casting
  - ➢ Surgical release

SPECIFIC THERAPY

N/A

FOLLOW-UP

N/A

COMPLICATIONS AND PROGNOSIS

N/A

ASPHYXIA, PERINATAL

RICHARD A. POLIN, MD

HISTORY & PHYSICAL

History: no single aspect of history diagnostic of asphyxia

- Fetal distress: decreased fetal heart rate variability; late decelerations; prolonged fetal bradycardia; abnormal biophysical profile; fetal scalp pH <7.2
- Meconium-stained amniotic fluid
- Resuscitation at birth
- Umbilical cord pH <7.0 & base excess >-12
- Apgar score <3 at 5 min of life

NOTE: ACOG defines asphyxia by constellation of findings (cord pH <7.0, Apgar score <3 at age 5 min, neurological findings c/w asphyxia & multiorgan system dysfunction)

Signs & symptoms

- Neurol
  - ➢ Birth-12 hr: impaired consciousness (coma)
    - Hypotonia
    - Seizures
  - ➢ 12–24 hr: variable changes in level of alertness
    - Seizures
    - Apnea
    - Jitteriness
    - Weakness
      - Preterm, lower extremity weakness
      - Full-term, upper extremity weakness
      - Some exhibit hemiparesis
  - ➢ 24–72 hr: persistent (but lessening) stupor
    - Disturbed sucking, swallowing, gag
    - Weakness
- Renal (oliguria/anuria, proteinuria, hematuria, electrolyte, acid-base disturbances: metabolic acidosis, hyponatremia, hyperkalemia, hypocalcemia)
- Hepatic (transaminase elevation, direct hyperbilirubinemia, hypoglycemia)
- Cardiopulm (pulmonary hypertension, hypotension, meconium aspiration syndrome)
- Gastrointestinal (ischemic bowel injury)
- Hematologic (thrombocytopenia, increase in nucleated RBCs, coagulopathy)

TESTS

- Neurol dysfunction
  - ➢ EEG
  - ➢ US at age 24 hours

- ➢ CT scan or MRI on day 4–7 (a diffusion MRI can be abnormal <24 hours)
- ➢ NMR spectroscopy (high lactate peak & decreased n-acetyl aspartate)
- ➢ Lumbar puncture in infants w/ seizures, lethargy or coma (to r/o other etiologies)
- ➢ Serum ammonia in infants w/ coma or seizures

- Venous or arterial blood gas for acid-base status
- Serum Na, K, Ca, K, BUN, creatinine
- Serum ALT/AST/total & direct bilirubin (liver function)
- Bedside monitoring of serum glucose (btwn 0.5 & 2 hr after birth, q4 h for 1st 24 hr)
- Platelet count (at least one determination)
- NOTE: Frequency of monitoring depends on degree of abnormalities detected

DIFFERENTIAL DIAGNOSIS

- Multiple organ systems injured w/ asphyxia
- However, w/ constellation of historical features, neurological abnormalities at birth & multisystem injury, perinatal asphyxia should be strongly suspected

MANAGEMENT

What to do first

- ABCs (airway, breathing, circulation); see **RESUSCITATION** in the "Procedures" section

General measures

- Fluid restriction to 60 cc/kg/day (infants w/ adequate urine output) or insensible H_2O loss + urine output (oliguric or anuric infants); avoid overhydration (unproven efficacy)
- No K until urine output established
- IV glucose (4–6 mg/kg/min)
- NPO for 48–72 hr w/ Hx of severe acidosis
- Monitor fluid intake, urine output
- Maintain BP; perfusion (avoid systemic hypotension, hypertension)
- Avoid marked hypercarbia or hypocarbia (optimal range 35–45 mmHg)
- Maintain normoxemia
  - ➢ Avoid overheating

SPECIFIC THERAPY

- The use of systemic hypothermia has been shown to decrease the risk of neurological morbidity.

FOLLOW-UP

- CT or MRI at age 6 mo if initial scan indicates injury
- Enrollment in high-risk neonatal follow-up clinic

COMPLICATIONS AND PROGNOSIS

- Neurol outcome in term infants depends on severity of neonatal neurological syndrome; death or sequelae (mental retardation or cerebral palsy) occur in ~25% of infants w/ hypoxic-ischemic encephalopathy
- Seizures increase risk of neurological sequelae by 2–5×
- Longer abnormal neurological signs persist, greater the risk of sequelae
- EEG, brain imaging provide prognostic information
- Permanent dysfunction in other organ systems very unlikely

CONGESTIVE HEART FAILURE

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HISTORY & PHYSICAL

- History
  - ➢ Time of onset
    - CHF in fetal life: commonly manifests as hydrops fetalis, suggests 1 of 6 problems:
      - Regurgitant lesions of atrioventricular valves (e.g., Ebstein anomaly or severe mitral regurgitation assoc w/ AV valve anomalies) or absent pulm valve (+/− tetralogy of Fallot)
      - Rhythm disturbances [bradyarrhythmias (<55 bpm), tachyarrhythmias]
      - Myocardial disease (myocarditis or intrauterine myocardial dysfunction)
      - Severe anemia
      - Arteriovenous fistulas
      - Premature closure of ductus arteriosus (indomethacin)
    - CHF PRESENTING in newborn infant suggests:

- Structural heart disease
  - LV outflow obstruction (aortic stenosis/severe coarctation or interrupted aortic arch)
  - Hypoplastic left heart syndrome
  - LV inflow obstruction (cor triatriatum)
  - Left-to-right shunts (e.g., ventricular septal defect) w/ falling pulm vascular resistance
  - Anomalous pulm venous return (obstructed)
  - Regurgitant lesions of atrioventricular valves
  - Rhythm disturbances [bradyarrhythmias (<55 bpm), tachyarrhythmias]
  - Arteriovenous fistulas
- Dilated, obstructive cardiomyopathies (e.g., metabolic diseases: fatty-acid oxidation defects, glycogen storage diseases, lysosomal storage diseases, respiratory chain defects); infant of diabetic mother, systemic hypertension, myocardial infarction, myosin mutations
- Sepsis
- Electrolyte disorders
- Hypoglycemia

➢ Maternal Hx
- Mothers w/ anti-Ro or anti-La antibodies because of lupus erythematosus: 5% risk of fetus w/ heart block
- Poor maternal control of phenylketonuria assoc w/ CHD
- Coxsackie B viral infection: myocarditis in newborns
- Maternal conditions assoc w/ cardiac defects
  - Diabetes mellitus
  - Alcohol abuse
  - Lithium & trimethadione use
- Hx of CHD in 1st-degree relatives of infant being eval should increase suspicion of CHD

■ Signs

➢ Cyanosis
- Acrocyanosis
  - Peripheral cyanosis commonly represents cutaneous vasoconstriction secondary to cool environment
  - Less commonly may indicate reduced cardiac output, poor tissue perfusion
- Central cyanosis
  - Cyanosis of oral mucous membranes indicative of generalized cyanosis due to reduction in systemic O_2 saturation (usually <70–80%)

- Commonly results from systemic conditions
- Differential cyanosis (upper normal/lower hypoxic or upper hypoxic/lower normal) strongly suggests CHD

➢ Vital signs
- Hypotension
  - Observed in any critically ill infant
  - BP measurements useful for following changes in clinical condition, but not helpful diagnostically
- BP >20 mmHg higher in arms than legs: consider coarctation of aorta
- Persistent systemic hypertension may cause CHF
- Tachycardia: nonspecific, not helpful diagnostically; extremely fast rates (>250 bpm) suggest supraventricular tachycardia
- Bradycardia: generally assoc w/ hypoxia, vagal stimulation (e.g., passage of nasogastric tube); rarely indicative of bradyarrhythmia such as congenital heart block
- Tachypnea: non-specific, not helpful diagnostically

➢ Pulm findings
- Tachypnea observed in any infant w/ CHF
- Rales & wheezing may be heard as pulm edema develops

➢ Systemic findings
- Poor perfusion
- Edema
- Hepatomegaly

➢ Cardiovascular findings
- Cardiac impulse
  - Displaced: dextrocardia or dextroposition
  - Increased: possible RV hypertrophy
- Murmurs
  - May be innocent or significant, persistent or transient
  - Loudness does not correlate w/ severity of lesion
- Heart sounds
  - Muffled heart sounds: pericardial effusions or pneumopericardium
  - 3rd & 4th heart sounds commonly heard w/ CHF
  - Single 2nd heart sound: lesions w/ pulm hypertension, some types of cyanotic CHD (e.g., transposition of great vessels & pulm atresia)
  - Wide fixed splitting: atrial communications (e.g., atrial septal defect) or Ebstein's anomaly
  - Increased intensity of 2nd heart sound: pulm hypertension

- Perfusion/capillary refill time: general indicator of cardiac output; refill >3 sec (on trunk in thermally appropriate environment) abnl

➢ Assoc findings
- Symptoms referable to heart (murmurs, cyanosis w/o resp distress, abnl heart sounds) suggest structural heart disease
- Multiple malformations suggest underlying CHD (e.g., VACTERL or CHARGE assoc) or inborn errors of metabolism (e.g., lysosomal disorders assoc w/ craniofacial dysmorphism, eye abnormalities, hepatosplenomegaly & skeletal abnormalities)
- Infants w/ cerebral AV malformation can present w/ cranial bruit, intracranial hemorrhage, seizures or hydrocephalus
- Pallor (indicative of poor perfusion, asphyxia or severe anemia)

TESTS

■ Pulse oximetry
➢ Best way to assess arterial O_2 saturation
➢ Measurements: always incl right hand, foot to detect shunting through ductus arteriosus
➢ Values <90% abnl (normal values >= 95%)
➢ Decreased perfusion, movement, bright lights affect accuracy of readings

■ Hyperoxia test
➢ Useful to distinguish infants w/ fixed right-to-left shunts from other causes of cyanosis
➢ Infant allowed to breathe 100% O_2 & arterial blood gas measurement (or O_2 saturation determination) made, compared w/ one obtained before O_2 administered
➢ Infants w/ pulm edema secondary to CHF will often but not invariably show rise in arterial PO_2 >= 20–30 mmHg (or rise in O_2 saturation >10%)
➢ Infants w/ fixed right-to-left shunts show small increase in oxygenation, but < these amounts

■ CXR
➢ Cardiomegaly invariably present (except in total anomalous pulm venous return w/ obstruction)
➢ Pulm edema
- Obstructed anomalous pulm venous return
- Cor triatriatum
- Critical aortic stenosis w/ LV dysfunction

- Hypoplastic left heart syndrome w/ restrictive atrial septal defect

- ECG
  - ➢ Rarely diagnostic except for arrhythmias
  - ➢ R or L axis deviation may narrow DDx
- Echocardiogram
  - ➢ Definitive diagnostic method for CHD
  - ➢ Anomalies of aortic arch, anomalous pulm venous return can be difficult to identify
  - ➢ Confirms pulm hypertension
- Arterial blood gas determination
  - ➢ Invasive
  - ➢ For oxygenation, not more helpful than pulse oximetry
  - ➢ Provides useful information about arterial pH, PCO_2 & metabolic acid-base status. NOTE: Metabolic acidosis can be observed in infants w/ resp chain defects, glycogen storage diseases, fatty-acid oxidation defects.
- Hemoglobin concentration
  - ➢ In presence of anemia, decrease in% O_2 saturation necessary to produce cyanosis will be greater
  - ➢ Polycythemia may increase blood viscosity & pulm vascular resistance
    - Polycythemic infants appear plethoric: plethora can be confused w/ cyanosis
    - Plethoric infants develop cyanosis w/ lesser reductions in O_2 saturation
    - In rare instances polycythemia can be a cause of CHF
- Serum glucose concentration
  - ➢ Hypoglycemia: rare but easily treatable cause of CHF, cyanosis
- When metabolic disorder suspected
  - ➢ Plasma carnitine
  - ➢ Serum amino acids
  - ➢ Serum lactate, pyruvate levels
  - ➢ Urine organic acids
  - ➢ Urine oligosaccharides
  - ➢ Electromyography
  - ➢ Skin, muscle or myocardial biopsy
- Serum electrolytes

DIFFERENTIAL DIAGNOSIS

- CHD

- Metabolic disorders
- Arrhythmias
- Myocarditis
- Arteriovenous malformation
- Cardiomyopathies
- Severe anemia
- Polycythemia
- Hypoglycemia

MANAGEMENT

- What to do first
  - ABCs (airway, breathing, circulation)
  - Breathing spontaneously: 100% O_2 (hyperoxia test)
  - Evidence of resp distress: 100% O_2 should be administered w/ continuous positive airway pressure (CPAP)
  - If persists despite 100% O_2 & CPAP, or ventilation perceived to be inadequate, intubate & place on mechanical ventilation (mechanical ventilation may not be indicated if cyanotic CHD documented & no signs of pulm dysfunction)
- General measures
  - Provide BP support prn
  - If ductal dependent lesion strongly suspected or confirmed, begin PGE1 (0.05–0.1 mcg/kg/min)
  - Correction of metabolic acidosis w/ bicarbonate

SPECIFIC THERAPY

For CHF secondary to underlying structural heart disease

- Diuretic therapy (furosemide) to decrease intravascular vol, treat edema
- Digoxin for direct enhancement of cardiac performance
- Ionotropes (dopamine, dobutamine & epinephrine) to improve cardiac output
- Amrinone has both inotropic, peripheral vasodilator effects
- Surgical palliation or correction

FOLLOW-UP

N/A

COMPLICATIONS AND PROGNOSIS

N/A

CYANOSIS

RICHARD A. POLIN, MD

HISTORY & PHYSICAL

History

- Time of onset
  - ➢ Generalized cyanosis that persists beyond 1st few min of life is abnormal & suggests 1 of 3 problems:
    - Most commonly, acquired or congenital pulmonary disorders
      - Persistence of fetal circulation (pulmonary hypertension w/ right-to-left shunting)
      - Cyanotic CHD
      - A combination of the above
  - ➢ Sudden onset of cyanosis (unaccompanied by resp distress) suggests closure of patent ductus arteriosus in infant w/ "ductal dependent" heart defect
  - ➢ Common finding in any infant w/ apnea, bradycardia; resolves when apneic episode ends
- Maternal Hx
  - ➢ Oligohydramnios (before 20 wk gestational age): pulmonary hypoplasia
  - ➢ Antepartum culture positive for group B streptococcus or chorioamnionitis: pneumonia, sepsis
  - ➢ Coxsackie B viral infection: myocarditis in newborn infants
  - ➢ Meconium-stained amniotic fluid: meconium aspiration syndrome
  - ➢ Maternal conditions assoc w/ cardiac defects
    - Diabetes mellitus
    - Alcohol abuse
    - Lithium & trimethadione usage
  - ➢ Hx of CHD in 1st-degree relatives of infant being evaluated should increase suspicion of CHD
  - ➢ Mothers w/ anti-Ro or anti-La antibodies because of lupus erythematosus: 5% risk of fetus w/ heart block
- Duration
  - ➢ Persistent & generalized: cardiac or pulmonary disorder until proven otherwise
  - ➢ Intermittent
    - Apnea & bradycardia
    - Hypoglycemia

Physical

- Distribution
  - ➢ Acrocyanosis
    - Peripheral cyanosis that commonly represents cutaneous vasoconstriction secondary to cool environment
    - Less commonly may indicate reduced cardiac output, poor tissue perfusion
  - ➢ Central cyanosis
    - Cyanosis of oral mucous membranes indicative of generalized cyanosis due to reduction in systemic O_2 saturation (usually <70–80%)
    - Commonly results from systemic conditions
  - ➢ Differential cyanosis (upper normal/lower hypoxic or upper hypoxic/lower normal) strongly suggests CHD
- Vital signs
  - ➢ Hypotension
    - Observed in any critically ill infant
    - BP measurements useful for following changes in clinical condition; not helpful diagnostically
  - ➢ BP >20 mmHg higher in arms than legs: consider coarctation of aorta
  - ➢ Tachycardia: nonspecific, not helpful diagnostically
  - ➢ Tachypnea: nonspecific, not helpful diagnostically
- Pulmonary findings
  - ➢ Indicate pulmonary dysfunction, resulting from pulmonary or cardiac disease
  - ➢ Hyperpnea (deep unlabored breathing): indicative of conditions w/ reduced pulmonary blood flow
- Cardiovascular exam
  - ➢ Cardiac impulse
    - Displaced: dextrocardia or dextroposition
    - Increased: possible RV hypertrophy
  - ➢ Murmurs
    - May be innocent or significant, persistent or transient
    - Loudness does not correlate w/ severity of lesion (e.g., transposition of great vessels may have no detectable murmur)
  - ➢ Heart sounds
    - Muffled heart sounds: pericardial effusions or pneumopericardium

- Single 2nd heart sound: lesions w/ pulmonary hypertension, some types of cyanotic CHD (e.g., transposition of great vessels & pulmonary atresia)
- Wide fixed splitting: atrial communications (e.g., atrial septal defect) or Ebstein's anomaly
- Increased intensity of 2nd heart sound: pulmonary hypertension

➢ Perfusion/capillary refill time: general indicators of cardiac output; refill >3 sec (on trunk in thermally appropriate environment) abnormal

➢ Hepatomegaly (nonspecific indicator of high venous pressure)

■ Assoc findings

➢ Pulmonary disorders: signs, symptoms of resp distress (retractions, grunting, rales, rhonchi, flaring tachypnea)

➢ Apnea, bradycardia: self-limited, recurrent episodes of cyanosis

➢ Cyanotic CHD or CHF: signs, symptoms referable to heart almost always present

➢ Multiple malformations suggest underlying CHD or pulm malformation as part of larger syndrome (e.g., VACTERL or CHARGE associations)

TESTS

■ Pulse oximetry

➢ Best way to assess arterial O_2 saturation

➢ Measurements: always incl right hand, foot to detect shunting through ductus arteriosus

➢ Values <90% abnormal (normal values >= 95%)

➢ Decreased perfusion, movement, bright lights can affect accuracy of readings

■ Hyperoxia test

➢ Useful to distinguish infants w/ fixed right-to-left shunts from those w/ pulmonary disease

➢ Infant allowed to breathe 100% O_2 & arterial blood gas measurement (or O_2 saturation determination) made, compared w/ one obtained before O_2 was administered

➢ Infants w/ pulmonary disease will often but not invariably exhibit rise in arterial PO_2 >20–30 mmHg (or rise in O_2 saturation >10%)

➢ Infants w/ fixed right-to-left shunts will exhibit small increase in oxygenation, but < these amounts

■ CXR

- ➢ Cardiomegaly or abnormally shaped heart: CHD or CHF
- ➢ Diffuse lung disease: primary pulmonary process, but may be difficult to distinguish from pulmonary edema secondary to heart failure or obstruction to venous return
- ➢ Localized "infiltrates": not helpful, chamber enlargement or edema may cause localized areas of atelectasis
- ➢ Pulmonary malformations usually evident; may be subtle
- ➢ Right-sided aortic arch: vascular rings, CHD
- ➢ Degree of pulm blood flow should be assessed
  - Idiopathic pulmonary hypertension: decreased pulmonary blood flow
  - Cyanotic CHD: increased or decreased pulmonary blood flow

■ ECG
- ➢ Rarely diagnostic except for arrhythmias
- ➢ R or L axis deviation may narrow DDx

■ Echocardiogram
- ➢ Definitive diagnostic method for CHD
- ➢ Anomalies of aortic arch & anomalous pulmonary venous return can be difficult to identify
- ➢ Confirms pulmonary hypertension

■ Arterial blood gas determination
- ➢ Invasive
- ➢ For oxygenation, not more helpful than pulse oximetry measurements
- ➢ Provides useful information about arterial pH, PCO_2, metabolic acid-base status

■ Hgb concentration
- ➢ In presence of anemia, decrease in % O_2 saturation necessary to produce cyanosis will be greater
- ➢ Polycythemia may increase blood viscosity & increase pulmonary vascular resistance
  - Polycythemic infants appear plethoric: plethora can be confused w/ cyanosis
  - Plethoric infants develop cyanosis w/ lesser reductions in O_2 saturation

■ Serum glucose concentration
- ➢ Hypoglycemia: rare but easily treatable cause of cyanosis

■ Pneumocardiogram
- ➢ Useful for quantifying, categorizing breathing, heart rate disturbances in infants w/ suspected apnea

■ Color of blood

- ➢ Blood from infant w/ methemoglobinemia will not turn red when exposed to O_2

DIFFERENTIAL DIAGNOSIS

- CHD
- Pulmonary disease
- Pulmonary hypertension
- Apnea
- Methemoglobinemia
- Hypoperfusion/hypotension

MANAGEMENT

- What to do first
  - ➢ ABCs (airway, breathing, circulation)
  - ➢ Breathing spontaneously: 100% O_2 (hyperoxia test)
  - ➢ Evidence of respiratory distress; 100% O_2 w/ continuous positive airway pressure (CPAP)
  - ➢ If persists despite 100% O_2 & CPAP, or ventilation perceived to be inadequate, intubate & place on mechanical ventilation (mechanical ventilation may not be indicated if cyanotic CHD documented & no signs of pulmonary dysfunction)
- General measures
  - ➢ Provide BP support prn
  - ➢ If ductal-dependent lesion strongly suspected or confirmed, begin PGE1 (0.05–0.1 mcg/kg/min)

SPECIFIC THERAPY

Varies with etiology

- CHD: balloon atrial septostomy, shunt placement or corrective surgery
- NO or ECMO for life-threatening persistent pulmonary hypertension of the newborn

FOLLOW-UP

N/A

COMPLICATIONS AND PROGNOSIS

N/A

DIAPER DERMATITIS

RICHARD A. POLIN, MD
REVISED BY MARIA C. GARZON, MD

HISTORY & PHYSICAL

History

- Irritant/contact diaper dermatitis
  - ➢ Affects nearly 50% of children during infancy
  - ➢ Onset: few wk to 18 mo of life
  - ➢ Less common during neonatal period because fecal enzymes found in low concentrations
- Candida diaper dermatitis
  - ➢ Affects 3% of infants btwn 2–4 mo of age

Signs

- Irritant diaper dermatitis
  - ➢ Erythema, scaling on convex surfaces of upper thighs, buttocks
  - ➢ May become deeply erythematous
  - ➢ Creases generally spared
- Candida diaper dermatitis
  - ➢ Erythematous patch over vulval & perineal areas w/ peripheral scale & satellite lesions
  - ➢ Pink papules covered by scale that may coalesce
  - ➢ Inguinal creases commonly involved

TESTS

- Potassium hydroxide preparation for detection of fungal dermatophytes

DIFFERENTIAL DIAGNOSIS

- Candida diaper dermatitis
- Allergic/contact dermatitis
- Acrodermatitis enteropathica
- Other metabolic diseases (e.g., cystic fibrosis)
- Psoriasis
- Langerhans cell histiocytosis

MANAGEMENT

- Irritant/contact diaper dermatitis
  - ➢ Frequent diaper changes
  - ➢ Use of diapers w/ absorbable gel material

SPECIFIC THERAPY

- Irritant diaper dermatitis
  - ➢ Emollients or pastes (zinc oxide, petrolatum)
  - ➢ Severe cases: non-fluorinated corticosteroid (1% hydrocortisone) for limited time period (days)
- Candida diaper dermatitis
  - ➢ Topical anti-candidal agents (e.g., clotrimazole, ketoconazole, nystatin)

FOLLOW-UP

- None required if the dermatitis resolves; follow-up is recommended if the lesions persist or recur

COMPLICATIONS AND PROGNOSIS

- Excellent
- Recurrences are common

GASTROINTESTINAL BLEEDING

RICHARD A. POLIN, MD

HISTORY & PHYSICAL

- Spurious causes of bleeding (e.g., swallowed maternal blood) must be distinguished from true bleeding disorders
- Etiology obscure in >= 50% of cases
- In non-idiopathic cases, swallowed maternal blood, fissures represent most common etiologies
- Hemodynamically significant hemorrhages usually caused by gastric or duodenal ulcer
- Hematemesis suggests recent hemorrhage proximal to ligament of Treitz
- Hematochezia (maroon, bright-red blood in stool) generally represents blood loss from colon, but can occur from upper GI tract w/ rapid transit time
- Fissures generally cause streaks of blood localized to exterior of stool
- Melena (black tarry stool) generally indicates bleeding proximal to ileocecal valve (rarely may indicate bleeding from right colon if transit time slow)

- Blood denatured by gastric contents appears as coffee grounds
- Coagulation disorders rarely present w/ GI bleeding
- Hemoptysis from bronchopulmonary malformation may be difficult to distinguish from GI bleeding
- History
  - ➢ Time of presentation
    - Swallowed maternal blood: commonly causes hematemesis 12–24 hr after birth (may present as hematochezia)
    - Hemorrhagic disease of newborn
      - Early disease occurs in 1st 24 hr of life in babies born to women taking oral anticoagulants or anticonvulsants
      - Classic disease presents 1–7 days after birth in infants who did not receive vitamin K
      - Late-onset disease presents 1–3 mo of life frequently in breast-fed babies who have difficulty absorbing fat-soluble vitamins
    - Gastric & duodenal ulcers: present at any time in critically ill infants, but more commonly in acute phases of illness (beyond age 3 days)
      - Drugs assoc w/ gastric mucosal injury include indomethacin, dexamethasone
    - Malrotation: commonly presents w/ obstruction after birth, but may cause GI bleeding when assoc w/ ischemic damage
    - Intestinal duplication: commonly presents w/ obstruction or as abdominal mass
      - Bleeding may occur at any time due to presence of ectopic gastric mucosa or stasis & bacterial overgrowth
    - Meckel's diverticulum
      - Found in 2% of population: often asymptomatic
      - Note: "rule of two's"
        - Twice as common in males, found w/in 2 ft of ileocecal valve w/ length of 2 in
      - Painless rectal bleeding (even massive bleeding) can occur at any time during infancy or childhood
    - Congenital vascular malformations (e.g., hemangiomas)
      - Present w/ GI bleeding in early infancy (25% of cases)
      - Commonly assoc w/ cutaneous hemangiomas, but in some conditions (e.g., Osler-Weber-Rendu disease), GI bleeding may occur before skin lesions noticeable
    - Necrotizing enterocolitis

- Time of presentation inversely related to gestational age, commonly after oral feedings begun
- Rare in 1st few days of life
- Hirschsprung-associated enterocolitis
  - Most common presentation of Hirschsprung disease is constipation w/ failure to pass meconium, abdominal distention, feeding intolerance
  - 10–30% present w/ GI bleeding
- Infectious enterocolitis uncommon in neonatal period
- Milk protein intolerance
  - Commonly presents later in infancy with bloody, mucoid diarrhea, but may occur in 1st few days of life
- Rectal fissure
  - Bright-red bleeding can occur at any time
  - Usually not massive
  - Rectal fissures may be difficult to demonstrate (if you look long enough, it is easy to create a rectal fissure)

➢ Maternal Hx
- Swallowed maternal blood at delivery
- Fetal distress or perinatal asphyxia may predispose the infant to ulcer development
- Oral anticoagulants or anticonvulsants

■ Physical

➢ In the absence of shock secondary to blood loss, decide whether infant is critically ill w/ life-threatening disease (e.g., necrotizing enterocolitis or malrotation) or relatively well, w/ unexpected bleeding in stool (e.g., anal fissure, Meckel's diverticulum, swallowed maternal blood)

➢ Signs of obstruction? Consider malrotation, Hirschsprung disease.

➢ Abdominal mass? Consider duplication.

➢ Signs of peritonitis? Consider necrotizing enterocolitis, malrotation w/ ischemic bowel.

➢ Assoc findings
- Syndromes assoc w/ vascular malformations of GI tract:
  Blue rubber bleb nevus syndrome
  Osler-Weber-Rendu disease
  Klippel-Trenaunay syndrome
  Down syndrome
  Hirschsprung disease
  Meckel's diverticulum

- Malrotation: assoc w/ other GI malformations (omphalocele, gastroschisis, diaphragmatic hernia & duodenal atresia)

TESTS

- Apt-Downey test: to distinguish swallowed maternal blood from neonatal blood
  - ➢ Sample of emesis diluted 1:4 w/ H_2O, centrifuged to remove particulate debris; supernatant mixed w/ .25 N (1%) sodium hydroxide in ratio of 5:1; pink color produced if blood came from baby, yellow-brown color if adult
- Coagulation tests if Hx or physical suggests coagulation disorder
- Blood, stool cultures if sepsis or infectious diarrhea suspected
- Nasogastric lavage: useful for identifying bleeding from stomach or first portion of duodenum
- Abdominal radiographs (supine, upright, decubitus)
  - ➢ Useful for diagnosing necrotizing enterocolitis or intestinal obstruction
- Endoscopy can be done but is rarely required
- Meckel's scan (technetium-99 m pertechnetate) will identify ectopic gastric mucosa in Meckel's diverticulum or duplication: more difficult in young infants

DIFFERENTIAL DIAGNOSIS

- See "History and Physical"

MANAGEMENT

- What to do first
  - ➢ ABCs (airway, breathing, circulation)
- General measures
  - ➢ NPO
  - ➢ Nasogastric tube to decompress abdomen (iced saline lavage not very effective in stopping bleeding, may cause hypothermia)
  - ➢ Correction of hypovolemia
  - ➢ Correction of acidosis
  - ➢ Correction of fluid, electrolyte disturbances
  - ➢ Fluid resuscitation
  - ➢ Vitamin K, platelets, fresh frozen plasma for pts w/ coagulation disorders
  - ➢ H_2 blockers, antacids for upper GI bleeding (maintain gastric pH between 5 & 6)
  - ➢ Surgery indicated for intestinal ischemia, presumed dead bowel

SPECIFIC THERAPY
N/A

FOLLOW-UP
N/A

COMPLICATIONS AND PROGNOSIS
N/A

HEMOLYTIC DISEASES OF THE NEWBORN

SUJIT SHETH, MD

HISTORY & PHYSICAL

Maternal history
- Family Hx of:
  - Anemia
  - Hyperbilirubinemia
  - Gallstones
  - Splenectomy
- Maternal hemolytic anemia
- Medications: penicillin, cephalothin, alpha-methyl DOPA
- History suggestive of sepsis or DIC
- History of transfusions: platelets, FFP or PRBCs
- Large vessel thrombosis

Physical exam of newborn
- Pallor
- Jaundice
- Edema
- Hepatosplenomegaly
- Signs of high-output cardiac failure: tachycardia, gallop
- Temp, heart rate, or BP instability
- Signs c/w arteriovenous malformations, hemangiomas
- Signs c/w congenital heart disease: severe coarctation, severe valvular pulmonary stenosis
- Signs c/w congenital infections

TESTS
- Basic tests
  - CBC

- ➢ Reticulocyte count
- ➢ Peripheral blood smear review by hematologist/clinical pathologist for evidence of nucleated RBC, intravascular hemolysis (schistocytes), spherocytes, etc.
- ➢ Liver function tests: bilirubin, LDH

- Specific diagnostic tests
  - ➢ Blood group: maternal/infant ABO & Rh
  - ➢ Direct antiglobulin test (DAT, direct Coombs'); if positive, specificity
  - ➢ Cultures: viral, bacterial, fungal, serologies for TORCH infections
  - ➢ Coagulation profile, D-dimer
  - ➢ Hemoglobin electrophoresis (review parents' if available)
  - ➢ G6PD, PK enzyme assays
  - ➢ Osmotic fragility

DIFFERENTIAL DIAGNOSIS

- Immune-mediated hemolysis (diagnosis based on blood group, DAT)
  - ➢ ABO/Rh incompatibility
  - ➢ Minor blood group incompatibility: c, C, e, Kell, Duffy, Jka, MNS
  - ➢ Drug-induced (maternal antibody): penicillin, cephalothin, alpha-methyl DOPA
  - ➢ Maternal autoimmune hemolytic anemia
- Infection (specific cultures, serologies)
  - ➢ Bacterial sepsis (*E. coli*, group B streptococcus)
  - ➢ Congenital malaria
  - ➢ Congenital TORCH infections, other viral infections
  - ➢ DIC (coagulation screen, D-dimers)
- Inherited RBC membrane defects (morphology, osmotic fragility, genetics)
  - ➢ Spherocytosis
  - ➢ Elliptocytosis
  - ➢ Stomatocytosis
  - ➢ Pyropoikilocytosis
- Inherited RBC enzyme defects (specific enzyme assays)
  - ➢ G6PD deficiency
  - ➢ Pyruvate kinase (PK) deficiency
  - ➢ Hexokinase deficiency
  - ➢ Glucose phosphate isomerase deficiency
  - ➢ Pyrimidine 5′-nucleotidase deficiency

- Hgb defects (Hgb electrophoresis, specific genetic tests)
  - ➢ Alpha- & gamma-thalassemia syndromes
- Microangiopathic hemolysis (smear, specific radiologic tests)
  - ➢ Cavernous hemangiomas
  - ➢ Arteriovenous malformations
  - ➢ Renal artery stenosis
  - ➢ Any large vessel thrombus
  - ➢ CHD (severe aortic coarctation, valvular stenoses)
  - ➢ After surgery in which a graft is placed ("Waring blender" effect)
- Other (appropriate specific tests)
  - ➢ Galactosemia
  - ➢ Lysosomal storage diseases
  - ➢ Prolonged metabolic acidosis
  - ➢ Transfusion reactions
  - ➢ Drug-induced hemolysis (valproic acid)

MANAGEMENT

- What to do first
  - ➢ Stabilize patient
  - ➢ Obtain blood samples for all appropriate diagnostic tests before specific therapy
- General measures
  - ➢ Hydration (if cardiac compromise, do not overhydrate)
  - ➢ Phototherapy for hyperbilirubinemia
  - ➢ Antibiotics as appropriate
  - ➢ FFP, platelets as indicated for DIC

SPECIFIC THERAPY

Varies w/ specific etiology

Anemia resulting from hemolytic process treated w/ transfusion

- Simple packed RBC transfusion
  - ➢ Indications
    - Severe anemia (Hgb <7 g/dL) w/o symptoms
    - Signs of cardiac compromise
    - Poor perfusion or oxygenation for other reasons (maintain Hgb >10 g/100 mL)
    - Ongoing hemolysis, falling Hgb

    NOTE: If hematocrit continues to fall, may need to transfuse repeatedly
  - ➢ Precautions
    - Appropriate cross-matching

- Irradiated, leukocyte-filtered blood products must be used
- Slow transfusion in aliquots of 5–10 cc/kg

➢ Absolute contraindication: none
➢ Relative contraindication: high-output cardiac compromise
➢ Complications
- Transfusion reactions (febrile, allergic, hemolytic)
- Transmission of bloodborne infections
- Alloimmunization

■ Double volume exchange transfusion
➢ Indication
- Hyperbilirubinemia (see **HYPERBILIRUBINEMIA, UNCONJUGATED**)
- High-output cardiac compromise
- Persistent high-titer DAT w/ continuing rapid hemolysis

➢ Precautions
- Appropriate cross-matching
- Irradiated, leukocyte-filtered blood products must be used
- Achieve appropriate post-transfusion Hgb

➢ Contraindications: none
➢ Complications
- Transfusion reactions (febrile, allergic, hemolytic)
- Thrombocytopenia, coagulopathy
- Hyperkalemia, hypocalcemia
- Transmission of bloodborne infections
- Alloimmunization
- Complications related to umbilical venous catheterization

FOLLOW-UP

■ During treatment
➢ Physical examination
➢ Hgb, bilirubin

■ Long-term
➢ Transient hemolytic disease: developmental as indicated for complications of anemia/hyperbilirubinemia
➢ Persistent hemolytic disease: hematology consultation & follow-up

COMPLICATIONS AND PROGNOSIS

■ Alloimmune hemolysis
➢ Self-limited

- ➢ Long-term outcome related to complications of anemia/hyperbilirubinemia
- Inherited hemolytic anemias
  - ➢ May be predisposed to gallstones
  - ➢ May require splenectomy
  - ➢ Counseling parents for future pregnancies

HEPATOMEGALY

RICHARD A. POLIN, MD

HISTORY & PHYSICAL

- Palpable liver does not equate w/ hepatomegaly
- In general, a palpable liver >3.5 cm below right costal margin indicates enlargement
- At 1 wk of life, normal liver span is 4.5–5 cm
- W/ inspiration liver moves down 1–3 cm
- Hepatomegaly: 5 possible causes
  - ➢ Inflammation
  - ➢ Excessive storage
  - ➢ Infiltration
  - ➢ Congestion
  - ➢ Obstruction
- History
  - ➢ Family Hx of early infant death or hepatic or neurodegenerative disease suggests metabolic etiology
  - ➢ Time of presentation
    - Biliary tract obstruction: onset in infancy (almost never at birth)
    - Concurrent w/ congestive heart failure (see **CONGESTIVE HEART FAILURE**)
    - Isoimmunization: at birth in infants w/ extramedullary hematopoiesis
    - Maternal diabetes: birth
    - Congenial cysts: birth
    - Parenteral nutrition: 2–6 wk after start of parenteral nutrition
    - Sepsis: concurrent w/ sepsis episode
    - Drugs: concurrent w/ drug therapy
      - Phenobarbital, Dilantin & corticosteroids lead to steatosis
    - Viral hepatitis/TORCH infection

- TORCH infections can produce hepatomegaly at birth
- Hepatitis B: 1–4 mo after birth (5% transmitted as congenital infection)

- Metastatic neuroblastoma (see **NEUROBLASTOMA** in the "Neonatal Conditions and Diseases" section)
  - Most common malignant tumor of liver
  - Liver most common site of metastasis, hepatomegaly may be present at birth
- Metabolic disorders
  - Alpha-1-antitrypsin deficiency
    - 10% of affected infants w/ PiZZ genotype present in neonatal period w/ cholestatic jaundice +/− hepatomegaly (generally 2–3 wk of life)
  - Neonatal hemochromatosis: commonly symptomatic at birth
  - Tyrosinemia: commonly detected at 3–4 mo of life (rarely presents in neonatal period)
  - Galactosemia: commonly symptomatic in newborn period w/ initiation of lactose intake (hepatomegaly uncommon). *E. coli* sepsis can be a presenting sign.
  - Glycogen storage disease types 1a, 1b: hypoglycemia, hepatomegaly in neonatal period
  - Mucopolysaccharidosis type VII: occasional presentation in neonatal period
  - Oligosaccharidoses (e.g., fucosidosis): onset in neonatal period
  - GM1 gangliosidosis: hepatosplenomegaly may be detected shortly after birth (usually w/in 3–6 mo)
  - Hereditary fructose intolerance: rarely presents in neonatal period because exposure to fructose limited
  - Wolman disease: w/in weeks of birth
  - Zellweger syndrome: onset at birth
  - Cystic fibrosis
    - Steatosis occurs in periods of poor nutrition
    - 5% develop neonatal cholestasis
  - Niemann-Pick disease
    - Type A: presents in utero to 1 y of age
    - Type C: commonly presents in neonatal period w/ conjugated hyperbilirubinemia, hepatosplenomegaly & liver dysfunction

- Gaucher disease type 2: onset of hepatomegaly at ~3 mo of age
- Beckwith-Wiedemann syndrome: onset at birth
- Mucolipidosis
  - I cell disease: onset at birth
  - Sialidosis type 2: onset at birth w/ infantile form
- Disorders of bile-acid metabolism: neonatal period to age 3 mo

- Starvation/malnutrition
- Budd-Chiari syndrome: rare presentation in infancy
  - Secondary to congenital diaphragmatic hernia w/ hepatic vein obstruction
  - Hepatic venous or caval obstruction secondary to prothrombotic disorder or polycythemia
- Hepatoblastoma: neonatal period to age 3 y
- Histiocytosis/familial erythrophagocytic lymphohistiocytosis: can present in neonatal period

➢ Maternal conditions
- Maternal diabetes
- Rh disease: extramedullary hematopoiesis

■ Physical
➢ Hepatomegaly may be subtle or missed in neonatal period
➢ Size, nodularity, consistency of liver should be noted
➢ Determine if splenomegaly also present
- Splenomegaly: more common w/ congenital infections or metabolic disease

➢ Infants w/ multiple malformations or suspected inborn error of metabolism should have eye exam by experienced ophthalmologist
➢ Associated findings
- Maternal diabetes
  - Hypoglycemia, macrosomia, hyperbilirubinemia, polycythemia, hypocalcemia, respiratory distress syndrome
- Biliary atresia
  - Extrahepatic: polysplenia heterotaxia syndrome in 10–15% of cases
- Isoimmunization: hydrops
- TORCH infections
  - Microcephaly/hydrocephaly
  - Organomegaly
  - Chorioretinitis

- Hepatoblastoma: Beckwith-Wiedemann syndrome/hemihypertrophy
- Beckwith-Wiedemann syndrome
  - Macrosomia, abdominal wall defect & macroglossia
- Metastatic neuroblastoma: blue subcutaneous nodules
- Metabolic disease
  - Alpha-1-antitrypsin deficiency
  - Neonatal hemochromatosis: hypoglycemia, hypoalbuminemia, edema, ascites, thrombocytopenia & bleeding
  - Tyrosinemia: cirrhosis, proximal renal tubular dysfunction, hypophosphatemic rickets & peripheral neuropathy
  - Galactosemia: poor growth, vomiting, poor feeding, jaundice, cataracts, *E. coli* sepsis, renal Fanconi syndrome
  - Glycogen storage disease
    - Type 1a: doll-like facies, lactic acidosis, hypoglycemia, hyperlipidemia
    - Type 1b: same as type 1a, but w/ neutropenia
  - Mucopolysaccharidosis type VII
    - Hydrops fetalis, hepatosplenomegaly, coarse facies, corneal clouding, inguinal & umbilical hernias, skeletal dysplasia
  - Oligosaccharidoses
    - Coarse facies, limitation of joint movement, hepatosplenomegaly, corneal clouding & gingival hypertrophy
  - Generalized GM1 gangliosidosis
    - Coarse skin & facial features, frontal bossing, depressed nasal bridge, maxillary hyperplasia, large, low-set ears, wide upper lip, gingival hypertrophy, cherry red spot & corneal clouding
  - Hereditary fructose intolerance
    - Poor feeding, vomiting, hypoglycemia & poor growth
  - Wolman disease: malnutrition, malabsorption, adrenal calcifications
  - Zellweger syndrome: dysmorphic facial features, hypotonia, seizures, multicystic kidneys, eye abnormalities, skeletal abnormalities
  - Cystic fibrosis
  - Niemann-Pick disease
    - Type A: constipation, feeding difficulties
    - Type C: hypotonia & delayed motor development

- Gaucher disease (type 2): hydrops fetalis, congenital icthyosis & collodion babies
- Mucolipidosis
  - I cell disease
    - Coarse features, corneal clouding, hypotonia & gingival hyperplasia
  - Sialidosis type 2: hydrops fetalis, ascites & bony abnormalities

TESTS

- CBC w/ differential count
- Hepatic profile
  - ➢ Fractionated bilirubin
  - ➢ Serum aminotransferases
  - ➢ Gamma-glutamyl transpeptidase
  - ➢ Alkaline phosphatase
  - ➢ Albumin
  - ➢ Prothrombin time
- If there is conjugated bilirubin elevated w/ splenomegaly:
  - ➢ TORCH infections
  - ➢ Metabolic disease
- If there is conjugated bilirubin elevated w/o splenomegaly:
  - ➢ Abdominal US
    - Choledochal cyst
    - Liver tumors
  - ➢ Liver biopsy +/− liver scan
    - Neonatal hepatitis
    - Biliary atresia
    - Parenteral nutrition
    - Toxins
- If there is mixed conjugated/unconjugated hyperbilirubinemia or only unconjugated hyperbilirubinemia:
  - ➢ US +/− liver biopsy
    - Congestive heart failure
    - Drug/toxins
    - Hemolytic anemia
- If no hyperbilirubinemia, but splenomegaly present:
  - ➢ Abdominal US
    - Vascular obstruction
    - Liver tumors

- Metabolic disease

■ If no hyperbilirubinemia, no splenomegaly:
  ➢ Abdominal US
    - Primary & metastatic tumors
    - Infants of diabetic mothers
    - Malnutrition
■ CT/MRI may be better at identifying small lesions
■ Genetics consultation for suspected metabolic disease

DIFFERENTIAL DIAGNOSIS
See "History and Physical"

MANAGEMENT
■ What to do first
  ➢ Correct metabolic disturbances (hypocalcemia, hypoglycemia, metabolic acidosis)
  ➢ Treat sepsis

SPECIFIC THERAPY
N/A

FOLLOW-UP
N/A

COMPLICATIONS AND PROGNOSIS
N/A

HYPERBILIRUBINEMIA, CONJUGATED

RICHARD A. POLIN, MD

HISTORY & PHYSICAL
■ Direct bilirubin concentration 50–90% of the total bilirubin concentration (a small amount of unconjugated bilirubin always present)

History
■ Time of presentation
  ➢ Extrahepatic biliary disease
    - Extrahepatic atresia: jaundice usually apparent 2nd-6th wk of life
    - Choledochal cyst: can be detected w/ prenatal US, rarely symptomatic in neonatal period
    - Bile duct stenosis: similar presentation to biliary atresia

- Perforation of bile duct: 3–8 wk of life w/ emesis, acholic stools, mild cholestasis, abdominal distention (ascites)
- Neoplasm: rare w/ variable time of presentation: malignant tumors (60–70%) include neuroblastoma, hepatoblastoma. Benign tumors include hemangioma, hemangioendothelioma, hamartoma.
- Cholelithiasis: time of presentation variable, usually related to anatomic malformation, hemolytic disease, cystic fibrosis or medical intervention (furosemide/TPN)

➢ Intrahepatic biliary disease
- Intrahepatic bile duct paucity
  - Familial (Alagille syndrome): jaundice usually apparent between 2nd-6th wk of life, but other manifestations may permit earlier diagnosis
  - Non-syndromic forms: variable time of presentation assoc w/ variety of conditions
- Inspissated bile: variable time of presentation, assoc w/ hemolytic disease & TPN; w/ intrauterine hemolysis cholestasis may be evident at birth
- Cystic dilatation of intrahepatic bile ducts, Caroli disease (rarely presents in neonatal period)
- Congenital hepatic fibrosis: typically presents as GI bleeding in older children; multiple associations, including autosomal recessive polycystic disease

➢ Hepatocellular disease
- Metabolic diseases
  - Disorders of amino acid metabolism (e.g., hereditary tyrosinemia): presents in 1st 6 mo of life w/ liver failure
  - Disorders of lipid metabolism
    - Wolman disease: presents in first few weeks of life w/ failure to thrive, vomiting, abdominal distention, hepatosplenomegaly
    - Niemann-Pick disease: may present in neonatal period w/ hepatosplenomegaly, jaundice
    - Gaucher disease: infantile form presents in 1st to 6th mo of life w/ hepatosplenomegaly & neurological deterioration
  - Disorders of carbohydrate metabolism
    - Galactosemia: onset of symptoms concurrent w/ intake of lactose, vomiting, diarrhea, cataracts, liver, renal dysfunction

- Hereditary fructose intolerance: infants asymptomatic in absence of fructose, sucrose or sorbitol intake; clinical symptoms include failure to thrive, vomiting, diarrhea, hepatomegaly, renal dysfunction, bleeding, anemia
- Type IV glycogen storage disease: presents in infancy w/ liver failure, occasionally muscle weakness

- Peroxisomal disorders
  - Zellweger syndrome: hepatomegaly, cholestasis usually present at birth, assoc w/ characteristic facies, hypotonia, seizures, profound retardation
  - Adreno-leukodystrophy: may present in infancy w/ liver dysfunction, neurol deterioration, evidence of adrenocortical dysfunction

- Endocrine disorders
  - Hypopituitarism: may present in neonatal period w/ conjugated or unconjugated hyperbilirubinemia, hypoglycemia, micropenis
- Familial "uncharacterized" excretory defects
  - Dubin Johnson: may present at any time from neonatal period to 4th decade w/ variable degrees of conjugated hyperbilirubinemia
  - Rotor syndrome: may present at any time from neonatal period to 4th decade with variable degrees of conjugated hyperbilirubinemia
  - Byler syndrome: presents in neonatal period w/ progressive cholestatic liver disease leading to chronic liver failure, death
  - Aagenaes syndrome: cholestasis assoc w/ lymphedema of lower extremities
  - Familial benign intrahepatic cholestasis: episodic jaundice, pruritus, elevated bile acids
- Defective bile acid synthesis: presents shortly after birth w/ cholestasis, liver failure
- Defective protein synthesis
  - Cystic fibrosis: multiple presentations, may present in neonatal period w/ cholestasis
  - Alpha-1-antitrypsin deficiency: typically presents w/ jaundice in 1st 4 months of life; 5–10% of infants w/ neonatal cholestasis will be deficient in alpha-1-antitrypsin
- Infections
  - TORCH: hepatitis may begin in utero

- Toxoplasmosis: 40% cholestasis, 60% hepatomegaly
- Syphilis: cholestasis develops in 1st 24 h of life
- Rubella: cholestasis 14%, hepatosplenomegaly 60%
- Cytomegalovirus: only 10% symptomatic, but 2/3 of these infants have cholestasis

- Hepatitis B: intrapartum acquisition commonly presents 4–8 wk of life
- Herpes simplex: fulminant infection w/ onset usually beyond 24 h of life
- Coxsackie B/ECHO virus: commonly presents in 1st wk of life w/ hepatitis
- Bacterial sepsis: onset cholestasis w/ sepsis episode

- Iatrogenic
  - Total parenteral nutrition: cholestatic jaundice appears 2–4 wk after beginning TPN
  - Drug or toxin: onset of symptoms concurrent w/ toxin exposure
- Idiopathic neonatal hepatitis: accounts for 40% of neonatal cholestasis; major manifestations: jaundice, hepatosplenomegaly
- Neonatal hemochromatosis: presents at birth w/ hepatomegaly, hypoglycemia, hypoprothrombinemia, hypoalbuminemia progressing to liver failure
- Shock or hypoperfusion

■ Maternal History
  ➢ History suggestive of infection w/ TORCH agent, enterovirus or colonization w/ herpes simplex virus

Physical

■ Neonatal cholestasis may occur in otherwise asymptomatic infant or be assoc w/ variety of other clinical manifestations (see above)
■ Assoc findings
  ➢ Clinical manifestations that suggest metabolic disease
    - Hepatomegaly (+/− splenomegaly), fulminant hepatic failure
    - Hypoglycemia, organic acidemia, lactic acidemia, hyperammonemia, coagulopathy
    - Recurrent vomiting, failure to thrive
    - Developmental delay, psychomotor retardation
    - Cardiac dysfunction/failure, unusual odor, rickets, cataracts
  ➢ Clinical manifestations that suggest TORCH infection

- Intrauterine growth restriction
- Hepatosplenomegaly
- Cataracts
- Retinopathy
- Microcephaly
- Hydrocephalus
- Cerebral calcifications
- Bone lesions

➢ Dysmorphic features
- Alagille syndrome: characteristic facies, pulmonary artery hypoplasia or stenosis (occasionally tetralogy of Fallot), butterfly vertebral defects, posterior embryotoxon in eye, tubulointerstitial nephropathy
- Aagenaes syndrome: lymphedema
- Zellweger: characteristic facial appearance, weakness, seizures, eye abnormalities, hypotonia

➢ Cystic fibrosis: meconium ileus/peritonitis

➢ Extrahepatic biliary atresia: assoc anomalies found in 10–25% of pts, organ systems most commonly involved cardiovascular, GI, urinary

➢ Neurological abnormalities
- Niemann-Pick (age 2–3 y)
- Zellweger
- Gaucher disease
- Sepsis/meningitis/encephalitis

➢ Metastatic diseases

➢ Renal disease
- Congenital hepatic fibrosis: renal cysts
- Galactosemia
- Tyrosinemia
- Hereditary fructose intolerance

➢ Hypopituitarism: hypoglycemia, micropenis

➢ Hepatomegaly
- Tyrosinemia
- Congenital hepatic fibrosis
- Glycogen storage disease type IV
- Wolman disease
- Niemann-Pick
- Gaucher disease
- Inborn errors of bile acid synthesis
- Neonatal hemochromatosis

- Galactosemia
- Hereditary fructose intolerance
- Alpha-1-antitrypsin deficiency
- Biliary atresias
- Hypopituitarism
- Idiopathic neonatal hepatitis
- Infectious hepatitis
- Byler disease

➢ Hepatocyte injury
- Metabolic & genetic disease
- Perinatal infections
- Idiopathic neonatal hepatitis
- TPN cholestasis (long-standing)

TESTS

- General screening of liver function
  - ➢ Total & direct serum bilirubin
  - ➢ Serum bile acids
  - ➢ Liver enzymes
    - Alkaline phosphatase
    - Aspartate (AST) & alanine (ALT) aminotransferases
    - Gamma-glutamyltransferase (GGT)
  - ➢ Liver synthetic function
    - Prothrombin time
    - Total protein
    - Albumin
  - ➢ Stool pigment
- Abdominal US: important first-line test; useful for detection of stones, choledochal duct cyst, stones, sludge, ascites; absence of gall bladder strongly suggests biliary atresia; presence of gall bladder does not exclude biliary atresia
- Hepatobiliary scintigraphy (DISIDA scans)
  - ➢ Hepatitis: poor uptake w/ delayed excretion
  - ➢ Biliary atresia: normal uptake w/ absent excretion on delayed images of up to 24 h
    - Presence of excretion excludes biliary atresia
    - Absence of excretion does not prove biliary atresia since infants w/ severe cholestasis may have absent excretion [oral administration of phenobarbital (5 mg/kg/day) for 5 days prior to study enhances biliary excretion of isotope in pts w/ hepatitis]

- Liver biopsy: operative cholangiogram often done at the time of surgery
- Disease-specific tests
  - Alpha-1-antitrypsin deficiency: proteinase inhibitor (Pi) typing & serum alpha-1-antitrypsin level
  - Hemolytic disease: Hgb, Hct, blood smear, reticulocyte count (Coombs test where indicated)
  - Tyrosinemia, Zellweger
    - Serum & urine amino acids
    - Urine organic acids
  - Galactosemia: urine reducing substances
  - Hypothyroidism: thyroxine & TSH
  - Cystic fibrosis: sweat chloride
  - Neonatal hemochromatosis: serum Fe, total Fe binding capacity, serum ferritin
  - Congenital infection: serologic tests for evidence of infection/viral culture

DIFFERENTIAL DIAGNOSIS

See "History and Physical"

MANAGEMENT

- General measures
  - Nutrition
    - Provide adequate calories
    - Supplement diet w/ medium-chain triglycerides
    - Supplement diet w/ fat-soluble vitamins
  - Pruritus/xanthoma
    - Phenobarbital
    - Cholestyramine
  - Ascites
    - Low-sodium diet/diuretics
  - Liver failure
    - Transplantation

SPECIFIC THERAPY

N/A

FOLLOW-UP

N/A

COMPLICATIONS AND PROGNOSIS

N/A

HYPERBILIRUBINEMIA, UNCONJUGATED

RICHARD A. POLIN, MD

HISTORY & PHYSICAL

History

- Time of presentation
  - ➢ Physiologic hyperbilirubinemia: 2nd DOL
  - ➢ Hemolytic disease: 1st DOL if hemolysis begins in utero (e.g., blood group incompatibility), or concurrent w/ hemolytic episode (e.g., sepsis)
  - ➢ Bruising/polycythemia/sequestered blood: prolonged & exaggerated physiologic hyperbilirubinemia
  - ➢ Breast-feeding jaundice: concurrent w/ physiologic hyperbilirubinemia
  - ➢ Breast milk jaundice: beyond 3–5 DOL
  - ➢ Crigler-Najjar syndrome: 1st DOL
  - ➢ Lucey-Driscoll syndrome: 1st 48 h of life
  - ➢ Pyloric stenosis: exaggerated physiologic hyperbilirubinemia or prolonged hyperbilirubinemia
  - ➢ Hypothyroidism: prolonged & exaggerated physiologic hyperbilirubinemia
  - ➢ G-6–PD heterozygotes (w/o hemolysis): exaggerated physiologic hyperbilirubinemia
- Duration
  - ➢ Self-limited
    - Physiologic hyperbilirubinemia: Mild jaundice can persist for 1–2 wk (duration inversely related to gestational age)
    - Bruising/polycythemia
    - G-6–PD heterozygotes
    - Breast-feeding jaundice
  - ➢ Prolonged
    - Hypothyroidism
    - Breast milk jaundice
    - Hemolysis (isoimmunization, erythrocyte biochemical defects, erythrocyte structural defects)
    - Lucey-Driscoll syndrome
    - Pyloric stenosis
    - Obstructive intestinal lesions

- ➢ Permanent
  - Crigler-Najjar syndrome
- Maternal history
  - ➢ Previous pregnancy w/ Rh-sensitized fetus
  - ➢ Gravidity
    - Maternal sensitization to Rh antigen rarely manifests itself w/ first pregnancy
    - ABO disease may occur in firstborn w/o prior sensitization
  - ➢ Ethnic differences
    - Serum unconjugated bilirubin levels are higher in certain Greek populations, Chinese, Japanese, Korean, American Indian, other Asian populations
  - ➢ Oxytocin (assoc w/ hyperbilirubinemia, cause/effect relationship unproven)
  - ➢ Breast feeding
- Associated findings
  - ➢ Hepatosplenomegaly
    - Intrauterine infection
    - Hemolytic disease
  - ➢ Pyloric stenosis
  - ➢ Hypothyroidism: 95% asymptomatic (occasional lethargy, hypotonia, periorbital edema, large fontanelles, perioral cyanosis, mottled skin, hoarse cry, constipation, hypothermia)

Signs

- Most infants w/ hyperbilirubinemia are asymptomatic except for jaundice
  - ➢ Jaundice: cephalocaudad progression so can ROUGHLY approximate serum bilirubin concentration based on degree of jaundice progression
    - Head: 5.9 +/− 0.3 mg/dL
    - Chest: 8.9 +/− 0.7 mg/dL
    - Knees: 11.8 +/− 0.8 mg/dL
    - Ankles: >15 mg/dL
  - ➢ Once phototherapy started, visual inspection unreliable
- Clinical signs occur w/ development of kernicterus (bilirubin encephalopathy)
  - ➢ Lethargy: nonspecific finding of bilirubin-induced neurological dysfunction
  - ➢ Preterm infants: appear ill w/o specific signs of kernicterus
  - ➢ Term infants

- Phase I: poor suck, hypotonia, diminished sensorium
- Phase II: fever, hypertonia (may progress to opisthotonos)
- Phase III: hypertonia lessens, high-pitched cry, hearing & visual abnormalities, poor feeding, athetosis

TESTS

- Total serum bilirubin
  - ➢ Generally not necessary to fractionate conjugated/unconjugated bilirubin when jaundice begins shortly after birth
  - ➢ When hemolysis begins in utero conjugated bilirubin levels can be increased at birth
  - ➢ Notoriously inaccurate measurement
  - ➢ For most infants, this is only measurement that is needed
- Additional studies indicated if:
  - ➢ Cord blood bilirubin concentration is >4 mg/dL
  - ➢ Serum bilirubin rising at rate >0.5 mg/h or >5 mg/day
  - ➢ Total serum bilirubin exceeds 17 mg/dL in full-term or 10 mg/dL in preterm infant
  - ➢ When phototherapy is begun
  - ➢ When clinical jaundice persists beyond 10 days in full-term or 21 days in preterm infant
- Further diagnostic studies depend on careful history & physical exam
  - ➢ For suspected hemolytic disease: maternal, infant blood types, direct/indirect Coombs test, smear for erythrocyte morphology, reticulocyte count

DIFFERENTIAL DIAGNOSIS

- Physiologic hyperbilirubinemia
- Hemolytic disease
- Breast-feeding jaundice
- Breast milk jaundice
- Hypothyroidism
- Pyloric stenosis
- Obstructive lesions of intestine
- Lucey-Driscoll syndrome
- Crigler-Najjar syndrome
- G-6–PD heterozygotes

MANAGEMENT

- What to do first

➢ Careful history & physical exam to exclude life-threatening problems like sepsis, to identify infants w/ hemolytic disease

■ General measures

➢ Phototherapy

- First-line treatment
- Generally begun 4–5 mg/dL below exchange transfusion level (see below)
- Clinical pearls
  - Maximize skin surface area exposed to phototherapy (if bilirubin levels high, use fiberoptic pad underneath infant AND lights from above)
  - Special blue/tungsten lights most effective (caution: tungsten halide lamps produce a lot of heat, can burn skin if placed too close)
  - Light does not have to be administered continuously; lights can be turned off briefly (for intervals of 15–30 min) w/o losing effectiveness
  - If meter available to measure energy output of phototherapy light, use doses of light >= 10 micro watts/cm^2/nm
    - Dose-response relationship between energy output of light, decrement in serum bilirubin
    - Doses of light up to 30 micro watts/cm^2/nm increasingly effective
- Risks
  - Increased insensible H_2O loss (minor issue)
  - Increased stooling (rare)
  - Bronze baby syndrome (rare)
  - Overheating/burning (preventable)

➢ Exchange transfusion (EXTX)

- Used when serum bilirubin concentration reaches level that places infant at risk for bilirubin-induced brain injury

■ General guidelines for phototherapy & exchange transfusion

➢ Preterm infants

- Birth wt <1250 g: photorx @ total serum bilirubin (TSB) 5–7, EXTX @ TSB 10–13
- Birth wt 1250–1499 g: photorx @ TSB 7–10, EXTX @ TSB 13–16
- Birth wt 1500–1999 g: photorx @ TSB 10–12, EXTX @ TSB 16–18
- Birth wt 2000–2500 g: photorx @ TSB 12–14, EXTX @ TSB 18–20

See Pediatrics 114:297–316, 2004

NOTE: Preterm infants w/ risk factors for kernicterus should be exchanged at lower part of range; risk factors incl perinatal

asphyxia, ongoing hypoxemia, persistent hypothermia, hypoalbuminemia (<2.5 g/dL), hemolysis, sepsis or CNS depression

➢ Healthy term newborns
- Age <24 h: TERM INFANTS WHO BECOME JAUNDICED IN FIRST 24 H OF LIFE NOT CONSIDERED HEALTHY
- Age 25–48 h: photorx @ TSB >15, EXTX @ TSB >20, if photorx fails, EXTX + photorx @ TSB >25
- Age 49–72 h: photorx @ TSB >18, EXTX @ TSB >25, if photorx fails, EXTX + photorx @ TSB >30
- Age >72 h: photorx @ TSB >20, EXTX @ TSB >25, if photorx fails, EXTX + photorx @ TSB >30

➢ Sick term newborns or term newborns w/ suspected/proven hemolysis
- Age <24 h: photorx @ TSB >10–14, EXTX @ TSB >20
- Age >= 24 h: photorx @ TSB >15, EXTX @ TSB >20

SPECIFIC THERAPY
N/A

FOLLOW-UP
N/A

COMPLICATIONS AND PROGNOSIS

Complications
- Kernicterus

Prognosis
- Excellent when unconjugated bilirubin levels maintained below exchange transfusion concentrations noted above

HYPERCALCEMIA

WINSTON KOO, MD

DEFINITION
- Serum or plasma total calcium (tCa) > 2.75 mmol/L (11 mg/dL)
- Serum or plasma ionized calcium (iCa) > 1.4 mmol/L (5.6 mg/dL)

HISTORY AND PHYSICAL

History
- Low or no phosphate, but Ca-containing parenteral nutrition

- Perinatal asphyxia & assoc complications (subcutaneous fat necrosis, alkali & ECMO therapy)
- Excessive infant or maternal vitamin D or A intake
- Family or maternal calcium or phosphorus disorders

Physical examination

- Most cases are asymptomatic
- May have poor growth parameters, lethargy, dehydration due to polyuria +/− vomiting, seizures, hypertension, band keratopathy (rare)
- Associated features: e.g., subcutaneous fat necrosis; "elfin" facies, CHD, mental retardation w/ underlying syndrome

TESTS

- Basic
  - ➢ Serum or plasma tCa & iCa, magnesium (Mg), phosphorus (P), alkaline phosphatase (AP) (total & bone specific), creatinine (Cr); blood gas; serial monitoring q12–24 h until normal ×2
  - ➢ Urine Ca, P, Cr
- Specific
  - ➢ Simultaneous serum or plasma "intact" or "whole" parathyroid hormone (PTH), vitamin D metabolites [25 OH- & 1,25 (OH)2-vitamin D]
  - ➢ Urine amino acids
  - ➢ Radiographs of hands (hyperparathyroidism) & chest (heart defect), abdomen (renal calcification)
  - ➢ ECG (shortened Q-T interval)
  - ➢ Ophthalmologic evaluation
- Other tests as appropriate
  - ➢ Serum PTH-related protein
  - ➢ Screening for occult tumors
  - ➢ Parental serum & urine Ca & P screening may lead to other tests for all family members, including molecular testing (e.g., Ca sensing receptor mutations)

DIFFERENTIAL DIAGNOSIS

DDX of signs and symptoms

- Any disorder that results in lethargy, refusal to feed, vomiting, failure to thrive, or complications & other symptoms & signs of hypercalcemia

DDX of pathogenesis

- Phosphate deficiency
  - ➢ Low or no phosphate, but Ca-containing parenteral nutrition
  - ➢ VLBW infants fed human milk or, less commonly, standard formula
- Parathyroid related
  - ➢ Hereditary primary hyperparathyroidism
    - Ca sensing receptor inactivating mutations: familial hypocalciuric hypercalcemia, severe neonatal hyperparathyroidism
    - PTH receptor mutation
  - ➢ Secondary hyperparathyroidism
    - Maternal: hypocalcemia, renal tubular acidosis
    - Neonatal: renal tubular acidosis
- Parathyroid hormone-related protein-secreting tumors
- Vitamin D
  - ➢ Excessive intake in:
    - Mother: increase milk vitamin D
    - Neonate: high-dose vitamin D prophylaxis, overfortification of milk
  - ➢ Increase 1,25 dihydroxyvitamin D
    - Subcutaneous fat necrosis
    - Histiocytic disorders
- Calcitonin response impairment (?) in congenital hypothyroidism
- Vitamin A excess
- Uncertain pathophysiologic mechanism
  - ➢ ECMO
  - ➢ Idiopathic infantile hypercalcemia (see **WILLIAMS SYNDROME** in the "Neonatal Conditions and Diseases" section)
  - ➢ Severe infantile hypophosphatasia
  - ➢ Microdeletion of 4q
  - ➢ Blue diaper syndrome
  - ➢ Congenital lactase, sucrase-isomaltase, disaccharidase deficiency, glycogen storage disease type 1a

MANAGEMENT

- Remove etiologic factor, if possible; e.g., discontinue vitamins D & A, & Ca supplementation

Acute

- Expansion of extracellular fluid compartment & induced diuresis w/ IV normal saline (20 mL/kg) & loop diuretic (furosemide 2 mg/kg);

reassess & repeat q4–6h as necessary; monitor fluid balance & serum Ca, Mg, sodium, potassium (K), P, & osmolality q6–12 h; prolonged diuresis may require Mg & K replacement
- Maintain nutritional support, but use lower-Ca-content milk or parenteral nutrition if possible
- In neonates w/ low serum P [<1 mmol (3 mg)/dL]
  - ➢ Oral phosphate supplement, 0.5–1 mmol (15–30 mg) elemental P/kg/d in 4 divided doses; may normalize serum P & Ca
  - ➢ In infants NPO, use parenteral nutrition containing standard amount of phosphate [1–1.5 mmol (31–46 mg)/100 mL]
- Minimal data on the use of subcutaneous, intranasal or intramuscular recombinant human calcitonin (4–8 IU/kg q6 h), or bisphonates (oral etidronate 25 mg bid, IV pamidronate 0.5 mg/kg) +/− oral glucocorticoid (prednisone 0.5–1 mg/kg/d)
- Peritoneal dialysis or hemodialysis w/ a low-calcium dialysate may be considered in severely symptomatic pt refractory to medical therapy
- Subtotal parathyroidectomy may be needed when clinically stabilized

Maintenance
- Depends on underlying cause
- Low-Ca, no-vitamin-D infant formula (Calcilo XD®, Ross Products Division, Abbott Laboratories, Columbus, OH) may be needed
- Minimal sunlight exposure to lower endogenous synthesis of vitamin D may be helpful

FOLLOW UP
- Check for resolution of:
  - ➢ Acute effects from symptomatic hypercalcemia
  - ➢ Residual effects from underlying disorder
- Family screening & genetic counseling as appropriate

COMPLICATIONS AND PROGNOSIS
- Acute: fluid electrolyte imbalance
- Chronic
  - ➢ Nephrocalcinosis due to underlying disorders
  - ➢ Failure to thrive, hypocalcemia & bone demineralization due to excessive limitation of Ca & vitamin D intake

HYPERGLYCEMIA

RICHARD A. POLIN, MD

Definition: plasma glucose >180 mg/dL

HISTORY & PHYSICAL

History

- Time of presentation
  - ➢ Glucose intolerance in very premature infant: at times of stress (e.g., sepsis, intraventricular hemorrhage), drug therapy (e.g., steroids, methylxanthines) or when rate of glucose infusion high (VLBW infants may not tolerate glucose infusion rates >4–5 mg/kg/min)
  - ➢ Neonatal diabetes mellitus: 1st month of life
- Duration
  - ➢ Self-limited
    - Transient neonatal diabetes mellitus (~50%, duration may be days to years)
    - Glucose intolerance in very premature infant
  - ➢ Recurrent or permanent
    - Neonatal diabetes mellitus
    - Wolcott-Rallison syndrome
    - Pancreatic hypoplasia
- Maternal Hx
  - ➢ Permanent neonatal diabetes mellitus
    - IUGR
  - ➢ Transient diabetes mellitus (self-limited, recurrent)
    - IUGR

Physical

- Clinical signs, symptoms of hyperglycemia
  - ➢ W/ serum glucose concentrations <200 mg/dL most infants will be asymptomatic
  - ➢ Osmotic diuresis/polyuria (rare)
  - ➢ Dehydration (rare)
  - ➢ Hyperosmolar state assoc w/ intraventricular hemorrhage (NOTE: Increase in osmolality is only 5.5 mOsm/L w/ every 100-mg/dL increase in plasma glucose concentration)
- Assoc findings

- ➢ Glucose intolerance in very premature infant: inversely related to degree of prematurity
- ➢ Wolcott-Rallison syndrome: multiple epiphyseal or spondyloepiphyseal dysplasia
- ➢ Pancreatic hypoplasia: CHD
- ➢ Leprechaunism: IUGR, large phallus, breast hyperplasia, hyperinsulinemia, insulin resistance

TESTS

- Glucosuria: Urine may be positive for glucose in preterm infants w/ plasma glucose <180 mg/dL
- Plasma glucose
  - ➢ >180 mg/dL (important to make sure blood sample not contaminated by glucose being infused)
- C-peptide
  - ➢ Low or undetectable in neonatal diabetes mellitus
  - ➢ Insulin levels normal in stressed preterm infant

DIFFERENTIAL DIAGNOSIS

- Glucose intolerance in very premature infant
- Stress (asphyxia, surgery, intracranial hemorrhage, sepsis)
- Drugs (steroids)
- Transient, permanent neonatal diabetes mellitus
- Wolcott-Rallison syndrome
- Pancreatic hypoplasia
- Leprechaunism (Donohue syndrome)
- Fictitious (poor sampling: dilution of sample from indwelling catheter by infusate containing dextrose)

MANAGEMENT

- What to do first
  - ➢ Repeat blood sample from site unlikely to be contaminated w/ glucose being infused
  - ➢ Consider possible sepsis or another stressful condition, treat if possible
- General measures (no intervention is generally needed if the serum glucose concentration is <200 mg/dL)
  - ➢ In VLBW infant, decrease rate of glucose infusion or reduce intake of IV fat
  - ➢ If possible, discontinue drugs assoc w/ hyperglycemia
  - ➢ Monitor urine output, serum electrolytes (if infant has polyuria)

- ➢ For persistent plasma glucose levels >250 mg/dL (unresponsive to measures outlined above), begin insulin (0.04–0.10 units/kg/h); monitor glucose levels qh using bedside test strip systems; adjust rate of regular insulin infusion to maintain serum level at 150–200 mg/dL
  - NOTE: When insulin used, tubing should be flushed w/ insulin solution to saturate binding sites
  - Insulin should be delivered using infusion pump
  - Insulin solutions are not compatible w/ aminophylline, dobutamine, phenobarbital, phenytoin, sodium bicarbonate or lidocaine

SPECIFIC THERAPY
N/A

FOLLOW-UP
N/A

COMPLICATIONS AND PROGNOSIS
N/A

HYPERKALEMIA

J.M. LORENZ, MD

- Definition
  - ➢ Plasma [K] > 5.0 mmol/L
  - ➢ Serum [K] > 5.5 mmol/L

  Note: Most auto-analyzers measure plasma [K]
- Clinical effects unusual w/ plasma [K] < 6.5–7.0 mmol/L
- Clinical effects potentiated by hypocalcemia
- Non-hemolyzed specimen required to accurately access plasma/serum [K]

HISTORY & PHYSICAL
- History
  - ➢ GA <= 28 wk
  - ➢ Oliguria/anuria
  - ➢ Drugs
    - K-sparing diuretic
    - Digoxin
    - Succinylcholine

- ➢ Poor feeding/growth w/ congenital adrenal hyperplasia (CAH; see **CONGENITAL ADRENAL HYPERPLASIA** in the "Neonatal Conditions and Diseases" section)

- Physical
  - ➢ Signs due to hyperkalemia: usually none other than arrhythmia (60% w/ plasma [K] > 7.5 mmol/L)
  - ➢ Edema w/ acute renal failure
  - ➢ Dehydration, shock w/ mineralocorticoid deficiency
  - ➢ Genital hyperpigmentation w/ CAH
  - ➢ Virilization in female w/ 21-hydroxylase or 3-beta-hydroxysteroid dehydrogenase deficiency
  - ➢ Hypospadias in male w/ 3-beta-hydroxysteroid dehydrogenase deficiency
  - ➢ Male pseudohermaphroditism w/ congenital lipoid hyperplasia

TESTS

- Urine [K]
  - ➢ High urine K (>~40 mmol/L) w/ K load or redistribution of K from intracellular fluid space
  - ➢ Low urine K (<~40 mmol/L) w/ impaired renal excretion
- Hyponatremia, hypoglycemia suggest possible adrenal insufficiency (see **ADRENAL INSUFFICIENCY** in the "Neonatal Conditions and Diseases" section)
- Increased plasma creatinine w/ renal failure
- ECG, as plasma [K] rises: peaking of T waves, prolongation of PR interval, flattening of P wave, widening of QRS complex, sine wave, & finally ventricular flutter/fibrillation/arrest
- Cortisol, renin, aldosterone if endocrine problem suspected

DIFFERENTIAL DIAGNOSIS

Spurious: specimen hemolysis; severe thrombocytosis; WBC > 50,000

True hyperkalemia

- Disorders w/ high urine K
  - ➢ Redistribution of K from intracellular fluid
    - Extreme prematurity in immediate newborn period (see **FLUID AND ELECTROLYTE THERAPY** in the "Supportive Care" section)
    - Succinylcholine
    - Digoxin toxicity
    - Hyperosmolality
  - ➢ Excessive K load

- Excessive, rapid administration
- Reabsorption of internal (including GI) hemorrhage
- Severe intravascular hemolysis
- Double volume exchange transfusion (transient)

■ Disorders w/ low urine K: impaired renal excretion
  ➢ Extreme prematurity during prediuretic period (see **FLUID AND ELECTROLYTE THERAPY** in the "Supportive Care" section)
  ➢ Acute or chronic renal failure
  ➢ K-sparing diuretics
  ➢ Mineralocorticoid deficiency: high plasma renin, low plasma aldosterone, hyperchloremic metabolic acidosis (see **RENAL TUBULAR ACIDOSIS** in the "Neonatal Conditions and Diseases" section)
    - CAH due to:
      - 21-hydroylase deficiency
      - 3-beta-hydroxysteroid dehydrogenase deficiency
      - Congenital lipoid hyperplasia
    - Bilateral adrenal hemorrhage (aka Waterhouse-Friderichson Syndrome)
    - Congenital isolated aldosterone deficiency (extremely rare)
  ➢ Pseudohypoaldosteronism type I (extremely rare)
    - Autosomal recessively inherited unresponsiveness of collecting duct to mineralocorticoids
    - Increased plasma renin, normal or increased plasma aldosterone, hyperchloremic metabolic acidosis (renal tubular acidosos, type IV)

MANAGEMENT

Spurious hyperkalemia: none

True hyperkalemia

■ Prevention: withhold/discontinue K in clinical situations w/ risk of hyperkalemia
■ Antagonize cardiac toxicity
  ➢ For arrhythmia: 0.5–1.0 mEq/kg elemental Ca (1–2 mL/kg of 10% Ca gluconate) by slow IV push; if no arrhythmia, treat co-existing hypocalcemia aggressively
  ➢ Correct metabolic acidosis
■ Stimulate cellular uptake of K
  ➢ Maximize dextrose administration, administer exogenous insulin prn to prevent hyperglycemia (see **HYPERGYLCEMIA** for insulin dosing)

- ➢ Albuterol, 0.1–0.5 mg/kg as nebulized solution q2–6h (limited efficacy/safety data)
- Remove K from body
  - ➢ Na polystyrene sulfonate (1 g in 10% sucrose in 1 g:4 mL ratio) by OG tube or retention enema; q6h as indicated
    NOTE: Hyperosmolar could damage immature or stressed bowel; may cause or exacerbate Na retention or hypernatremia
  - ➢ Peritoneal dialysis
- Rx underlying disease

SPECIFIC THERAPY
- As indicated for underlying disease

FOLLOW-UP
- Long-term
  - ➢ None for hyperkalemia per se
  - ➢ Other as indicated for complications or underlying disorders

COMPLICATIONS AND PROGNOSIS
- Complications: sinus bradycardia, ventricular flutter/fibrillation/arrest, death
  - ➢ Prognosis: depends on underlying etiology if pt survives acute episode

HYPERMAGNESEMIA

WINSTON KOO, MD

DEFINITION
- Serum or plasma total magnesium (Mg) >1.1 mmol/L (2.6 mg/dL)
- Data insufficient to define based on serum or ionized Mg

HISTORY AND PHYSICAL

History
- Maternal intrapartum Mg therapy
- Mg administration w/ poor renal function (prematurity & perinatal asphyxia)
- Excessive Mg intake
  - ➢ High Mg content or high rate of infusion of parenteral nutrition
  - ➢ Mg-containing antacid or enema

Physical examination
- Lethargy, floppiness, weak or absent tendon reflex
- Poor respiratory effort; may require ventilatory support
- Bradycardia & hypotension [unusual in term infants with serum Mg <2 mmol/L (4.8 mg/dL)]

TESTS
- Basic
  - ➢ Serum or plasma total Mg, ionized Mg if available, total & ionized calcium (Ca), phosphorus (P), glucose, creatinine (Cr); serial measurement q12–24h until normal ×2
  - ➢ Urine Ca, Mg, P, Cr as baseline
- Other tests as appropriate
  - ➢ EKG, CXR if cardiac arrhythmia +/− hypotension

DIFFERENTIAL DIAGNOSIS

DDX of signs and symptoms
- Neuromuscular disorder (see **HYPOTONIA**)

DDX of pathogenesis
- Increased Mg load
  - ➢ Maternal Mg sulfate administration
  - ➢ Neonatal: Mg therapy, excessive Mg in parenteral nutrition, Mg-containing antacid or enema
- Decreased Mg excretion
  - ➢ Prematurity
  - ➢ Asphyxia
  - ➢ Chronic renal failure

MANAGEMENT
- Supportive: cardiorespiratory, nutrition & fluid
- Symptomatic
  - ➢ IV 10–20 mg elemental Ca/kg infused w/ dextrose water or normal saline w/ continuous EKG monitoring
    - 10% Ca gluconate provides 9 mg elemental calcium/mL
    - 10% Ca chloride provides 27 mg elemental calcium/mL
  - ➢ Loop diuretic (furosemide 2 mg/kg/dose); ensure adequate fluid intake
  - ➢ Exchange transfusion w/ citrated blood
  - ➢ Peritoneal dialysis or hemodialysis may be considered in refractory pts

- Treat underlying disorder if possible (e.g., discontinue Mg-containing antacid)

FOLLOW UP

- Check for resolution of:
  - ➢ Acute effects of symptomatic hypermagnesemia
  - ➢ Residual effects from underlying disorder

COMPLICATIONS AND PROGNOSIS

- Cardiorespiratory, CNS depression
- May have hypocalcemia secondary to suppression of parathyroid hormone & 1,25-dihydroxyvitamin D
- Usually resolves spontaneously if renal function is normal & no persistent underlying problem

HYPERNATREMIA

J.M. LORENZ, MD

- Definition: plasma [Na] > 145 mmol/L
- CNS signs unusual w/ plasma [Na] < 150 mmol/L
- CNS signs more likely w/ rapid rate of rise

HISTORY & PHYSICAL

- History
  - ➢ Drugs: hypertonic $NaHCO_3$
  - ➢ Extreme prematurity, care under radiant warmer (high insensible water loss)
  - ➢ Unusual loss of hypotonic body fluid (usually GI)
  - ➢ Polyuria (diabetes insipidus)
- Physical
  - ➢ Seizures w/ CNS complications
  - ➢ Edema w/ hypertonic Na intake

TESTS

- Plasma, urine osmolality
- Body fluid [Na]
- Head US, CT, or MRI w/ CNS signs

DIFFERENTIAL DIAGNOSIS

- Spurious: contamination of sample drawn from indwelling catheter by infusate w/ [Na] $\gg$ 150 mmol/L

- Free water intake < free H_2O loss (total body Na normal)
  - ➢ W/ unexpectedly high insensible water loss
  - ➢ During postnatal diuresis
  - ➢ Renal concentrating defects
    - Hypokalemia
    - Hypercalcemia
    - Chronic renal failure
    - Obstructive uropathy
    - Diabetes insipidus
      - Central
      - Nephrogenic
- Dehydration w/ total body water deficit > total body Na deficit: GI losses replaced w/ solution w/ higher [Na] than of GI fluid lost
- Excessive sodium intake
  - ➢ During postnatal diuresis
  - ➢ Hypertonic $NaHCO_3$ for acidosis
  - ➢ Improperly diluted (i.e., too concentrated) formula

MANAGEMENT

Too rapid correction can result in cerebral edema; rate of correction should be proportional to the time over which hypernatremia developed

- Free H_2O intake < free H_2O loss (total body Na normal)
  - ➢ Increase free water intake
  - ➢ Alter environment to decrease insensible water loss (see **FLUID AND ELECTROLYTE MANAGEMENT** in the "Supportive Care" section)
  - ➢ Rx underlying disorder
- Dehydration w/ total body water deficit > total body Na deficit
  - ➢ Emergent normal saline (>= 20 mL/kg) if plasma volume critically depleted
  - ➢ Hypotonic NaCl solution to replace H_2O & Na deficits
  - ➢ Increase H_2O & Na intake to replace ongoing losses
  - ➢ Rx underlying problem
- Excessive Na intake
  - ➢ If hypernatremia or volume overload critical
    - Give loop diuretic
    - Replace resulting urine output w/ free H_2O
    - Monitor plasma [Na] & for CNS signs closely
  - ➢ Otherwise, restrict Na intake

SPECIFIC THERAPY
As indicated for underlying condition (e.g., diabetes insipidus)

FOLLOW-UP
- During Rx
  - ➢ Plasma [Na]
  - ➢ I&O
  - ➢ Change in body wt
  - ➢ CNS status
- Long-term
  - ➢ Neurodevelopmental w/ CNS signs
  - ➢ Other as indicated for underlying disorders

COMPLICATIONS AND PROGNOSIS
- Complications
  Due to hypernatremia
  - ➢ Intracranial hemorrhage, subdural effusion
  - ➢ Intravascular thrombosis
  - ➢ Prerenal failure w/ severe dehydration
  - ➢ Pulm edema w/excessive Na intake

  Due to Rx
  - ➢ Cerebral edema (bulging fontanel, lethargy, seizures) w/ too rapid correction of hypernatremia
- Prognosis: depends on CNS involvement, underlying etiology

HYPERTENSION

RICHARD A. POLIN, MD

- Definition
  - ➢ BP that persistently exceeds mean +/− 2 SD for normal subjects of similar gestational age, size, postnatal age
  - ➢ Hypertension probable in full-term infant w/ persistent elevation of BP >90/60 & in preterm infant >80/50
  - ➢ After neonatal period, systolic BP >113 mmHg considered hypertensive

HISTORY & PHYSICAL

History
- Time of presentation
  - ➢ Variable depending on etiology

- ➢ Iatrogenic hypertension (e.g., fluid overload, meds): onset of hypertension concurrent w/ iatrogenic episode
- ➢ Renovascular hypertension: rarely manifest at birth (except w/ congenital malformations of renal artery); onset generally coincides w/ vascular insult (e.g., renal artery or renal vein thrombosis)
- ➢ Renal disorders: infants w/ congenital malformations (e.g., polycystic kidneys) may exhibit hypertension at birth; acquired disorders (e.g., acute tubular necrosis) result in hypertension at time of insult
- ➢ Coarctation: hypertension evident at birth
- ➢ Neurological hypertension (e.g., seizures or increased intracranial pressure): onset of hypertension concurrent w/ clinical event
- ➢ Endocrine causes (e.g., congenital adrenal hyperplasia)
  - 11 beta-hydroxylase deficiency: onset of hypertension at birth can occur, but BP usually normal in neonate
  - 17-alpha-hydroxylase deficiency: severe hypertension in infancy
  - 11-beta-hydroxysteroid dehydrogenase: onset of severe hypertension in early childhood
  - Primary hyperaldosteronism: extremely rare in infancy
  - Cushing disease: extremely rare in infancy
  - Congenital hyperthyroidism
  - Neuroblastoma/pheochromocytoma

■ Duration
- ➢ Self-limited
  - Iatrogenic
  - Renovascular hypertension (most)
  - Neurological hypertension (w/ Rx of underlying disorder)
- ➢ Recurrent or permanent
  - Uncorrected coarctation
  - Renal artery hypoplasia or stenosis
  - Congenital renal malformations
  - Untreated endocrine disorders

■ Maternal History
- ➢ Oligohydramnios w/ congenital renal malformations
- ➢ Unexplained maternal tachycardia w/ fetal neuroblastoma or pheochromocytoma
- ➢ Maternal cocaine abuse
- ➢ Maternal Graves disease

Physical

- Clinical signs, symptoms of hypertension
  - ➢ Hypertension often asymptomatic
  - ➢ Overt CHF relatively uncommon (subtle LV dysfunction on echocardiogram probably more common)
  - ➢ Hypertension of upper extremities w/ decreased or absent femoral pulses diagnostic for coarctation
  - ➢ Failure to thrive
  - ➢ Neurological manifestations (lethargy, alterations in muscle tone, seizures, stroke)
- Assoc findings
  - ➢ Any etiology of hypertension can cause CHF
  - ➢ Meds causing hypertension: steroids, theophylline, adrenergic agents (PO, topical, IV or aerosolized), cocaine, pancuronium & doxapram; almost all cause tachycardia
  - ➢ Retinal findings can be observed in >1/2 of affected infants
  - ➢ Coarctation assoc w/ a variety of congenital cardiac malformations leading to CHF. NOTE: Coarctation produces upper extremity hypertension w/ decreased femoral pulses.
  - ➢ Congenital adrenal hyperplasia
    - 11 beta-hydroxylase deficiency: hypertension variable, female infants virilized, hyperpigmentation of genitalia & areolae
    - 17-alpha-hydroxlase deficiency: female infants appear normal at birth, male infants undervirilized, may be phenotypic females
    - 11-beta-hydroxysteroid dehydrogenase: failure to thrive, polydipsia, polyuria, hypokalemia
    - Hyperaldosteronism: chronic hypokalemia leading to clear cell nephrosis (polyuria & polydipsia)
  - ➢ Large kidneys: renal vein thrombosis, cystic kidney disease, obstructive uropathy w/ hydronephrosis, renal tumors
  - ➢ Other manifestations of renal disorders include:
    - Increased or decreased urine output
    - Hematuria or proteinuria
    - Increased BUN & creatinine

TESTS

- If physical examination (incl 4-extremity BPs) & Hx unrevealing, diagnostic workup should focus on renal & renovascular causes of hypertension
  - ➢ Urinalysis

- ➢ Serum electrolytes
- ➢ Serum calcium
- ➢ Plasma renin activity
- ➢ Renal US

- If renovascular hypertension suspected, renal blood flow should be evaluated using a radionuclide scan, Doppler flow study
- If suspicion of hydronephrosis or reflux, urine should be sent for culture

DIFFERENTIAL DIAGNOSIS

- Iatrogenic hypertension
  - ➢ Na, fluid overload
  - ➢ Meds (see "History and Physical")
  - ➢ ECMO
  - ➢ Surgical repair of omphalocele & gastroschisis
  - ➢ Bronchopulmonary dysplasia
- Renovascular hypertension
  - ➢ Thromboembolism of renal artery
  - ➢ Stenosis or hypoplasia of renal artery
  - ➢ Renal vein thrombosis
  - ➢ Extrinsic compression of renal artery
  - ➢ Hematoma of wall of renal artery
  - ➢ Idiopathic arterial calcification of infancy
- Renal hypertension
  - ➢ Acute tubular necrosis; medullary or cortical necrosis
  - ➢ Renal tumor
  - ➢ Congenital renal malformation (dysplasia, hypoplasia, glomerular dysgenesis, polycystic/multicystic kidney)
  - ➢ Coarctation of the aorta
  - ➢ Neurological hypertension (intracranial hypertension or seizures)
  - ➢ Endocrine hypertension (congenital adrenal hyperplasia, primary hyperaldosteronism, Cushing disease, hyperthyroidism, neural crest tumors)

MANAGEMENT

- What to do first
  - ➢ Confirm that hypertension persistent, measurement has been made accurately w/ appropriate-size BP cuff
  - ➢ Discontinue or taper any non-essential drugs capable of causing hypertension

- ➢ Remove umbilical arterial line
- General measures
  - ➢ Treat underlying cause of hypertension (e.g., fluid overload should be treated w/ Na+ & H_2O restriction, judicious use of diuretics)
- Drug Rx
  - ➢ Systolic & diastolic BPs that require treatment controversial
  - ➢ Mild hypertension (diastolic <80 mmHg) should be treated with Na+ & H_2O restriction plus diuretics
  - ➢ Moderate hypertension (diastolic BP >80 mmHg) should initially be treated as above; if BP remains elevated anti-hypertensives should be initiated
  - ➢ For chronic or subacute hypertension, initial goal of Rx only to achieve 75% correction of initial value; too rapid a correction may place infant at risk for cerebral ischemia, renal failure
  - ➢ Drug of first choice for persistent hypertension: hydralazine (often used in conjunction w/ diuretic)
  - ➢ Severe hypertension considered life-threatening can be treated w/:
    - Salt restriction, diazoxide or nitroprusside
    - ACE inhibitors (captopril/enalapril)

SPECIFIC THERAPY
N/A

FOLLOW-UP
N/A

COMPLICATIONS AND PROGNOSIS
N/A

HYPOCALCEMIA

Winston KOO, MD

DEFINITION
- Serum or plasma total calcium (tCa)
  - ➢ Term: <2 mmol/L (8 mg/dL)
  - ➢ Preterm: <1.75 mmol/L (7 mg/dL)
- Serum or plasma ionized calcium (iCa)
  - ➢ <1–1.1 mmol/L (4.0–4.4 mg/dL) depending on electrode used

HISTORY AND PHYSICAL

History

- Prematurity; perinatal asphyxia; congenital heart defect (DiGeorge syndrome & variants); complicated clinical course; diet (cow's milk-based infant formula, very early cereal intake); winter birth in northern latitude coupled w/ poor maternal vitamin D status; phosphate enema use
- Maternal complications: diabetes, hyperparathyroidism, vitamin D or magnesium deficiency (diet, sunlight exposure, malabsorption problems, etc.), anticonvulsant or illicit drug use
- Family history: calcium or endocrine disorders, especially in mother (e.g., maternal hypercalcemia)

Physical examination

- Peripheral & central nervous system
  - ➢ Apnea, bradycardia
  - ➢ Neuromuscular irritability
    - Jitteriness, seizures
    - Percussion of facial nerve w/ muscle twitching (Chvostek sign)
    - Carpopedal spasm (uncommon in neonates)
    - Laryngospasm (uncommon in neonates)
- Features assoc w/ predisposing causes: prematurity, infant of diabetic mother, birth asphyxia, congenital heart defect, etc.

TESTS

- Basic
  - ➢ Serum or plasma tCa & iCa, magnesium (Mg), phosphorus (P), albumin (parallels changes in total Ca), creatinine (Cr); blood gas (acidosis increases & alkalosis decreases iCa)
  - ➢ Serial serum tCa & iCa q12–24 h until normal ×2
  - ➢ Urine Ca, Mg, P, Cr
  - ➢ ECG: prolonged QT interval
  - ➢ Meconium/urine drug screen
- Specific: serum or plasma intact parathyroid hormone, vitamin D metabolites [25 OH- and 1,25 (OH)2-vitamin D] done simultaneously w/ serum Ca
- Other tests as appropriate
  - ➢ Glucose, EEG, intracranial imaging, lumbar puncture for seizure & septic workup

- ➢ CXR (thymic & cardiac silhouette, pulmonary vascular marking) & FISH test for 22q11 deletion if suspect DiGeorge syndrome; other molecular genetic tests (e.g., Ca sensing receptor mutation)
- ➢ Malabsorption workup
- ➢ Response to exogenous PTH, including urine cyclic adenosine monophosphate
- ➢ Parental serum & urine Ca & P screening may led to other tests for all family members including molecular testing (e.g., Ca sensing receptor mutations)

DIFFERENTIAL DIAGNOSIS

DDx of signs and symptoms

- Hypoglycemia
- Hypomagnesemia
- Intracranial hemorrhage
- Sepsis/meningitis
- Narcotic withdrawal

DDX of pathogenesis

- Maternal
  - ➢ Insulin-dependent diabetes
  - ➢ Hyperparathyroidism
  - ➢ Vitamin D or magnesium deficiency
  - ➢ Anticonvulsant use (?)
  - ➢ Narcotic use (?)
- **Peripartum**
  - ➢ Birth asphyxia
- **Infant**
  - ➢ Intrinsic
    - Prematurity
    - Malabsorption of Ca +/− Mg
    - Parathyroid hormone: impaired synthesis or secretion, regulation, or responsiveness
    - Ca sensing receptor activating mutations
    - Calcitonin elevation
    - Vitamin D deficiency or decreased response to 1,25 (OH)2D
    - Absent osteoclast activity: malignant infantile osteopetrosis
  - ➢ Extrinsic
    - Diet
      - Inadequate calcium

- Excess phosphorus
- Enema: phosphate
- Hungry bone: refeeding syndrome
- Severe diarrhea
- Exchange transfusion w/ citrated blood
- High rate of IV lipid infusion
- Phototherapy (?)
- Alkali therapy (?)

MANAGEMENT

- Prevention
  - ➢ Minimize the predisposing risk factors if possible
  - ➢ Early feeding of gestational age-appropriate formula or use of calcium-containing parenteral nutrition
- Symptomatic
  - ➢ IV 10–20 mg elemental Ca/kg as 10% Ca gluconate or 10% Ca chloride (provide 9 mg & 27 mg, elemental calcium respectively per mL); infuse w/ dextrose water or normal saline under constant EKG monitoring; repeat as necessary
  - ➢ Treat hypomagnesemia if present (see **NEONATAL HYPOMAGNESEMIA**)
  - ➢ Continue until symptom resolution & iCa is normal, then continue w/ Ca-containing parenteral nutrition or appropriate milk feeding
- Asymptomatic
  - ➢ Oral 50–75 mg elemental Ca/kg/d as calcium carbonate (40 mg/mL), glubionate (23 mg/mL), gluconate (9 mg/mL), lactate (13 mg/mL), or chloride (27 mg/mL) in 4–6 divided doses until iCa normalized; then decrease Ca supplement by half each 24 hours for 2 days; then discontinue
  - ➢ For non-breast-fed infants: several wks of very-low-phosphorus milk formula (PM 60/40®, Ross Products Division, Abbott Laboratories, Columbus, OH) may be useful
  - ➢ Long-term Ca +/− vitamin D metabolite may be needed for some disorders
- Treat underlying disorder if possible (e.g., discontinue or lower the high P intake)

FOLLOW UP

- Check for resolution of:
  - ➢ Acute effects of symptomatic hypocalcemia

- ➢ Residual effects from underlying disorder
- Family screening & genetic counseling as appropriate

COMPLICATIONS AND PROGNOSIS

- Acute: primarily treatment-related; minimized w/:
  - ➢ Continuous EKG monitoring during Ca infusion
  - ➢ No infusion of calcium solutions into arterial lines (causes arterial spasm)
  - ➢ Confirm patency of venous lines prior to infusion (extravasation causes tissue necrosis)
  - ➢ Risk for nephrocalcinosis & nephrolithiasis in pts w/ absent or non-functional parathyroid hormone, as protective effect of calciuria is absent
- Short term
  - ➢ Depends on the symptomatic manifestations (e.g., seizure, apnea, cyanosis, bradycardia, hypotension, etc.)
  - ➢ Risk of metastatic calcification from aggressive Ca treatment in the presence of hyperphosphatemia; the latter should be treated if present
- Long term: primarily dependent on underlying cause (e.g., DiGeorge syndrome-associated neurodevelopment delay & cardiovascular anomaly)

HYPOGLYCEMIA

RICHARD A. POLIN, MD

- Definition: plasma glucose <= 50 mg/dL

HISTORY & PHYSICAL

History

- Time of presentation
  - ➢ Infant of diabetic mother: 30–90 min of life (usually asymptomatic)
  - ➢ Hyperinsulinism: 24–48 h w/ seizures, hypotonia (onset of hypoglycemia w/in hours of birth)
  - ➢ Hypothermia: concurrent w/ hypothermia
  - ➢ Asphyxia: w/in hours of birth
  - ➢ Infection: concurrent w/ sepsis episode
  - ➢ IUGR: first 24 h after birth (but may persist for several days)
  - ➢ Hyperviscosity: 1st day of life (concurrent w/ polycythemia)

- ➢ Inborn errors of metabolism: variable times of onset related to dietary intake, severity of metabolic defect
- ➢ Pituitary insufficiency: 1st hours of life

- Duration
  - ➢ Transient: limited to neonatal period, assoc w/:
    - Changes in maternal metabolism
      - Intrapartum administration of glucose
      - Drug treatment (terbutaline, ritodrine, propranolol)
      - Diabetes in pregnancy
      - IUGR
    - Neonatal problems
      - Idiopathic (failure of adaptation)
      - Asphyxia
      - Infection
      - Hypothermia
      - Hyperviscosity
      - Erythroblastosis fetalis
      - Iatrogenic (malpositioned umbilical arterial catheter)
      - Congenital cardiac malformations
  - ➢ Persistent or recurrent
    - Hyperinsulinism
    - Endocrine disorders
    - Inborn errors of metabolism
    - Defective glucose transport
- Maternal History
  - ➢ Maternal diabetes
  - ➢ IUGR
  - ➢ Drugs
    - Oral hypoglycemic agents
    - Terbutaline, ritodrine
    - Propranolol

Physical

- Clinical signs & symptoms of hypoglycemia
  - ➢ Abnormal cry
  - ➢ Apnea/cyanotic spells
  - ➢ Feeding difficulty
  - ➢ Grunting/tachypnea
  - ➢ Hypothermia
  - ➢ Hypotonia
  - ➢ Irritability

- ➢ Jitteriness
- ➢ Tremors
- ➢ Lethargy
- ➢ Seizures
- ➢ Sweating
- ➢ Tachycardia

■ Associated findings (in addition to hypoglycemia)

- ➢ Infant of diabetic mother: macrosomia, birth trauma/bruising, hypertrophic cardiomyopathy, hyperbilirubinemia, hypocalcemia, congenital anomalies, polycythemia, renal vein thrombosis, small left colon syndrome
- ➢ Hyperinsulinism: large-for-gestational-age (LGA) infants
- ➢ Beckwith-Wiedemann syndrome: LGA infants, polycythemia, macroglossia, omphalocele, visceromegaly, ear pits/creases, cardiac defects
- ➢ Pituitary insufficiency: males predominate, antenatal growth normal, physical exam may reveal microphallus, poorly developed scrotum, cleft lip/palate, poorly developed nasal septum, hypotelorism, hypertelorism & widely spaced nipples
- ➢ Galactosemia: jaundice, hepatomegaly, vomiting, seizures, poor feeding & *E. coli* sepsis
- ➢ Glycogen storage diseases
  - GSD type I: increased plasma free fatty acids, ketone bodies, hepatomegaly, lactic acidosis, hypertriglyceridemia, hyperuricemia, neutropenia (type Ib)
  - GSD type III: hepatomegaly
- ➢ Gluconeogenesis defects
  - Hereditary fructose intolerance: after introduction of sucrose or fructose in diet, jaundice (transaminase elevation), hepatomegaly, vomiting, lethargy, irritability, convulsions
  - Fructose-1,6 diphosphatase deficiency: after intro of sucrose or fructose in diet, shock, convulsions, hyperlacticacidemia
  - Pyruvate carboxylase deficiency: severe acidosis, hyperammonemia, hypercitrullinemia, hyperlysinemia
- ➢ Organic acidemias
  - Isovaleric acidemia: vomiting, acidosis, seizures, neutropenia, thrombocytopenia, odor of "sweaty feet"
  - Maple syrup urine disease: poor feeding, vomiting, coma, hypertonicity, muscular rigidity, odor of maple syrup
  - Methylmalonic acidemia: ketosis, acidosis, hyperammonemia, neutropenia, thrombocytopenia, coma

- Propionic acidemia: poor feeding, vomiting, acidosis, seizures, ketosis, hyperammonemia, neutropenia, thrombocytopenia
- Multiple carboxylase deficiency: breathing difficulties (tachypnea/apnea), hypotonia, seizures, vomiting, metabolic acidosis, ketosis, "tomcat" odor to urine, occasionally hyperammonemia

➢ Ketogenesis defects (30% present in neonatal period)
- 3-hydroxy-3-methyl glutaric acidemia: hyperammonemia, acidosis, abnl liver function tests

➢ Fatty acid oxidation defects
- Defects of long-chain fatty acid oxidation more likely to present in neonatal period (cardiomyopathy, hyperammonemia)

TESTS

■ Plasma glucose
➢ In high-risk populations (e.g., infant of diabetic mother, premature infants, LGA & SGA infants, etc.) glucose should be monitored using bedside test strip system at 1–2 h of life, then q4h for at least 48 h
➢ Routine testing not indicated for low-risk infant populations
➢ In enterally fed high-risk infants, repeat testing should occur once/shift (pre-feeding) until full feedings achieved (parenteral glucose discontinued), glucose levels have stabilized in normal range
➢ In infants receiving glucose parenterally, bedside testing should occur once/shift
➢ When total parenteral nutrition (containing high concentrations of glucose) is discontinued abruptly, plasma glucose concentration must be monitored closely until stable values achieved
➢ Any value <50 mg/dL by test strip should be confirmed w/ lab determination

DIFFERENTIAL DIAGNOSIS

■ Idiopathic (failure of adaptation)
■ Infant of diabetic mother
■ Asphyxia
■ Infection
■ Hypothermia

- Hyperviscosity
- Erythroblastosis fetalis
- Iatrogenic
- Congenital cardiac malformations
- Hyperinsulinism
  - ➢ Nesidioblastosis/adenoma
  - ➢ Beckwith-Wiedemann syndrome
- Endocrine disorders
  - ➢ Pituitary & adrenal insufficiency
- Inborn errors of metabolism (see "History and Physical")
- Defective glucose transport

MANAGEMENT

- What to do first
  - ➢ ABCs (airway, breathing, circulation)
- General measures
  - ➢ Plasma glucose concentration requiring intervention: 45 mg/dL
    - For asymptomatic infants able to tolerate enteral feedings
      - Begin enteral feeding, advance as tolerated
      - Recheck glucose after 30 min of feeding
    - For symptomatic infants
      - Increase the rate or concentration of glucose infusion (preferred intervention)
      - Administer 2 cc/kg of 10% dextrose over 1–2 min followed by an infusion supplying 4–6 mg/kg/min
      - Begin enteral feedings if appropriate
    - For asymptomatic infants unable to tolerate enteral feedings
      - Begin 10% dextrose & H_2O infusion supplying 4–6 mg/kg/min
    - Plasma glucose must be monitored q1–2 h until stabilized
    - If plasma glucose concentration does not normalize, rate of infusion should be increased 1–2 mg/kg/min q3–4 h (this may require insertion of central line)
    - If symptoms persist, or glucose remains <= 50 mg/dL despite a dextrose infusion rate >12 mg/kg/min, begin hydrocortisone (5 mg/kg/day PO or IV)

SPECIFIC THERAPY

N/A

FOLLOW-UP

N/A

COMPLICATIONS AND PROGNOSIS

- Asymptomatic hypoglycemia has an excellent prognosis
- Long-term neurological handicaps related to duration of signs (before correction), underlying disorder
- Seizures in neonatal period assoc w/ poorer prognosis

HYPOKALEMIA

J.M. LORENZ, MD

- Definition
  - ➢ Plasma [K] <3.0 mmol/L
  - ➢ Serum [K] <3.5 mmol/L

  Note: most auto-analyzers measure plasma [K]
- Clinical effects potentiated by digoxin, hypercalcemia
- Hypokalemia cannot be excluded if whole blood sample hemolyzed

HISTORY & PHYSICAL

- History
  - ➢ Polyhydramnios w/ congenital etiology
  - ➢ Loop or thiazide diuretic Rx
  - ➢ Hyperinsulinemia or insulin Rx
  - ➢ Amphotericin B Rx
  - ➢ Beta-catecholamine Rx
  - ➢ Poor growth
  - ➢ Vomiting
  - ➢ Polyuria
- Physical
  - ➢ Signs of hypokalemia: abd distention, lethargy, arrhythmias
  - ➢ Congenital adrenal hyperplasia (see **CONGENITAL ADRENAL HYPERPLASIA** in the "Neonatal Conditions and Diseases" section)
    - W/ 11-beta-hydroxylase deficiency: hypertension & virilization of female
    - W/ 17-alpha-hydroxylase deficiency: hypertension & incomplete masculinization of male

TESTS

- Nonspecific
  - ➢ Serum electrolytes, urine [K] & [Cl], blood gas for acid-base status

- Specific
  - ➢ Plasma [Mg]
  - ➢ ECG: increased P-wave amplitude, prolonged P-R interval; widened, decreased QRS voltage; depressed ST segment; widened, flattened, or inverted T waves; U waves
  - ➢ If endocrine cause suspected: plasma renin, aldosterone, cortisol

DIFFERENTIAL DIAGNOSIS

- Spurious: w/ severe leukocytosis (WBC >100,000/mm^3) due to uptake of K by WBC in whole blood sample if latter stands at room temp
- Redistribution of K from extracellular fluid w/o change in total body potassium (TBK)
  - ➢ Alkalosis
  - ➢ Hyperinsulinemia or insulin Rx
  - ➢ Beta-catecholamine Rx
  - ➢ Mineralocorticoid excess
    - Congenital adrenal hyperplasia (see **CONGENITAL ADRENAL HYPERPLASIA** in the "Neonatal Conditions and Diseases" section)
      - 11-beta-hydroxylase deficiency
        - Hypertension, female virilization
        - Low cortisol, increased 11-deoxycorticosterone, increased 11-deoycortisol, low renin, aldosterone
      - 17-alpha-hydroxylase deficiency
        - Hypertension, incomplete masculinization
        - Low cortisol; increased 11-deoxycorticosterone, increased corticosterone, low renin, aldosterone
    - Antenatal, hypercaluric variant of Bartter's syndrome (aka hyperprostoglandin E syndrome)
      - Autosomal recessive
      - Polyhydramnios, premature delivery, hypokalemia, hypercalcuria, metabolic alkalosis, polyuria (marked variability in phenotype)
    - Secondary hyperaldosteronism (low plasma renin activity, high aldosterone)
      - Plasma volume depletion
      - CHF
      - Severe cirrhosis
      - Nephrotic syndrome
      - Renovasular disease

- Decrease in total body potassium (TBK)
  - ➢ High urine K losses
    - Normal pH
      - Diuresis/natriuresis: physiologic, diuretic phase of acute tubular necrosis, postobstructive
      - Amphotericin B Rx
      - Hypomagnesemia (see **NEONATAL HYPOMAGNESEMIA**)
    - Hypochloremic metabolic alkalosis
      - Low urinary Cl
        - Vomiting, gastric suctioning; loop or thiazide diuretics (after acute effects dissipated)
        - After hypercapnia
      - High urinary Cl
        - Loop or thiazide diuretics
        - Severe K depletion
        - 11-beta-hydroxylase deficiency
        - 17-alpha-hydroxylase deficiency
        - Antenatal, hypercaluric variant of Bartter's syndrome (aka hyperprostoglandin E syndrome)
        - Secondary hyperaldosteronism (low plasma renin activity, high aldosterone)
    - Hyperchloremic metabolic acidosis
      - Renal tubular acidosis types I, II, III (see **RENAL TUBULAR ACIDOSIS** in the "Neonatal Conditions and Diseases" section)
  - ➢ Low urine K losses
    - Normal pH: insufficient intake
    - Hypochloremic metabolic alkalosis: vomiting, gastric suction
    - Hyperchloremic metabolic acidosis: ostomy losses, diarrhea

MANAGEMENT

- No Rx indicated for spurious hypokalemia
- No Rx usually necessary for hypokalemia solely due to transcellular shift of K
- K ***deficiency*** requires increased K intake regardless of cause
  - ➢ To prevent life-threatening cardiac complications: 1 mmol/kg of KCl IV over 1 hr
  - ➢ NOTE: Infusate [K] should be <40 mmol/L by peripheral & <80 mmol/L by central vein
  - ➢ Otherwise, replace K deficit & increase intake K as necessary to cover ongoing losses
  - ➢ Hydration as indicated

SPECIFIC THERAPY

- Diuresis/natriuresis (physiologic, diuretic phase of acute tubular necrosis, postobstructive): none
- Amphotericin B Rx: none
- Na/water overload: restrict Na/water intake
- Hypomagnesemia: see **NEONATAL HYPOMAGNESEMIA**
- Alkalosis w/ K deficiency: correct underlying cause of alkalosis
- Loop or thiazide diuretic: may add K-sparing diuretic
- 11-beta- or 17-alpha-hydroxylase deficiency: cortisol
- Antenatal, hypercaluric variant of Bartter's syndrome: long-term Rx w/ prostaglandin synthesis inhibitor
- Secondary hypoaldosteronism: treat underlying condition
- Renal tubular acidosis (types I, II, III): long-term $NaHCO_3$ & K-citrate (see **RENAL TUBULAR ACIDOSIS** in the "Neonatal Conditions and Diseases" section)
- Inadequate intake: replace deficit & increase intake to meet requirements
- GI losses: Rx underlying cause as necessary

FOLLOW-UP

- During Rx
  - ➢ Plasma electrolytes, blood gases, ECG
  - ➢ Other as indicated for underlying disorder
- Long-term
  - ➢ None for hypokalemia per se
  - ➢ Other as indicated for underlying disorders

COMPLICATIONS AND PROGNOSIS

- Complications
  - ➢ Sinus bradycardia, premature atrial contractions, paroxysmal atrial tachycardia, junctional tachycardia, AV block, atrial fibrillation, multifocal premature ventricular contractions, ventricular tachycardia, ventricular fibrillation
  - ➢ Myocardial necrosis
  - ➢ Dehydration due to polyuria
  - ➢ Death
- Prognosis: depends on myocardial effects, underlying etiology

HYPOMAGNESEMIA

WINSTON KOO, MD

DEFINITION

- Serum or plasma total magnesium (Mg) <0.06 mmol/L (<1.5 mg/dL)
- Data insufficient to define based on serum or ionized Mg

HISTORY & PHYSICAL

History

- Maternal complications: diabetes, hyperparathyroidism, magnesium deficiency
- Small for gestational age
- Exchange transfusion w/ citrated blood
- Excessive glucose, sodium & fluid intake resulting in extracellular fluid compartment expansion and/or osmotic diuresis
- Chronic loop diuretic therapy
- Extensive small bowel resection
- Draining enteric fistula
- Chronic diarrhea
- Renal tubular disorder
- Family Hx of Mg malabsorption

Physical examination

- Jitteriness, hyperreflexia, tetany, seizures (indistinguishable from hypocalcemia)
- Hypokalemia
- Features assoc w/ underlying disorder (e.g., infant of diabetic mother)

TESTS

- Basic
  - ➢ Serum or plasma total Mg, ionized Mg if available, total & ionized calcium (Ca), phosphorus (P), glucose (q12–24h until normal × 2)
  - ➢ Creatinine (Cr)
  - ➢ Meconium drug screen
- Specific
  - ➢ Intact parathyroid hormone
  - ➢ Enteric fluid (Mg, K, & Zn) from draining fistula

- Other tests as appropriate (e.g., maternal serum Mg & Ca screening may led to other tests for herself & family members)

DIFFERENTIAL DIAGNOSIS

DDX of signs and symptoms

- Hypoglycemia
- Hypocalcemia
- Intracranial hemorrhage or infection
- Sepsis
- Narcotic withdrawal

DDX of pathogenesis

- Decreased Mg intake
  - ➢ Mother
    - Mg deficiency
    - Maternal insulin-dependent diabetes mellitus
  - ➢ Infant
    - IUGR
    - Extensive small bowel resection
    - Specific intestinal Mg malabsorption (isolated, familial)
- Increased Mg loss
  - ➢ Intestinal fistula or diarrhea
  - ➢ Hepatobiliary disorders
  - ➢ Decreased renal tubular reabsorption
    - Primary
    - Secondary to extracellular fluid compartment expansion, osmotic diuresis, loop diuretics, aminoglycosides
- Other
  - ➢ Excessive P intake
  - ➢ Maternal hyperparathyroidism

MANAGEMENT

- Early milk feeding or parenteral nutrition
- Symptomatic
  - ➢ IV 0.1–0.2 mmol (2.5–5 mg) elemental Mg (0.05–0.1 mL/kg of 50% Mg sulfate heptahydrate) over 15–20 min
  - ➢ May repeat q8–12h or sooner depending on clinical & lab findings
  - ➢ May give same dose IM if lack of venous access
  - ➢ Oral supplement (see below) started simultaneously if clinically indicated
- Asymptomatic

- ➢ Oral 0.2 mL/kg/d 50% Mg sulfate heptahydrate diluted 4- to 6-fold to allow more frequent administration, maximizing absorption & minimizing side effects
- ➢ In the newborn period, data on the use of other Mg salts such as Mg L-lactate dihydrate, citrate, gluconate, hydroxide, oxide are extremely limited

- Treat underlying disorder if possible
- In pts w/ chronic enteric loss, potassium & zinc deficiency may coexist & require treatment

FOLLOW UP

- Check for resolution of:
  - ➢ Acute effects of symptomatic hypomagnesemia
  - ➢ Residual effects from underlying disorder
- Family screening & genetic counseling as appropriate

COMPLICATIONS AND PROGNOSIS

- Acute: primarily treatment-related; minimized with:
  - ➢ Continuous ECG monitoring during Mg infusion
  - ➢ Check venous line patency prior to infusion
- Short term: depends on the symptomatic manifestations (i.e., seizures, apnea, etc.)
- Long term: primarily dependent on underlying cause

HYPONATREMIA

J.M. LORENZ, MD

- Definition: plasma [Na] <135 mmol/L

HISTORY & PHYSICAL

- CNS signs unusual w/ plasma [Na] > 125–130 mmol/L
- CNS signs more likely w/ rapid rate of fall
- Hx
  - ➢ Excessive maternal intrapartum IV fluid or hyponatremia?
  - ➢ Prematurity
  - ➢ Drugs
    - Diuretics
    - Amphotericin B
    - Indomethacin
  - ➢ I&O

- H_2O intake $\ll$ (urine output + estimated IWL + other fluid losses) leads to Na balance even more neg than H_2O balance = hyponatremic dehydration
- H_2O intake $>>$ (urine output + estimated IWL + other fluid losses) leads to water intoxication = dilutional hyponatremia

➢ Body wt
- Decreased inappropriately for caloric intake c/w dehydration
- Increased inappropriately for caloric intake c/w H_2O, Na retention

➢ Oliguria/anuria w/ acute renal failure
➢ Unusual GI, pleural, peritoneal, CSF losses
➢ Consider SIADH w/ asphyxia, intracranial hemorrhage, meningitis, hydrocephalus, air leak syndromes, air trapping, positive-pressure ventilation, pain, drugs (e.g., opiates)
➢ Poor feeding/growth w/ adrenal insufficiency

■ Physical
➢ Due to hyponatremia: bulging fontanel, lethargy, seizures
➢ Edema w/ Na & water retention (e.g., renal failure, CHF)
➢ Genital hyperpigmentation, shock w/ congenital adrenal hyperplasia (CAH) (see **CONGENITAL ADRENAL HYPERPLASIA**)
➢ Virilization in female w/ 21-hydroxylase or 3-beta-hydroxysteroid dehydrogenase deficiency
➢ Hypospadias in male w/ 3-beta-hydroxysteroid dehydrogenase deficiency
➢ Male pseudohermaphroditism w/ congenital lipoid hyperplasia

TESTS
■ Plasma electrolytes, creatinine
■ Urine [Na], calculated Na output, fractional excretion of Na
■ Plasma & urine osmolality
■ If endocrine cause suspected: plasma renin, aldosterone, cortisol

DIFFERENTIAL DIAGNOSIS
■ Spurious
➢ Hyperlipemia if [Na] measured by flame photometry (not if measured by direct ion-specific electrode); Dx: measured plasma Osm WNL & > calculated Osm
➢ Dilution of sample drawn from indwelling catheter by infusate w/ low [Na]; Dx: measured plasma Osm low & = calculated Osm

■ Dehydration w/ TBNa deficit > TBW deficit
➢ High urine Na

- Renal immaturity
- Excess diuretic
- Osmotic diuresis (e.g., glucosuria)
- Adrenal insufficiency (see **CONGENITAL ADRENAL HYPERPLASIA, ADRENAL INSUFFICIENCY**)
  - CAH due to:
    - 21-hydroxylase deficiency
    - 3-beta-hydroxysteroid dehydrogenase deficiency
    - Congenital lipoid hyperplasia
  - Bilateral adrenal hemorrhage (aka Waterhouse-Friderichson syndrome)
- Congenital isolated aldosterone deficiency (extremely rare)

➢ Low urine Na
- Third-space losses
- GI losses
- External CSF drainage
- Peritoneal or pleural fluid drainage
- SIADH w/Na deficiency

■ Dilutional hyponatremia

➢ Water intoxication (increased TBW w/ nl TBNa)
- Maternal hyponatremia due to excess intrapartum IV fluid intake
- Excess H_2O intake w/ low GFR
  - During prediuretic period (see also FLUID AND ELECTROLYTE THERAPY in the "Supportive Care" section)
  - Prerenal failure
  - Indomethacin
- Excess H_2O intake w/ diuretic Rx
- SIADH (high urine Na, plasma Osm $<$ 280 mOsm/L, urine Osm $>$ 300 mOsm/L)

➢ H_2O & Na retention (excessive wt gain, edema)
- High urine Na
  - Acute tubular necrosis
  - Chronic renal failure
- Low urine Na
  - Excess H_2O, Na intake w/ low GFR
  - CHF
  - Cirrhosis

MANAGEMENT

■ No Rx indicated for spurious hyponatremia

- Emergent Rx for CNS signs: 3% (0.5 mmol/L) or 5% (0.85 mmol/L) NaCl solution to raise plasma [Na] 10–12 mmol/L in 24 h & 16–18 mmol/L in 48 h; Na to be administered (mmol) = {plasma [Na] target – plasma [Na] actual} × body wt (kg) × 0.80
- Dehydration
  - ➢ Emergent normal saline admin if plasma volume critically depleted
  - ➢ Replace H_2O, Na deficits; increase intake to replace ongoing losses
  - ➢ Reduce freq of diuretic
  - ➢ Rx underlying problem
- H_2O intoxication
  - ➢ Restrict H_2O intake
  - ➢ Alter environment to increase IWL
  - ➢ Rx underlying problem
- H_2O & Na retention
  - ➢ Restrict H_2O, Na intake
  - ➢ Alter environment to increase IWL
  - ➢ Diuretic Rx
  - ➢ Rx underlying problem

SPECIFIC THERAPY

N/A

FOLLOW-UP

- During Rx
  - ➢ Plasma [Na]: q4–6h (if correcting w/ hypertonic saline) to q12–24h to monitor rate of change
  - ➢ I&O
  - ➢ Change in body wt
  - ➢ CNS status
- Long-term
  - ➢ Neurodevelopmental w/ CNS signs
  - ➢ Other as indicated for underlying disorders

COMPLICATIONS AND PROGNOSIS

- Complications
  - ➢ Cerebral edema
  - ➢ Prerenal failure w/ severe dehydration
  - ➢ Pulm edema w/ severe H_2O, Na retention
- Prognosis: depends on CNS involvement, underlying etiology

HYPOTONIA

RICHARD A. POLIN, MD
REVISED BY M. RICHARD KOENIGSBERGER, MD

- May be due to non-neurological systemic disease or primary neurologic disorder
- Hypotonia may be:
  - Central: upper motor neuron (UMN)
  - Peripheral: lower motor neuron (LMN) – i.e., anterior horn cell (AHC), peripheral nerve, neuromuscular junction (NMJ), or muscle
- Central hypotonia far more common than peripheral in newborns

HISTORY AND PHYSICAL

- History
  - Maternal Hx
    - Maternal diabetes → ? hypoglycemia, hypocalcemia
    - Maternal preeclampsia → ? hypermagnesemia, asphyxia, hypoglycemia
    - Maternal group B streptococcus, herpes simplex, toxoplasmosis → ? sepsis, meningitis, encephalitis
    - Maternal myopathic facies, myotonia → ? myotonic dystrophy or other congenital myopathy
    - Hx of myasthenia gravis → ? transient neonatal myasthenia
    - Hx of consanguinity → ? autosomal recessive disorder
  - Intrapartum Hx
    - Perinatal/postnatal asphyxia → ? hypoxic-ischemic encephalopathy, hypoglycemia, hypocalcemia
    - Traumatic or rapid vaginal delivery → ? subarachnoid or subdural bleed
    - PROM, chorioamnionitis → sepsis
    - Reduced fetal movements: nonspecific, but → ? LMN disorders
    - Polyhydramnios due to decreased swallowing w/ either UMN or LMN lesions
    - Maternal treatment w/ analgesics, sedatives, antidepressants, anesthetics, magnesium
  - Time of presentation may be helpful in DDx

- Physical
  - ➢ Abnormally decreased muscle tone; manifested as:
    - Decreased resistance of joints to passive movements
    - Increased range of motion of joints
    - Bizarre or unusual postures
  - ➢ ± weakness (characterized by inability to generate antigravity power)
  - ➢ Pinpoint anatomical site pinpointed by determining:
    - Distribution of weakness:
      - Proximal (muscle) vs. distal (nerve)
      - Symmetrical vs. asymmetrical
    - Absent deep tendon reflexes → AHC or peripheral nerve disorder
    - Cranial nerve abnormalities
      - Ptosis, extraocular abnormal muscle → muscle or NMJ disorder
      - Fasciculations → AHC disorder
    - Sensory abnormalities (difficult to assess) → dysautonomia, neuropathies
  - ➢ Associated findings (other than hypotonia) w/specific etiologies
    - See **HYPOXIC-ISCHEMIC ENCEPHALOPATHY** in the "Neonatal Conditions and Diseases" section: depressed consciousness, seizures, jitteriness; multiorgan system dysfunction
    - Intracranial hemorrhage
      - See **SUBARACHNOID HEMORRHAGE** in the "Neonatal Conditions and Diseases" section: well child; rarely symptomatic, unless associated CNS hemorrhage
      - See **SUBDURAL HEMORRHAGE** in the "Neonatal Conditions and Diseases" section: neurologically asymptomatic or just depressed, some show contralateral hemiparesis; large pupil on side of bleed is neurosurgical emergency
    - Hypoglycemia: see **HYPOGLYCEMIA**
    - Inborn errors of metabolism: vomiting, stupor, unusual odor, seizures, metabolic acidosis, hypoglycemia, elevated lactate, hyperammonemia, hypocapnia,
    - Congenital infection: hepatosplenomegaly, rash, thrombocytopenia
    - See **HYPOTHYROIDISM, CONGENITAL** in the "Neonatal Conditions and Diseases" section: temperature instability, hoarse cry, prolonged jaundice; may be muscular
    - Riley-Day syndrome: absent corneal reflexes, absent deep tendon reflexes, temperature instability, skin blotching,

absence of fungiform papillae of tongue, absent axonal flare to histamine injection

TESTS

- Serum electrolytes, Ca, Mg, glucose
- Arterial blood gas, lactate
- Serum ammonia
- Serum CPK: increased → ? muscle disorders, particularly congenital myotonic dystrophies; ± mild increase w/ congenital myopathies, severe AHC disease
  NOTE: May be increased w/o muscle disease for as long as a week after delivery, esp w/ difficult vaginal
- Lumbar puncture
  - ➢ >20–30 WBC/mm^3 (in the absence of RBCs) → ? bacterial or viral infection
    Note: May be elevated after intraventricular hemorrhage
  - ➢ Protein >150–200 mg/dL, w/o other CSF abnormalities → ? neonatal neuropathy
    Note: May be very elevated after intraventricular hemorrhage
  - ➢ CSF lactate: helpful in hypoxic-ischemic encephalopathy for prognosis, mitochondrial diseases
  - ➢ CSF amino acids, esp for non-ketotic hyperglycinemia
  - ➢ Culture
- DNA testing
  - ➢ Specific testing for suspected myotonic dystrophy, Prader-Willi, spinal muscular atrophy (SMA) I, others w/ known DNA abnormalities
  - ➢ May obviate invasive procedures (e.g., EMG, muscle biopsy)
- Tensilon or neostigmine tests for transient neonatal myasthenia & some congenital myasthenic syndromes
- Nerve conduction velocities, motor (MNCV) & sensory (SNCV)
  - ➢ MNCV gestational age-dependent
  - ➢ Best confirmatory tests for peripheral nerve disorder
  - ➢ As a rule, lower in demyelinating disorders than in axonal neuropathies
  - ➢ MNCV wnl w/ disorders of muscle, NMJ, AHC (however, may be reduced by as much as half of normal values in a variety of instances w/ the latter)
- Repetitive nerve stimulation (RPS): best confirmatory test for myasthenia gravis; useful in botulism
  - ➢ Decrement of muscle action potential as stimulation rates increase in myasthenic disorders

- ➢ Increments in muscle action potential at high rates of stimulation w/ botulism; also w/ hypermagnesemia
- Electromyography (EMG) needle studies
  - ➢ AHC disorders
    - At rest, fibrillations, positive waves, fasciculations
    - W/ muscle contraction, diminished # of motor unit potentials
  - ➢ Peripheral nerve disorders
    - At rest, fibrillations & positive wave
    - W/ muscle contraction: diminished # of small motor units
  - ➢ NMJ disorders: usually normal; sometimes single fiber exam exhibits jitter
  - ➢ Muscle disorders
    - At rest, usually normal in myotonic dystrophy, myotonia
    - W/ muscle contraction, increased, low-amplitude units; but may be normal
- Muscle biopsy
  - ➢ Most specific test for LMN disorders
  - ➢ AHC & peripheral nerve disorders: atrophy of muscle fibers
  - ➢ Muscle disorders
    - Histology diagnostic at time of onset
      - Central core disease, nemalinemyopathy, myotubular myopathy, congenital fiber type disproportion, other congenital myopathies w/ abnormal structure
      - Mitochondrial myopathies (cytochrome c-oxidase deficiency, mitochondrial DNA depletion)
      - Metabolic myopathies (disorders of glycogen & fatty acid metabolism), onset in neonatal period or infancy
    - Histology non-diagnostic at time of onset
      - Myotonic dystrophy
      - Congenital muscular dystrophies
      - Facioscapulohumeral myopathy: rare at birth; when occurs, deafness & Coats disease coexist
- Nerve biopsy, usually sural nerve; helpful in determining type of neuropathy
- Other tests as indicated for specific disorders

DIFFERENTIAL DIAGNOSIS

Non-neurologic systemic disease

- Other signs of underlying etiology usually dominate the clinical picture

Primary neurologic

- UMN disorders
  - ➢ See **HYPOXIC-ISCHEMIC ENCEPHALOPATHY** in the "Neonatal Conditions and Diseases" section: most common cause of hypotonia presenting at birth, but Dx requires consistent Hx
  - ➢ Intracranial hemorrhage, cerebral infarct: focal or generalized hypotonia, often with seizure; onset at time of occurrence
  - ➢ Intracranial infection: onset at birth w/ congenital infections or concurrent w/ nosocomial meningitis or encephalitis
  - ➢ Metabolic disturbances: onset concurrent w/ or shortly after development of electrolyte disturbances, hypoglycemia, hyperbilirubinemia, aminoacidopathies, organic acidemia
  - ➢ Intrapartum administration of analgesics, sedatives, anesthetics
  - ➢ Hypothyroidism
  - ➢ Congenital anomalies of cerebrum, cerebellum
  - ➢ Multiple chromosomal syndromes (e.g., Prader-Willi syndrome)
  - ➢ Degenerative encephalopathies of white & gray matter: peroxysomal diseases – e.g., Zellweger syndrome (cerebro-hepato-renal syndrome), adrenaleukodystrophy
  - ➢ Traumatic spinal cord injury (esp cervical)
- AHC disorders
  - ➢ SMA I, aka Werdnig-Hoffman disease: usually presents at 2–4 months, but may present in first days; rarely even causes intrauterine arthrogryposis
  - ➢ See **GLYCOGEN STORAGE DISEASE TYPE II** (aka Pompe's disease) in the "Neonatal Conditions and Diseases" section: usually presents w/ cardiac symptoms before hypotonia ~1 month of age; involves muscle as well as AHC
  - ➢ Poliomyelitis:- presents at age 2–3 mo after attenuated live-polio vaccination
- Peripheral nerve disorders
  - ➢ Traumatic
    - See **BIRTH TRAUMA: BRACHIAL PLEXUS INJURY** in the "Neonatal Conditions and Diseases" section
    - Postpartum trauma/pressure: median nerve(carpal tunnel syndrome), radial n (wrist drop), peroneal n (foot-drop)
  - ➢ Chronic motor-sensory polyneuropathy
    - Congenital hypomyelinating neuropathy
    - Chronic inflammatory demyelinating neuropathy: rare at birth

- Subcellular–cytoskeletal disorders (e.g., giant axonal neuropathy): may present in neonatal period

➢ Congenital sensory & congenital sensory & autonomic neuropathies (HSAN) – e.g., congenital sensory neuropathy w/ anhydrosis, Riley-Day syndrome (Ashkenazi-Jewish parents)
- Can present w/ hypotonia in infancy
- Sensory & autonomic difficulties hard to recognize in newborn

➢ Acute polyneuropathy (Guillain-Barre syndrome): very rare in newborn

■ NMJ disorders
➢ Hypermagnesemia due to maternal administration: onset at birth (aminoglycosides may worsen hypotonia)
➢ Myathenias (see **MYASTHENIA GRAVIS, TRANSIENT AND CONGENITAL** in the "Neonatal Conditions and Diseases" section)
- Transient neonatal myasthenia (mother w/ myasthenia gravis): presents sometime in 1st 12 hrs of life
- Congenital myasthenic syndromes (at least 9 types known; some present at birth)

➢ Infantile botulism: generally presents in infancy after birth

■ Muscle disorders (see **MUSCLE DISEASES CAUSING NEONATAL WEAKNESS & HYPOTONIA** in the "Neonatal Conditions and Diseases" section)
➢ See **MYOTONIC DYSTROPHY, CONGENITAL** in the "Neonatal Conditions and Diseases" section: apparent in first few hours of life
➢ Congenital muscular dystrophies: apparent at birth; histology does not distinguish various types; some are assoc w/ CNS involvement
➢ Facioscapulohumeral myopathy: rare at birth; when it occurs, deafness & Coats disease coexist
➢ Minimal change myopathy: presents at birth
➢ Central core disease, nemalinemyopathy, myotubular myopathy, congenital fiber type disproportion, other congenital myopathies w/ abnormal structure: all present at birth
➢ Mitochondrial myopathies (e.g., cytochrome c-oxidase deficiency, mitochondrial DNA depletion): often present in neonatal period
➢ Metabolic myopathies (disorders of glycogen & fatty acid metabolism): present in neonatal period or infancy

MANAGEMENT

- What to do first
  - ➢ ABCs (airway, breathing, circulation)
  - ➢ Initiate diagnostic evaluation after stabilization (important to interview & examine parents)

SPECIFIC THERAPY

Depends on etiology

FOLLOW-UP

Depends on etiology

COMPLICATIONS AND PROGNOSIS

Depends on etiology

INTESTINAL OBSTRUCTION

RICHARD A. POLIN, MD

HISTORY & PHYSICAL

- Intestinal obstruction can be functional (e.g., secondary to sepsis, hypermagnesemia, increased intracranial pressure, prematurity) or mechanical
- High intestinal obstruction (above ampulla of Vater) leads to excessive salivation, non-bilious vomiting; abdominal distention rare except in epigastric area
- Obstruction beyond ampulla of Vater leads to bilious vomiting, marked abdominal distention
- Delayed passage of meconium occurs w/ lesions closer to anus
- Failure to pass meconium w/in 24 h suggests colonic lesion
- Bilious vomiting: always investigate, should be considered medical emergency
- Persistent non-bilious vomiting often related to feeding practices
- Gastric content >15 mL before first feeding a sign of intestinal obstruction

History

- Time of presentation
  - ➢ Gastric antral webs, pyloric atresia: complete obstruction produces symptoms (non-bilious vomiting) shortly after birth, incomplete obstruction may not present for wk or mo after birth

- Pyloric stenosis: symptoms (non-bilious vomiting) commonly begin 3–6 wk of age, but can appear in first wk of life
- Lactobezoars: 3–12 days after feeding begun
- Gastric perforation: 2–7 days of age
- Duodenal atresia: onset of symptoms (bilious vomiting) in first 24 h of life; abdominal distention localized to upper part of abdomen
- Malrotation: 80% of affected infants present in first month of life w/ bilious vomiting, occasional rectal bleeding, shock; malrotation w/o volvulus formation produces more subtle symptoms (vomiting, failure to thrive, abdominal pain) NOTE: IN ANY INFANT W/ BILIOUS VOMITING, MALROTATION (SURGICAL EMERGENCY) SHOULD BE R/O.
- Extrinsic compression (annular pancreas, duplication, retroperitoneal tumors): annular pancreas presents in similar fashion to duodenal atresia & these two malformations often coexist; enteric duplications may be asymptomatic, but can present in first few wks of life
- Jejunoileal atresia (most common atresia): onset of symptoms in 1–2 days of life (bilious vomiting, abdominal distention, failure to pass meconium)
- Meconium ileus
  - Simple meconium ileus (2/3 of cases): clinical presentation similar to other mid-ileal obstructions (first 1–2 days of life)
  - Complicated meconium ileus (occurs when meconium ileus complicated by intestinal necrosis, perforation, peritonitis or pseudocyst formation): signs of peritonitis superimposed on those of intestinal obstruction
- Meconium plug syndrome/small left colon syndrome: signs of low intestinal obstruction in first few days of life
- Imperforate anus: infants w/ complete obstruction commonly present w/ signs of low intestinal obstruction in first few days of life; fistulous connections to perineum usually recognized in first few days of life; infants w/ fistulous connections to the urinary tract may present w/ recurrent urinary tract infection
- Hirschsprung disease
  - Failure to pass meconium in first 24 h of life or delayed passage of meconium beyond 48 h most common sign
  - Complete obstruction may lead to abdominal distention w/ bilious vomiting in first few days of life

- Some infants present w/ constipation, intermittent bouts of obstruction in first few wk of life relieved by digital rectal exam or enema
- Infants may be symptom-free for several weeks
- Incomplete obstruction can lead to diarrhea/enterocolitis, protein-losing enteropathy, failure to thrive
- Dilated megacolon may obstruct the urinary tract, cause urinary tract infection

- Maternal History
  - ➢ Polyhydramnios: suggests possibility of high intestinal obstruction
  - ➢ Maternal stress in last trimester assoc w/ pyloric stenosis
  - ➢ Maternal diabetes: meconium plug/small left colon
  - ➢ Toxemia of pregnancy: hypermagnesemia used to treat preeclampsia assoc w/ meconium plug

Physical

- Note magnitude, location of abdominal distention
- High intestinal obstruction: less distention & when present, localized in upper abdomen
- Low intestinal obstruction: generalized distention
- Increased salivation: high intestinal obstruction
- Peritoneal tenderness: common w/ meconium ileus, NEC or any condition w/ perforation (e.g., malrotation)
- Assoc findings
  - ➢ Pyloric stenosis
    - Male infants more commonly affected (4:1)
    - More common in firstborn infants
    - Assoc w/ blood types O & B
  - ➢ Duodenal atresia
    - 30% of affected babies have Down syndrome
    - Assoc w/ malrotation, CHD, tracheoesophageal fistula, renal anomalies
    - 20% have annular pancreas (70% of these infants: assoc anomalies)
  - ➢ Malrotation: assoc w/ other GI malformations (omphalocele, gastroschisis, diaphragmatic hernia & duodenal atresia)
  - ➢ Jejunoileal atresia: assoc w/ IUGR
  - ➢ Meconium ileus: cystic fibrosis (observed in 10–15% of CF patients)

- ➢ Meconium plug/small left colon
  - Infants of diabetic mothers represent 50% of affected patients
  - Assoc w/ sepsis & hypermagnesemia
  - May be manifestation of Hirschsprung disease
  - 14–25% have cystic fibrosis
- ➢ Imperforate anus
  - Anomalies occur in half of affected infants (cryptorchidism, spinal dysraphism, single umbilical artery, cloacal exstrophy, omphalocele and sacral agenesis)
  - Assoc w/ deficits in neural innervation to perineum
  - Part of VATER assoc
- ➢ Hirschsprung disease
  - 80% male
  - 10% have Down syndrome
  - Assoc w/ neural crest abnormalities (e.g., neuroblastoma, pheochromocytoma, neurofibromatosis)
  - Sensorineural deafness & Ondine's curse

TESTS

- Abdominal radiographs (supine, upright, decubitus) provide best info
  - ➢ "Double bubble" not specific for duodenal atresia (also observed w/ annular pancreas, malrotation)
  - ➢ Higher intestinal obstruction leads to small bowel dilatation
  - ➢ Lower intestinal obstruction leads to generalized dilatation
  - ➢ Peritoneal calcification: evidence of antenatal bowel perforation; cystic fibrosis, ileal atresia most common causes
  - ➢ Meconium ileus may cause bubbly appearance in distal small bowel
  - ➢ Pneumoperitoneum indicates perforated viscus
- Abdominal ultrasound
  - ➢ Useful for pyloric stenosis (occasional infant may req barium study)
  - ➢ In anomalies assoc w/ renal malformations, US mandatory
  - ➢ Useful for differentiating high from low atresia
- Upper GI study
  - ➢ Useful for malrotation
- Barium enema

- ➢ Useful for differentiating jejunoileal atresia, meconium ileus, meconium plug, Hirschsprung disease
- Rectal manometry: Hirschsprung disease
- Rectal biopsy: Hirschsprung disease

DIFFERENTIAL DIAGNOSIS
- See "History and Physical"

MANAGEMENT
- What to do first
  - ➢ ABCs (airway, breathing, circulation)
- General measures
  - ➢ NPO
  - ➢ Nasogastric tube to decompress abdomen
  - ➢ Correction of acidosis
  - ➢ Correction of fluid, electrolyte disturbances
  - ➢ Fluid resuscitation
  - ➢ Pediatric surgical consultation

SPECIFIC THERAPY
N/A

FOLLOW-UP
N/A

COMPLICATIONS AND PROGNOSIS
N/A

INTRAUTERINE GROWTH RESTRICTION (IUGR)

RICHARD A. POLIN, MD

HISTORY & PHYSICAL
- IUGR may begin early or late in fetal development
  - ➢ Note: IUGR & small for gestational age are NOT synonymous
  - ➢ IUGR: deviation from expected fetal growth pattern due to factors that inhibit normal growth potential of fetus
  - ➢ SGA describes infant whose wt is >2 standard deviations below population standards
- Infants demonstrating IUGR early in gestation are symmetrically growth-restricted (i.e., head circumference, wt, length are proportionately affected to similar degree)

- IUGR of later onset characterized by "head sparing"; body wt, length reduced to greater degree

History

- Time of onset
  - ➢ Infants w/ early-onset IUGR
    - Decreased growth potential
    - May exhibit signs of congenital infection, anomalad syndrome, or chromosomal abnormality
    - Normal ponderal index [birth wt × 100/length(to the third power)]
    - Low risk of asphyxia, hypoglycemia
  - ➢ Infants w/ late-onset IUGR
    - Low ponderal index
    - "Brain sparing"
    - Increased risk for hypoglycemia, asphyxia
- Maternal History
  - ➢ Higher incidence of IUGR in women who were SGA themselves or have had SGA infant (recurrence risk may be 25–50%)
  - ➢ Early IUGR
    - Congenital infections
  - ➢ Late IUGR
    - Chronic fetal hypoxia
    - Multiple gestations
    - Preeclampsia
    - Chronic hypertension
    - Class D-F diabetes
    - Poor nutrition (more common in adolescents, women w/ chronic diseases, dietary faddists, low pre-pregnancy weight, Hx of frequent conceptions, heavy physical work during pregnancy, low socioeconomic groups)
    - Uteroplacental vascular insufficiency
  - ➢ Drugs assoc w/ IUGR
    - Diphenylhydantoin, isotretinoin, trimethadione, valproic acid, antimetabolites, alkylating agents, alcohol, warfarin, cigarettes

Physical

- Early-onset growth restriction
  - ➢ Head circumference, length, wt proportionately small
  - ➢ Physical exam may be entirely normal; however, some infants will exhibit signs consistent w/ specific syndrome, congenital infection or chromosomal abnormality

- Late-onset growth restriction
  - Head appears large in comparison w/ undergrown trunk
  - Decreased subcutaneous tissue (reduced skin fold thickness)
  - Anterior fontanelle may be larger than expected
  - Cranial sutures may be widened or overriding
  - Bone ossification may be retarded
  - Neurological assessment of GA should be consistent w/ GA
  - Physical assessment of GA may be misleading (decreased vernix caseosa, increased sole creases, decreased breast tissue, immature appearance to genitalia)

TESTS

- Plasma glucose concentration
  - Hgb concentration (IUGR infants at risk for polycythemia, hyperviscosity)
  - Eval for congenital infection if infant has assoc signs
  - Karyotype w/ assoc dysmorphic features or congenital anomaly

DIFFERENTIAL DIAGNOSIS

- SGA infant who has grown normally
- DDx of etiology of IUGR
  - Congenital infection
  - Chromosomal abnormality
  - Anomalad syndrome
  - Fetal teratogen exposure
  - Maternal malnutrition
  - Maternal diseases (preeclampsia, diabetes, collagen vascular disease)
  - Uteroplacental vascular insufficiency

MANAGEMENT

- What to do first
  - ABCs (airway, breathing, circulation)
- General measures
  - Careful attention to thermal environment
  - Early institution of enteral feedings if infant ready to accept enteral nutrition
  - IV dextrose (4–8 mg/kg/min) if infant unable to accept enteral feedings

SPECIFIC THERAPY

N/A

FOLLOW-UP

- In neonatal period
  - ➢ Body temp
  - ➢ Plasma glucose (bedside assessment w/in 2 h of birth, then prior to each feeding for 24–48 h; infants maintained on IV dextrose should have bedside testing done once/shift after plasma glucose concentration has stabilized)
  - ➢ Hct
- Long-term
  - ➢ Growth & development

COMPLICATIONS AND PROGNOSIS

- Complications
  - ➢ Asphyxia
  - ➢ Meconium aspiration syndrome
  - ➢ Hypothermia
  - ➢ Hypoglycemia
  - ➢ Polycythemia
  - ➢ Pulm hemorrhage
- Prognosis
  - ➢ Depends on underlying etiology

MALABSORPTION

RICHARD A. POLIN, MD

HISTORY & PHYSICAL

- Malabsorption in neonates manifested as loose stools, which can quickly cause dehydration
- Diarrhea may be manifestation of systemic infection
- Most common causes of diarrhea include excessive fluid & nonabsorbable carbohydrate intake, enteric infections, inflammatory processes, drugs
- Neonate highly susceptible to enteric pathogens due to:
  - ➢ Lack of colonization w/ protective flora
  - ➢ Decreased gastric acid production
  - ➢ Lack of secretory IgA
- Types of diarrhea
  - ➢ Osmotic diarrhea (e.g., lactose intolerance): diarrhea caused by ingesting substances that cannot be absorbed or digested,

or cannot be absorbed because of underlying intestinal disease
- Non-absorbed solute draws H_2O, electrolytes into intestine
- Fresh diarrheal stool has osmolality (2× ([Na+] + [K+]) of 280–300 mOsm
- In osmotic diarrhea, stool osmolality is <280 mOsm & the osmotic gap [serum osmolality – stool osmolality] is high (>160 mOsm)
- Diarrhea ceases when poorly absorbed solute not ingested

➢ Secretory diarrhea (e.g., congenital chloride diarrhea)
- Diarrhea occurs throughout day & night
- Underlying mechanism excessive chloride secretion
- Osmotic gap low (<20 mOsm)
- Persistence of diarrhea beyond 24–48 h w/o enteral intake suggests secretory diarrhea

■ History

➢ Acute diarrhea
- Enteric pathogens: can occur at any time, but bacterial etiologies less common in breast-fed infants
  - *E. coli, Salmonella, Shigella, Campylobacter, C. difficile, Vibrio cholerae, Yersinia enterocolitica, Rotavirus*, other viruses, parasites & fungi
- Antibiotic assoc
  - In presence of antibiotic pressure, *C. diff* overgrowth, toxin production occurs
  - Antibiotics can alter bowel flora, resulting in diarrhea
  - Penicillins, cephalosporins can directly compete w/ absorption

➢ Chronic diarrhea
- Post-infectious enteritis: secondary to mucosal damage, can last 1–2 mo
- Carbohydrate malabsorption
  - Acquired intolerance much more common than primary carbohydrate malabsorption (onset symptoms w/ intro of carbohydrate in diet)
    - Congenital lactase deficiency
    - Sucrase-isomaltase deficiency
    - Glucose-galactose malabsorption
- Lipid disorders
  - Abetalipoproteinemia: severe fat malabsorption, failure to thrive from birth

- Hypobetalipoproteinemia: severe fat malabsorption, failure to thrive from birth
- Chylomicron retention disease: steatorrhea, failure to thrive from birth
- Wolman disease: presents in 1st few wks of life w/ vomiting, diarrhea, abd distention
- Intestinal lymphangiectasia (may be primary or secondary): diarrhea, protein-losing enteropathy in infancy

- Electrolytes, trace minerals
  - Congenital chloride diarrhea: severe diarrhea in first few wks of life w/ massive H_2O & electrolyte loss
  - Congenital sodium diarrhea: phenotypically similar to congenital chloride diarrhea, but acidotic
  - Acrodermatitis enteropathica: may present as early as 3 wks w/ severe diarrhea
  - Menkes syndrome
- Primary bile acid malabsorption: diarrhea, steatorrhea in early infancy
- Congenital enterocyte disorders
  - Microvillus inclusion disease: high-output diarrhea in early life
  - Tufting disease: persistent diarrhea in first few wks of life
- Hirschsprung disease: colitis w/ bloody diarrhea
- Acquired defects
  - Short bowel syndrome after intestinal resection
  - Necrotizing enterocolitis w/ stricture formation leading to "overflow" diarrhea
- Abnormalities of pancreas secretion
  - Cystic fibrosis: diarrhea usually does not occur until 4–6 wk of age
  - Shwachman syndrome: may present in 1st 6 months of life
- Overfeeding: may occur at any time
- Immune defects: abnormalities can be primary or secondary, diarrhea a common manifestation
- Hormonal disorders
  - Hyperthyroidism: most commonly caused by transplacental transfer of TSH receptor-stimulating antibodies
    - In infants born to untreated mothers, signs of hyperthyroidism begin in first 24 h of life
- Inflammatory, allergic disorders

- Cow's milk or soy protein intolerance: symptoms begin in first 5 months of life, often bloody diarrhea

➢ Maternal History
- Infectious diarrhea in mother

■ Physical
➢ Assess degree of dehydration
➢ Determine adequacy of growth
➢ Signs of intestinal obstruction or peritoneal tenderness
➢ Assoc findings
- Abetalipoproteinemia & hypobetalipoproteinemia: acanthocytes, decreased deep tendon reflexes, low levels of plasma cholesterol
- Wolman disease: organomegaly, calcification of the adrenals
- Primary intestinal lymphangiectasia: Turner, Noonan syndromes, abnormalities of lymphatic drainage
- Congenital chloride diarrhea: hypochloremic, hypokalemic metabolic alkalosis
- Acrodermatitis enteropathica: vesiculobullous, eczematous & psoriasiform eruptions about mouth, genitals, anus, ocular changes
- Cystic fibrosis: meconium ileus/peritonitis, intestinal obstruction, cholestasis
- Shwachman syndrome: neutropenia, recurrent infection, bony abnormalities
- Hyperthyroidism: irritability, flushing, hyperthermia, high-output congestive heart failure, generalized lymphadenopathy, hepatosplenomegaly & thrombocytopenia

TESTS

■ Acute diarrhea
➢ By definition, these are self-limited episodes
➢ Minimal workup should include CBC, serum electrolytes if dehydrated, blood & stool cultures

■ Chronic diarrhea
➢ CBC for evidence of infection, anemia, acanthocytes (abetalipoproteinemia), lymphopenia (intestinal lymphangiectasia) or neutropenia (Shwachman syndrome)
➢ Serum electrolytes
➢ Total protein, albumin levels
➢ Stool culture for enteric pathogens, rapid screen for rotavirus (winter months), stool for ova & parasites

- ➢ Exam of stool for leukocytes, pH, reducing substances, occult blood
- ➢ Exam of the chloride content of serum, urine & stool (to exclude congenital chloride or sodium diarrhea)
- ➢ Sweat chloride (inaccurate w/ severe malnutrition)
- ➢ Qualitative test for stool fat
- ➢ Serum immunoglobulins, in vitro tests of T-cell function
- ➢ Fecal, serum bile acids (to exclude primary bile salt malabsorption)
- ➢ Proctosigmoidoscopy (to rule out enterocolitis)
- ➢ Small bowel biopsy (useful for cow's milk/soy protein allergy, familial villous atrophy, intestinal lymphangiectasia, abetalipoproteinemia)

DIFFERENTIAL DIAGNOSIS

- See "History and Physical"

MANAGEMENT

- What to do first
  - ➢ Fluid resuscitation if dehydrated
- General measures
  - ➢ NPO
  - ➢ Systemic broad-spectrum antibiotics if sepsis suspected
  - ➢ Correction of acid-base, electrolyte disturbances
  - ➢ TPN if diarrhea has been persistent or infant malnourished
  - ➢ If diarrheal episode has been brief, infants can be restarted on breast milk or standard formula
  - ➢ If the diarrhea has been persistent, begin elemental formula such as Pregestemil (volume & concentration of feedings should be cautiously advanced)

SPECIFIC THERAPY

N/A

FOLLOW-UP

- Varies w/ etiology & effect on growth

COMPLICATIONS AND PROGNOSIS

- Varies w/ etiology & effect on growth

METABOLIC ACIDOSIS

RICHARD A. POLIN, MD

HISTORY & PHYSICAL

- Normal serum pH does not exclude lactic acidemia
- Metabolic acidosis may be divided into anion gap/non-anion gap acidoses.
- Anion gap = Na+ minus HCO_3- minus Cl- (K+ not generally used in equation because this eliminates hemolysis as confounding variable)
- An elevated anion gap may be due to:
  - ➢ Increased serum concentrations of unmeasured anions
  - ➢ Decreased concentrations of unmeasured cations (rare in neonate)
- Metabolic acidosis w/ normal anion gap is due to immature renal function, diarrhea or renal tubular acidosis
- Metabolic acidosis w/ elevated anion gap is due to lactic acidosis or organic acidosis resulting from inborn error of metabolism
- In infants w/ dehydration or renal failure, anion gap modestly elevated
- Anion gap of 10–15 (<8 mmol/L) considered normal
- Elevated anion gap (>16 mmol/L) indicates organic acidosis
- Anion gaps ranging 8–16 mmol/L not diagnostic, may/may not be assoc w/ organic acidosis
- Normal lactate level <2 mM or 18 mg/dL
- Normal pyruvate level <0.1 mM
- Normal lactate/pyruvate (L/P) ratio <25
- Normal beta-hydroxybuterate/acetoacid (BOHB/AcAc) ratio <= 3.3
- Lactate/pyruvate ratio: index of redox state of cytoplasm
- BOHB/AcAc ratio: index of redox state of mitochondria
- History
  - ➢ Time of presentation
    - Lactic acidosis
      - Secondary
      - Lactic acid increases whenever tissue O_2 delivery diminished (hypoxia or shock)
      - Occurs as secondary phenomenon w/ abnormalities of organic acid metabolism, fatty acid oxidation, urea cycle (see below)

- Primary
  - ➢ Defects in gluconeogenesis, glycogenolysis or pyruvate metabolism
    - Fructose 1,6-bisphosphatase deficiency
      - Onset symptoms w/ fasting
      - Fructose intake not very important in precipitating crises
    - Hereditary fructose intolerance
      - Remains disease-, symptom-free until exposed to sucrose- or fructose-containing products
    - Glycogen storage disease (GSD) I
      - Onset in neonatal period
    - Glycogen storage disease (GSD) III
      - May present in infancy
    - Pyruvate carboxylase deficiency
      - Several types, but can present w/ severe neonatal encephalopathy, hyperammonemia, lactic acidosis
    - Pyruvate dehydrogenase complex deficiency
      - Severe defects present in neonatal period (<20% residual enzyme)
  - ➢ Krebs cycle defects: rare disorders that may present in neonatal period w/ severe acidosis
  - ➢ Respiratory chain defects
    - Nuclear DNA mutations
      - Benign infantile mitochondrial myopathy +/− cardiomyopathy
        - Onset at birth
      - Lethal infantile mitochondrial myopathy
        - Severe illness in first few weeks of life
      - Barth syndrome
        - Onset in neonatal period
    - Mitochondrial DNA mutations
      - Leigh syndrome
        - Usually presents beyond the neonatal period
      - Pearson syndrome: onset in neonatal period
    - Organic acidurias: usually present early, but can be delayed
      - Isovaleric acidemia: onset in 1st 2-4 days of life
      - Methylmalonic aciduria: onset in 1st 2-4 days of life
      - Propionic acidemia: onset in 1st 2-4 days of life
      - Maple syrup urine disease: onset in 1st 2-4 days of life
      - Holocarboxylase synthetase deficiency: onset in 1st few days of life

- 3-hydroxy, 3-methylglutaryl-CoA (HMG) Lyase deficiency: onset in neonatal period in 30% of cases
- Glutaric acidemia type 2: onset w/in 24 h of birth
- Molybdenum cofactor deficiency (sulfite oxidase deficiency): onset in 1st few days of life

- Fatty acid oxidation defects
  - Medium-chain acyl-CoA dehydrogenase deficiency
    - Onset w/ beginning of breast-feeding (time of relative fasting)
- Ketogenesis defect
  - 3-hydroxy-3-methylglutaric acidemia
    - Onset in neonatal period
- Disorders of ketolysis: onset in neonatal period
  - Beta-ketothilase deficiency
  - Succinyl-CoA 3-ketoacid CoA transferase deficiency
- Renal tubular acidosis
  - Several types have onset in neonatal period or infancy

➢ Maternal conditions
- HELLP syndrome: long-chain acyl-CoA dehydrogenase deficiency

■ Physical

➢ Careful physical exam (including exam of retina by experienced ophthalmologist) mandatory since multiple systems can be involved

➢ Assoc findings (other than acidosis)
- Primary lactic acidosis
  - Defects in gluconeogenesis, glycogenolysis or pyruvate metabolism
    - Fructose 1,6-bisphosphatase deficiency
      - Ketosis, lactic acidosis, hypoglycemia w/ fasting
    - Glycogen storage disease (GSD) I
      - Hepatomegaly, hypoglycemia, ketosis, hypertriglyceridemia, hyperuricemia & neutropenia (type Ib)
    - Glycogen storage disease (GSD) III
      - Hypoglycemia & liver disease
    - Pyruvate dehydrogenase complex deficiency
      - Cystic lesions in cerebral hemispheres & basal ganglia
      - Cerebral atrophy
      - Facial dysmorphism
      - Impaired migration of neurons
      - Agenesis of corpus callosum

- Respiratory chain defects
  - Nuclear DNA mutations
    - Benign infantile mitochondrial myopathy +/− cardiomyopathy
      - Hypotonia, feeding abnormalities, resp difficulties
    - Lethal infantile mitochondrial myopathy
      - Hypotonia, failure to thrive
    - Barth syndrome
      - Dilated cardiomyopathy, cataracts & neutropenia
  - Mitochondrial DNA mutations
    - Leigh disease
      - Optic atrophy, ophthalmoplegia, hypotonia, spasticity, seizures, myopathy, renal tubular dysfunction, cardiomyopathy, liver dysfunction, microcephaly
    - Pearson syndrome
      - Sideroblastic anemia, exocrine pancreatic dysfunction, neutropenia, thrombocytopenia
      - Some affected children may develop Kearns-Sayre syndrome
    - Mitochondrial depletion syndrome
      - Acute hepatic failure, renal disease & hypotonia
- Organic acidurias
  - Isovaleric acidemia, methylmalonic aciduria, propionic acidemia
    - Coma, ketoacidosis, hyperammonemia, hypoglycemia, hyperglycinemia, abnormal carnitine metabolism, lactic acidosis, neutropenia, thrombocytopenia or pancytopenia
  - Maple syrup urine disease
    - Ketoacidosis, hypoglycemia, lethargy, seizures, coma & maple syrup odor to urine
  - Holocarboxylase synthetase deficiency
    - Apnea, lethargy, coma, peculiar odor, hyperammonemia
  - Glutaric acidemia type 2
    - Hypotonia, hepatomegaly, nephromegaly, rocker bottom feet, anterior abdominal wall defects, external genitalia anomalies
  - 3-hydroxy, 3-methylglutaryl-CoA Lyase deficiency
    - Hypoketotic hypoglycemia, organic acidosis
    - Hypotonia, stupor, tachypnea & vomiting

- Molybdenum cofactor deficiency (sulfite oxidase deficiency)
  - Vomiting, seizures, eye abnormalities, skin rash in later infancy
- Fatty acid oxidation defects
  - Medium-chain acyl-CoA dehydrogenase deficiency
    - Hypoglycemia, mild acidosis, hyperammonemia, dicarboxylic aciduria
- Ketogenesis defect
  - Nonketotic acidosis, seizures, hypotonia & hypoglycemia
- Renal tubular acidosis
  - Proximal RTA
    - May be primary or assoc w/ other disorders causing Fanconi syndrome
  - Distal RTA
    - Sensorineural hearing loss

TESTS

- Metabolic acidosis due to hypoxemia or shock: no further workup required (acidosis will disappear once underlying defect corrected)
- Persistent metabolic acidosis
  - ➢ Arterial blood gas determination
  - ➢ CBC & platelet count
  - ➢ Serum electrolytes
  - ➢ Plasma lactate
  - ➢ CSF lactate
  - ➢ Serum glucose
  - ➢ Plasma pyruvate
  - ➢ Serum amino acids
  - ➢ Urine organic acids
  - ➢ Serum beta-hydroxybutyrate & acetoacetate (difficult to measure)
  - ➢ Urine pH, ketones
  - ➢ Plasma ammonia
- Metabolic acidosis WITHOUT lactic acidosis
  - ➢ If serum glucose normal
    - AND ketosis present
      - Ketolysis defect
      - Organic acidemia
    - AND ketosis absent

- Renal tubular acidosis

➢ If serum glucose decreased
- AND ketosis present
  - Organic acidemia
  - Normal adaptation to fasting
- AND ketosis absent
  - Fatty acid oxidation defect
  - Ketogenesis defect

■ Metabolic acidosis w/ lactic acidosis
➢ If urinary organic acids abnormal
- Fatty acid oxidation defect
- Organic acidemia

➢ If urinary organic acids normal
- Assess lactate/pyruvate (L/P) ratio

■ If L/P ratio increased, assess beta-hydroxybuterate/acetoacid (BOHB/AcAc) ratio
➢ If BOHB/AcAc ratio increased
- Resp chain defect

➢ If BOHB/AcAc ratio decreased or normal
- Krebs cycle defect
- Pyruvate carboxylase deficiency

■ If L/P normal, assess serum glucose AND BOHB/AcAc ratio
➢ If normoglycemia w/o ketosis
- Pyruvate dehydrogenase complex deficiency

➢ If hypoglycemia +/− ketosis
- Gluconeogenic defect

DIFFERENTIAL DIAGNOSIS

■ See "History and Physical"

MANAGEMENT

■ What to do first
➢ If resp/circulatory compromise, begin w/ ABCs (airway, breathing, circulation)

■ General measures for metabolic acidosis (no suspected metabolic disorder)
➢ Assure adequate O_2 delivery (circulatory, ventilatory support as needed)

➢ For chronic metabolic acidosis associated w/ prematurity, add sodium acetate (in place of some of sodium chloride) to IV solution

- ➢ Sodium bicarbonate (0.5–2 mEq/kg) for correction of acute metabolic acidosis; repeat as needed
- General measures for suspected metabolic disorder
  - ➢ Vigorous correction of metabolic acidosis w/ sodium bicarbonate or THAM
  - ➢ No protein intake until diagnosis established
  - ➢ NPO
  - ➢ Maintenance IV fluids
  - ➢ Maintain plasma glucose concentration 60–120 mg/dL
  - ➢ Megavitamin therapy
  - ➢ Dietary manipulation

SPECIFIC THERAPY
N/A

FOLLOW-UP
N/A

COMPLICATIONS AND PROGNOSIS
- Varies w/ etiology
- Acidosis secondary to immature renal function in premature infants: self-limited, has excellent prognosis

NEPHROCALCINOSIS AND NEPHROLITHIASIS

RICHARD A. POLIN, MD

HISTORY & PHYSICAL
- Most instances of nephrolithiasis are assoc w/ hypercalciuria
- Nephrolithiasis, nephrocalcinosis are much more common in preterm infants
- Hypercalciuria in full-term infants defined as urinary Ca/creatinine ratio >0.15 mg/mg
- Normal values for Ca excretion in preterm infants controversial, but calcium/creatinine ratios higher (50th percentile in 1study = 0.29 mg/mg)

History
- Time of presentation
  - ➢ Intrauterine development of nephrocalcinosis has been described in neonatal hyperparathyroidism, distal renal tubular acidosis

- ➢ Infants w/ hereditary causes of "hypercalciuria" may be symptomatic in infancy, but often present w/ signs unrelated to hypercalciuria, nephrocalcinosis
  - Distal renal tubular acidosis type I (presenting signs related to metabolic acidosis)
  - Arthrogryposis multiplex congenita w/ renal, hepatic anomalies (>150 syndromes assoc w/ arthrogryposis, joint deformities the initial presenting sign)
  - Bartter syndrome (hypercalciuria may be presenting sign)
  - Infantile hypophosphatasia (severe rickets evident at birth)
  - Hyperparathyroidism (primary, secondary can lead to diffuse bone demineralization & nephrocalcinosis)
- ➢ Infants w/ acquired causes of hypercalciuria usually asymptomatic (nephrocalcinosis detected by renal US)
  - Increased Ca intake +/− hypercalcemia
    - Excessive Ca intake
    - Rapid Ca infusion
    - Hypervitaminosis D
    - Low phosphate intake
  - Decreased renal tubular reabsorption
    - Furosemide, ethacrynic acid, Aldactone
    - Osmotic diuresis
    - Phosphate depletion syndrome
    - Extracellular volume expansion
    - Methylxanthines
  - Factors favoring precipitation of Ca, phosphate
    - Low urine output
    - Alkaline urine
    - Absence of inhibitors (citrate, inorganic phosphate, Mg)
- ➢ Misc causes of nephrolithiasis
  - Type I primary hyperoxaluria: rarely presents in neonatal period, but common in infancy (anorexia, failure to thrive, vomiting, diarrhea, fever)
  - Cystinosis: earliest symptoms appear in 2nd half of 1st year of life (polyuria, polydipsia, anorexia, failure to thrive, dehydration)
  - Gitelman syndrome (hyperprostaglandinuric tubular syndrome w/ hypercalciuria & hypokalemia (increased propensity for oxalate stones, may be assoc w/ hypocalcemia)
  - TPN (increases oxalate secretion)

- Pyridoxine deficiency (may result in hyperoxaluria)
- Corticosteroid therapy (increases calcium excretion)

■ Maternal History
  ➢ Chronic maternal hypocalcemia may cause secondary hyperparathyroidism in neonate

Physical
Most preterm infants w/ nephrocalcinosis secondary to hypercalciuria are asymptomatic; renal function usually normal, but nephrolithiasis can impair GFR or distal tubular function

TESTS
■ Infants at risk for nephrocalcinosis (primarily sick preterm infants <1500 g, infants receiving chronic diuretics) should have screening renal US study at 2-4 wk of life

DIFFERENTIAL DIAGNOSIS
■ See "History and Physical"

MANAGEMENT
■ General measures for nephrocalcinosis secondary to hypercalciuria
  ➢ Discontinue or decrease drugs assoc w/ increased Ca excretion
  ➢ Consider adding thiazide to a diuretic regimen
  ➢ Maintain urine flow rates, prevent dehydration
  ➢ Prevent phosphate depletion

SPECIFIC THERAPY
N/A

FOLLOW-UP
N/A

COMPLICATIONS AND PROGNOSIS
■ Duration
  ➢ Nephrocalcinosis occurs most often in preterm infant; self-limited disorder
  ➢ Recurrent/permanent nephrolithiasis can be observed in hereditary disorders listed above

NEUTROPENIA

RICHARD A. POLIN, MD

HISTORY & PHYSICAL

- Neutropenia clinically defined as absolute neutrophil (PMN) count below lower limit of values in age-defined population
- In term & late preterm infants infant, PMN counts should remain $>1750/mm^3$
- In VLBW infants, lower limit of normal is $1100/mm^3$
- PMN counts $>1{,}000/mm^3$ have no increased risk of infection
- PMN counts $<500/mm^3$ greatly increase risk of infection
- PMN counts $500–1{,}000/mm^3$ may have intermediate risk of infection
- Etiology of neutropenias can be divided into decreased production, increased usage or destruction & excessive neutrophil margination
- History
  - ➢ Time of presentation
    - Decreased production
      - Infants of hypertensive women: onset at birth (3–5 days in duration)
      - Donors of twin-twin transfusion
        - Onset at birth, can last 8–10 days
      - Rh hemolytic disease: onset at birth, lasts 3–5 days
      - Drug/chemical-induced: concurrent w/ drug use
        - Drugs causing neutropenia by direct suppression include indomethacin, chloramphenicol, sulfonamides, semisynthetic penicillins, H_2 blockers
      - Kostmann syndrome: severe neutropenia w/ onset at birth
      - Cyclic neutropenia: cycles occur every $21 +/- 3$ days, often accompanied by thrombocytopenia, reticulocytopenia
      - Shwachman-Diamond syndrome: onset in infancy
      - Reticular dysgenesis: severe neutropenia & lymphopenia w/ onset at birth
      - Neonatal aplastic anemia: pancytopenia at birth
      - Chronic idiopathic neutropenia: onset at birth, commonly in preterm infants
      - Neutropenia assoc w/ metabolic disease: onset in first hours to days of life
        - Hyperglycinemia

- Isovaleric acidemia
- Methylmalonic acidemia
- TORCH infections: onset at birth

- Accelerated neutrophil usage
  - Bacterial or fungal sepsis (usually resolves in 48–72 h w/ appropriate therapy)
  - Autoimmune neutropenia: observed in infants born to women w/ autoimmune neutropenia
  - Alloimmune neutropenia: onset at birth, can last 2–4 wk
  - Drug/chemical-induced: ibuprofen, aminopyrine, phenytoin, propylthiouracil, hydralazine, procainamide, quinidine, chlorpropamide, levamisole
- Excessive PMN margination
  - Endotoxemia

➢ Maternal conditions
- Pregnancy-induced hypertension
- Autoimmune neutropenia w/ transplacental transfer of antibodies
- Drugs: numerous drugs assoc w/ neutropenia

➢ Assoc findings
- Shwachman syndrome: Steatorrhea, failure to thrive, eczema, metaphyseal chondrodysplasia
- Reticular dysgenesis: absence of lymph nodes
- Kostmann syndrome: monocytosis, eosinophilia, frequent episodes of fever, pyogenic infections in first few months of life
- Metabolic disease
  - Organic acidemias: metabolic acidosis, coma (occasionally pancytopenia)
- Pancytopenia
  - Neonatal aplastic anemia
  - Reticular dysgenesis
  - Alloimmune
- Hydrops: Rh hemolytic disease
- TORCH infections
  - Microcephaly/hydrocephaly
  - Organomegaly
  - Chorioretinitis

■ Physical

➢ Infant appears critically ill?
- Consider sepsis or metabolic disease

- ➢ Manifestations of congenital infection?
- ➢ Hydrops? Consider Rh hemolytic disease

TESTS

- Most neutropenias self-limited, have obvious etiologies (sepsis or pregnancy-induced hypertension)
  - ➢ Neutropenia of sepsis usually resolves in 48–72 h
  - ➢ Neutropenia assoc w/ pregnancy-induced hypertension lasts 3–5 days
  - ➢ Persistence of neutropenia beyond these limits should prompt evaluation
- Persistent neutropenia
  - ➢ CBC w/ smear to evaluate PMN morphology
    - Infants w/ persistent neutropenia should have counts obtained 2× weekly for 6 wk to evaluate periodicity
  - ➢ Maternal PMN count: to exclude autoimmune neutropenia
  - ➢ If mother's count normal, "type" maternal & paternal neutrophils, obtain anti-neutrophil Ab screen
    - (Ab generally directed at neutrophil-specific NA antigen system)
  - ➢ Bone marrow
    - Reserved for infants w/ severe neutropenia ($<500/mm^3$) lasting >1 wk
    - Note: Exam of bone marrow rarely provides definitive Dx, but does identify underlying mechanism (decreased production or increased destruction)

DIFFERENTIAL DIAGNOSIS

- See "History and Physical"

MANAGEMENT

- What to do first
  - ➢ Determine if sepsis responsible for neutropenia, provide supportive measures (antibiotics/fluids, etc.) as needed
- General measures
  - ➢ If absolute PMN persistently remains $<500/mm^3$, use prophylactic antibiotics (ampicillin/aminoglycoside) until count is $>1{,}000/mm^3$
  - ➢ rG-CSF
    - rG-CSF indicated if absolute PMN count remains $<500/mm^3$ for 2 or 3 day or in $501–999/mm^3$ for 5–7 days
    - Effective in:

- Kostmann syndrome
- Shwachman-Diamond syndrome
- Cyclic
- Alloimmune
- Chronic idiopathic
- Note: rG-CSF not helpful in infants w/ sepsis

➢ IVIG may help raise blood PMN count in infants w/ bacterial sepsis

SPECIFIC THERAPY
N/A

FOLLOW-UP
N/A

COMPLICATIONS AND PROGNOSIS
N/A

NONIMMUNE HYDROPS FETALIS (NIHF) AND CONGENITAL ASCITES

RICHARD A. POLIN, MD

HISTORY & PHYSICAL

- Hydrops fetalis: generalized fetal edema (fluid accumulation in fetal tissues, serous cavities)
- The term "hydrops" should be reserved for fluid accumulation at >1 site
- Note: An isolated fluid collection (e.g., pleural effusion) may be initial manifestation of hydrops, before generalized edema develops
- Hydrops may be secondary to immune causes (e.g., Rhesus immunization) or nonimmune causes (NIHF)
- NIHF results from 1 of 6 mechanisms
  - ➢ Primary myocardial failure
  - ➢ High-output cardiac failure
  - ➢ Decreased plasma oncotic pressure
  - ➢ Increased capillary permeability
  - ➢ Obstruction of venous return
  - ➢ Obstruction of lymphatic flow
- Congenital ascites
  - ➢ Fluid localized to abdominal cavity

- ➢ Can be chylous, urinary, biliary, pancreatic or manifestation of ruptured ovarian cyst or peritonitis

■ History
- ➢ Time of presentation
  - Hydrops fetalis: always evident at birth, but can be detected prenatally w/ US
  - Congenital ascites: abdominal distention may/may not be present at birth
- ➢ Duration
  - Depending on etiology, some cases of NIHF resolve spontaneously
  - Only certain conditions amenable to therapy (e.g., NIHF secondary to tachyarrhythmias or fetal anemia); those conditions resolve w/ treatment of underlying disorder
  - Congenital ascites can resolve spontaneously (e.g., chylous ascites), but most infants require surgical intervention
- ➢ Assoc findings
  - NIHF
    - Cardiac conditions (structural defects or arrhythmias) resulting in CHF (25–40% of cases)
      - AV septal defect, hypoplastic left heart, aortic stenosis, ectopia cordis, cardiomyopathy, Ebstein's anomaly, AV malformations, pulmonary atresia, cardiac tumors (tuberous sclerosis)
      - Tachyarrhythmias & bradyarrhythmias
        - Supraventricular tachycardia most common tachyarrhythmia
        - Congenital heart block in absence of structural anomalies only rarely causes hydrops
    - Chromosomal abnormalities (account for ~15% of cases): Turner syndrome, trisomies, triploidy
    - Anemia (accounts for 5–15% of cases): alpha-thalassemia, fetal hemorrhage, twin/twin transfusion (including acardia twinning), G6PD (hemolysis can be spontaneous or secondary to maternal ingestion of oxidants), RBC enzymatic disorders
    - Congenital infections (~4% of cases): parvovirus B19, cytomegalovirus, toxoplasmosis, Coxsackie virus, syphilis, trypanosomiasis, herpes simplex type I, respiratory syncytial virus, leptospirosis
    - Congenital hepatic dysfunction: cirrhosis, necrosis

- Nephrotic syndrome (Finnish variety)
- Thoracic causes (~8% of cases): congenital diaphragmatic hernia, congenital cystic adenomatoid malformation (CCAM; MOST COMMON PULM CAUSE), pulmonary sequestration, pulmonary leiomyosarcoma, pulmonary effusions, hamartomas, lymphangiectasia
- Neoplasms: teratomas (cause high-output failure), neuroblastoma (may cause severe anemia, venous obstruction or arrhythmias), congenital leukemia, hemangioendothelioma of liver
- Skeletal dysplasias, other malformation syndromes (pathogenesis uncertain): achondroplasia, achondrogenesis, osteogenesis imperfecta, thanatophoric dysplasia, short rib polydactyly syndrome, asphyxiating thoracic dystrophy, multiple pterygium syndrome, arthrogryposis
- Placental causes: chorangiomas (act as high-volume A/V shunts), hemorrhagic endovasculitis, angiomyxoma of umbilical cord, cord vein thrombosis, umbilical vein torsion
- Inborn errors of metabolism (associated finding in 1–2% of cases): beta-glucuronidase defect, Gaucher disease, GM1 gangliosidosis, sialidosis, Hurler syndrome, other mucopolysaccharidosis & Niemann-Pick disease, myotonic dystrophy
- Idiopathic

- Congenital ascites
  - Chylous (most common cause of neonatal ascites): may be assoc w/ intestinal malrotation, volvulus
  - Urinary (accounts for 25% of ascites): male/female ratio 5:1, posterior urethral valves most common cause, but may occur w/ any obstructive uropathy
  - Biliary ascites: due to rupture of biliary tree, often assoc w/ clinical jaundice (and a rise in direct reacting bilirubin)
  - Pancreatic ascites: infants usually asymptomatic
  - Ruptured ovarian cyst: may cause ascites or hemoperitoneum
  - Meconium peritonitis: secondary to bowel obstruction or ischemic bowel injury (meconium ileus, intussusception, volvulus, incarcerated inguinal hernia, imperforate anus & meconium plugs, necrotizing enterocolitis, appendicitis)

➢ Maternal History (hydrops)

- Flu-like syndromes in mother
- Polyhydramnios (75% of cases)
- Malpresentation (24% of cases)
- Preterm labor
- Uterine size > expected for gestational age
- Preeclampsia (or preeclampsia-like disease): 34–50% of cases
- Assoc w/ tocolytic agents (fenoterol, ritodrine, indomethacin)
- Fetal distress
- Higher incidence of postpartum hemorrhage, retained placenta

■ Physical
  ➢ Frequently premature delivery
  ➢ W/ hydrops, respiratory distress common (pleural effusions may lead to pulmonary hypoplasia)
  ➢ Hydrops: fluid accumulation in serous cavities, generalized body edema
  ➢ Infants w/ congenital ascites may be symptomatic at birth or have marked abdominal distention, which can interfere w/ ventilation

TESTS

■ NIHF (most important step: to rule out isoimmunization)
  ➢ Maternal studies
    - CBC
    - Hgb electrophoresis
    - Kleihauer Betke test
    - RPR
    - Serological tests for parvovirus, toxoplasmosis
    - Screen for G6PD
  ➢ Fetal studies
    - US
      - Hydrops: generalized skin thickening (>5 mm), + 2 or more of following: ascites, pleural effusion, pericardial effusion or abnormally thickened placenta (>6 cm)
    - Echocardiogram
    - Amniocentesis
      - Viral cultures (CMV)
      - PCR for toxoplasmosis
      - Alpha-fetoprotein
    - Umbilical blood sampling
      - Karyotype

- CBC
- Hgb electrophoresis
- Lysosomal storage enzymes

➢ Neonatal studies
- CBC, smear
- Blood type & Hgb electrophoresis
- Blood chemistry studies
- Skeletal radiographs
- US (cardiac, thoracic, abdomen)
- Dysmorphology evaluation
- Karyotype
- Metabolic studies
- Autopsy

■ Congenital ascites

➢ Fetal
- If no evidence of hydrops: assess for oligohydramnios (suggests obstructive uropathy)
- If oligohydramnios not present: look for dilated bowel loops, intraperitoneal calcifications (indicative of in utero perforation)

➢ Neonatal
- Single most informative test: exam of ascitic fluid (red cell count, white cell count, total protein, culture, triglycerides, amylase, urea, bilirubin)
- Total/direct bilirubin
- Serum Na (hyponatremia observed in ~70% of infants)
- If obstructive uropathy suggested, further evaluation of urinary tract indicated (US, IVP, VCUG)
- If biliary ascites suspected: technetium liver scan

DIFFERENTIAL DIAGNOSIS

■ See "History and Physical"

MANAGEMENT

■ What to do first

➢ ABCs (airway, breathing, circulation)

➢ Correction of acid/base disturbances

➢ Treatment of CHF (see **CONGESTIVE HEART FAILURE**)

■ General measures

➢ Once infant has been stabilized, diagnostic evaluation takes precedence

SPECIFIC THERAPY

- Hydrops
  - ➢ Fetal intervention (depends on underlying etiology; examples shown below)
    - Correction of fetal anemia
    - Treatment of tachyarrhythmias
    - Ablation of shunts btwn twins
    - Fetal surgery for CCAM
  - ➢ Neonatal (depends on underlying etiology; examples shown below)
    - Correction of anemia (usually accomplished by partial exchange transfusion)
    - Treatment of tachy/bradyarrhythmias
- Congenital ascites
  - ➢ Chylous: treatment consists of repeated parancentesis, use of formula containing medium-chain triglycerides
  - ➢ All other etiologies require surgical intervention

FOLLOW-UP

N/A

COMPLICATIONS AND PROGNOSIS

- Mortality 40–90%
- Prognosis for tachyarrhythmias, isolated ascites or hydrothorax probably better

RENAL FAILURE

RICHARD A. POLIN, MD

HISTORY & PHYSICAL

- Definitions (multiple)
  - ➢ Serum urea nitrogen >20 mg/dL, creatinine concentration 1.5 mg/dL
    - Serum creatinine at birth a function of maternal serum creatinine
    - Serum urea nitrogen may be >30 mg/dL in the first days of life & in infants receiving a high parenteral protein intake, but serum creatinine does not increase
    - Serum urea nitrogen usually <10 mg/dL in growing preemies

- ➢ 50% increase in plasma creatinine (above baseline)
- ➢ <0.5–1.0 mL/kg/h of urine output
- ➢ Sudden decrease in GFR to <50% of normal for gestational, postnatal age (best definition)

■ History
- ➢ Time of presentation
  - Prerenal failure: concurrent w/ hemorrhage, hypovolemia, low cardiac output or sepsis episode
  - Intrinsic renal failure
    - Varying time of presentation depending on etiology
      - Bilateral agenesis, severe cystic dysplasia, renal tubular dysgenesis & severe non-cystic dysplasia: onset may be prenatal (oligohydramnios) or at birth
      - Renal hypoplasia: can be symptomatic in neonatal period when assoc w/ renal dysplasia
      - Autosomal recessive, autosomal dominant polycystic kidney disease: varying time of presentation but either may cause life-threatening disease in neonatal period
        - Severe respiratory distress, renal failure at birth (more common w/ autosomal recessive disease)
        - Asymptomatic infant w/ flank masses (more common w/ autosomal dominant disease)
  - Obstructive renal disease
    - Severe lesions: present in infancy w/ renal failure, may cause renal maldevelopment
    - Less severe lesions: may be asymptomatic until later in childhood
- ➢ Maternal History
  - Fetal hemorrhage
    - Twin-twin transfusion
    - Fetal-maternal hemorrhage
    - Cordocentesis
    - Amniocentesis
    - Maternal idiopathic thrombocytopenic purpura (ITP)
    - Birth trauma
    - Umbilical cord accidents
    - Abruptio placentae/placenta previa
  - Oligohydramnios
    - Suggests antenatal onset to renal failure
  - Use of angiotensin-converting enzyme inhibitors in pregnancy

- Assoc w/ renal tubular dysgenesis
- Fetal hydronephrosis
- Stillbirth (up to 40% of infants w/ bilateral agenesis stillborn)
- Renal teratogens: cocaine, indomethacin, lead, phenacetin, salicylate, warfarin

■ Physical
➢ Wide range depending on etiology, associations
➢ Oligohydramnios sequence w/ prenatal onset of renal failure
➢ Hypertension
➢ Assoc findings
- Perinatal/neonatal hemorrhage: signs & symptoms depend on site of bleeding (most common locations: intracranial, pulmonary, gastrointestinal & adrenal)
- Oligohydramnios sequence: indicates decreased fetal urine production (but does not suggest specific etiology)
  - Abnormal face (wizened appearance, low-set ears, often w/ folded helices, down-turned nose, small chin)
  - Bowed legs
  - Clubbed feet
  - Amnion nodosum
  - Pulmonary hypoplasia
- Prune belly syndrome
  - Absent or wrinkled anterior abdominal muscles
  - Undescended testes (females infrequently affected)
  - May display features of oligohydramnios sequence
  - Deficiency of smooth muscle in internal sphincter, bladder wall, ureters
  - May be assoc w/ posterior urethral valves or anatomic obstruction of lower urinary tract
  - Renal abnormalities range from minor to severe dysplasia
  - Prognosis worse w/ lower urinary tract obstruction
- Multicystic kidney
  - No continuity between glomerulus, calyces
  - Opposite kidney may be normal, absent, cystic, dysplastic, ectopic or hydronephrotic
  - Most common abdominal mass in newborn
- Renal agenesis
  - Autosomal recessive syndromes
    - Acrorenomandibular syndrome
      - Ectrodactyly & hypoplastic mandible
    - Digitocerebrorenal syndrome

- MURCS association: Mullerian duct aplasia & cervicothoracic somite dysplasia
- C-trigonocephaly
  - Trigonocephaly, polysyndactyly, abnormal ears, joint dislocations
- Fraser syndrome
  - Cryptophthalmos, ear anomalies, syndactyly & genital anomalies
- Adrenogenital
  - 21-hydroxylase deficiency
- Pena-Shokeir syndrome
  - Failure to thrive, microcephaly, prominent nose, large ears, hypotonia, flexion contractures
- Ellis-van Creveld syndrome
  - Acromelic dwarfism, polydactyly, hypoplasia, dystrophy of nails & teeth, CHD
- Ivemark syndrome
  - Spleen agenesis or hypoplasia, cyanotic CHD, trilobulated left lung, gut malrotation
- Neu-Laxova syndrome
  - IUGR, microcephaly, abnormal facies, short neck, arthrogryposis & CNS malformations

- Autosomal dominant syndromes
  - Acrorenal syndrome
    - Radial & renal anomalies
  - Ectodermal dysplasia-ectrodactyly-cleft lip/palate syndrome
  - Lacrimo-auricular-dento-digital
    - Nasolacrimal duct obstruction, cup-shaped ears, enamel dysplasia & digital malformations
  - LEOPARD syndrome
    - Multiple lentigines syndrome
  - CHARGE association
  - VACTERL association
  - Sorsby syndrome
    - Pigmented macular coloboma, brachydactyly
- Associated anomalies
  - Pulmonary hypoplasia
  - Single umbilical artery
  - Anal, duodenal, esophageal atresia
  - Colonic atresia

- Meckel's diverticulum
- Abnormal internal genitalia

- Renal dysplasia (cystic or non-cystic)
  - 70% of non-cystic dysplasias have other urinary tract anomalies (vesicoureteral reflux most common)
  - Dysplastic kidneys can be unilateral or bilateral
  - Associated malformations
    - Cardiovascular
    - Gastrointestinal
    - Scoliosis (associated w/ unilateral dysplasia)
    - Congenital dislocation of hip (associated w/ unilateral dysplasia)
    - Turner syndrome (associated w/ unilateral dysplasia)
- Renal adysplasia/dysplasia (note: adysplasia refers to renal agenesis, hypoplasia or dysplasia)
  - Trisomy 9 & 13
  - Prune belly syndrome
    - Renal abnormalities range from minor to severe dysplasia
  - Posterior urethral valves
    - Renal abnormalities range from minor to severe dysplasia
  - Branchio-oto-renal syndrome
    - Dandy-Walker malformation, corneal opacities, cleft lip/palate, diaphragmatic hernia & digital abnormalities
    - Assoc w/ spectrum of abnormalities, unilateral dysplasia to bilateral agenesis
  - Ectodermal dysplasia-ectrodactyly-cleft lip/palate syndrome
  - Fanconi pancytopenia syndrome
    - Pancytopenia, radial ray defects & hyperpigmentation
    - Assoc w/ renal anomalies, adysplasia
  - Thrombocytopenia absent radius syndrome
  - Fraser syndrome (see above for associated anomalies)
    - Assoc w/ cystic dysplasia & agenesis
  - Fryns syndrome
    - Dandy-Walker malformation, corneal opacities, cleft lip/palate, pulmonary hypoplasia, diaphragmatic hernia & digital hypoplasia
    - Assoc w/ cystic dysplasia
  - Pallister-Hall syndrome

    - Hypothalamic-hamarblastoma hypopituitarism, imperforate anus, polydactyly
    - Assoc w/ renal dysplasia/ectopia
  - VACTERL association
    - Assoc w/ renal anomalies
- Polycystic kidney disease
  - Autosomal recessive (ARPKD)
    - Presents in infancy w/ large flank masses, oligohydramnios sequence (Potter's phenotype & pulmonary hypoplasia)
    - Hypertension common
    - Sterile pyuria common
    - Concentrating defect
    - Hepatic fibrosis, biliary dysgenesis
  - Autosomal dominant
    - Wide range of manifestations from severe clinical disease (indistinguishable from ARPKD) to asymptomatic
  - Tuberous sclerosis (fibrous angiomatosis, seizures, mental deficiencies, cardiac tumors)
  - Roberts syndrome (tetraphocomelia, cleft lip/palate & genital hypertrophy)
  - Meckel syndrome (postaxial polydactyly, microphthalmia, encephalocele, cystic kidneys, ambiguous genitalia & hepatic fibrosis)
  - Goldston syndrome (cystic kidneys, hepatic fibrosis, Dandy-Walker malformation)
  - Chondrodysplasias, include Jeuene syndrome (resp distress, dysostoces, short ribs, small thoracic cage, small pelvis, cone-shaped epiphyses, handle-bar clavicle, short limbs, renal cystic disease, hepatic fibrosis)
  - Ivemark syndrome (see above)
  - Type 2 glutaric aciduria (prematurity, hypotonia, hepatomegaly & nephromegaly w/ renal cystic dysplasia)
  - Zellweger syndrome (cerebro-hepato-renal syndrome)
- Glomerulocystic kidneys
  - May resemble polycystic kidney disease
  - Kidneys may be large or small
  - Familial hypoplastic glomerulocystic kidney
    - Onset of chronic renal failure in infancy
    - May be associated w/ marked prognathism
- Dysgenetic kidneys

- Congenial hypernephronic nephromegaly w/ tubular dysgenesis
  - Late-onset oligohydramnios, large non-functioning kidneys
  - Underdeveloped calvarium w/ wide sutures
- Perlman syndrome
- Polyhydramnios, macrosomia, bilateral nephromegaly w/ nephroblastomatosis, visceromegaly & cryptorchidism

TESTS

- Urinalysis
  - ➢ Protein concentration should not exceed 5–10 mg/dL
  - ➢ WBC count <2–3/HPF
  - ➢ RBC count <5/HPF
  - ➢ Cellular casts not generally seen, suggest renal parenchymal disease or dehydration
  - ➢ RBC casts suggest glomerulonephritis
- Renal US
  - ➢ Best first-line test for evaluation of renal size, texture
  - ➢ Allows identification of hydronephrosis & cystic kidney disease
- Doppler scan
  - ➢ Useful for assessing renal artery, vein thrombosis
- Radioisotope studies
  - ➢ Valuable in locating anomalous kidneys, determining kidney size, demonstrating abnormalities in blood flow distribution
  - ➢ Provide information on contribution of each kidney to overall renal function
- Intravenous pyelography
  - ➢ Less commonly used because high doses of radiocontrast material are required for visualization
- Voiding cystourethrogram
  - ➢ Essential test when vesicoureteral reflux suspected or urinary tract infection has been diagnosed
- Evaluation of renal function
  - ➢ Assessment of GFR
    - Serum urea nitrogen: generally <20 mg/dL after first wk of life; abnormal values may indicate dehydration, excessive protein intake or diminished renal function
    - Creatinine
      - Serum creatinine values in first couple days of life reflect maternal values; thereafter:

- Term infants: values should be <1.0 mg/dL (mean 0.5 mg/dL)
- Infants 25–28 wk gestation: values may be >1.0 mg/dL for up to 8 wk
- Infants 28–34 wks gestation: values may be >1.0 mg/dL for up to 4 wk

- After first wk of life, estimate of GFR can be made using creatinine length method (may not be accurate w/ acute renal failure)
  - Full-term infants: GFR = 0.45 × length (cm)/plasma creatinine value
  - Infants <34 wk: GFR = 0.34 × length (cm)/plasma creatinine value
  - Average GFR in term infant: ~40 mL/min/1.73 M2 (rapidly increases postnatally)
  - Preterm infants 25–28 wk gestation have average GFR of ~10 mL/min/1.73 M2 (slowly increases postnatally)

➢ Renal tubular function
- Fractional excretion of Na+: fractional excretion Na = urine Na x plasma creatinine/ plasma Na x urine creatinine × 100
- In the presence of oliguria, a fractional excretion of Na >3% suggests intrinsic renal failure, but preterm infants can have fractional excretion >3%

■ Arterial BP

DIFFERENTIAL DIAGNOSIS

■ Systemic hypovolemia
➢ Fetal hemorrhage
➢ Neonatal hemorrhage
➢ Septic shock
➢ Peritonitis
➢ Dehydration
- Increased insensible H_2O losses in infants <1000 g
- Excessive use of diuretics
- Severe fluid restriction
- Increased losses (renal/GI)

■ Renal hypoperfusion
➢ Perinatal asphyxia
➢ Hemodynamic
- Congestive heart failure
- High mean airway pressure (decreased venous return)

- Pneumothorax
- Patent ductus arteriosus
- Cardiac surgery: concurrent w/ surgery

➢ Polycythemia-hyperviscosity

➢ Pharmacologic
- Indomethacin
- Tolazoline
- Captopril

■ Obstructive renal failure

➢ Congenital malformations
- Imperforate prepuce
- Urethral stricture
- Posterior urethral valves
- Massive vesicoureteral reflux
- Ureterocele
- Megacystis/megaureter/megacolon syndrome
- Eagle-Barrett syndrome
- Ureteropelvic junction obstruction

➢ Extrinsic compression
- Sacrococcygeal teratoma
- Hematocolpos

➢ Intrinsic obstruction
- Renal calculi
- Fungus balls

➢ Neurogenic bladder
- Meningomyelocele
- Tethered cord

➢ Blocked catheter or urethra (clot)

➢ Pancuronium w/ heavy sedation

■ Intrinsic renal failure

➢ Acute tubular necrosis

➢ Congenital malformations
- Bilateral agenesis
- Renal dysplasia
- Polycystic kidney disease
- Glomerular maturational arrest
- Hypoplasia
  - Vesicoureteral reflux
  - Fetal alcohol syndrome
  - Wolf-Hirschhorn syndrome
- Renal tubular dysgenesis

- Infection
  - Congenital (syphilis/toxoplasmosis)
  - Pyelonephritis
- Renal vascular
  - Renal artery thrombosis
  - Renal vein thrombosis
  - Disseminated intravascular coagulation
- Nephrotoxins
  - Indomethacin
  - Aminoglycosides
  - Amphotericin
  - Contrast media
- Intrarenal obstruction
  - Uric acid nephropathy
  - Myoglobinuria
  - Hemoglobinuria

MANAGEMENT

- General measures
  - Make sure BP, perfusion normal
  - Bladder catheterization
    - Eliminates possibility of outlet obstruction
  - Fluid challenge
    - 20 mL/kg over 2 h of normal saline to correct volume depletion followed by furosemide (1 mg/kg) if oliguria/anuria persists
  - Intrinsic renal failure
    - Low-dose dopamine (2–4 mcg/kg/min)
  - Persistent anuria/oliguria
    - Restrict fluid intake to insensible H_2O loss (IWL) + urine output w/ electrolyte free fluids unless urinary Na loss high
    - Monitor serum Na, K, Ca & P concentrations at least once/d, make corrections as necessary
    - Monitor serum glucose concentrations once/shift
      - Glucose requirements: 4–8 mg/kg/min
    - Provide essential amino acid solution designed for renal failure 1 g/kg/d, glucose, Intralipid
    - Correct metabolic acidosis w/ sodium bicarbonate
  - Treat hypertension
  - Avoid nephrotoxic drugs, monitor drug concentrations closely

➢ Dialysis: indications include severe fluid overload, electrolyte abnormalities – e.g., hyperkalemia, severe hyponatremia (unresponsive to medical management), symptomatic uremia, rapidly rising BUN & creatinine, hypertension

SPECIFIC THERAPY
N/A

FOLLOW-UP
N/A

COMPLICATIONS AND PROGNOSIS
- 50% mortality for acute renal failure caused by congenital malformations or acquired diseases
- The majority of infants w/ renal failure secondary to congenital malformations will progress to chronic renal failure
  - ➢ Chronic hypertension
  - ➢ Poor growth
  - ➢ Acidosis

RESPIRATORY DISTRESS

RICHARD A. POLIN, MD

HISTORY & PHYSICAL
- History
  - ➢ Presentation
    - Transient respiratory distress (duration <4 h) common, generally signifies infant who is undergoing slow transition to postnatal life
      - May signify delayed absorption of fetal lung fluid (commonly observed in infants w/ perinatal depression)
      - May result from hypothermia
- Transient respiratory distress should resolve w/in 4 h; at that point infant's O_2 saturation should be >= 95% in room air
- NOTE: In infant w/ "transient" respiratory distress, it is frequently difficult to determine whether symptoms will be transient or persistent, so interventions & diagnostic studies are often indicated before infant improves & signs of respiratory distress resolve.
  - ➢ Persistent resp distress: pulmonary etiologies
    - Respiratory distress syndrome (RDS)

- Transient tachypnea of newborn (TTN)
- Bacterial pneumonia/sepsis
- Viral pneumonia/sepsis
- Meconium aspiration syndrome (MAS)
- Pulmonary hypoplasia
- Pneumothorax (generally follows initiation of respiratory support, but may occur spontaneously)
- Pulmonary hemorrhage
- Congenital pulm malformations: congenital diaphragmatic hernia, cystic adenomatoid malformation (and other cystic anomalies), chylothorax, congenital lobar emphysema, pulmonary lymphangiectasia
- Airway obstruction: nose (e.g., choanal atresia); mouth (e.g., Pierre Robin syndrome); larynx (e.g., laryngeal web or vocal cord paralysis); trachea/bronchi (e.g., tracheomalacia, bronchomalacia, tracheostenosis); airway compression (e.g., vascular ring, hemangioma, mediastinal masses, goiter)
- Disorders of surfactant protein metabolism
- Persistent pulmonary hypertension of the newborn (PPHN)

➢ Persistent respiratory distress: extrapulmonary causes
- Neuromuscular disorders
- CHF
- Rib cage abnormalities
- Hematological disorders (anemia/polycythemia)
- Metabolic acidosis
- Cyanotic CHD

■ Importance of gestational age
➢ RDS: incidence correlates inversely w/ gestational age
➢ MAS: rarely occurs in preterm infants
➢ Sepsis/pneumonia: incidence correlates inversely w/ gestational age
➢ Pulmonary hemorrhage: more common in preterm infants (esp those w/ RDS)
➢ TTN: more common in term or near-term infants
➢ Pulmonary lymphangiectasia: more common in term or near-term infants

■ Time of presentation
➢ RDS: immediately after birth
➢ TTN: immediately after birth
➢ "Early-onset" sepsis/pneumonia usually presents in 1st day of life, but may present as late as day 5

- ➢ "Late-onset" sepsis/pneumonia may present at any time 5 days to 3 mo of life
- ➢ MAS: immediately after birth
- ➢ Pulmonary hypoplasia: immediately after birth
- ➢ Congenital pulmonary malformations may be asymptomatic at birth or present w/ severe respiratory distress almost immediately
- ➢ Pneumothorax: may occur as spontaneous event immediately after delivery, or at any time following initiation of respiratory support
- ➢ Severe upper airway obstruction (e.g., bilateral choanal atresia, laryngeal web, tracheal stenosis) presents immediately after birth; less severe forms of airway obstruction (e.g., Pierre Robin sequence) may cause minimal or no symptoms at birth
- ➢ Pulmonary hemorrhage: presents in preterm infants who are generally receiving mechanical ventilation

■ Assoc findings
- ➢ Pulmonary disorders: signs & symptoms of respiratory distress (retractions, grunting, rales, rhonchi, flaring tachypnea)
- ➢ Cyanotic CHD or CHF: signs & symptoms referable to heart are usually but not invariably present
- ➢ Multiple malformations suggest underlying CHD or pulmonary malformation as part of larger syndrome (e.g., VACTERL or CHARGE associations)

■ Maternal Hx
- ➢ Oligohydramnios (before 20 wk gestational age): pulmonary hypoplasia
- ➢ Antepartum culture positive for group B streptococcus or chorioamnionitis: pneumonia, sepsis
- ➢ Coxsackie B viral infection: myocarditis in newborn infants
- ➢ Meconium-stained amniotic fluid: MAS
- ➢ Hydrops fetalis: may be noted w/ congenital cystic anomalies
- ➢ Many malformations can be detected antenatally

■ Physical Exam
- ➢ Distribution of cyanosis
  - Most infants demonstrate central cyanosis
    - Cyanosis of oral mucous membranes indicates generalized cyanosis resulting from reduction in systemic oxygen tension (usually <70–80%)
  - Infants w/ upper airway obstruction w/o pulmonary parenchymal disease may not be cyanotic

- Differential cyanosis (upper normal/lower hypoxic or upper hypoxic/lower normal) strongly suggests CHD

➢ Vital signs
- Hypertension
  - May be cause of CHF
  - More common in infants w/ bronchopulmonary dysplasia
- Hypotension
  - May be observed in any critically ill infant
  - BP measurements useful for following changes in clinical condition but not helpful diagnostically
- BP that is >20 mmHg higher in arms than legs: consider coarctation of aorta
- Tachycardia: nonspecific, not helpful diagnostically
- Tachypnea: nonspecific, not helpful diagnostically

➢ Pulmonary findings
- Indicate pulmonary dysfunction, resulting from pulmonary or extra-pulmonary causes
- Nasal flaring: decreases total lung resistance, work of breathing
- Grunting: maintains stable functional residual capacity, improves ventilation perfusion ratio
  - Common in infants w/ RDS, other pulmonary parenchymal diseases
  - Uncommon in infants w/ TTN
- Retractions: nonspecific
  - Because the newborn's chest is so compliant, retractions can be observed w/ even minimal alterations in lung mechanics
  - Severity of retractions generally correlates w/ severity of lung disease
- Tachypnea: minimizes work of breathing
  - In infants w/ decreased lung compliance, respiratory rate rapid & shallow
  - In infants w/ increased resistance (e.g., subglottic stenosis), respirations slower & deeper
- Hyperpnea (deep unlabored breathing): indicative of conditions w/ reduced pulmonary blood flow or metabolic acidosis

TESTS

■ Pulse oximetry

➢ Best way to assess arterial O_2 saturation

- ➢ Measurements: always include right hand, foot to detect shunting through ductus arteriosus
- ➢ Values <90% abnormal (normal values >= 95%)
- ➢ Decreased perfusion, movement, bright lights can affect accuracy of readings

■ CXR
- ➢ Useful for determining tube, line position
- ➢ Pneumothoraces, pleural effusions usually evident on plain radiograph; when unsure, lateral decubitus film can help
  - Pneumothorax (side w/ suspected air leak up)
  - Effusions (affected side down)
- ➢ Diffuse lung disease: primary pulmonary process, but may be difficult to distinguish from pulmonary edema secondary to heart failure or obstruction to venous return
- ➢ Cardiomegaly or an abnormally shaped heart: CHD or CHF
- ➢ Localized "infiltrates": not helpful diagnostically
  - May indicate infection or aspiration syndrome
  - Chamber enlargement or edema may cause localized areas of atelectasis that look like infiltrates
- ➢ Pulmonary malformations usually evident, but may be subtle
- ➢ Right-sided aortic arch: vascular rings & CHD

■ Echocardiogram
- ➢ Definitive diagnostic method for CHD
- ➢ Anomalies of aortic arch, anomalous pulmonary venous return can be difficult to identify
- ➢ Confirms pulmonary hypertension

■ Arterial blood gas determination
- ➢ Invasive
- ➢ For oxygenation, not more helpful than pulse oximeter measurements
- ➢ Provides useful info about arterial pH, PCO_2, metabolic acid-base status

■ Hemoglobin concentration
- ➢ In presence of anemia, decrease in% O_2 saturation necessary to produce cyanosis will be greater
- ➢ Polycythemia may increase blood viscosity & pulmonary vascular resistance
  - Polycythemic infants appear plethoric: plethora can be confused w/ cyanosis
  - Marked polycythemia may cause respiratory distress

- Plethoric infants develop cyanosis w/ lesser reductions in O_2 saturation

- Serum glucose concentration
  - ➢ Hypoglycemia: rare but easily treatable cause of cyanosis

DIFFERENTIAL DIAGNOSIS

- Pulmonary diseases (note detailed list in "History and Physical" section)
- Sepsis
- Cyanotic CHD
- CHF
- Anemia
- Polycythemia/hyperviscosity
- Neuromuscular diseases
- Rib cage abnormalities
- Upper airway obstruction
- Metabolic acidosis

MANAGEMENT

- What to do first
  - ➢ ABCs (airway, breathing, circulation)
  - ➢ Breathing spontaneously: apply 100% O_2 to infant's face (hyperoxia test)
  - ➢ Evidence of respiratory distress: 100% O_2 should be administered w/ continuous positive airway pressure (CPAP)
  - ➢ If persists despite 100% O_2 & CPAP, or ventilation perceived to be inadequate, infant should be intubated, placed on mechanical ventilation (may not be indicated if CHD documented & no signs of pulmonary dysfunction)
- General measures
  - ➢ Provide BP support as needed
  - ➢ If ductal-dependent lesion strongly suspected/confirmed, begin PGE1 (0.1 mcg/kg/min)

SPECIFIC THERAPY

N/A

FOLLOW-UP

N/A

COMPLICATIONS AND PROGNOSIS

N/A

SEIZURES

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- Definition: paroxysmal alteration in neurologic function due to abnormal hypersynchronous discharge on EEG
- Classification
  - Clonic, focal or multifocal
  - Tonic, focal or generalized
  - Myoclonic, focal,* multifocal,* or generalized
  - Subtle*: some ocular phenomena, buccal-lingual movements, rowing or pedaling limb movements, apnea; perhaps should be called abnormal phenomena as EEG is + only 13% of time
  - Electrographic neonatal seizures (ENS): seizure w/o clinical concomitant; common after Rx of clinical seizures; may be present in some unresponsive newborns

    * EEG abnormality uncommon

HISTORY AND PHYSICAL

- History
  - Maternal/pregnancy Hx
    - Maternal diabetes → ? hypoglycemia, hypocalcemia, hypomagnesemia
    - Intrauterine growth retardation → ? hypoglycemia
    - Maternal group B streptococcus, herpes simplex, toxoplasmosis → ? sepsis, meningitis, encephalitis
    - Maternal narcotic addiction
    - Hx of consanguinity → ? autosomal recessive disorder
  - Intrapartum Hx
    - Perinatal/postnatal asphyxia → ? hypoxic-ischemic encephalopathy, hypoglycemia, hypocalcemia
    - Traumatic or rapid vaginal delivery → ? subarachnoid or subdural bleed
    - PROM, chorioamnionitis → ? meningitis
    - Prematurity → ? intraventricular hemorrhage
  - Family Hx of neonatal seizure limited to the neonatal period
  - Time of presentation – helpful in DDx (see "Differential Diagnosis" section)
- Physical

- ➢ Type of seizure rarely diagnostic of etiology
- ➢ Associated focal neurologic abnormalities
- ➢ Associated findings w/specific etiologies
  - See **HYPOXIC-ISCHEMIC ENCEPHALOPATHY** in the "Neonatal Conditions and Diseases" section: depressed consciousness, hypotonia, hyporeflexia, jitteriness, multiorgan system dysfunction
  - Intracerebral hemorrhage
    - See **SUBARACHNOID HEMORRHAGE** in the "Neonatal Conditions and Diseases" section: well child; rarely symptomatic, unless other associated CNS hemorrhage
    - See **SUBDURAL HEMORRHAGE** in the "Neonatal Conditions and Diseases" section: neurologically asymptomatic or depressed consciousness, some show contralateral hemiparesis; large pupil on side of bleed is neurosurgical emergency
  - Inborn errors of metabolism: vomiting, stupor, unusual odor, hypotonia, metabolic acidosis, hypoglycemia, elevated lactate, hyperammonemia, hypocapnia
  - Congenital infection: hepatosplenomegaly, rash, thrombocytopenia
  - Neonatal narcotic withdrawal (see **NARCOTIC USE/ABUSE, MATERNAL** in the "Maternal Conditions and Diseases" section): hyperactivity, irritability, high-pitched cry, coarse tremors, jitteriness, myoclonic jerks, hypertonia, hyperreflexia, facial scratches, pressure point abrasions (elbows & knees), sneezing, hiccupping, yawning, nasal stuffiness, sweating, fever, tachypnea, feeding difficulties, vomiting, diarrhea

TESTS

- ■ CBC w/ diff, blood culture
- ■ Bedside eval of serum glucose
- ■ Serum NA, K, Ca, P, Mg, arterial lactate, ammonia
- ■ Cranial US; CT; MRI w/ spectroscopy if possible
- ■ Lumbar puncture
  - ➢ Cell count, protein, glucose, culture in all cases
  - ➢ Special studies (e.g., lactate, amino acids) as indicated
- ■ EEG
  - ➢ Amplitude integrated EEG, a simple test, identifies 70–90% of seizures; of limited use

- ➢ EEG obtained during seizures
  - May confirm abnormal jerks or posturing to be seizures
  - May confirm electrographic neonatal seizures, especially w/ sedation associated w/ anticonvulsant Rx
  - May require continuous EEG monitoring for 24 h or more
- ➢ Interictal (btwn seizures) EEG may provide useful prognostic info
- Other tests indicated for specific disorders

DIFFERENTIAL DIAGNOSIS

- See **HYPOXIC-ISCHEMIC ENCEPHALOPATHY** in the "Neonatal Conditions and Diseases" section
  - ➢ Onset of seizures usually by 6–12 hr of life
  - ➢ Most common etiology for neonatal seizures, but Dx requires consistent Hx
- Acute, severe hypoxia
- Intracranial hemorrhage
  - ➢ See **SUBARACHNOID HEMORRHAGE** in the "Neonatal Conditions and Diseases" section: DOL 2 (if not associated w/ hypoxic-ischemic encephalopathy)
  - ➢ See **SUBDURAL HEMORRHAGE** in the "Neonatal Conditions and Diseases" section: 50% of seizures in 1st 48 h of life (day 2–3 most common)
- See **STROKE, ISCHEMIC, PERINATAL AND NEONATAL** in the "Neonatal Conditions and Diseases" section
- See **MENINGITIS** in the "Neonatal Conditions and Diseases" section; encephalitis
  - ➢ Bacterial, at time of occurrence
  - ➢ Congenital infection (TORCH): seizures occur in 1st wk of life
- Congenital brain malformations: seizures occur in 1st wk of life
- Neonatal narcotic withdrawal (see **NARCOTIC USE/ABUSE, MATERNAL** in the "Maternal Conditions and Diseases" section)
  - ➢ 1st 3 days of life most common; later w/ methadone
  - ➢ Seizure rare manifestation, but may be precipitated in delivery room by naloxone for neonatal depression
- Local anesthetic intoxication (e.g., lidocaine after caudal): presents in 1st 6 hrs w/ apnea, bradycardia, pupils unresponsive to light
- Metabolic disturbances
  - ➢ See **HYPOGLYCEMIA**: at time of occurrence; duration of hypoglycemia most critical
  - ➢ See **HYPOCALCEMIA**: at time of occurrence

- Onset in 1st 2–3 days of life, commonly assoc w/ prematurity, infant of diabetic mother, asphyxia
- Onset day 7–10, neonatal tetany seen with high PO_4 formula

➢ See **HYPOMAGNESEMIA**: at time of occurrence
➢ See **HYPONATREMIA/HYPERNATREMIA**: at time of occurrence or during Rx; depends on rate of change in serum Na
➢ Amino acid & organic acid disorders: DOL 1–5; some only after protein intake
➢ Pyridoxine dependency: intrauterine onset of seizures possible; then, usually in first few hr of life
➢ Mitochondrial (e.g., Leigh syndrome) or peroxysomal (e.g., Zellweger syndrome) disorders: neonatal period or later in infancy or early childhood

■ Miscellaneous syndromes
➢ Benign familial neonatal seizures, K+ channel disorder (rare): onset of seizures 2nd or 3rd DOL, do not usually persist beyond DOL 15; chromosome 20q13.3 or 8q24
➢ Benign idiopathic neonatal seizures, multifocal clonic w/ apnea: onset of seizures 4th to 6th DOL
➢ Early myoclonic encephalopathy, myoclonus & clonus → tonus: may have in utero onset of seizures; most commonly due to inborn errors of metabolism
➢ Early infantile epileptic encephalopathy, tonic spasms: onset of seizures may be in utero; most commonly due to bilateral CNS malformation or destruction

MANAGEMENT

■ What to do first: ABCs (airway, breathing, circulation)
■ General measures: Correction of simple metab disturbances (e.g., see **HYPOGLYCEMIA**, **HYPOMAGNESEMIA**, **HYPONATREMIA**, **HYPERNATREMIA**)
■ Anticonvulsants
➢ Acute mgt
- Phenobarbital, 20 mL/kg, slow IV push
  If seizures continue, give another 10 mg/kg
  If seizures continue, give up to 2 more doses of 5 mg/kg for total dose of 40 mg/kg
- Phenytoin, only after failure of response to max phenobarbital, 20 mg/kg IV over at least 30 min
- Lorazepam, 0.05–0.1 mg/kg slow IV push
  or
  Midazolam, 0.05–0.15 mg/kg IV over at least 5 min

- ➢ Maintenance
  - Phenobarbital, 3–5 mg/kg/day, 12-24 h after loading dose, divided q12h, IV, IM, PO, to maintain serum levels 15–40 mcg/mL
  - Phenytoin, 4–8 mg/kg/day in 2 or 3 divided doses, IV or PO (not IM), to maintain trough serum levels 6–15 mcg/mL in 1st wks, then 10–20 mcg/mL
    Note: oral absorption erratic

SPECIFIC THERAPY

Treat underlying condition if possible

FOLLOW-UP

- Monitor anticonvulsant levels
- Neurologic, neurodevelopmental; other depending on cause of seizure

COMPLICATIONS & PROGNOSIS

Complications

- During loading w/ anticonvulsant
  - ➢ Phenobarbital: respiratory depression, phlebitis
  - ➢ Phenytoin: phlebitis, tissue necrosis w/ extravasation, cardiac arrhythmias
  - ➢ Lorazepam: respiratory depression, phlebitis; myoclonus in preterms
  - ➢ Midazolam: respiratory depression, hypotension (w/ rapid IV administration or in association w/ narcotic Rx); myoclonus in preterms or w/ rapid IV administration or CNS disorders

Prognosis

- Survival: depends on underlying etiology & associated conditions
- Seizure disorder, cerebral palsy, mental retardation depending on the cause of seizures – risk:
  - ➢ Those w/ seizures due to late hypocalcemia (due to excessive PO_4 intake), benign familial neonatal seizures, benign idiopathic neonatal seizures do well
  - ➢ Low risk: 50% w/ seizures due to early-onset hypocalcemia, depending on underlying etiology & associated conditions
  - ➢ 10% w/ seizures due to subarachnoid hemorrhage
  - ➢ 50% w/ seizures due to hypoxic-ischemic encephalopathy, hypoglycemia, bacterial meningitis

- ➢ Variable, but usual high risk w/ early myoclonic encephalopathy
- ➢ 100% w/ seizures due to CNS anomaly, early infantile epileptic encephalopathy

SKIN INFECTIONS

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HISTORY & PHYSICAL

History

- Impetigo
  - ➢ Usually no constitutional signs
  - ➢ Common in first 2 wk of life
- Cutaneous abscesses
  - ➢ Disruption of skin barriers or abnormalities in the immune system (e.g., hyper-IgE syndrome & leukocyte adhesion deficiency syndrome) predispose to infection
  - ➢ Breast abscess
    - Term infants in the first 6 wk of life
    - Male-female incidence equal in first 2 wk of life; more common in females thereafter
- Omphalitis
  - ➢ Infection of the umbilical stump
  - ➢ Onset on 3rd DOL
  - ➢ More common in premature infants
- Necrotizing fasciitis
  - ➢ Rapidly spreading infection preceded by few or no signs
  - ➢ Deep tenderness out of proportion to cutaneous signs
- Staphylococcal scalded skin syndrome (SSSS)
  - ➢ May occur sporadically or in epidemics
  - ➢ Toxin-mediated disease; exfoliative toxins elaborated by certain strain of *Staphylococcus aureus*
  - ➢ Focus of infection can include nasopharynx, umbilicus, urinary tract, cutaneous wound or blood

Signs

- Impetigo
  - ➢ Bullous impetigo
    - Can be considered a localized form of SSSS

- Exfoliative toxin produced by certain *S. aureus* strains induces cleavage plane in the superficial epidermis
- Flaccid, transparent subcorneal bullae
- Single or clustered w/o surrounding erythema
- Bullae may contain pus that layers out
- Lesions rupture easily, leaving shallow erosions w/ narrow rim of scale
- W/ healing, pigmentary alteration may occur

➢ Non-bullous impetigo
- Erythematous, honey-colored, crusted plaques
- Lesions tend to be localized, but more generalized on diseased skin
- Intertriginous, periumbilical areas commonly involved

■ Cutaneous abscesses
➢ Firm, tender, erythematous nodule, eventually becomes fluctuant
➢ Breast abscess
- Breast enlargement
- Firm, erythematous, indurated area
- ~1/3 of infants have constitutional symptoms
- Cellulitis occurs in 5–10% of infants
- Abscesses due to *S. aureus* assoc w/pustules or bullae in perineal region in 25–50% of cases
- Infants w/ abscesses due to *Salmonella sp* may exhibit diarrhea

➢ Omphalitis
- Periumbilical erythema/induration +/− drainage
- Red streaking following umbilical vein or cellulitis may develop

■ Necrotizing fasciitis
➢ Most commonly involves abdominal wall
➢ Constitutional symptoms common
➢ Warmth, swelling, erythema leading to ischemia over 24–48 h
➢ Bullae containing straw-colored or hemorrhagic fluid may develop

■ SSSS
➢ Generalized macular erythema, evolves quickly into scarlatiniform eruption prominent in flexural, periorificial areas
➢ Erythematous areas acquire wrinkled appearance, desquamate over a few days

- ➢ In the most severe cases, blistering & widespread desquamation of large areas of skin
- ➢ Exposed skin develops crusted, flaky appearance
- ➢ Crusting, fissuring around eyes, mouth, nose develops 2–5 days after erythroderma
- ➢ Nikolsky's sign: separation of skin due to gentle shear force
- ➢ Secondary cutaneous infections may occur

TESTS

- Staphylococcal impetigo
  - ➢ Diagnosis made clinically, confirmed by culture & Gram stain of material from w/in a pustule or vesicle, or under lifted edge of a crusted plaque
- Cutaneous abscesses/omphalitis
  - ➢ Gram stain, culture of involved area or bullae
  - ➢ Blood, urine, CSF cultures for all systemically ill infants
  - ➢ Culture of aspirated pus
  - ➢ Blood culture for infants w/o constitutional signs
- Necrotizing fasciitis
  - ➢ Surgical exploration w/ biopsy
  - ➢ Blood, urine, CSF cultures
- SSSS
  - ➢ Bullae are sterile
  - ➢ Blood, urine, CSF, umbilicus, & nasopharynx

DIFFERENTIAL DIAGNOSIS

- Staphylococcal impetigo
  - ➢ Streptococcal impetigo
  - ➢ Erythema toxicum
  - ➢ Transient neonatal pustular melanosis
  - ➢ Incontinentia pigmenti
  - ➢ Epidermolysis bullosa
  - ➢ Pemphigus
  - ➢ Pemphigoid
  - ➢ Herpes simplex virus infection
  - ➢ Varicella
  - ➢ Enterovirus infection
  - ➢ Congenital cutaneous candidiasis
- Cutaneous abscesses
  - ➢ Breast abscess

- Physiological, postnatal breast enlargement

- Omphalitis
  - ➢ Vitelline duct remnant
  - ➢ Patent urachus
  - ➢ Umbilical papilloma
- Necrotizing fasciitis
  - ➢ Cellulitis (w/o pain or ischemia)
- SSSS
  - ➢ Bullous impetigo
  - ➢ Epidermolysis bullosa
  - ➢ Toxic epidermal necrolysis
  - ➢ Diffuse cutaneous mastocytosis
  - ➢ Familial peeling skin syndrome w/ eosinophilia
  - ➢ Epidermolytic hyperkeratosis
    - Drug eruption
    - Methylmalonic acidemia
    - Graft-versus-host disease (seen in severe combined immunodeficiency syndrome)
    - Neonatal lupus erythematosus (rare cases of newborns w/ erosions)
    - Transplacental passage of antibodies from a mother w/ an autoimmune bullous disorder such as pemphigus foliaceus, pemphigus vulgaris or pemphigoid gestationis

MANAGEMENT

General Measures

- SSSS
  - ➢ Careful attn to fluid, electrolyte balance, temp regulation
  - ➢ Non-adherent semi-occlusive dressings
  - ➢ Isolation

SPECIFIC THERAPY

- Staphylococcal impetigo
  - ➢ Bullous impetigo
    - IV therapy w/ penicillinase-resistant penicillin (e.g., nafcillin, oxacillin, methicillin) × 7–10 days
    - First-generation cephalosporin also suitable
    - Culture & consider empiric coverage for methicillin-resistant *Staphylococcus aureus* (MRSA)
  - ➢ Non-bullous impetigo

- In absence of fever, soft tissue infection (e.g., lymphadenitis) or cellulitis, oral therapy w/ beta-lactamase-resistant antibiotic (e.g., cloxacillin, dicloxacillin, cephalexin) × 7 days is appropriate
- If any of above complications noted, parenteral treatment indicated (see treatment for bullous impetigo above)

- Cutaneous abscesses
  - ➢ Empiric therapy: broad-spectrum antibiotics to cover both gram-positive & gram-negative organisms (oxacillin & gentamicin)
  - ➢ Targeted antibiotic therapy once organism is identified
  - ➢ If fluctuance present, incision & drainage indicated, send fluid for culture
- Omphalitis
  - ➢ Empiric therapy
    - <5 days of age: ampicillin & gentamicin × 7–10 days
    - <= 5 d of age: oxacillin & gentamicin × 7–10 days
  - ➢ Monitor for signs of peritonitis or necrotizing fasciitis
- Necrotizing fasciitis
  - ➢ Ampicillin or penicillinase-resistant penicillin, gentamicin & clindamycin or metronidazole
- SSSS
  - ➢ Parenteral therapy w/ a penicillinase-resistant penicillin × 7–10 days
  - ➢ Consider empiric coverage for MRSA and/or adjust treatment as appropriate based on culture results or response to therapy

FOLLOW-UP

- None required unless complications occur (e.g., portal vein thrombosis w/ omphalitis)
- Any infant w/ bacteremia is at risk for osteomyelitis or CNS infection

COMPLICATIONS AND PROGNOSIS

- Complications
  - ➢ Sepsis, meningitis, osteomyelitis w/ any bacterial skin infection
    - Omphalitis
      - Portal vein thrombosis
      - Liver abscess(es)
      - May progress to necrotizing fasciitis
    - Necrotizing fasciitis

- Skin necrosis
- Distal ischemia due to edema w/ extremity involvement

➢ SSSS
- Secondary infection
- Dehydration

■ Prognosis
➢ Excellent for all superficial infections
➢ Breast growth may be affected by abscesses in that location

THROMBOCYTOPENIA

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HISTORY & PHYSICAL

■ Premature infants have platelet counts slightly lower than but in same range as older children, adults (150,000–450,000/mm^3)
■ Platelet counts 100,000–150,000/mm^3 may occur in otherwise healthy neonates
■ Platelet counts <100,000/mm^3 definitely abnl
■ Thrombocytopenia a risk factor for intracranial hemorrhage (ICH)
■ About 20% of sick infants have thrombocytopenia
■ Thrombocytopenia may be due to:
➢ Decreased production
➢ Increased destruction
➢ Sequestration
➢ Very often a combination of these processes
■ 60% of neonatal thrombocytopenias are idiopathic, no specific etiology will be found

1. Neonatal alloimmune thrombocytopenia (NAIT)
   - Caused by transplacental transfer of maternal anti-platelet antibodies
   - First pregnancy commonly affected
   - Neonatal thrombocytopenia due to increased platelet destruction
   - Incidence: 1/1000–1/2000 live births
   - Thrombocytopenia occurs early in gestation
   - Platelet counts low at birth (<50,000/mm^3 in 80%)
   - Risk of severe thrombocytopenia increased if Hx of antenatal ICH in sibling

- Due to platelet antigen incompatibility btwn mother, fetus
  - Over 15 types of human platelet antigens (HPA)
  - Frequency of particular HPA in given population related to ethnic background

    HPA-1a: most common antigen responsible for NAIT in Caucasian populations. Only 1 in 20 HPA-1a neg women make antibodies.
- Risk of any thrombocytopenia in subsequent pregnancy depends on father's zygosity
  - Homzygous father for HPA-1a: 100% affected
  - Heterozygous father for HPA-1a: 50% affected

    HPA-4: most frequently responsible in Asian populations

2. Other immune thrombocytopenias

   Assoc w/ maternal conditions
   - Idiopathic thrombocytopenic purpura (ITP)
   - Systemic lupus erythematosus (SLE)
   - Lymphoproliferative disorders
   - Hyperthyroidism
   - Maternal drugs
     - Quinine
     - Thiazide diuretics
     - Hydralazine
     - Tolbutamide
   - Maternal antibodies passively transferred to fetus
     - Maternal platelet counts may be normal
     - Incidence of neonatal thrombocytopenia in infants born to women w/ ITP is 13%–56% (severe neonatal thrombocytopenia in 5–20%)
     - Thrombocytopenia reaches its nadir 2-3 days after birth
     - Usually mild, Rx rarely required

       Neonatal autoimmune thrombocytopenia (neonatal ITP)
3. Infections
   - In infants w/ congenital infections or early-onset bacterial infections, thrombocytopenia is present at or shortly after birth
   - Bacterial infections
     - 55–65% of infants w/ proven bacterial infections have platelet counts $<10{,}0000/mm^3$
     - Mechanism is accelerated platelet destruction, but not usually DIC
     - Bleeding manifestations rare
   - Viral infections

- Thrombocytopenia due to increased destruction, decreased production
- All TORCH agents capable of causing thrombocytopenia (particularly CMV)
- Other viral agents
  - Coxsackie virus
  - Parvovirus
  - Epstein-Barr virus
  - Adenovirus

4. Congenital syndromes
   - Thrombocytopenia w/ absent radii (TAR)
     - Autosomal recessive disorder due to decreased response to thrombopoietin (TPO)
     - Severe neonatal thrombocytopenia
       - ~60% at birth or age 1 wk
       - 90% by age 4 mo
     - Thrombocytopenia exaggerated by viral illnesses, cow's milk allergy or intolerance
     - Highest mortality in first 4 mo
     - Thrombocytopenia resolves by school age
   - Fanconi's anemia
     - Autosomal recessive disorder
     - Radial ray defects
       - Hypoplasia to aplasia of thumb & supernumerary thumbs
     - May present w/ isolated neonatal thrombocytopenia in neonatal period, but pancytopenia commonly presents in childhood (median age 6–7 y)
   - Congenital amegakaryocytic thrombocytopenia
     - More than half of affected infants present in the 1st wk of life w/ severe thrombocytopenia
   - Familial macrocytopenias
     - Congenital thrombocytopenia assoc w/ increased platelet vol
   - Chromosomal abnormalities
     - Trisomy 13, 18 & 21
     - Turner syndrome
     - Onset in fetal life
     - Wiskott-Aldrich syndrome
       - Onset in infancy (not infrequently at birth)
     - Noonan syndrome

- Thrombocytopenia assoc w/ myeloproliferative disorder or hemostatic abnormalities
- Inherited metabolic diseases
  - Onset at birth
    - Methylmalonic academia
    - Ketotic glycinemia
    - Isovaleric academia
    - Holocarboxylase synthetase deficiency

5. Misc neonatal disorders
   - DIC
   - Necrotizing enterocolitis
   - Kasabach-Merritt syndrome
     - Assoc w/ giant hemangioma
   - Asphyxia
   - Heparin-induced thrombocytopenia
   - Thrombosis
     - Renal vein thrombosis
     - ECMO
     - Atrial thrombosis

Assoc findings

- NAIT
  - ICH occurs in 10–15% of affected infants (1/2 occur in utero)
  - Petechiae 80%
  - Assoc disorder 6.5%
- Autoimmune thrombocytopenia
  - Incidence of bleeding incl ICH is low (<= 3%)
  - If etiology of thrombocytopenia in mother is SLE, assoc w/ congenital complete heart block
- TAR syndrome
  - Bilateral absent radii
  - Ulnar abnormalities
  - Thumbs & digits are always present
  - CHD (33%)
- Fanconi's anemia
  - Radial ray defects
    - Hypoplasia to aplasia of thumb & supernumerary thumbs
  - Short stature (prenatal onset)
  - Microcephaly
  - Eye abnormalities
  - Renal & urinary tact abnormalities

- ➢ Brownish skin pigmentation
- ➢ Pancytopenia (manifests in childhood)
- ➢ Increased chromosomal breaks
- ➢ Predisposed to myeloid leukemias, myelodysplastic syndromes

- Congenital amegakaryocytic thrombocytopenia
  - ➢ ~1/2 of infants develop aplastic anemia (median age 3.5 y)
- Chromosomal abnormalities
  - ➢ Trisomy 13 & 18
- Wiskott-Aldrich syndrome
  - ➢ Eczema
  - ➢ Severe bleeding tendency
    - GI bleeding

Physical examination

- Infant appears critically ill?
  - ➢ Consider sepsis or metabolic disease
- Manifestations of congenital infection?
- Multiple malformations
  - ➢ Consider genetic syndrome
- Well-appearing
  - ➢ NAIT or alloimmune thrombocytopenia

TESTS

- Most thrombocytopenias are self-limited, require no eval
- Persistent thrombocytopenia
  - ➢ Thrombocytopenias due to increased platelet destruction suggested by:
    - Large platelets seen on the peripheral blood smear
    - Less-than-expected rise in platelet counts after platelet transfusions
  - ➢ Platelet typing
    - Useful for suspected NAIT
  - ➢ Anti-platelet antibodies in maternal serum
  - ➢ Specific genetic tests for congenital causes described above
  - ➢ Head US in high-risk infants

DIFFERENTIAL DIAGNOSIS

See “History & Physical”

MANAGEMENT

- What to do first
  - ➢ Determine if sepsis responsible for thrombocytopenia, provide supportive measures (antibiotics/fluids, etc.) as needed

- General measures
  - ➢ Rx of underlying disorder responsible for thrombocytopenia (e.g., sepsis)
  - ➢ Replacement of RBC if significant bleeding has occurred
  - ➢ Cesarean section for fetuses w/ NAIT & platelet counts <= 50,000/mm^3
- Specific measures
  - ➢ Platelet transfusion
    - Indications controversial
    - Usual dose: 5–10 mL/kg of standard platelet suspension administered over 1–2 h
    - Maintain platelet counts >= 75,000/mm^3
      - Infants w/ ongoing significant hemorrhage
      - Infants undergoing surgery
      - Infants on ECMO
    - Maintain platelet counts >= 50,000/mm^3 in preterm infants at risk for ICH
    - Maintain platelet counts >= 25,000/mm^3 in asymptomatic infants w/ thrombocytopenia
    - NOTE: Infants w/ NAIT may receive random donor platelets if they have bleeding, unless the diagnosis has already been established, in which case they should receive washed, irradiated maternal platelets
  - ➢ Intravenous immunoglobulin (IVIG; 1 g/kg)
    - Reserved for infants w/ NAIT or autoimmune thrombocytopenia, severe thrombocytopenia (<= 50,000/mm^3)
  - ➢ Corticosteroids (methylprednisolone 2 mg/kg/d)
    - Used in infants w/ immune-mediated thrombocytopenias (along w/ IVIG) when platelet counts <= 50,000/mm^3

SPECIFIC THERAPY

N/A

FOLLOW-UP

N/A

COMPLICATIONS AND PROGNOSIS

- Varies w/ etiology
- Most thrombocytopenias are self-limited; if ICH does not occur, prognosis favorable

TRANSIENT SKIN LESIONS

RICHARD A. POLIN, MD
REVISED BY MARIA C. GARZON, MD

HISTORY & PHYSICAL

History

- Erythema toxicum neonatorum
  - ➢ Common in term infants, rare in premature & <2,500-g infants
  - ➢ Most cases occur btwn 24 & 48 h of age
  - ➢ Occasionally present at birth
- Transient neonatal pustular melanosis
  - ➢ More common in term newborn infants
  - ➢ Always present at birth
- Miliaria
  - ➢ More common in warmer climates
  - ➢ Miliaria crystallina
    - Due to blockage of sweat ducts beneath stratum corneum
    - Occasionally present at birth, commonly follows excessive warming
  - ➢ Miliaria rubra
    - Due to blockage of sweat ducts in stratum corneum: leaks into dermis causing inflammatory response
    - More common after 1st wk of life
    - Associated w/ excessive warming
- Sucking blisters
  - ➢ Always present at birth
  - ➢ Hands/forearms
- Neonatal acne (neonatal cephalic pustulosis)
  - ➢ Onset 2–3 wk of life
  - ➢ Hallmarks of true acne (comedones) absent
  - ➢ Possibly due to infection w/ Malassezia

Signs

- Erythema toxicum neonatorum
  - ➢ Four distinct lesions: erythematous macules, wheals, papules, pustules
  - ➢ Erythematous macules, wheals vary in size from a few mm to cm
  - ➢ Papules, pustules 1–2 mm, superimposed on macules, wheals
  - ➢ Rash waxes, wanes
  - ➢ New lesions can appear for several days

- ➢ Begins on face; however, buttocks, torso, extremities common sites of involvement

- Transient neonatal pustular melanosis
  - ➢ Three kinds of lesions
    - Pustules w/ little/no underlying erythema
    - Ruptured pustules appear as hyperpigmented macules w/ surrounding scales
    - Hyperpigmented lesions w/o scales (2–3 mm)
  - ➢ Affected areas
    - Forehead, behind ears, under chin, neck, back, hands, feet (including palms, soles)
- Miliaria (prickly heat)
  - ➢ Most commonly affects forehead, upper trunk
  - ➢ Miliaria crystallina
    - Tiny vesicles resembling dewdrops without background redness
  - ➢ Miliaria rubra
    - Erythematous papules, pustules
- Sucking blisters
  - ➢ Flaccid bullae, 5–15 mm
  - ➢ May evolve quickly to erosion
  - ➢ Resolve in days to weeks
  - ➢ Characteristic locations
    - Radial forearm, wrist, hand (incl dorsal thumb, index fingers)
- Neonatal acne (neonatal cephalic pustulosis)
  - ➢ Papulopustular facial eruption usually on the cheeks
  - ➢ May appear anywhere on face, scalp, upper chest

TESTS

- Erythema toxicum neonatorum
  - ➢ Wright's stain of pustule demonstrates eosinophils
  - ➢ Occasionally, peripheral eosinophilia
- Transient neonatal pustular melanosis
  - ➢ Wright's stain of pustule demonstrates neutrophils, occasionally eosinophils
  - ➢ Gram stain will not show bacteria
- Miliaria (prickly heat)
  - ➢ No diagnostic test
  - ➢ If uncertain of diagnosis, skin biopsy can be performed
  - ➢ Miliaria crystallina
  - ➢ Dewdrop vesicles rupture easily

- Sucking blisters
  - ➢ Infants w/ sucking blisters may suck on extremities
  - ➢ Tests for herpes simplex virus and bacteria will be negative
- Neonatal acne (neonatal cephalic pustulosis)
  - ➢ Giemsa stain of pustules can demonstrate fungal spores, neutrophils
  - ➢ Gram stain will not show bacteria

DIFFERENTIAL DIAGNOSIS

- Erythema toxicum neonatorum
  - ➢ Neonatal pustular melanosis
  - ➢ Congenital candidiasis
  - ➢ Miliaria rubra
  - ➢ Incontinentia pigmenti
  - ➢ Eosinophilic pustular folliculitis
- Transient neonatal pustular melanosis
  - ➢ Erythema toxicum
  - ➢ Staphylococcal impetigo
  - ➢ Congenital candidiasis
  - ➢ Miliaria
  - ➢ Acropustulosis of infancy
- Miliaria (prickly heat)
  - ➢ Erythema toxicum
  - ➢ Transient neonatal pustular melanosis
- Sucking blisters
  - ➢ W/ well appearance, characteristic location, diagnosis usually evident
  - ➢ Other possibilities
    - Bullous impetigo
    - Neonatal herpes simplex
    - Epidermolysis bullosa
- Neonatal acne (neonatal cephalic pustulosis)
  - ➢ Miliaria rubra
  - ➢ Congenital candidiasis

MANAGEMENT

General measures

- None required

SPECIFIC THERAPY

- Erythema toxicum: none
- Transient neonatal pustular melanosis: none

- Miliaria: avoid overheating
- Sucking blisters: none
- Neonatal acne
  - ➢ Often remits spontaneously
  - ➢ Use of imidazole anti-yeast creams may promote resolution
  - ➢ Low-potency topical steroids may improve some cases but must be used w/ caution

FOLLOW-UP

- None required if the lesions resolve; by definition all of these conditions are transient

COMPLICATIONS AND PROGNOSIS

- Resolution w/o scarring

VASCULAR ABNORMALITIES OF THE SKIN

RICHARD A. POLIN, MD
REVISED BY MARIA C. GARZON, MD

HISTORY & PHYSICAL

History

- Salmon patch ("angel kiss" or "stork bite")
  - ➢ Capillary malformation
  - ➢ Present at birth
  - ➢ Common locations: eyelids, glabella, nape of neck
  - ➢ Usually disappears by age 1–2 y
  - ➢ Must be distinguished from partial port wine stain or hemangioma
- Port wine stains
  - ➢ Capillary malformations
  - ➢ Present at birth
  - ➢ Usually sporadic, but may be inherited in an autosomal dominant fashion
- Venous malformations
  - ➢ Slow-flow vascular malformations present at birth Two types:
    - "Typical" venous malformations may arise on skin or mucosa
    - Glomuvenous malformations anomalous channels lined w/ glomus cells
- Lymphatic malformations
  - ➢ May be superficial or deep, assoc w/ other lymphatic anomalies

- ➢ Intrathoracic or intra-abdominal lymphatic malformations account for 8% of malformations
- ➢ Classification
  - Macrocystic lymphatic: present at birth
    - Usually found in neck or axilla, called cystic hygromas
  - Microcystic lymphatic malformations (lymphangioma circumscriptum) congenital lesions but uncommon to be clinically apparent in the neonatal period
    - Areas of predilection include oral mucosa, proximal limbs, flexures
  - Combined macro-, microcystic lesions: most common on head (cheek & mouth)
  - Congenital hemangiomas
  - Differ from common infantile hemangiomas (IH)
    - Fully formed at birth (intrauterine proliferation), little if any postnatal growth
    - Histology
      - GLUT-1staining negative
    - Two types
      - Rapid involuting congenital hemangiomas (RICH)
        - Involute w/in the first 14 months of life
      - Non-involuting congenital hemangiomas (NICH)
        - Persist w/o involuting

- Arteriovenous malformations (AVMs)
  - ➢ 40% visible at birth
  - ➢ May be quiescent at birth
  - ➢ >AVMs are staged based upon flow
- Vascular tumors
  - ➢ **Infantile Hemangiomas**
    - Become visible in first few wks of life (50–60% present at birth); precursor lesions are common
    - Phase of rapid growth, followed by regression
    - M:F ratio = 2.5:1 to 5:1
    - More common in prematures
    - Incidence increased in infants born to mothers who have had chorionic villus sampling
    - Histology

GLUT-1staining positive

- Morphology/Classification
- 75–90% solitary lesions

- Depth
  - ➢ Superficial: 50–60%: proliferate up to 9mo/longer
  - ➢ Mixed (25–35%)
  - ➢ Deep (15%)
- Patterns
  - Localized – appear to arise from a central focus
  - Segmental – diffuse, often plaque-like, can be superficial, mixed or deep lesions

Multiple

Multiple superficial hemangiomas or solitary large IH may suggest visceral involvement

Liver, airway most common

Hemangiomas on lower face in beard distribution suggest involvement of airway

- Diffuse neonatal hemangiomatosis term used to describe multiple skin lesions w/ visceral lesions
- Benign neonatal hemangiomatosis: multiple lesions w/o visceral involvement

Most IHs are sporadic

50% involute by 5 y, 70% by 7 years, 90% by 10–12 y

Other Associations

PHACE(S) syndrome: large segmental facial hemangioma plus one:

P – posterior fossa & other brain anomalies

H – large IH (segmental)

A – arterial anomalies (often aortic arch & CNS vessel anomalies)

C – cardiac anomalies & coarctation of the aorta

E – eye anomalies (structural malformations)

S – sternal anomalies & supraumbilical raphe

Endocrinologic anomalies are increasingly reported in PHACE(S) syndrome

Hypothyroidism

Assoc w/ hepatic hemangiomatosis & "large" IH

IH can produce a deidodinase that inactivates thyroxine

Congenital hemangiomas

- Differ from common IH
  - ➢ Fully formed at birth (intrauterine proliferation), little if any postnatal growth
  - ➢ Histology
    - GLUT-1staining negative

- ➢ Two types
  - Rapid involuting congenital hemangiomas (RICH)
    - Involute w/in the first 14 months of life
  - Non-involuting congenital hemangiomas (NICH)
- ➢ Persist w/o involuting

Other vascular tumors

Kaposiform hemangioendothelioma
Tufted angioma
Histology differs from IH & are GLUT-1negative
These tumors are assoc w/ Kasabach-Merritt syndrome
Kasabach-Merritt syndrome
Rapid enlargement of a vascular tumor
Thrombocytopenic coagulopathy

Signs

- Salmon patch ("angel kiss" or "stork bite")
  - ➢ Bilateral symmetrical defect
  - ➢ Commonly involves upper eyelids, nape of neck, glabella, nose
  - ➢ May also occur sacral area, where it tends to persist
- Port wine stains (capillary malformations)
  - ➢ Pink or red macular patches, occur anywhere on body, blanch at birth
  - ➢ Port wine stains darken w/ age & may become more nodular
  - ➢ Grow proportional to child's growth
  - ➢ Facial port wine stains may be assoc w/ bony & soft tissue overgrowth
- Venous malformations
  - ➢ Blue, compressible ill-defined birthmarks
  - ➢ Usually subtle, but may be large
  - ➢ No thrill or bruit
    - Can be located on the skin or mucosa
    - Glomuvenous lesions often have a pebbly surface; can be small or extensive
  - ➢ Calcifications may cause phleboliths visible on x-ray
  - ➢ During infancy & early childhood, these malformations expand, may become deep blue
  - ➢ Extensive venous malformations on the limbs commonly lead to localized intravascular coagulopathy
  - ➢ Extensive blue malformations in leg or arm must be distinguished from Klippel-Trenaunay
- Lymphatic malformations

- ➢ Microcystic lymphangiomas
  - Infiltrate the skin, resulting in clear or hemorrhagic vesicles that leak lymph
- ➢ Macrocystic lesions
  - Large cystic structures usually located on neck or axilla
  - May result in a chronic coagulopathy
  - Assoc w/ Turner's syndrome
- ➢ Combined lesions
  - May involve tongue, mouth; interfere w/ normal development of jaw

■ AVMs
- ➢ Resemble port wine stain or involuting hemangiomas
- ➢ Increased local warmth
- ➢ Thrill or bruit in active cases

■ Syndromes assoc w/ vascular anomalies
- ➢ Sturge-Weber
  - Facial port wine stain (forehead, eyelid "V-1"), vascular malformation of the eye, glaucoma, leptomeningeal vascular malformation, seizures
- ➢ Klippel-Trenaunay
  - Capillary malformations of the limb, varicose veins, persistent embryonic veins, overgrowth of bone, soft tissue of affected limb
- ➢ Servelle-Martorell
  - Capillary stains of the limb, dysplastic veins & limb undergrowth
- ➢ Parkes Weber
  - Limb overgrowth assoc w/ capillary stains, multiple AVMs
- ➢ Proteus
  - Hemihypertrophy, visceral lipomas, visceral vascular malformations, endocrine tumors, epidermal nevi, thickened palms & soles
- ➢ Bannayan-Riley-Ruvalcaba
  - Macrocephaly, mental retardation, visceral lipomas, intestinal polyposis, capillary venous malformations, pigmented macules on the genitalia
- ➢ Beckwith-Wiedemann
  - Macroglossia, macrosomia, omphalocele, renal disorders, embryonic tumors, capillary stain on mid-forehead
- ➢ Cutis marmorata telangiectatica congenita (CMTC)
  - May be localized, segmental or diffuse

- More common in females
- Reticulate purple network noted at birth
- Focal areas of atrophy
- Diffuse CMTC may be assoc w/ developmental defects

➢ Adams-Oliver
- Cranium defects, limb anomalies, CMTC-like vascular malformation

➢ Blue rubber bleb nevus
- Venous malformations of the skin, GI tract assoc w/ bleeding, iron deficiency anemia

➢ Wyburn-Mason
- AVM overlying facial skin (can mimic a port wine stain), retinal & intracranial AVM

➢ Cobb
- Posterior truncal vascular malformation overlying a vascular abnormality that involves the spinal cord

➢ Maffucci syndrome
- Mixed vascular malformations & enchondromas

■ Vascular tumors

➢ IH
- Precursor lesions: halo of pallor, pale or erythematous patches, bruise-like macules
- Occasionally appears as ulceration on lip or perineum
- On rare occasions may be fully developed at birth

Superficial IH

■ Bright-red erythematous plaques (strawberry hemangioma)
➢ Deep hemangiomas
■ Warm subcutaneous mass
■ Superficial skin normal or has bluish color
■ Large lesions may have bruit
➢ Mixed (superficial & deep)
■ Well-circumscribed superficial portion w/ ill-defined bluish deeper component

Congenital hemangiomas

■ Raised violaceous tumor w/radiating veins
■ Hemispheric tumor w/ overlying telangiectasia
■ Firm pink violaceous tumor w/ a pale halo

TESTS

- Salmon patch ("angel kiss" or "stork bite")
  - ➢ Clinical diagnosis
- Port wine stains (capillary malformations)
  - ➢ Clinical diagnosis
  - ➢ Cranial MRI indicated in infants w/ facial port wine stains
- Venous malformations
  - ➢ Clinical diagnosis
  - ➢ MRI to define extent
- Lymphatic malformations
  - ➢ Dx confirmed by MRI or US
- Vascular tumors
  - ➢ IH
    - Most diagnosed by physical exam
    - Doppler US or MRI may assist Dx
    - Congenital hemangioma
      - Biopsy may be needed to rule out other neoplasms
    - Multiple IH
      - May be assoc w/ visceral involvement
      - Screening abdominal USG recommended for 5 or more skin lesions
      - CBC to assess for anemia
      - Stool guaiac to assess for GI tract involvement
      - More extensive work-up: cardiac echo, MRI or CT may be required depending on physical exam & initial screening
      - Thyroid function tests for pts w/ large lesions or internal involvement
- AVMs
  - ➢ MR angiography
  - ➢ Color Doppler US

DIFFERENTIAL DIAGNOSIS

- Salmon patch ("angel kiss" or "stork bite")
- Port wine stains (capillary malformations)
  - ➢ Sturge-Weber syndrome
  - ➢ Beckwith-Wiedemann syndrome
  - ➢ Quiescent AVMs may mimic port wine stains
- Venous malformations
  - ➢ Venous malformation on central forehead must be distinguished from sinus pericranii, in which there is a direct

communication btwn superficial veins & intracranial venous sinuses
  - ➢ In sinus pericranii, the veins bulge w/ crying
- Lymphatic malformations
  - ➢ IH
  - ➢ Venous malformations

Other tumors
- Vascular tumors
  - ➢ IH
  - ➢ Congenital hemangiomas must be differentiated from other neoplasms (fibrosarcoma & infantile myofibromatosis)
  - ➢ Deep IH
    - AVM
    - Fibrosarcoma
    - Rhabdomyosarcoma
    - Infantile myofibromatosis
- AVMs
  - ➢ Port wine stain
  - ➢ Deep hemangioma

MANAGEMENT

N/A

SPECIFIC THERAPY
- Salmon patch ("angel kiss" or "stork bite")
  - ➢ None required
- Port wine stains (capillary malformations)
  - ➢ Flashlamp-pumped pulsed dye laser
- Venous malformations

  Depends on location
  - ➢ Percutaneous sclerotherapy
  - ➢ Extensive venous malformations of limb
    - Managed conservatively w/ elastic stockings
  - ➢ Localized venous malformations may be excised
- Lymphatic malformations
  - ➢ Macrocystic
    - Treated w/ fine-needle aspiration & sclerotherapy
    - Surgery is alternative
  - ➢ Microcystic
    - Depends on size, location

- Surgery
- Recurrences common
- May require skin grafting

➢ Combined
- Less amenable to surgery, sclerotherapy, due to disfigurement, bleeding, airway compression, esophageal obstruction

■ AVMs
➢ Depends on the stage
➢ Pharmacologic treatment of congestive heart failure
➢ Embolization if failure persists
➢ Caution: Partial treatment/excision, laser treatment, cryotherapy may promote growth & expansion of the AVM

■ Vascular tumors
➢ MAJORITY OF HEMANGIOMAS WILL REGRESS SPONTANEOUSLY, NEED NO TREATMENT
➢ Indications for treatment
- Life-threatening or function-threatening lesions (compromise of vision, respiratory system or CHF)
- Hemangiomas in locations (e.g., nose, glabella or ears) that may cause permanent disfigurement or scars
- Large facial hemangiomas
- Ulcerated hemangiomas

➢ Infection & ulcerations should be treated aggressively w/ topical & systemic antibiotics
➢ Systemic corticosteroids
- Administered during the proliferating phase (first several months of life)
- Numerous potential side effects
- Effectively controls growth in majority of IHs

➢ Intralesional corticosteroids
- Reserved for small focal hemangiomas in critical areas
- Injection into periorbital lesions may cause blindness

➢ Interferon-alfa
- Variable response
- Risk of spastic diplegia

➢ Flashlamp-pumped pulsed dye laser
- More effective for superficial lesions
- Promotes lightening
- May help heal ulcerations

- Side effects: transient pigmentary abnormalities & atrophic scarring

➢ Surgical excision reserved for involuting/involuted hemangiomas, occasionally for IH in problematic locations or persistently ulcerated
- Arterial embolization employed for some IHs assoc w/ high-output failure

FOLLOW-UP

- Dermatology
- Other medical, surgical specialists may be needed, depending on extent of visceral involvement or anatomic location

COMPLICATIONS AND PROGNOSIS

- Salmon patch ("angel kiss" or "stork bite")
  - ➢ Excellent
- Port wine stains (capillary malformations)
  - ➢ Isolated (non-syndromic) port wine stains have an excellent prognosis, but can be disfiguring
  - ➢ May darken & thicken w/ maturity if untreated
  - ➢ Significant lightening w/ laser treatment in most cases
- Venous malformations
  - ➢ In the older child, venous malformations may cause joint limitation, bony deformities
- Lymphatic malformations
  - ➢ May cause disfigurement
  - ➢ Increased risk for infection
- Venous malformations
  - ➢ Complications
    - Deformity of facial structures as veins expand
    - Painful episodes & pathologic fractures for extremity lesions
    - Localized coagulopathy
- AVMs
  - ➢ Complications incl CHF, bleeding, disfigurement
- Vascular tumors
  - ➢ Ulceration is the most common complication (lip, perineum, skin folds)
  - ➢ Large size, facial location, and/or segmental morphology are the most important predictors of poor short-term outcomes
  - ➢ Diffuse neonatal hemangiomatosis

- High mortality
- GI bleeding
- High-output CHF (also seen w/ large hemangiomas)
- Hypothyroidism

➢ IH

- 50% involute by 5 y
- 70% involute by 7 y
- 90% involute by 10–12 y

PART FOUR

Procedures

ARTERIAL CATHETERIZATION, PERIPHERAL, PERCUTANEOUS

VADIM TEN, MD

INDICATIONS

- Measurement of blood gases for PaO_2 tension (esp if PREDUCTAL monitoring desired)
- Direct, continuous measurement of arterial BP
- Facilitate frequent blood sampling (usually not sole indication)

CONTRAINDICATIONS

- Skin infection at site
- Preexisting circulatory insufficiency in distribution of artery or inadequate collaterals
- Uncorrected coagulopathy

SPECIAL CONSIDERATIONS

- Candidate arteries
  - ➢ Radial artery (R for preductal monitoring)
  - ➢ Ulnar artery (R for preductal monitoring)
  - ➢ Posterior tibial artery
  - ➢ Dorsalis pedis artery
  - ➢ Temporal artery: not recommended unless necessary because of risk of significant CNS sequelae (allows preductal monitoring)
- Always ensure adequate collateral circulation (Allen test for radial or ulnar artery)
- Technique
  - ➢ Avoid wrist hyperextension
  - ➢ Transillumination extremely useful
  - ➢ Prepare flush of heparinized (1 unit/1 cc) normal saline in 1-cc syringe
  - ➢ Insert 22 or 24G angiocatheter at 30-degree angle very slowly, observing for flashback
- Precautions
  - ➢ Leave tips of digits exposed to detect ischemia
  - ➢ Use minimal (0.5–1.5 mL/h) infusion rates
  - ➢ Ensure normal arterial waveform, easy blood withdrawal
  - ➢ Avoid large or rapid withdrawal of blood or bolus injections of infusate
  - ➢ Do not infuse hypertonic/irritating solutions or blood products

COMPLICATIONS

- Ischemia if collateral circulation inadequate
  - Frequency: rare
  - Mgt: remove catheter immediately; insert no other vascular catheters in affected extremity
- Vasospasm, thromboembolism, air embolism
  - Frequency: uncommon
  - Prevention: minimize infusion rate, avoid large or rapid withdrawals/infusions, avoid hypertonic/irritating solutions & blood products
  - Mgt: controversial; usually self-limited; remove if dampening of waveform or difficulty in withdrawing blood is not resolved w/ repositioning or if thromboembolism suspected
- Infection: sepsis, cellulitis, abscess
  - Frequency: rare
  - Prevention: attention to aseptic technique; prophylactic antibiotic ineffective
  - Mgt: catheter removal, antibiotics if necessary
- Hemorrhage due to catheter accident or coagulopathy
  - Frequency: rare
  - Mgt: local hemostasis; platelets, coagulation factors if deficient

CENTRAL VENOUS CATHETER INSERTION, PERCUTANEOUS

VADIM TEN, MD
REVISED BY DAVID BATEMAN, MD, AND CATHERINE A. HANSEN, MD

INDICATIONS

- To administer IV solutions w/ high osmolality (e.g., hypertonic glucose, parenteral nutrition solution)
- To secure access for critical medications (e.g., ionotropes, PGE1)

CONTRAINDICATIONS

Absolute

- Unstable vital signs
- Infection of skin at site of insertion
- Arterial insufficiency of extremity

Relative

- Ongoing bacteremia

SPECIAL CONSIDERATIONS

Site preparation and insertion

- Percutaneous central venous line insertion is a sterile procedure, optimally requiring 2 persons scrubbed & third non-scrubbed assistant
- 70% isopropyl alcohol preferable to 10% povidone-iodine solution for site preparation
- Choice of venous site: antecubital > scalp > axillary > saphenous > external jugular > femoral
- Prepare hemostatic cotton "ball" to tamp bleeding
- Do not remove tourniquet until catheter advanced into vein 2–3 cm beyond needle tip
- If catheter meets resistance, gentle massage along vein w/ sterile cotton-tipped swab may help to advance
- Position of catheter tip in superior or inferior vena cava; confirm by x-ray
- Do not to cut catheter to length; coil excess outside of skin & fix with Steri-strips
- If catheter tip directed retrograde into a vein, it may flip into the central vein by blood flow; recheck x-ray in 12–24 hr

Site maintenance

- Insertion point should remain visible; do not obscure insertion site w/ dressing
- Cover site with clear occlusive dressing (e.g., Tegaderm or OpSite)
- Dressing should not be circumferential
- If small cotton or gauze piece used to tamp bleeding, remove in 24 hours & redress site
- Site redressing should be routine (weekly suggested) & PRN if occlusive dressing is loose or site contamination

Anti-infection measures

- Incidence of percutaneous central venous line infection reduced by minimizing catheter entry, standardizing access (multiple ports, in-line flushes, etc.) & by ensuring line is entered only under sterile conditions
- 3-way stopcocks should not be used on percutaneous central venous lines
- Establish & follow protocols to maintain hand hygiene, hub disinfection, hub-port integrity, & for percutaneous central venous line insertion & maintenance

- Insert & use percutaneous central venous lines only when necessary; remove as soon as no longer essential
- See CHCA website: www.chca.com/mm/misc/change˙package˙bsi.pdf

COMPLICATIONS

- Infection: sepsis-bacteremia, cellulitis, septic thrombophlebitis, endocarditis
  - ➢ Frequency: common; may be related to catheter duration
  - ➢ Prevention: see above
  - ➢ Mgt: remove catheter, provide appropriate antibiotic Rx
- Thrombosis, occlusion
  - ➢ Frequency: more often with low infusion rates through small-bore catheters
  - ➢ Prevention: heparin, 1 unit/mL in infusate
  - ➢ Mgt: catheter removal
- Catheter leak
  - ➢ Frequency: infrequent
  - ➢ Prevention: depends on quality of catheter care
  - ➢ Mgt: some catheters have repairable tubing, but repair increases risk of bacteremia; removal/replacement of catheter preferable
- Bleeding
  - ➢ Frequency: rare w/ appropriate hemostatic technique; usually not significant
  - ➢ Mgt: temporarily tamp insertion site; blood-soaked gauze piece may be risk for infection; remove when bleeding stops

ENDOTRACHEAL INTUBATION

VADIM TEN, MD

INDICATIONS

- Mechanical ventilation
- Relieve upper airway obstruction
- Direct endotracheal suctioning
- Exogenous surfactant administration

CONTRAINDICATIONS

- None

SPECIAL CONSIDERATIONS

- Pre-oxygenate pt w/ 100% O_2 +/− bag & mask ventilation for 30 sec if non-emergent (latter contraindicated in pts w/ suspected diaphragmatic hernia)
- Make sure suction setup, laryngoscope, endotracheal tube (ETT), bag & mask, O_2 are prepared & function properly
- Pre-medication
  - ➢ Standard
    - Fentanyl, 2.0 micrograms/kg IV over 5 min

    and
    - Atropine, 0.02 mg/kg IV over 1 min

    ±
    - Short-acting neuromuscular blocking agent (e.g., rocuronium or mivacurium)
  - ➢ Increased intracranial pressure: ultra-short-acting barbiturate
  - ➢ Persistent pulmonary hypertension of the newborn: fentanyl, 2.0 micrograms/kg IV over 5 min
  - ➢ Severe spasm of vocal cords
    - Succinylcholine

    and
    - Versed
- Route of intubation
  - ➢ Nasotracheal (most secure ETT fixation, but assoc w/ increased prevalence of post-extubation atelectasis)
  - ➢ Orotracheal
- ETT size should allow small air leak around it at peak pressure of 20 cm H_2O: GA/birth wt:
  - ➢ <28 wk, <1 kg – 2.5
  - ➢ 28–34 wk, 1–2 kg – 3.0
  - ➢ 34–38 wk, 2–3 kg – 3.5
  - ➢ >38 wk, >3 kg – 3.5–4.0
- Technique
  - ➢ Position patient in "sniffing position" on flat surface
  - ➢ Blade size
    - <3 kg – Miller 0
    - >3 kg – Miller 1
  - ➢ Attach thin catheter to side of blade to provide O_2 during intubation
  - ➢ Advance ETT, directing it posteriorly through naris or from right side of mouth (not ALONG blade); pass ETT tip through vocal cords under direct vision

- ➢ Depth of insertion: 1–1.5 cm beyond vocal cords
  - Nasotracheal tube distance from naris
    - Body length 32 cm – 7 cm
    - Body length 36 cm – 8 cm
    - Body length 40 cm – 8.7 cm
    - Body length 44 cm – 9.5 cm
    - Body length 48 cm – 10.2 cm
    - Body length 52 cm – 11 cm
    - Body length 56 cm – 12 cm
  - Orotracheal tube distance from upper lip
    - Birth wt <0.5 kg – 6 cm
    - Birth wt 1 kg – 7 cm
    - Birth wt 2 kg – 8 cm
    - Birth wt 3 kg – 9 cm
    - Birth wt >4 kg – 10 cm
- Confirm placement clinically
  - ➢ Equal breath sounds over both lung fields, absent over stomach
  - ➢ Chest rise w/ each positive-pressure ventilation
  - ➢ No gastric distention
  - ➢ H_2O vapor in ETT w/ expiration
  - ➢ Colorimetric CO_2 detection

  Note: If in doubt or heart rate & oxygenation are not improving or are deteriorating, extubate & mask ventilate, then reintubate
- Verify ETT placement by x-ray w/ neck & head in NEUTRAL position; tip should be 1–1.5 cm above carina

COMPLICATIONS

- Hypoxia, hypoventilation, bradycardia (due to prolonged intubation attempt, inadvertent mainstem bronchus or esophageal intubation), apnea, vagal reflex, ETT obstruction, accidental dislodgement of ETT from trachea
  - ➢ Frequency: most common complications
  - ➢ Prevention: provide free flow O_2 during intubation, limit duration of attempt, allow recovery btwn attempts, verify position by direct visualization & auscultation; adequate ETT fixation; IF CYANOSIS OR BRADYCARDIA PERSISTS, EXTUBATE & PLACE A NEW ETT
  - ➢ Mgt: interrupt attempt or extubate, remove ETT; provide mask & bag positive-pressure ventilation w/ O_2
- Atelectasis/pneumothorax due to mainstem bronchus intubation, usually right
  - ➢ Frequency: common w/o attention to depth of insertion

- ➢ Prevention: verify position by auscultation, x-ray; record depth of insertion at naris or upper lip regularly
- ➢ Withdraw ETT appropriate distance

- Hypopharyngeal or tracheal laceration/penetration
  - ➢ Frequency: very rare, mostly in premature infants; possible complications – subcutaneous emphysema, mediastinitis, vocal cord injury
  - ➢ Prevention: proper positioning of head & neck; always maintain visualization of tip of tube, avoid excessive pressure in advancing; if intubating orally w/ stylet, be sure stylet is w/in the ETT & the tip is not beyond the tip of the ETT
  - ➢ Mgt: NPO for 10 days, usually heals spontaneously
- Subglottic stenosis
  - ➢ Frequency: 1–5% of intubated infants; risk factors: tight-fitting ETT, repeated intubation, poor ETT fixation, prolonged intubation
  - ➢ Prevention: proper site ETT, secure ETT fixation, extubate ASAP
  - ➢ Mgt: ENT consultation if airway compromised; tracheostomy may be required
- Deformation
  - ➢ Naris
  - ➢ Palate (grooved)
  - ➢ Defective dentition
- Infection: tracheobronchitis, pneumonia, otitis media
  - ➢ Frequency: uncommon
  - ➢ Prevention/mgt: strictly aseptic approach to ETT insertion, care/antibiotics for infection
- Post-extubation atelectasis: post-extubation nasal continuous positive airway pressure, esp after nasotracheal intubation & w/ extreme prematurity

EXCHANGE TRANSFUSION

MANDIR SURI, MBBS, MD
REVISED BY RICHARD A. POLIN, MD

INDICATIONS

- **Double volume**
  - ➢ Urgent reduction of serum bilirubin level to reduce risk of kernicterus (most common indication); see **HYPERBILIRUBINEMIA, UNCONJUGATED** in the "Neonatal Presenting Signs" section

- ➢ Removal of infant's sensitized RBC & circulating antibodies in severe alloimmune hemolytic anemia (rarely required)
- ➢ Alloimmune thrombocytopenia to remove circulating antibodies (rarely required)
- ➢ Removal of drugs, toxins (e.g., amino acids, ammonia w/ inborn errors of metabolism) if peritoneal dialysis is not effective
- ➢ Severe sepsis (efficacy unproven)
  - Remove bacterial toxins
  - Provide antibody

■ **Partial**
- ➢ Reduce Hct w/ polycythemia
- ➢ Increase Hct w/ severe anemia w/o concurrent hypovolemia

CONTRAINDICATIONS

■ Related to umbilical vein catheterization (see **UMBILICAL VEIN CATHETERIZATION**)
■ Related to umbilical artery catheterization (see **UMBILICAL ARTERY CATHETERIZATION**)
■ Severely unstable cardiopulmonary status

SPECIAL CONSIDERATIONS

■ Routes
- ➢ Double volume: via umbilical vein catheter (to infuse, withdraw), +/− umbilical artery catheter (to withdraw)
- ➢ Partial via peripheral vein (to infuse), umbilical artery catheter (to withdraw)

■ Calculations
- ➢ Double volume
  - Volume exchanged = blood volume × 2
  - Blood volume = 80 mL/kg in full-term infants, 100 mL/kg in preterms
- ➢ Partial exchange transfusion
  - Polycythemia
    Volume exchanged = [Blood volume × (Hct observed – Hct desired)]/Hct observed
  - Isovolumetric exchange transfusion for severe anemia:
    Volume exchanged = [Blood volume × (Hct desired – Hct observed)]/(Hct PRBC – Hct observed)

■ Blood product infused
- ➢ Double volume for hemolytic disease of newborn
  - ABO: O, Rh-specific, CMV-neg, irradiated PRBC, reconstituted w/ FFP to Hct 45–60

- Rh: O or type-specific, Rh-neg, CMV-neg, irradiated PRBC, reconstituted w/ FFP to Hct 45

➢ Other double volume: O or type-specific, Rh-specific, CMV-neg, irradiated PRBC, reconstituted w/ FFP to Hct 45–60

➢ Partial
- Polycythemia: 5% albumin
- Severe anemia: O or type-specific, Rh-specific, CMV-neg, irradiated PRBC

■ Precautions w/ double volume

➢ ABCs & medical stabilization

➢ Continuous cardiorespiratory monitoring, oximetry; periodic BP monitoring

➢ NPO for 4 h prior if possible; otherwise empty stomach w/ orogastric tube

➢ Verify appropriateness of blood product

➢ Meticulous, continuous monitoring of blood volume withdrawn & infused

➢ Slow, steady pace: 3–5 min per pass w/ push-pull technique; interrupt procedure if pt becomes unstable

➢ Avoid excessive suction when withdrawing, excessive pressure when infusing

➢ Use no more than 1 unit per exchange

➢ Volume of aliquot withdrawn/infused per pass
- Minimum in ELBW infant: 5 mL
- Maximum in term infant: 20 mL

➢ Post-exchange studies
- Hct, platelet count
- Bilirubin (if for hyperbilirubinemia)
- Electrolytes, glucose, ionized Ca
- Crossmatch (if repeat exchange transfusion may be required)

COMPLICATIONS

■ Complications assoc w/ umbilical vein catheter (if used), see **UMBILICAL VEIN CATHETERIZATION**

■ Complications assoc w/ umbilical artery catheter (if used), see **UMBILICAL ARTERY CATHETERIZATION**

■ Transmission of blood product-assoc infections

■ Others w/ double volume

➢ Hypothermia, hyperthermia w/ inappropriate blood temp

➢ Hypoxemia

- ➢ Electrolyte disturbances: hyperkalemia, hypoglycemia, hypernatremia, hypocalcemia, acidosis (acutely), alkalosis (delayed)
- ➢ Hemolysis due to overwarming, excessive infusion pressure
- ➢ Thrombocytopenia (common, usually transient)
- ➢ Neutropenia (uncommon)
- ➢ Cardiovascular
  - Hypovolemia/hypervolemia if error in replacement
  - Arrhythmias related to electrolyte disturbances
  - Cardiac arrest

LUMBAR PUNCTURE

VADIM TEN, MD

INDICATIONS
- Obtain CSF for diagnostic purposes
- Temporary mgt of communicating hydrocephalus
- Measurement of CSF pressure (rare)

CONTRAINDICATIONS
- Increased intracranial pressure
- Cardiopulmonary instability
- Platelet count <50,000 or coagulopathy
- Skin infection at puncture site
- Lumbosacral anomalies

SPECIAL CONSIDERATIONS
- Monitor vital signs (consider oximetry as well), airway
- Position
  - ➢ Lateral decubitus, spine flexed
  - ➢ Sitting, spine flexed (less respiratory compromise)
- Always use needle w/ stylet
- Puncture site: midline at vertebral interspace just above (L3-L4) or below (L4-L5) plane of iliac crests; direct needle slightly cephalad
- Often no clear sensation of puncturing dura mater: remove stylet frequently, checking for CSF
- Depth of needle insertion (cm) estimated as 0.03 x body length (cm)
- CSF volume removed
  - ➢ Diagnostic: 0.5–1 mL in each of 3 or 4 tubes
    - 1st: Gram stain, bacterial culture

- 2nd: chemistries (at least glucose & protein; others if metabolic disease suspected)
- 3rd: cell count
- 4th: viral culture as indicated

➢ Hydrocephalus: until flow ceases, but usually not >10 min

COMPLICATIONS

- Contamination of CSF specimen w/ blood: correction of WBC for RBCs not valid
  - ➢ Frequency: most common complication
  - ➢ Prevention: advance needle in small increments, withdraw stylet to check for CSF
  - ➢ Mgt: repeat LP in 12–24 h
- Resp compromise
  - ➢ Frequency: common
  - ➢ Prevention: avoid neck flexion, excessive spinal flexion, cardiopulmonary monitoring
  - ➢ Mgt: ABC
- Infection: meningitis due to concomitant bacteremia; abscess; osteomyelitis
  - ➢ Frequency: very rare
  - ➢ Prevention: strict aseptic technique, avoid penetration of infected skin
- Brain stem herniation
  - ➢ Frequency: very rare
  - ➢ Prevention: rule out increased intracranial pressure
- Bleeding, hematoma (spinal epidural; spinal or intracranial, subdural or subarachnoid)
  - ➢ Frequency: rare
  - ➢ Prevention/mgt: correction of clotting factor deficits, correction of thrombocytopenia if $<50{,}000/mm^3$
- Spinal cord/nerve injury if needle inserted above L2
- Acquired spinal cord epidermoid tumor formation
  - ➢ Frequency: very rare
  - ➢ Prevention: always use stylet

SUPRAPUBIC BLADDER ASPIRATION

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INDICATIONS
- Obtain urine for culture & sensitivity

CONTRAINDICATIONS
- Absolute
  - ➢ Localized skin infection in suprapubic area
- Relative
  - ➢ Dilated bowel
  - ➢ Marked organomegaly
  - ➢ Genitourinary tract anomalies
  - ➢ Bleeding diathesis, platelet count $<50{,}000/mm^3$

SPECIAL CONSIDERATIONS
- Infant should not have voided w/in 1 h of procedure
- Use aseptic technique
- Site of puncture 1–2 cm above symphysis pubis in midline
- Needle should be inserted perpendicular to plane of body & not advanced >2.5 cm

COMPLICATIONS
- Hematuria
  - ➢ Frequency: common
  - ➢ Mgt: usually microscopic, resolves spontaneously w/o bleeding diathesis
- Hematoma: abdominal wall, bladder wall, pelvis
  - ➢ Frequency: rare in absence of bleeding diathesis
  - ➢ Mgt: usually resolves spontaneously
- Bleeding
  - ➢ Frequency: rare in absence of bleeding diathesis
  - ➢ Mgt: local hemostasis measures
- Intestinal perforation
  - ➢ Frequency: rare
  - ➢ Prevention: do not advance needle >2.5 cm
- Abdominal wall cellulitis/sepsis/pubic bone osteomyelitis
  - ➢ Frequency: rare
  - ➢ Prevention: strict aseptic technique

THORACENTESIS

J.M. LORENZ, MD

INDICATIONS

- Emergent evacuation of tension pneumothorax pending definitive Rx w/ thoracotomy tube insertion
- Obtain pleural fluid for Dx

CONTRAINDICATIONS

- No emergent indication for evacuation of pneumothorax

SPECIAL CONSIDERATIONS

- 18- to 20-gauge angiocatheter
- Insertion site
  - ➢ Pneumothorax
    - Over top of 5th or 6th rib in midclavicular line
    - Direct catheter cephalad at 45-degree angle to plane of chest until pleural space entered, then decrease to 15 degrees, advance cannula as stylet withdrawn
  - ➢ Diagnostic tap of pleural fluid
    - Over top of 6th or 7th rib btwn anterior & midaxillary lines, below pectoralis major muscle & breast tissue
    - Direct catheter posteriorly
- Avoid excessive depth of insertion
- Connect 20-mL syringe via 3-way stopcock, aspirate
- Cover puncture site w/ petroleum gauze & dressing after catheter removal

COMPLICATIONS

- Iatrogenic pneumothorax if care not taken to limit time catheter open to atmosphere or puncture site not appropriately sealed after catheter removal
- Punctured lung
  - ➢ Frequency: depends on the operator skill
  - ➢ Prevention: appropriate angle, depth of insertion
  - ➢ Mgt: usually none required
- Bleeding
  - ➢ Frequency: rare; usually significant only w/ coagulopathy
  - ➢ Prevention
    - Appropriate insertion site, depth

- Enter pleural space over top of rib
- Correct coagulation factors prn

➢ Mgt
- Local pressure
- Drain hemothorax if present

THORACOTOMY TUBE PLACEMENT

VADIM TEN, MD

INDICATIONS
- Evacuation of air (pneumothorax) or fluid (hemothorax, chylothorax, pleural effusion or empyema) from pleural space

CONTRAINDICATIONS
- Absolute: none
- Relative: bleeding diathesis

SPECIAL CONSIDERATIONS
- Position: supine w/ affected side elevated w/ towel roll
  - ➢ 60–75 degrees off bed to evacuate air
  - ➢ 15–30 degrees off bed for fluid, chyle, blood, pus
- Anesthesia: local infiltration w/1% lidocaine +/− conscious sedation & analgesia
- Tube size: 10F–14F; most commonly 12F (4 mm)
- Point of insertion
  - ➢ Skin (after incision w/ scalpel): 6th or 7th intercostal space; remain lateral to the edge of the pectoralis major muscle & avoid breast tissue
  - ➢ Chest wall (after blunt dissection w/ curved mosquito hemostat)
    - Always enter pleural space over top of a rib to avoid inferior blood vessels
    - To evacuate air: direct tube cephalad & anteriorly, entering pleural space in 4th or 5th intercostal space, midway btwn anterior & midaxillary lines, directing tube anteriorly
    - To evacuate fluid: direct tube posteriorly in same intercostal space as skin incision, entering pleural space midway btwn anterior & midaxillary lines
- Attach the tube to vacuum drainage at -10 to -20 cm H_2O via infant thoracostomy tube set

- Observe for vapor or bubbles in tube to confirm intrapleural location
- Check tube position by AP & lateral x-ray

COMPLICATIONS

- Pulmonary laceration
  - ➢ Frequency: depends on operator skill
  - ➢ Prevention
    - If thoracentesis performed prior to thoracotomy, allow some air/fluid to remain in pleural space
    - Do not insert hemostat >1 cm into pleural space
- Bleeding
  - ➢ Frequency: rare; usually significant only w/ coagulopathy
  - ➢ Prevention
    - Appropriate insertion site, depth
    - Enter pleural space over top of rib
    - Correct coagulation abnormalities
  - ➢ Mgt
    - Blood replacement as needed
    - Drain hemothorax if present
- Diaphragm, liver/spleen puncture
  - ➢ Frequency: very rare; depends on operator skill
  - ➢ Prevention: appropriate insertion site, depth
  - ➢ Mgt: usually self-limited; surgical repair if laceration significant
- Infection (cellulitis, empyema)
  - ➢ Frequency: rare
  - ➢ Prevention: strict aseptic technique
  - ➢ Mgt: antibiotics, drainage as needed
- Fluid/electrolyte imbalance, hypoproteinemia
  - ➢ Prevention: appropriate replacement of chest tube fluid drainage
- Damage to breast tissue
  - ➢ Prevention: appropriate insertion site

UMBILICAL ARTERY CATHETERIZATION

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INDICATIONS

- Measurement of blood gases for O_2 tension or content

- Continuous measurement of arterial BP
- Cardiac catheterization
- Resuscitation (umbilical venous line better choice)
- Exchange transfusion (to WITHDRAW blood)
- Infusion of maintenance glucose-electrolyte solution or meds (not ideal; usually not sole indication)
- Facilitate freq blood sampling (usually not sole indication)

CONTRAINDICATIONS

- Omphalitis
- Omphalocele
- Peritonitis
- Evidence of local vascular compromise in lower extremity or buttocks
- Necrotizing enterocolitis (no proven cause/effect relationship)

SPECIAL CONSIDERATIONS

- Use size 3.5 Fr for VLBW infants & 5 Fr for larger infants
- Position
  - ➢ High position: level of thoracic vertebra 6–10 (preferred)
  - ➢ Low position: level of lumbar vertebra 3–4
- Insertion distance to T6–T10 (cm) = 2.5 cm/kg × birth wt (kg) + 9.7 cm + length of cord remaining (cm)
- Must confirm position of catheter by x-ray
- If repositioning required, catheter may be withdrawn, but should never be advanced
- Infusate should contain 0.5–1 units of heparin per mL
- Umbilical artery catheter may remain in situ for 7–10 days, but should be removed as soon as indication for insertion no longer exists

COMPLICATIONS

- Malpositioned catheter
  - ➢ Frequency: Common
  - ➢ Mgt: Reposition it (should never be advanced)
- Vascular complications: arterial perforation, vasospasm, thromboembolism, air embolism, ischemia of bowel/buttock/lower extremity, hypertension
  - ➢ Frequency: catheter thrombi (most asymptomatic), vasospasm common; others uncommon
  - ➢ Prevention: Avoid hyperosmolar (e.g., $NaHCO_3$, glucose, parenteral nutrition), irritating (i.e., Ca), rapid infusions

- ➢ Mgt
  - If vasospasm suspected, warm contralateral extremity for 5–10 min w/ warm soak; if problem does not resolve, remove catheter
  - Remove catheter if waveform dampens, blood cannot be withdrawn, or any of above complications are suspected
- Hemorrhage due to catheter accident
  - ➢ Frequency: rare
  - ➢ Mgt: local hemostasis
- Sepsis/cellulitis/omphalitis/septic emboli
  - ➢ Frequency: rare
  - ➢ Prevention: strict aseptic technique (prophylactic antibiotics ineffective)
  - ➢ Mgt: catheter removal, antibiotic therapy

UMBILICAL VENOUS CATHETERIZATION

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INDICATIONS

- Administration of resuscitation drugs
- Central venous access
  - ➢ Infusion of hypertonic solutions
  - ➢ Administration of critical drugs (e.g., PGE1, ionotropes)
  - ➢ Delivery of blood & blood products, except platelets
- Measurement of central venous pressure
- Double volume exchange transfusion

CONTRAINDICATIONS

- Omphalitis
- Omphalocele
- Peritonitis

SPECIAL CONSIDERATIONS

- Use size 3.5 Fr for VLBW infants, 5 Fr for larger infants
- Position catheter tip 1 cm above diaphragm on lateral CXR, but never within the heart
- Depth of insertion (cm) = 1.5 cm/kg × birth wt (kg) + 5.6 cm + length of cord remaining (cm)
- Must confirm catheter position by x-ray

- If repositioning required, catheter may be withdrawn, but never advanced
- Never open umbilical vein catheter to atmosphere
- Infusate should contain 0.5–1 units of heparin/mL
- Umbilical vein catheter may remain in situ for 7–14 days, but no longer than clinically indicated

COMPLICATIONS

- Vessel perforation
  - ➢ Frequency: rare
  - ➢ Prevention: do not force if catheter does not advance easily
- Infection: sepsis, cellulitis, septic emboli, omphalitis, endocarditis
  - ➢ Frequency: sepsis common; others less common
  - ➢ Prevention: aseptic technique, minimize interruption of line (risk/benefit does not justify prophylactic antibiotic)
  - ➢ Mgt: remove catheter, antibiotic therapy
    NOTE: *Staphylococcus epidermidis* bacteremia may be treated w/o removal; if bacteremia persists >2 days, remove the line
- Air embolism
  - ➢ Frequency: rare
  - ➢ Mgt: never open umbilical vein catheter to atmosphere
- Thromboembolism: pulmonary, paradoxical, portal vein (w/ resulting portal hypertension
  - ➢ Frequency: rare
  - ➢ Mgt: remove catheter; other controversial
- Catheter malposition: myocardial perforation w/ tamponade, arrhythmias, segmental pulm hemorrhagic infarction, hydrothorax, hepatic necrosis, necrotizing enterocolitis; ALL POTENTIALLY LETHAL
  - ➢ Frequency: uncommon
  - ➢ X-ray verification of proper positioning, then note & monitor depth of insertion
  - ➢ Mgt: urgent specific therapy of complication may be required (e.g., pericardiocentesis, thoracentesis); remove catheter

PART FIVE

Supportive Care

FLUID AND ELECTROLYTE THERAPY

J.M. LORENZ, MD

SPECIAL CONSIDERATIONS

- Insensible water loss (IWL)
  - ➢ Relatively large component of total H_2O requirement: ~1/3rd the total H_2O requirement in term newborns; greater proportions w/ decreasing GA
  - ➢ Highly variable: affected by many factors
    - Increased w/ **immaturity**, increased ambient temp, fever, increased minute ventilation, increased air flow velocity, phototherapy, increased activity, exposed bowel
    - Decreased w/ antenatal steroid therapy, increasing postnatal age, IUGR, **increased ambient humidity**, increased inspired humidity, plastic blanket
  - ➢ Infant has no ability to modulate IWL in response to perturbations in fluid, electrolyte therapy: **IWL is obligate free water loss**
  - ➢ IWL (mL/kg/day) on day 1 of life in AGA infants in incubator w/ 50% humidity*:

    GA/ IWL
    23–24 wk/100 – >200
    25–27 wk/ 60 – 200
    28–30 wk/ 20 – 75
    31–36 wk/ 10 – 30
    37–42 wk/ 10 – 20

    * IWL will be 15–35% > under radiant warmers w/o vapor barrier over infant
- Contraction of the extracellular fluid (ECF) space
  - ➢ Roughly, magnitude of contraction in ECF space inversely proportional to GA
  - ➢ Fluid & electrolyte therapy should allow wt loss of 5–10% in term infants, 10–20% in preterm in 1st wk of life
- Phases of renal, fluid, and electrolyte adaptation: usually 3 phases can be distinguished:
  - ➢ Ante diuretic
    - 1st 12–48 h of life
    - Urine output low regardless of intake
    - Na, K excretion minimal
    - Ability to excrete H_2O load restricted

- ➢ Diuretic/natriuretic
  - Age 1–5 days
  - Urinary H_2O, Na, K outputs increase abruptly w/o regard to intake
  - Majority of postnatal wt loss occurs
- ➢ Homeostatic
  - Age 2–5 days
  - Urinary H_2O, Na, K outputs decrease and vary appropriately w/ intake

■ Intracellular fluid (ICF) to ECF shift of K
- ➢ In infants <= 28 wk GA, K shifts from ICF to ECF space in immediate postnatal period
- ➢ Magnitude of shift correlates roughly w/ degree of prematurity
- ➢ May lead to life-threatening hyperkalemia even w/o K intake

■ Limitations of renal function
- ➢ Glomerular filtration rate (GFR) lower in preterm than full-term infant; lowest in the ante diuretic phase; limits excretion of H_2O, Na, K
- ➢ Na reabsorptive capacity of kidney limited in preterm infant
  - Ability to conserve Na < full-term infants, adults
  - Ability of preterm to excrete Na loads > full-term infants
- ➢ Maximum urine concentration ~ 600 mOsm/L in full term, ~ 500 mOsm/L in preterm infants: minimal H_2O required to excrete given solute load > in preterm than full-term infant and > in full-term infant than adult
- ➢ Serum [HCO_3] at which HCO_3 will appear in urine < in preterm than full-term infant and < in term infant than adult
- ➢ Acid secretory capacity limited
- ➢ Serum glucose concentration at which glucose will appear in urine < in preterm than full-term infant, adult

MANAGEMENT

Depends on phase of adaptation:

■ Ante diuretic
- ➢ H_2O intake should approximate estimated IWL or minimum req to provide adequate dextrose (whichever higher); in incubator w/ 50% humidity:

  GA/IWL
  23–24 wk/100 – >200
  25–27 wk/ 60 – 200
  28–30 wk/ 20 – 75

31–36 wk/ 10 – 30
37–42 wk/ 10 – 20

- ➢ No Na or K
- ➢ Dextrose intake
  - Preterms: 4–6 mcg/kg/min
  - Full-terms: 4–8 mcg/kg/min

  Note: Dextrose administration rate (mg/kg/min) = dextrose concentration (%) x infusion rate (mL/kg/day) × 0.006
  - 200 mL/kg/d D5W will provide ~ 6 mcg/kg/min glucose; higher rates in extreme preterms (which may be necessary for high IWL) will result in hyperglycemia
  - 65 mL/kg/d D12.5W (> concentration should not be given by peripheral vein)~ minimum necessary to prevent hypoglycemia

- Diuretic/natriuretic
  - ➢ Increase H_2O intake to prevent hypernatremia
  - ➢ Begin Na intake when serum [Na] is decreasing or nl & stable w/ wt loss
  - ➢ Begin 1–2 mmol/kg/day K if serum [K] < 5–6 mmol/L & NOT INCREASING
- Homeostatic
  - ➢ Adjust H_2O intake to optimize caloric intake, but avoid H_2O overload
  - ➢ Approximate Na loss +/− growth allowance; urinary Na losses, and therefore Na required, inversely proportional to GA
  - ➢ >= 2–3 mmol/kg/day K to maintain serum [K] normal
  - ➢ Gradually increase glucose administration rate as tolerated to optimize caloric intake

SPECIFIC THERAPY

- See individual conditions or diseases for therapy for abnormalities of fluids and electrolytes

FOLLOW-UP

- H_2O balance: body wt, H_2O intake, urine output, serum [Na], +/− urine osmolality
- Na balance: body wt, Na intake, serum [Na], +/− urine Na excretion
- K balance: serum [K], +/- urine K excretion
- Serum glucose concentration

COMPLICATIONS

- Ante diuretic

- ➢ Hypernatremia if H_2O intake ≪ IWL
- ➢ H_2O intoxication (hyponatremia) if H_2O intake ≫ IWL
- ➢ Hyperkalemia in very premature infants
- ➢ Hyperglycemia due to high H_2O (& so glucose) intake

■ Diuretic natriuretic
- ➢ Hypernatremia w/ inadequate H_2O intake
- ➢ Hyperglycemia due to high H_2O (& so glucose) intake

■ Homeostatic
- ➢ Hyponatremia in preterms
- ➢ Hypokalemia

NUTRITION, ENTERAL

SUDHA KASHYAP, MD

SPECIAL CONSIDERATIONS

■ Recommended macronutrient and mineral intakes for VLBW infants
- ➢ Protein: 3.5–4.0 g/kg/day – 24-kcal/oz preterm formulas and fortified expressed breast milk (EBM) provide:
  - 3.6 g/kg/day when fed 150 mL/kg/day
  - 4 g/kg/day when fed 165 mL/kg/day
- ➢ Energy: 110–135 kcal/kg/day – 24-kcal/oz preterm formulas and fortified EBM provide:
  - 120 kcal/kg/day when fed 150 mL/kg/day
  - 134 kcal/kg/day when fed 165 mL/kg/day
- ➢ Ca: 140–230 mg/kg/day – 24-kcal/oz preterm formulas and fortified EBM provide 170–220 mg/kg/day when fed 150 mL/kg/day
- ➢ Phosphorus: 70–140 mg/kg/day – 24-kcal/oz preterm formulas and fortified EBM provide 85–120 mg/kg/day when fed 150 mL/kg/day

■ Digestive and metabolic limitations
- ➢ Relative deficiency of pancreatic lipase, bile salt
  - Poor fat absorption
  - Preterm formulas fat source, 40–50% medium-chain triglycerides
- ➢ Decreased mucosal lactase activity
  - Difficulty digesting lactose
  - Preterm formulas carbohydrate source (50% lactose, 50% glucose polymers)

- ➢ Unmodified bovine milk protein (whey/casein ratio 18:82) produces:
  - Metabolic acidosis
  - Azotemia
- ➢ Preterm formulas protein source – modified bovine milk protein (whey/casein ratio 60:40)

MANAGEMENT

- Feedings available
  - ➢ Term infants
    - Human milk
    - Bovine milk-derived formulas (Similac Advance® & Enfamil Lipil®)
  - ➢ Preterm infants
    - Human milk + human milk fortifier
      - Add fortifier when tolerating 100 mL/kg/day of EBM
    - Bovine milk-derived preterm infant formulas (Similac Special Care Advance® & Enfamil Premature Lipil®)
      - Initially 20-kcal/oz formula
      - If fluid restriction required, feed 24-kcal/oz formula
    - Follow-up formulas for VLBW infants (Similac Neosure Advance® & Enfamil Enfacare Lipil®)
      - Recommended for 6–9 mo after discharge
- Methods of enteral feeding
  - ➢ Nipple feed: infants > 34 wk gestation
  - ➢ Gavage feed: infants < 32–34 wk gestation
    - Naso- or orogastric
      - Intermittent
      - Continuous
    - Transpyloric
      - Confirm catheter position by x-ray
      - Feedings delivered continuously (intermittent feeding may cause dumping syndrome)
      - May result in fat malabsorption: bypasses salivary & gastric lipases
- Guidelines for feeding sick VLBW infants
  - ➢ Start trophic feeds as soon as infant hemodynamically stable at 10–20 mL/kg/day
  - ➢ Attempt intermittent gavage feeds
  - ➢ If not tolerated, trial of continuous gavage feeds
  - ➢ If not tolerated, transpyloric feeds

- ➢ If tolerated, increase feeds 10–20 mL/kg/day (controversial)
- ➢ As feedings tolerated, rate of advancement can be increased 20–30 mL/kg/day

SPECIFIC THERAPY
N/A

FOLLOW-UP
- Assessment of feeding tolerance
  - ➢ Gastric residuals
  - ➢ Vomiting
  - ➢ Abdominal distention
  - ➢ Stool consistency, frequency
  - ➢ Stool guaiac, reducing substance
- Growth
  - ➢ Wt gain
  - ➢ Head circumference
  - ➢ Length
- Biochemical variables
  - ➢ Albumin
  - ➢ Serum urea N (nl 5–10 mg/dL in growing preemie)
  - ➢ Serum electrolytes
  - ➢ Ca, phosphorus, alkaline phosphatase

COMPLICATIONS
- Necrotizing enterocolitis (see **NECROTIZING ENTEROCOLITIS** in the "Neonatal Conditions and Diseases" section)
- Bovine milk protein intolerance: may cause vomiting, diarrhea, bloody stool, colic, irritability, atopic dermatitis
- Lactose intolerance: may cause diarrhea, abdominal distention
- Fat malabsorption may cause large, bulky, foul-smelling stools

NUTRITION, PARENTERAL

SUDHA KASHYAP, MD

SPECIAL CONSIDERATIONS
- Indications
  - ➢ VLBW infants: unable to tolerate enteral feeding due to GI immaturity &/or respiratory distress syndrome

- ➢ Infants w/ necrotizing enterocolitis, surgically correctable GI malformations (gastroschisis, omphalocele, tracheo-esophageal fistula, malrotation w/ volvulus), short bowel syndrome
- ➢ Infants undergoing surgical correction of diaphragmatic hernias, congenital cardiac anomalies
- ➢ Infants on ECMO

MANAGEMENT

- When indicated TPN should be initiated by 24–48 h of life
- Components of infusate
  - ➢ H_2O: in general 120–150 mL/kg/day (see **FLUID & ELECTROLYTE THERAPY**)
  - ➢ N2 source: pediatric amino acid mixtures (Trophamine®, Aminosyn-PF®)
    - Provides 4 kcal/g
    - Maintain protein:energy ratio 1 g:20–25 kcal(N2:E ratio 1:125–150)
    - VLBW infants
      - Begin 2.0 g/kg/day
      - Increase by 0.5 g/kg/day to 3–3.5 g/kg/day
    - LBW & term infants
      - Begin w/ 2–2.5 g/kg/day
      - Increase 0.5 g/kg/day to 3 g/kg/day
    - Add cysteine 30–40 mg/g of amino acid mixture
  - ➢ Carbohydrate source: dextrose – provides 3.4 kcal/g
    - Infants < 1,000 g
      - Begin 3.5–5 mg/kg/min (5–7 g/kg/day)
      - Increase by 1.0–2.0 mg/kg/min each day (1.5–3 g/kg/day) as tolerated (monitor chemstrip, urine dipsticks)
    - Infants > 1,000 g
      - Begin 5–7 mg/kg/min (7.5–10 g/kg/day)
      - Increase by 2–3 mg/kg/min each day (3–4 g/kg/day)
  - ➢ Lipids source: 20% Intralipid®, soyabean oil emulsion
    - Provides 2 kcal/mL
    - Begin 1 g/kg/day
    - Increase 0.5 g/kg/day to a maximum of 3 g/kg/day
  - ➢ Electrolytes & minerals
    - Requirements vary from infant to infant (see **FLUID & ELECTROLYTE THERAPY**)
    - Adjustments made based on close monitoring

- Ca & phosphorous content should be maximized, esp for ELBW infants

➢ Trace elements
- Add Zn, Cu if TPN for >1 wk
- Add other trace elements (Se, Cr, Mn, Mo) for infants requiring TPN for longer period

➢ Vitamins: Add multivitamin TPN mixture for all infants receiving parenteral nutrition
- Wt < 2,000 g: add 1.5–2.0 mL/kg/day
- Wt > 2,000 g: add 3 mL/day

■ Route of administration
➢ Peripheral: can provide 60–90 kcal/kg/day, suitable for infants likely to tolerate adequate enteral intakes w/in 1–2 wk
- Max dextrose conc 12.5%
- Max osmolality ~ 800 mOsm/L

➢ Central: can provide >100 kcal/kg/day, suitable for infants likely to require longer period of TPN

SPECIFIC THERAPY
N/A

FOLLOW-UP
■ Daily wt
■ Daily BUN, creatinine, electrolyte, mineral determination initially, then 2×/wk (1 wk) until stable, then weekly
■ Bedside serum glucose monitoring (confirm abnormal values w/ serum glucose) & urine dipsticks w/ every change in dextrose rate &/or lipid infusion & in clinical status of the infant
■ Triglycerides, 24 h after every 1-g increase in lipid infusion, then weekly (<150 mg/dL is normal)
■ LFTs weekly
■ Acid/base status when amino acids being increased
■ NH3 as indicated for azotemia

COMPLICATIONS
■ Catheter-related
➢ Peripheral infusions: thrombophlebitis, skin necrosis w/ infiltration, infection
➢ Central vein infusions: malposition, dislodgement w/ bleeding, thrombosis, infection
■ Metabolic

- ➢ Related to infant's limited metabolic capacity: hyperglycemia, hypoglycemia, azotemia, electrolyte & mineral disorders
- ➢ Related to infusate: abnormal plasma aminograms, hypercholesterolemia/phospholipidemia, hypertriglyceridemia, cholestasis, abnormal liver enzymes, hepatomegaly, cholestasis

RESPIRATORY SUPPORT

ALAN R. SPITZER, MD
ADRIANN COMBS, RNC, BSN

SPECIAL CONSIDERATIONS

- Neonate must overcome several challenges in assuming breathing at birth
  - ➢ Fluid forces in lung (alveolar fluid fills lung prior to birth)
  - ➢ Elastic forces of lung
  - ➢ Surfactant deficiency in premature infants
  - ➢ Surfactant inactivation by meconium
  - ➢ Increased pulmonary vascular resistance prior to birth
  - ➢ Ductus arteriosus must close
- Signs of neonatal respiratory disease
  - ➢ Cyanosis (>3–5 g/dL desaturated Hgb)
  - ➢ Tachypnea (respiratory rate >60 bpm)
  - ➢ Retractions (indicates decreased alveolar volume)
  - ➢ Grunting (attempt to maintain lung inflation)
  - ➢ Nasal flaring (attempt to increase air entry)
  - ➢ Apnea, early (due to fatigue)

MANAGEMENT

- Available neonatal respiratory support therapies
  - ➢ Supplemental O_2
  - ➢ Continuous positive airway pressure (CPAP)
    - Nasal or endotracheal
  - ➢ Surfactant administration
    - Natural surfactants (Survanta, Infasurf, Curosurf)
    - Artificial surfactants (Exosurf, Surfaxin)
  - ➢ Conventional mechanical ventilation (CMV)
  - ➢ Synchronized intermittent mandatory ventilation (SIMV)
  - ➢ Assist/control (A/C) ventilation
  - ➢ High-freq ventilation (HFV)
    - Jet ventilation (HFJV)

- Oscillatory ventilation (HFOV)
- High-freq flow interrupter (HFFI)

➢ Inhalational nitric oxide therapy (iNO)
➢ Extracorporeal membrane oxygenation (ECMO)
➢ Liquid ventilation (experimental): perfluorocarbon-assisted ventilation

■ General principles of respiratory support
➢ Assessment of respiratory status
- Clinical signs (esp related to work of breathing)
- Pulse oximetry (oxygen saturation)
- Arterial blood gas (ABG – pH, PaO_2, $PaCO_2$, base excess)
- Transcutaneous monitoring ($tcpO_2$, $tcpCO_2$; now rarely used)

➢ Do not wait for respiratory failure before initiating Rx; early intervention usually preferable to rescue Rx, but caution indicated to avoid unnecessarily aggressive Rx & assoc complications
➢ Criteria for respiratory failure
- pH < 7.20
- pO_2 < 50 mmHg on 100% O_2
- pCO_2 > 60 mmHg

NOTE: As infants undergo physiologic transition after birth, initial pH may be <7.2, initial PCO_2 may be >55 mmHg; if O_2 saturation >90%, these infants should be allowed time to make transition; repeat ABG should be obtained w/in 30 min, infants must be closely observed

Persistent apnea: only absolute criterion for mechanical ventilation

■ Initial steps: w/ respiratory distress
➢ Place child on 40–50% FiO_2, observe response over 15 min
➢ If stable, follow w/ serial physical exams & pulse oximetry, consider ABG (to assess pH & PCO_2), wean oxygen as symptoms subside
➢ If respiratory distress increases, increase O_2 admin, obtain ABG
➢ Initiate CPAP or mechanical ventilation prn as symptoms progress or if respiratory failure develops
➢ Early CPAP use in delivery room may help avoid subsequent intubation
- Initiation of respiratory support

➢ Surfactant administration
- Consider surfactant for infants w/ respiratory distress syndrome who require IMV w/ >0.40 FiO_2

- Administration of 1st dose of surfactant <4 h of life optimal
- Often 1 dose sufficient; >3 doses rarely indicated
- Surfactant rarely necessary in DR; concentrate on resuscitation (ABCs; see **RESUSCITATION** in the "Procedures" section)
- Surfactant may be valuable in diseases other than respiratory distress syndrome (meconium aspiration syndrome, pneumonia, congenital diaphragmatic hernia, etc.)

➢ CPAP
- Nasal CPAP highly effective for many preterm/term infants
- Start at 5–6 cm H_2O & adjust O_2 gradually upward
- Higher pressures may be admin using nasal CPAP (8–10 cm H_2O), but may not be more effective, since mouth serves as "pop-off" valve for increased airway pressure
- Observe clinical response & obtain ABG
- If respiratory failure develops or apnea frequent, intubate & initiate mechanical ventilation

➢ Initiation of mechanical ventilation
- Begin w/ conventional or A/C ventilation for most respiratory problems; SIMV or CMV may be appropriate for clinical situations where more control is desired & during weaning from ventilator support
- Manual ventilation (increases risk of volutrauma due to inadvertently excessive peak inspiratory pressure [PIP]; may not be possible to admin positive end-expiratory pressure [PEEP])
  Suggested starting points for hand ventilation
  - FiO_2 at 0.50–0.60
  - IMV 20–40 bpm
  - PIP at 12–15 cm H_2O
  - PEEP at 4–5 cm H_2O
- Increase FiO_2 gradually to maintain O_2 saturation 90–95%; increase PIP to provide air entry, visible chest movement
- Follow pulse oximetry & obtain ABG
- Adjust support as indicated by ABG (see below); pulmonary graphics monitoring is available on many ventilators to assist in decision-making

■ Suggested ventilator adjustments during mgt or weaning

➢ To decrease pCO_2, increase PIP by 2–3 cm H_2O or rate by 5–10 bpm NOTE: W/ assist/control ventilation, increasing rate has no effect if infant is breathing at more than set rate

➢ To increase pCO_2, reduce PIP by 1–2 cm H_2O or rate
NOTE: Decreasing set rate in A/C of little value

- ➢ To increase pO_2, increase FiO_2 by 3–5% or PEEP by 1–2 cm H_2O
- ➢ To decrease pO_2, decrease FiO_2 by 2–3% or PEEP by 1cm H_2O
- ➢ Obtain ABG ~15–30 min following each ventilator change
- ➢ PEARL #1: Pressure-support ventilation may be helpful to minimize airway & ventilator resistance for the VLBW baby as weaning progresses

NOTE: Ventilator mgt can be very complex, but the above guidelines will cover majority of circumstances commonly encountered in both term & preterm infants.

- Sudden deterioration on ventilator
  - ➢ Remove infant from ventilator; hand ventilate w/ bag
  - ➢ Examine ventilator, be sure cycling at appropriate pressures/rate
  - ➢ If ventilator appears to be functioning, consider other possibilities
    - ET tube occlusion
    - Accidental extubation
    - ET tube too high/low
    - Pneumothorax
    - Inadequate gas exchange
    - Patent ductus arteriosus
    - Septicemia
- Extubation from conventional ventilator
  - ➢ Extubation may be facilitated by starting Rx w/ methylxanthines (caffeine or theophylline) 24 h prior to extubation
  - ➢ Extubate when PIP ~10 cm H_2O, FiO_2 <0.35–0.40
  - ➢ Remove ET tube while giving prolonged, low-pressure breath by hand
  - ➢ Place on nasal CPAP or O_2 by hood
  - ➢ Role of peri-extubation racemic epinephrine controversial
  - ➢ PEARL #2: When weaning ventilation, frequent small changes are preferable to less-frequent large changes in order to avoid "flip-flop," the up/down pattern of improvement/deterioration often seen w/ large weaning changes
- Rescue Rx w/ HFV
  - ➢ PEARL #3: Most infants (>90%) can be very successfully treated w/ CMV, SIMV, or A/C; HFV should be reserved primarily for rescue therapy; early use of HFV in some studies assoc w/ increased risk of intraventricular hemorrhage &/or periventricular leukomalacia
  - ➢ HFV appears to be an effective treatment for:

- Air leaks (pulmonary interstitial emphysema, pneumothorax; HFJV may be superior to HFOV)
- Severe V/Q mismatch syndromes
- Severe respiratory failure (consider when PIP > 25–30 cm H_2O)
- W/ iNO for persistent peripheral hypertension of the newborn
- Some cases of meconium aspiration syndrome & persistent peripheral hypertension of the newborn (~30–50% respond)
- Lung hypoplasia syndromes

➢ HFJV approach
- Initiate Rx w/ 15–20% higher PIP than used w/ SIMV or A/C
- Set PEEP at 5–6 cm H_2O & increase by 1–2 cm H_2O as needed
- FiO_2 usually near 1.0
- Start at IMV 420 bpm & inspiratory time of 0.02 sec
- Background sigh rate of 5–10 bpm on conventional ventilator (2 ventilators used in tandem); defer sighs initially w/ severe air leak
- Obtain ABG after 30 min
- Adjust ventilator by:
  - Increasing PIP to lower $paCO_2$
  - Decreasing PIP to raise $paCO_2$
  - Decreasing FiO_2 or PEEP to lower paO_2
  - Increasing FiO_2 or PEEP to raise paO_2
  - Rate changes usually of little benefit
- PEARL #4: Weaning must be very gradual w/ HFJV, as slow volume loss w/ PIP weaning may not become apparent until after several decreases in PIP & result in excessive rise in $paCO_2$

➢ HFOV approach
- HFOV settings NOT comparable to conventional ventilator settings
- MAP usually increased ~2 cm H_2O above that used w/ conventional ventilation to stabilize lung volume
- Start amplitude at ~20–25 & rate of 10 Hz; watch for chest vibration
- Amplitude (peak-to-peak pressure) & rate control $paCO_2$, MAP, FiO_2, control paO_2
  - To decrease $paCO_2$, increase amplitude or decrease frequency
  - To increase $paCO_2$, decrease amplitude or increase rate
  - To increase paO_2, increase MAP or FiO_2
  - To decrease paO_2, decrease MAP or FiO_2

- Obtain ABG 30 min after ventilator changes
- Serial CXRs required to monitor for hyperinflation from excessive MAP
- Weaning MAP should be gradual
- Consider returning to conventional ventilation when FiO_2 <~0.5, amplitude <~20, MAP ~12

SPECIFIC THERAPY

- Persistent pulmonary hypertension of the neonate (PPHN)
  - ➢ iNO (see **PULMONARY HYPERTENSION OF THE NEWBORN** in the "Neonatal Conditions and Diseases" section)
  - ➢ PEARL #5: Continued hyperventilation or normocapnic ventilation at high pressures in PPHN appears to be assoc w/ an increased risk of bronchopulmonary dysplasia, neurodevelopmental handicap
- Extracorporeal membrane oxygenation (ECMO)
  - ➢ Use of prolonged cardiac bypass to rest both heart & lung in many cases of severe neonatal respiratory failure
  - ➢ Should only be used for diseases w/ reasonable likelihood of recovery
    - Meconium aspiration syndrome
    - PPHN
    - Congenital diaphragmatic hernia
    - Respiratory distress syndrome

    Survival >95% in all of above, except congenital diaphragmatic hernia (45–55%)
  - ➢ Used only in infants >2.0 kg & 34 wk gestation
  - ➢ Infant must be heparinized; coagulation tests must be monitored extremely closely; monitor for intracranial hemorrhage w/ head US
  - ➢ May be applied via arteriovenous (A-V) route (cannulation of carotid artery & internal jugular vein) or venovenous (V-V) route (only internal jugular vein cannulated)
  - ➢ V-V ECMO requires reasonably stable cardiac function; otherwise, A-V is indicated
  - ➢ ECMO should be used only in centers performing >12–15 cases/yr
  - ➢ Duration of Rx ranges from 2 days-4 wk, depending on disease

FOLLOW-UP

- Neurodevelopmental

- Pulmonary for increased risk of pneumonia during 1st year of life, esp w/ bronchopulmonary dysplasia
- Growth
- Ophthalmology

COMPLICATIONS AND PROGNOSIS

Acute

- Complications related to endotracheal intubation (see **ENDOTRACHEAL INTUBATION** in the "Procedures" section)
- Air leaks
  - Pulmonary interstitial emphysema
  - Pneumothorax
  - Pneumomediastinum
  - Pneumopericardium
  - Pneumoperitoneum
- Hyperinflation w/ secondary decrease in lung compliance & venous return
- Cardiovascular
  - Decreased cardiac output
  - Patent ductus arteriosus
  - Intraventricular hemorrhage
  - Ventriculomegaly
  - Periventricular leukomalacia
- Others
  - Nosocomial pneumonia & other infections
  - Feeding intolerance, GERD

Long-term

- Bronchopulmonary dysplasia
  - Definition: see **BRONCHOPULMONARY DYSPLASIA** in the "Neonatal Conditions and Diseases" section)
  - Prevalence
    - Depends on BW & GA
    - 5–50% of ventilated premature neonates
    - ~3–5% of ventilated term neonates
    - Considerable variation from center to center
  - Management: see **BRONCHOPULMONARY DYSPLASIA** in the "Neonatal Conditions and Diseases" section)
- Neurodevelopmental
  - Cognitive impairment
  - Cerebral palsy (5–25% of ventilated infants)

- ➢ Hearing loss
- ➢ Speech delay

- Misc
  - ➢ See **RETINOPATHY OF PREMATURITY** in the "Neonatal Conditions and Diseases" section)
  - ➢ Pneumonia (risk increased in 1st year of life)
  - ➢ Otitis media
  - ➢ Abnormalities of dentition (due to intubation)

RESUSCITATION

J.M. LORENZ, MD
REVISED BY HELEN M. TOWERS, MD

See also **ENDOTRACHEAL INTUBATION**

SPECIAL CONSIDERATIONS

- Anticipate need for resuscitation
- Most newborns vigorous
- All newborns req initial assessment after birth
  - ➢ 90% need not be separated from mother
  - ➢ 10% req assistance
  - ➢ 1% require resuscitation
- Apgar score ***not*** useful to guide need for resuscitation
- If ventilation & oxygenation required, ***increasing heart rate is primary sign of effective ventilation***; other signs include improving color, spontaneous breathing, improved muscle tone
- If meconium-stained fluid is present, intubate only if infant is depressed
- O_2 blender recommended: provide 100%* O_2 only w/ cyanosis or positive-pressure ventilation
  - * May start w/ O_2 <100% & increase after 90 seconds w/o improvement
- Maintain normothermia

Personnel

If delivery is high risk, recruit at least 1 additional experienced person to assist

Equipment

- Radiant warmer
- Gloves

- Stethoscope
- Suction equipment
  - ➢ Bulb syringe & 12F or 14F suction catheter w/ meconium aspirator
  - ➢ Suction source w/ neg pressure regulator
- Bag & mask
  - ➢ 200- to 750-mL self-inflating resuscitation bag capable of delivering 1.0 FiO_2 +/− manometer
    OR
  - ➢ 200- to 750-mL anesthesia bag w/ manometer
    OR
  - ➢ Flow-controlled pressure-limited device (Neopuff®)
- Masks – term, preterm sizes
- Feeding tube, syringe
- Intubation equipment
  - ➢ Laryngoscope w/ straight blades
    - No. 1 for term infant
    - No. 0 for preterm infant
  - ➢ Appropriate-size endotracheal tube for gestational age (see **ENDOTRACHEAL INTUBATION**)
  - ➢ Stylet (optional)
  - ➢ Shoulder roll, tape, bulbs, batteries
  - ➢ Scissors
  - ➢ Warmed linens
  - ➢ O_2 source w/ flow meter
  - ➢ CO_2 detector or capnograph
  - ➢ Laryngeal mask airway
  - ➢ Clock w/ second hand
- Meds
  - ➢ Epinephrine 1:10,000, 3-ml or 10-mL ampules
  - ➢ Normal saline or Ringer's lactate
  - ➢ Sodium bicarbonate 4.2%
  - ➢ Naloxone hydrochloride 1.0 mg/mL ampule
  - ➢ Syringes, umbilical vessel catheters, flush solutions

Prepare/test equipment

- Turn on radiant warmer
- Connect O_2 source to bag & adjust flow to 5 L/min; test bag:
  - ➢ O_2 flowing?
  - ➢ Good pressure generated?
  - ➢ Pressure-release valve working?
  - ➢ Valve assembly present & working?

- ➢ Pressure manometer (if any) working?
- Connect suction tubing, turn on source, adjust neg pressure to 80 mmHg, test suction
- Check laryngoscope light
- Review NRP resuscitation flow chart

MANAGEMENT

Overview

- WITHIN FIRST 30 SEC
  - ➢ Provide warmth
  - ➢ Position head & clear airway
  - ➢ Assess ventilation & color
  - ➢ Provide positive-pressure ventilation for lack of spontaneous respirations or blow-by O_2 for cyanosis
- WITHIN NEXT 30 SEC
  - ➢ Ensure that ventilation is effective
  - ➢ Initiate ECM if HR < 60
- WITHIN NEXT 30 SEC
  - ➢ Again ensure that ventilation is effective
  - ➢ Reassess HR
  - ➢ Evaluate for complications
  - ➢ Administer epi if HR < 60

Resuscitation steps

- AT BIRTH: immediately assess:
  - ➢ Amniotic fluid clear of meconium?
  - ➢ Breathing/crying?
  - ➢ Good muscle tone?
  - ➢ Term gestation?

    YES – Routine Care
    - Provide warmth
    - Clear airway prn, suction mouth & then nose (direct endotracheal suctioning is indicated if the amniotic fluid is meconium-stained AND the baby is depressed)
    - Dry, stimulate
    - Assess color

    NO
    - Provide warmth
    - Clear airway prn, suction mouth then nose (direct endotracheal suctioning is indicated if the amniotic fluid is meconium stained AND the baby is depressed)
    - Reposition head in "sniffing" position

- Briefly stimulate (flick soles of feet or gently rub trunk or extremities)

■ BY 30 SECONDS: assess respirations, HR & color
  ➢ Apnea or HR < 100+
    - Provide positive-pressure ventilation w/ 1.0 FiO_2 & 40–60 breaths/min by mask
      NOTE: if no supplemental O_2 available, use room
  ➢ Breathing & HR > 100
    - PINK: supportive care
    - CYANOTIC: provide free-flowing FiO_2

■ BY 60 SEC: reassess ventilation, HR, color
  ➢ Not ventilating or HR < 100
    - Reposition head
    - Reapply mask to face w/ good seal
    - Ventilate w/ newborn's mouth open
    - Increase ventilatory pressure
    - Consider endotracheal intubation
  ➢ Ventilating, but HR < 60
    - Continue positive-pressure ventilation
    - Initiate chest compressions: 3 chest compression btwn each positive-pressure ventilation q2 sec (1-and-2-and-3-and breath, 1-and-2-and-3-and breath, . . .), providing 90 chest compressions & 30 breaths per min
    - Consider endotracheal intubation
  ➢ Ventilating, but HR 60–100 or cyanotic: continue positive-pressure ventilation
  ➢ Ventilating, HR > 100, pink: spontaneously breathing?
    - NO: continue positive-pressure ventilation
    - YES: gradually discontinue positive-pressure ventilation & provide free-flowing O2

■ BY 90 SEC: reassess ventilation, HR, color
  ➢ HR < 60
    - Reconfirm effectiveness of ventilation
      - Chest movement?
      - If not intubated, consider endotracheal intubation
      - If continuing w/ mask ventilation, insert orogastric tube
      - If intubated:
        Check that depth of insertion is appropriate (see **ENDOTRACHEAL INTUBATION**)
        Check for exhaled CO_2 to confirm tube placement
    - Continue positive-pressure ventilation w/100% O_2

- Continue/initiate ECM, confirm palpable umbilical artery pulse w/ compressions
- Epinephrine (1:10,000)
  - Via ETT, 0.3–1 mL/kg

OR PREFERABLY

- Insert umbilical vein catheter (see **UMBILICAL VENOUS CATHETERIZATION**) and give IV 0.1–0.3 mL/kg rapidly; flush w/ 0.5–1 mL NS; may repeat q 3–5 min
- If hypovolemia highly suspected (pale or Hx c/w maternal or fetal blood loss): NS 10 mL/kg via umbilical vein over 5–10 min; repeat as indicated
- If metabolic acidosis confirmed & ventilation adequate: $NaHCO_3$ (4.2% = 0.5 mmol/mL), 4 mL/kg via umbilical vein no faster than 2 mL/kg/min (caution: caustic, hypertonic solution)

➢ Ventilating, HR 60–100
- Discontinue ECM (if previously initiated)
- Continue positive pressure ventilation
- Consider endotracheal intubation if not previously performed
  - HR > 100, pink w/ effective spontaneous respirations
    - Gradually discontinue positive-pressure ventilation
    - Provide free-flowing O_2

■ If ventilation ineffective or HR < 60, consider:
➢ Pneumothorax
➢ Diaphragmatic hernia
➢ Pulmonary hypoplasia
➢ Airway anomalies

■ If ventilation effective & HR > 100, but cyanosis persists, consider cyanotic congenital heart disease

■ NOTE:
➢ Naloxone recommended only:
- W/ history of maternal narcotics w/in 4 hr of delivery
- After HR & color restored

➢ Discontinuation of resuscitative efforts may be appropriate after 10 min of complete & adequate resuscitation efforts if HR remains absent

SPECIFIC THERAPY
N/A

FOLLOW-UP

- Monitor:
  - ➢ HR, respiratory rate, color, mental status, tone
  - ➢ Pulse oximetry (optional)
  - ➢ Monitor for and Rx hypoglycemia (see **HYPOGLYCEMIA** in the "Neonatal Presenting Signs" section)
  - ➢ Avoid hyperthermia or hypothermia (see **THERMAL MANAGEMENT** in the "Supportive Care" section)
- Check blood gas from umbilical venous catheter or arterial puncture (optional)
- Monitor for feeding problems

COMPLICATIONS

- Pneumonia, pneumothorax
- Transient tachypnea, meconium aspiration syndrome
- Hypotension
- Airway trauma due suctioning or intubation
- W/ asphyxia
  - ➢ Hypoxic-ischemic encephalopathy (see **HYPOXIC ISCHEMIC ENCEPHALOPATHY** in the "Neonatal Conditions and Diseases" section)
  - ➢ Acute tubular necrosis
  - ➢ Ileus, necrotizing enterocolitis
  - ➢ Anemia, thrombocytopenia
- Intraventricular hemorrhage w/ rapid administration of NS or $NaHCO_3$

THERMAL MANAGEMENT

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SPECIAL CONSIDERATIONS

- Heat loss from preterm infants increases geometrically w/ lower gestation: THE SMALLER THEY ARE, THE COLDER THEY GET, FASTER
- Heat loss occurs via 4 routes (down a temp gradient): HEAT GOES FROM WHERE IT IS TO WHERE IT'S NOT
  - ➢ EARTH: CONDUCTION
    - Solid-solid body contact
    - Temp gradient = **T**skin – **T**mattress

- Negligible w/foam mattress

➢ AIR: NATURAL CONVECTION (heat rises from the skin) & FORCED CONVECTION (wind passing over skin)
- Temp gradient = **T**skin – **T**air

➢ FIRE: RADIATION
- Infrared heat transfer from skin to solid object w/ which it is not in contact (black body), mW/cm^2
- Temp gradient = **T**skin – **T**wall

➢ WATER: EVAPORATION
- From skin & respiratory tract
- 0.68 Kcal/mL H_2O evaporated

■ Fetal/neonatal temp maintenance depends on environment
➢ Heat loss in utero by convection (placental blood flow); **T**mother < **T**fetus by 0.2° C: MOTHER KEEPS BABY COOL, NOT WARM
➢ Heat loss at birth in delivery room (radiation, convection, evaporation); uncorrected may decrease **T**axillary by 0.5 degrees C/min (at 5 min **T**axillary 34.5° C, at 10 min 32 degrees C)
➢ INCUBATORS CONTROL METABOLIC HEAT LOSS, BUT DO NOT ACTUALLY WARM BABY; heat loss inside incubators determined by:
- Non-evaporative **T**operant = [0.6 (**T**incubator walls) + 0.4 **T**air w/in incubator]; INCUBATOR AIR TEMP > ROOM AIR, BUT SLIGHTLY < BABY
- Evaporation 0.68 kcal/mL H_2O loss from skin & respiratory tract

➢ Convective & evaporative heat loss under radiant warmers >>> w/in incubators
- Must be balanced w/ RADIANT HEAT GAIN
- RADIANT WARMERS ACTUALLY "INJECT" HEAT THROUGH SKIN, SKIN BLOOD FLOW

MANAGEMENT

■ Interventions in delivery room: WORK FAST, SPEND LEAST TIME IN COLDEST PLACE
➢ Place under radiant warmer on full power
➢ Dry w/ warm blankets, discard wet blankets
➢ Avoid cold O_2 from mask blowing over baby's skin
➢ Consider plastic blanket (Saran blanket or polyethylene bag, see below)

■ Rewarming & temp stabilization in NICU
➢ Place UNDRAPED under RADIANT WARMER servo-controlled to **T**skin abdomen = 36.5° C until

- All procedures done (umbilical artery/vein catheter, IV, ET tube, etc.)

and

- **T**axillary = 36.0–37.0° C (see below)

➢ If hypothermic

- **T**skin abdomen < 35.5° C & radiant warmer alarms: set servo control to **T**skin abdomen + 0.5° C (eg, if **T**skin abdomen = 33.3° C, set servo contol to **T**skin abdomen 33.8° C)
- Monitor **T**axillary, advance servo control dial q ~15 min to **T**skin abdomen + 0.5° C until **T**skin abdomen = 36.5° C and **T**axillary >= 36.0° C
- Rate for rewarming CORE BODY TEMP (**T**axillary = **T**deep rectal – 0.5°C) is ~2 C/h, where normal **T**rectal ≈ 37.0° C, normal **T**axillary ≈ 36.5°

■ Transfer to conventional, convection-warmed incubator to minimize stimulation & optimize growth

➢ Goal to achieve THERMAL NEUTRAL ENVIRONMENT: set of environmental conditions (**T**wall, **T**air, % relative humidity) that results in lowest metabolic rate (infant O_2 consumption increases w/ cold stress) at normal body temp; also called "thermal comfort zone"

➢ MONITOR & MAINTAIN **T**axillary 36.0–37.0° C (BABY'S HIGHEST PRIORITY) by varying servo control **T**skin abdomen 36.5–37.5° C (may be lower in larger babies, but consider radiant warmer if higher temp required for micropremie w/ birth wt < 700 g)

➢ AIR TEMP SERVO CONTROL may be used alternatively

➢ Incubator **T**air required increases w/ decreasing gestational age at birth

➢ Incubator **T**air required decreases as baby matures postnatally (skin, size)

➢ Incubator **T**air required lower w/ double wall than single (higher **T**inner wall)

➢ Incubator **T**air required may be lower w/ phototherapy (varies w/ phototherapy unit)

➢ Humidification of incubator air reduces evaporative H_2O/heat loss: **T**air required lower w/ higher % relative humidity

- Use incubator manufacturer devices only; don't use respirator humidifiers
- AAP/ACOG recommends 50% relative humidity w/in incubators

- Micropremies w/ birth wt < 700 g may benefit from 50–80% for 1st 1–2 wk
- ANY VISIBLE MIST IS RAIN-OUT & PROMOTES INFECTION (e.g., *Pseudomonas*), so maintain set humidity <=80% & below dew point

➢ HEAT SHIELDS DECREASE RADIANT, CONVECTIVE, EVAPORATIVE HEAT LOSSES; incubator **T**air required lower w/ heat shields

- BODY HOOD (transparent plastic 1–3 mm thick): may be useful, but only in single-walled incubators
  - NOT recommended under radiant warmers (impedes heat transfer)
  - Cumbersome inside incubators
- SARAN BLANKETS (thin, flexible plastic): seal edges w/ tape, cover head-to-toe
  - ONLY if endotracheally intubated or on nasal CPAP; may obstruct breathing (mouth, nose) in infants not intubated & not on nasal CPAP
  - Minimize contact w/ skin using blanket rolls at baby's sides; occlusive skin contact may macerate skin, promote infection
  - Most useful under radiant warmers
  - May be useful in closed incubators

➢ SKIN PROTETION (further research required)

- Adherent semipermeable polyurethane dressings (e.g., Opsite®, Tegaderm®)
- Petroleum-based ointment (eg, Aquaphor®) may promote staphylococcal or yeast colonization

■ Radiant warmers: Critically ill babies requiring freq interventions (interrupting closed incubation) may be managed alternatively under radiant warmers

➢ MONITOR, MAINTAIN **T**axillary 36.5–37° C (BABY'S HIGHEST PRIORITY) by varying servo control **T**skin abdomen 36.5–37.2° C (may be lower in larger babies)

➢ Consider plastic blanket in micropremies w/ birth wt < 700 g

➢ Cover **T**skin abdomen thermistor probe tip w/ adhesive foil shield

➢ Avoid surgical drapes, which obstruct radiant warming; partially drape from side

➢ Side effects

- Increased transcutaneous evaporation: consider Saran blanket

- Hyperthermia if probe poorly attached under foil shield
- Hypothermia if probe left under baby, between mattress & skin when baby turned

SPECIFIC THERAPY
N/A

FOLLOW-UP
- Monitor/record baby's temp q2–4h
  - ➢ CORE BODY TEMPS (**T**axillary = **T**deep rectal – 0.5° C); measure w/ calibrated alcohol glass or electronic thermometer (device equilibrium time varies from <1 to 5 min)
  - ➢ **T**abdomen skin
- Monitor/record incubator air & servo-control temps & environmental conditions
  - ➢ Nursery **T**ambient air: set room thermostat to at least 24° C (75° F)
  - ➢ If **T**ambient air < 27° C (< 80° F) may need to raise air control set-point for **T**incubator air
  - ➢ Record **T**incubator air temp during both servo control & air control modes
  - ➢ Record % relative humidity if humidification used

COMPLICATIONS
- HYPERTHERMIA: ANY BABY T > 37.5° C A CONCERN FOR OVER-HEATED INCUBATION
  - ➢ Exam: lobster pink skin color, posture extended, tone flaccid, tachycardia, seizures
  - ➢ Also caused by maternal fever or baby fever
  - ➢ Must r/o inappropriately warm environment: "Tummy-Toe Gradient"
    - If **T**abdomen = **T**foot, consider iatrogenic hyperthermia (check incubator)
    - If **T** abdomen – **T** foot > 2° C, consider fever
  - ➢ Reduce servo-controlled/incubator air temp immediately; change temp probe/incubation device if not improving in <30 min
- HYPOTHERMIA: ANY BABY T < 36.0° C: CONCERN FOR COLD STRESS
  - ➢ Exam: gray skin color, posture flexed, irritable, baseline tachy- or bradycardia (& normal % sat O_2)
  - ➢ Caused by:

- Environmental cold stress (e.g., in delivery room, near window, w/ bath)
- Sepsis, hypothyroidism; r/o under heated incubation

➢ Acute cold stress
- Place under radiant warmer, rewarm as above
- Assoc w/ acidosis, pulm hypertension, pulmonary hemorrhage, shock, hypoglycemia, increased mortality

➢ Chronic cold stress
- Assoc w/ low NORMAL **T**core, increased O_2 consumption, irritability, failure to thrive, increased mortality
- Increase servo control/incubator temp immediately, change probe/incubation device if not improving in <30 min