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Neonatology

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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