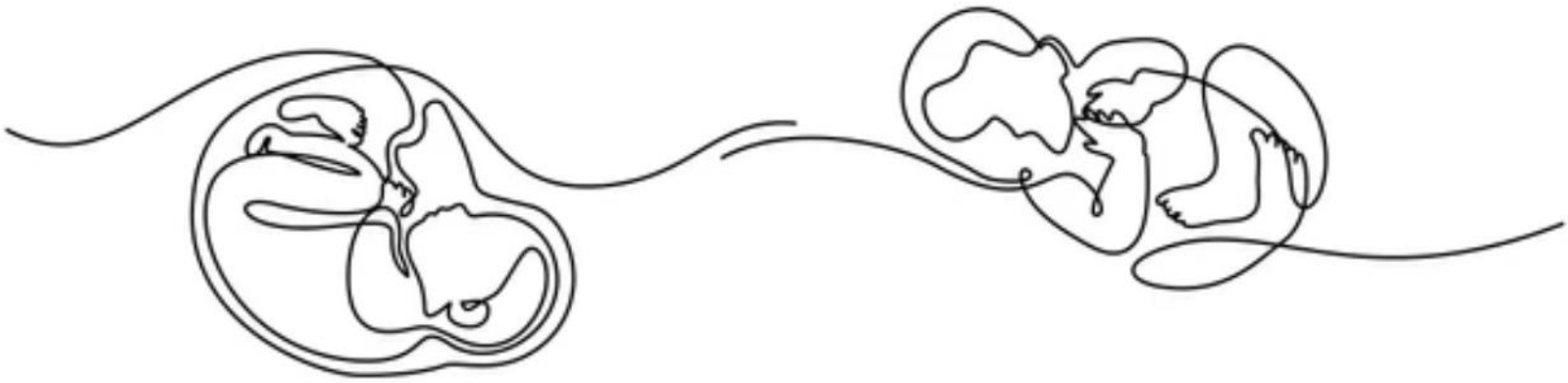
TORONTO RESIDENT'S HANDBOOK OF NEONATOLOGY

FOR RESIDENTS BY RESIDENTS

FIRST EDITION



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Acknowledgements

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We would like to acknowledge the land on which the contributors to this handbook live and work. For thousands of years it has been the traditional land of the Huron-Wendat and Petun First Nations, the Seneca, and most recently, the Mississaugas of the Credit River. Today, Toronto is home to Indigenous Peoples from across Turtle Island. Indigenous Peoples on the land now-called Canada face social and political barriers to health related to systemic discrimination, both current and historical. As a result, Indigenous Peoples have unique healthcare needs and can face challenges related to healthcare resources. Resources related to Indigenous health, cultural safety, reconciliation, and Jordan's Principle can be found on the Canadian Paediatric Society website.

Preface

The Toronto Resident's Handbook of Neonatology was created for residents, by residents. It is the culmination of 2 years of work (2020 to 2022) by 27 residents, and 18 content experts based in Toronto, Canada. It is meant to be used as a quick on-call reference for residents, study guide for final year residents, and clinical resource for general paediatricians. The content is broadly applicable to any Canadian context where neonates are cared for. Canadian Paediatric Society position statements form the foundation of the content. In the absence of CPS statements, national / international guidelines, hospital-specific guidelines, and expert opinion were used. Content references can be found at the end of each chapter. The chapters represent an overview of common clinical neonatal problems and are not meant to be in-depth detailed reviews. We endeavor to update the chapters every 5 years.

Table of Contents

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Common NICU Abbreviations

A/B = apnea/bradycardia
A/B/D = apnea/bradycardia/desaturation
AC = assisted control ventilation
AEDF = absent end diastolic flow
AFP = alpha-fetoprotein
AGA = appropriate for gestational age
AOP = apnea of prematurity
ASD = atrial septal defect
AUS = abdominal ultrasound
AVSD = atrioventricular septal defect
AXR = abdominal x-ray
BP = blood pressure
BPD = bronchopulmonary dysplasia
BPP = biophysical profile
CCHD = critical congenital heart disease
CGA = corrected gestational age
CLD = chronic lung disease
CoA = coarctation of the aorta
CP = cerebral palsy
CPAP = continuous positive airway pressure
CPR = cardiopulmonary resuscitation
CPS = Canadian Paediatric Society
C/S = cesarean section
CSF = cerebral spinal fluid
CVS = chorionic villus sampling
CXR = chest X-ray
DAT = direct antiglobulin test
DBM = donor breast milk
DCC = delayed cord clamping
DTR = deep tendon reflex
EBM = expressed breast milk
ELBW = extremely low birth weight
EOS = early onset sepsis
ET or ETT = endotracheal tube
FTS = first trimester screen
GA = gestational age
GBS = group B strep
GDM = gestational diabetes mellitus
GIR = glucose infusion rate
GTPAL = gravida, term, preterm, abortions, living
HC = head circumference
HF = high flow oxygen
HFJV = high frequency jet ventilation
HFOV = high frequency oscillatory ventilation
HIE = hypoxic ischemic encephalopathy
HLHS = hypoplastic left heart syndrome
HMF = human milk fortifier
HTN = hypertension
HUS = head ultrasound
IAP = intrapartum antibiotic prophylaxis
IDM = infant of diabetic mother
IMV = intermittent mandatory ventilation
iNO = inhaled nitric oxide
IUFD = intrauterine fetal demise
IUGR = intrauterine growth restriction
IV = intravenous
IVF = in vitro fertilization
IVH = intraventricular hemorrhage
LF = low flow oxygen
LGA = large for gestational age
LISA = less invasive surfactant administration
LP = lumbar puncture
MAP = mean airway pressure or mean arterial pressure
MAS = meconium aspiration syndrome
MIST = minimally invasive surfactant therapy
MFM = maternal fetal medicine
NAS = neonatal abstinence syndrome
NBS = newborn screen
NEC = necrotizing enterocolitis
NG = nasogastric tube
NICU = neonatal intensive care unit
NIPPV = non-invasive positive pressure ventilation
NIPT = non invasive prenatal testing
NPO = nil per os
NST = non-stress test
NTD = neural tube defect
O2 = oxygen
OG = orogastric tube
OIT = oral immune therapy
ONBS = ontario newborn screen
PC = pressure control ventilation
PCP = primary care provider
PDA = patent ductus arteriosus
PEEP = positive end expiratory pressure
PFO = patent foramen ovale
PGE1 = prostaglandin E1
PICC = peripherally inserted central catheter
PIH = pregnancy induced hypertension
PIP = positive inspiratory pressure
PNV = prenatal vitamins
PO = per os (by mouth)
PPHN = persistent pulmonary hypertension of the newborn
PPROM = preterm premature rupture of membranes
PPV = positive pressure ventilation
pRBCs = packed red blood cells
PSV = pressure support ventilation
PTL = preterm labour
PVHD = post hemorrhagic ventricular dilation
PVL = periventricular leukomalacia
PVR = peripheral vascular resistance
RDS = respiratory distress syndrome
ROM = rupture of membranes
ROP = retinopathy of prematurity

RSV = respiratory syncytial virus
SGA = small for gestational age
SIDS = sudden infant death syndrome
SIMV = synchronized intermittent mechanical ventilation
STI = sexually transmitted infection
SVR = systemic vascular resistance
TA = tricuspid atresia or truncus arteriosus
TAPVD = total anomalous pulmonart venous drainage
TFI = total fluid intake
TGA = transposition of the great arteries
ToF = tetralogy of fallot
TPN = total parenteral nutrition
TSB = total serum bilirubin
TTN = transient tachypnea of the newborn
UA = umbilical artery
UAC = umbilical arterial catheter
US = ultrasound
UTI = urinary tract infection
UVC = umbilical venous catheter
VLBW = very low birth weight
VS = vital signs
VSD = ventricular septal defect

Chapter 1 – Routine Newborn Care

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1.1 – Newborn History

Pregnancy and maternal history

- Gestational Age
- Singleton or Multiples (if multiple mono- or di- amniotic/chorionic and any complications)
- Maternal Age
- GP (Gravida, Para) or GTPAL (Gravida, Term, Preterm, Abortions, Living)
- Type of conception (spontaneous vs. assisted i.e. IVF)
- Screening investigations
  - Serologies and infectious screen (HIV, hepatitis, rubella, syphilis, gonorrhea, chlamydia, UTI)
  - GBS +/-/unknown
  - Blood type and antibody status
- Antenatal screening
  - First Trimester Screen (FTS)
  - Non invasive prenatal testing (NIPT)
  - Anatomy scan
  - If applicable – fetal echo, amniocentesis, chorionic villus sampling (CVS)
  - Follow up ultrasounds: biophysical profile (BPP) for fetal growth and wellbeing
- Maternal conditions and pregnancy complications
  - GDM (diet controlled vs. insulin dependent), pregnancy induced hypertension (PIH), etc.
  - Pre-eclampsia, antepartum haemorrhage, etc.
  - Any fetal medications give i.e. Corticosteroids
- Maternal medications (prenatal vitamins (PNV), Insulin, Labetalol, SSRI's etc.)
- Maternal exposures/substances (alcohol, cigarettes, opioids, etc.) – see Table 1.1
- Was an antenatal consult done?

Labour and Delivery

- Time of rupture of membranes (ROM)
- Septic risk factors (See Common Neonatal Consults)
  - Maternal fever (also consider person of interest for COVID)
  - Prolonged ROM (>18 hours)
  - Maternal intrapartum GBS colonization during the current pregnancy
  - GBS bacteriuria at any time during the current pregnancy
  - A previous infant with invasive GBS disease
  - Inadequate antibiotic prophylaxis

- Delivery
  - Vaginal vs. C-section (elective vs. emergency)
    - Indication for emergency delivery if applicable
  - Use of instrumentation: forceps, vacuum
  - Complications (i.e. fetal distress, meconium, nuchal cord etc.)
  - Attendants at delivery (Pediatrician, RT, NICU etc.) and indication
- Resuscitation
  - Need for stimulation, suction, CPAP, PPV, CPR, epinephrine (timing and vitals/appearance at each intervention)
  - APGAR Scores at 1 and 5 minutes (and every 5 minutes thereafter until 20 minutes or score of 7 reached)
  - Where did they go? Routine care and stay with parents vs. admitted to NICU
- Measurements
  - Birth weight; Head circumference; Length
  - Determine if appropriate, small, or large for gestational age (AGA, SGA, LGA)
  - Plot measurements on appropriate growth curves (WHO for term infants, Fenton for preterm infants)
- Investigations
  - Cord gas results
    - Healthy term infants: umbilical artery pH 7.27 ± 0.07 with a base deficit of -2.7 ± 2.8 mM (pH <7.0 suggests risk of neonatal neurologic morbidity, see Neurology)
  - Other investigations depending on scenario (consider CBC if septic risk factors)

Table 1.1a – APGAR Score criteria.

	0	1	2
Appearance (Colour)	Blue, pale	Pink body, blue extremities	Pink
Pulse (Heart Rate)	Absent	Below 100 bpm	Over 100 bpm
Grimace (Reflex)	No response	Minimal response to stimulation	Cry or active withdrawal
Activity (Muscle Tone)	Absent	Some flexion	Active
Respiratory effort	Absent	Slow and irregular	Vigorous cry

Table 1.1b – Neonatal exposures and outcomes.

Exposure	Neonatal presentation	Management	Long-term impact
SSRI/SNRI	- Poor neonatal adaptation syndrome: respiratory distress, tremors, jitteriness, feeding difficulties, weak cry - rarely hypoxemia from PPHN	- Often scored with modified Finnegan scoring (but not required) - Quiet environment, swaddling, skin-to-skin, encourage breastfeeding, small frequent feeds, resolves in days to weeks	- Neurodevelopmental impacts unclear but impact of untreated depression & anxiety concerning
Alcohol	- Low birth weight - Tremors, fussiness, poor feeding, diarrhea - Dysmorphisms related to Fetal Alcohol Syndrome: epicanthal folds, flat nasal bridge, small palpebral fissures, smooth philtrum, thin upper lip, microcephaly	- Early identification, education and anticipatory guidance, social support - Referral to neurodevelopmental follow-up program	- Fetal alcohol syndrome - Neurologic sequelae
Cocaine	- Preterm delivery - Low birth weight - Abruption	Treat complications	- Neurodevelopmental impact, limb anomalies, congenital heart defects, cleft palate
Marijuana	- Low birth weight	May need quiet environment, reduce maternal use if possible	- Neurodevelopmental impact is concerning but prenatal vs postnatal exposure unclear
Cigarettes	- Low birth weight - placental insufficiency	May need quiet environment, reduce maternal use if possible	- Risk of SIDS
Opioids	See Chapter 8 - Neurology		

1.2 – Newborn Physical Examination

1.2.1 Normal Newborn Exam

Sample note for newborn examination

- General appearance: well-appearing, vigorous, pink, non-dysmorphic appearing
- HEENT: normocephalic, atraumatic, PERRL, red reflex x 2, palate intact
- Respiratory: good air entry bilaterally, no adventitious sounds, no work of breathing
- Cardiac: heart sounds 1, 2 normal, no murmur heard, femoral pulses palpable bilaterally, warm and well perfused, capillary refill < 2 sec
- Abdomen: soft, non-tender, non-distended, no organomegaly, no masses, 3-vessel cord, anus appears patent
- GU: normal (male/female) genitalia, ± testes descended bilaterally
- MSK: spine straight and intact, hips stable
- Neuro: strong suck, symmetric moro, symmetric grasp x 4, normal axial and extra-axial tone

1.2.2 - Skin

Normal neonatal skin findings

- Vernix caseosa
    - White, watery biofilm that serves as a barrier for water loss and thermoregulation
    - Do not remove after birth, provides hydration and decreases skin inflammation
- Cutis marmorata
    - Transient lace-like mottling appearance of the skin due to vasomotor instability
    - Benign, improves with heat, time
    - Persistent cutis marmorata seen in: T21, Cornelia de Lange, homocystinuria
    - Differential diagnosis: cutis marmorata telangiectatica congenita
- Congenital dermal melanocytosis (aka. Slate grey nevus, previously Mongolian blue spot)
    - Flat, hyperpigmented lesion with a grey-blue colour
    - Most often seen on the lower back or buttocks in neonates of colour
    - Benign, fades over years

Table 1.2.2a - Benign newborn rashes

Rash	Timing	Characteristics	Special Features and Management
Erythema Toxicum Neonatorum	- Appear days to weeks after birth - Resolves in days	- Erythematous papules may progress to pustules on erythematous base - Whole body sparing palms and soles	- Contains eosinophils - Minority may have transient systemic eosinophilia
Transient Neonatal Pustular Melanosis	- Appear at birth - Self-limited	- Pustules which rupture and lead to post inflammatory hyperpigmentation - Whole body, in neonates of colour	- Contains neutrophils
Neonatal Cephalic Pustulosis (aka. Neonatal Acne)	- Appear 2-3 weeks after birth - Resolves in weeks-months (vs infantile acne at 3-6 months)	- Inflammatory papules and pustules on face and scalp - Lacks comedones (vs. infantile acne)	- Associated with *Malassezia* colonization - Contains yeast and neutrophils - Treatment: ketoconazole shampoo or 2% ketoconazole cream with low potency steroid
Miliaria	- Appear 2-3 weeks after birth - Resolves in days with removal of heat	- Affects areas prone to overheating - Can erode and leave mild desquamation Subtypes (level of obstruction): - Crystallina (superficial): clear 'dew drop' vesicles without erythema, 'dew drops, rupture on palpation - Rubra (mid): small erythematous papules and vesicles - Profunda (deep): more inflammatory	- Caused by blocked eccrine (sweat) ducts - Cooling measures, remove occlusive clothing
Milia	- Appear any time after birth - Resolve spontaneously	- Firm, tiny white or yellow papules on face and scalp - "Epstein's pearls" if on mucosa (often seen on palate)	- Inclusion cysts containing keratinized stratum corneum (not fluid filled)
Seborrheic Dermatitis (aka. Cradle cap)	- Appears at 2 weeks-12 months - Self resolving weeks-months	- Salmon-coloured patches with greasy scales - Commonly on scalp but may be seen on whole body and intertriginous areas (may have fissuring in diaper area)	- Overgrowth of *Malassezia furfur* - Treatment: emollients, gentle combing, ketoconazole shampoo or cream, low potency topical steroid
Irritant contact dermatitis (diaper dermatitis)	- May appear at any time	- Diaper area, spares folds/creases - Sharply demarcated, no satellite lesions - DDx: Acrodermatitis enteropathica (Zinc deficiency) with triad of diarrhea, failure to thrive, and alopecia	- Treatment: frequent diaper changes, gentle cleansing, barrier cream (zinc oxide), 1% hydrocortisone if needed, topical antifungal if secondary candida

Table 1.2.2b - Newborn rashes of clinical concern

Rash	Timing	Characteristics	Special Features and Management
Blueberry muffin rash	- Present at birth	- Violaceous (blue-red) papules and nodules	- Differential includes: TORCH infection, cutaneous neoplastic manifestation (leukemia, neuroblastoma), LCH - Rash represents extramedullary hematopoiesis
Herpes Simplex Virus (HSV)	- Transmitted congenitally (in utero) or acquired perinatally (during labour, most common) or postnatally	- Small vesicles with surrounding erythema and spectrum of disease - Localized skin, eye, mouth (SEM): vesicles progress to pustules and crusting, conjunctival edema and eye pain, mouth ulcers - CNS ± SEM (14% mortality, 70% poor neurodevelopmental outcome): seizures, lethargy, irritability, poor feeding, fever, hypothermia - Disseminated disease involving multiple organs (29% mortality)	- Diagnosis: Tzanck-stained smear of lesions, HSV DNA by PCR - Treatment: systemic acyclovir, early diagnosis and treatment can prevent progression
Varicella Zoster Virus (VZV)	-Transmitted congenitally (primary maternal infection in first 20 weeks of gestation, rare) or acquired perinatally or postnatally (infantile)	- Range of limited skin disease to disseminated infection - Erythematous macules, vesicles with progression to papules and crusting - Disseminated: pneumonia, hepatitis, meningoencephalitis, coagulopathy (30% mortality)	- Lesions usually heal in 7-10 days - Antiviral therapy recommended - If acquired 5 days prior to or 2 days after delivery (no maternal IgG protection) aggressive therapy with VZV immunoglobulin and IV acyclovir
Bullous Impetigo/ Staphylococcal scalded skin syndrome (SSSS)	- Onset days to weeks after birth	- Bullous Impetigo: erythema, flaccid bullae, superficial erosions - SSSS: flaccid ruptured bullae, generalized erythema, desquamation, Nikolsky sign, malaise, fever	- Staph aureus, strep A/B - SSSS: Epidermolytic toxin producing S. Aureus - Treatment: topical mupirocin, oral or IV antibiotics if widespread
Neonatal Langerhans cell histiocytosis (LCH)	- Diagnosed in weeks to months from birth	- Various rash morphologies - Mimics seborrheic dermatitis in intertriginous areas - Erythematous red-brown papules and patches with superficial erosions and crust - May have multisystem disease	- Skin biopsy: histiocyte aggregates with granulomatous formation - Supportive treatment, depends on manifestations - Oncology: evaluate long term for signs of progression or recurrence (3% risk of mortality, 10% risk of relapse)
Congenital cutaneous candidiasis	- Transmitted congenitally or acquired neonatally	- Congenital: diffuse erythema with or without pustules, occasionally bullae, systemic infection - Neonatal: oral thrush or diaper dermatitis (erythema with satellite vesicles or pustules) with or without systemic disease	- Benign in term neonates (cutaneous only) but potentially fatal in preterm (disseminated disease) - Diagnosis: KOH (spores and pseudohyphae) and culture - Treatment: topical antifungal (term), systemic antifungal (preterm)

Vascular rashes

- Nevus simplex (aka. Stork bite, Angel's kisses)
  - Benign and self-limiting flat pink or red birthmarks
  - Collection of vessels often seen on the eyelids, forehead, back of the neck
  - More prominent with crying, blanchable

- Infantile hemangioma
    - Presentation:
        - Appears in first days to months of life
        - Typically not present at birth
        - May be a precursor lesion present
        - Range in size, may be superficial, deep or mixed
    - Pathogenesis:
        - Benign and self-limiting
        - Rapid proliferation initially then slower until 9-12 months, involute by 1-several years
        - Of concern if interference with vision, vital organs, circulatory system or central nervous system (beard distribution of face risk factor for airway hemangioma)
        - If several, consider abdominal US to look for liver hemangiomas
        - May cause ulceration or permanent disfigurement
    - Associations: Rule out PHACES syndrome if segmental distribution on the face
    - Treatment:
        - Conservative management, beta blockers (close monitoring), topical steroids
- Port wine stain (nevus flammeus)
    - Capillary malformation common on the face, neck, scalp, arms, legs
    - Does not self-resolve; darkens as the infant gets older and grows in proportion to child
    - If the face consider Sturge-Weber syndrome and screen for associated symptoms including leptomeningioma and glaucoma

1.2.3 - Head

Head Shape and Size

- Head circumference (HC)
    - Accurate measurement: flat surface of forehead (glabella) and occipital protuberance as reference - plot on appropriate growth chart
    - Note abnormalities in head shape that may affect measurement (ie. molding, craniosynostosis, scalp swellings/haemorrhage)
- Craniosynostosis
    - Premature closure of one or more sutures of the skull
    - May have asymmetric head shape
    - Complications include developmental delay, facial abnormality and neurological dysfunction
    - Associated syndromes: Pfeiffer syndrome, Apert syndrome
    - Management: requires monitoring and possible surgical intervention
- Microcephaly (<3rd percentile)
    - Congenital: chromosomal/genetic abnormalities, TORCH infections, maternal drug/toxin exposures
    - Acquired (normal HC at birth): infection in the 3rd trimester, perinatal hypoxic ischemic insults, metabolic derangements
    - Investigations: send urine CMV and serologies, refer to neonatal follow up clinic

Scalp Injuries

- Caput succedaneum
    - Common, benign localized swelling of the scalp after delivery
        - May cross midline and suture lines, may have overlying skin changes (erythema, ecchymoses)
    - Self-limited, presents at birth and resolves within 4-6 days

- Cephalohematoma
    - Subperiosteal collection of blood due to broken capillaries (bleeding contained within a cranial plate)
        - Does not cross midline or suture lines with sharp boundaries
    - Self-limited, develops in hours-days from birth and may take weeks to months to resolve
- Subgaleal haemorrhage
    - Collection between the epicranial aponeurosis and periosteum of the skull
        - Bleeding into subcutaneous tissues can be life threatening and sequester 40% or more of the newborn's blood volume causing hemorrhagic shock
        - Associated with vacuum delivery, skull fracture
    - Presents with large, boggy skull with fluid wave often palpable
        - Enlarging head circumference - expect 40 cc blood loss for every 1cm increase in head circumference
    - Requires urgent monitoring of vital signs (tachycardia), serial head circumference measurements, and CBC (fall in hematocrit)
        - Consider coagulation studies (looking for consumptive coagulopathy)
        - Emergency stabilization with fluid boluses (volume resuscitation) and transfusions (pRBC, FFP, cryo, platelets) and transfer to tertiary centre

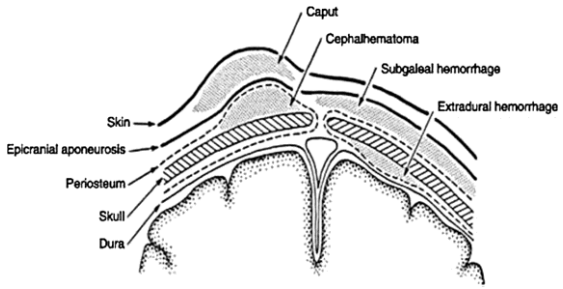

Figure 1.2.3a – Extradural fluid collections (Image from Pediatr Rev.)

! Subgaleal haemorrhage is a potential life threatening emergency requiring emergent resuscitation and massive transfusion !

1.2.4 - Facial Features

Abnormal Red Reflex

- If white, absent or asymmetric – urgent referral to ophthalmology
- Etiology:
    - Cataracts (most common), retinoblastoma (most concerning)
    - Congenital (coloboma, Coats disease), intraocular infections (toxoplasmosis), late stage retinopathy of prematurity

Choanal atresia

- Nasal passage blocked either by abnormal bony or soft tissue
- Presentation
    - Bilateral choanal atresia presents with upper airway obstruction, noisy breathing, cyanosis that worsens during feeding and improves with crying
    - Unilateral choanal atresia usually presents later
- Investigations: failed attempt pass catheter down nares
- Etiology: consider CHARGE syndrome

Cleft lip and palate

- Usually diagnosed antenatally with ultrasound
    - Consider amniocentesis and detailed anatomy ultrasounds +/- fetal echo

- Etiology
    - Cleft lip alone occurs in ~ 1 in 2500 and cleft lip and palate occurs in ~ 1 in 750
    - Up to 50% of babies with cleft palate have other associated anomalies
    - Associated with 22q11.2, trisomy 13, trisomy 18, Pierre Robin Sequence etc.
- Presentation
    - Feeding issues in the newborn period: use Haberman nipple, NG feed PRN, OT assessment
- Management: Refer to plastic surgery for repair

Ankyloglossia (tongue tie) (see Feeding and Nutrition)

- Should be assessed as a possible cause of breastfeeding difficulty and cracked nipples
- Option for frenotomy performed by some Paediatricians or Paediatric dentists

Facial palsies

- Usually results from forceps delivery and affects the mandibular branch of the facial nerve
- Clinical presentation
    - Loss of nasolabial fold and cannot contract the lower facial muscles on the affected side
    - Mouth appears drooped and when crying draws over to the affected side
    - Affected eye does not close fully
- Management
    - Expect resolution in days to weeks, may use artificial tears in affected eye

Asymmetric crying faces

- Congenital absence or hypoplasia of depressor anguli oris muscle
- Presentation
    - Muscles of the upper face are spared and nasolabial fords are normal
    - When the infant cries the forehead wrinkles, both eyes close normally
- Associations: renal or cardiac anomalies, 22q11 microdeletion
- Management
    - Benign, usually becomes less noticeable as the child gets older

Ear tags and pits

- Etiology
    - Isolated minor external ear anomalies including preauricular skin tags or pits are not associated with increased risk of renal anomalies and do not need screening
    - External ear anomalies are associated with additional anomalies of the middle or inner ear and hearing loss as well as syndromes of multiple congenital anomalies including renal anomalies
- Investigations
    - If hearing screen abnormal, refer to audiology
    - Consider renal ultrasound or other investigations if not isolated

1.2.5 – Cardiac (see Chapter 10 – Cardiology)

Femoral Pulses

- Diminished femoral pulses or brachial-femoral delay is concerning for coarctation of the aorta
- Order 4 limb BPs, pre and post ductal saturations

Murmurs

- Transient, benign murmurs very common in the newborn period, usually caused by a patent ductus arteriosus or pulmonary branch stenosis
    - PDA murmurs are continuous “machinery-like”, harsh and best heard under the left clavicle or radiating along the left sternal border
    - Peripheral pulmonary stenosis murmur is a systolic ejection murmur best heard in the upper left sternal border which radiates to the infraclavicular region, axillae and back (depending on the stenosis location)
        - Often benign but needs follow-up

- Benign murmur features
    - Grade 2 or less
    - Short systolic duration (not holosystolic or diastolic)
    - Minimal radiation
    - Musical or vibratory quality
- If concerned about a murmur
    - Pre and post ductal saturations, 4-limb BP (abnormal if >20 systolic difference), ECG
    - Consider hyperoxia test if cyanotic to differentiate cardiac and respiratory etiologies
    - Echocardiogram and refer to Paediatric Cardiology

1.2.6 – Abdominal

Diastasis Recti

- Normal in newborns due to non-union of the rectus muscles
- Resolves over time but may result in umbilical hernia

Umbilical hernia

- Due to persistent opening of the umbilical ring (incarceration is very rare)
- Majority will close by 5 years of age, refer to surgery for repair if large defect remains by 4 years of age

Two vessel cord/single umbilical artery

- May be isolated finding or associated with IUGR, heart or renal anomalies

1.2.7 – Musculoskeletal

Hands

- Syndactyly (fusion of digits) or Polydactyly (extra digits)
    - Can be normal variant, often a strong family history (consider VACTERL)
- Clinodactyly (5th finger curvature)
    - Associated with T21 – look for single palmar crease and other features of T21

Clavicle fracture

- Risk factors: shoulder dystocia (see brachial plexus injury), operative delivery, increased maternal age, increased birth weight (>4 kg)
- Presents with irritability, decreased motion on the affected side
- On exam: tenderness, crepitus, swelling on the bone, asymmetric moro
- Treatment: can pin sleeve of affected arm to front of clothes, no specific treatment necessary
    - Oral or rectal acetaminophen for pain in first week until callus forms

Developmental Dysplasia of the Hips (DDH) (see Chapter 5 – Common Neonatal Consults)

- Clinical screening (until walking age, note Barlow/Ortolani only present until 3-4 mo of age)
    - Hip 'clicks' are clinically unimportant
    - Asymmetric abduction or limited abduction
    - Barlow's sign: 'clunk of dislocation' with posterior force and gentle adduction
    - Ortolani Sign: 'clunk of reduction' on abduction as you relocate a dislocated hip into the socket
    - Galeazzi sign: thighs in midline, difference in height of two knees

Sacral dimple

- Benign features: single sacral dimple, midline, overlying the coccyx, visible intact base, less than 0.5 cm in diameter (no further investigation required)
- Concerning features: greater than 0.5 cm deep or large, in the superior portion of the gluteal cleft or above the gluteal cleft (>2.5 cm from the anal verge) or associated with other cutaneous markers of neural tube defects (hypertrichosis, discolouration)
    - Recommend spine US to screen for neural tube defect

Clubfoot (Talipes Equinovarus)

- Foot excessively plantar flexed with forefoot swung medially and sole facing inward
    - Does not correct with manual manipulation of the foot

- Contrast with positional clubfoot (positional calcaneovalgus feet or metatarsus adductus) due to intrauterine crowding or breech position
    - Corrects with manual manipulation of the foot

1.2.8 – Neurologic (See Neurology)

Primitive reflexes in the newborn

- Suck
- Grasp
    - Elicited by putting pressure on the palmar or plantar surface of a relaxed hand/foot and the infant should close their fingers or toes
    - Well established by 32 weeks and present until 3 months for palmar and 6 months for plantar
- Moro
    - Sudden dropping of the infant's head in relation to their trunk should result in abduction and extension of the infant's arms and opening of the hands followed by flexion
    - Should be symmetric between left and right
    - Present at 32 weeks, strong by 37 weeks
- Asymmetrical tonic neck reflex ("fencing position")
    - With an infant lying on their back, turning their head and neck to one side should cause the infant's upper and lower extremities on that side to extend and the contralateral upper extremity to flex
    - Disappears by 4 months of age allowing an infant to roll over
- Galant
    - Place the baby in ventral suspension and stroke the paravertebral region from the thorax to lumbar area, should cause the trunk and hips to move towards the side of the stimulus
- Stepping response
    - Hold infant in vertical position with their feet in contact with flat surface, should exhibit an alternate stepping action of flexion and extension of the legs
    - For infants >32 weeks
- Rooting
    - Stroking the cheek should lead turning of the head to that side

Hypotonia

- At term should exhibit strong flexion in all four limbs
- Test resistance to passive movements of the limbs
- Signs of hypotonia
    - Scarf sign (arm easily pulled across midline without resistance)
    - Slips through hands when lifted under the arms
    - U shape in ventral suspension
- Etiology: associated with brisk tendon reflexes suggest CNS dysfunction, associated with absent tendon reflexes suggests neuromuscular etiology

Neonatal Brachial Plexus Palsy (NBPP)

- Caused by lateral traction on the fetal head, usually secondary to shoulder dystocia, occasionally no known cause
- Risk factors
    - Difficult delivery, instrumented delivery, LGA infant, maternal diabetes, shoulder dystocia
    - Assess for other associated birth injuries (humeral / clavicular fractures, Horner syndrome, hemiparesis)
- Types
    - Erb's palsy (most common): injury to C5, C6 and occasionally C7
        - Adduction and internal rotation of the arm and forearm extension with hand movement preserved
    - Total brachial plexus injury
        - Flail arm (total paralysis), may be associated with Horner's syndrome

- Ddx: Pseudoparesis, myotonia congenita, anterior horn cell injury (congenital varicella syndrome or congenital cervical spinal atrophy), pyramidal tract or cerebellar lesions
- Management:
    - Consider XR if concern for bony injury. Elevated hemidiaphragm can suggest Horner's
    - If incomplete recovery by 1 month, this predicts severe NBPP and should be referred to multidisciplinary team
    - Most require physical or occupational therapy, surgery rare
- Prognosis
    - 75% recover completely within the first month
    - 25% may have permanent impairment
    - Full recovery unlikely if symptoms persist at 3-4 weeks

1.2.9 – Genitourinary

Hypospadius

- Abnormal location of the meatal opening with failure of closure of urethral folds
- Common congenital malformation (1 in 300), often isolated and not associated with underlying disorder (if cryptorchidism present should raise concern for problem of sexual development)
- Urology consultation with repair by 18mo of age
    - Defer circumcision as foreskin required for repair

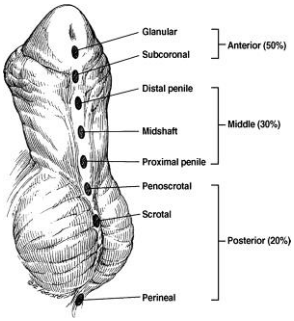

Figure 1.2.9a – Anatomy of hypospadias with abnormal locations of the ventral opening (Image from Kraft et al., 2010)

Other genitourinary differences

- Undescended testes and Inguinal hernia (see Chapter 11 - General Surgery)
- Ambiguous genitalia (see Chapter 14 – Endocrinology)

1.3 – Newborn Medications and Vaccines

Medications

- Vitamin K
    - To prevent hemorrhagic disease of the newborn (see Haematology) caused by insufficient prenatal storage of Vitamin K and Vitamin K in breastmilk
    - CPS and AAP suggest 1.0 mg dose of Vitamin K given IM after birth in all infants (0.5 mg for infants weighing ≤1,500 g)
    - Oral Vitamin K is inferior to IM and should only be considered for patients who's parents refuse IM as harm reduction strategy
- Erythromycin eye ointment
    - To prevent neonatal opthalmia due to *Neisseria gonorrhoeae*
    - Does not prevent transmission of *Chlamydia trachomatis*
    - Not routinely recommended by the CPS due to routine screening for gonorrhoea and chlamydia during pregnancy
        - For infants born to mothers who screen positive, should be monitored clinically at delivery (see Infectious Diseases)

Vaccines

- Hepatitis B vaccine (see Infectious Diseases)
    - Not recommended routinely in Ontario
    - Recommended in Ontario for infants whose mothers have a history of Hepatitis B (HBsAg positive) (concurrently with HepB IG) or for household contacts with Hepatitis B (vaccine only)
    - Schedule: 1st dose within 24hr of birth, 2nd dose at 1 month and 3rd dose at 6 months old (schedule differs for low birth weight infants)

1.4 - Postpartum Advice and Discharge Criteria

Readiness for discharge

- Provider assessments
    - Antenatal and perinatal risk factors reviewed by healthcare provider
    - Physical exam (with stable vital signs) by a healthcare provider with measurements complete and follow-up of any abnormal findings planned
    - Newborn screening complete (at 24hrs) (see Chapter 5 – Common Neonatal Consults)
        - Ontario Newborn Screen (see section 1.5)
        - Hearing screen (may not be done in hospital, referred to public health)
        - Critical congenital heart disease (CCHD) screen
        - Bilirubin check (transcutaneous if no risk factors and/or serum)
            - May check serum bilirubin earlier if risk factors present
    - Car seat safety
        - Rear facing until 2 years of age or approximately 40lb (depending on seat restrictions)
- Infant readiness
    - Feeding
        - Breastfeeding encouraged as desired by parent (see Chapter 7 – Feeding and Nutrition)
            - Consider follow-up with breastfeeding clinic/lactation support
        - Feeding established (minimum 2 successful feeds) and feeding plan in place
        - APNO prescription (Dr. Newman's All Purpose Nipple Ointment) for cracked nipples
            - Betamethasone ointment 0.1% 15 grams and Mupirocin ointment 2% 15 grams to which is added Miconazole powder to a concentration of 2% Miconazole (total about 30 grams combined)
                - Optional addition of Ibuprofen powder to a concentration of 2% Ibuprofen
                - To be used sparingly after each feed, do not wash or wipe off
    - Weight loss
        - Term, AGA infants may lose up to 11% of their birth weight in the first days after birth (nadir at days 3-5).
        - Should re-gain birth weight by 10 days of life
    - Voided
        - Urate crystals (pink/orange "brick dust") in the diaper may be normal for the first week of life but may indicate dehydration
        - May see vaginal discharge (clear, yellow, white, or blood stained) as infant withdraws from maternal hormones
    - Passed meconium (within 24-48 hours of life)
        - Failure to pass meconium in the first 48 hours may prompt further investigation (consider radiopaque marker study, anal manometry)
        - DDx: Hirschprung disease (look for "squirt sign"), intestinal obstruction including atresia, webs or volvulus, imperforate anus, meconium ileus, meconium plug
    - Newborn medications received: vitamin K, +/- erythromycin eye ointment, vaccines as indicated per provincial guidelines

- Parental readiness
    - Postpartum counselling (see below) on routine newborn care, infant safety, feeding, when to seek care, and follow up plans
    - Information regarding circumcision if requested (see Common Neonatal Consults)
    - Screen for and educate about postpartum depression/baby blues and refer to appropriate maternal provider as needed
    - Maternal drug exposures
        - Emphasize sensitive, non-stigmatizing care including supporting breastfeeding, parental presence if possible (consider rooming in programs) and social work support

Postpartum counselling and newborn care advice

- Follow up: with family doctor, paediatrician, or midwife within 24-72 hours
- Feeding & Growth
    - Conversation around breastfeeding and support (referral to lactation support as needed)
    - Term, AGA newborns without complications should feed every 2-3 hours (allow for up to 4-6 hour stretch overnight if no weight concerns), encourage feeding on demand
    - Vitamin D supplementation (400 IU per day)
    - Spitting up is generally tolerated as long as gaining weight, green vomit always an emergency
- Voiding
    - Expect the same number of wet diapers as they are days old up to day 5 of life and 5+ wet diapers thereafter
- Bowel movements
    - Variable stool patterns: usually 2-3 per day in the first week, after the first month may have many stools per day or periods of days between stooling
    - Expect transition from meconium (black/sticky) to green to yellow seedy if breastfeeding or yellow pasty if formula fed
    - Blood in stool is never normal
- Cleansing and skin care
    - Newborns do not require frequent bathing, use mild cleanser and water
    - Keep umbilical stump clean and dry, sponge bath until cord detaches (within first 3 weeks)
        - Do not apply alcohols or antibiotic ointments to the cord
        - Delayed separation of the cord may indicate Leukocyte Adhesion Deficiency type I (LAD1)
    - Care of the penis: gentle cleansing with regular bathing
        - Uncircumcised penis: do not retract the foreskin, expect natural separation of the foreskin from the glans over time
        - Circumcised penis: apply petroleum ointment (ie. Vaseline) and clean gauze to the exposed glans after each diaper change until site healed
    - Nail care: use nail file or safety nail clippers to trim nails
- Safe Sleep
    - Back to sleep campaign has led to a significant reduction in the incidence of SIDS
        - Firm, infant safety certified mattress with no loose pillows, toys or blankets
        - Infant strollers, swings, bouncers and car seats are not safe sleep places
        - Prevent exposure to tobacco smoke before and after birth
        - Prevent overheating – use one-piece sleepwear that is comfortable at room temperature
        - Breastfeeding and pacifier use are protective from SIDS
    - Co-sleeping (same room with own sleeping surface) is recommended until 6-12 months and protective against SIDS
    - Bed-sharing (shared sleeping surface) is not recommended and increases risk for SIDS
        - If it is practiced, avoid intoxication, sleeping on a couch or against a wall where the baby could get wedged, no heavy blankets, firm mattress

- Fever and other emergencies
    - Fever is >=37.5 C axillary or 38 C rectal (preferred)
        - Infrared/forehead or tympanic thermometers not accurate in newborns
    - If a baby has a fever in the first 3 months of life they should be seen immediately by a medical professional
    - Other concerning signs prompting urgent medical care:
        - Lethargy/difficult to rouse, inconsolability, not feeding/having few voids (<4 wet diapers per day in a newborn), difficulty breathing, blood in the stool, green vomit

1.5 – Ontario Newborn Screening

Ontario Newborn Screening Test

- Bloodspot test completed within 24-38 hours after birth to screen for treatable diseases that are usually asymptomatic in the newborn period
- Screens for > 25 diseases including
    - Metabolic, Endocrine, Sickle Cell, Cystic Fibrosis, SCID, SMA, CCHD
- Results: Not diagnostic rather screening test to identify risk for disease
    - Baby may screen positive, negative, or unsatisfactory
    - Results sent to the hospital or midwifery practice that did the test
    - Parents/guardian or health care providers can request that results be sent to the PCP
- If baby screens positive
    - Referred to a follow up centre for confirmatory/diagnostic tests
    - Family informed of result and possibility of false positive

Ontario Newborn Screen:
Argininosuccinic Acid Lyase Deficiency (ASA)
Biotinidase Deficiency
Carnitine Uptake Defect (CUD)
Citrullinemia
Cobalamin A & B Defects
Congenital Adrenal Hyperplasia (CAH)
Congenital Hypothyroidism (CH)
Critical Congenital Heart Disease (CCHD)
Cystic Fibrosis (CF)
Galactosemia
Glutaric Acidemia Type 1 (GA1)
Homocystinuria
Hurler Disease ("Mucopolysaccharidosis type 1H" or "MPS1H")
Isovaleric Acidemia (IVA)
Long Chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency (LCHAD)
Maple Syrup Urine Disease (MSUD)
Medium Chain Acyl CoA Dehydrogenase Deficiency (MCADD)
Methylmalonic Acidemia (MMA)
Phenylketonuria (PKU)
Propionic Acidemia (PA)
Severe Combined Immune Deficiency (SCID)
Sickle Cell Disease (Hemoglobin SC)
Sickle Cell Disease (Hemoglobin SS)
Sickle Cell Disease (Sickle/Beta-Thalassemia)
Spinal Muscular Atrophy (SMA)
Trifunctional Protein Deficiency (TFP)
Tyrosinemia Type 1
Very Long Chain Acyl CoA Dehydrogenase Deficiency (VLCAD)

Table 1.5 – Diseases screened on routine Ontario newborn screen (newbornscreening.on.ca)

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Chapter 2 - Maternal Medical Illness

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2.1 – Increased Fetal Surveillance

- Maternal medical illness in pregnancy is typically closely monitored by high-risk obstetrical care and increased fetal surveillance during the pregnancy
- First-trimester screen in conjunction with an ultrasound assessment of nuchal translucency or maternal serum screen in the second trimester to screen for chromosomal abnormalities
- A detailed ultrasound to assess fetal anatomy is typically performed between 18-20 weeks
- After 26 weeks, growth scans can be done as often as biweekly with weekly biophysical profiles if indicated
- Serial biophysical profile (BPP) scored by 4 domains and if reassuring gets 2 points per domain
    - Tone (limb extension then flexion): at least one episode of limb extension followed by flexion
    - Movement: three discrete movements
    - Breathing: at least one episode of breathing lasting at least 30s
    - Amniotic fluid volume: a fluid pocket of 2cm in 2 axes
- Non-stress test (NST)
    - A NST is reactive from 32 weeks to term if there are two or more fetal heart rate accelerations reaching a peak of at least 15 beats per minute (BPM) above the baseline rate and lasting at least 15 seconds from onset to return to baseline (15 x 15) in 20 minutes
- Umbilical artery dopplers
    - Measures blood flow velocities in the maternal and fetal vessels to provide information about uteroplacental blood flow and fetal responses to physiologic challenges. Indicates fetal hypoxemia if Doppler indices are altered (increased, decreased, reversed or absent)

2.2 – Maternal Hematologic/Rheumatologic Diseases (Common)

2.2.1 – Systemic Lupus Erythematosus

- Maternal medications for SLE
    - Corticosteroids and hydroxychloroquine are safe with pregnancy and breastfeeding
    - For high dose maternal corticosteroids, using prednisolone rather than prednisone and avoiding breastfeeding for 4 hours after a dose reduces the dose received by the infant. However, for short-term steroid use, this delay is typically unnecessary
    - Azathioprine is safe but advised to avoid breastfeeding or pumping for the first 4 hours after taking the dose
- Neonatal lupus
    - Associated with the transplacental passage of autoantibodies such as anti-Ro/SSA and anti-La/SSB
    - Clinical features – rash (annular lesions, periocular scaly rash, can be photosensitive), heart block, rarely structural heart disease and pulmonary hypertension, elevated liver enzymes, cytopenias, rarely neurologic manifestations
    - Risk for neonatal heart block
        - Independent of the severity of maternal illness and often the first sign of neonatal lupus
        - If high anti-Ro/SSA or anti-La/SSB antibodies during pregnancy, ECG monitoring from 18-25 weeks assessing for prolonged PR interval
    - Mothers can be treated with anticoagulants and corticosteroids
    - At birth, assess for neonatal lupus and congenital heart block
        - Physical examination assessing for erythematous skin lesions, typically on the face or scalp (commonly not present at birth but develops in the first few weeks of life)
        - Blood work assessing for thrombocytopenia, anemia, neutropenia and abnormal liver function tests
        - 15 lead ECG assessing for heart block
    - Prior to discharge, refer to paediatric rheumatology clinic for follow-up and counsel parents on the appearance of a neonatal lupus rash

2.2.2 – Red Cell Alloimmunization

- See Hemolytic Disease of the Newborn
- The formation of maternal antibodies against fetal antigens on RBCs that go through the placenta and attack fetal RBCs. This occurs if a mother is exposed to the fetal blood cells
    - Sources include fetal-maternal bleeding, blood transfusions and needle sharing
    - With the initial exposure, the mother creates IgM antibodies followed by IgG antibodies
    - With repeat exposure, IgG is made more rapidly
- Common maternal antigens include Rh factor, Kell, Duffy, MNS, Kidd, anti-u
- Can result in haemolytic disease of the fetus and newborn
    - Intrauterine fetal demise, fetal hydrops, fetal/neonatal anemia, fetal/neonatal high-output heart failure and neonatal hyperbilirubinemia
    - ABO incompatibility may be protective against a primary Rh sensitization because of the rapid clearance of the fetal blood cells, therefore shorter potential Rh response by the maternal immune system
- Screening during pregnancy
    - Maternal blood type, Rh status, indirect Coombs test and antibody titres
    - Paternal zygosity testing

- Monitoring during pregnancy
    - Ultrasound for fetal hydrops
        - Hydraminos, increased placenta thickness, enlargement of the fetal liver, hydrops, increased splenic circumference
    - Middle cerebral artery doppler for the degree of fetal anemia where increased flow demonstrates anemia
    - Percutaneous umbilical blood sampling for fetal antigenic determination and fetal haemoglobin
    - Amniocentesis for bilirubin measurement assessing the degree of haemolysis
- Monitoring for ABO incompatibility after birth
    - If a mother is blood type O, the baby will be screened with blood type and antibody screen at birth due to being high risk for hyperbilirubinemia
- Treatment and Prevention
    - Rh factor red cell alloimmunization
        - Mothers who are Rh-negative are given Rhogam© (anti-D IgG) at 28 weeks and within 72 hours after delivery
        - This helps prevent mothers from developing Rh antigens, which would affect a Rh+ fetus in future pregnancies
    - Intrauterine fetal transfusions help prevent significant anemia and thus hydrops
    - Exchange transfusion indicated if the postnatal rise of unconjugated bilirubin >17mmol/L/h in Rh incompatibility
    - Management of hydrops fetalis
        - Initial resuscitation at birth is important to minimize morbidity and mortality
        - Increased risk of birth trauma due to soft tissue edema
        - Airway/breathing
            - Intubation and ventilation are needed but likely difficult due to edema of the head
        - Circulation
            - UVC, UAV insertion, fluid resuscitation, inotropes (i.e. Dopamine), isovolumic partial exchange transfusion with pRBCs
        - Drainage of fluid via thoracocentesis, cardiocentesis or paracentesis may be needed
        - Determine the cause
            - Blood gas, CBC, type and cross match, ECG, echo, CXR, congenital bacterial and viral infections (CMV, parvovirus B19, toxoplasmosis, coxsackie virus), blood smear, Kleihauer-Betke test for fetal maternal hemorrhage, chromosomal microarray and WES

2.2.3 – Maternal Arthritis

- NSAIDs should be avoided between 20-30 weeks gestation due to rare risks of fetal renal dysfunction leading to oligohydramnios and neonatal renal impairment, as well as during the 3rd trimester due to risk of premature ductus arteriosus closure
- Some immunosuppressive medications (TNFa inhibitors) may lead to some fetal immunosuppression, and live vaccines should be avoided in neonates for the first 6 months of life (BCG and rotavirus vaccines)
    - Inactivated vaccines can be given as per the regular vaccine schedule

2.3 – Maternal Renal Diseases

2.3.1 – Acute kidney injury
2.3.2 – Chronic kidney disease

2.3.1 – Acute Kidney Injury

- Wide variety of causes such as pre-eclampsia, haemolytic-uremic syndrome, thrombotic thrombocytopenic purpura, acute fatty liver of pregnancy, acute pyelonephritis, urinary tract obstruction
- Many of these conditions will require urgent delivery of the fetus

2.3.2 – Chronic Kidney Disease

- Increased risk of growth restriction, prematurity, and still-birth
- Increased fetal surveillance and a placental scan to assess placental morphology and doppler flow at approximately 22 weeks due to increased risk for pre-eclampsia

2.4 – Maternal Endocrinologic Diseases

2.4.1 – Thyroid disease
2.4.2 – Diabetes

2.4.1 – Thyroid Disease

- Hypothyroidism
    - Untreated hypothyroidism is associated with pregnancy loss, prematurity, pre-eclampsia, low birth weight, cognitive impairment
    - Mother's at risk screened and treated in early pregnancy
- Grave's disease (see Figure 2.4.1)
    - 1-5% of neonates born to women with Graves' disease have hyperthyroidism due to transplacental transfer of TSH-receptor-stimulating antibodies (TSHR-Ab)
        - Often tested with "TR-Ab" assay
    - The higher the maternal TSHR-Ab concentration during the third trimester, the greater the likelihood of neonatal Grave's hyperthyroidism
    - Clinical features of fetal hyperthyroidism
        - High fetal heart rate (>160bpm), fetal goitre, advanced bone age, IUGR, craniosynostosis, hepatosplenomegaly, exophthalmos

Figure 2.4.1 - Maternal hypothyroidism and monitoring of the neonate
TSHR-Ab: TSH-receptor-stimulating antibodies

2.4.2 – Diabetes

- Type 1 diabetes mellitus (T1DM)
    - Increased risk of congenital anomalies such as congenital heart disease and open neural tube defects
- Type 2 Diabetes mellitus (T2DM) and gestational diabetes mellitus
    - Risk of **"SMASH":**
        - **S**houlder dystocia, **m**acrosomia, **a**mniotic fluid excess (polyhydraminos), **s**till-birth, neonatal **h**ypoglycaemia
- Infants of diabetic mothers should be monitored for hypoglycaemia after delivery

2.5 – Pregnancy -Related Hypertension

- Hypertension in pregnancy is defined as ≥140/90mmHg; severe hypertension is ≥160/110mmHg
    - Pregnancy-induced hypertension
        - Hypertension without proteinuria or other signs of pre-eclampsia related end-organ dysfunction that develops after 20 weeks of gestation
    - Pre-eclampsia
        - New onset of hypertension and proteinuria/significant end-organ dysfunction after 20 weeks of gestation and may develop post-partum
        - Eclampsia – pre-eclampsia with seizures
    - HELLP syndrome
        - **H**aemolysis, **e**levated **l**iver enzymes, **l**ower **p**latelets
- Severe hypertension increases the risk of IUGR, oligohydraminos, pre-term delivery and placental abruption
- Fetal well-being is monitored with BPP or non-stress test with amniotic fluid estimation and serial growth ultrasounds
- May require early delivery

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Chapter 3 - Antenatal, Obstetrics, and Delivery

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3.1 – Antenatal History

- GTPAL = Gravida, Term, Para, Abortus, Living
- Maternal pregnancy history
    - Previous pregnancies
        - Previous delivery method, gestational age, losses, and complications
    - Medical conditions in pregnancy
        - Gestational diabetes, gestational hypertension, pre-eclampsia
    - Prenatal screening results
        - Gestational diabetes, infections , genetics
    - Ultrasound results
        - First trimester dating ultrasound at 11-14 weeks, anatomy scan at 18-20 weeks, and biophysical profiles if performed
- Maternal medical history
    - Maternal medical and surgical history
        - Note maternal autoimmune conditions such as lupus, thyroid disease, diabetes, myasthenia gravis, and ITP that can cause neonatal concerns
- Maternal medications
    - Medications for diabetes (insulin, metformin) and for blood pressure (labetalol)- can cause neonatal hypoglycemia
    - Maternal SSRIs- can cause SSRI neonatal behavioural syndrome and a rarely persistent pulmonary hypertension
    - Maternal opioids- can cause neonatal abstinence syndrome (NAS)
- Exposures
    - Drugs, alcohol, and teratogenic medications during pregnancy
- Social
    - Children's Aid Society (CAS) involvement, living situation, partner safety concerns, healthcare coverage status

3.2 - Maternal Infections and Gestational Diabetes Screening

- HIV, hepatitis B and hepatitis C serologies
- Rubella immunity
    - If non-immune, mother may receive an MMR booster after delivery. Consider status if infant demonstrates signs of congenital rubella
- Gonorrhea, chlamydia, and syphilis
    - If evidence of untreated disease, baby requires evaluation and intervention after delivery
- HSV
    - Important to know whether this is a first or recurrent episode, mode of delivery, and rupture of membranes (ROM)

- Group B streptococcus status. Vaginal swab at 35-37 weeks, therefore premature infants may not have this information available
- Gestational diabetes screening
    - One hour glucose tolerance test performed at 24-28 weeks
        - A value >11.1 mmol/L confirms the diagnosis of gestational diabetes
    - If one hour glucose test between 7.8-11 mmol/L, to perform a two-hour glucose tolerance test

3.3 - Prenatal Genetic Screening

- Non-invasive prenatal screening (note these are SCREENING tests)
    - Enhanced first trimester screening (eFTS) at 11+2 to 13+3 weeks gestation
        - Includes maternal bloodwork (measuring Papp-A, hCG, AFP, and PIGF) and nuchal translucency on ultrasound
        - Screens for trisomy 21 and 18
        - Combines risk of image and blood results with maternal age to give overall risk
    - Maternal serum screen (MSS) at 14+0 to 20+6 weeks gestation
        - Includes maternal bloodwork (hCG, AFP, inhibin-A, uE3)
        - Screens for trisomy 21 and 18
        - Combines risk of blood results with maternal age to give overall risk
    - Non-invasive prenatal testing (NIPT) after 9+0 weeks gestation
        - Funded only for high-risk mothers (>40, positive screen on eFTS or MSS, NT ≥3.5mm, history of trisomy)
        - Includes maternal bloodwork looking for placental DNA
        - Screens for Trisomy 21, 18 and 13 and sex chromosomal abnormalities
- Invasive diagnostic testing (note these are DIAGNOSTIC tests)
    - Chorionic villus sampling (CVS) typically at 11-14 weeks gestation
        - Samples from placental tissue
        - Can determine a diagnosis for trisomies or chromosomal abnormalities
        - Also possible to run more specific genetic tests
    - Amniocentesis after 15+0 weeks gestation
        - Samples amniotic fluid for fetal DNA
        - Can determine a diagnosis for trisomies or chromosomal abnormalities
        - Also possible to run more specific genetic tests

3.4 – Labour and Delivery

- Risk factors for neonatal sepsis
    - ROM>18 hours, maternal fever, chorioamnionitis, maternal or fetal tachycardia, untreated or not adequately treated GBS (a dose of antibiotics given <4 hours from delivery), a previous infant with invasive GBS disease
- Type of delivery
    - Spontaneous vaginal delivery or c-section (emergency vs planned)
        - Planned c-section ("cold" c-sections) can put baby at risk of TTN
        - In emergency c-sections, consider the reason for the emergency in evaluating the risk for neonatal consequences such as HIE
- Instrumentation used (forceps or vacuum)
    - A sign of a difficult delivery that may put baby at risk of birth injury- bruising, skull fracture or laceration, HIE, subgaleal hemorrhage, clavicle or humeral fractures, brachial plexus injury
- Medications in labour, especially opioids, can cause transient respiratory depression in the newborn
- APGAR scores
    - Scores <5 at 5 and 10 minutes need further evaluation for HIE
- Cord gases
    - Cord gas pH ≤7 or base deficit ≥ 10 need further evaluation for HIE

3.5 – Fetal Monitor Tracings

- Bradycardia on fetal tracings
    - It can be normal to see bradycardia (or decelerations) with contractions
    - When decelerations are frequent, deeper, or take longer to recover from, they become a cause for concern, signalling that the fetus is not handling the stress of labour well
        - This may signal peripartum hypoxia, raising the concern for prenatal depression and HIE
- Tachycardia on fetal tracings
    - This may signal maternal infection, raising concern for fetal infection

3.6 – Twin to Twin Transfusion Syndrome

- Abnormal distribution of placental blood supply between monochorionic twins
- Both twins are at risk of premature delivery
- Potential consequences in donor twin include
    - Oligohydramnios, SGA/IUGR, chronic anemia, hydrops, hypertension, in utero fetal death
- Potential consequences in recipient twin include
    - Polyhydramnios, LGA, polycythemia, high-output cardiac failure, hydrops, pulmonary stenosis, hypertension, in utero fetal death

3.7 – Oligohydramnios and Polyhydramnios

- Oligohydramnios- lower than normal amniotic fluid levels (<5th percentile)
    - Causes include prolonged rupture of membranes, placental insufficiency, kidney anomalies (fetal renal agenesis or dysplastic kidneys), urinary obstruction
    - Sequelae can include pulmonary hypoplasia leading to severe respiratory distress at birth and muscle contractures
- Polyhydramnios-higher than expected amniotic fluid levels (>95th percentile)
    - Causes include fetal intestinal obstruction (preventing the fetus from swallowing), maternal diabetes, macrosomia, anemia, genetic abnormalities, and twin to twin transfusion syndrome
    - Sequelae include premature birth or breech presentation from uterine overdistension, risk of cord prolapse at rupture, and consequences of any genetic condition or structural abnormality causing the polyhydramnios

3.8 – Intrauterine Growth Restriction (IUGR)

- IUGR = A rate of growth below expected growth potential for a fetus
- Small for gestational age = weight < 10th percentile
    - Not necessarily an abnormal finding
- Possible consequences include premature birth, feeding intolerance, hypoglycemia, hyperglycemia, risk of refeeding syndrome, hypothermia, polycythemia, leukopenia, thrombocytopenia, respiratory distress

Table 3.8 - Causes of IUGR

Maternal	Placental	Fetal
Inadequate prenatal care or nutrition	Placental insufficiency or disease	Intrauterine infections
Smoking or drug use	Abnormal umbilical cord insertion	Genetic conditions including trisomies
Maternal illness (diabetes, hypertension, preeclampsia, or stress)	Single umbilical artery	Multiple gestation

3.9 – Antenatal Counselling

- Prepare
    - Ensure you have as much uninterrupted time as possible
    - Ensure all decision makers are present if possible
- Introduce yourself and the reason for the discussion
    - This may include providing information around the NICU course for a preterm infant or a discussion around decisions about whether to provide active resuscitation or not
- Ask the family about who they are (religious background, culture, employment, education, family support), what they know already (about current reason for consultation, possible knowledge around and experience with disability), and try to get a sense of what is important to them
- Speak slowly and pause often to allow for questions or for information to be repeated
- Counselling should be tailored to the specific situation and the family. Each family has goals and values that will impact the information they wish to know and how they will make decisions
- Describe what stabilisation may look like depending on location and gestational age
    - Whether baby will be brought to a separate area, who will be present, what interventions may be needed after delivery, and when parents will be able to see their baby
- Neurodevelopmental outcomes are affected not only by gestational age, but by a baby's NICU course and complications
    - In general, the more premature the baby, the higher the possibility of impairments. This can range from mild impairments that can be supported with extra resources or therapies, neurobehavioural diagnoses such as ADHD / learning disability, and more significant impairments that can impact a child's ability to walk, talk, or live independently
    - Discussions of neurodevelopmental outcome are challenged by differences in how healthcare providers (and parents) may interpret medical labels, small sample sizes, inconsistent resuscitation practices and continually evolving data, as well as difficulties in correlating developmental outcome and quality of life as perceptions vary. Generally, families want the F words for outcomes: Fun, Function, Family, Future, Fitness, Friends, and these things are available to individuals with and without disability (CanChild)
- For a woman <26+0 weeks gestation at risk of delivery
    - Transfer to a tertiary care centre if possible
        - Where there are systems in place to best assist both mother and infant
    - Many tertiary NICU centres in Canada will offer resuscitation from 22-24 weeks, with an assumption of automatic resuscitation at 25 weeks and above
    - Goal is to determine the course of action that will be taken if fetus is born in the immediate future (active resuscitation or comfort care measures)
        - Framed discussion around the family's goals and the information they wish to know (specific numbers and outcomes, general information about what to expect)
        - Survival of extreme preterm significantly impacted by centre approach and care (this applies to both survival and outcomes)
        - The length of stay is likely to be at least until the child's due date but more immature babies may require longer hospitalizations
        - A discussion on the potential outcomes and challenges is warranted as well as awareness of medical bias and ableism. The more extremely preterm the child, the greater the possibility of challenges, but many will not have a significant disability. Most will however have neurobehavioral challenges and impacts on school performance
- For a woman 26+0 – 35+0 weeks gestation at risk of delivery
    - Transfer to a tertiary care center as per NICU team's comfort level/Level of care
    - 2019 Canadian Neonatal Network data shows survival to discharge rates of 90% at 26 weeks and 95% at 28 weeks
    - Focus on routine NICU care, tailor to the anticipated gestational age and birth weight
        - Information on expected stay (likely until around due date)
        - support with feeding and nutrition infant cues develop at 32-34 weeks, transfer of milk from 34-38 weeks

    - support with breathing (CPAP, intubation) & routine bloodwork and monitoring
    - May include information on routine screening (head ultrasounds, ROP exams, neonatal follow up clinics)
    - Transfer expectations should be reviewed
- Generally, discussions at these ages can be kept broad, with the opportunity to discuss more details about specific complications should they arise after baby is born

The tables below provide some information that may help in antenatal counselling discussions. It is important to remember that numbers are only part of the overall discussion, if they are used at all. Data about survival and outcomes are constantly evolving, making published numbers out-of-date quickly. Additionally, this data reflects inconsistent resuscitation approach and, therefore, likely represents an underestimation of survival and overestimation of impairment.

Table 3.9a - Survival Rates for Infants <25 weeks in Canada 2010-2015 (adapted from Moore & Lemyre, 2017)

GA (weeks + days)	Number of live births (n)	Infants who received palliative care at birth (n, [% of live births])	Infants who received early intensive care at birth (n, [% of live births])	Delivery room deaths in newborns who received early intensive care (n, [%])	Survivors to NICU discharge in newborns who received early intensive care (n, [%; 95% CI])
≤22 + 6	332	226 (68%)	106 (32%)	56 (53%)	19 (**18%**; 11, 25%)
23 + 0–23 + 6	723	196 (27%)	527 (73%)	82 (16%)	218 (**41%**; 37, 45%)
24 + 0–24 + 6	1200	68 (6%)	1132 (94%)	26 (2%)	753 (**67%**; 64, 70%)
25 + 0–25 + 6	1575	24 (1.5%)	1551 (98.5%)	66 (4%)	1225 (**79%**; 78, 80%)

CI Confidence interval; GA Gestational age; NICU Neonatal intensive care unit

Table 3.9b - Significant or moderate-to-significant Neurodevelopmental Disability (NDD) rates at 4 to 8 years of age in surviving children born extremely preterm (adapted from Moore & Lemyre, 2017)

Gestational age	Rate of significant NDD (%, 95% CI)	Rate of moderate-to-significant NDD (%, 95% CI)
22 weeks (n=12 for both severe and moderate-to-severe NDD rates)	31% (12, 61)	43% (21, 69)
23 weeks (n=73 for severe NDD rates) (n=75 for moderate-to-severe NDD rates)	17% (9, 28)	40% (27, 54)
24 weeks (n=175 for severe NDD rates) (n=210 for moderate-to-severe NDD rates)	21% (14, 30)	28% (18,41)
25 weeks (n=337 for severe NDD rates) (n=441 for moderate-to-severe NDD rates)	14% (10, 20)	24% (17, 32)
*Most children have no or mild NDD with estimates of: 57% at 22 weeks GA, 60% at 23 weeks, 72% at 24 weeks and 76% at 25 weeks. Mild NDD include neurobehavioural difficulties (e.g., autism, attention-deficit) that could challenge a child and their family		

CI Confidence interval; NDD neurodevelopmental disability

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Chapter 4 – Neonatal Resuscitation Program, Procedures, and Checklists

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4.1 - Resuscitation Equipment Overview

- Positive Pressure Ventilation (PPV) equipment (standard peak end expiratory pressure "PEEP" 5 mmH2O, peak inspiratory pressure "PIP" 20mmH2O, FiO2 set by O2 blender on the wall or warmer)
    1. Flow inflating bag (aka an anesthesia bag)
        - Min flow 10L for the bag to inflate
        - Set the PEEP by turning the blue dial on the side of the mask
        - PIP is determined how hard the bag is squeezed, and can be seen on manometer
    2. T-piece
        - Set the PIP with the dial on the warmer or device
        - Set the PEEP with the blue or gray dial attached to the mask
    3. Self-inflating bag (this is not commonly used)
        - No PEEP can be provided and so cannot provide CPAP (unless special attachment valves are used)
        - PIP is determined how hard the bag is squeezed
        - No supplemental O2 unless attached to an O2 reservoir
- Suction equipment
    - 10 or 12 Fr suction catheter attached to wall suction at 80-100mmHg
- Intubation equipment
    - Laryngoscopes: Miller 1 term, Miller 0 preterm and Miller 00 early preterm
    - Endotracheal tubes: Have sizes 2.5, 3.0 and 3.5 ready
    - Stylet for oral intubations, Magill forceps for nasal intubations
        - Oral intubation is quickest in an emergency setting
    - CO2 detector
- Emergency UVC insertion equipment
    - Cleaning supplies (ie chlorhexidine swabs)
    - Umbilical tie
    - Scalpel
    - UVC line (see section 4.52)
    - Normal saline flush
    - Suture materials
- Medications
    - Epinephrine 1:10,000 (0.1 mg/mL)
    - Normal saline for volume expansion
    - Normal saline flushes
    - pRBC if concern for acute blood loss

4.2 - Before the Delivery

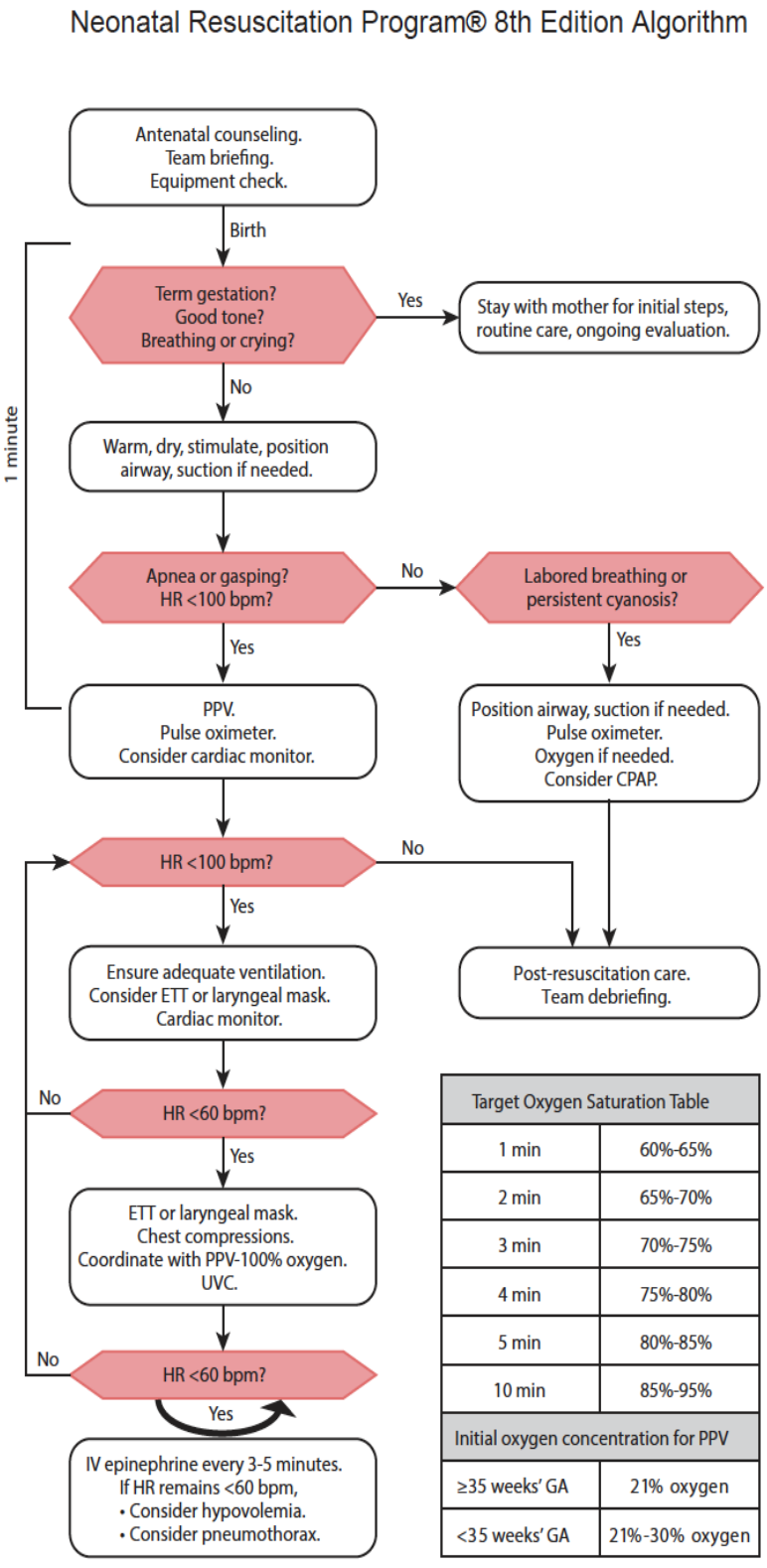
- Gather a brief history, when possible
    a. What is the expected gestational age?
    b. Is the amniotic fluid clear?
    c. Are there any additional risk factors?
    d. What is the cord management plan?

Table 4.2 – Perinatal Risk Factors Increasing the Likelihood of Neonatal Resuscitation (from *Textbook of Neonatal Resuscitation, 8th edition*)

Antepartum Risk Factors	
GA < 36 weeks	Oligohydramnios
GA >/= 41 weeks	Fetal hydrops
Preeclampsia or eclampsia	Fetal macrosomia
Maternal HTN	Intrauterine growth restriction
Multiple gestation	Significant fetal malformations/anomalies
Fetal anemia	No prenatal care
Polyhydramnios	
Intrapartum Risk Factors	
Emergency C/s	Intrapartum bleeding
Forceps or vacuum-assisted delivery	Chorioamnionitis
Breech or other abnormal presentation	Narcotics administered to mother within 4 hours of delivery
Concerning fetal heart rate pattern	Shoulder dystocia
Maternal general anesthesia	Meconium-stained amniotic fluid
Maternal magnesium therapy	Prolapsed umbilical cord
Placental abruption	

- Assign team-member roles: team leader, airway management, medications/lines, documentation
- Discuss anticipated management depending on identified risk factors
- Check equipment
    - Warmer on with towels and hat ready
    - Attach PPV device to flowmeter (minimum 10L/min)
        - Verify PIP (20 cm H2O) and PEEP (5 cm H2O)
        - FiO2 21% if term and 21-30% if preterm
    - Suction to 80-100 mmHg
    - Connect monitoring equipment (ECG, saturation and temperature leads)
- Special equipment to consider
    - Meconium aspirator
    - Plastic bag if < 32 weeks GA
    - UVC insertion kit
    - Intubation equipment
    - Medications (epinephrine, normal saline, blood products, surfactant)

4.3 - Resuscitation



Don't hesitate to call a code pink!

Figure 4.3 – Neonatal Resuscitation Program Algorithm (from *Textbook of Neonatal Resuscitation, 8th edition*)

- Ventilatory correction measures: "MR. SOPA"
  1. M&R: Mask fit, reposition (extend neck or place shoulder roll)
  2. S&O: Suction (mouth before nose), open mouth
  3. P: Pressure (increase by 5-10 mmHg, to a max of 40 mmHg)
  4. A: Alternate airway (ETT or LMA)
- Intubation
    - Always have both the anticipated ETT size and one size smaller ready

Table 4.3a – Recommended Laryngoscope and ETT Sizes
(adapted from *Textbook of Neonatal Resuscitation, 7th edition*)

Weight (g)	Gestational age (weeks)	Laryngoscope size	ETT size
<1000	<28	Miller 00	2.5
1000-2000	28-34	Miller 0	3.0
>2000	>34	Miller 0 or 1	3.5

Table 4.3b – Initial ETT insertion depth for orotracheal intubation
(from *Textbook of Neonatal Resuscitation, 7th edition*)

Gestational age (weeks)	Endotracheal tube insertion depth at lips (cm)	Baby's weight (g)
23-24	5.5	500-600
25-26	6.0	700-800
27-29	6.5	900-1000
30-32	7.0	1,100-1,400
33-34	7.5	1,500-1,800
35-37	8.0	1,900-2,400
38-40	8.5	2,500-3,100
41-43	9.0	3,200-4,200

    - If there is unexpected deterioration while intubated: consider "DOPE"
        - D: Displacement of ETT
        - O: Obstruction of ETT
        - P: Pneumothorax
        - E: Equipment failure
- Compressions
    - Should try at least 30 seconds of effective ventilation prior to start of compressions (ideally 30 seconds of PPV through an alternate airway)
    - 3:1 ratio of compressions to breaths
    - Goal compression rate of 90/minute
    - Compression depth of 1/3 AP diameter
    - Always ensure FiO2 is at 100% when giving compressions

- Epinephrine
    - 1:10,000 concentration
    - IV or IO = 0.01-0.03 mg/kg = 0.1-0.3 ml/kg (suggested initial dose of 0.02 mg/kg = 0.2 ml/kg)
        - **Think 0.6ml IV for 3kg baby**
        - Flush with 3 ml of normal saline (for all weights and gestational ages)
    - ETT = 0.05 to 0.1 mg/kg = 0.5-1ml/kg (suggested initial dose 0.1 mg/kg = 1 ml/kg, max 3 ml total)
        - **Think 3ml via ETT for 3kg+ baby**
    - IV or IO is preferred, but ETT may be used while obtaining access
- Emergency UVC insertion
    - Insert as low-lying in emergencies: 2-4 cm + stump length, until blood return
    - See section 4.5 – "Procedures" for further details

4.4 - After the Delivery

Table 4.4 – Clinical signs, laboratory findings and management after resuscitation (from *Textbook of Neonatal Resuscitation, 7th edition*)

Organ system	Clinical signs and lab findings	Management considerations
Neurological	Apneas, seizures, irritability, poor tone, altered neuro exam, poor feeding coordination	Monitor for apnea Support ventilation as needed Check glucose and electrolytes Avoid hyperthermia Consider anticonvulsants Consider therapeutic hypothermia Consider delayed initiation of feeds
Respiratory	Tachypnea, grunting, retractions, nasal flaring, low oxygen saturations, pneumothorax	Maintain adequate oxygenation and ventilation Avoid unnecessary suctioning Consider antibiotics Consider X-ray and blood gas Consider surfactant therapy Consider delayed initiation of feeds
Cardiovascular	Hypotension, tachycardia, metabolic acidosis	Monitor blood pressure and heart rate Consider volume replacement or inotrope administration if baby is hypotensive
Renal	Decreased urine output, edema, electrolyte abnormalities	Monitor urine output Monitor serum electrolytes Monitor weight Restrict fluids if baby has decreased urine output and vascular volume is adequate
Gastrointestinal	Feeding intolerance, vomiting, abdominal distention, abnormal liver function test, gastrointestinal bleeding	Consider abdominal X-ray Consider delayed initiation of feeds Consider parenteral nutrition
Endocrine-Metabolic	Metabolic acidosis, hypoglycemia, hypocalcemia, hyponatremia, hyperkalemia	Monitor blood glucose Monitor serum lytes Consider IV fluids Replace lytes as needed
Hematological	Anemia, thrombocytopenia, delayed clotting, pallor, bruising, petechiae	Monitor hematocrit, platelets and coagulation studies
Constitutional	Hypothermia	Delay bathing

4.5 - Procedures

4.51 – Lumbar Puncture (LP)
4.52 – Umbilical Vein Catheter (UVC)/Umbilical Artery Catheter (UAC) insertion
4.53 – Needle decompression

4.51 - Lumbar Puncture

Indications and Contraindications

- Indications
  - Diagnostic (evaluation for meningoencephalitis)
  - Therapeutic (post-hemorrhagic ventricular dilatation)
- Contraindications
  - Absolute
    - Local infection
    - Increased intracranial pressure
  - Relative
    - Bleeding disorder (do not need to check coagulation function routinely unless you have a suspicion for a bleeding disorder), generally aim for platelets >50

Consent

- Indication for procedure
- Who will be doing the procedure
- Risks: Infection, bleeding, failure of procedure and need for repeat LP

Materials

- Local anesthetic of choice (EMLA patch, maxilene, lidocaine 2%)
- 3-4 sterile cleaning swabs
- Sterile LP kit
- Needles (typically 22 gauge 1.5 inch needles)
- Sterile gloves and gown

Steps

1. Landmark: Typical sites are L4-5 and L3-4
   - L3-4 is at the level of the posterior superior iliac spine
   - Ensure proper positioning of the patient:
     - Hips in line and parallel
     - Back flexed (but make sure neck is not over-flexed to prevent airway obstruction)
2. Place EMLA patch/maxilene and wait 30 minutes. If infiltrating with lidocaine, no need to wait
3. Open LP kit and open other sterile materials (ie needles, cleaning swabs) into sterile field
4. Wash hands and scrub appropriately
5. Clean area with 3 sterile cleaning swabs and place sterile drape
6. Re-landmark over the sterile drapes
7. Gently and slowly insert the needle, bevel up, angling the needle towards the umbilicus
   - Make sure the needle is parallel to the floor, not tilted up or down
   - If the infant initially jerks as the needle is inserted, pause for 1-2 seconds
8. Remove stylet as needed to check for CSF flow. Always re-insert the stylet completely before adjusting depth.
9. If needed, adjust the angle of the needle by coming back to just below the skin and aiming again
10. Collect CSF (~5-10 drops per tube). Usually need at least 4 tubes to send:
    - Cell count (can use last tube if bloody initially)
    - Glucose and protein count
    - Bacterial culture
    - Viral cultures
11. Insert the stylet back into the needle prior to removing it. Once removed, hold direct pressure to the site of LP for a few seconds then place a band-aid.

4.52 – Umbilical Vein Catheter (UVC)/Umbilical Artery Catheter (UAC) Insertion

Table 4.5a – Umbilical venous and arterial catheter placement and use guidelines (adapted from *Toronto Centre for Neonatal Health*)

	Insertion Depth	Anatomical Target	Catheter/Material	Radiographic Confirmation	Duration of use
UVC	[(Birth weight in kg x 3 + 9) ÷ 2] + 1 + cord stump 2-4cm if low-lying	T8-T9 (Junction of the IVC and Right atrium, at level of diaphragm)	< 1.5 kg = 3.5F >1.5 kg = 5F (may trial 3.5F if difficult insertion	AP + Lateral X-ray Lateral most important	Remove after 5-7 days and replace with PICC if anticipated >7 days of use or PIV if <7 days of use
UAC	(Birth weight [kg] x 3) + 9 + cord stump	T6-9 (preferred) L3-4 (acceptable)	< 1.5 kg = 3.5F >1.5 kg = 5F (may trial 3.5F if difficult insertion	AP + Lateral X-ray AP most important	Max 5 days of use Remove if any signs of vascular insufficiency to extremities or buttocks

Indications and contraindications

- Indications
    - Medication, fluid, TPN administration (UVC only)
    - Frequent blood sampling (UAC only)
    - Monitoring of arterial pressure (UAC only)
- Contraindications
    - Midline defects (omphalocele, gastroschisis)
    - Infection (omphalitis, NEC, peritonitis)

Materials

- Sterile drapes
- 3-4 sterile cleaning swabs
- Umbilical tie
- Scalpel
- Hemostats (Kelly clamps)
- Vessel dilator
- Umbilical vein and/or artery catheter
- Saline flushes
- Suturing material

Non-emergency UVC/UAC insertion

1. Identify insertion depth (see above)
2. If umbilical cord is shriveled, wrap in saline-soaked gauze for 20-30 minutes
3. Open central line kit and open other sterile equipment (ie catheter, flush) into sterile field
4. Wash hands and scrub appropriately
5. Attach saline flush to the catheter and flush to remove air. Check unit policy for connectors for UVs and UAs. Flush connectors and attach to catheters.
6. Ask an assistant to hold the umbilical cord up with a hemostat on the cord clamp
7. Clean umbilical stump with cleaning swabs
    - Be cautious with using alcohol in very preterm infants as this can cause skin burns; refer to local guidelines
8. Lay down drapes to create sterile field
9. Tie base of the umbilicus with umbilical tie
10. Cut the umbilical cord below the clamp with the scalpel. Aim to have a stump of about 1-2cms.
    - Can use closed forceps or clamp to stabilize the other side of the cord as you cut

11. Identify the vessels (there are 2 smaller muscular arteries, and 1 larger vein) and dilate the one of choice with the dilator or forceps
12. Insert catheter until at the pre-measured depth (with added length of umbilical stump)
    - If there is resistance, dilate the opening further. Do not force the catheter as it can create a false tract.
    - *Tips for veins:* If there is resistance before your pre-measured depth, it is possible you went into the liver (Figure 4.5a). Remove the catheter and restart procedure.
    - *Tips for arteries:* Arteries will spasm. If you feel resistance and feel confident you are in the vessel, hold a bit of pressure without pushing for about 30s and you may then feel the catheter insert smoothly once the spasm has ended.
13. Once at the desired depth, draw back to ensure good blood return
14. If good blood return, flush the catheter (be mindful of volume)
15. Suture the catheter in place:
    - Pull needle through jelly of the umbilicus and anchor the suture
    - Wrap the suture around the catheter 3-4 times then tie down to your anchor
16. To draw labs: Start by drawing off 'waste', then draw up required blood and give back the 'waste'. Ensure there are no air bubbles in the waste before putting it in the patient.
17. Check position with a chest x-ray (see below)

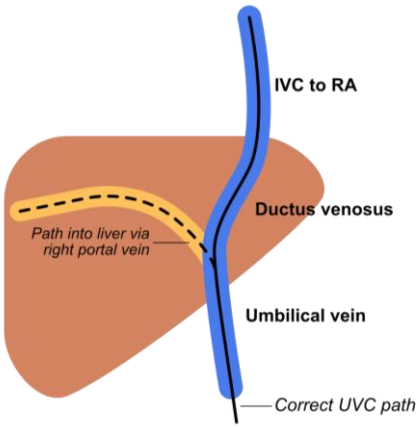


Figure 4.5a – UVC path

Emergency UVC insertion

1. Attach a saline flush to the UVC and
2. Clean the cord with sterile cleaning swabs
3. Tie the umbilical tie at the base of the umbilical stump
4. Cut the cord with the scalpel
5. Insert the UVC about 2-4cm until you get blood return
6. Administer medications

4.53 - Needle Thoracocentesis (Decompression)

Indications and contraindications

- Indications
    - Pneumothorax relief
- Contraindications
    - Known congenital diaphragmatic hernia
    - Local infection

Materials

- 3-4 sterile cleaning swabs
- Butterfly needle
    - 25 gauge for <32 weeks or <1500 g
    - 23 gauge for >32 weeks or >1500g
- 10-20cc syringe
- 3-way-stopcock
- Sterile gloves and gown

Steps

1. Position the infant supine
2. Locate 2nd intercostal space, mid-clavicular line
3. If infant is stable, wash hands and scrub appropriately
4. Clean the area
5. Attach the syringe to the butterfly needle using the 3-way-stopcock (stopcock closed to the empty opening)
6. Insert needle directly over the 3rd rib (as neurovascular bundle runs inferior to the bone) in the previously located space
7. Aspirate air with the syringe
8. Close the 3-way-stopcock to the butterfly needle, and empty the syringe
9. Repeat aspiration if necessary
10. Following stabilization, reassess clinically and with an X-ray, and insert a chest tube if required

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- Weiner GM, Zaichkin J, editors. Textbook of Neonatal Resuscitation (NRP), 8th Ed. American Academy of Pediatrics; 2021.
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Chapter 5 – Common Neonatal Consults

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Antenatal Consults

Perinatal Consults

Antenatal Consults

5.1 – Ventriculomegaly

- Definition
  - Dilation of the fetal cerebral ventricles seen on an antenatal scan, with atrial diameter of the lateral ventricles ≥ 10 mm
    - Mild: 10-12 mm
    - Moderate: 13-15 mm
    - Severe: > 15 mm
  - May be unilateral or bilateral
- Incidence and pathology
  - Estimated incidence – 1% of all pregnancies
  - May be a normal variation, particularly if mild, no other structural abnormalities are noted, and genetic screening is normal
  - May also reflect an underlying congenital syndrome, or obstructive hydrocephalus if severe
- Associations
  - Structural CNS abnormalities – agenesis of the corpus callosum, Dandy-Walker malformation, neural tube defects, neuronal migration abnormalities
    - Most common cause of severe ventriculomegaly is aqueductal stenosis
  - Congenital infections (CMV, toxoplasmosis, Zika) – often other sonographic features present
  - Genetic disorders – most commonly Trisomy 21 in mild cases
- Management and prognosis
  - Expert consensus: lateral ventriculomegaly ≥ 10 mm diameter on antenatal ultrasound is abnormal and should be investigated
  - Antenatal workup: pediatric antenatal consult should be obtained + MFM referral
    - Genetic – NIPT, amniocentesis
    - Detailed ultrasound to assess for other fetal anomalies + evidence of IUGR
    - Consideration of:
      - Fetal MRI
      - Anti-platelet Ab – fetal IVH can lead to posthemorrhagic hydrocephalus in the case of neonatal alloimmune thrombocytopenia (NAIT)
      - TORCH serologies

- Postnatal workup: pediatric consult, including detailed physical exam + measurements, consideration of cranial US after delivery
    - If well baby, non-dysmorphic and normal head circumference, obtain head ultrasound (HUS). Consider outpatient MRI only if HUS abnormal
    - If unwell, dysmorphic, or large head circumference, further work up is indicated (may include genetic testing, MRI, TORCH, etc.)
    - Consider CBC after birth if concern for IVH on imaging
- Normal postnatal evaluation and normal development in > 90% of mild cases, although 5% of mild to moderate cases have an abnormal karyotype
- Risk of morbidity increases as severity of ventriculomegaly increases

5.2 – Echogenic Intracardiac Focus (EIF)

- Definition
    - Small bright echoic focus within the fetal heart on a four-chamber view (as bright as bone and usually < 3 mm) seen on an antenatal ultrasound scan
- Incidence and pathology
    - Present in about 4-5% of karyotypically normal fetuses
    - May be more common in Asian populations
    - Represents mineralization within the papillary muscles
    - Majority are unilateral and most frequently in the left ventricle
- Associations
    - Trisomy 21 (Down syndrome) – may be present in up to 12% of fetuses with trisomy 21
    - Trisomy 13
    - Biventricular EIFs or multiple foci have higher risk for aneuploidy
- Management and prognosis
    - Needs to be interpreted in the context of maternal risk factors and other sonographic anomalies
    - In low-risk pregnancies in isolation – considered a benign variant / incidental finding
    - In high-risk pregnancies or if multiple or bilateral foci are present – considered a soft marker for aneuploidy. May warrant further work-up (MFM referral, fetal Echo, antenatal karyotype)
    - Postnatal workup: no routine investigations – depends on prenatal workup and exam/clinical course at birth

5.3 – Echogenic Bowel

- Definition
    - Observation in antenatal ultrasound imaging where fetal bowel appears to be brighter than expected (brighter than surrounding bone)
    - Most common in the right lower quadrant
- Incidence and pathology
    - Seen in 0.2-1.8% of second trimester fetuses
    - May be due to thickened meconium from absorption of water – this may be normal and transient, or reflect slow meconium passage in the gut (hypoperistalsis)
    - Alternatively, may be due to intra-amniotic hemorrhage (after amniocentesis or placental abruption) when blood is then ingested by the fetus
- Associations
    - Aneuploidies – Trisomy 21 and less commonly Trisomy 13, 18, and Turner syndrome
    - Small bowel obstruction/atresia, and Hirschsprung's disease
    - Cystic fibrosis, more likely if concurrent bowel dilatation (seen in 2-11% of fetuses with cystic fibrosis)
    - IUGR, possibly due to bowel ischemia
    - Intrauterine fetal demise later in pregnancy (9x increased risk of demise if echogenic bowel present, particularly if AFP also increased)
    - CMV infection

- Management and prognosis
    - Normal variant / isolated finding in up to 70% of cases, and often resolves on subsequent antenatal scans
    - Antenatal workup – MFM referral +/- antenatal pediatric consult; detailed ultrasound for other fetal anomalies; serial imaging to monitor for resolution, fetal growth, and placental function; consider cystic fibrosis carrier testing, TORCH serology, and amniocentesis; referral to genetic counselling
    - Postnatal workup – peds to assess after birth, ensure anus is patent and passes meconium, and monitor for signs of bowel obstruction after feeding starts (emesis, abdominal distension)
        - Particularly if concurrent bowel dilation is seen antenatally, consider abdominal Xray at 4-6 hours of life (AP and lateral views) with large NG in place (8 Fr)
        - Low threshold for NICU admission

5.4 – Pelviectasis and Hydronephrosis

- The following is based on guidance from the Canadian Urologic Association. However, significant variation in practice exists between sites. Consult site-specific guidelines where available
- Definition
    - Dilation of the renal pelvis and/or calyces on an antenatal scan

Table 5.4a - Severity of antenatal hydronephrosis (AHN) by antero-posterior renal pelvic diameter (APD) (adapted from Capolicchio, 2018).

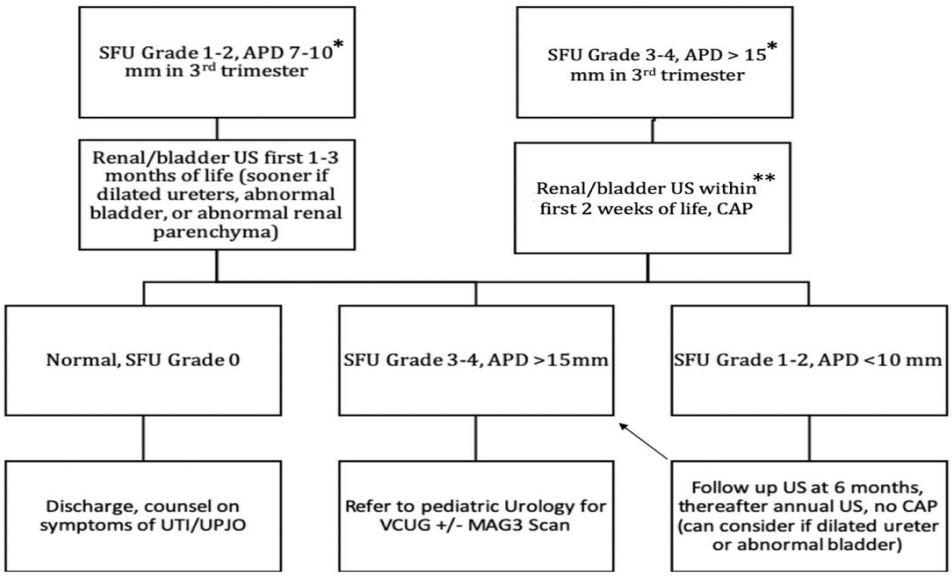
Severity of AHN	Second Trimester	Third Trimester
Mild	4 to <7 mm	7 to <9 mm
Moderate	7 to ≤10mm	9 to ≤15 mm
Severe	>10 mm	>15 mm

Table 5.4b – Society for Fetal Urology (SFU) grading of hydronephrosis (adapted from Capolicchio, 2018).

SFU Grade	Ultrasound Findings
0	Normal kidney (resolved ANH)
1	Pyelectasis
2	Pyelectasis with dilation of 1 or more major calyces (caliectasis)
3	Pyelectasis with dilation of all 3 major calyces
4	Pyelectasis with parenchymal thinning compared to contralateral kidney

- Incidence and pathology
    - 1 to 5% of all pregnancies
    - Differential diagnosis, in order of likelihood – transient hydronephrosis, uretero-pelvic junction (UPJ) obstruction, vesicoureteric reflux (VUR), uretero-vesical junction (UVJ) obstruction, primary non-obstructive megaureter, ureterocele, ectopic ureter, causes of megacystis (posterior urethral valves, and other less common causes)
    - Higher grade AHN is more likely to be associated with pathology except for VUR, which is equally likely with any grade of AHN
- Associations
    - Some of the above diagnosis have sex and genetic underpinnings that should be investigated once the etiology of AHN is determined
    - More common in conditions with serious chromosomal anomalies
    - Severe, bilateral hydronephrosis or oligohydramnios may indicate associated renal failure

- Management and prognosis
  - Antenatal investigations
    - In isolated AHN, no genetic testing is required. If multiple system anomalies, consider amniocentesis and karyotype
    - In utero interventions may be available for severe or complicated AHN. Antenatal referral to urology is indicated in these cases.
  - Postnatal investigations
    - Postnatal abdominal ultrasound with attention paid to genitourinary structures
      - Mild AHN has a 12% likelihood of pathology. The Canadian Urological Association suggests a post-natal u/s for all cases of mild AHN (≥7mm APD on 3rd trimester u/s). Some sites only investigate moderate and severe AHN.
      - SFU grade 3-4 (APD > 15mm) should be imaged soon after birth (between Day 2 and 14 if possible). SFU grade 1-2 (APD 7-10mm) can be imaged later (see figure 5.4)
      - If concern for obstructive uropathy such as PUV, conduct work up without delay
      - If bladder is full on u/s, consider re-imaging post-void to ensure adequate emptying
    - Serum creatinine (ideally after DOL 2), electrolytes, BP measurement, and consultation with urology in severe HN, solitary kidney, or abnormal renal echogenicity
    - VCUG should be conducted (in consultation with urology) if there is concern for bladder outlet obstruction (high grade HN, bladder anomalies, hydroureter)
      - VCUG is most useful in diagnosing PUV, VUR, ureteroceles
    - Other tests for high grade HN (consider in consultation with urology) – MAG3 diuretic renogram is helpful in diagnosing UPJ and UVJ obstruction, DMSA study to assess differential renal function
  - Prophylactic antibiotics
    - SFU grade 3-4, dilated ureter, or abnormal bladder (see figure 5.4)
    - Antibiotic choice varies by site. Typically trimethoprim, amoxicillin, or cephalexin
  - Postnatal resolution in 25 to 50% of cases. Majority that persist postnatally are low grade



*If APD between 10 and 15 mm, manage by SFU grading
**Ultrasound ASAP if concern for obstructive uropathy (PUV)
CAP: Continuous antibiotic prophylaxis

Figure 5.4 – Approach to Antenatal Hydronephrosis (adapted from Capolicchio, 2018)

5.5 – Limited Antenatal Care

- Routine antenatal care has been shown to improve maternal and neonatal health
- When mothers experience limited, fragmented, or no antenatal care, their infants are at risk of adverse outcomes
- Mothers may be at increased risk for food insecurity, mental illness, intimate partner violence, homelessness
- Efforts should be focused on supporting the mother, engaging in a full history, being careful not to further stigmatize a mother who is requiring help. All efforts should be made to mobilize an interdisciplinary team (nursing, social work, lactation support, etc) to ensure short and long term care of the family is preserved
- The following is a list of considerations in the management of mothers in labour:
    - Routine care
        - CBC, blood type, rubella immunity, urine culture, cervical cytology, STI screening, random blood glucose
        - Ultrasound for GA, biophysical profile (BPP), congenital anomalies
        - If unsure of GA or EFW, have necessary equipment at delivery in preparation for premature or SGA baby
    - Infections
        - Rapid antibody testing for HIV, syphilis, hepatitis B, and C
        - GBS prophylaxis – manage as GBS unknown
        - Erythromycin eye ointment for chlamydia exposure after delivery
    - Substances
        - Consider meconium and urine testing for substances if indicated
        - Exposures – SSRI/SNRI and other medications, cigarettes, alcohol, cannabis, cocaine
        - Neonatal abstinence syndrome / Neonatal opioid withdrawal syndrome - infants born to mothers using opioids should be monitored in hospital for 3-5 days for withdrawal symptoms
    - Endocrine
        - Consider postnatal hypoglycemia screening if concern for untreated GDM, possible prematurity
    - Multidisciplinary team for family support

5.6 – Intrauterine Growth Restriction (IUGR)

- Definitions
    - IUGR – a fetus has not reached its growth potential because of a potential pathology
    - Small for gestational age (SGA) – birth weight < 10th percentile for GA
    - IUGR is typically used to define abnormal fetal growth while SGA is used to describe the size of the infant after delivery
    - Low birth weight – birth weight < 2500g, regardless of GA
    - Very low birth weight (VLBW) – birth weight < 1500g, regardless of GA
    - Extremely low birth weight (ELBW) – birth weight < 1000g, regardless of GA
- Approach to IUGR
    - Symmetric IUGR (10-30%)
        - HC, length, and weight are decreased proportionally
        - Can be a normal variant related to genetic tendencies of parents as different GA birth weight curves do exist for different populations (constitutional smallness)
        - If pathologic cause, it typically occurs early in pregnancy; genetic or early infection (TORCH) that interferes with early growth are common considerations
        - Severe maternal disease, prolonged drug exposure possible but less likely
    - Asymmetric IUGR (70-90%)
        - HC is spared relative to decreased weight and length
        - Occurs later in pregnancy
        - Adaptation to hostile environment by redistributing blood flow in favor of vital organs

Table 5.6 - Causes of IUGR (adapted from Smitten, 2011)

Maternal	Placental	Fetal
Inadequate prenatal care or nutrition	Placental insufficiency or disease	Intrauterine infections (TORCH)
Substance use (cigarettes, alcohol, drugs)	Abnormal implantation	Chromosomal disorders
Maternal illness (diabetes, hypertension)	Vascular anomalies	Multiple gestation
Pre-eclampsia	Placental abruption	Metabolic disorders
Early or advanced age	Infarction	Congenital anomalies
Malnutrition		Constitutional smallness
Uterine malformations		
Medications (warfarin, anticonvulsants)		

- Antepartum Investigations
    - Serial monitoring with biophysical profile, non-stress test, fetal weight assessments, amniotic fluid volume
        - Blood flow velocity in fetal vessels with doppler
            - Absent or reversed end diastolic flow in the umbilical artery (UA) suggests the fetus is in poor condition
            - Abnormal UA doppler warrants investigation of the fetal circulatory system (middle cerebral artery, ductus venosus, and umbilical vein dopplers)
        - Monitor for signs of maternal pre-eclampsia (BP, CNS exam, blood work, urinalysis)
        - Monitoring should increase and/or referral to maternal fetal medicine (high risk obstetrics) if growth plateaus, amniotic fluid index declines, or fetal tone diminishes
    - Investigation of underlying cause with detailed fetal anatomic survey by ultrasound, detailed placental ultrasound (at 19 to 23 weeks), and testing for congenital infections, karyotype, non-invasive pregnancy testing, etc. are considered on an individual basis based on results from above
- Management
    - Low-dose aspirin for prevention in women with risk factors for placental insufficiency from 12 to 36wks gestation
    - Abnormal UA / fetal vascular doppler in the presence of IUGR is ominous and should trigger consideration of delivery
    - If fetus is preterm consider transfer to appropriate facility, consider antepartum steroids for lung maturation, and weigh the risk of prematurity against risk of intrapartum demise / asphyxia
- Post-natal Care
    - Prepare for resuscitation at delivery, particularly if concerning fetal monitoring
    - Monitoring for hypoglycemia, hypothermia
    - Assessment for underlying cause with history and physical exam
        - Findings of concern: symmetric IUGR, dysmorphic features, petechiae, HSM, jaundice, other abnormalities on antenatal screening
    - Consider genetic testing, HUS, and/or TORCH screening
- Outcomes
    - Increased risk of morbidity and mortality
    - Antepartum complications – pre-eclampsia, still birth
    - Neonatal complications – prematurity, hypoglycemia, hypothermia, polycythemia, thrombocytopenia, impaired immune function, asphyxia, jaundice, hypocalcemia
    - Long term complications - Infants with asymmetric growth restriction are more likely to experience catch up growth. IUGR infants are at increased risk of metabolic conditions (obesity, diabetes), and cardiovascular disease

Postnatal Consults

5.7 - Hypoglycemia

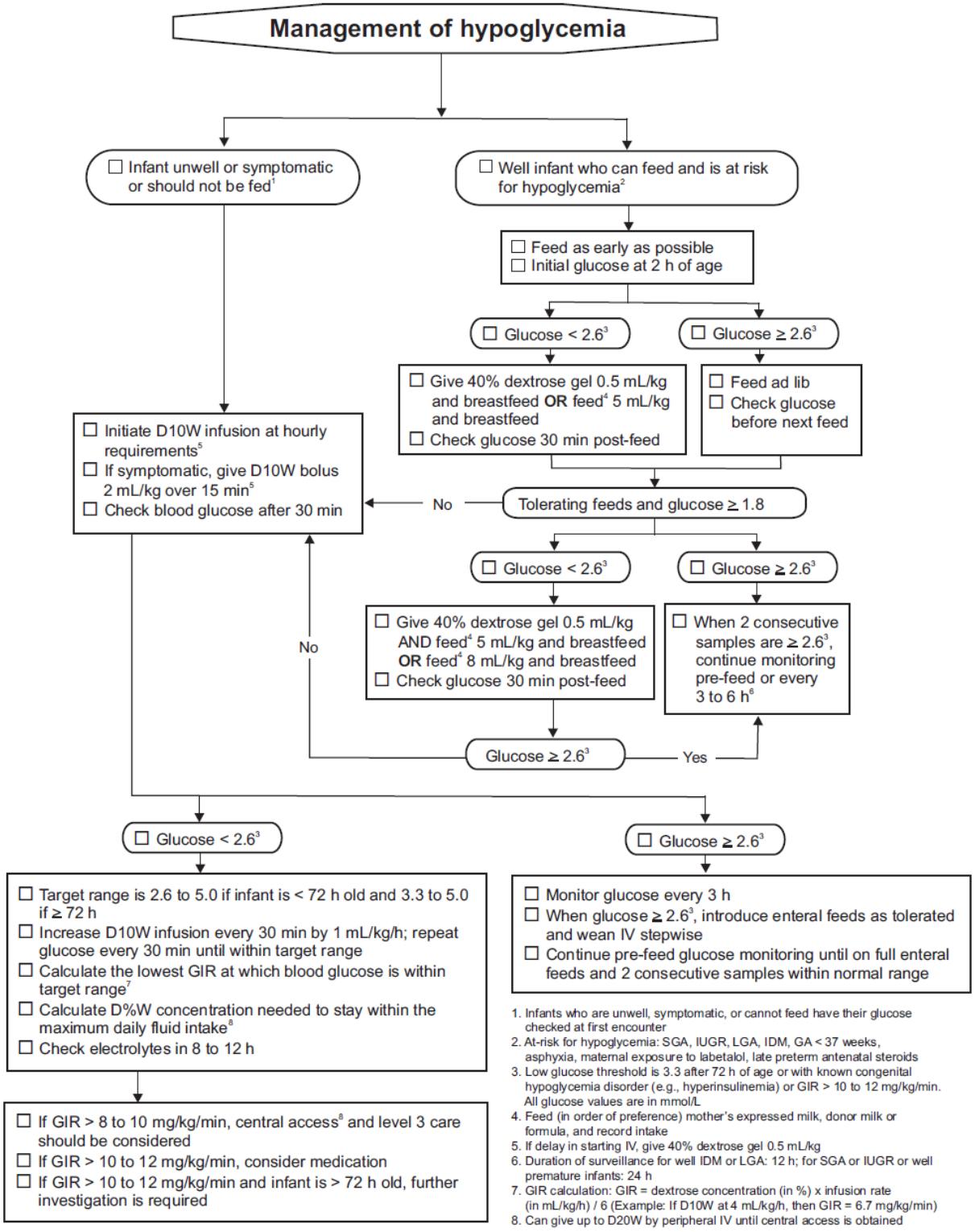
- Definition
    - Transitional hypoglycemia in the first 72 hours post-birth: blood glucose <2.6 mmol/L
    - Persistent hypoglycemia after 72 hours post-birth: blood glucose <3.3 mmol/L

- Incidence and pathology
    - In the first 72 hours of life, hypoglycemia occurs in 12-14% of well, appropriate for gestational age (AGA), breastfed newborns
    - Transient hypoglycemia occurs following the disruption of glucose supply at birth and is impacted by the hormonal environment in utero as well as fetal glycogen stores
- Signs and symptoms
    - In approximate order of frequency – jitteriness, cyanosis, seizures, apneas or tachypnea, high-pitched or weak cry, lethargy or limpness, feeding difficulty, and eye-rolling
        - Note: differential diagnosis for jitteriness includes hypoglycemia, hypocalcemia, prematurity, hypothermia, SSRI/SNRI exposure, or other exposures (cigarettes, marijuana, cocaine).
    - Sweating, pallor, hypothermia, or cardiac failure may also occur
- Screening and risk factors
    - No routine screening for all infants
    - Screening applies to infants with the following risk factors
        - Weight – IUGR or SGA <10th percentile, LGA > 90th percentile
        - Maternal – IDM, beta blocker exposure (labetalol)
        - Newborn – prematurity (< 37 weeks GA), exposure to antenatal steroids, perinatal asphyxia, genetic syndromes (Beckwith-Wiedemann), metabolic conditions
- Investigation and management
    - Symptomatic infants should have their blood glucose tested without delay
    - Asymptomatic infants with risk factors should be monitored for 12 to 24h (see figure 5.7)
    - Treatment and investigation thresholds vary depending on hours of life (see table 5.7)
    - Suggested investigations and critical sample blood work if persistent/unexplained hypoglycemia can be found in Endocrinology
    - Persistent hypoglycemia should be confirmed by laboratory assays, as whole blood glucose readings are lower than plasma within a 10% range
    - Acute management may be initiated based on point-of-care samples using feeds, dextrose gel, and/or IV fluids (see figure 5.7)
    - Glucose infusion rate (GIR) for intravenous dextrose may be calculated as follows
        - GIR units = mg glucose/kg/minute
        - GIR = [ml/hr x (10 x % dextrose concentration) / (60 minutes x kg)]
        - Simple GIR at birth: [% dextrose concentration x infusion rate (ml/kg/hr)] / 6
        - If feeding don't forget to include PO/NG feeds in total GIR
    - If GIR > 8-10 consider central access, and tertiary care. If GIR > 10-12 consider medications

Table 5.7 – Blood glucose thresholds for treatment and investigation depending on infant age in hours (adapted from Narvey, 2019).

Infant age (hours)	BG threshold for treatment (mmol/L)	BG threshold for investigation (mmol/L)
0 to 72	2.6	2.6
>72	3.3	2.8

- Outcomes and follow up
    - Symptomatic hypoglycemia can contribute to neuronal injury and should be treated immediately
        - Can treat with formula feeding and/or dextrose gel first (Figure 5.7) but may ultimately need IV dextrose to maintain normoglycemia
    - Blood glucose levels <2.6 mmol/L in at-risk infants, particularly when persistent, may be associated with adverse neurodevelopmental outcomes
    - Neonates being monitored for persistent hypoglycemia (BG < 3.3 after 72h) should have specific medical management initiated and have a 5-6 hour fast before discharge for safety at home



Abbreviations: Ca - calcium, D%W - %age dextrose in water (e.g., D10W = dextrose 10% in water), GA - gestational age, GIR - glucose infusion rate, h - hours, IDM - infants of diabetic mothers, IUGR - intrauterine growth restriction, IV - intravenous, K - potassium, LGA - large for gestational age, min - minutes, Na - sodium, SGA - small for gestational age

Figure 5.7 - Management and care of infants at risk for neonatal hypoglycemia in the first 72 hours of life (Narvey, 2019)

5.8 – Early Onset Sepsis (EOS)

- Definition and etiology
  - Sepsis in the first 7 days of life – most infants are symptomatic within 24 hours of birth
  - The most common pathogen is Group B Streptococcus (GBS) followed by E. coli, S. viridans, S. pneumoniae, Enterococcus, Enterobacter, S. aureus, and H. influenzae.
- Incidence
  - Estimated at 0.77 cases/1000 live births in the United States (case fatality – 10.9%)
  - In the absence of intrapartum antibiotic prophylaxis (IAP), approximately 1-2% infants born to mothers colonized with GBS develop EOS
- Risk factors
  - Presence of more than one risk factor (see below) increases the likelihood of EOS
  - Preterm labour (<37 weeks) should also be considered a risk factor for neonatal sepsis
  - The sepsis calculator here may help estimate the probability in asymptomatic babies
- Prophylaxis
  - Adequate intrapartum antibiotic prophylaxis (IAP) consists of ≥ 1 dose at least 4 hours before birth of IV penicillin G or ampicillin. For penicillin allergy with low risk of anaphylaxis, IV cefazolin is considered adequate IAP
  - IAP is not needed for a caesarean section before labour onset if membranes are intact
- Investigation and management
  - For term infants at risk of sepsis, see Table 5.8
  - Infants with clinical signs of sepsis must be investigated and treated promptly
    - If presentation in keeping with TTN (stable with respiratory distress and no sepsis risk factors), consider observation for 4-6 hours before initiating work up and treatment for sepsis
  - Lumbar puncture should be performed if blood culture is positive, or at the outset if there is strong clinical suspicion or signs of meningitis
    - In term infants, cerebrospinal fluid pleocytosis (>20-25 cells/mm3) is abnormal
  - Urine, gastric aspirates, and body surface cultures are not recommended
  - Well late preterm infants (35 or 36 weeks) can be managed similarly to term infants but should be monitored in hospital for 48 hours prior to discharge

Table 5.8 - Management of term infants at risk for early onset sepsis (adapted from Narvey, 2019 and S. Bitnun)

Clinical Status	GBS Status	Other risk factors	Adequate IAP	Recommendation
Unwell	-	-	-	Investigate and treat promptly
Well	Positive	No	Yes	Routine care
			No	Close observation
		Yes	Irrespective	Individualized care
	Negative / unknown	No	-	Routine care
		1	Yes	Routine care
			No	Close observation
		≥ 2 or chorioamnionitis	Irrespective	Individualized care

Unwell – respiratory distress, temperature instability, tachycardia, seizures, hypotonia, lethargy, poor peripheral perfusion, hypotension, and acidosis
GBS status – GBS colonization, GBS bacteruria in pregnancy
Risk factors – previous infant with invasive GBS disease, ROM ≥ 18 hours, maternal fever ≥ 38C
Chorioamnionitis – maternal fever >38C plus two other signs (uterine tenderness, maternal or fetal tachycardia, foul/purulent amniotic fluid, maternal leukocytosis)
Adequate IAP – ≥ 1 dose at least 4 hours prior to delivery of IV penicillin G, ampicillin, or cefazolin.
Investigate and treat promptly – CBC, blood culture, LP, and chest xray if respiratory distress present. Start IV antibiotics (ampicillin and aminoglycoside).
Close observation: Examine at birth. Observe 24-48 hours. Vitals Q3-4H. Reassess and counsel pre-discharge.
Individualized care: At minimum, examine at birth. Observe 24-48 hours. Vitals Q3-4H. Reassess and counsel pre-discharge. Consider CBC at 4 hours of life.

5.9 – Unconjugated Hyperbilirubinemia in Term/Late Preterm Infants (>35 week gestation)

- Overview
  - Hyperbilirubinemia is common and usually benign in the newborn period, but is screened for and treated to prevent neurologic toxicity
  - At high levels, unconjugated bilirubin unbound to albumin can cross the blood brain barrier, leading to acute and chronic bilirubin encephalopathy, and/or kernicterus (staining of the basal ganglia and brainstem nuclei)
  - A total serum bilirubin (TSB) concentration ≥ 340 umol/L is severe hyperbilirubinemia, and ≥ 425 umol/L is critical. Above this level, the risk of toxicity progressively increases
    - TSB is the combined value of both conjugated and unconjugated bilirubin
  - Red flags (clinical scenarios that are always abnormal)
    - A conjugated bilirubin that is greater than 20% of the TSB
    - Jaundice in the first 24h of life: check a bilirubin at the first sign of jaundice; do not wait until 24h especially if there are risk factors for hemolysis
    - Jaundice at ≥ 3 weeks of life: consider TSH and galactosemia/tyrosinemia screen
  - Certain conditions, like G6PD deficiency and ABO incompatibility, require intervention at a lower TSB level because they are more likely to progress to severe hyperbilirubinemia
- Pathophysiology
  - Non-pathologic
    - Physiologic jaundice
      - Expected in the newborn period, peaking at day 3-5 of life; caused by naturally elevated hematocrit, shorter lifespan of blood cells, impaired ability to excrete bilirubin from the body
    - Breastfeeding-associated jaundice
      - Exclusive breastfeeding can exaggerate physiologic jaundice due to a combination of: mild dehydration, delayed passage of meconium, and increased enterohepatic circulation of bilirubin
      - Newborns should not lose more than 10% of their birth weight. This is a sign of dehydration and risk for hyperbilirubinemia
    - Breast milk jaundice
      - Peaks at 10-14 days but can last longer
      - May increase enterohepatic circulation
  - Pathologic or other risk factors
    - Increased bilirubin production through breakdown of RBCs
      - Hemolytic disease – isoantibodies (ABO, Rh incompatibility), RBC enzyme or structural defects (G6PD, pyruvate kinase deficiency, spherocytosis)
      - Non-hemolytic – cephalohematoma/excessive bruising, polycythemia
    - Impaired bilirubin metabolism or excretion
      - Congenital syndromes – Gilbert, Crigler-Najjar, galactosemia, hypothyroidism
      - Biliary obstruction – biliary atresia, Dubin-Johnson
    - Other
      - Prematurity (less than 38 weeks)
      - Asian ethnicity
      - Sepsis
- Evaluation
  - Screening all infants with TSB or (TcB) measurement at 24-72h of life, coupled with clinical risk score, is the best available method for predicting severe hyperbilirubinemia
  - Nomograms use TSB, age in hours, gestational age, and risk factors to guide management and follow up

1) Use the phototherapy nomogram (Figure 5.9a) to determine if phototherapy is required. The thresholds used are determined by the infants' gestational age and risk factors for bilirubin encephalopathy
2) If phototherapy is not required, the TSB concentration is plotted on the predictive nomogram (Figure 5.9b and Table 5.9). This information is used in conjunction with the infant's risk factors for progression to severe hyperbilirubinemia to guide the timing of follow up
    - These risk factors are different than the ones used in the phototherapy nomogram and do not change the phototherapy treatment line (exclusive breastfeeding, sibling requiring phototherapy, East Asian ethnicity, cephalohematoma/bruising)

- Other investigations to consider:
    - Blood group and DAT in infants with early jaundice, mother's blood group O, or who are antibody positive
    - If possible, obtain 2 bilirubin measurements to calculate a Rate-of-Rise (RoR) of bilirubin. RoR of 1-4 umol/L/hr is normal.
    - G6PD screening – if family history or ethnicity suggestive, or if hyperbilirubinemia is severe
        - In the presence of hemolysis, G6PD levels can be overestimated, and screening results can be misleading. Screening tests may also take several days to result, which would not aid in management decisions
    - CBC + differential with attention to hemoglobin and hematocrit levels, blood smear, red cell morphology
    - Conjugated bilirubin (particularly if hyperbilirubinemia is prolonged >2 weeks)
    - If jaundice is persistent at 3 weeks, consider TSH and galactosemia / tyrosinemia screen

- Management
    - Phototherapy – is the mainstay of treatment. It breaks down bilirubin in areas of exposed skin, and should cause the TSB RoR to slow or decline within 4-6 hours
        - Intensive phototherapy should be used for infants with severe hyperbilirubinemia or those at greatest risk – achieved by using multiple lights and/or a fibre optic blanket, maximizing exposed skin area and time spent under lights
        - Discontinue phototherapy when TSB is 20-35 umol/L below the initiation level
        - Once phototherapy is discontinued, consider follow up TSB measurement to ensure it does not continue to rise, particularly if concern for hemolytic process
            - Check 6-12 hours after discontinuing to assess for rebound
    - Rehydration - IV fluids are indicated if there is significant dehydration, otherwise enteral nutrition (+/- formula supplementation) is adequate
    - IVIG – indicated in infants who have isoimmune hemolytic disease (DAT+) who have rising TSB despite phototherapy or are nearing exchange transfusion levels
    - Exchange transfusion– indicated when phototherapy fails to control rising bilirubin concentrations, if TSB levels are above the thresholds in Figure 5.9c, or if there are clinical signs of acute bilirubin encephalopathy (hypertonia, arching, retrocollis, opisthotonos, fever, high-pitched cry)
- Can use BiliTool link here to generate bilirubin nomogram based on TSB and age in hours
- See Figure 5.9d and 5.9e for guidelines for infants below 35 weeks gestational age. Note that these are SickKids specific, and different thresholds may be used at different centers

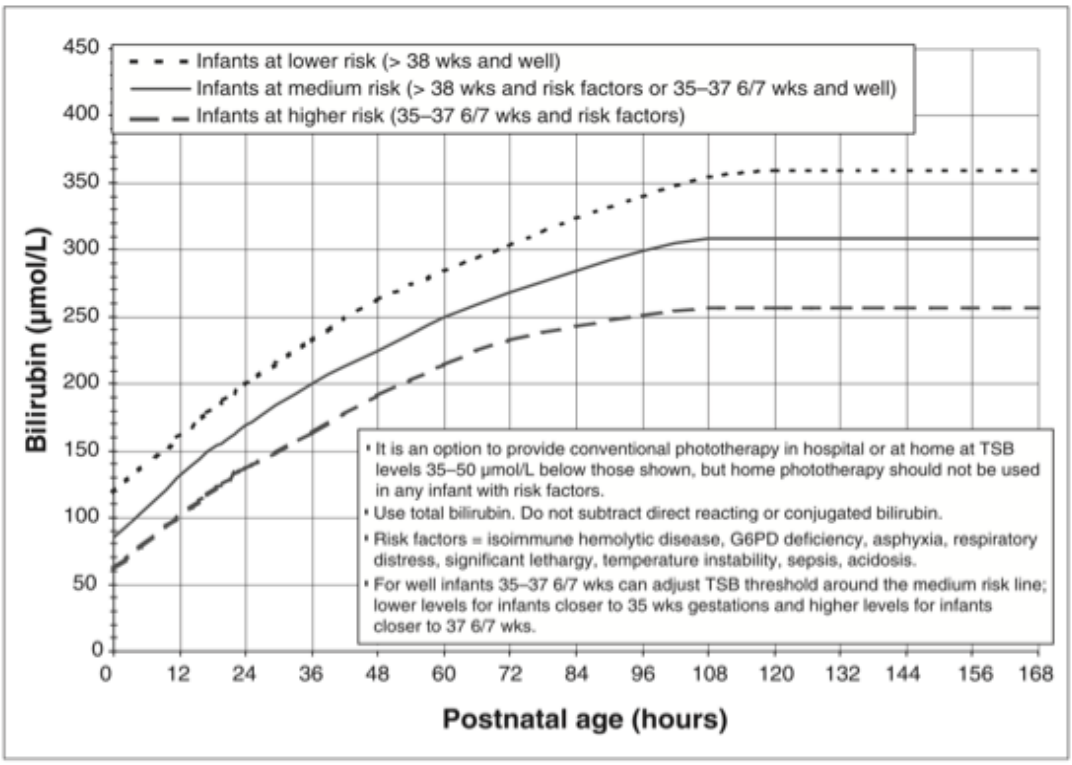


Figure 5.9a: Phototherapy thresholds for term or late preterm infants (Barrington, 2007).

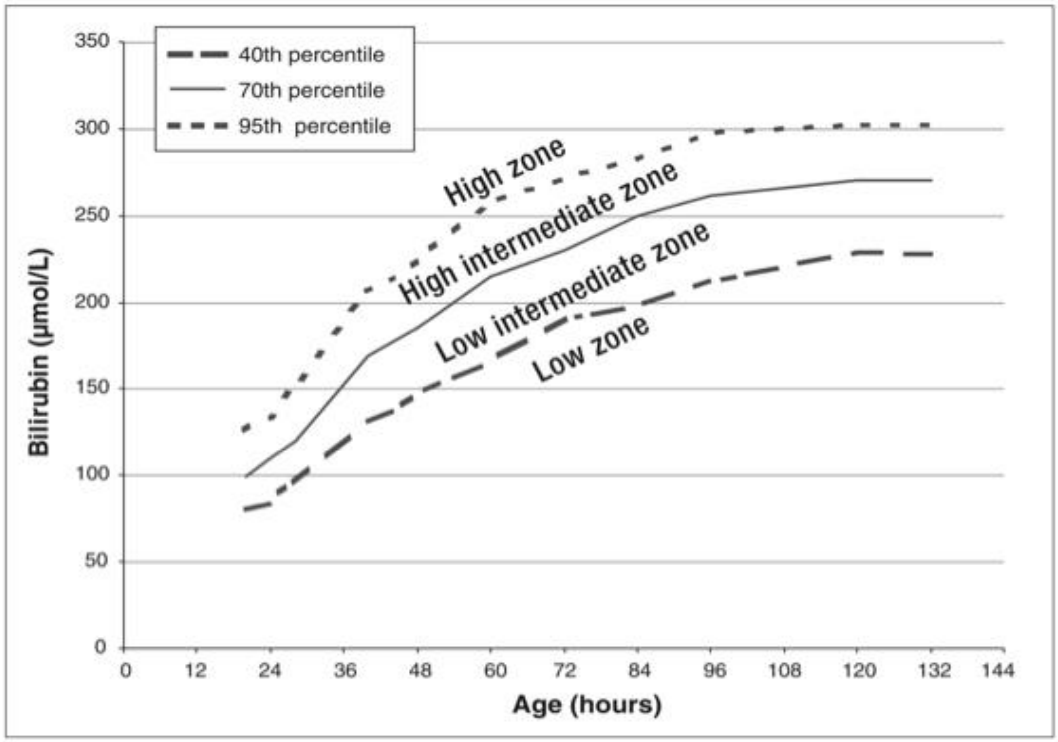


Figure 5.9b: Risk stratification zones based on TSB levels that will guide follow up (Barrington, 2007).

Table 5.9 - Suggested interventions based on risk zone from Figure 5.9b (adapted from Barrington, 2007).

Zone	> 37wks AND DAT neg	35 to 37+6wk OR DAT pos	35 to 37+6wk AND DAT pos
High	Further testing or treatment required	Further testing or treatment required	Phototherapy required
High-intermediate	Routine Care	Follow up within 24-48h	Further testing or treatment required
Low-intermediate	Routine Care	Routine Care	Further testing or treatment required
Low	Routine Care	Routine Care	Routine Care

Further testing or treatment required: timely (within 24h) re-evaluation of bilirubin by serum testing

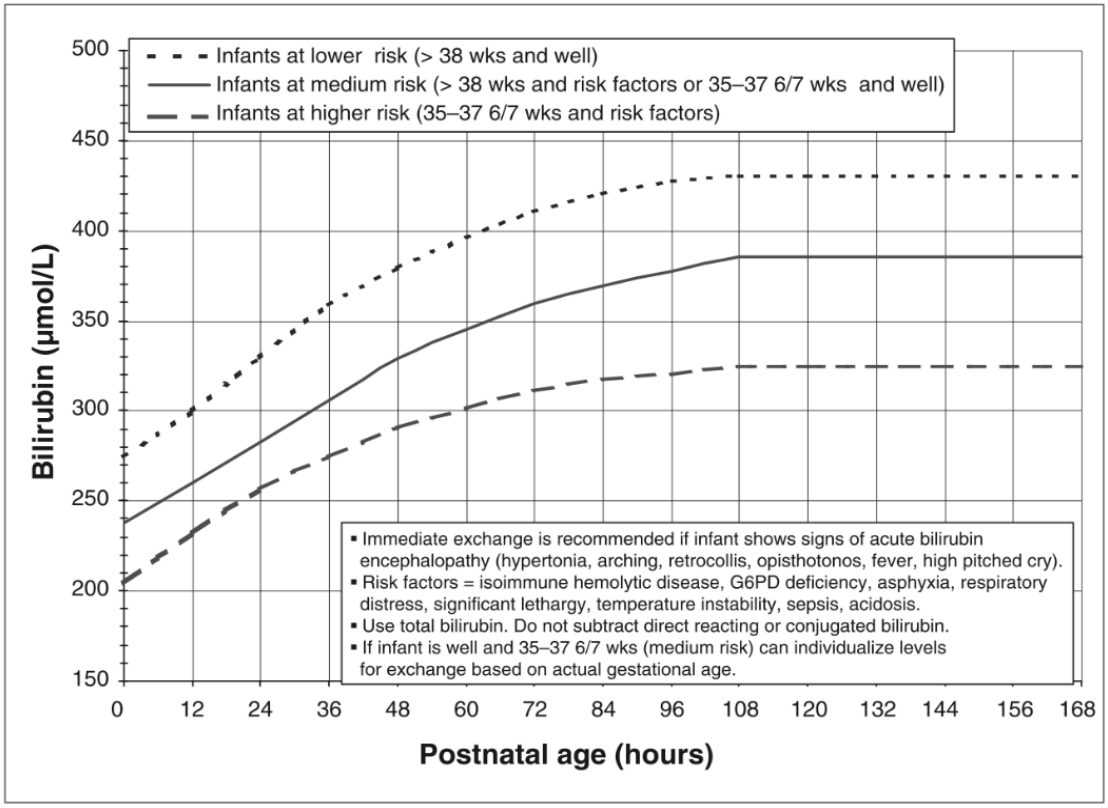


Figure 5.9c: Exchange transfusion thresholds for term and late preterm infants (Barrington, 2007).

PHOTOTHERAPY INITIATION LEVELS

Total serum bilirubin (TSB) (micromol/litre)

- **For infants > 1000 grams use INTENSIVE phototherapy (irradiance ~30µW/cm2/nm)**
- **For infants ≤ 1000 grams use STANDARD phototherapy (irradiance ~10µW/cm2/nm) unless TSB is rapidly rising or TSB continues to rise while receiving phototherapy** (less irradiance used to reduce risk of oxidative tissue injury by phototherapy in extremely immature infants)

Gestational Age (weeks)	Age in Hours	<24 hours	24-48 hours	49-72 hours	> 72 hours
	<28 0/7 and at risk*	70	80	80	90
	<28 0/7	80	90	90	100
	28 0/7 to 29 6/7 and at risk*	80	90	90	100
	28 0/7 to 29 6/7	90	100	120	140
	30 0/7 to 31 6/7 and at risk*	90	100	120	140
	30 0/7 to 31 6/7	100	120	140	170
	32 0/7 to 33 6/7 and at risk*	100	120	140	170
	32 0/7 to 33 6/7	100	130	170	200
	34 0/7 to 34 6/7 and at risk*	110	140	170	200
	34 0/7 to 34 6/7	110	160	210	230

Figure 5.9d: Phototherapy thresholds for infants below 35 weeks GA (The Hospital for Sick Children, 2019).

*Risk factors for bilirubin toxicity include: serum albumin < 25 g/L, rapidly rising TSB levels greater than 8.5 micromol/L/h suggesting hemolytic disease, clinically unstable infants (acidotic, septic, apnea or bradycardia requiring cardiorespiratory resuscitation, hypotensive on pressors, mechanical ventilation)

EXCHANGE TRANSFUSION LEVELS

Total serum bilirubin (TSB) (micromol/litre)

- Exchange transfusion is recommended for infants whose TSB levels continue to rise to exchange levels despite receiving intensive phototherapy to the maximal surface area
- Exchange transfusion is recommended if infant shows signs of acute bilirubin encephalopathy (hypertonia, arching, retrocollis, opisthotonos, high-pitched cry); even if below exchange levels (but note that these signs can be subtle in very low birth weight infants and may be difficult to detect)

Gestational Age (weeks)	Age in Hours	<24 hours	24-48 hours	49-72 hours	> 72 hours
	<28 0/7 and at risk*	190	190	210	220
	<28 0/7	190	200	210	240
	28 0/7 to 29 6/7 and at risk*	200	200	210	220
	28 0/7 to 29 6/7	200	210	220	240
	30 0/7 to 31 6/7 and at risk*	220	220	230	260
	30 0/7 to 31 6/7	220	230	260	270
	32 0/7 to 33 6/7 and at risk*	240	240	260	300
	32 0/7 to 33 6/7	240	250	290	300
	34 0/7 to 34 6/7 and at risk*	250	260	290	310
	34 0/7 to 34 6/7	260	270	310	320

Figure 5.9e: Exchange transfusion thresholds for infants below 35 weeks GA (The Hospital for Sick Children, 2019).

5.10 – Routine Newborn Screening

- Metabolic Screen
  - Blood spot at 24-48h to screen for treatable metabolic conditions that usually show no symptoms in the newborn period. If completed prior to 24h, the test is not valid and must be repeated within 7 days
  - For premature infants born at less than 33 weeks gestational age, repeat again at 21 days of life. See here for other indications for a repeat newborn screen
- Bilirubin Screen – see 5.9, often done in conjunction with metabolic screen
- Critical Congenital Heart Disease Screen
  - Some types of CCHD, including duct-dependent lesions, may not present with obvious clinical features (murmur, cyanosis, respiratory signs) prior to discharge home
    - Pulse oximetry screening identifies otherwise clinically undetectable degrees of cyanosis
  - All term and late preterm infants should be screened between 24-36 h of age
    - Screening prior to 24h increases the false positive rate, but is better than no screen at all

    - Test by using the right hand and one foot
        - A normal screen is ≥95% oxygen saturation in both hand and foot, and ≤3% difference between the two
        - Borderline = any limb with SpO2 90-94% OR >3% difference between the two
        - Can repeat screen in 1 hour x2
        - Fail = any limb with SpO2 <90% or more than 3 borderline attempts
        - See here for chart
    - Failed screening test requires further evaluation
        - Detailed cardiovascular examination (heart sounds/presence of murmurs, femoral and peripheral pulses, perfusion, respiratory status, presence of hepatomegaly)
        - Consider 4 limb BPs, ECG, CXR
        - If concern for cardiac origin or unclear → cardiology consult + echocardiogram
- Newborn Hearing Screen
    - Screens for congenital hearing loss, with estimated incidence of 1-3/1000 live births
        - Majority (70%) have non-syndromic deafness, other causes are syndromic deafness, congenital infections, severe hyperbilirubinemia, and ototoxic medications
        - Risk factors – family history, craniofacial abnormalities, admission to NICU
    - Goal is early diagnosis and intervention (auditory therapy, hearing aids, cochlear implants)
    - Otoacoustic emission (OAE) is used as a first test in newborns with no risk factors, followed by automated auditory brainstem response (AABR) in infants who do not pass the OAE
        - Screening should be completed or scheduled prior to discharge home
        - If not passed, needs follow up testing arranged (usually by 3 months)

5.11 – Developmental Dysplasia of the Hip (DDH)

- Definition: congenital abnormality in the size, shape, orientation, or organization of the femoral head, acetabulum, or both
- Risk factors – female (6x increase), family history (20% of affected), breech (30% of affected), first born, twin pregnancy, swaddling, presence of neuromuscular disorder
- Assessment – Barlow and Ortolani maneuvers at birth, 2 weeks, and all well baby visits until walking
- Management
    - Ultrasound of the hip joint if abnormal exam or to screen infants with risk factors (limited evidence to determine who needs screening). X-ray in children over 6mo.
    - Orthopaedic opinion for abnormal ultrasound. Treat with Pavlik harness up to 6mo of age.

5.12 – Circumcision

- Potential benefits of circumcision include
    - Reduction of early/infant UTI. Number needed to treat (NNT) is very high (111-125)
        - More beneficial if other risk factors (urinary tract anomalies, recurrent infections)
    - Reduced incidence of some STIs (particularly HIV, HSV and HPV) – NNT varies depending on the population studied
    - Prevention of future phimosis (NNT 67)
- Common risks of circumcision include pain, minor bleeding, local infection, unsatisfactory cosmesis, and meatal stenosis, with a median complication rate of 1.5% in infants and 6% in children
    - Severe complications are rare
- Contraindications – hypospadias (must consult with urologist) and bleeding disorder
- Recommendations
    - CPS does not recommend routine circumcision of every newborn male, although there may be benefits for some boys in some high-risk populations or circumstances
    - If circumcision is performed it should be with informed and documented consent, an experienced provider, adequate analgesia, attention paid to immediate and delayed complications of procedure (bleeding)

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Chapter 6 – Routine Preterm Care

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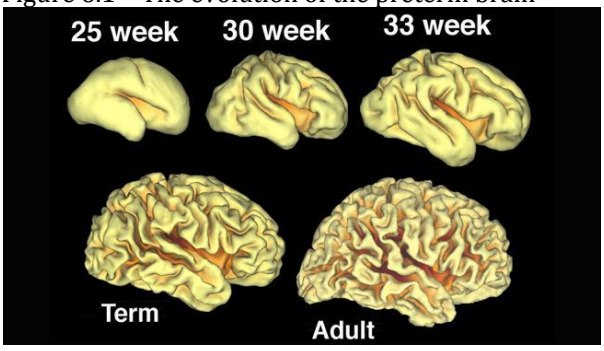
Expert Reviewer – Dr. Eugene Ng

6.1 – Foundations of care for the preterm infant

- Family-Centered Care
    - Psychological bonding of the parent and child start during the pregnancy and is interrupted by preterm birth. This can negatively impact this relationship as the infant is born often unexpectedly with unnatural separation of the infant and parents
    - The behaviour of the preterm infant is different than a term infant and can often be misinterpreted by parents which can further complicate the infant-parent bond
    - Supporting and promoting infant-parent bonding during the whole NICU journey - from the antenatal consultation, through the NICU, and during outpatient follow up mitigates these negative impacts
- Infant-centered care
    - Growth spurt of infant's brain occurs in the third trimester. Infants born preterm are undergoing neuronal migration and organization in the NICU instead of in utero (Figure 6.1)
    - The development of the infant brain is largely governed by sensory input
    - Any negative sensory input or noxious stimuli can impact the brain development (both the anatomy and the function of the brain)
    - Positive or nurturing stimuli are important for neuropromotion and include skin-to-skin care, touch, and parental voices
    - Examples of stresses/painful procedures are heel pricks, noises, bright lights, feeding, repositioning, etc.
- A three-step approach to developmental care of the neonate
    1. Create a nurturing physical environment for babies, families, and caregivers
    2. Promote parent involvement in newborn care and parent holding as much as possible
    3. Promote a multi-disciplinary inter-professional developmentally supportive care philosophy

Figure 6.1 – The evolution of the preterm brain



6.2 - Antenatal Preterm Care

See Chapter 3 for general antenatal care and preterm counselling Table 6.2 – Corticosteroids and MgSO4 as part of antenatal preterm care

What	Corticosteroids	MgSO4
When	Timing: maximal efficacy reached within 7 days of last dose Steroids may be re-dosed within 24 hrs between the last administration, for a maximum of 2 doses. In deliveries where doses may not be able to be given 24 hrs apart, they may be re- dosed within 12 hrs. Steroids are effective for 2 to 4 weeks from time of administration Optimal interval: greater than 48 hrs between last dose and birth	Consider in all women experiencing imminent preterm delivery (≤ 33+6 weeks GA)
Why	Lower risk for RDS Reduce IVH (especially if >48 hrs interval)	Decreases risk of neurodevelopmental impairment Decreases risk of CP In preeclampsia ● Neuroprotection for baby ● Prevention of seizures for mom ● Short-term tocolysis to allow for administration of antenatal corticosteroids
Indications	Mothers at **≤34+6 weeks** gestation with risk of delivery in the next 7 days should be routinely offered a course of antenatal corticosteroids Women at risk for extremely preterm birth at **≥22 weeks GA** when early intensive care is a management option.	Consider intrapartum magnesium sulphate for mothers at risk for imminent delivery of an infant **≤33+6 weeks GA** in the next 24 hours
Contraindications		Not for long-term use

6.3 – Neuroprotection

Table 6.3 – Neuroprotection at different stages (adapted from Ryan, Lacaze-Masmonteil, and Mohammad, 2019)

See Neurology

Time Period	Intervention
Antenatal Period	Infection prophylaxis ● Mothers at risk of/experiencing PPROM (≤ 32 +6wk GA) should receive penicillin and a macrolide (or macrolide alone if penicillin allergy) Steroids ● Mothers at ≤34+6wk GA at risk of delivery in the next 7 days should be offered antenatal steroids ● Repeat doses of steroids are not recommended as they do not improve outcomes but can negatively affect infant growth, head circumference, and increase the risk of NDI
During Delivery	Steroids/MgSO4 ● Consider intrapartum MgSO4 for mothers at risk of imminent delivery of infant ≤33+6wk GA in coming 24hr Delivery ● Consider C/S when infant is mal-presenting ● Delay cord clamping when possible if no immediate resuscitation required. Cord milking can be considered if this is not possible Hypothermia/Environment ● Routine use of polyethylene bag/wrapping, a thermal mattress, preheated radiant warmer with servo-control, hat and room temperature 25-26C should be used for all infants ≤31+6wk GA ● Minimal handling should be promoted within the first 72 hours of life, especially for infants of lower gestational age
Neonatal period	Infection prophylaxis ● Infants ≤32+6wk GA born to mothers with chorioamnionitis or PPROM should receive antibiotics for 36-48hrs pending a negative blood culture Vital Sign Changes ● Avoid inotropes for hypotension unless other clinical signs of tissue hypoperfusion also present (elevated lactate, prolonged capillary refill, decreased urine output or low cardiac output) ● Avoid iatrogenic causes of hypotension (lung hyperinflation or dehydration) Environment ● Minimal handling especially in the first 72 hours ● In first 72 hours preterm infant's head should be in neutral, midline position, with the head of the bed elevated 30 degrees Cardiorespiratory Function ● Consider prophylactic indomethacin in high-risk, extremely preterm infants, based on risk factors (as hemodynamically significant PDA increases risk of brain injury) ● Maintain a PCO2 of 45 mmHg to 55 mmHg, to a maximum of 60 mmHg (to help prevent periventricular leukomalacia (PCO2 below 35 mmHg) and IVH (PCO2 above 60 mmHg)) ● Volume-targeted ventilation should be first choice for all preterm infants in the first 72 hours ● When treating hypotension in preterm infants, consider the fact that rapid fluid boluses and the use of vasopressors may cause rapid fluctuations in cerebral perfusion pressure leading to a higher risk of IVH.

6.4 – Basic Orders for Preterm Delivery

Table 6.4 – Basic Orders for Preterm Delivery (for babies <32 weeks GA)

Most units will have order sets for preterm infants. These can differ for the smaller babies (<26 weeks). This is an overview of what most order sets will contain and what to monitor for however the *specifics* are different based on each hospital's policy.

	Orders
Monitoring	● Vitals Q1hr for at least 72 hours ● Routine BP ○ Initially via UAC for 72hr, ensuring that it correlated with cuff CP every 8 hr ● Transcutaneous pCO2 (change site Q6hr) or spot checks if concerns about skin integrity ● Target O2 saturation 88-95% ● No abdominal girth measurements for 72 hours unless clinical concern ● Weight should be taken at admission, 48 hours, then every 24 hours (2 person procedure)

Access and Fluid	● Vascular access
	  ○ IV: Recommended for infants ≥30 wks
	  ○ UVC: Recommended for infants ≤ 30 wks and in infants ≥30wks with difficult PIV access or hemodynamic instability
	  ▪ Should have heparin flush as per unit policy
	  ▪ Consider double lumen UV for infants that may require multiple medications (ex. Inotropes or glucagon)
	  ○ UAC: Recommended for infants ≤26wks and in infants >26wks with hemodynamic instability, requiring frequent blood sampling and altered skin integrity requiring regular blood sampling
	  ▪ Must run heparin solution as per unit policy
	  ○ PICC: Try to avoid insertion in first 72 hours, insert if will require PIV for >3-5 days or difficult access
	  ○ PAL: insert if need frequent blood sampling or invasive BP monitoring
	  ▪ Must run heparin solution as per unit policy

Nutrition	● Weight
	  ○ BW should be used for medication dosing for 72-120hr or until it is regained
	● TPN (generally electrolyte free immediately after birth until the neonate has established urine output and then individualized as per institutional practices)
	● NG/OGT feeds
	  ○ Increasing volume as per unit policy based on weight
	● Consider expressed breast milk (EBM) or donor milk (will need consent as human product)
	● Oral immune therapy (OIT) by giving a few breastmilk drops in the baby's mouth is to be initiated 2hr after birth

Ventilation	● Target capillary blood gas values
	  ○ pH 7.25-7.4 (allow lower pH in younger infants to allow for permissive hypercapnia)
	  ○ PaCO2 40-60 (see above)
	● Intubation
	  ○ Pre-intubation medications (check unit policy). Below is an example to be given in the following order
	  ▪ IV atropine 0.02mg/kg/dose (push)
	  ▪ IV fentanyl 2 mcg/kg (slow administration over 2 min)
	  ▪ IV succinylcholine 2mg/kg/dose (push)
	● Consider surfactant administration
	  ○ Intratracheal surfactant (can be given to intubated patient or patient can be intubated for surfactant administration and extubated shortly after (INSURE method – INtubation-Surfactant-EXtubation))
	  ○ Less invasive surfactant administration (LISA)/Minimally invasive surfactant therapy (MIST)
	  ○ Follow guidelines of institution

Medications	● Vitamin K 0.5mg IM
	● Consider erythromycin 0.5% eye ointment to both eyes to prevent ophthalmia neonatorum
	● Probiotics PO q24hr with commencement of feeds
	● Sucrose 24% 0.5ml to anterior tongue 2 min prior to painful procedures (max 4 doses/24hr period)
	● Antibiotics
	  ○ Ampicillin and gentamicin for empiric coverage
	  ○ Consider in infants born after spontaneous preterm labour at ≤32+6
	  ○ Consider in infants born to mothers with chorioamnionitis, PPROM, or non-reassuring fetal status, should be carefully evaluated
	● Caffeine
	  ○ 10mg/kg load then 5mg/kg/dose daily for maintenance
	● Consider prophylactic indomethacin in ELBW (for PDA closure and IVH prevention)
	  ○ 0.1mg/kg IV q24hr for total three doses
	  ● Fluid boluses or inotropes as needed

Skin Care	● Blood and vernix should be removed with warm water when cardiorespiratory and thermal stability achieved ● Only use neutral pH soap if needed ● Infants <27wks of life - sterile warm water should be used to cleanse skin surfaces for first 5 days (avoid chlorhexidine as it can burn the skin) ● Incubator humidity should be maintained between 75-80% for the first week of life ● Open diaper for 4-7 days (to prevent diaper dermatitis) in infants <27wks ● Swab skin for candida culture (one swab) as per unit policy in ELBW

Investigations	● Bloodwork:
	  ○ On admission
	  ▪ CBC and differential
	  ▪ Glucose
	  ▪ Group and Screen
	  ▪ Blood gas, lactate
	  ▪ CRP and Blood culture if indicated
	  ○ 12-hour bloodwork
	  ▪ Electrolytes + Bilirubin (if baby is very bruised or ABO setup)
	  ▪ Blood gas and lactate (if respiratory or metabolic concern)
	  ○ 24-hour bloodwork
	  ▪ Electrolytes
	  ▪ Newborn screening bloodwork + Bilirubin
	  ○ Further bloodwork is completed depending on ventilation and feeding status
	  ○ POCT glucose testing (ideally from UAC if available) starting at 2 hours of life and every 3-6 hours after that, as per unit hypoglycemia policy
	● Imaging
	  ○ Chest X-ray as needed (whenever a baby requires respiratory support)
	  ○ Abdominal X-ray (AP and lateral dorsal decubitus - Cross Table) – required to check UVC +/- UAC placement or for other indications
	  ○ Head ultrasound at 4 days of life, 10 and 1 month (please see section below)

Handling, Development and Behaviour	● Minimal and gentle handling “Eyes on, Hands Off”. Minimize handling to Q6hr or according to cues ● Hand hugging by family/staff as soon as possible after birth ● No prone positioning until after 72hrs of age (unless required due to respiratory distress) ● Hand hugs and Kangaroo (skin-to-skin) care as soon as possible ● Midline head positioning (use gel rolls to support head). ● Head of bed elevated 15-30 degrees for 72 hours ● Handling and positioning by 2 people whenever possible
Family Centered Care	● Encourage families to touch and photograph infant ● Obtain consent for donor milk and blood transfusions ● Discuss plan and goals of care

6.5 – Preterm Surveillance and Screening

Table 6.5 – General guidelines for initiation of postnatal interventions and screening based on gestational age

Intervention	<29	30	31	32	33 +
Infection prophylaxis until negative culture				≤32+6 or if indicated	
Probiotics			-	≤ 32+6 or ≤ 1500g	
IVH screening 4-7 days post birth			≤31+6 or ≤1500g		
Caffeine initiation			≤31+6 until 34-35		-
Repeat newborn screening at 21d			≤31+6	-	-
ROP Screening		≤30+6 or ≤1250g			
RSV prophylaxis	≤29+6 (or as per unit policy)				

6.6 – Neuroimaging and Intraventricular Hemorrhage

- Pathophysiology
  - Intracranial hemorrhage and white matter insult are the two most significant brain injuries that occur in the preterm period, with the potential for significant adverse neurodevelopmental outcomes (CP, sensory difficulties)
  - The preterm brain is at higher risk of hypoxic or hemorrhagic injury due to its vascular and cellular features. In particular, the germinal matrix, which is present until 34-36wks PMA, is fragile and susceptible to changes in cerebral blood flow that may occur secondary to acidosis, severe RDS, fluctuations in blood pressure, etc.
  - 50% within 24 hours and 90% within 72 hours of delivery
- Complications
  - Subependymal germinal matrix - primary source of bleeding within ventricles
  - Periventricular hemorrhagic infarction (PVHI) and parenchymal lesion (venous infarct) associated with severe IVH. Infarcts can lead to cystic changes in periventricular white matter (forming porencephalic cyst)
  - Post-hemorrhagic ventricular dilation (PHVD) - occurs commonly following severe IVH. Babies with severe IVH will require serial HUS to monitor for PHVD. Depending on the degree of PHVD, babies may require serial LPs to relieve the pressure +/- ventricular shunts – this management is guided by neurosurgery.
    - PHVD occurs typically 7 – 14 days after IVH in 30-50% of severe IVH, may be progressive or non-progressive, and may require surgical drainage or shunt
  - Cerebellar injury - occurs in preterm infants less than 32-34wk GA

- White matter injury (WMI) - may present as cystic periventricular leukomalacia (PVL)
    - Periventricular region located at watershed area and prone to hypoperfusion and ischemia, leading to white matter injury (WMI) and PVL with neurodevelopmental sequelae (spastic diplegia)
    - Typically occurs 2-6 weeks after ischemia, infection, or inflammatory process
  - Grades of PVL
    - Grade 1 - transient increased echogenicity for 7 days or more in periventricular area
    - Grade 2 - small, localized frontoparietal cysts
    - Grade 3 - extensive periventricular cystic lesions
    - Grade 4 - increased echogenicity in deep white matter with extensive cystic lesions
- Papile Grading System
  - Most commonly used grading system for abnormal head ultrasound findings
  - Grade 1-2: Mild IVH
  - Grade 3-4: Severe IVH

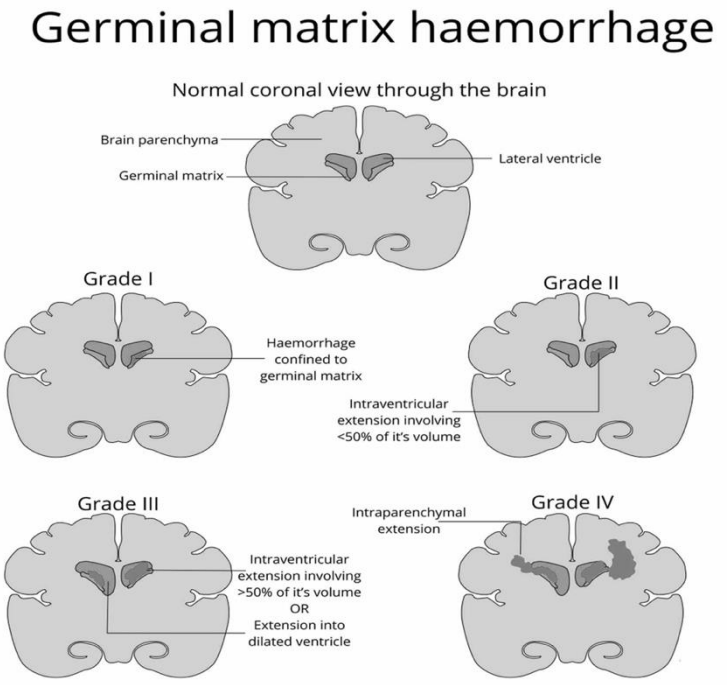


Figure 6.6 Germinal Matrix Hemorrhage Grading
(obtained from https://healthjade.net/germinal-matrix-hemorrhage)

Table 6.6.a – Papile Grading System for IVH

Grade	Description
I	Hemorrhage restricted to subependymal region/germinal matrix (seen in the caudothalamic groove)
II	Hemorrhage into the ventricles and occupying <50% of ventricular space
III	Extension of hemorrhage into dilated ventricles
IV	Intraventricular hemorrhage with parenchymal extension

Table 6.6.b – Neuroimaging Modalities

Modality	Advantage	Disadvantage
Ultrasound	Ideal for detection of IVH, cerebellar bleeds, large cysts and echogenic regions involving WM	Operator dependant quality of images
MRI	Highest standard resolution for assessing WM, low grade IVG, posterior fossa anomalies and cerebral malformations. Also helpful in diagnosing inborn errors of metabolism.	Expensive with higher time requirements. May require sedation and more intensive transportation needs.
CT	Detects calcifications, hemorrhage, edema secondary to VST, masses and structural changes	Exposure to ionizing radiation. Avoided in newborns

Routine head ultrasound (HUS) surveillance for preterm neonate

- < 32 weeks (or ≥ 32+0 to 36+6 weeks GA with additional risk factors)
    - Risk factors - critical care or complicated neonatal course, complicated monochorionic twin pregnancy, microcephaly, sepsis, necrotizing enterocolitis, major surgery, abnormal neurological symptoms or seizures
- Initial imaging - HUS within 4 – 7 days post-delivery
    - Detects most GM-IVH and may detect early dilation
    - Consider early HUS if < 26 weeks for prognosis and decision-making regarding goals of care
- Repeat imaging
    - If < 32 weeks GA - repeat at 4-6 weeks post-delivery to assess for WMI
    - If ≥ 32+0 to 36+6 weeks G - repeat at 4-6 weeks post-delivery only if initial HUS abnormal
- If initial HUS abnormal (> Grade 2 IVH), repeat at 7-10 days later to assess for PHVD
    - If dilation present, weekly repeat imaging initially, then as clinically indicated
- Repeat imaging as needed in the weeks after acute illness (sepsis, NEC) to assess for WMI
- Term-corrected imaging at 37-42 weeks cGA for infants born at < 26 weeks, infants with moderate-severe abnormalities (≥ grade 3 IVH, PHVD or ≥ grade 3 PVL), or additional risk factors/critical illness

Table 6.6.c – Indications for neuroimaging by gestational age

Gestational Age	First Neuroimaging	Repeat Imaging	Presence of Abnormal findings
<26 wks	4-7 days post-birth to detect IVH and early ventricular dilatation	4-6 wks after birth (to detect WMI) Repeat HUS at term-corrected age	If abnormality present on initial imaging (Grade II IVH or higher, or WMI) --> repeat HUS in 7-10 day. If ventricular dilatation or worsening PHVD → higher frequency of HUS (at least 1x/week) Additional imaging to be considered in presence of acute illness (sepsis, NEC) or rapidly increased head circumference MRI at term-corrected age may be considered if mod-severe anomalies on HUS (Grade III or higher IVH, PVHD, PVL, WMI)
26 to 31+6 wks	4-7 days post-birth	4-6 wks after birth (to detect WMI) Repeat HUS at term corrected age only recommended if additional risk factors present or at least moderate anomalies on HUS (Grade III or higher IVH, PVHD)	
32 wks to 36+6wks	4-7 days post-birth only if risk factors present (extensive resuscitation, sepsis, NEC, surgery, abnormal neurologic signs)	Only as necessary	

6.7 – Retinopathy of Prematurity

- Definition
  - A proliferative disorder of the developing retinal blood vessels in preterm infants
  - ROP occurs when the vessels that feed the retina stop growing for a time and then begin growing abnormally and randomly
- Outcomes – poor visual acuity, blindness
- Classification
  - Zones – location of blood vessels
    - Zone 1 - a small area at the heart of the retina (surrounding the central visual area, including the optic nerve)
    - Zone 2 - covers the middle of the retina
    - Zone 3 - runs along the retina's outer edge
    - The lower the zone number, the more serious the ROP
  - Stages – severity of abnormal vascularization
    - Stage 1 - demarcation line separating avascular from vascularized retina
    - Stage 2 - ridge arising in region of demarcation line
    - Stage 3 - extraretinal fibrovascular proliferation/neovascularization extending into the vitreous
    - Stage 4 - partial retinal detachment
    - Stage 5 - total retinal detachment
  - Plus disease
    - Dilation or increased tortuosity of retinal blood vessels in at least two quadrants of the retina
    - Pre-plus disease - more vascular dilatation and tortuosity than normal but not sufficient to be called plus disease
- ROP Disease
  - Threshold ROP - 50% risk of retinal detachment if left untreated therefore should be treated
    - ROP with more than 5 contiguous or 8 cumulative clock hours of stage 3 plus ROP in zone 1 or 2
  - Pre-threshold ROP - ROP with high likelihood of progressing to threshold ROP. Needs very close follow-up or treatment. Includes:
    - Any zone 1 ROP less than threshold
    - Zone 2 stage 2 with plus
    - Zone 2, stage 3 without plus
    - Zone 2, stage 3 with plus but less than 5 contiguous or less than 8 cumulative clock hours of ROP
  - Type 1 ROP - significant changes that require treatment (includes threshold ROP)
  - Type 2 ROP - without significant changes that do not require treatment but must be carefully monitored

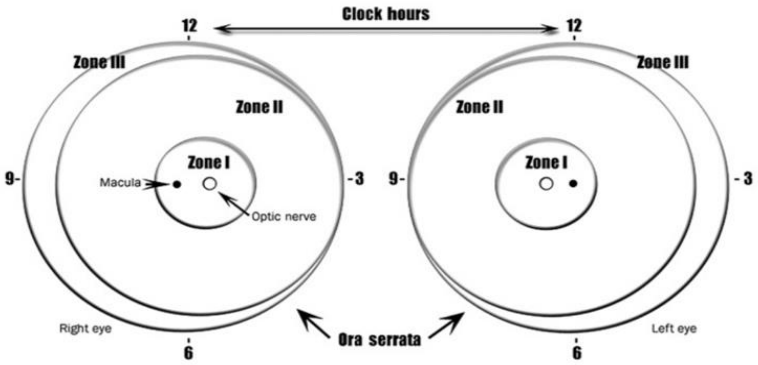


Figure 6.8 – Zones of ROP (from the CPS statement)

- Screening
    - Who
        - All infants born ≤30+6 weeks' GA (regardless of birth weight)
        - Infants having a birth weight ≤1250 g
        - More mature infants believed to be at high risk for ROP
    - When
        - Timing of the first examination should be based on corrected gestational age: GA plus 4 weeks but is never done before CGA = 31 weeks or 4 weeks of age, whichever is later
        - Ex: GA 22 weeks => ROP exam at 31 weeks, GA 30 weeks = >ROP exam at 34 weeks
- Treatment of ROP
    - Retinal laser ablation – decreases production of angiogenic growth factors
    - Recent developments – anti-VEGF therapy (bevacizumab intravitreal injection)
    - Post-treatment follow-up with ophthalmologist as per CPS guidelines

6.8 – Ballard Scoring

- Maturational assessment of gestational age in newly born infants, based on physical and neuromuscular maturity
- Allows estimation of GA from 20-44 weeks of gestation
- Assessment conducted between 30 mins and 96 hours of age (4 days), usually within first 24 hours

Neuromuscular Maturity

Score	-1	0	1	2	3	4	5
Posture							
Square window (wrist)	>90°	90°	60°	45°	30°	0°	
Arm recoil		180°	140°–180°	110°–140°	90°–110°	<90°	
Popliteal angle	180°	160°	140°	120°	100°	90°	<90°
Scarf sign							
Heel to ear							

Physical Maturity

Skin	Sticky, friable, transparent	Gelatinous, red, translucent	Smooth, pink; visible veins	Superficial peeling and/or rash; few veins	Cracking, pale areas; rare veins	Parchment, deep cracking; no vessels	Leathery, cracked wrinkled
Lanugo	None	Sparse	Abundant	Thinning	Bald areas	Mostly bald	
Plantar surface	Heel-toe 40-50 mm: –1 <40 mm: –2	>50 mm, no crease	Faint red marks	Anterior transverse crease only	Creases anterior ⅔	Creases over entire sole	
Breast	Imperceptible	Barely perceptible	Flat areola, no bud	Stippled areola, 1–2 mm bud	Raised areola, 3–4 mm bud	Full areola, 5–10 mm bud	
Eye/Ear	Lids fused loosely: –1 tightly: –2	Lids open; pinna flat; stays folded	Slightly curved pinna; soft; slow recoil	Well curved pinna; soft but ready recoil	Formed and firm, instant recoil	Thick cartilage, ear stiff	
Genitals (male)	Scrotum flat, smooth	Scrotum empty, faint rugae	Testes in upper canal, rare rugae	Testes descending, few rugae	Testes down, good rugae	Testes pendulous, deep rugae	
Genitals (female)	Clitoris prominent, labia flat	Clitoris prominent, small labia minora	Clitoris prominent, enlarging minora	Majora and minora equally prominent	Majora large, minora small	Majora cover clitoris and minora	

Maturity Rating

Score	Weeks
-10	20
-5	22
0	24
5	26
10	28
15	30
20	32
25	34
30	36
35	38
40	40
45	42
50	44

Figure 6.8 - Ballard Scoring System for Maturational Assessment of Gestational Age

6.9 – Pain Management in the Neonate

- Mitigating pain associated with routine neonatal procedures
    - Infants often experience a number of painful procedures in the NICU - suctioning, NG placement, needle insertion. It is important that newborns be routinely assessed for pain using multidimensional tools. If procedures can be avoided, this should be taken into careful consideration
    - Procedures that inflict pain in neonates include the following:
        - Blood sampling (heel lance, venipuncture, arterial puncture)
        - Cannulation of blood vessels (PICC, PIV, PAL)
        - Injections (IM, SQ)
        - Other sampling procedures (LP, suprapubic tap)
        - Chest tube insertion
        - Intraosseous line insertion

Table 6.9 - Mitigating Pain Associated with Routine Neonatal Procedures

Procedure	Analgesic Interventions
Bedside care procedures (needle insertion, suctioning, gavage tube placement, diaper care)	Oral sucrose/glucose Nonpharmacological interventions (non-nutritive sucking, kangaroo care, swaddling) Topical anesthetics may be used with IV insertions, lumbar punctures and venous punctures
Surgery	Opioids or regional anesthesia should be used postoperatively A specified postoperative pain scale should be used with appropriate postoperative analgesia as dictated by the scale Acetaminophen may be used as an adjunct medication (although inadequate data related to dosing <28wks GA)
Intercostal Drains	Insertion: ● Non-pharmacologic measures ● Slow infiltration of skin with local anesthetic (if vitally stable, or once vitally stable) ● Systemic analgesia with rapidly acting opioid (fentanyl) Removal: ● Non-pharmacologic measures ● Systemic analgesia with rapidly acting analgesic
Retinal Examination	Oral sucrose Local anesthetic eye drops
Circumcision	Dorsal penile nerve block (ring block) is most effective form of analgesia Ideally should be combined with oral sucrose and EMLA (lidocaine-prilocaine 5%) cream Glucose and tylenol are not sufficient as independent measures

6.10 – Neonatal Follow-up and Discharge Criteria of the Preterm Infant

Neonatal follow up for infants born at <34 weeks
Discharge between 37 and 42 weeks cGA

1. Infant competencies (physiological maturity)

- Usually achieved between 34 and 36 weeks cGA

Thermoregulation	Maintenance of normal body temperature (approximately 37°C) when fully clothed, in an open cot
Control of breathing	Resolution of apnea of prematurity An apnea-free period of sufficient duration (at least five to seven days is suggested)
Respiratory stability	Maintenance of SaO2 >90% to 95% in room air
Feeding skills and weight gain	Sustained weight gain and successful feeding by breast and/or bottle without major cardiorespiratory compromise

2. Family and home preparation

- Determine family's caregiving and psychosocial readiness for infant's discharge
- Parents should be able to
    - Independently and confidently care for their infant
    - Provide medications, nutritional supplements and any special medical care
    - Recognize signs and symptoms of illness and respond appropriately, especially in emergency situations; and understand the importance of infection control measures and a smoke-free environment.

Preparing for discharge

- Starts at the time of NICU admission
- Promoting family involvement in care
- Discuss anticipated time of discharge with family
- Parental education: Safe sleep/SIDS prevention, CPR, car seat safety, minimizing infection risks
- Evaluation prior to discharge
    - Provincial newborn screening
    - Assessment for RSV prophylaxis and administration
    - Cranial imaging at near-term, if indicated
    - ROP screening, if indicated
    - Hearing screen
    - Immunizations according to chronological age and provincial schedule
    - Pre-discharge physical examination including weight, length, and HC
- Follow-up plan
    - Identification and communication with PCP
    - Follow up with a qualified HCP within 72 hours
    - Medical and surgical follow-up appointments as required, including ROP
    - Neonatal neurodevelopmental follow-up, if indicated
    - Follow-up of hearing and newborn screening results
    - RVS prophylaxis, if required
    - Community resources and supports

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Chapter 7 - Feeding and Nutrition

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7.1 – Total Fluid Intake

- The total amount of all fluids given over a day, expressed in ml/kg/day
- Comprises the total of enteral feeds + continuous IV infusions + parenteral nutrition (usually bolus drugs are excluded, although on occasion, can amount to large volumes)
- Ensure your calculations are accurate as small differences can have a significant impact in neonates; know the actual rate at which infusions are running
- Tracking ins and outs is essential to detect fluid overload or dehydration
- For stable patients, aim for positive fluid balance of ~25-50% of daily fluid intake to account for insensible losses and fluid requirements for growth
    - Consider patient's 24-hour weight change when assessing fluid balance
    - Understand clinical expectations (diuresis in first days of life, fluid retention after surgery)
- Prior to bedside rounds, ensure you are aware of each patient's 24-hour fluid balance and urine output; assess for any acute changes to urine output in recent hours

Table 7.1 - Total fluid intake daily increase (adapted from Jochum et a., 2018)

Age	Preterm**	Term
Day 1	80ml/kg/day	60ml/kg/day
Day 2	100ml/kg/day	80ml/kg/day
Day 3	120ml/kg/day	100ml/kg/day
Day 4	140ml/kg/day	120ml/kg/day
Day 5	160ml/kg/day	140ml/kg/day
Day 6	160ml/kg/day	160ml/kg/day

Note - Some infants require significantly faster TFI increases to meet fluid requirements during diuresis, while some will not need to be advanced as quickly. Use fluid balance, weight change, biochemistry (sodium especially), clinical status to help guide changes to fluid management plan.

7.2 - Breastfeeding, Human Milk, Formula & Feeding Practices

- Breast milk
    - Recommend exclusive breastfeeding for the first 4-6 months of life, then introduction of appropriate complementary foods with continued breastfeeding for up to two years and beyond
    - Breast milk has a unique composition of live cellular components, antibodies, hormones, and other essential components required for growth which cannot be replicated by formulas

    - Benefits of breastfeeding - decrease risk of Sudden Infant Death Syndrome (SIDS), improved neurodevelopment, reduced risk of metabolic disease, decreased incidence of infections including bacterial meningitis, bacteremia, diarrhea, respiratory infections, otitis media, and UTIs, cost savings, maternal health benefits
    - Breast milk is indicated for virtually all infants, including preterm infants. The only exclusions are HIV, HTLV infections and certain chemotherapy drugs.
    - Breast milk may not meet the protein, energy, calcium, or phosphorus requirements of a preterm infant alone. Fortification with a multi-nutrient fortifier (Human Milk Fortifier (HMF)) is required.
    - Lactation milestones
        - Human milk provision and lactation support in the NICU is an area of focus early in an admission. This is because the benefit of human milk early on is like that of other medications provided to a preterm baby. However, support can decrease over the course of the admission which can decrease the likelihood of parents providing milk long-term
        - Monitor for the expression volumes listed in Table 7.2a

Table 7.2a – Milestones for expression of breastmilk (adapted from AboutKidsHealth, 2019)

Day of life	Volume (mL/d)
First days of life	Drops
By day 7	350-500
By day 14	750

    - Breast feeding should be supported at all levels of government and the health system in accordance with WHO's 'Ten Steps to Successful Breastfeeding'
    - Helpful Breastfeeding resources/links
        - AboutKidsHealth
        - Public Health Agency of Canada
- Donor milk (DM)
    - Best milk for a baby is mother's own milk. DM can be used as a bridge for sick, hospitalized neonates while mom establishes her milk supply
    - DM in Ontario is provided to hospital from Roger's Hixon Ontario Human Milk Bank
    - Must meet specific criteria in the NICU to be eligible (currently at SickKids < 34 weeks, < 2000g, post-NEC, post-GI or cardiac surgery).
        - Note - eligibility and discontinuation criteria are site-dependent
    - Parents must consent to use. Counseling should include
        - DM is pasteurised which deactivates any viruses or bacteria
        - Donors are required to be seronegative for Hepatitis B and C, HIV, HTLV
        - Discourage use of unpasteurized informal donor milk sharing which may occur in the community or via the Internet
        - No reported cases of infections with pasteurized DM in Ontario to date
    - DM use in the NICU decreases rate of infections, and necrotizing enterocolitis (NEC) and results in shorter admissions
    - DM contains less protein and fat than mom's own milk. Suboptimal growth is anticipated and must be monitored and intervened on appropriately
- Infant formula
    - Preterm formula
        - Available as ready-to feed, in-hospital only (0.68 or 0.8 kcal/mL)
        - High in protein, calcium, phosphorus, vitamin D, and iron
        - Enfamil A+ Premature, Similac Special Care

- Post-Discharge formula
  - Indicated for preterm infants born <1.2 kg now >2 kg
  - Available as ready-to feed or powder, available in hospital and in the community
    - Can be used exclusively as formula or can be added to human milk
  - High in protein, calcium, phosphorus, vitamin D, and iron (less than preterm formula)
  - Enfamil A+, EnfaCare, Similac Neosure
- Term formula
  - Cow's milk-based formula designed to meet the needs of most term infants
  - Enfamil A+, Similac Advance
- Therapeutic formula
  - Designed for specific clinical indications (i.e. malabsorption, chylothorax)
  - Less palatable, expensive
  - Extensively hydrolyzed - Nutramigen A+, Alimentum,
  - Amino-acid based - PurAmino A+, Neocate

Table 7.2b - Nutrient Content per Litre of breast milk and common formulas (adapted from the SickKids Yellow Card)

Nutrient	Expressed Breast Milk (EBM)				Standard Formulas					Therapeutic Formulas	
	Mature EBM (Donor EBM)	Fortified EBM		EBM + EnfaCare	Enfamil A+ Premature (Preterm Formula)		Enfamil A+ EnfaCare (Post-Discharge Formula)	Enfamil A+ (Term Formula)		Good Start (Whey)	PURAMINO A+ (Free AA)/ Nutramigen A+ (Hydrolyzed Casein)
		EBM +Similac LHMF (Liquid Human Milk Fortifier)									
Concentration (kcal/ml)	0.68	0.74 (1pk HMF: 50ml EBM)	0.8 (1pk HMF: 25ml EBM)	0.8	0.68	0.8	0.74	0.68	0.8	0.67	0.68
Energy (kcal/L)	680	745	800	809	680	810	740	680	810	670	680
Protein (g/L)	12 (9)	20.0	26.7	15.8	20	24	21	14	17	15	18.9
Fat (g/L)	39	39.3	39.5	46	34	41	39	36	43	34	36
Carbohydrate (g/L)	72	79.1	85.0	85	74	89	77	76	88	75	72/70
Sodium (mmol/L)	7.8	11.1	13.8	9.9	17.1	20	11.3	7.9	9.5	7.8	13.8
Potassium (mmol/L)	13.5	22.1	29.3	17.1	17	20	20	18.7	22	18.4	19
Calcium (mmol/L)	7	20.0	30.8	11.2	28	33	22	13.2	15.8	11	15.9
Phosphorus (mmol/L)	4.5	14.1	22.6	7.5	18.1	22	15.8	9.4	11.3	7.8	11.3
Iron (mg/L)	0.4	2.4	4.0	3	12.2	14.6	13.3	12.2	14.6	10	12.2
Vitamin D (IU/L)	20	655	1183	122	1620	1950	520	410	490	400	340

- Advancing feeds
  - Initiation and advancement of enteral feeds can differ based on centre
  - See the following links for protocols at SickKids and Mt. Sinai regarding working up on feeds

- Trophic feeds
    - Small volume (trophic) feeds (<15 mL/kg/d) are not meant to provide nutrition rather, they stimulate the gut in advance of physiologic volume feeds
    - Starting with trophic feeds and then advancing at a weight-appropriate rate promotes feed tolerance and may promote faster achievement of full feeds overall
    - Trophic feeds are particularly important for sick neonates to prevent gut atrophy and to decrease the time it takes to achieve full feeds
- Early total enteral feeding
    - Involves initiating feeds on day of life 1 at 80 mL/kg/d of pasteurized donor human milk via feeding tube, thereby preventing the need for vascular access and parenteral nutrition
- Feed concentration conversions
    - Feed orders often expressed using different units of energy (kcal/mL or kcal/oz)

Table 7.2b - Conversion units for energy

Energy (kcal/mL)	Energy (kcal/oz)	With the addition of HMF
0.68	20	-
0.74	22	1 package in 50 mL EBM (1:50)
0.8	24	1 package in 25 mL EBM (1:25)
0.9	27	-
1.0	30	-

- Oral Feeding
    - Preterm infants should be assessed for oral feeding readiness using a cue-based approach at every feed
    - Infants ≥ 32 weeks PMA and not requiring respiratory support should be allowed to attempt oral feeds if alert and cuing
- Ankyloglossia (tongue-tie)
    - Controversy regarding the diagnosis, implications, and management.
    - Infants with significant breastfeeding difficulty may benefit from frenotomy, but there is limited evidence
    - Refer to Lactation Consultant and Occupational therapist to assist with oral feeding.

7.3 – Growth

- Growth and Nutrition Targets
    - Growth at normal rate using Fenton (preterm) or WHO (term) growth chart (see below)
    - Meet protein-energy requirements
    - See Yellow Card for detailed information
- Growth
    - Main indicator of adequate nutrition in neonates
    - Weight is measured each day as a way of assessing fluid status, not growth
        - Monitor weight gain trends over a longer period of time to better assess growth
    - Length and head circumference must be measured weekly and are better indicators of long-term growth than weight
        - Must measure length using length board for accurate measurement
    - Preterm babies from 28 weeks gestation usually will double weight in 6 weeks, triple in weight in 12 weeks
    - Generally, babies lose ~10% of birthweight in first 4-6 days of life and regain their birthweight by 14 days

Table 7.3a - Growth parameters and expectations for preterm and term babies (adapted from SickKids, 2020)

Measurements	Preterm	Term (first 3 months)
Initial Weight Loss	≤15%	≤10%
	Expect maximum weight loss to occur by ~4-6 days of life	
Weight	15-20 g/kg/day	20-30 g/day
Length	1 cm/week	0.69-0.75 cm/week
Head Circumference	22-30 wks:1 cm/week 30+ wks: 0.5 cm/week	0.5-1 cm/week

- Growth Charts
    - Preterm growth chart
    - Standard WHO growth chart
    - PediTools calculator
    - Down syndrome growth chart
    - Be aware, certain conditions may have specific growth charts

7.4 – IV Fluids, Parenteral Nutrition and Electrolytes

- Fluids
    - Which fluid should be started at birth?
        - If PN is not indicated, D10W is indicated for most infants
            - Na and K are generally not indicated in the first 24-48 hours of life as infants are not yet diuresing
        - Add electrolytes to fluid after 24-48 hours
            - Consider fluid balance, biochemistry
        - Do not delay enteral feeding unnecessarily
- Parenteral Nutrition (PN)
    - Indications for parenteral nutrition
        - Birth weight < 1500g - start electrolyte free PN and lipids as soon as possible after birth
        - Clinically unable to tolerate enteral feeds (NEC, GI obstruction)
    - Availability of PN may differ depending on centre, and pharmacy
        - In some NICUs, standard electrolyte free PN is stocked on the floor which can be started on admission to the unit. Electrolyte Free PN contains protein, D10W, and calcium (usually no Na or K)
    - In newborns requiring prolonged parenteral nutrition, central access is usually required in the form of Umbilical Venous Catheter (UVC) or PICC. Some sites use a BW cut off of 1500g as an indication for UVC insertion at birth.
- Electrolytes
    - Electrolyte panel is usually drawn at 24 hours of life if baby is on IV fluids
    - Pay attention to Na trend
        - If Na high - most likely hypernatremic dehydration as preterm babies have high urine output and insensible losses. Assess fluid balance, clinical status, and increase TFI based on assessment
        - If Na low - may be dilutional hyponatremia so assess fluid balance. If fluid balance is appropriate, baby may be losing Na in the urine due to renal immaturity. Consider increasing PN Na or adding oral Na supplements for infants tolerating feeds

7.5 – Supplementation - Vitamins and Minerals

- Metabolic bone disease (osteopenia) of prematurity (values may vary depending on site)
    - Screen babies born < 34 weeks
    - Monitor ionized calcium, phosphorus and urea at baseline and every 2-3 thereafter
        - Target Phosphate > 2 mmol/L
        - If alkaline phosphatase (ALP) > 500 U/L, will require close monitoring
        - Supplement with phosphate and calcium, as required
- Vitamins
    - Most babies will require a daily vitamin (D-Vi-Sol, Tri-Vi-Sol)
    - Provide Vitamin D daily
        - All infants in the first year of life should receive
            - 400IU vitamin D (either as a supplement or from diet)
            - Formula-fed infants require 1L or more of formula to achieve the recommended amount before they should stop their vitamin D supplement
            - 800IU vitamin D for infants in Northern or indigenous communities during winter months
        - Note - some infants will not require vitamin D supplementation as their intake requirements will be met by their feeds

Table 7.5a - Common vitamin brand and content

	Tri-Vi-Sol	D-Vi-Sol
Vitamin D (IU/mL)	400	400
Vitamin C (mg/mL)	30	0
Vitamin A (IU/mL)	750	0

- Probiotics
    - Prescribed to preterm babies for NEC prevention
    - Evidence shows reduced mortality and decreased time to reach full enteral feeds
    - Initiated with first enteral feed
- Iron
    - Routinely recommended for infants with BW < 2.5 kg AND predominantly breastfed (more than 50% of intake) to be started at 10-14 days of life
        - Note - some infants will not require iron supplementation in NICU as their intake requirements will be met by their feeds

Table 7.5b - Dosing for iron (adapted from Unger et al., 2019)

Elemental iron supplementation	Birth weight	
	2.0 to 2.5 kg	Less than 2.0 kg
Dose (usually start day 10-14)	1 - 2mg/kg/day	2 -3 mg/kg/day
Duration	6 months	1 year

- Sodium
    - Poor growth can occur when sodium is depleted, even in the presence of appropriate caloric and protein intake.
    - Consider renal losses (immature kidneys), stoma losses
    - Sodium depletion can occur even if the patient's serum sodium level is normal (135 – 145 mmol/L) as serum sodium is influenced by the patient's fluid status
    - Monitoring urine sodium is recommended for a more accurate reflection of total body sodium. Urine sodium monitoring is indicated for patients with stomas and preterm patients exhibiting suboptimal weight gain
        - Aim for urine sodium 30-50 mmol/L and urine sodium > urine potassium
    - Diuretics can increase sodium losses in the urine. Therefore, urine sodium is not an appropriate indicator of total body sodium for patients receiving diuretics

7.6 – Discharge, Nutrition & the Preterm Infant

- CPS outlines general criteria preterm infants must meet before discharge home. Nutrition, recommendations include ability to safely feed orally and gaining weight appropriately
- HMF and preterm formulas are only available in hospital. Adjust feeding plan when approaching discharge, as required, to include products available to family at home. Ensure adequate oral intake and growth with this plan before discharge.

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Chapter 8 – Neurology

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8.1 – Comprehensive Neurological Examination

- Considerations
  - Neurological findings change with maturation of the newborn
  - Medications, interventions, or physiological state may alter examination (sedatives, cooling, stage of sleep)
- Level of consciousness
  - Multiple behavioural states of healthy newborns (active sleep, quiet sleep, alert)
  - Abnormal states - coma, lethargy, irritability, hyperexcitability, high-pitched/abnormal cry
- General features
  - Dysmorphic features, dermatologic manifestations (port wine stain, cafe au lait macules)
  - Head shape, circumference (plot on growth chart), fontanelles
- Posture and tone
  - Preterm limbs in passive extension at rest, progressive increases in flexion with maturation
  - Arthrogryposis/contractures (congenital myasthenia gravis, myopathies, etc.)
  - Assessing tone - head lag, head control on sitting position, ventral and vertical suspension, arm/leg traction and recoil, scarf sign, popliteal angle; Note rigidity, spasticity, opisthotonus
- Movements
  - Normal - smooth, symmetric, and varied movements of all limbs
  - Jitteriness - suppressible (hypoglycemia, drug withdrawal, mild HIE)
  - Unilateral limb immobility (plexus injury, clavicle fracture)
  - Exaggerated startle (glycine encephalopathy, CNS injury)
  - Persistent choreoathetoid movements (>2-3 weeks old) (injury localizing to basal ganglia)
- Vision and abnormal eye movements
  - Pupillary light response (not present until 30 weeks GA) and red reflexes
  - Abnormal eye movements - horizontal jerky (seizure in contralateral hemisphere), tonic horizontal (ipsilateral CNS lesion), tonic downward/sun-setting (pretectal brainstem, increased ICP), unilateral dilated non-reactive pupil (uncal herniation).
- Hearing - hearing screen, startle, head turning to noise
- Facial movements
  - Should be symmetrical including crying and blinking, attention to palpebral fissures, nasolabial folds and mouth corners may reveal subtle asymmetry.
  - Assess suck and rooting reflexes, tongue fasciculation is abnormal (SMA or brainstem injury)
- Deep tendon reflexes
  - Absent reflexes suggest anterior horn cell lesion or neuropathy, depressed suggest myopathy or neuromuscular junction disorder, increased in upper motor neuron lesions
  - A few beats of clonus may be seen in healthy neonates
- Primitive Reflexes (see Chapter 1 – Routine Newborn Care)
  - Palmar/plantar grasp, Moro, asymmetric tonic neck reflex, stepping reflex, Galant reflex

8.2 – Hypotonia

Table 8.2a - Features of central vs peripheral hypotonia

	Central	Peripheral
Tone	Axial > appendicular hypotonia Fisting of hands, scissoring of legs	Axial = appendicular hypotonia
LOC	Variable, obtundation, encephalopathy	Alert, awake, preserved social interactions
Weakness	Normal to mild	Marked
Muscle bulk	Normal to disuse atrophy	Reduced
Reflexes	DTR normal to increased Extensor plantar response Sustained ankle clonus Preserved or exaggerated postural reflexes	DTR reduced or absent Diminished or absent postural reflexes
Associations	Seizures Apneas Feeding difficulties Microcephaly or macrocephaly Global developmental delay Dysmorphic appearance	Feeding difficulties Congenital contractures Fasciculations Respiratory difficulties Paradoxical chest wall movement Myopathic facies

Table 8.2b - Causes of neonatal hypotonia by location in the nervous system.

Cerebrum	Spinal cord	Motor neuron
Encephalopathy (HIE) Drugs/Substances Genetic disorders - Down syndrome, Prader-Willi, Edwards, etc. CNS malformations	Spinal cord injury Spinal muscular atrophy Hypoxic-ischemic myelopathy Neurogenic arthrogryposis	Myelination disorder
Neuromuscular junction	**Muscle**	**Metabolic or multisystem disease**
Transient acquired neonatal myasthenia Congenital myasthenia Magnesium toxicity Aminoglycoside toxicity Infantile botulism	Congenital myotonic dystrophy Congenital muscular dystrophy Congenital myopathy	Prematurity Sepsis Inborn error of metabolism Hypoglycemia

Approach to management of hypotonia

- Respiratory support, rule-out reversible/life-threatening causes (sepsis, hypoxia, hypoglycemia, dyselectrolytemia), empiric antibiotics if sepsis suspected, and cranial ultrasound to assess for hemorrhage

8.3 – Hypoxic-Ischemic Encephalopathy (HIE)

Pathophysiology

- Acute or chronic impairment of gas exchange → hypoxia and ischemia of brain
- Etiology - placental (contractions, abruption, insufficiency), umbilical (cord compression/prolapse), maternal (hypotension/hypoxia) or neonatal (difficult delivery, inadequate resuscitation)
- Other causes of neonatal encephalopathy
    - Sepsis, meningitis, maternal substance use/neonatal abstinence syndrome, maternal sedation/anesthesia, metabolic disturbances or diseases (hypoglycemia, hyperbilirubinemia, hyponatremia, hypocalcemia, amino acidopathy, molybdenum cofactor deficiency), CNS disease/malformations, seizures, etc.
- Neuroprotective interventions (therapeutic hypothermia) targeted during latent period (1 to 6 hours following resuscitation/reperfusion) before irreversible failure of mitochondrial function

Criteria for therapeutic hypothermia
(Adapted from Lemyre & Chau, 2018)

Must meet all of the following criteria

1. GA ≥ 36 weeks*
2. Age ≤ 6 hours post-delivery
3. Evidence of intrapartum hypoxia defined as either a. OR b. below
    a. Cord or postnatal blood gas within 1 hour pH ≤ 7.0 or BE ≥ -16
    b. Gas not available or cord/1 hour postnatal blood gas pH 7.01 to 7.15 or BE ≥ -10 to -15.9 AND both of the following
        i. Evidence of an acute perinatal event (abruption, uterine rupture, maternal trauma or cardiopulmonary arrest, late or variable decelerations, cord prolapse, inadequate resuscitation, etc.)
        ii. APGARS ≤ 5 at 10 minutes or continued assisted ventilation/resuscitation at 10 minutes
4. Signs of moderate to severe encephalopathy defined as presence of clinical seizures or ≥3 of the 6 items in the moderate to severe categories using the modified Sarnat score (see below)

* The Hospital for Sick Children clinical pathway includes gestational age ≥ 35 weeks and weight over 1.8kg

Exclusion criteria

1. Significant coagulopathy refractory to treatment
2. Severe morbidity/ major congenital abnormalities for which no further aggressive management is indicated
3. No severe head trauma or intracranial hemorrhage
4. Severe intrauterine growth restriction

Assessment and Management

- See Criteria for Therapeutic Hypothermia above
- Clinical assessment includes evidence of acute perinatal event, APGAR scores, physical examination to determine modified Sarnat or Thompson score (see Table 8.3a and 8.3b)
- Investigations - cord or early postnatal (within 1 hour of life) blood gas
- Management - therapeutic hypothermia (see Figure 8.3b) initiated within 1-6 hours from injury
- Supportive care during therapeutic hypothermia
    - FEN - NPO with maintenance fluids (avoid fluid overload)
        - Glucose q4-6h, maintain normoglycemia (2.6 - 8.0 mmol/L)
        - Monitor electrolytes - correct hypocalcemia, hypomagnesemia, hyponatremia
    - Cardiovascular - maintain MAP 40-50, consider invasive BP monitoring
        - If hypotensive - fluid resuscitation, ionotropes as needed, R/O cardiac dysfunction and/or adrenal insufficiency
    - Respiratory - adequate oxygenation, avoid hyperoxia/hypocapnea, trend blood gas and monitor acidosis
    - Renal - trend Cr, urea, electrolytes, and urine output, monitor for fluid overload, SIADH or acute tubular necrosis (ATN)
    - Hepatic - monitor for hyperbilirubinemia, liver enzymes for hepatic injury
    - Metabolic - consider metabolic screen including lactate and ammonia
    - Neurological - arrange for aEEG +/- cEEG, prompt treatment of seizures per protocol (see Section 8.4)
    - Hematologic - monitor for anemia, pRBC if Hb low (consider IVH if downtrending Hb)
        - Monitor for coagulopathy/DIC and correct as indicated
    - Pain/Sedation - sedation if excessive shivering or agitation (dexmedetomidine)
        - Monitor and consider treatment for pain with low dose opioid infusion

Table 8.3a - Modified Sarnat score

	Mild	Moderate	Severe
LOC	Hyper-alert	Lethargy	Stupor/coma
Spontaneous activity	Normal	Decreased activity	No activity
Posture	Mild distal flexion	Distal flexion, full extension	Decerebrate (arms extended and internally rotated, legs extended with feed in forced plantar flexion)
Tone	Normal	Hypotonia (focal, general)	Flaccid
Primitive reflexes	Suck weak Moro strong	Suck weak Moro incomplete	Suck absent Moro absent
Autonomic system	Pupils dilated Tachycardia Normal respirations	Pupils constricted Bradycardia Periodic breathing	Pupils skew deviation, dilated, non-reactive to light Variable HR Apnea

Table 8.3b - Thompson score (Score of 0-10 indicates mild HIE, 11-14 moderate HIE, >=15 severe HIE)

Score	0	+1	+2	+3
Tone	Normal	Hypertonia	Hypotonia	Flaccid
LOC	Normal	Hyperalert, stare	Lethargic	Comatose
Fits	Normal	Infrequent (<3/day)	Frequent >2/day	
Posture	Normal	Fisting/cycling	Strong distal flexion	Decerebrate
Moro reflex	Normal	Partial	Absent	
Grasp	Normal	Partial	Absent	
Sucking reflex	Normal	Poor	Absent/bites	
Respiration	Normal	Hyperventilation	Brief apnea	Intermittent PPV (apnea)
Fontanelle	Normal	Full not tense	Tense	

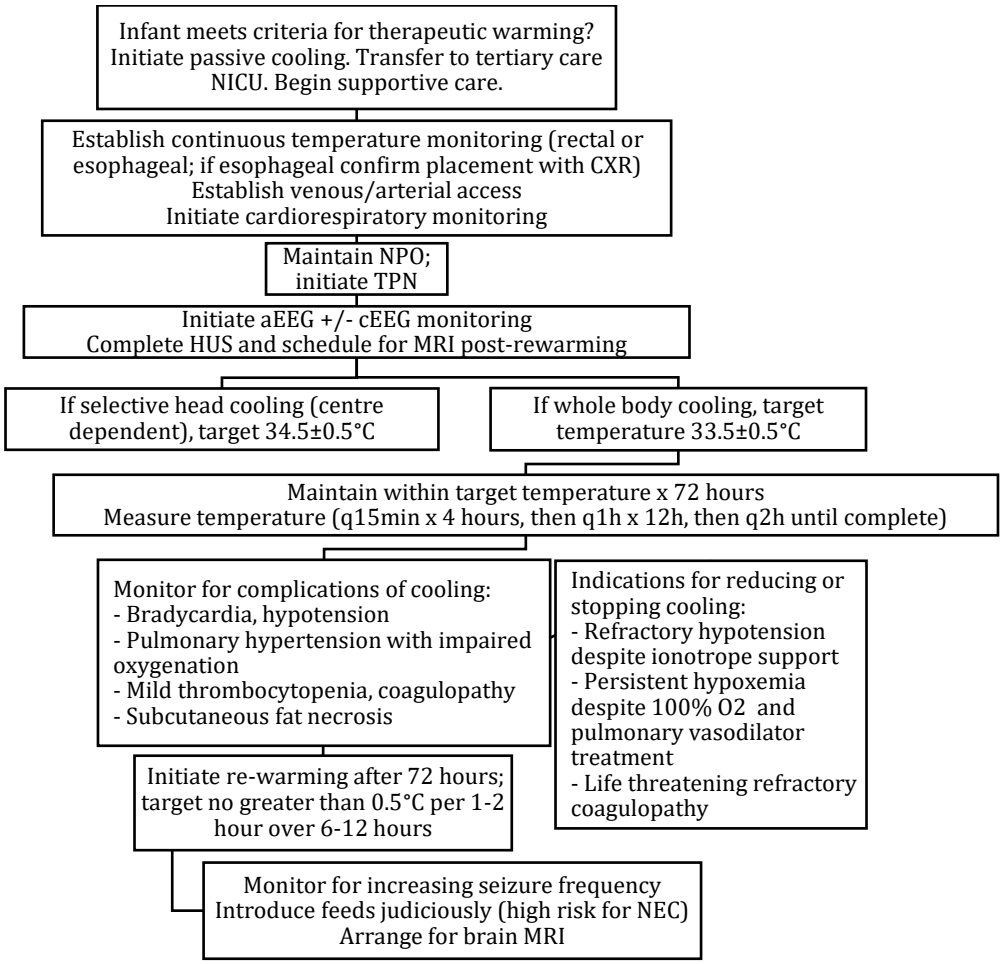

Figure 8.3b - Management of hypoxic-ischemic encephalopathy (Adapted from Hypoxic Ischemic Encephalopathy Clinical Pathway, The Hospital for Sick Children, 2020)

8.4 – Neonatal Seizures

Causes

- Neurologic
  - HIE, CNS malformation, intracranial hemorrhage (intraventricular, intraparenchymal, subarachnoid, subdural), neonatal stroke
- Neonatal-onset epilepsy
  - Benign neonatal or benign familial neonatal seizures
  - Neurocutaneous syndromes
  - Early myoclonic epilepsy
  - Early infantile epileptic encephalopathy (Ohtahara syndrome, infantile spasms)
  - Genetic epilepsy syndromes
- Infection
  - Sepsis, bacterial meningitis/encephalitis, viral encephalitis (HSV, enterovirus, parechovirus), TORCH/congenital infection
- Drug - withdrawal or intoxication

- Metabolic
    - Hypoglycaemia, hypocalcemia, hypomagnesemia, hyperbilirubinemia, etc.
    - Inborn errors of metabolism (urea cycle defects, nonketotic hyperglycemia, organic acidurias, aminoacidopathies)
    - Pyridoxine-dependent epilepsy, pyridoxamine 5'-phosphate oxidase deficiency, biotinidase deficiency, molybdenum cofactor deficiency

Clinical features (seizure semiology)

- *Note - generalized tonic-clonic seizures are rare in this age group*
- Focal clonic (rhythmic, uni- or multifocal synchronous or asynchronous, non-suppressible)
- Focal tonic (sustained posturing or eye deviation, non-suppressible, non-provokable)
- Myoclonic (random single contractions of muscle groups, generalized, focal or fragmentary, may be provoked or intensified by stimulation)
- Spasms (flexor or extensor, often clustered, non-suppressible and non-provokable)
- Generalized tonic (sustained symmetric posturing, non-epileptic without EEG correlate)
- Motor automatisms (random/roving eye movements, sucking, chewing, tongue protrusion, rowing/swimming movements, pedaling/bicycling, complex purposeless movements; non-epileptic without EEG correlate)
- Subclinical seizures (by definition asymptomatic)

Assessment and management

- If seizures identified, EEG monitoring should continue until minimum 24 hours seizure-free
- See Figure 8.4a for guidelines on management of neonatal seizures

EEG modalities

- Continuous EEG (cEEG) - gold standard is multi-channel video cEEG
    - For newborns with
        - Definite or suspected clinical seizures
        - Definite or suspected electrographic seizures on aEEG
        - Abnormal background activity on aEEG
- Cerebral function monitoring (CFM)/Amplitude integrated EEG (aEEG)
    - aEEG uses compressed signals and fewer leads than cEEG
    - Lower sensitivity and specificity than cEEG but more readily available
    - Allows for monitoring of trends in brain signalling by non-expert bedside staff
    - Characterization of abnormal baseline signalling patterns and detection of clinical and subclinical seizures
    - Data collected includes - background activity, sleep-wake cycling, presence of seizures
        - Background activity (upper and lower margin μVolts)
            - Continuous normal voltage (upper >10, lower >5)
            - Discontinuous normal voltage (upper > 10, lower <5)
            - Burst suppression (upper <10, lower <5 with bursts)
            - Suppression/Low voltage (upper <10, lower < 5 without bursts)
            - Flat tracing (upper <5, lower <5; isoelectric)

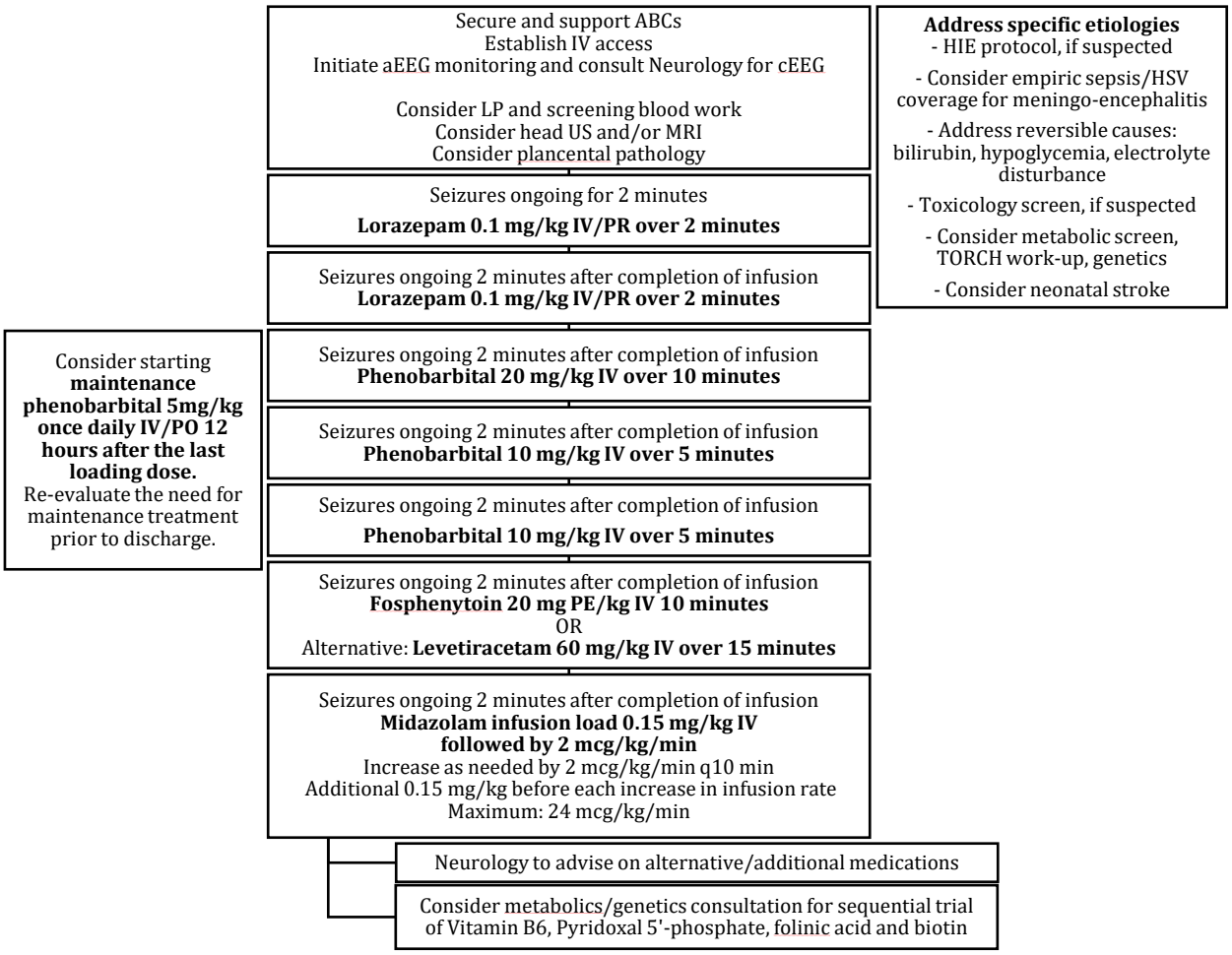

Figure 8.4 - Management of seizures - GA ≥ 34 weeks and PMA < 44 weeks (Adapted from The Hospital for Sick Children Electronic Formulary, 2020)

8.5 – Neonatal Stroke

Types of stroke

- Arterial ischemia, cerebral sinovenous thrombosis, hemorrhagic stroke

Clinical features

- Seizures (particularly focal seizures), altered mental status or encephalopathy, abnormal tone (diffuse or focal), focal motor or sensory abnormality, apnea, poor feeding

Risk factors

- Maternal
  - Autoimmune/prothrombotic conditions (APLA), diabetes, pre-eclampsia, cocaine use
  - Complicated L&D (chorioamnionitis or infection, prolonged ROM, placental thrombosis)
- Neonatal/fetal
  - Dehydration, hypoglycaemia, infection, polycythemia, twin-twin transfusion, congenital heart disease (CHD), neonatal encephalopathy, inherited thrombophilia
- Arterial ischemia
  - Embolic disease - CHD, endocarditis, transcardiac (placental thrombus via PFO)
  - Meningitis/sepsis, trauma
  - Prothrombotic condition - genetic thrombophilia, DIC/sepsis, polycythemia
  - Arteriopathy - malformations (PHACES), trauma (cervical artery dissection)
  - Collagenopathy - COL4A
  - Degenerative (Menkes disease)

- Hemorrhagic
    - Hemorrhagic conversion of arterial or venous ischemia
    - Periventricular hemorrhage in prematurity
    - Primary intracerebral hemorrhage
        - Idiopathic
        - Bleeding diathesis (thrombocytopenia, coagulopathy, hemophilia, Vit K deficiency)
        - Vascular anomalies (cavernous malformation, AVM, aneurysm)

Investigations

- Investigations dependent on type of stroke
- Neuroimaging - MRI > HUS, consider CT only when necessary (radiation)
- Neurovascular imaging - consider MRA/MRV to assess for vascular malformation or arteriopathy
- EEG for seizures
- Consider echocardiogram for assessment of shunt, thrombus, congenital heart disease
- Consider assessment for coagulopathy/thrombophilia as indicated (maternal antibodies/APLA testing, protein S and C, placental pathology, etc.)

Management considerations

- Arterial ischemia - in rare circumstances where recurrence is higher risk, consider antiplatelet therapy or LMWH/UFH anticoagulation
- Cerebral sinovenous thrombosis - consider anticoagulation with UFH or LMWH
- Hemorrhagic stroke - correction of severe thrombocytopenia, coagulopathy, factor deficiency
- Ventricular drainage ± shunt if hydrocephalus present

Supportive measures

- Oxygenation and ventilation, maintain hydration, manage seizures, antibiotics if infection suspected
- Correct anemia, electrolyte/metabolic disturbances (acidosis, hypoglycemia, hypocalcemia, etc.)

8.6 – Neurological Complications of Prematurity

Risk factors

- Prematurity and low birth weight (especially < 32 weeks GA or <1000g)
- Birth outside tertiary care centre
- Absence of prenatal corticosteroid use
- Complicated twin pregnancy
- Chorioamnionitis
- Cerebral blood flow instability - respiratory distress, acidosis, hypo- or hypercarbia, hypotension/hypertension or BP variability, patent ductus arteriosus
- Critical illness (need for mechanical ventilation, need for early inotropes)
- Post-natal illness (sepsis, NEC, surgery, etc.)
- Coagulopathy

Prevention of acute brain injury in preterm infants – see chapter 6

Intraventricular hemorrhage (IVH)

Periventricular leukomalacia (PVL)

Management of neurological complications of prematurity

- Management involves monitoring and supportive measures including
    - Correcting coagulopathy, pRBC as needed, maintaining normotension +/- inotropic support, appropriate ventilation, correction of acidosis, seizure treatment and HUS surveillance

Routine head ultrasound (HUS) surveillance for preterm neonate

8.7 – Hydrocephalus

Etiology

- Acquired - post-hemorrhagic/traumatic, post-infectious (bacterial meningitis, encephalitis, tuberculosis), obstructive (tumour, cyst, etc.), choroid plexus papilloma

- Congenital - aqueductal stenosis, CNS malformation (Dandy-Walker, Chiari malformation, etc.), genetic or syndromic (X-linked hydrocephalus, trisomies, etc.) craniosynostosis, neural tube defects (myelomeningocele, encephalocele, etc.), hydranencephaly, intrauterine infection (Rubella, CMV, toxoplasmosis, lymphocytic choriomeningitis, syphilis, Zika), CNS tumour

Clinical features

- Irritability, lethargy, poor feeding, recurrent vomiting, high-pitched cry, seizures, apneas, macrocephaly or inappropriate increase in head circumference
- Bulging fontanelle, splayed sutures, prominent scalp veins, "sunsetting" eyes, papilledema, pupillary changes, stiffness

Assessment and management

- Antenatal diagnosis of ventriculomegaly accomplished by fetal US +/- fetal MRI
- Postnatal diagnosis and monitoring accomplished by HUS (consider MRI to assess for etiology)
- Medical therapy for raised ICP often ineffective
- Mainstay of treatment is neurosurgical intervention
    - Temporary CSF diversion - ventricular access device, external ventricular drain, ventriculosubgaleal shunt, and serial lumbar punctures
    - Permanent CSF diversion - ventriculoperitoneal shunt, ventriculopleural shunt, ventriculoatrial shunt, endoscopic third ventriculostomy +/- choroid plexus cauterization
- Complications of shunts include obstruction/underdrainage, infection, and overdrainage (slit ventricle syndrome, subdural hematomas, craniosynostosis, etc.)

8.8 – Degenerative Disorders

- In general, disorders of gray matter manifest as early-onset seizures, myoclonus, spikes or sharp activity on EEG, failure of cognitive development, and retinal disease
- Disorders of white matter are characterized by early marked motor deficits and slow activity on EEG
- Others involve specific organelles or brain regions; or involve both grey and white matter

Table 8.8 - Clinical features and examples of degenerative disorders

	Grey matter		**White matter**	**Grey and white matter**
	No visceral storage	Visceral storage		
Clinical Features	• Myoclonus • Hypotonia • Weakness • Cherry-red macula • Seizures • Macrocephaly or microcephaly • Apnea • Developmental arrest • Visual or auditory deficit	• Hepatosplenomegaly • Feeding impairment • Hypotonia • Weakness or spasticity • Cherry-red macula • Developmental arrest • Strabismus • Trismus • Failure to thrive • Coarse facies • Dermatologic abnormalities	• Hypotonia or hypertonia • Spasticity • Tonic spasms • Opisthotonus • Macrocephaly or microcephaly • Seizures • Poor visual fixation • Developmental arrest • Poor feeding • Abnormal eye movements • Oral-facial dyskinesia • Head titubation	• Facial dysmorphisms • Hypotonia • Weakness • Feeding impairment • Visual and/or auditory deficit • Oculomotor deficit • Seizures • Developmental arrest • Microcephaly • Cardiac, liver, or renal abnormalities • Extrapyramidal or pyramidal motor features

Examples	• Tay-Sachs disease (GM2 gangliosidosis) • Congenital neuronal ceroid-lipofuscinosis • Alpers disease • Menkes kinky hair disease	• GM1 gangliosidosis • GM2 gangliosidosis (Sandhoff variant) • Niemann-Pick disease • Gaucher disease • Farber disease • Infantile sialic acid storage disease	• Canavan disease • Alexander disease • Krabbe disease • Pelizaeus-Merzbacher disease • Leukodystrophy with cerebral calcifications and cerebrospinal fluid pleocytosis (Aicardi-Goutieres disease)	• Peroxisomal disorders - neonatal adrenoleukodystrophy, Zellweger syndrome • Mitochondrial disorder - Leigh syndrome, other mitochondrial encephalopathies • Disorders with cerebellar pontine hypoplasia (congenital disorders of glycosylation, pontocerebellar hypoplasia) • Neurotransmitter defects (serine synthesis deficiency) • Rett syndrome

8.9 – Neuromuscular Disorders

Table 8.9 - Clinical features, investigations, and management of neuromuscular disorders of the newborn

	Clinical Features	**Investigations**	**Management**
Congenital myotonic dystrophy	• Antenatal polyhydramnios, reduced fetal movements, prematurity • Facial diplegia • Hypotonia • Respiratory muscle weakness • Feeding difficulties • Talipes equinovarus, flexion contractures of the hips and knees • Atrophy • Weakness or paralysis • Areflexia or hyporeflexia • Maternal facial weakness or delayed relaxation of fist	• Normal CSF and NCS • CPK level variable • CXR thin ribs +/- diaphragmatic elevation • Immature muscle on biopsy • Myotonia on EMG • Genetic testing of DMPK gene on chromosome 19	• Respiratory support • Feeding support • Myopathy support (orthotics) • Arthrogryposis typically non-surgical management
Congenital muscular dystrophy	Clinical features dependent on specific etiology (Walker-Warburg syndrome, muscle-eye-brain disease, merosin-negative or merosin-positive congenital muscular dystrophy) • Hypotonia • Weakness • Micro- or macrocephaly • Ocular abnormalities • CNS malformations • Contractures • Feeding difficulties	Investigations dependent on etiology • Often elevated CPK • Myopathy on EMG • Neuroimaging suggestive of diagnosis • Dystrophic changes on muscle biopsy • Genetic testing may be diagnostic	• Stretching exercises for contracture prevention • Feeding support
Spinal muscular atrophy	• Antenatal reduced fetal movements • Severe generalized hypotonia • Severe weakness, proximal > distal, generalized • Areflexia • Bell-shaped thorax, paradoxical breathing • Weak cry, poor suck/swallow • Tongue fasciculations • Relatively preserved facial movements, extraocular movements, and sensorium	• Normal or near normal CPK and NCS • EMG and biopsy rarely utilized due to molecular testing • Genetic testing for pathogenic mutations of SMN1 is diagnostic	• Respiratory support • Feeding support • Novel disease-modifying therapies (nusinersen, onasemnogene abeparvovec, risdiplam)

Congenital myopathy (nemaline myopathy)	Onset dependent on etiology, clinical course is typically non-progressive • Antenatal polyhydramnios and reduced fetal movements • Hypotonia • Weakness (proximal > distal) • Tendon reflexes decreased proportional to weakness • Congenital hip dislocation • Arthrogryposis • Respiratory muscle weakness • Feeding difficulties	• Muscle biopsy often diagnostic • Normal or mildly elevated CPK • Normal or myopathic EMG • Genetic testing may be diagnostic	• Stretching exercises for contracture prevention • Feeding support • Respiratory support
Transient myasthenia gravis	10-20% of mothers with myasthenia gravis, onset within hours of delivery (<3 days) • Suck/swallow impairment, feeding difficulty, need for gavage feeds • Respiratory muscle weakness • Poor secretions handling • Weak cry • Facial diplegia • Generalized weakness • Hypotonia • Ptosis and/or oculomotor abnormalities less common • In severe cases, fetal akinesia deformation sequence (polyhydramnios, short umbilical cord, pulmonary hypoplasia, arthrogryposis, craniofacial anomalies)	• Normal CPK and CSF • Standard EMG is normal • Normal muscle biopsy (often not required) • Diagnosis often established by clinical improvement with AChEI • Diagnosis may be confirmed by myasthenic phenomenon on nerve stimulation studies with improvement after AChEI administration	• Feeding support (smaller feed volume, frequent feeds, gavage feeds) • Respiratory support/ventilation as required • AChEI IM or SC (neostigmine), transition to PO once swallowing improved • Typical improvement within 2 – 4 weeks • Average duration of pharmacotherapy is 4 weeks
Congenital myasthenic syndromes	Variable onset and symptoms based on specific etiology • Fatigable weakness • Prominent bulbar and oculomotor weakness (ophthalmoplegia, ptosis, respiratory distress, feeding difficulties) • Hypotonia • Apnea • Arthrogryposis	• Diagnosis may be established by clinical improvement with AChEI • Genetic testing may be diagnostic	• Feeding support • Respiratory support/ventilation as required • Specific therapies dependent on etiology/mutation (pyridostigmine, albuterol, ephedrine, etc.)

8.10 – CNS Malformations

Neural tube defects

- Primary neural tube defects (myelomeningocele, encephalocele, anencephaly) and secondary neural tube defects (meningocele, lipomeningocele, sacral agenesis/dysgenesis, diastematomyelia, and myelocystocele)
- Risk factors - folic acid deficiency, maternal anticonvulsant use (VPA, carbamazepine), maternal diabetes, prenatal irradiation, maternal hyperthermia, consanguinity, positive family history, chromosomal or syndromic disorders
- Diagnosis - often established with prenatal testing (maternal serum AFP, prenatal US +/- fetal MRI) or post-natal examination

- Physical examination
    - If open defect, inspect for CSF leak, size of defect, and spine curvature
    - If suspected closed defect, note hemangioma, hairy patch, sinus tract or deep dimple especially if outside gluteal cleft
    - Record head circumference and monitor anterior fontanelle/sutures
    - Defer Barlow and Ortolani examination for open defects until post-operative
- Management (open defects)
    - Neurosurgical intervention - fetal vs. post-natal surgery defect closure, hydrocephalus management
    - Obstetrical - elective Caesarian delivery preferred
    - Neurological - prone position with sterile saline-soaked gauze over defect with plastic wrap, HUS for hydrocephalus/Chiari malformation, seizure management
    - ID - empiric meningitis prophylaxis (ampicillin + gentamicin)
    - Urologic - assess for renal/urinary abnormalities, assess for urinary retention/neurologic bladder
- Complications
    - Neurological - hydrocephalus, hearing and/or visual impairment, motor impairment, cognitive/intellectual impairment
    - Growth and nutrition - feeding difficulties, choking/aspiration, may require gavage feeding, often require bowel regimen for bowel-bladder dysfunction
    - Urologic - assess for elevated post-void residuals, consider VCUG and/or urodynamic studies, CIC as needed, consider prophylactic antibiotics as indicated
    - Orthopedic - CXR for rib or cardiac abnormalities, spine X-ray for vertebral abnormalities, consider limb X-rays if concern for abnormality, consider hip US if concern for hip dysplasia, monitor for scoliosis, osteopenia/fractures, contractures
    - ID - surgical site infection, shunt infection
    - Other - decubitus ulcers, latex allergy, endocrinopathy

Holoprosencephaly

- Developmental defect of embryonic forebrain, often associated with midfacial defects (single central upper incisor, depressed/narrow nasal bridge, hypotelorism, ophthalmologic abnormalities including cyclopia, proboscis, single nostril, etc.)
- Etiology likely multifactorial (genetic + environmental)
- Clinical presentation includes
    - Failure to thrive, feeding difficulties, lethargy, hypotonia, seizures/epilepsy, hydrocephalus, dystonia, movement disorders, autonomic dysfunction, and hypothalamic/pituitary dysfunction (including diabetes insipidus, growth hormone deficiency, adrenal hypoplasia, hypogonadism, or thyroid hypoplasia)
- Investigations
    - Prenatal diagnosis often via prenatal US/fetal MRI
    - Post-natal diagnosis via MRI
- Management (if compatible with life)
    - Genetics consultation to assess for syndromic/chromosomal causes
    - Assess for complications/associations (consider EEG if seizures/epilepsy, dystonia management, pituitary function screen)
    - Feeding support (tube feeding, dysmotility and gastroesophageal reflux management)
    - Assess for hydrocephalus and need for surgical intervention
    - If midfacial defects present, consider ENT or ophthalmology assessment
    - Long-term neurodevelopmental follow-up and therapy

Agenesis of the corpus callosum

- Causes include genetic (syndromic or monogenic), infectious (TORCH infections, Zika virus), vascular, or toxic (fetal alcohol syndrome)
- Associated with other CNS anomalies and non-CNS anomalies
- Diagnosis established by prenatal or postnatal neuroimaging
- Clinical manifestations and outcomes dependent on cause and presence of associated abnormalities

Septo-optic dysplasia

- Absent septum pellucidum, optic nerve hypoplasia, +/ – absent pituitary
- Associated with endocrinopathy/hypopituitarism and requires regular screening

Non-visualization of the cavum septi pellucidi

- Normal finding in fetuses < 18 weeks GA, > 37 weeks GA and in up to 90% of infants
- May be isolated abnormality, however thorough fetal CNS assessment required
- May be associated with other CNS malformations including septo-optic dysplasia, holoprosencephaly, schizencephaly, hydranencephaly, Chiari type II malformation, agenesis of the corpus callosum, etc.

Anomalies of the posterior fossa and cerebellum

- Dandy-Walker malformation
    - Developmental malformation including posterior fossa cyst communicating with the 4th ventricle, hypoplasia of the cerebellar vermis
    - Associated with other CNS malformations, chromosomal abnormalities, syndromic anomalies and/or hydrocephalus/ventriculomegaly
- Other examples include megacisterna magna, Blake's pouch cyst, cerebellar hypoplasias/dysplasias

Choroid plexus cysts

- May be isolated finding in 1-2% of the normal population
- If associated with additional anomalies, increased risk of chromosomal abnormalities/trisomies requiring further evaluation

Aneurysm of the vein of Galen

- Rare vascular malformation of arteriovenous shunts from the carotid/vertebrobasilar system to the vein of Galen
- High blood flow leads to vein dilation and may result in hydrocephalus
- May result in high output cardiac failure, hydrops fetalis or polyhydramnios
- Diagnosis established by sonography
- Outcome dependent on severity of hydrocephalus and/or cardiac involvement

Hydranencephaly

- Significant cystic change of the cerebral hemispheres due to massive brain infarction with preservation of cerebellum, midbrain, thalami and basal ganglia
- Findings may include micro- or macrocephaly, polyhydramnios, impaired fetal swallowing
- Prognosis is poor

Abnormalities of cortical development

- Examples include lissencephaly, pachygyria, microgyria/polymicrogyria, and heterotopias
- Often associated with other CNS or extra-CNS anomalies and/or genetic abnormalities

8.11 – Neonatal Abstinence Syndrome

Overview

- Often used as an umbrella term for the clinical presentation associated with substance exposure in utero. However it was originally described specifically for opioid exposure. Neonatal Opioid Withdrawal Syndrome (NOWS) is now the preferable term when describing specific withdrawal from opioid.
- Opioid use in pregnancy is associated with prematurity, low birth weight, risk of spontaneous abortion, SIDS, and long term developmental outcomes including neurobehavioural abnormalities
- History - substances used, most recent dose and route, and assess for associated health risks (hepatitis B and C, HIV, maternal nutrition, access to antenatal care, and social risk factors)
- Symptoms of opioid withdrawal typically appear within 2 – 3 days. If fentanyl or carfentyl use in pregnancy expect rapid onset of symptoms with potential severe consequences without medical treatment; long-acting opioid use in last few weeks of pregnancy (methadone or buprenorphine) may have delayed neonatal clinical presentation up to 5 -7 days
- Acute symptoms may persist for 10 – 30 days, whereas mild symptoms (feeding difficulties, irritability, sleep disorders) may persist for 4 – 6 months.
- 30-75% of infants will require medical treatment for withdrawal symptoms

Assessment

- Modified Finnegan score guides standardized assessment - score 1-2 hours after birth then q3-4h for minimum 72 hours
- Finnegan tool specifically developed for opioid exposure only, not necessarily a guide for treatment options in polysubstance drug exposure
- Longer duration may be warranted with polysubstance use and/or long-acting opioid use

Management

- Non-pharmacologic - skin to skin, rooming in, swaddle, low stimulation environment, breastfeeding (ensure no contraindications), nutrition
- Pharmacologic - if score >=8 on 3 consecutive assessments or average >=12 on 2 assessments (see algorithm in Table 8.11a)
- Note - avoid naloxone in infant born to opioid-dependent mother, risk for seizure
- Discharge - if treatment threshold avoided for 72 hours (120 hours if long-acting opioid use), or after treatment (may be discharged on medication if adequate follow up available and weaning plan established)

Table 8.11a – Modified Finnegan scoring system

System	Signs and symptoms	Score	System	Signs and symptoms	Score
Central Nervous System Disturbances	Excessive high-pitched cry < 5 min Continuous high-pitched cry > 5 min	+2 +3	Metabolism, vasomotor, and respiratory disturbances	Sweating	+1
	Sleeps < 1 hour after feeding Sleeps < 2 hours after feeding Sleeps < 3 hours after feeding	+3 +2 +1		Fever 38°C – 38.3°C Fever > 38.3°C	+1 +2
	Hyperactive Moro reflex Markedly hyperactive Moro reflex	+2 +3		Frequent yawning > 3-4 times per scoring interval	+1
	Mild tremors when disturbed Mod-severe tremors when disturbed Mild tremors undisturbed Mod-severe tremors undisturbed	+1 +2 +3 +4		Mottling	+1
	Increased muscle tone	+1		Nasal stuffiness	+1
	Excoriation (specify location _____)	+1		Sneezing > 3-4 times per scoring interval	+1
	Myoclonic jerks	+3		Nasal flaring	+2
	Generalized convulsions	+5		RR > 60/min without retractions RR > 60/min with retractions	+1 +2
Gastrointestinal disturbances	Excessive sucking	+1			
	Poor feeding	+2			
	Regurgitation (≥2 during/post feed)	+2			
	Projectile vomiting	+3			
	Loose stools (curds/seedy) Watery stools	+2 +3			

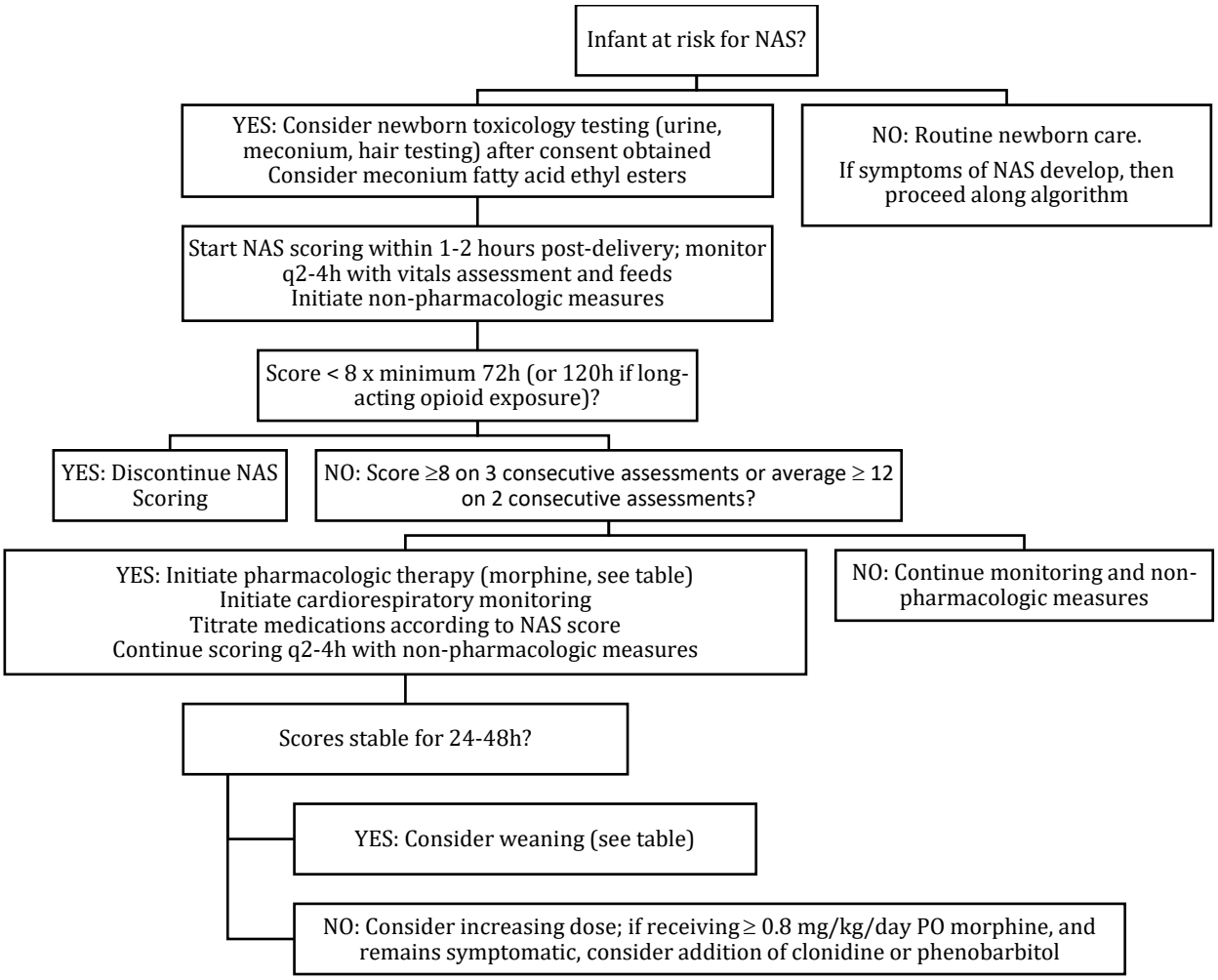

Figure 8.11 – Clinical pathway for assessment and management of a newborn with NAS

Table 8.11b – Pharmacologic management of NAS (Adapted from CPS Position Statement Lacaze-Masmonteil, T., & O'Flaherty, P., 2018)

Medication	Dose	Comments

Morphine	Score ≥8 on 3 consecutive assessments or average ≥ 12 on 2 consecutive assessments
	• Starting dose
	  ○ Score 8-10: 0.32 mg/kg/day PO, divided q4-6h
	  ○ Score 11-13: 0.48 mg/kg/day PO, divided q4-6h
	  ○ Score 14-16: 0.64 mg/kg/day PO, divided q4-6h
	  ○ Score ≥ 17: 0.8 mg/kg/day PO, divided q4-6h
	• If persistently elevated score, increase by 0.16 mg/kg/day every 4-6h, to maximum of 1.0 mg/kg/day.
	• If score < 8 for 24 – 48 hours, consider weaning 10% of total daily dose q24-48 hours
	• Once total daily does < 0.2mg/kg/day, consider extending dosing interval to q8h then q12h.
	• Morphine can be discontinued once scores remain stable on dose less than 0.05 – 0.1 mg/kg/day.
		Typical first-line treatment
		Short half-life (9h)
		No alcohol in preparation
		PO to IV - Divide by 3

Clonidine	May be used as adjunct with morphine, particularly when autonomic symptoms predominate or symptoms not well controlled on morphine ≥ 0.8 mg/kg/day PO • Maintenance: 0.5 – 2 mcg/kg/dose PO, q4-6h • Wean by 25% total daily dose every other day once symptoms controlled (q4h to q6h x 48h, to q8h x 48h, to q12h x 48h, to qHS x 48h, then discontinue)	Alcohol free available Long half-life (44-72h) Abrupt discontinuation may cause rebound tachycardia or hypertension If unable to tolerate PO consider phenobarbital
Phenobarbital	May be used as adjunct with morphine, particularly for polysubstance • Loading dose: 10mg/kg PO, q12h x 3 doses, THEN • Maintenance dose: 5mg/kg/day PO daily • Wean by 10-20% total daily dose every 1-2 days once symptoms controlled	Long half-life (45-100h) Requires level monitoring Sedative effect Contains 15% alcohol May worsen GI symptoms
Methadone	Alternative to morphine therapy • Start dose: 0.05-0.1 mg/kg/dose PO, q6-12h • Titrate increase dose by 0.05 mg/kg q48h • Maximum dose 1 mg/kg/day	Long half-life (26h) Used in many countries as a first-line treatment when mother is on methadone
Buprenorphine *	Alternative to morphine therapy at some institutions • Start dose: 4–5 mcg/kg/dose SL q8h • Maximum dose 60 mcg/kg/day	Sublingual administration Half-life (24-60h) Contains 30% alcohol

*Not approved for neonatal use in Canada

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Chapter 9 – Respirology

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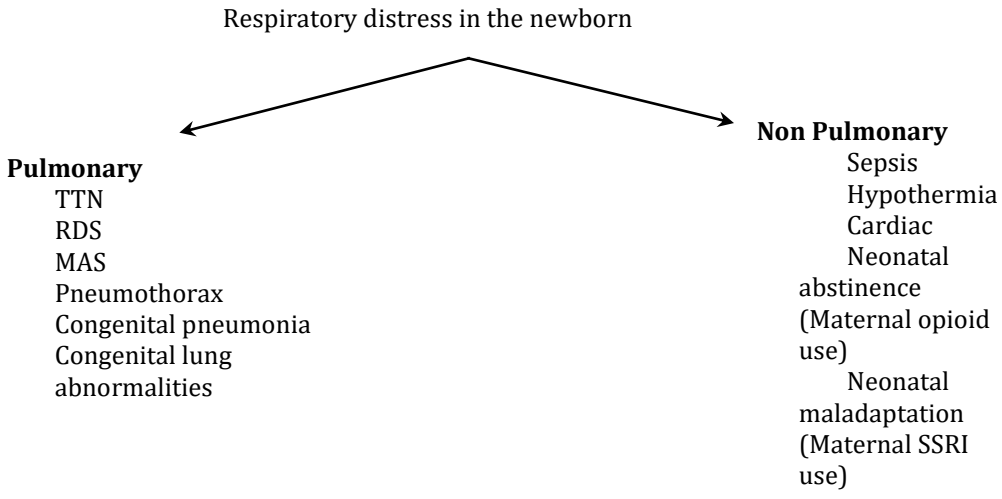
Expert Reviewer – Dr. Michael Dunn

9.1 - Respiratory Distress in the Newborn

9. 1.1 - Differential diagnosis and initial approach to the newborn with respiratory distress



- Initial approach to respiratory distress in a newborn
    - Relevant History - gestation, ROM duration, type of delivery, meconium, maternal GDM, etc.
    - Consider the following investigations
        - Blood gas
        - Glucose
        - CXR
        - +/- partial septic workup - CBC, blood culture

9.1.2 - Apnea

- Definition - respiratory pause >20 s, or <20 s associated with bradycardia and/or cyanosis
- Incidence - decreases with increasing gestational age
    - For premature babies, incidence usually peaks in 2nd week of life
    - 50% incidence at 30–31 weeks
    - Majority resolve by 34–35 weeks (7% incidence)
- Pathophysiology
    - Central (10-25%) - absent respiratory drive
    - Obstructive (10-25%) - airway obstruction impairing airflow despite effort
    - Mixed (50-75%) - central + obstructive
- DDx/Exacerbating factors
    - Apnea of prematurity (dx of exclusion, if no other treatable cause)
    - Neuro - Intracranial hemorrhage, Seizures, Hydrocephalus/CNS malformations, Vagal stimulation (common with feeding related apnea. suctioning), Congenital hypoventilation syndrome
    - Respiratory - Atelectasis/Hypoxemia, upper airway obstruction and malformations
    - GI - Gastroesophageal reflux
    - Infection - sepsis, meningitis, UTI, pneumonia, NEC
    - Hematology - anemia, polycythemia
    - Endocrine - hypoglycemia
    - Other - prostaglandins, hypo/hyperthermia, maternal medications (narcotics, magnesium, beta-blockers)
- Intervention
    - Gentle stimulation, oxygen, suction, escalating respiratory support if not responding, including non-invasive options (CPAP or NIPPV) or invasive ventilation if severe
    - Treat underlying cause, contributory pathologies
- Prevention
    - Caffeine
    - Benefits of caffeine - decrease extubation failure, decrease CLD rates.
    - Indications - All infants <32 weeks. Can also be given for frequent apnea/bradycardia events (≥5 per day)+/-significant intervention required (vigorous stimulation or CPR)
    - Dosing - Caffiene citrate, loading 10mg/kg, maintenance 5mg/kg/day
- Weaning off caffeine
    - >32 weeks CGA (Extremely premature may require more prolonged caffeine)
    - No apneic episodes x 5 days
    - Wean well before discharge given long half-life (3-7 days)

9.1.3 - Bronchopulmonary Dysplasia (BPD)/ Chronic Lung Disease (CLD)

- Definition - Requirement for supplementary oxygen +/- respiratory support >28 days and >36 weeks corrected GA. Severity based on level of support and oxygen requirements.
    - +/- typical CXR changes
        - Generalized opacification of lung fields initially
        - Progression to streaky areas of opacification; later changes in severe cases include areas of patchy opacification and over-inflation

    - Risk of pulmonary hypertension in severe cases
    - Contributing factors - arrest of alveolar development, infection, inflammation, oxygen toxicity, ventilator associated injury, pulmonary edema
- Risk factors
    - Increased risk with lower gestational age
    - Maternal - chorioamnionitis
    - Respiratory - severe RDS, prolonged PPV, lung over-inflation ('volutrauma'), hyperoxia, pulmonary air leak (pneumothorax and PIE)
    - Other - PDA, postnatal sepsis, GERD
- Prevention
    - Lung protective ventilation - avoid lung over-inflation (lowest tidal volumes and pressures), avoid hyperoxia, permissive hypercapnia)
    - Medications - antenatal steroids, caffeine
    - Feeding with breast milk has been shown to decrease the risk of BPD
- Treatment
    - Optimize nutrition (alveolar growth)
    - Medications
        - Steroids for BPD prevention
            - Dexamethasone in the first week of life no longer indicated in the prevention of CLD due to concerns for long term developmental effects
            - Consider low-dose hydrocortisone in the first 24 to 48 h after birth for highest risk infants (<28 weeks GA or chorioamnionitis), to increase likelihood of BPD free survival
        - PREMILOC DOSING Physiologic replacement dose - 1 mg/kg per day x 7 days, then 0.5 mg/kg per day x 3 days) x 10 days
    - Other considerations
        - Increased risk for late-onset sepsis
        - Contraindications - indomethacin prophylaxis
- Steroids for extubation- DART protocol
    - Dexamethasone for ELBW (<1000g) or very preterm infants (<28 weeks) who remain ventilator dependant after the first 1 week of life and at high risk of BPD
        - Facilitated extubation
        - Improved ventilation and oxygen requirements
        - Decreased duration of intubation
        - No increase in short term complications
    - Dose - 10-day tapering course of dexamethasone sodium phosphate (0.15 mg/kg per day for 3 days, 0.10 mg/kg per day for 3 days, 0.05 mg/kg per day for 2 days, and 0.02 mg/kg per day for 2 days; total of 0.89 mg/kg over 10 days)
    - Some clinicians may choose different steroids, doses, durations
- Selective use of nebulized bronchodilators, diuretics
- Other management considerations
    - Monitoring - Echo in all oxygen dependent babies at 34-36 weeks (r/o PHTN)
    - Maintain oxygen saturations >95% in babies with evidence of pulmonary hypertension
- Prognosis
    - Most weaned off O2 by 1 year of age
    - Increased probability of neurodevelopmental and respiratory morbidity

9.1.4 - Congenital lung malformations

- Types
    - Congenital Pulmonary Airway Malformation (CPAM) - previously known as congenital cystic adenomatoid malformations (CCAM). Connected to the tracheobronchial tree. Supplied by pulmonary circulation.
        - Pathophysiology - Stages of CPAM corrolate with the lung development stage (stages 0-4)
        - Generally grows until ~28 weeks, plateaus and then regresses
        - 1/3 will develop non-immune hydrops - RF for hydrops include everted ipsilateral hemidiaphragm, predominantly cystic lesions, lesions in the third trimester, CPAM volume ratio > 1.6
- Bronchopulmonary Sequestration - rare malformations made up of nonfunctional lung parenchyma. Not connected to the tracheobronchial tree. Supplied by systemic arterial supply.
    - Pathophysiology
        - Extralobar sequestration - has own pleura and systemic venous drainage. Likely originates from independent bud from the foregut. More common.
        - Intralobar sequestration - integral to lung pleura and has pulmonic venous drainage. Unclear whether congenital or acquired.
    - Diagnosis and workup
        - Prenatally - ultrasound can often identify these lesions. If identified, workup for other congenital anomalies indicated. Further workup with fetal MRI can help distinguish CCAM from BPS by identifying arterial supply.
        - Postnatally - US, CT, MRI with angiography can all help further delineate the lesion and the arterial supply
        - For BPS - Upper GI can identify post natally if communication with GI tract
- Management
    - Most will regress
    - Most infants with CCAM/BPS will be asymptomatic at birth
    - Remainder can present with respiratory distress ranging from mild to severe with pulmonary hypertension. Hydrops is poor prognostic factor.
    - Both require general surgery referral. Controversial whether to resect CCAM. Resection recommended for BPS that are symptomatic early in life

9.1.5 - Meconium Aspiration Syndrome (MAS)

- Incidence - 5% of babies where there is meconium stained amniotic fluid
- Pathophysiology
    - Ball-valve obstruction of airways leading to overinflation, air leaks and atelectasis
    - Chemical pneumonitis, inactivation of endogenous surfactant
    - Hypoxaemia due to right to left shunting as a result of pulmonary hypertension
    - Secondary infection
- Complications of MAS
    - Pneumothorax
    - Pneumomediastinum
    - PPHN
    - Long term sequelae are rare (CLD, wheezing, chronic cough)
- Management
    - Oral/nasal suction
    - Endotracheal suction via meconium aspirator used if obstruction below vocal chords
        - Used sparingly and cautiously
    - O2 to maintain saturations
    - Respiratory support - CPAP, mechanical ventilation - applied catiously given increased risk of air trapping
    - Surfactant lavage (not routinely used)

9.1.6 - Acute Persistent Pulmonary Hypertension (PPHN)

- Overview
  - PPHN occurs when pulmonary vascular pressure remains abnormally elevated after birth leading to right to left shunting (across PDA and PFO) and oxygenation failure.
  - *Acute PPHN is to be differentiated from chronic pulmonary hypertension seen in patients with BPD/CLD that usually develops around 34-36 weeks of corrected age.*
  - Incidence - 0.2% of liveborn term infants have severe PPHN
- Pathophysiology
  - Categorized in two types
    - Primary
      - Maldeveloped - normal lung parenchyma with remodelled pulmonary vasculature (idiopathic PPHN)
    - Secondary
      - Maladaptation - Abnormally constricted pulmonary vasculature with parenchymal diseases (MAS, RDS, sepsis) - most common
      - Underdeveloped - Hypoplastic vasculature (CDH, pulmonary hypoplasia, alveolar capillary dysplasia)
- Risk factors - MAS, HIE, acidosis, maternal SSRI use, PPROM but can be idiopathic
- Diagnosis
  - Echo is gold standard - flattening or displaced ventricular septum, tricuspid regurgitation, R to L shunting through PDA or PFO
    - Mild - Estimated RVp is ~1/2 systemic
    - Moderate - estimated RVp is ~3/4 systemic
    - Severe - estimated RVp is > systemic, RV dysfunction
  - Differential cyanosis – often have >10% differential in pre- and post-ductal sats
  - Hyperoxia test - PaO2 <100 despite being on 100% oxygen
  - Chest Xray can be normal or show associated pulmonary condition. Pulmonary vasculature can be normal or reduced
  - Severity often assessed by calculating the Oxygenation Index = (MAP x FiO2)/ postductal PaO2 x 100. Consider ECMO if severe (OI >25)
- Treatment
  - Supportive care including oxygen and circulatory support
  - Treat metabolic derangements - correct acidosis, hypoglycemia, hypoglycemia
  - Optimize lung recruitment (mechanical ventilation, high frequency ventilation, surfactant)
  - Pulmonary vasodilatory - inhaled nitric oxide
  - Decrease oxygen requirements - sedation and paralysis

9.1.7 – Pneumonia

- Pathogenesis
  - Early onset – acquired from the mother/during delivery, congenital pneumonia (presents at or shortly after birth)
  - Late onset – late onset sepsis or nosocomial including Ventilator Associated Pneumonia (VAP)
- Risk factors - early onset sepsis risk factors, intubation, anomalies of the airway, reflux
- Common pathogens
  - Early - GBS, E. Coli, Klebsiella, Listeria, Candida
  - Late - above plus S. Aureus, Pseudomonas, fungal, Chlamydia
  - Other - RSV, enterovirus
- Signs and symptoms
  - Resp - respiratory distress, increasing FiO2/ventilation requirements, excess secretions, PPHN
  - Systemic - signs of sepsis (temperature instability, poor perfusion, hypotension, metabolic acidosis, abdominal distention, feeding intolerance, jaundice)

- Diagnosis - combination of clinical, radiographic and microbiology findings (+/- Tracheal aspirates)
    - CXR diffuse or local consolidations, pleural effusions
- Treatment
    - Supportive - ventilatory support, oxygen, etc.
    - Antibiotics - usual duration 14 days
    - Early - think GBS and treat with Amp and Gent/Tobra
    - Late - consider local pathogens, antibiogram and tracheal aspirate

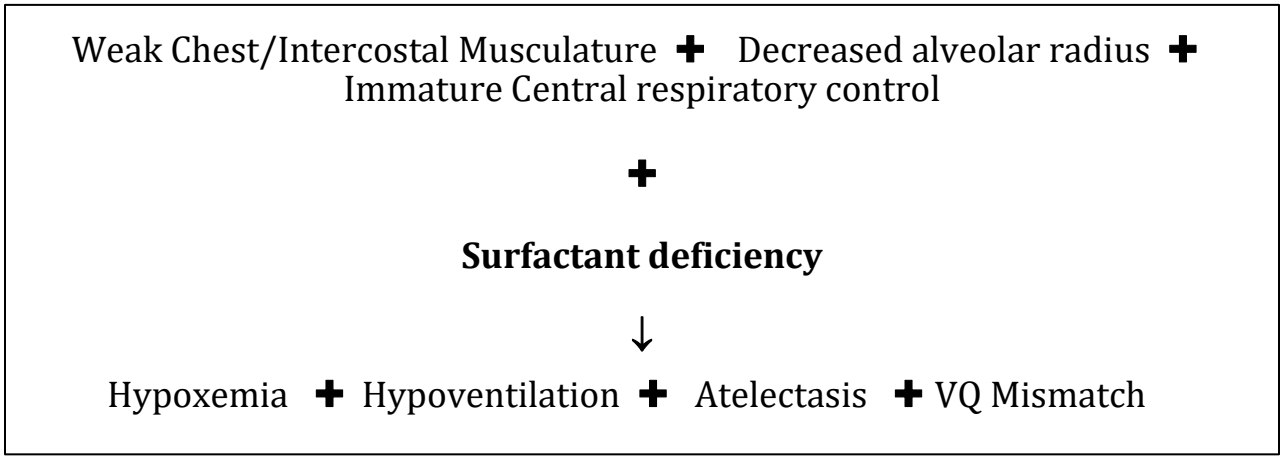
9.1.8 - Pulmonary Hemorrhage

- Incidence - ~11% in infants <1500g.
- Pathophysiology - acute fulminant lung edema with leakage of RBC and capillary filtrate into airspaces
- Differential - trauma from ETT tube/suction
- Risk factors - LBW infants, IUGR, surfactant administration, PDA, coagulopathy
- Signs and symptoms - fresh blood/frothy pink secretions from mouth or ETT, hypotension, hypoxia, DIC, hypoglycemia, metabolic acidosis, 'white out' on CXR
- Workup - CXR, BW (CBC and coags, biochemical, blood gas, sepsis w/u)
- Treatment - resuscitation, ventilation, surfactant, circulation, antibiotics
- Complications - BPD/CLD, air leak syndrome, neurological damage, mortality

9.1.9 - Respiratory Distress Syndrome (RDS)

- Pathophysiology - deficiency of pulmonary surfactant
    - Surfactant
        - Composed of phospholipids (80%), proteins (10%) and neutral lipids (10%)
        - Produced by type II alveolar cells between 24-34 weeks of gestation
        - Rationale for antenatal steroids for GA <34 weeks
        - Reduce surface tension in the alveolus, preventing collapse during end-exhalation
        - Surfactant deficiency drives atelectasis, VQ mismatch, hypoxia and hypoventilation
    - Exacerbated by weak respiratory muscles, decreased alveolar radius, and immature central respiratory control in the preterm neonate

Figure 9.1.9 - Pathophysiology of RDS



- Management
    - CPAP, O2, invasive ventilation
    - CPAP should be applied to preterm infants at risk of RDS; if increasing or sustained levels of oxygen requirement (eg. FiO2 > 0.3) or if other concerns for severe RDS, consider surfactant
    - Surfactant administration
        - Prophylactic surfactant is no longer recommended. CPAP acceptable alternative to elective intubation and administration of prophylactic surfactant
        - INSURE method - INtubation-SURfactant-Extubation - infants are intubated for the administration of surfactant, surfactant is administered during a very brief period of mechanical ventilation and then extubated to noninvasive respiratory support
        - Early administration (before RDS is severe) is favoured
        - Dosing - hospital dependant (natural bovine/porcine vs. synthetic)
        - Re-dosing - repeat surfactant if evidence of ongoing moderate to severe RDS, escalating resp support requirement, generally within the first 24-48 hours
        - Use of surfactant for MAS and pulmonary hemorrhage can be considered as per staff on call
    - Other methods of surfactant administration
        - Less invasive surfactant administration (LISA)
            - Administration of surfactant through a thin catheter via Magill forceps under direct laryngoscopy
            - MIST is a modified LISA technique using a more rigid catheter
            - Goal - avoidance of mechanical ventilation, ETT tube, intubation, and thus BPD
            - Combined with avoidance of positive pressure ventilation, use of antenatal steroids, early use of CPAP, and caffeine administration in the delivery room
            - Initial data suggests reduced BPD/death

9.1.10 – Transient Tachypnea of the Newborn (TTN)

- Incidence - 5.7/1000 term live births, higher in late preterm births and in babies born to C-section
- Pathophysiology
    - Pulmonary edema due to delayed fluid clearance from alveoli
    - Circulatory catecholamines and hormones in late gestation and labour cause the respiratory epithelium to switch from secretory (chlorine and liquid) to absorptive (sodium and liquid); absence of catecholamines (no labour) can result in delayed resorption and clearance of fetal alveolar fluid
    - Active Na transport from the alveolar space into the interstitium responsible for fluid reabsorption, hence why prenatal steroids has proven to improve symptoms of TTN
    - Resorptive function also upregulated by oxygen tension and glucocorticoids after birth
- Risk factors - C/S delivery, maternal diabetes, perinatal depression, maternal sedation, precipitous delivery
- Management – Support, O2, CPAP has been shown to have some benefit

Table 9.1.10 - Respiratory Distress in the Newborn

Pathology	Pathophysiology	Risk factors	CXR	Treatment
TTN Onset: first 6 hours of life (but steadily improves) Duration: 12-24 hours	Multifactorial Lack of circulatory catecholamines and hormones to promote switch of channels in respiratory epithelium secretory to absorptive	C/S more commonly but can occur with SVD Any gestational age ↑ risk in babies born to diabetic mothers	Bilateral perihilar streaking, fluid in fissure, normal to hyperinflated lung volumes (>8ribs - flat diaphrams)	O2, CPAP, PPV (more rarely)
RDS Peak severity at 1-3 days Onset of recovery usually around ~72 hours	Surfactant deficiency ↓ lung maturity	Premature babies as late as 37 wks Male gender Maternal diabetes, hypertension Caesarean section Perinatal hypoxia/ischaemia/acidosis	"Ground glass" "Reticulogranular pattern" Air bronchograms	CPAP/HFNC (positive pressure- minimizes atelectasis and VQ mismatch). If persistent O2 requirement/ intubated give surfactant, r/o sepsis. Supportive Prevention via maternal steroids
MAS	Chemical pneumonitis secondary to meconium aspiration, and functional surfactant inactivation	Meconium-stained amniotic fluids	Bilateral patchy opacities, hyperinflated lung, flattened diaphragms	Suction O2 Caution with CPAP: increase risk of air trapping and pneumothorax

9.2 - Respiratory Support

**outside of NRP*

9.2.1 - Aims of respiratory support

- Maintain adequate oxygenation, ventilation (CO_2 clearance)
- Minimize lung injury (ventilator associated lung injury - VALI)
- Minimize hemodynamic impairment
- Avoid injury to other organ systems (neuro, renal, GI)
- Reduce work of breathing

9.2.2 - Low flow O2 Therapy by Nasal Prongs

- Indications - desaturations without significant WOB, normal blood gas (pH >7.25; PCO_2 <6.5)
- Benefits - Non-invasive. Provides oxygen, no positive pressure.
- Risks - Hyperoxia and downstream effects
- Parameters - Flow Rate <1L/min, non-humidified

9.2.3 - Heated Humidified High flow O2 therapy

- Indications - Increased O2 requirement and WOB on low flow, no upper airway obstruction
- Mechanism
    - Provides some positive airway pressure
    - Minimizes or eliminates the inspiration of room air
    - Provides a constant, steady flow of gas (airway pressures vary during inhalation and exhalation)
- Benefits
    - Non-invasive
    - Decrease in upper and lower airway resistance
    - Wash out of anatomic dead space in in upper and lower airways reduces WOB
    - Decrease total ventilator days, occurrence of BPD, re-intubation rates, compilations including IVH, NEC, and ROP
    - Less nasal injury compared to CPAP
- Risks
    - Gastric distention
    - Need to escalate therapy
- Parameters
    - Rate <2-7L/min

9.2.4 - Continuous Positive Airway Pressure (CPAP)

- Indications
    - Respiratory distress, increased work of breathing hypoxia
    - Apnea of prematurity
    - All babies at risk of RDS (<30weeks GA) who do not require intubation are electively placed on CPAP
    - Post extubation
- Mechanisms of effect
    - Provides positive airway pressure that splints open airways and increases residual lung volume
    - ↓V/Q mismatch, ↓airway resistance
    - Stabilize respiratory pattern and ↓work of breathing
    - Prevents alveolar collapse and preserves endogenous surfactant
- Benefits
    - Reduces apnea of prematurity, extubation failure/ reintubation, CLD/BPD
- Risks
    - Trauma to nasal septum
    - Gastric distention
- Parameters
    - CPAP 5-8 mmHg (may go up even further if indicated)

9.2.5 - Nasal Intermittent Positive Pressure Ventilation (NIPPV)

- Indications
    - No improvement on CPAP
    - FiO2 >0.4 in preterm or >0.5–0.6 in term infants
- Mechanism of effect
    - Provides intermittent bursts of positive pressure ('breaths') delivered by ventilator via nasal prongs or mask
    - Positive pressure (CPAP) cycles between higher and lower pressures, asynchronous to breaths
    - ↑ mean airway pressure (↑PaO2)
    - 'Washout' of upper airway anatomical dead space (↓PaCO2) ↓work of breathing
- Benefits
    - Decreases extubation failure, apnea of prematurity, WOB and chest wall dysynchrony, need for intubation/mechanical ventilation, and duration of respiratory support

- Risks
    - Increased risk of air leak syndromes
    - Gastric distention

9.2.6 - Conventional Mechanical Invasive Ventilation

- Definitions and acronyms
    - VT - Tidal volume
    - PEEP - Positive End Expiratory Pressure
    - PIP - Peak inspiratory pressure
    - MAP Mean Airway Pressure (area under the curve)
    - Ti - Inspiratory time
    - Te - expiratory time
    - MV minute ventillation
- Goal - Optimize gas exchange (oxygenation, ventilation) while minimizing associated lung injury
- Basic principles
    - Saturation target - 90-95% (for preterms)
    - Oxygenation is dependant on MAP and FiO2
    - $MAP = \frac{(Ti \times PIP) + (Te \times PEEP)}{Ttotal}$
    - MAP (and oxygenation) can be improved by (in order of greatest impact)
        - ↑ PEEP
        - ↑ Inspiratory time (Ti)
        - ↑PIP
- Carbon dioxide clearance is dependent on alveolar ventilation which is proportional to minute ventilation
    - $MV = TVxRR$
    - Ventilation can be increased by increasing
        - Tidal volume (VT)
            - Normal 4-6 ml/kg, up to 8cc/kg in CLD/BPD
            - Increased by increasing ΔP (PIP-PEEP)
        - Ventilator rate
- Unique considerations in neonates
    - ↑ metabolic rate, ↓↑ functional residual capacity, ↓ lung compliance.
- Ventilator support required if
    - PaO2 <45, with FiO2>0.5–0.6
    - PaCO2 >65 mmhg with acidosis
    - Arterial pH <7.20
    - Poor oxygenation - FiO2>0.6 to maintain sats 85-94%
    - Significant circulatory failure
    - Recurrent or severe apneas of prematurity
    - Muscle paresis
    - Respiratory depression

Types of invasive mechanical ventilation

- No patient control
    - Intermittent positive pressure ventilation (IPPV)
    - Delivers a fixed breath at a fixed frequency (set the PEEP, PIP, itime, rate, FiO2)
- With patient control
    - Assist Control Ventilation (AC)
        - Delivers a fixed tidal volume at set intervals or when the patient initiates a breath
        - PIP adjusted to ensure the expired tidal volume (V_{Te}) is close to the set V_{Te}
    - Pressure support ventilation (PSV)
        - Delivers a fixed PIP at set intervals or when the patient initiates a breath
        - Tidal volume fluctuates

- Synchronized intermittent mechanical ventilation (SIMV)
  - Can be volume or pressure controlled (ie you can limit the pressure or the volume you will give with each breath)
  - Will deliver a mandatory set number of breaths with a set volume or pressure while at the same time allowing spontaneous breaths. Breaths from the machine are delivered when the airway pressure drops below the end-expiratory pressure
  - If patient takes a breath, the ventilator will support the breath

Table 9.2.6 - Ventilator Variables (Adapted from St. Paul NICU Resident Manual)

Ventilator Variable	Effect on PaO2	Effect on PaCO2
↑PIP	↑ (marginal effect)	↓
↑PEEP	↑	↑ (marginal effect)
↑ Frequency (rate)	N/A	↓
↑ IE ratio	↑	N/A
↑ FIO2	↑	N/A
↑ Volume target	↑	↓

9.2.7 - High Frequency Oscillation (HFO)

- Constant distending pressure (MAP) with pressure oscillating around the MAP at a very high frequency
- Oscillation using a piston-diaphragm – forward-backward motion of the piston produces alternating positive and negative pressures changes that are superimposed on the MAP
- HFO delivers tidal volume smaller than the dead space using a piston-diaphragm unit at rates of 300-900 breaths/minute (= 5-10Hz)
- Both inspiration and expiration are active in HFO
- Settings - MAP, amplitude, frequency (Hz = cycles per minute therefore 10Hz = 10 cycles/sec = 600 cycles/min) and FiO2

Table 9.2.7 – Troubleshooting HFO settings

Poor oxygenation	Over oxygenation	Under ventilation	Over ventilation
Increase FiO2	Decrease FiO2	Increase Amplitude	Decrease amplitude
Increase MAP	Decrease MAP	Decrease frequency (if amp maximized)	Increase frequency (if amplitude is minimized)

9.2.8 - High Frequency Jet Ventilator (HFJV)

- Uses a conventional ventilator + the jet ventilator that are connected to the ETT via a three-way adaptor
- Useful in disease states such as meconium aspiration syndrome (MAS), pulmonary interstitial emphysema (PIE)
- Incoming gas is propelled into the lungs like a stream (active inhalation) and the expiration is passive by spiraling out around the incoming jet
- You can add conventional breaths or 'sigh' breaths on top of the jet to help reverse atelectasis
- Settings: PIP, rate, I-time (generally kept at 0.02s), PEEP, FiO2

Table 9.2.8 – Troubleshooting HFJV settings

Poor oxygenation	Over oxygenation	Under ventilation	Over ventilation
Increase FiO2	Decrease FiO2	Increase PIP	Decrease PIP
Increase PEEP	Decrease PEEP	Increase rate	Decrease rate

9.3 - Blood Gas Interpretation

- Step 1: PH: Acidosis (<7.3) or alkalosis (>7.4)?
- Step 2 CO_2: Does the CO_2 'align' with the pH?
    - If there is an acidosis, is the CO_2 high? If alkalosis, is it low?
    - If yes, respiratory acidosis/alkalosis.
- Step 3 HCO3: Does the bicarbonate align with the pH?
    - If there is an acidosis, is the bicarbonate low? If alkalosis, is it high?
    - If yes, metabolic acidosis/alkalosis.
- Step 4: Compensated? Is there an appropriate compensation for the primary disturbance

Table 9.3a - Normal blood gas values

	Arterial	Venous	Capillary
pH	7.35-7.45	7.32-7.42	7.35-7.45
PO2	80-100	24-48	60-80
PCO2	35-45	38-52	35-45
HCO3	19-25	19-25	19-25

Table 9.35b - Summary of uncompensated acid base disturbances

	Respiratory Acidosis	**Metabolic Acidosis**	**Respiratory Alkalosis**	**Metabolic Alkalosis**
pH	<7.3	<7.3	>7.4	>7.4
PCO2	>45mmHg	Normal range	<35	Normal
HCO3	Normal (22-26)	Low	Normal	High

Table 9.35c - Summary of uncompensated acid base disturbances

Disorder	Primary disturbance	Expected compensation	Correction factor
Metabolic acidosis	Decrease in HCO3-	PaCO2 = (1.5 x [HCO3-]) +8	**± 2**
Acute respiratory acidosis	Increase in PCO2	Increase in [HCO3-] = Δ PCO2/10	**± 3**
Chronic respiratory acidosis (3-5 days)	Increase in PCO2	Increase in [HCO3-] = 3.5(Δ PaO2/10)	
Metabolic alkalosis	Increase in HCO3-	Increase in PCO2 = 40 + 0.6(ΔHCO3-)	
Acute respiratory alkalosis	Decrease in PCO2	Decrease in [HCO3-] = 2(Δ PaCO2/10)	
Chronic respiratory alkalosis	Decrease in PCO3	Decrease in [HCO3-] = 5(Δ PaCO2/10) to 7(Δ PaCO2/10)	

- Target neonatal blood gas values
    - PaCO2 45-60mmHg (hypocapnia is a risk factor for PVL therefore permissive hypercapnia is recommended for neonatal neuroprotection)
    - pH > 7.25

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Chapter 10 - Cardiology

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10.1 – Approach to Suspected Congenital Heart Disease (CHD)

Overview

- Cyanotic lesions (T's)
  - Tetralogy of Fallot, Truncus arteriosus, Transposition of the great vessels, Total anomalous pulmonary venous drainage (TAPVD), Tricuspid valve abnormalities including Tricuspid Atresia and Ebstein's Anomaly, Pulmonary Atresia/Stenosis, Transitional circulation
- Acyanotic lesions
  - Ventricular Septal Defect (VSD), Atrial Septal Defect (ASD), Atrioventricular Septal Defect (AVSD), Aortopulmonary window (AP window), Patent Ductus Arteriosus (PDA)
- Obstructive lesions (typically present with shock)
  - Coarctation of the aorta, Interrupted aortic arch, Hypoplastic left heart, Aortic stenosis

Cyanosis and Hypoxemia

- Cyanosis - bluish discolouration of skin or mucous membranes due to low oxygen saturation classically described as >5.0 g/dL of deoxyhemoglobin
- Causes of hypoxemia (abnormally low level of O2 in the blood)
  - Apnea/hypoventilation
  - V/Q mismatch (pulmonary edema from HF caused by L to R shunts, pneumonia, pneumothorax)
  - Intrapulmonary shunt (arteriovenous malformation (AVM), hepatopulmonary syndrome)
  - Intracardiac shunt (R to L shunting, or obstruction to pulmonary flow)
  - Diffusion deficit (interstitial or alveolar edema or fibrosis such as alveolar capillary dysplasia)

Hemodynamic changes in the newborn

- Fetal circulation
    - Two parallel circuits and equal left and right ventricular pressures (slightly more cardiac output from right ventricle, approximately 60%)
    - Flow of oxygenated blood from placenta through umbilical vein through the ductus venosus to the RA, preferentially directed via the foramen ovale (FO) to the LA – LV – ascending aorta
    - Flow of deoxygenated blood from the SVC and IVC to the RA directed preferentially to the RV to PA then shunting of up to 90% of blood from PA to descending aorta via two umbilical arteries to low resistance placental circulation
- Transitional newborn circulation
    - Loss of the low resistance placental flow on clamping of the umbilical cord results in a sudden increase in systemic vascular resistance (SVR)
    - Initiation of ventilation at birth leads to reduction in pulmonary vascular resistance (PVR) and increased pulmonary blood flow leading to an increase in LA pressure and closure of the FO
    - Transductal blood flow after birth switches from predominantly R to L to L to R within 30 minutes of birth (may remain bidirectional for up to 10-15 hours)
        - PDA remains patent before spontaneous functional closure within hours of birth followed by structural remodelling over weeks to months

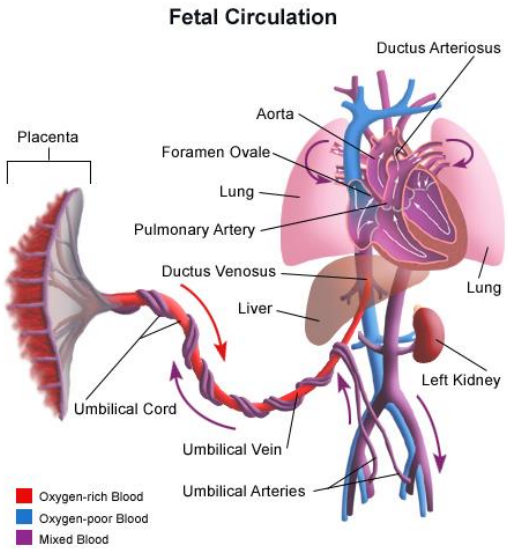


Figure 10.1a - Illustration of fetal circulation (Image from Stanford Children's Health)

Diagnostic algorithm

- History and exam (murmur not always present in severe defects), ABCDEs
- Pre- and post-ductal saturations (see Table 10.1a)
    - CCHD screening - <90% abnormal, persistently 90-94% or >3% difference abnormal
- 4 limb BPs - no consensus, consider >10-20mmHg systolic upper vs. lower limb difference as possibly pathologic
- Hyperoxia test (to elucidate cardiac vs. pulmonary etiology) (see Table 10.1a)
    - Measure arterial O2 pre-ductal (right radial) then give O2 - 100% O2 for 10 min
    - Repeat measurement of arterial oxygen in right radial

Table 10.1a – Anticipated pre and post ductal saturation differences based on etiology (adapted from lecture by Dr. O. Zulan)

Differential	Pre-ductal SpO2	Post-ductal SpO2	Etiology
Cyanosis	85%	85%	• Cyanotic congenital heart lesion • Pulmonary hypertension with lung pathology • Non-cardiac cause of cyanosis (ie. sepsis, airway pathology, neurologic, congenital methemoglobinemia, profound anemia)

Differential cyanosis	95%	75%	• Pulmonary hypertension (PPHN)/delayed transition
			• Duct dependent systemic blood flow
			  • Aortic arch abnormality (coarctation, interrupted arch, critical aortic stenosis)
			  • LV outlet obstruction
			  • Poor LV contractility (sepsis, myocarditis, myopathy, hypoplastic left heart)

Reverse differential cyanosis (both saturations are cyanotic)	75%	90%	• TGA with aortic arch anomaly or pulmonary HTN • Supracardiac TAPVD (streaming of oxygenated blood from SVC to the right heart through the PDA to the descending aorta leading to higher saturations in the post ductal circulation - depends on degree of obstruction, more obstruction leads to pulmonary edema and more cyanosis)

Table 10.1b – Expected PaO2 and SpO2 values following the hyperoxia test given different underlying conditions (Adapted from Marino 2001)

Etiology	Room Air PaO2 (SpO2)	FiO2 1.00 PaO2 (SpO2)
Normal	70 (95%)	> 300 (100%)
Lung Disease	50 (85%)	> 150 (100%)
Cyanotic CHD	< 40 (75%)	< 50 (<85%)* or <150(100%)$

*Parallel circulations or mixing lesions with restricted pulmonary blood flow
$Mixing lesions without restricted pulmonary blood flow

Management of critical cardiac lesions

- Transfer to tertiary care centre, maintain normoglycemia/normal temp/normal pH
- Acceptable level of oxygenation for cyanotic lesions is a SpO2 of 75-85% and CO2 40-45 mmHg to balance Qp:Qs
- ECG or CXR may have suggestive features
- Echocardiogram (definitive diagnostic test for all heart lesions)
- Cardiac MRI or CT (may be used for visualization of difficult lesions, supracardiac TAPVD)
- Majority of cardiac lesions will require surgical correction

Post-operative considerations

- Post-operative complications
  - Occur in 30-40% of patients
  - May include: need for prolonged mechanical ventilation, poor cardiac output, infection, bleeding, thrombosis, acute renal failure, acquired brain injury/stroke (up to 2/3rds of those requiring cardiopulmonary bypass), and death (<4%)
- Post-operative anticoagulation
  - Heparin or low molecular weight heparin (LMWH)) +/- antiplatelet therapy (ASA) required in shunted and stented physiology as well as Fontan circulation
    - High risk of shunt thrombosis (8-12%) and death
  - General approach (courtesy of Dr. L. Benson, Sick Kids)
    - For BT shunts or bare metal PDA stents - heparin x 24hr ⟶ LMWH x 1 month ⟶ ASA 3-5mg/kg OD
    - For drug eluting PDA stents - heparin x 24 hr ⟶ Plavix (Clopidogrel) 0.5mg/kg ⟶ ASA 3-5mg/kg OD
    - No anticoagulation required for RVOT, pulmonary artery, CoA or PDA stent in Hybrid Stage I

- Guidelines for infective endocarditis prophylaxis for dental procedures
    - Unrepaired cyanotic CHD (saturations <75%)
    - Repaired congenital heart defect with prosthetic material or device or adjacent defects to the site of the material or device
    - Cardiac transplant recipients
    - Prior history of infective endocarditis

? To PGE1 or not to PGE1 ?

TGA, ToF, PA, Tricuspid Atresia, Coarctation of the aorta, HLHS - duct dependent lesions require PGEs for duct patency
Ebstein's - caution with PGE1, may worsen circular shunt and precipitate HF
TAPVR - will clinically worsen therefore PGE1 not indicated
TA - no duct therefore PGE1 not indicated (unless in the case of IAA)

Prostaglandin E1 (PGE1)/Alprostadil

Initial dosing - 0.01-0.1 mcg/kg/min IV to establish patency of closing ductus
Maintenance dosing - 0.01-0.02 mcg/kg/min IV to maintain ductal patency
Titration - always start low and titrate to effect
Adverse effects - edema, apnea, respiratory depression, and hypotension. Pyloric hypertrophy and hyperostosis from long term use

10.2 - Patent Ductus Arteriosus (PDA)

Overview

- Persistent connection between the main pulmonary trunk (or proximal left pulmonary artery) and descending aorta
- Relative occurrence is 6-8% of all known cardiac anomalies (F:M 2:1)
- Closure in full-term healthy newborns - 50% within first 24hr, 90% by 48hr, and approaches 100% by 96hr after birth
- Increased risk of PDA
    - Prematurity, RDS, fluid overload, asphyxia, congenital syndromes
- Decreased risk of PDA
    - Antenatal steroid, fetal growth restriction, prolonged rupture of membrane

Pathophysiology

- PDA patency and closure driven by a balance between relaxing (prostaglandin) and constricting (oxygen) measures
- The muscular layer is more sensitive to the relaxing agents at younger gestational age and more responsive to constricting agents at older age
- In stable neonate (without PPHN), PDA shunts the blood L to R from the aorta to the pulmonary artery, also called stealing phenomena, resulting in increased pulmonary flow resulting in increased capillary hydrostatic pressures, alveolar edema, reduced pulmonary compliance and increased respiratory work
- Increased blood flow returning to the left heart resulting in LV dilatation

Clinical presentation

- Auscultation - systolic "machinery" murmur increasing in intensity from S1 to S2 and weaning at mid diastole (loss of the diastolic component with increasing pulmonary pressures)
- Bounding peripheral pulses (due to widened pulse pressure)
- Wide pulse pressure - DBP < ½ of SBP (steal from aorta to pulmonary circulation results in lower end diastolic aortic pressure)
- Other manifestations
    - Hypotension, hyperactive pericardium, respiratory distress and congestive heart failure

Investigations

- ECG - may show LVH
- CXR - prominent pulmonary artery and increased pulmonary vascular markings, cardiomegaly with large PDA

- Echo - definitive, Doppler can show size and direction of flow, assess LV overload and dilatation and RV pressure
- BNP and NTpNBP - may be used to help assess hemodynamic significance of PDA or used to predict closure after treatment (for resource limited settings where echo not available)

Approach to treatment in term infants

- Different pathophysiology and anatomy to preterm infants, usually not responsive to pharmacological therapy
- Surgical intervention recommended before 1 year of life if large PDA to decrease risk of pulmonary hypertension

Pharmacologic closure

- Indomethacin
    - Side effects - renal (decreased GFR, urine output), risk of GI bleeding and intestinal perforation, platelet dysfunction
    - Contraindications - elevated creatinine, GI bleeding, NEC, coagulopathy, sepsis
- Ibuprofen
    - Same efficacy for PDA closure as indomethacin with less AKI and NEC
- Acetaminophen
    - Side effects - theoretical risk of hepatic dysfunction in preterm infants

Table 10.2 – Approach to medical and surgical treatment in preterm infants.

Approach	Timing	Advantages	Disadvantages
Prophylactic intervention (Indomethacin only)	DOL1 - Suggested for preterm with BW <1000g or <1250g with RDS requiring surfactant	Reduced short term complications of PDA including IVH, pulmonary haemorrhage, need for ligation	Exposure to needless medication given that 40% will have an asymptomatic course and close spontaneously
Early asymptomatic	Echo guided early screening DOL 2-4	Reduces the need of surgical intervention and reduces incidence of pulmonary haemorrhage	Medication side effects
Late symptomatic	After development of symptoms (DOL 7-10)	Chance to close spontaneously and avoid medication side effects	Will need CHF management
Surgical approach - Device Closure	After medical trial in symptomatic infants (persistent O2 or ventilation requirements)	No weight limit (as low as 700g) Early age (>3 days of life) Good safety profile in preterm infants	Requires straight and large size duct Risk of coarctation or LPA stenosis Risk of post ligation cardiac syndrome (sudden change in loading conditions results in LV decompensation)

Among moderately preterm (>28 weeks) all three medications have comparable closure rates
Recent studies have shown that in very early prematurity (<26 weeks) acetaminophen has low effectiveness and standard ibuprofen dosing after day 7 is inefficacious

10.3 – Acyanotic Heart Disease

10.3.1 – Atrial septal defect
10.3.2 – Atrioventricular septal defect
10.3.3 – Ventricular septal defect
10.3.4 – Coarctation of Aorta

10.3.1 – Atrial Septal Defect (ASD)

- A pathological defect which results in a shunt across the atrial septum, the direction of which depends on hemodynamic status
    - For example, in the setting of pulmonary hypertension the ASD will be bidirectional or R to L

- Usually asymptomatic, may require closure if persistently large beyond 4-6 years of age
- Note - a patent foramen ovale (PFO) differs from ASD as it is a normal physiological shunt across the atrial septum which persists in 25% of adults
- Types of ASD (Figure 10.3.1a)
    - Ostium Secundum (70%)
    - Ostium primum (20%)
    - Sinus venosus (5%)
    - Coronary sinus septal defect (<1%)

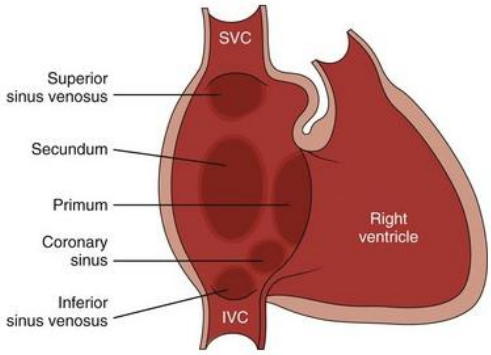


Figure 10.3.1a – Types of atrial septal defects (Image from Radiologykey.com)

Ostium Secundum ASD

Overview

- May be sporadic or inherited (autosomal dominant)
- Usually isolated but often associated with complex congenital heart disease
- Associations
    - Holt Oram (absent radii, thumb, triphalageal thumb, heart block)

Pathophysiology

- Flow across the ASD is determined by the size of the ASD, RV compliance, and pulmonary to systemic pressure ratio (Figure 10.3.1b)
- Reduced RV compliance leads to RV dilatation and a larger shunt
- A hemodynamically important shunt (pulmonary to systemic ratio >1.5:1) can technically be determined by catheterization or a nuclear scan, not often performed

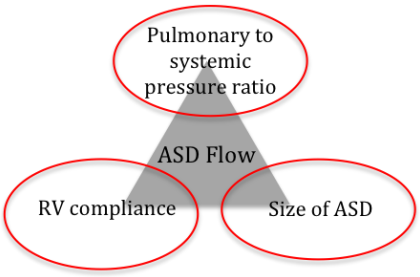


Figure 10.3.1b – Diagram demonstrating factors that contribute to flow across the ASD

Clinical presentation and manifestations

- Usually asymptomatic in neonates and infants, can have failure to thrive and/or respiratory symptoms of wheezing, similar to reactive airways disease
- Complications generally do not manifest symptoms until 3rd decade of life or in pregnancy
- On exam - RV heave, asymmetric chest appearance (due to enlarged RV from volume overload)
- Auscultation -widely split and fixed second heart sound LUSB (rarely heard in newborn), soft systolic ejection murmur due to increased flow in pulmonary outflow tract
    - Note - a fixed split S2 in ASD is due to the relative overcirculation and increased flow on the right side of the heart

Investigations

- ECG - RAD, rsR' conduction delay (incomplete RBBB), RVH
- CXR - cardiomegaly, prominent main pulmonary artery, increased pulmonary vascular markings
- Echo - definitive, demonstrates size, number and location of ASD, RV size and function, associated lesions

Management

- Small-to-moderate ASD with no RV enlargement is generally left untreated and typically closes spontaneously
- Criteria for closure
    - Symptomatic patients despite maximal medical management (e.g. nutrition support for failure to thrive)
    - Asymptomatic if persistently enlarged right ventricle and moderate to large ASD
- Timing of intervention - 4-6 years of age, earlier if symptomatic
    - Recommended closure during childhood because of increased morbidity/mortality and risk of arrhythmia in adulthood if intervention at >20 years of age
- Percutaneous device closure is preferred if anatomically feasible (weight of patient, the device requires the ASD to have adequate rims to strut the device), surgical closure otherwise (newer option is minimally invasive with smaller sternotomy or via thorax)

Ostium primum ASD

- This is usually isolated and not associated with genetic conditions
- Defect in the lower atrial septum near the AV valve
- Spectrum of isolated ostium primum (with intact ventricular septum) to a complete endocardial cushion defect (see AVSD below)
- Clinical presentation for ostium primum is similar to ostium secundum ASD
- ECG - left axis deviation
- The majority of ostium primum defects require surgical closure with repair of the cleft left AV valve at 4-5 years of age

Sinus venosus ASD

- Defect associated with the SVC or IVC (abnormally inserted SVC straddles the defect)
- Similar clinical course to moderate to large secundum ASD
- Almost all are associated with partial anomalous pulmonary venous return of 1-3 right pulmonary veins which drain into the SVC
    - This often leads to a greater left to right shunt than an isolated secundum ASD

- All require surgical repair at 4-5 years of age with re-direction of the anomalous pulmonary veins to the LA

Unroofed coronary sinus/coronary sinus septal defect

- Often associated with persistent left SVC which drains by unroofed fenestration(s) into the LA
- All require surgical repair at 4-5 years of age

10.3.2 – Atrioventricular septal defect (AVSD)

Overview

- Complete endocardial cushion defect with common 'AV valve' formed by leaflets of the malformed tricuspid and mitral valves
- Associations
    - 70% of AVSD associated with Trisomy 21 (typically balanced AVSD, rarely in combination with Tetralogy of Fallot (ToF))
    - Unbalanced lesions are usually isolated
    - May be associated with right or left isomerisms (heterotaxy syndromes) and other abnormalities

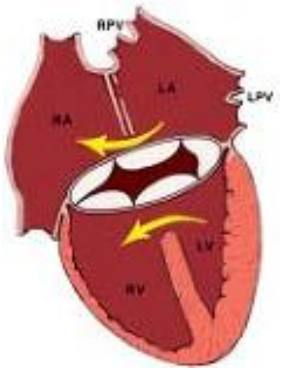


Figure 10.3.1c – AVSD anatomy demonstrating the common AV valve and flow across the septum (Image rom Thoracickey.com)

Pathophysiology

- May be 'balanced' or 'unbalanced' with the AV valve committed equally or unequally to the L and R ventricular chambers +/- corresponding hypoplasia of either the RV or LV
- If the AVSD is severely unbalanced, full repair may not be possible

Investigations

- ECG - left axis deviation
- Echo - RV/LV size, characteristics of the AV valves, other defects such as coarctation, ToF

Management

- Medical management of CHF/failure to thrive for small infants until optimized for surgery
- Surgical repair depends on anatomy
    - Complete, balanced AVSD - full repair at 4-6 months of age with closure of the ASD, VSD components and repair of the cleft left AV valve
    - Unbalanced AVSD - a full repair may not be possible and single ventricle palliation would be considered

Outcomes

- Poorer outcome with residual left AV valve stenosis or regurgitation requiring re-repair or prosthetic valve plavement
- Outcome of AVSD with heterotaxies is guarded, given the multiple other anomalies
    - In particular right atrial isomerism with AVSD and total anomalous pulmonary venous drainage has a very poor prognosis

10.3.3 – Ventricular septal defects (VSD)

Overview

- Usually asymptomatic at birth with risk of developing CHF after the first month of life as the pulmonary vascular resistance gradually falls
- Classified based on location in the septum
    - Perimembranous VSD (most common) - isolated or associated with other CHD (e.g ToF), often close spontaneously
    - Muscular VSD - single or multiple defects (swiss-cheese septum; rare), most close spontaneously
    - Inlet VSD - can be isolated, an extension of a perimembranous VSD or part of the AVSD anatomy, the majority require surgery
    - Doubly committed/outlet VSD (rare) - more common in Asian descent, most small and do not require surgery
- Associations
    - Large isolated perimembranous +/- inlet VSD + dysplastic valves is associated with Trisomy 13 and 18

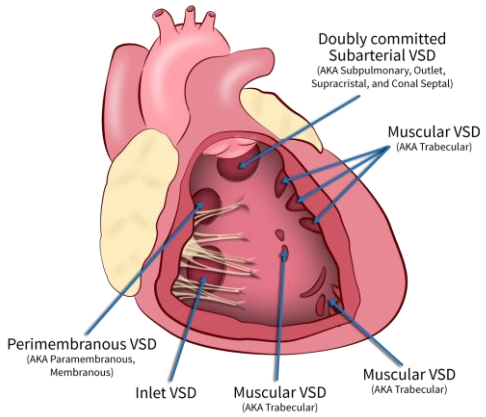


Figure 10.3.3 – Types of ventricular septal defects (Image from Pediatric Echocardiography)

Pathophysiology

- Clinical presentation and outcome depends on
    - Type of VSD
    - Degree of shunt – unrestrictive vs restrictive, direction of shunt (L-R, R-L or bidirectional)
    - Associated cardiac lesions and genetic abnormalities
    - Risk of developing pulmonary hypertension (early vs. late)
    - Natural history
    - Flow determined by (1) VSD size and (2) pulmonary vascular resistance
- Eisenmenger syndrome - reversal of shunting and cyanosis due to irreversible pulmonary hypertension (very late finding in adolescence/adulthood in unrepaired lesions)

Clinical Presentation

- Auscultation
    - Muscular VSD - typical soft, “blowing” murmur
    - Small restrictive VSD - holosystolic murmur at apex and LLSB
    - Large unrestrictive VSD - softer holosystolic murmur +/- diastolic rumble
    - Rarely audible at birth but will usually appear after 3 days of life as pulmonary pressures fall

Management

- Spontaneous closure - more common with perimembranous/muscular VSD
- Monitoring - large unrestrictive VSDs require monitoring and treatment for CHF with optimized nutrition and weight gain
    - Medications include diuretics, ACE inhibitors

- Indications of surgery
    - Persistent symptomatic CHF despite maximal medical therapy
    - Large VSD with pulmonary hypertension (repair should be before12 months of age to reduce risk of irreversible pulmonary hypertension)
    - For perimembranous VSD - associated lesions such as progressive aortic valve insufficiency/right coronary cusp prolapse, severe RVOTO due to right ventricular muscle bundles, severe LVOTO due to subaortic stenosis
    - History of endocarditis
- Contraindication
    - Irreversible pulmonary hypertension (confirmed by cardiac catheterization)

10.3.4 – Coarctation of Aorta (CoA)

Overview

- Male to female ratio 2:1
- Associations - bicuspid aortic valve (in up to 70% of CoA), Turner syndrome (35% of whom have CoA), Shone complex, as well as other complex cardiac lesions
    - Shone complex - left sided obstructive lesions - CoA, subaortic stenosis, and parachute mitral valve (supravalvular mitral ring)

Pathophysiology

- Tubular hypoplasia
    - Transverse hypogenesis in the wall of the aorta, usually originating at the distal end of the left subclavian artery and extending toward the ductus arteriosus
- Discrete juxtaductal obstruction
    - Defect of the aortic wall opposite to the entrance of the ductus arteriosus
    - "Posterior shelf" seen on echocardiography/cardiac catheterization
    - May not become symptomatic until adulthood unless severely obstructive

Clinical presentation

- Difficulty palpating or absent femoral pulses, cool legs with decreased perfusion, brachial-femoral delay
- Often asymptomatic and not recognized until presentation with shock
    - Obstructive effect once PDA closes leading to hypoperfusion, acidosis and shock
    - Severe forms, as in tubular hypoplasia, may present before PDA closure with R to L shunt and differential cyanosis
- 4-limb BP - upper limb arterial hypertension with differential of >10-20 mmHg as compared to the lower limb

Investigations

- ECG - can be normal but may see LVH or ST changes
- CXR - non-specific, increased pulmonary vascular markings, cardiomegaly
- Echo - diagnostic, location and severity of CoA, LVOTO, BAV, LV function, mitral valve regurgitation/stenosis, PDA flow, associated congenital heart lesions such as TGA/AVSD

Management

- In neonates presenting with shock – acute management with PGE1 (lifesaving)
- Definitive management - balloon angioplasty +/- stent (age and weight dependent) or surgical intervention
    - Surgical approach of thoracotomy or midline sternotomy depending on cardiac anatomy

Complications

- Risk of post-operative systemic arterial hypertension that may persist into adulthood
- Possibility of residual CoA or re-coarctation

10.4 – Critical Congenital Heart Lesions

10.4.1 – Transposition of the great arteries
10.4.2 – Tetralogy of Fallot/Pulmonary atresia VSD
10.4.3 – Pulmonary Atresia Intact Ventricular Septum (IVS)
10.4.4 – Ebstein's Anomaly
10.4.5 – Tricuspid Atresia
10.4.6 – TAPVR
10.4.7 – Truncus Arteriosus
10.4.8 – Hypoplastic Left Heart Syndrome

10.4.1 - Transposition of the great arteries (d-TGA + IVS)

Pathophysiology

- Great arteries switched resulting in two parallel circulations
    - De-saturated blood from RV to aorta to body and oxygenated blood from LV to PA back to lungs
    - O2 saturations depend on ability to mix (with ASD, VSD, PDA)
    - The most critically ill neonates have a severely restrictive ASD, intact atrial septum and/or severe pulmonary hypertension
- Multiple variations/terminology
    - d-TGA (dextro-positioned aorta) - aorta anterior and to the right of the PA
        - d-TGA with intact ventricular septum (IVS) - also referred to as simple or isolated TGA (*focused on in this chapter*)
        - d-TGA with VSD - if small, similar to d-TGA with IVS; if large, anticipate clinical manifestations of CHF
    - ccTGA (congenitally corrected, aka L-TGA)
        - Note - this is corrected physiology and management differs from d-TGA
        - Ventricular inversion resulting in 'physiologically corrected' circulation but with incorrect ventricle placement
            - De-saturated blood from RA to LV to pulmonary artery and oxygenated blood to LA to RV to aorta
- Abnormal coronary arrangement (minority of cases) - single or intramural coronaries
    - Highest mortality with intramural coronary (surgical complexity increases)
- Often isolated lesion, rarely associated with underlying genetic conditions

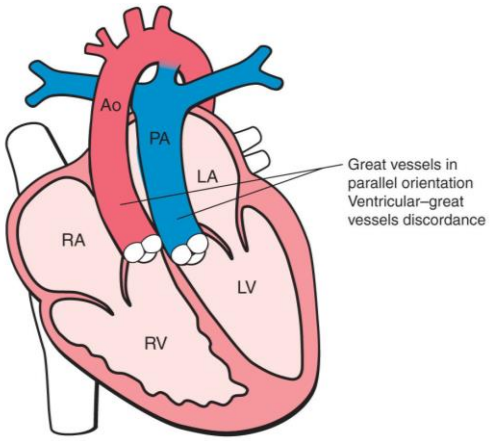


Figure 10.4.1.a – Cardiac anatomy in d-TGA with IVS (Image from OBGYNKey)

Clinical presentation

- Clinical - early cyanosis, born blue
  - Moderate/severe hypoxemia depending on degree of atrial and ductal shunting
- Reverse differential saturations if associated with aortic arch abnormality or PPHN
- Auscultation - single S2 (loud), usually without murmur

Investigations

- ECG - may show R axis deviation, RVH pattern
- CXR - "egg on string" from narrowed mediastinum, mild cardiomegaly; increased pulmonary blood flow apparent within first several weeks of life
- Echo is diagnostic (can identify coronary artery arrangement on echo)

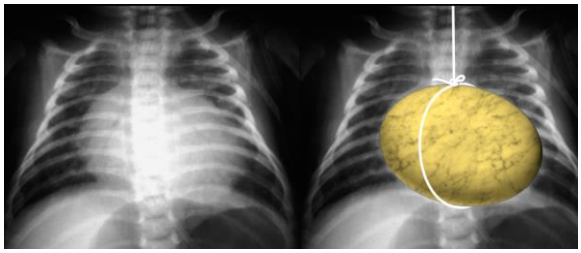


Figure 10.4.1b – Chest x-ray in a patient with TGA showing characteristic "egg on string" appearance (case courtesy of Dr Vincent Tatco, Radiopaedia.org, rID: 43062)

Management

- PGE1 buys time and improves oxygenation
  - Keep patient warm, prompt correction of acidosis and hypoglycemia
- Early transfer for Balloon Atrial Septostomy (BAS) (Rashkind procedure)
  - Bedside procedure with echo guidance via the umbilical vein usually 1st 24-48 hrs of life
  - Can defer if early surgery planned and patient stable
- Definitive operation (anatomy dependent)
  - Arterial switch operation (Jatene) (7-10 days of life) - for simple dTGA + IVS
    - If aorta and PA are adequate size with good size ventricles (if other anatomical complicating factors may wait 4-6 weeks after BAS for the switch)
    - Aorta and PA transected above coronary sinuses and re-anastomosed in correct position with coronary button reimplantation in old pulmonary root (neo-aorta)
    - As PVR declines after birth, LV pressure declines resulting in a decrease in LV mass – must repair prior to LV pressure/mass degradation to ensure LV pump adequacy
  - Nikaidoh operation - for d-TGA + VSD + severe PS
  - Damus-Kaye-Stansel (DKS) + VSD closure + RV-PA conduit - for d-TGA + large VSD + subaortic stenosis

Outcomes

- Short-term - better outcome with more favourable coronary artery anatomy, may have earlier mortality with concomitant PPHN
- Long-term - survival rate >95% for uncomplicated d-TGA, many have long term neurodevelopmental delays including cognitive and behavioural challenges

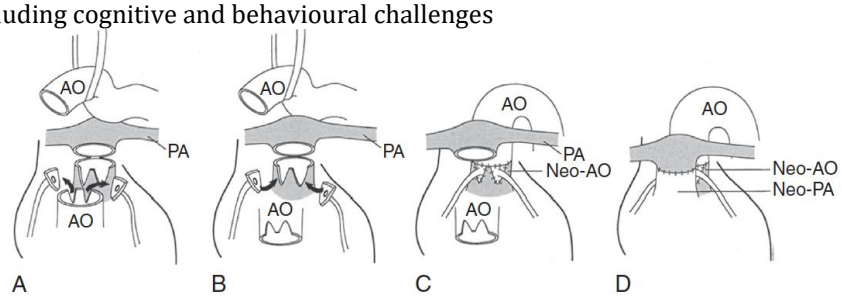


Figure 10.4.1c – Arterial Switch Operation (Image from ThoracicKey)

10.4.2 – Tetralogy of Fallot (including PA+VSD)

Pathophysiology

- Anterior-superior deviation of infundibular septum (muscular septum that separates aortic and pulmonary outflows) which causes RV outflow obstruction
- Tetralogy (four components)
    1. VSD - large, subaortic, unrestrictive
    2. RVOT obstruction (RVOTO) - decreased pulmonary blood flow, frequently multi-level (including subvalvar, pulmonary valvar, supravalvar)
    3. Overriding aorta
    4. Right ventricular hypertrophy
- Clinical heterogeneity dependent on extent of RVOTO and PA anatomy
    - Mild RVOTO – "pink" tet, clinically well
    - Moderate to severe RVOTO – severely reduced flow to pulmonary arteries, duct dependent cyanotic lesion
- Associated with other congenital defects in 25% of cases including DiGeorge syndrome (microdeletion 22q11) and Down Syndrome
- When the aorta overrides VSD by >50%, defect may be classified as a form of double outlet right ventricle (DORV) though circulatory dynamics and repair is similar to ToF.

Clinical Presentation

- Clinical - Cyanosis depends on degree of RVOTO (spectrum of normal pulmonary valve to complete pulmonary atresia)
    - PGE1 may be required to keep the PDA open and ensure adequate pulmonary blood flow (in this case will require early neonatal intervention)
    - Can present immediately after birth (severe) or within first few months as increasing hypertrophy of RV infundibulum develops
- Auscultation - Grade 2-4/6 SEM at LUSB (secondary to RVOTO)

- 'Tet-Spell" - paroxysmal hyper-cyanotic attack or hypoxic spell
    - Characterized by hyperpnea (rapid/deep breathing), irritability/crying, increased cyanosis, and reduced murmur intensity
    - Pathophysiology - triggered by any cyanotic or hypoxic event with either increased RVOTO, increased PVR, or decreased SVR leading to a vicious cycle of fall in arterial PO2 worsening hyperpnea, increasing systemic venous return, and upregulating catecholamines which results in increased contractility and further RVOTO, all exacerbating the R to L shunt
    - Can result in severe systemic hypoxia, metabolic acidosis, syncope, convulsions, or death

Investigations

- ECG - RAD, RVH
- CXR - "boot appearance", AP view showing narrow base, concave L heart border, normal cardiac size, decreased pulmonary vascularity
- Echo - diagnostic, determine severity of RVOTO and location (subvalvular, pulmonary valvar, supravalvar), size of branch pulmonary arteries (confluent vs non-confluent)
    - Severity depends on degree of RVOTO (mild, moderate, or severe as defined by % obstruction on echo) and levels of valvular obstruction

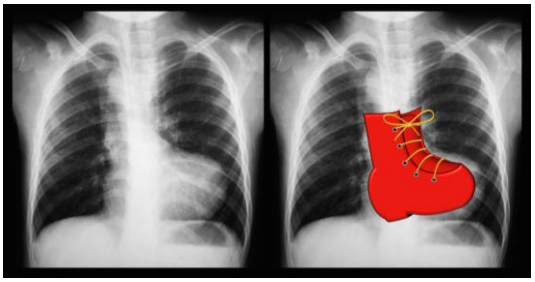


Figure 10.4.2a – Chest x-ray in a patient with ToF showing characteristic "boot" appearance (Image from Radiopedia.org)

Management

- Immediate/early management
    - Severe ToF or PA+VSD with marked RVOTO (duct-dependent) - immediate PGE1 until surgery or intervention
    - If severe RVOTO can place RVOT stent (or PDA stent if RVOT not favourable) by cardiac catheterization or a surgical modified Blalock-Taussig (BT) shunt (goretex connection between innominate artery and RPA)
        - Systemic to pulmonary shunts in those with unfavourable anatomy or who are not candidates for definitive surgery
- Medical management for stable vs. unstable infants
    - In stable acyanotic ToF, no medical management indicated
    - In unstable, cyanotic ToF (SpO2 persistently <75-85% in room air
        - PO Propranolol 0.5-1mg/kg/dose BID-QID to prevent hypoxic spells while waiting for surgical intervention (to avoid tet spells by stabilizing peripheral vascular reactivity and preventing falls in SVR)
- Definitive repair at 4-6 months (depends on anatomy)
    - Valve sparing repair - VSD repair, RVOT resection
        - If the pulmonary valve is of good size and not severely dysplastic
        - Not possible if RVOT stent placed as it destroys the pulmonary valve
    - Transannular patch repair - VSD repair, RVOT resection, with excision of the pulmonary valve and patch placed across it
- Acute Tet Spells
    - (1) Conservative/supportive measures
        - Calm baby, avoid agitation
        - Knee-chest - increases afterload, decreasing R-L shunting
        - Fluid bolus (increases preload)
        - O2 therapy (vasodilation of the pulmonary vascular bed to encourage pulmonary blood flow, however limited efficacy)
    - (2) Beta blockers
        - IV propranolol (0.05-0.1 mg/kg slow IV push over 10min) - blocks beta receptors in infundibulum reducing RVOTO
        - Esmolol infusion if refractory
        - Switch to oral propranolol once stable (0.5-1mg/kg/dose BID-TID or QID)
    - (3) Sedation
        - SC or IM Morphine (0.1-0.2 mg/kg) to suppress respiratory centre and stop hyperpnea
    - Other medications
        - IV Phenylephrine (5 mcg/kg/dose, followed by IV infusion 0.1-0.4 mcg/kg/min) - increases SVR, decreasing R-L shunting
        - IV bicarbonate to correct metabolic acidosis if severe

Outcomes

- Overall reasonably good outcomes following total correction
- Surgical consequences - pulmonary regurgitation can be moderate to severe, restrictive RV physiology (usually post operative only)
- Arrhythmias - SVT, VT, PVC's early post operative and long term
- Pulmonic valve replacement in late adolescence to adulthood (due to progressive RV dilatation secondary to severe pulmonary regurgitation, can lead to RV dysfunction)

10.4.3 – Pulmonary Atresia (PA + IVS)

Pathophysiology

- Very rare lesion with guarded prognosis which depends on the size of the RV/TV and presence of RV dependent coronary sinusoids
    - Spectrum of good to very poor outcomes (biventricular vs. single ventricle anatomy)
- Note - characteristics and outcomes differ from PA + VSD (spectrum of ToF as in section 10.4.2)

- Anatomical characteristics
    - All have an ASD
    - RV size can vary between normal to severely hypoplastic
    - TV size can vary between normal to severely hypoplastic, or even Ebstein's anomaly
    - PDA dependent pulmonary blood flow
    - RV dependent coronary sinusoids (occur with high pressure RV, acts as offload pathway), associated with increased mortality

Clinical Presentation

- Clinical - severe cyanosis from birth as ductus closes
- Auscultation - single, loud S2 (no P2 component), usually no murmur (unless PDA)

Investigations

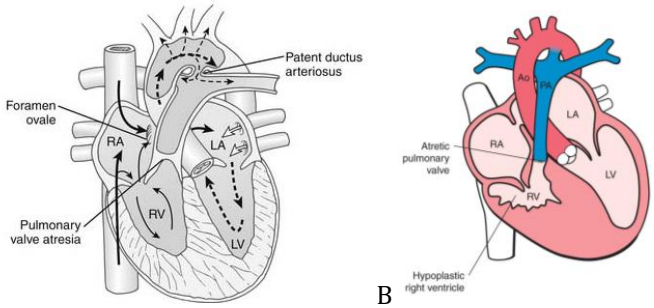
- ECG - frontal QRS (0 to +90 deg), RA enlargement, LVH +/- RVH
- CXR - decreased pulmonary vascularity
- Echo - defines RV size and function, TV size and degree of TR, presence of an RVOT infundibulum, size of branch pulmonary arteries, presence of coronary artery stenosis or sinusoids
- Cardiac catheterization - determines if there are RV dependent coronary sinusoids, intervention can be done at the same time if favourable RVOT anatomy

Management

- Immediate - PGE1 infusion for ductal patency
- Surgical intervention
    - Surgery depends on anatomy – biventricular (BiV) vs single ventricle palliation
    - Depends on RV/TV size and presence of RV-dependent coronary circulation
    - Favourable anatomy (imperforate valve with RVOT infundibulum)
        - Cardiac catheter radiofrequency ablation or RVOT stent +/- PDA stent
        - Pulmonary valvotomy +/- modified BT shunt followed by one and a half or two-ventricle repair depending on anatomy
    - Unfavourable anatomy (atretic pulmonary valve) or RV dependent coronary circulation
        - Three-stage single ventricle palliation - (modified BT shunt or PDA stenting) followed by Glenn and Fontan procedure (see Figure 10.4.8a)
        - High risk for ischemia and arrhythmias

Outcome

- Guarded prognosis with poor transplant-free survival due to infantile mortality and mortality between stages of palliation
- Overall 20-year survival approximately 66%, however best prognosis for those that survive all stages of palliative surgery (up to 98%)



A B

Figure 10.4.3a – Anatomy of pulmonary atresia with IVS. A. Imperforate pulmonary valve. B. Atretic pulmonary valve with a 'seagull' appearance.
(Image A from Thoracickey.com, Image B from Obgynkey.com)

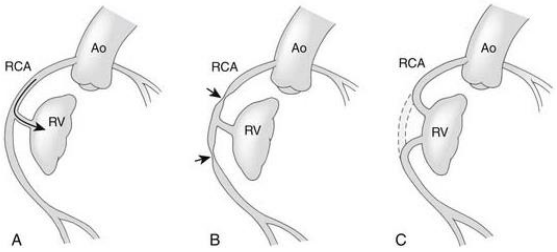


Figure 10.4.3b – Examples of an RV dependent coronary circulation. A. Without coronary stenosis. B. With coronary stenosis. C. With coronary obstruction (Image from Thoracickey.com)

10.4.4 – Ebstein's Anomaly

Pathophysiology

- Most are prenatally diagnosed and earlier age of presentation predicts severity
- Downward displacement of septal and posterior TV leaflets with "atrialization" of RV and RA enlargement
- Associated with ASD R-L, RV size ranges from normal to severely hypoplastic, TV displacement can be mild to severe, leading to varying degrees of TR, varying degrees of pulmonary obstruction to pulmonary atresia
    - With pulmonary atresia and severe TR may die of hydrops in utero
- "Circular shunt" concept - blood never goes forward to the lungs when PDA open
    - TR moves blood away from lungs and blood from ductus via pulmonary regurgitation moves back to R heart and away from lungs leading to hemodynamic instability and demise

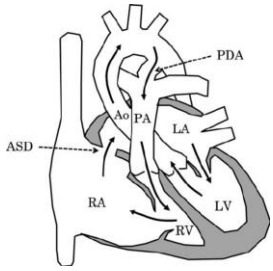


Figure 10.4.4a – Demonstration of a circular shunt in Ebstein's anomaly (Image from Yanase et al. 2012)

Clinical Presentation

- Clinical - pink and well to severe cyanosis, CHF, SVT
- Auscultation - S2 widely split, gallop rhythm, holosystolic murmur LLSB

Investigations

- ECG - RBBB without increased R precordial voltage, WPW is common (pathways near TV)
- CXR - "wall-to-wall heart" due to thin-walled atria enlargement
- Echo - shows degree of TV displacement and TR, RV size and function, RA dilatation, severity of RVOTO

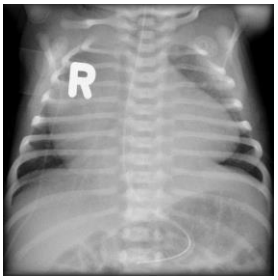


Figure 10.4.4b – Chest X-ray of a newborn with severe Ebstein's anomaly showing the classical "wall-to-wall" heart (Image from Radiopedia.org)

Management

- Prenatal intervention
  - In utero, in the setting of a circular shunt and evolving hydrops, maternal oral indomethacin is considered to prenatally close the PDA
- Post-natal management depends on the physiology, from monitoring clinically and no intervention, to starting PGE1 and delivering at a surgical centre
  - In the most severe prenatal cases with a circular shunt, planned delivery of the baby in the Sick Kids OR with ECMO on standby (very rare)
  - Caution with PGE1 as may precipitate CHF (increase PA pressure and worsen PR/TR)
  - Diuretics can be useful if there is severe TR and right sided failure
- Surgical options
  - Indications - critically ill neonates, severe cyanosis with polycythemia, PDA dependent circulation, severe RVOTO
  - Early surgical options depend on anatomy
    - Can include modified BT shunt, PDA stenting, or a Starnes operation (RV exclusion operation with patch over TV orifice + modified BT shunt)
  - Later surgery includes a Cone operation (complex TV repair) or TV replacement
  - Single ventricle palliation to a Fontan is sometimes required
  - Avoiding surgical intervention is preferable

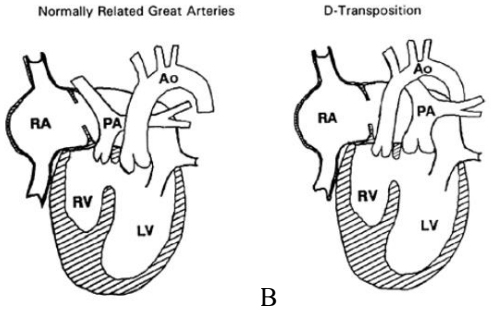
Outcome

- Mortality correlated to earlier presentation and severity of lesion
- 18% of symptomatic neonates die in the neonatal period

10.4.5 – Tricuspid Atresia

Pathophysiology

- Absent tricuspid valve with hypoplastic RV and PA
  - Requires associated defects for survival - ASD, VSD, or PDA
  - All systemic venous return shunts from RA to LA
- Relation of the great arteries (ventriculoarterial (VA) concordance)
  - VA concordant (70%) - TA with normally related great arteries
    - Typically, small VSD + PS with hypoplastic PAs
  - VA discordant (30%) - TA + d-TGA
    - Typically, VSD without PS
    - Commonly associated with coarctation, interrupted arch
- Degree of cyanosis dependent on size of VSD and severity of pulmonary stenosis (PS)
  - Pulmonary blood flow may be augmented by or dependent on a PDA
- In patients with TA + TGA, LV blood flows directly into pulmonary artery, whereas systemic blood has to go through VSD + RV to reach aorta; as a result, pulmonary blood flow is usually significantly increased with early heart failure development



A B

Figure 10.4.5a – Tricuspid atresia. A. TA with normally related great arteries (VA concordant). B. TA with d-TGA (VA disconcordant) (Image from pedscards.com)

Clinical Presentation
- Clinical - cyanosis evident at birth (SpO2 75-85%), tachypnea, poor feeding, hepatomegaly if inadequate ASD
- Auscultation - single S2, grade 2-3/6 holosystolic murmur of VSD, LLSB

Investigations
- ECG - LAD (specifically L superior QRS, usually -30 to -90), LVH
    - Cyanosis + LAD on ECG is highly suggestive of TA
- Echo - TA +/- associated defects (VSD, great vessel relationship), degree of PS, arch obstruction

Management
- Immediate intervention (if severe cyanosis, SpO2 <75%) - PGE1 for ductal patency
- Early interventions
    - Pulmonary artery banding if increased pulmonary blood flow via unobstructed RVOT (TA + d-TGA)
    - Infrequently, BAS to improve R to L atrial shunting
    - Follow for signs of developing cyanosis (usually indicates VSD closure, which occurs over 6-12 months)
- Staged surgical palliation
    - Stage 1 - Ensure favourable anatomy for future palliation (aim for normal LV function and low PVR)
        - Either modified BT shunt (volume offloading)
        - or PA banding (maintain PVR)
        - or DKS + modified BT shunt (for TA + d-TGA + restrictive VSD)
    - Stage 2 - Bidirectional Glenn operation or Hemi-Fontan (4-6mo of age)
    - Stage 3 - Fontan operation (2-5 years of age)

Outcome
- Good overall early survival of 90% at 1 month and 80% at 1 year with poor late survival of 60% at 20 years

10.4.6 – TAPVR (Total anomalous pulmonary venous return)

(a.k.a. TAPVC (connection) or TAPVD (drainage))

Pathophysiology
- Pulmonary veins do not drain into LA directly, but rather into a confluence
- Confluence drains then into one of three main locations
    - Supracardiac (50%) - all PV drain into SVC (predominantly L via *vertical vein*)
    - Cardiac (25%) - PV drain into coronary sinus or RA
    - Infra cardiac (20%) - all PV drain into portal vein, ductus venosus, hepatic veins or IVC (always considered obstructed)
    - Mixed type (5%)
- Mix of desaturated and fully oxygenated blood mix in RA - obligate R to L shunt at ASD

Clinical Presentation
- Often missed on prenatal screening
- Obstructed TAPVR
    - Profound cyanosis (SpO2 50-60%), respiratory distress from pulmonary edema
    - Loud and single S2, gallop
    - Behaves like PPHN with all R to L shunting
- Unobstructed TAPVR
    - Mild cyanosis, FTT, CHF
    - S2 split and fixed, accentuated P2, grade 2-3/6 SEM ULSB (increased flow through PV)

Investigations
- ECG - RVH
- CXR - small (underfilled heart) pulmonary edema and “snowman” (if supracardiac)
    - If not obstructed, have cardiomegaly with pulmonary artery and RV prominence, and increased pulmonary vascularity

- Echo - ASD R-L, dilated RV with abnormal pulmonary connections (vein with doppler flow away from heart is pathognomonic for TAPVR), echo evidence of pulmonary hypertension with PDA R-L
- Pre-op MRI or CT if non-emergent and question of drainage for 1+ pulmonary vein

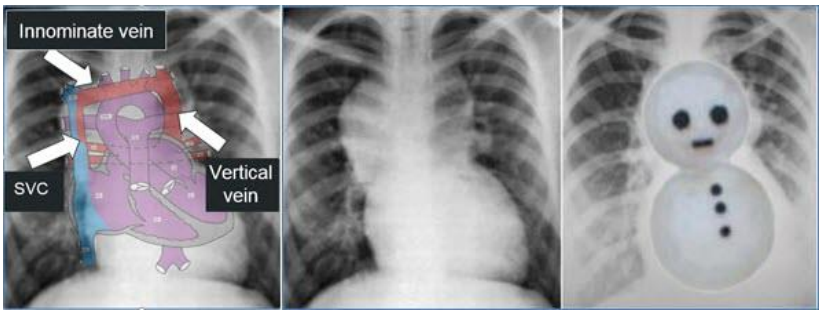


Figure 10.4.6a – Chest X-ray illustrating the "snowman" sign in a case of supracardiac TAPVC (Image from UTMB)

Management

- Obstructed TAPVR is a SURGICAL EMERGENCY! No PGE1! (will worsen clinically due to worsened obstruction)
    - While awaiting surgery may require intubation with careful PEEP (if overventilated will worsen venous obstruction)
- Unobstructed TAPVR - may require diuretics
- Surgical correction
    - May require ECMO if surgery cannot be performed urgently for obstructed TAPVR
    - Various surgical correction techniques depend on specific anatomy but all operations aim to reimplant all pulmonary veins to left atrium and close the ASD

10.4.7 – Truncus Arteriosus

(a.k.a. persistent truncus arteriosus, common arterial trunk)

Pathophysiology

- Both ventricles supply blood through common outlet – total mixing lesion
- Classified as 3 separate types
    - Type 1 - pulmonary artery arises from posterior L side of persistent truncus, then divides into L and R pulmonary arteries
    - Types 2/3 - no main pulmonary artery, R and L pulmonary arteries arise from orifices on posterior (type 2) or lateral (type 3) aspects of truncus
- Most do not have a duct except in the case of interrupted aortic arch (IAA)
- Coronary artery abnormalities are always present
- Associated with DiGeorge Syndrome (microdeletion 22q11) is high (approximately 30% of those with truncus arteriosus have 22q11)

Clinical Presentation

- Clinical - acyanotic to cyanotic (not profound), CHF, hemodynamic instability
- Auscultation - normal S1 and loud single S2, harsh 2-4/6 SEM if truncal stenosis or diastolic murmur if truncal insufficiency

Investigations

- ECG - biventricular hypertrophy
- CXR - cardiac enlargement, increased pulmonary vascularity
- Echo - diagnostic, with large truncal vessel overriding a large subarterial VSD +/- aortic arch abnormalities, truncal valve can have between 2-6 cusps and have varying degrees of regurgitation and/or stenosis.

Management
- Careful management of ventilation, oxygenation and diuretics with close monitoring of perfusion and saturations (aim for 75-85%) – delicate hemodynamics as blood must choose direction to flow (coronaries, lungs, or body)
- PGE1 generally not indicated unless IAA present
- Immediate surgical intervention
    - Close the VSD, commit the truncal valve/outflow to the LV, RV-PA conduit, +/- repair of truncal valve
- Common issues - truncal regurgitation, truncal stenosis, myocardial ischemia

Outcome
- Mortality associated with degree of truncal valve stenosis or regurgitation, for complex anatomy 4-6x more likely to die within 30 days of surgery

10.4.8 – Hypoplastic Left Heart Syndrome

Pathophysiology
- Spectrum of anomalies characterized by underdevelopment of the left heart structures (any defect along the path from MV to LV to AoV to aortic arch)
    - Mitral valve - normal, hypoplastic to atretic, varying degrees of mitral stenosis
    - Aortic valve - hypoplastic to atretic, bicuspid, varying degrees of obstruction
    - LV - mild-borderline hypoplastic to complete absence of an LV cavity, to a small, "hypertensive" LV (seen with mitral stenosis + aortic atresia, and can have coronary sinusoids)
    - ASD - can be unrestrictive, restrictive or intact (an intact atrial septum is the most severe, leading to early demise of the infant if not treated)
- Blood flows from pulmonary veins via ASD to RA-RV via PDA to the descending aorta and lower body
    - Flow from ductus also fills ascending aorta/brain and CAs in retrograde fashion
- Can have inadequate maintenance of systemic circulation and potentially pulmonary venous HTN (if restrictive ASD)
- May be isolated lesion or associated (5-15%) with Turner syndrome, trisomy 13, 18, or 21 or Jacobsen syndrome (11q deletion)

Clinical Presentation
- Critically ill in first hours-days of life as duct closes with cyanosis and shock state with poor systemic perfusion and weak/absent pulses

Investigations
- ECG - RV dominance with eventual P wave prominence
- CXR - variable in first few days of life with rapid cardiomegaly associated with increased pulmonary vascularity
- Echo - diagnostic, absence or hypoplasia of mitral valve and aortic root, with variably small LA/LV and correlated large RA/RV, varying degrees of TR and RV dysfunction, ASD size/shunting crucial

Management
- Pre-operative medical management
    - PGE1 to maintain ductal patency
    - Avoid excessive pulmonary blood flow
        - Maintain O2 saturations 80-85% with FiO2 0.21 (careful not to over oxygenate and shunt blood to lungs away from systemic perfusion)
        - May require hypoxic oxygen mixture in a hood (FiO2 0.19)
- Staged surgical palliation
    - Stage 1a - Norwood procedure
        - PA divided with closure of the distal stump allowing for a neo-aorta to be created using the proximal PA and hypoplastic aorta
        - Modified BT shunt (R subclavian to RPA) or Sano connection (RV to PA)
        - Atrial septectomy

        - New anatomy - flow from PV to RA to RV to neo-aorta to systemic circulation with pulmonary circulation supplied only by the shunt (requires anti-coagulation until next stage)
    - Stage 1b - Hybrid operation
        - Bilateral PA banding with PDA stent to palliate to next stage (along with atrial septostomy)
    - Stage 2 - Bidirectional Glenn operation (3-6 months of age)
        - Anastomosis of SVC to PAs, either RSVC to PA or if bilateral SVCs then both are anastomosed
        - If hybrid approach in Stage 1b, combined Norwood + Glenn in Stage 2
    - Stage 3 - Modified Fontan procedure (2-5 years of age)
        - Connection of IVC to PAs with fenestration to RA (fenestration closed by device in cath lab 6-12 months later if tolerated)
- Anticoagulation by low molecular weight heparin between Stage 1 and Stage 2
- Cardiac transplantation less in favour given chronic risk of organ rejection, need for lifelong immunosuppressive therapy, and organ availability

Outcome

- Early outcomes - hospital survival approximately 70% (90% for standard risk)
- Late outcomes - approximately 65% survive to the Fontan, overall survival to 20 years of age approximately 50%
- Poorest neurodevelopmental outcomes of all heart lesions with a range of disabilities from CP to intellectual disability, to functional limitations in over 50% of the cohort
- Other morbidities including RV failure, ischemia, stroke, protein losing enteropathy, and arrhythmias

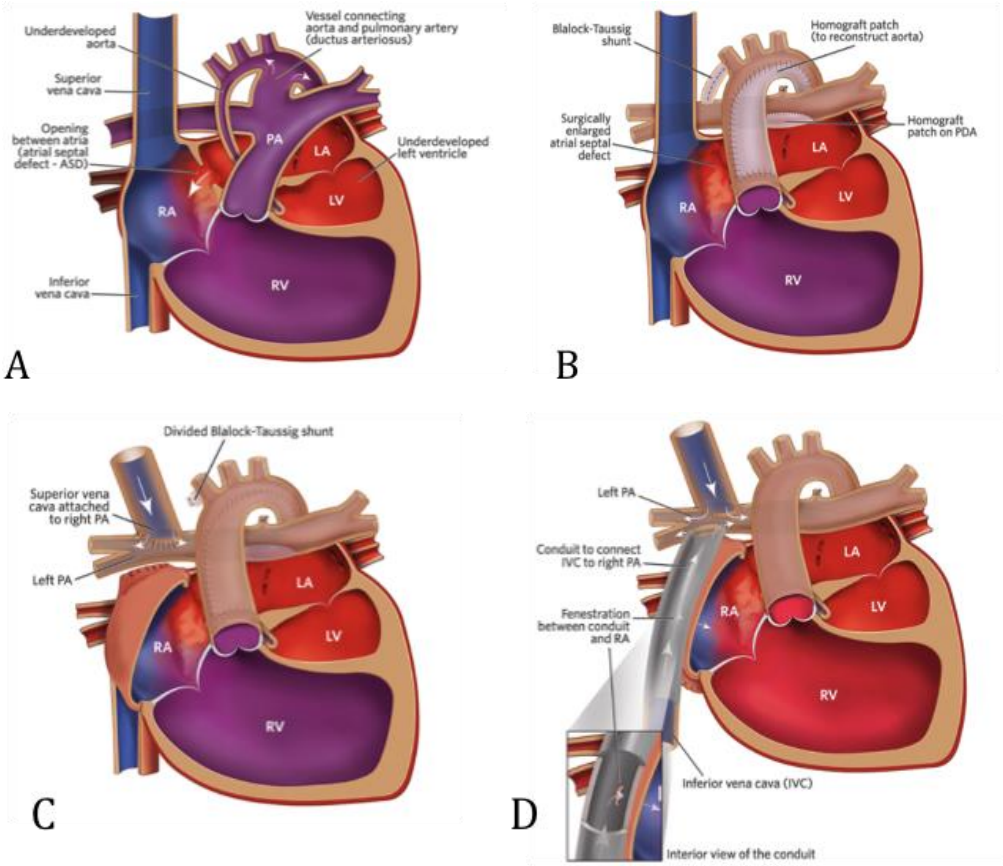


Figure 10.4.8a – Hypoplastic left heart anatomy and the three-staged palliative procedure. A. Hypoplastic left heart anatomy, B. Stage 1 Norwood procedure with modified BT shunt, C. Stage 2 Bidirectional Glenn with divided BT shunt, D. Stage 3 Extracardiac fenestrated Fontan procedure (Image from CHOP)

10.5 – Arrhythmias

10.5.1 – General principles and ECG interpretation
10.5.2 – Tachyarrhythmias
10.5.3 – Bradyarrhythmias
10.5.4 – Long QT Syndrome
10.5.5 – PACs and PVCs

10.5.1 – General principles and ECG Interpretation

ECG Interpretation in the term newborn

- Normal to right axis deviation
- RV dominance in precordial leads (predominantly R in V1, predominantly S in V6)
- T waves
    - Upright in right precordial leads (V1, V3R) for first 72hr is normal
        - Should invert in 1 week, if remain upright may signal pathology with RVH
    - T wave in V3, V2, V1 inverted in childhood then becomes upright in sequence V3, V2, V1
    - T wave in V5, V6 always upright (if not may signal coronary abnormality)
        - May see flat T waves in inferior-lateral leads transiently (signal transient myocardial ischemia of the newborn)
    - All T waves upright by adulthood

Lead	0–1 months	1–3 months	3–6 months	6–12 months	1–3 years
Heart rate (beats . min $^{-1}$)	160 (129, 192)	152 (126, 187)	134 (**112**, **165**)	128 (106, 194)	**119** (97, **155**)
	155 (136, 216)	154 (126, 200)	139 (**122**, **191**)	134 (106, 187)	**128** (95, **178**)
P axis (°)	56 (13, 99)	52 (10, 73)	49 (− 5, 70)	49 (9, 87)	48 (− 12, 78)
	52 (24, 80)	48 (20, 77)	51 (16, 80)	50 (14, 69)	47 (1, 90)
P duration (ms)	78 (64, 85)	79 (65, 98)	81 (64, 103)	80 (66, 96)	80 (63, 113)
	79 (69, 106)	78 (62, 105)	78 (63, 106)	80 (64, 07)	83 (62, 104)
PR interval (ms)	99 (77, 120)	98 (85, 120)	106 (87, 134)	114 (82, 141)	118 (86, 151)
	101 (91, 121)	99 (78, 133)	106 (84, 127)	109 (88, 133)	113 (78, 147)
QRS axis (°)	97 (75, 140)	87 (37, 138)	66 (− 6, 107)	68 (14, 122)	64 (− 4, 118)
	110 (63, 155)	80 (39, 121)	70 (17, 108)	67 (1, 102)	69 (2, 121)
QRS duration (ms)	67 (50, 85)	64 (52, 77)	66 (54, **85**)	**69** (52, **86**)	**71** (54, 88)
	67 (54, 79)	63 (48, 77)	64 (50, **78**)	**64** (52, **80**)	**68** (54, 85)
QTc interval (ms)*	413 (378, 448)	419 (**396**, 458)	422 (391, 453)	411 (379, 449)	412 (383, 455)
	420 (379, 462)	424 (**381**, 454)	418 (386, 448)	414 (381, 446)	417 (381, 447)

Bold values indicate that the 95% confidence intervals of the percentile estimates for boys and girls do not overlap.

*Corrected QT interval, according to Bazett's formula: $QTc = QT \cdot \sqrt{\frac{\text{heart rate}}{60}}$.

Figure 10.5.1a - Lead-independent ECG measurements for boys (upper row) and girls (lower row) showing the median value and range (2nd percentile to 98th percentile) (Image from Rijnbeek et al., 2001)

Approach to arrhythmias

- Is the baby hemodynamically stable or unstable?
- Intermittent or prolonged? Regular or irregular?
- Known underlying congenital heart disease or suspected CHD?
- Suspected arrhythmias should have a 15 lead ECG, baseline echo for structural/functional assessment
- Consider Holter monitor for better characterization
- Exclude non-cardiac causes of any arrhythmia - electrolytes, Ca, Mg, TSH, CNS

Sinus Tachycardia

- Causes - sepsis, hypovolemia, shock, anemia, thyrotoxicosis, congestive heart failure, myocardial disease
- ECG - regular rapid heart rate defined as >98th percentile for patient's age, 1:1 conduction ratio of P to QRS complexes with a P wave preceding every QRS complex and upright P wave morphology in I/avL/II/III/avF and inverted in avR

Sinus Bradycardia

- Causes - increased intracranial pressure, hypothyroidism, hypothermia, hypoxia, drugs, elevated intra-abdominal pressure (may stimulate vagal nerve)
- ECG - slow heart rate defined as <2nd percentile for patient's age, 1:1 conduction ratio of P to QRS complexes with a P wave preceding every QRS complex
- Generally benign, heart rate should be variable (differentials include 2:1 AV block, complete heart block, long QT syndrome)
- Specific treatment is not required, treat underlying cause

10.5.2 – Tachyarrhythmias

Supraventricular tachycardia (SVT)

Pathophysiology

- Most common tachyarrhythmia in newborn period
- Most often due to re-entrant pathway or AET (atrial ectopic tachycardia)
- SVT can occur due to indwelling lines such as UV catheters or PICC lines too far in the RA
- Maternal prenatal therapy may include sotalol, flecainide, digoxin
    - Pregnancies are closely followed. with risk of fetal hydrops
    - Early delivery can be indicated which can resolve the fetal SVT

Clinical Presentation

- May have a history of SVT in utero
- History of restlessness, tachypnea, irritability, poor feeding
    - May develop abruptly with SVT or 12-24 hours later
    - Without treatment, prolonged SVT can result in rapid cardiovascular compromise (tachycardia induced cardiomyopathy)

Investigations

- ECG showing
    - Persistent regular ventricular rate >220 bpm
    - QRS complex is narrow (<0.08 sec)
    - Absent P wave or P wave seen after QRS
    - Fixed and regular R-R interval
    - Little variability in HR with activities (crying, feeding, apnea)
- Must run rhythm strip throughout interventions to determine underlying rhythm

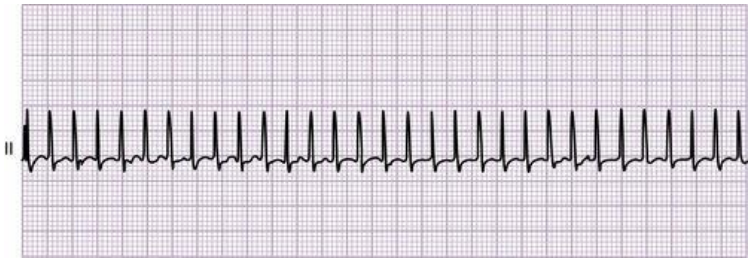


Figure 10.5.2a – ECG showing SVT (Image from Gardner et al. 2015)

Management

- Vagal maneuvers (first line for hemodynamically stable neonate)
    - Stimulation of diving reflex with ice bag applied to face (must cover entire face and be aggressively applied for >15 seconds)
- Acute management
    - Adenosine, 0.1 mg/kg IV, max 6 mg (can increase to 0.2 mg/kg, max 12 mg)
        - Administered as rapid IV push followed by normal saline bolus through venous access because of very short half-life (do not give through arterial line)
        - Always run a rhythm strip when delivering adenosine

        - Mechanism - slows the sinus rate resulting in a transient AV block
            - Will break re-entrant SVT (AV-nodal dependent tachycardias) but will NOT break atrial tachycardias such as AET
- Maintenance therapy
    - First line agent - beta blocker (e.g. IV Esmolol or PO Propranolol) assuming normal cardiac function
        - Monitor for hypoglycemia and hypotension in infant on beta blocker
    - Second line agent - class I antiarrhythmics (Procainamide, Flecanide) or class III agents (Sotalol or Amiodarone)
- Synchronized cardioversion (if hemodynamically unstable)
    - Consult cardiology for further management prior to cardioversion
    - Sedation of neonate prior to cardioversion
    - Direct current (DC) cardioversion (starting at 0.5-1 J/kg, can increase to 2 J/kg)
- Other interventions - Esophageal pacing

10.5.3 – Bradyarrhythmias

Congenital Complete Heart Block

Pathophysiology

- Caused by neonatal lupus in 60-90% of cases (maternal anti-Ro and anti-La antibodies)
    - May also be associated with congenital heart lesions (most commonly ccTGA, left atrial isomerism (interrupted IVC +/- AVSD), neonatal myocarditis
    - Mortality is very high if associated with congenital heart disease
- Frequently diagnosed prenatally by fetal echo

Investigations

- ECG
    - Marked, persistent bradycardia (HR<80bpm)
    - Regular ventricular rate
    - Faster regular atrial rate (P waves are seen dissociated from the QRS complex "marching through" at a rate usually 2:1)
    - Measure P-P and R-R intervals and compare
- 24-hour Holter - determines range of heart rate and its variability and longest pause (>3 secs is criteria for pacemaker)
- Echo - rule out structural heart disease and determine ventricular function

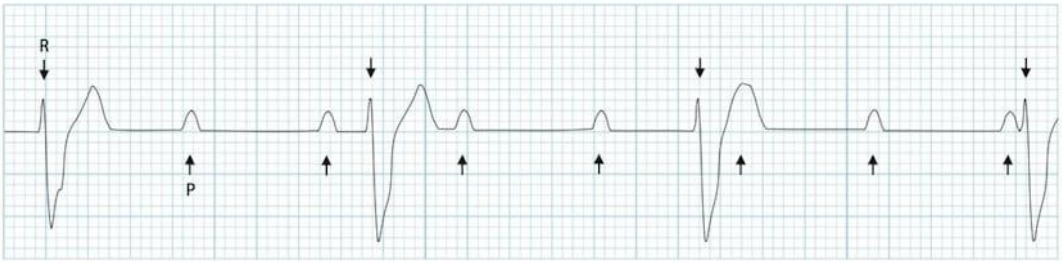


Figure 10.5.3a – ECG showing complete heart block with AV dissociation (Image from litfl.com)

Management

- In utero may include maternal therapy with dexamethasone +/- IVIG (only if associated with anti-Ro/La antibodies)
- May not require treatment as newborn if asymptomatic with normal ventricular function and acceptable heart rate (>55 bpm)
- If symptomatic may use IV isoproterenol, atropine (2nd line) and ultimately epicardial ventricular pacing
- Complications in utero include hydrops fetalis, LV dysfunction, fetal demise
- Complications in early infancy include congestive heart failure

10.5.4 – Long QT Syndrome

Pathophysiology

- Genetic disorder (>300 mutations identified) of ventricular repolarization (disorder of cardiac Na+ and K+ channels) that can cause VT and/or torsades des pointes and sudden cardiac death (consider family history)
- Acquired causes - drugs, electrolyte disturbances (hypokalemia, hypocalcemia, hypomagnesemia), bradycardias (including in cooled newborns), myocardial dysfunction, endocrinopathies, neurologic conditions (stroke, subarachnoid hemorrhage, encephalitis)

Investigations

- ECG - rhythm can present as sinus bradycardia, pseudo-2:1 AV block, PVCs or as ventricular tachycardia
- Manual measurement of QTc (Bazett formula)
    - QTc = QT divided by the square root of the preceding R-R interval (in seconds)
    - Measure QTc in lead II at the shortest and longest RR interval
- Multiple ECGs may be required to confirm the diagnosis
- Normal intervals in neonates - QTc <440 ms within normal range (female > male)
    - QTc >450 ms repeat in 1-2 weeks
    - QTc >470 ms requires further work up
- 24 hr Holter - assess overall heart rhythm, heart rate range/variability, presence of PVCs/VT
- Echo - mainly to assess ventricular function

Management

- Propranolol 0.5-1mg/kg/dose PO q6-8h is first line therapy
- Pacemaker or defibrillator may be required

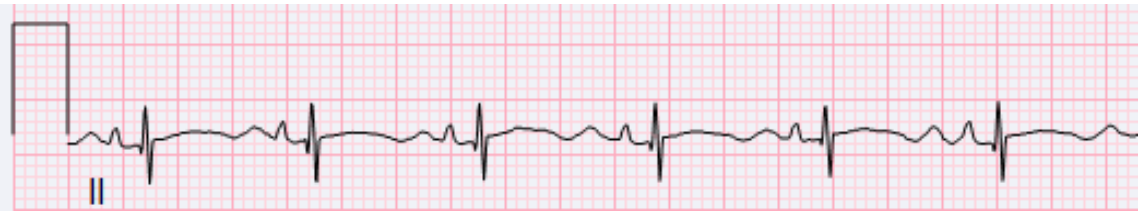


Figure 10.5.4a - Infant with LQTS with a QTc of 590 msec (Image provided by Dr. L. Nield)

10.5.5 – PACs and PVCs (ectopic beats)

Premature Atrial Contractions (PACs)

Pathophysiology

- May occur in healthy newborns
- Premature beats originate in the RA or LA
- If PACs are frequent, can lead to SVT in those predisposed to re-entrant SVT

Investigations

- ECG - an early, narrow complex QRS with a preceding P wave is seen on ECG or monitor
    - Occasionally a PAC can have a wide QRS complex (PAC with aberrancy)
    - Note - a wide complex rhythm is ventricular until proven otherwise
- Blood work to exclude non-cardiac causes

Management

- Occasional, isolated PACs are of no hemodynamic significance and treatment not indicated

Premature Ventricular Contractions (PVCs)

Pathophysiology

- Premature beats can originate from the RV or LV (risk of ventricular tachycardia)
- Rarely normal in an infant but can benign
    - Generally signifies an underlying electrolyte/cardiac or metabolic abnormality

- Associated with cardiomyopathies, myocardial ischemia, Long QT syndrome, metabolic disorder, genetic disorders
    - Family history of sudden cardiac death, cardiomyopathies

Investigations

- Blood work to exclude non-cardiac causes
- ECG -wide complex early beats, can be monomorphic or polymorphic,
    - Bigeminy = abnormal beat between 2 normal beats
    - Couplets/Triplets = 2 or 3 abnormal beats in a row
    - Ventricular tachycardia = > 3 abnormal QRS beats in a row
- Echo - rule out structural heart disease and assess ventricular function
- 24-hour Holter - determine frequency and type of PVCs and if VT is seen
- Cardiac MRI - can be performed to determine if there is an underlying myocardial abnormality such as LV non compaction, ARVD (arrhythmogenic RV dysplasia)

Management

- Treat underlying cause
- If PVCs are intermittent, asymptomatic and no underlying cardiac disease has been found, can be monitored clinically
- Indication for treatment (PO propranolol) includes hemodynamically unstable VT or ventricular dysfunction

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Chapter 11 – General Surgery

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11.1 - Perioperative Fluid Management

Key points

- Peri-operative stress leads to risk of electrolyte abnormalities requiring specific consideration of fluid administration in neonates.

Physiology

- Neuroendocrine response to surgery/stress → ↑ ADH → retention → ↑ free body water, can lead to ↓ Na+ (rationale for reduction in TFI)
- Neonates at baseline - ↑ risk of hypoglycemia + lipolysis 2º to increased metabolism, decreased glycogen stores, impaired gluconeogenesis
- Response to anesthesia - stress, decreased metabolism and O_2 consumption = decreased glucose requirements and risk of hyperglycemia

Management

- TPN should be stopped and IV fluids without potassium should be started ≤2hrs pre op
- GIR should aim to be reduced by ~20-25% for a neonate on a TFI of 150-160mg/kg/day (general guiding principal)
- Any change to TFI or GIR should ideally occur ≤2hrs pre op
- Special considerations for patients with dehydration, fluid overload, unstable blood glucose, glucagon within 7 days

Perioperative fluid management algorithm in brief (see Sick Kids policy as example)

- Maintain current TFI (unless >120 then reduce to 120ml/kg/d)
- Use 0.45 normal saline (unless <48hr old and postnatal weight loss has not occurred then use dextrose only)
- Match current dextrose concentration unless if D12.5W change to D10W (special considerations for >D12.5W)
- Monitor blood glucose pre and post-op if changes to dextrose concentration

Perioperative challenges

- Post-op hyponatremia
    - Contributing Factors - increase ADH secretion, hypotonic fluids
    - Rationale for use of hypotonic fluids - Risk with isotonic fluids due to tolerability of increased Na+, concern for delay in contraction of ECF + postnatal diuresis
- Post-op glucose
    - Hypoglycemia - expect operative stress to increase BG, caution not to decrease GIR dramatically for risk of hypoglycemia
    - Hyperglycemia - due to stress response, can lead to osmotic diuresis (BG >12mmol/L), increased lactate production, and acidosis (rationale for decreased GIR with reduction in TFI if >120)

11.2 - Post-op Pain Management

Pain assessment

- Premature Infant Pain Profile Revised (PIPP-R) scale
    - 0-6 = none, 7-11 = moderate, >/= 12 = severe
- Face, Legs, Activity, Cry, Consolability (FLACC-R) scale (>2mo corrected age)
    - 0-3 = none, 4-6 = mild to moderate, 7-10 = severe
- Neonatal Pain, Agitation and Sedation scale (N-PASS)
    - Measures level of sedation for those receiving opioids or sedatives

Post-op pain algorithm (adapted from Sick Kids Post-Operative Pain Guidelines)

- Algorithm A - Mild pain
    - Scheduled Acetaminophen x 48 hours
    - Intermittent IV morphine (0.05 mg/kg/dose) q4h PRN for breakthrough pain
- Algorithm B - Moderate pain
    - Scheduled Acetaminophen x 72 hours
    - Continuous morphine infusion 5mcg/kg/hour (alternative = Fentanyl)
    - Intermittent morphine 0.1mg/kg/dose q4h prn for breakthrough pain
- Algorithm C - Severe pain
    - Scheduled Acetaminophen x 72 hours
    - Acute Pain Service (APS) will order continuous regional/epidural infusion and PRN morphine
- Key points
    - Assess pain (PIPP-R or FLACC-R) and sedation (N-PASS) scores q1h for 4 hours
    - Morphine is the recommended agent for post-op pain management
    - Fentanyl indicated for moderate to severe procedural pain (or in place of morphine if concern regarding hypotension)
    - Dexmedetomidine = adjunct for sedation and minor analgesia (common side effects include hypotension and bradycardia)
    - Benzodiazepines used for sedation adjunct (no analgesic activity), used in GA >/= 4 weeks (side effects include respiratory depression, apnea)

Table 11.2 – Classification of procedures based on potential severity of post-operative pain (adapted from Sick Kids Post-Operative Pain Guidelines)

Potential mild pain	Potential moderate pain	Potential severe pain
Bronchoscopy, laparoscopic surgery	Chest tube insertion	Congenital diaphragmatic repair
Ventricular shunt insertion	Gastrostomy tube insertion	EA/TEF repair
Colostomy creation	Omphalocele repair	Laparotomy
Uncomplicated inguinal hernia repair	Abdominal drain insertion	Operative necrotizing enterocolitis
See Algorithm A	*See Algorithm B*	*See Algorithm C*

11.3 – Tracheoesophageal Fistula/Esophageal Atresia (TEF/EA)

Overview

- 33-41% premature (preterm labour may be impacted by polyhydramnios)
- Etiology includes environmental, biomechanical, genetic and other factors leading to abnormal foregut development
- 10% of TEF/EA associated with genetic syndromes: T18, T21, T13, CHARGE, DiGeorge, etc, 30-50% have VACTERL findings

Classification (Gross Classification System)

- Type A – Esophageal atresia without fistula/pure esophageal atresia (8%)
- Type B – Esophageal atresia with proximal TEF (<1%)
- Type C – Esophageal atresia with distal TEF (86%, most common)
- Type D – Esophageal atresia with proximal and distal TOF (<1%)
- Type E – TEF without esophageal atresia, also called H-type fistula (4%)

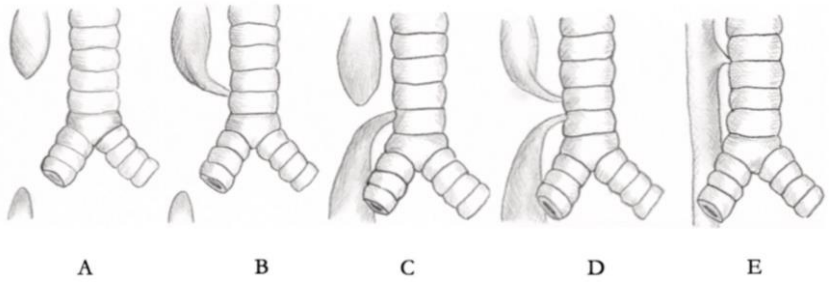

Figure 11.3 – Classification of EA and TEF by type (Image from Adler, 2019)

Presentation

- Antenatal US - polyhydramnios, absence of stomach bubble (if proximal or no fistula)
- Feeding difficulties (choking, coughing, cyanosis), emesis, excess oral secretions, tachypnea/respiratory distress
- Abdominal distension (if distal fistula) or scaphoid abdomen (if proximal or no fistula)
- +/- dysmorphic features related to VACTERL including cardiac murmurs
- Inability to pass orogastric tube into stomach

Investigations

- Attempt to place NG or OG tube (expect resistance at approximately 10cm from lips)
- CXR/AXR - determine placement of tube (coiled in pouch) and presence or absence of abdominal gas
    - Double bubble = concomitant duodenal atresia (2-5% of TEF/EA)
- Echocardiogram - 50% incidence of cardiac anomalies (VSD, ToF, ASD etc.)

Management

- Goal to preserve circulation and oxygenation prior to repair
- NPO and nasal/oral esophageal sump suction tube (Replogle tube) in upper pouch on continuous suction
- Elevate bed to 45 degrees to prevent reflux and aspiration of gastric content
- IV hydration follow by parenteral nutrition
- Respiratory - spontaneous breathing with supplemental oxygen is preferred
    - Be cautious with mechanical ventilation - PPV can lead to gastric distension impairing ventilation and risk of gastric perforation
    - If PPV required in patient with duodenal atresia, then urgent repair required to avoid gastric perforation
- Ligation of TEF is the most urgent step for respiratory stabilization
- Primary repair if esophageal atresia
- Delayed repair with placement of gastrostomy (G tube) to decompress stomach and establish enteral nutrition
    - If long gap or unable to complete primary repair at the same time as TEF ligation
    - If high operative risk due to prematurity, cardiac anomalies or very low weight
- At risk of reflux, dysmotility, feeding intolerance, and feeding aversion

Post-operative care

- Parenteral nutrition, broad spectrum antibiotics
- Avoid continuous positive airway pressure
- Reflux can lead to aspiration - elevate head of bed 45 degrees, frequent suctioning , acid blockage (no evidence for prophylactic PPI use)
- Monitor for complications - anastomotic leak and strictures, esophageal stenosis
    - If cyanotic spells - concern for recurrent aspiration od tracheomalacia
    - Consider missed/recurrent fistula, laryngotracheal cleft, vocal cord paralysis

11.4 - Congenital Diaphragmatic Hernia

Definition

- Abdominal viscera herniates into the thoracic cavity via diaphragmatic defect
- Mass effect on lungs, heart leading to pulmonary hypoplasia, respiratory distress and risk of obstructive shock

Pathophysiology

- Failure of pleuroperitoneal closure ~4-10 wks leading to reduction in bronchiolar branching, altered pulmonary vasculature, reduced surfactant, pulmonary hypoplasia, ipsilateral cardiac hypoplasia
- 95% posterio-lateral (Bochdalek) vs anterior retrosternal/peristernal (Morgagni), rarely central
- 80% left sided, bilateral <2%
- Up to 30% will have associated anomalies - malrotation, chromosomal abnormalities

Presentation

- Antenatal - detection on routine antenatal US (polyhydramnios also a clue)
- Postnatal
    - Severe respiratory distress immediately after birth
    - Heart sounds on right side of chest with
    - Decreased/absent breath sounds on left with bowel sounds in left chest
    - Scaphoid abdomen

Investigations

- CXR - air filled loops of bowel in hemithorax, mediastinal displacement
- DDx - CCAM/CPAM, diaphragmatic eventration

Management

- Antenatal
    - Risk stratification (lung-to-head ratio (LHR), total lung volume observed to expected MRI, position of liver)
    - Screening for associated anomalies (amniocentesis, fetal echo)
    - Parental counselling
    - ?Use and timing of steroids
    - Role of fetal surgery - Fetoscopic Endoluminal Tracheal Occlusion (FETO)
        - Balloon occlusion of the trachea in utero to promote lung growth
    - Fetal surveillance and delivery planning
- Postnatal
    - Delivery at or immediate transfer to surgical centre
    - Initial Stabilization - respiratory stabilization, mitigate mass effect in thorax
    - Immediate intubation with PPV (avoid BMV!) – intubation often performed in OR as baby is delivered (aka first breath intubation)
    - Ventilator settings - CMV, HFOV, JET with pressure limits to avoid barotrauma
    - Wide bore NG - aspirate then leave to free drain
    - Maintain standard CDH physiologic targets (ventilation, oxygenation, blood pressure, airway pressures)
    - Monitor pre and post ductal oxygen saturation
    - Surfactant, Nitric Oxide, Inotropes, sedation, fluid and diuretics usage as required
    - Postnatal testing/ confirmation of associated anomalies
    - Use of ECHO targeted function for therapies
    - Role of ECMO

- Surgical Treatment
    - Surgical closure once stabilized (primary vs. synthetic patch, open vs. minimally invasive surgery)
    - If malrotation present may repair concurrently

Outcomes

- May require significant post operative respiratory support
- Persistent pulmonary hypertension common (HFOV, iNO may be needed and in some cases prolonged use of oxygen and sildenafil)
- Other complications - pulmonary hypoplasia, GERD, feeding intolerance, chylothorax, CLD

11. 5 - Abdominal Wall Defects - Omphalocele & Gastroschisis

Table 11.5 - Key similarities and differences of abdominal wall defects.

	Omphalocele	Gastroschisis
Presentation	- Prenatal AFP elevation - Central/umbilical mass with sac membrane covering (pre- and postnatal ruptures are possible) - Bowel ± liver involvement or hernia into cord (smaller defect) - Minor <5cm, major >5cm	- Prenatal AFP elevation - Paracentral defect (commonly to the right of the umbilicus) with no covering sac - May include bowel, stomach, testes/ovaries
Associations	- 40% have associated syndromes or chromosomal anomalies (Trisomy 13, 18, 21, cardiac defect, Beckwith-Wiedemann syndrome) - Malrotation in all cases	- Less likely to have associated anomalies - Linked to young maternal age, substance use (cocaine) - May have intestinal atresia, stenosis, malrotation, cryptorchidism
Complications	- Respiratory insufficiency (giant omphalocele) - Sac rupture is a surgical emergency, treat as Gastroschisis - Post-op - compartment syndrome	- Higher risk of GI complications (infection, fluid loss, GI motility issues, loss of bowel length) - Post-op - compartment syndrome
Management	- Vaginal delivery possible (C-section if large) - Sterile wrapping of the defect - High TFI (100-120 ml/kg/day), non-umbilical IV access, antibiotics until abdominal wall closure - Bowel decompression - Surgical reduction and wall closure - Paint-and-wait or Silo placement and delayed reduction (if giant)	- Vaginal delivery possible (C-section if liver herniation) - Sterile wrapping of the defect - High TFI (100-120 ml/kg/day), non-umbilical IV access, antibiotics until abdominal wall closure - Bowel decompression - Primary or delayed closure depending on size - Silo insertion and reduction by gravity + active Silo size reduction

Management of Omphalocele

- Initial Stabilization
    - Sterile wrapping of the defect
    - Respiratory support (may have respiratory distress due to pulmonary hypoplasia or pulmonary hypertension)
    - NPO, NG - aspirate + straight drain
    - IV fluids, may feed via NG (less commonly TPN), monitor blood glucose
    - Rupture of the sac at ANY time is a surgical emergency!
- Investigations - upper GI study, karyotype, echocardiogram
- Surgical Management
    - Small defect - direct closure
    - Larger defect - plain sac to induce epithelialisation and development of ventral hernia or Silo/sheath with gradual volume reduction (7-10 days) then surgical closure of the fascia

Management of Gastroschisis

- Initial Stabilization
    - Support the prolapsed content, wrap in cellophane or plastic sheath at delivery
    - Monitor bowel for signs of poor perfusion, avoid tissue damage
    - NPO, NG - aspirate + straight drainage
    - IV Fluids/TPN, IV Abx , monitor electrolytes, consider fluid boluses

- Definitive Management
    - Prolapse enclosed in silo, closed gradually over 5-10 days followed by primary closure of the fascia or dressing to allow secondary closure (known as “plastic “ sutureless closure)
    - Occasionally can undergo primary closure immediately
- Post-Op Management
    - Monitor for abdominal compartment syndrome, anuria, decreased distal pulses, respiratory difficulties
    - Parenteral nutrition until gut function is established
- Prognosis - 90% survival, often issues with gut motility and absorption

11.6 - Intestinal atresia

Pathophysiology

- Congenital intestinal obstruction classified by anatomical region (pyloric, duodenal, jejunoileal, colonic)
- Theories on etiology
    - Lack of revascularization of the solid cord intestinal stage (Tandler’s concept)
    - Late intrauterine vascular accident
- Multiple atresia may be related to diffuse inflammatory cause (vs. vascular)
- Small bowel atresia can occur as a result of volvulus, internal hernias, vanishing gastroschisis, intussusception, etc.

Table 11.6 – Classification of intestinal atresias

	Presentation	**Diagnosis**	**Associations and Complications**	**Management**
Pyloric stenosis	- Non-bilious progressive projectile emesis with feeds - Hypochloremic, hypokalemic metabolic alkalosis - Onset 3-5 weeks of life	- AXR - dilated gastric bubble - US - thickened enlarged pylorus		- Rehydration, electrolyte correction (correct alkalosis to prevent postop apnea!) - Gastric decompression, NPO - Surgical repair (pyloric-myotomy)
Pyloric atresia	- Polyhydramnios - Enlarged gastric bubble - Non-bilious projectile emesis with feeds - Upper abdominal distension	- AXR dilated gastric bubble and absence of distal air	- Epidermolysis bullosa - Other intestinal atresias	- Rehydration, electrolytes correction - Gastric decompression, NPO - Surgical repair (pyloroplasty) or gastroduodenostomy
Duodenal atresia	- Polyhydramnios - Double bubble - Bilious or non-bilious emesis - Upper abdominal distension	- AXR - double bubble and absence of distal air	- Annular pancreas and duodenal webs could present similarly - Other intestinal atresias - Trisomy 21	- Gastric decompression, NPO - Surgical repair and primary duodeno-duodenostomy and duodeno-jejunostomy
Jejunal atresia	- Polyhydramnios - Bilious emesis - Abdominal distension	- AXR - dilated bowel loops and absence of distal air	- Other intestinal atresias - Microcolon	- Gastric decompression, NPO - Surgical repair
Ileal atresia	- Polyhydramnios - Abdominal distension	- AXR - dilated bowel loops and absence of distal air	- Cystic fibrosis - Microcolon	- Gastric decompression, NPO - Surgical repair
Colonic atresia	- Signs of bowel obstruction - No passage of meconium	- AXR - dilated bowel loops and absence of distal air	- Small bowel atresia - Hirschsprung's disease	- Gastric decompression, NPO - Primary anastomosis or colostomy and delayed anastomosis

Presentation

- Maternal polyhydramnios, prenatal US findings of dilated or echogenic bowel (signs of obstruction)
- Bilious emesis/gastric output in first 24-48 hours of life (if atresia distal to duodenum)
- +/- Abdominal distension (may have scaphoid abdomen)
    - More common in distal intestinal atresia (eg. ileal atresia)
    - May not be apparent until 24-48 hours of life in isolated colonic atresia
- +/- Respiratory compromise, signs of intestinal perforation, jaundice (indirect bilirubin)
- Screen for other anomalies - chromosomal syndromes, murmurs, genitourinary abnormalities
    - If jejunoileal atresia suspected in fetus consider screening for cystic fibrosis

Investigations

- Abdominal x-ray (2 views) - dilated bowel loops and absence of distal air
    - May see air fluid levels, free air, calcifications (in utero perforation)
- Note - if suspecting colonic atresia, early x-ray will not rule out obstruction, will need to repeat to see progressive distension
- Contrast enema
    - Can demonstrate microcolon (commonly present in intestinal atresias)
    - Demonstrates colonic patency
    - Screens for functional obstruction (e.g. Hirschsprung disease)
    - Screen for associated anomalies

Management

- Nasogastric decompression as temporizing measure
- Surgical intervention necessary
- Prenatal diagnosis - no indication for fetal intervention or early delivery, delivery with access to paediatric surgery centre

Post-operative management

- Labs - electrolytes, glucose, CBC, acid base balance
- Parenteral nutrition started after 24 hours post op
- Prophylactic antibiotics for first 24 hours post op (controversial)
- NG outputs - replace if >30 ml/kg/day
- Oral feeding - 5-15 mL q3h with slow advance to 120 ml/kg/day
- If extensive loss of bowel length – risk for dumping syndrome and malabsorption
    - Protein hydrolysate formula (medium chain triglycerides) or elemental formula
- Monitor for complications of intestinal atresia repair
    - Infection (pneumonia, sepsis, peritonitis), anastomotic leak, stricture, obstruction (dysmotility, bacterial overgrowth, functional obstruction)
- Malabsorption of fats, bile salts, vitamin B12, calcium, magnesium
    - More common in ileal atresia (may also see steatorrhea)
- Residual small bowel length and the preservation vs. loss of ileocecal valve are important indicators of prognosis and short bowel syndrome.
    - Less than 25 cm of bowel length requires long term TPN
    - Less than 100 cm requires temporary TPN usage
    - Premature babies will have bowel growth and better adaptation with time

11.7 - Malrotation and Midgut Volvulus

Overview

- Malrotation (incomplete rotation) - intestinal anomaly with failure of complete rotation during embryogenesis leading to malposition of gut and narrow mesenteric base
    - Predisposes to abnormal bands or twisting of the bowel's own blood supply
    - Bowel rotates 180 degrees (instead of 270) resulting in the duodenojejunal limb positions in the right epigastrium and the cecum in the left epigastrium
- Volvulus - twisting of bowel/mesentery leading to obstruction and ischemia and subsequent bowel necrosis

- Normal physiology
    - ~4th week midgut (supplied by SMA), herniates into the extraembryonic coelom due to intestinal growth beyond abdominal growth
    - Midgut returns to the abdominal cavity and proximal jejunal loop rotates 270º posterior and to the left, distal cecocolic moves anterior and to the right
    - 10th week - midgut in abdomen, intestinal fixation secures duodenojejunal junction at Ligament of Trietz in LUQ
    - Cecum will eventually fixate in RUQ, timing variable
    - Normal process will create broad, anchoring mesentery that decreases the risk of volvulus
        - Any error in this process = intestinal rotational abnormality (IRA)
        - Without proper fixation, risk of volvulus increases due to narrow based mesentery
- Risk of volvulus in a normally rotated individual due to omphalomesenteric duct remnants, meconium ileus (segmental volvulus), intestinal atresia
- Associated with heterotaxia/situs inversus, T21, intestinal hernia, intestinal atresia, intussusception, biliary atresia, anorectal malformation, hirschsprung

Presentation

- Bilious vomiting, abdominal distension, +/- hematemesis/hematochezia (late)
- Irritability, lethargy, hemodynamic instability, abdominal sepsis/shock

Diagnosis

- AXR - initially non-specific, abnormal gas pattern (SB on R, LB on L +/- double bubble)
- Upper GI series (gold standard)
    - Duodenum does not cross midline
    - Duodenojejunal flexure on right, cecum in upper abdomen
    - Volvulus - duodenal obstruction (birds beak appearance)+ corkscrew appearance
- Abdominal US with dopplers
    - Abnormal orientation of mesenteric vessels SMA:SMV (technician dependent)
    - Volvulus by whirlpool appearance on doppler
- Can be seen on other imaging modalities (MRI, CT) but not typically done

Management

- Volvulus = surgical emergency!
    - Prevent ischemia, necrosis, and to resect necrotic tissue if need
- Malrotation alone - consider expedited surgery if well monitored
- Ladds Procedure
    - Detorsion of volvulus with lysis of abnormal peritoneal bands/Ladds Bands and widening of the mesentery
    - Placement of small bowel on right, large bowel on left (non rotation)
    - Appendectomy (not part of the original Ladd's procedure but commonly done because of location of cecum in the LLQ)

Table 11.7 – Malorotation and volvulus key points.

	Presentation	Diagnosis	Associations	Management
Malrotation/volvulus	- Malrotation may be asymptomatic or present with emesis, distension, & poor weight gain - Midgut volvulus is the most severe complication - Risk of volvulus is higher during the neonatal period -Volvulus will present with bilious emesis - Volvulus can happen prenatally (intraperitoneal calcifications)	- X-ray (may not be diagnostic) - signs of obstruction - US - signs of malrotation (abnormal SMA-SMV) or volvulus (whirlpool sign) - Upper GI contrast study is diagnostic - Direct surgical evaluation if acute abdomen	- Gastroschisis - Omphalocele - Congenital diaphragmatic hernia - Heterotaxy - Trisomy 21 - Small bowel atresia - Post-op obstruction secondary to adhesions is not uncommon	- Volvulus is a surgical emergency - Gastric decompression, NPO, antibiotics - Surgical repair - Ladd´s procedure (malrotation) and volvulus reduction with bowel resection if necrotic segment
Segmental volvulus	-Bilious emesis, abdominal distension	- X-ray (may not be diagnostic) - dilated bowel loops, signs of obstruction -US (whirlpool sign)	- Meconium ileus - Intestinal atresia - Prematurity	- Volvulus is a surgical emergency - Gastric decompression, NPO, antibiotics - Volvulus reduction and bowel resection if necrotic segment

11.8 - Spontaneous Intestinal Perforation

Overview

- Clinically indistinguishable from NEC with similar management but different pathophysiology

Pathophysiology

- Perforation usually of the distal ileum with necrosis of the external muscle layer without signs of bowel inflammation beyond the area of perforation

Risk Factors

- Very/extreme low birth weight <1500g
- Exposure to postnatal Indomethacin
- Exposure to postnatal steroids (synergistic effect of indomethacin and steroids together)
- Candidiasis and staph epidermidis have high incidence/ association

Presentation and diagnosis

- Typically occurs in the first week of life
- Abdominal distension, increased aspirates, change in aspirate quality (bilious), decreased bowel sounds, less likely to be septic appearing as may be seen in NEC
- AXR (two views including cross table lateral or 'shoot through') - extensive pneumoperitoneum with lack of pneumatosis (a gasless abdomen does not exclude the diagnosis)

Management

- Peritoneal drainage (with Penrose drain) may stabilize and be the definitive treatment
- Operative - primary anastomosis vs. enterotomy and mucus fistula

11.9 - Hirschsprung Disease

Pathogenesis

- Functional obstruction of the intestine due to absence of ganglion cells in the rectum and along variable length of intestine
- Incomplete caudal migration, lack of maturation or disappearance of migrated ganglion progenitor cells absence of ganglion cells in the submucosal plexus of the lower intestinal tract
- Ganglion cells produce local nitric oxide which relaxes enteric smooth muscle, needed for peristalsis and internal anal sphincter relaxation results in functional intestinal obstruction

Associations

- Isolated cases (70%), familial (20%), Trisomy 21 (2.3% of patients with T21), Multiple endocrine neoplasia type 2A (MEN2A), Waardenburg-Shah, congenital central hypoventilation syndrome, neuroblastoma, Hirschsprung's associated enterocolitis

Presentation

- Failure to pass meconium in first 24 hours (present in ~90% of pts with HD)
- Signs of bowel obstruction - feeding intolerance, obstipation, bilious emesis
- Abdominal distension, explosive stool/gas post digital rectal exam
- Fever/sepsis secondary to Hirschsprung's associated enterocolitis

Investigations

- Abdominal x-ray - signs of distal intestinal obstruction, saw-tooth mucosal pattern in the sigmoid colon or rectum
- Water-soluble contrast enema
    - Transition zone - proximal dilated bowel and distal contracted aganglionic bowel
    - Abnormal rectosigmoid diameter ratio (normal is greater than 1)
    - Persistence of unevacuated bowel contrast after 24 hours in term newborn
- Anorectal manometry
    - Useful in diagnosing ultrashort segment HD or internal sphincter achalasia (both of which are uncommon)
- Rectal biopsy (gold standard)
    - Bedside procedure using suction biopsy device
    - Complications - inadequate specimen (10%), rectal perforation (0.06%), pelvic sepsis (0.06%), significant hemorrhage (0.5%)

Management

- Medical management
    - Gastric decompression, NPO, IV antibiotics if enterocolitis present
    - Rectal irrigations/stimulation to relieve obstructive symptoms
- Surgical management - Pull through surgery
    - Primary or two stage procedure with temporizing colostomy (if enterocolitis present)
- Post-op care
    - IV fluids until tolerating oral feeds
    - Barrier cream to reduce perianal excoriation
    - Nil per rectum post op
    - Routine dilation may be needed if concern for anastomotic stricture
    - Long term risk of enterocolitis decreased post pull through but not zero.
        - Important to maintain bowel regimen and avoid constipation.
        - Some patients require irrigation, antibiotics +/- botox sphincter injection for recurrent post op enterocolitis

11.10 - Anorectal malformation (ARM)

Definition

- Group of congenital hind gut anomalies in a spectrum ranging from ectopic anal position to complex malformation such as persistent cloaca
- Imperforate anus/lack of anal opening therefore rectum empties
    - Anteriorly into perineum (recto-perineal fistula) or
    - Towards labia minora in females (recto-vestibular fistula, most common ARM in females) or
    - Into urethra (recto-urethral fistula is the most common ARM in males)
- Complex ARM includes bladder neck fistula and cloacal anomalies.
- Association of T21 and imperforate anus without fistula

Anatomy

- Normal anus = adequate size, lined by mucosa, dentate line, located within sphincter complex
- Abnormal anus = absent, flat perineal area, no orifice but anal pit, abnormal anterior position may be fistula
    - In females - one opening common cloaca, two openings normal, three openings vestibular fistula
- Features which predict lower vs. higher fistulas outlined in Table 11.10a
- More complex ARMs may involved the genitourinary tract
- Up to 60% of ARM have associated anomaly
- VACTERL (see Genetics)
    - Vertebral (hemivertebrae, fused, missing, extra or, misshaped vertebrae)
    - Anal (anal atresia)
    - Cardiovascular (eg. ASD, PDA, tetralogy of Fallot, VSD)
    - Tracheo-Esophageal fistula, GI anomalies
    - Renal, GU (eg. vesicouretral reflux, hydronephrosis, renal agensis/dysplasia), Gyne (eg. uterine malformation such as bicornate, vaginal anomalies)
    - Limb anomalies
- Currarino triad - (1) ARM, (2) Sacral defect, (3) Presacral mass (seen with anal stenosis and rectal atresia)

Presentation

- Close examination of the perineal area
- Other findings on physical exam - cardiac murmur, esophageal atresia (NG pass through), abdominal mass (hydrocolpos), inguinal hernia
- Note - meconium passage does not rule out the diagnosis (look out for recto-vaginal, urinary or perineal fistulas)

Table 11.10 – Perineal features which predict lower vs. higher fistulas (adapted from Speck et al., 2020)

Lower	Higher
Normal appearing buttocks	Flat buttocks
Perineal or vestibular fistula	Obvious lack of musculature
Subepithelial raphe fistula	Lack of buttock crease
Midline skin bridge (bucket handle)	Lack of anal dimple
Funnel anus (skin lined)	Sacral abnormalities

Investigations

- X-ray - esophageal atresia, vertebral anomalies, limb anomalies
- AUS - GU anomalies
- Echo - congenital heart disease
- Spinal ultrasound - tethered spinal cord and presacral mass

Management - Surgical anoplasty

- Initially gastric decompression and NPO
- Early surgical repair for low ARM +/- anorectal dilations prior to anoplasty
    - Diverting colostomy may be required if primary repair not possible and no fistula present
- +/- prophylactic antibiotics if suspected urinary tract fistula or vesicoureteral reflux
- Reasons for delayed repair
    - Cardiac anomalies, may consider colostomy as a temporizing measure
    - Complex anomalies (cloaca) require neonatal stoma and later repair
- Post-op complications include anal stenosis, constipation, incontinence

11.11 - Inguinal Hernia

Definition and Pathophysiology

- Weakness in the anterior abdominal wall resulting in exit of tissue through the wall of the cavity in which it normally resides
    - Indirect (more common): patent processus vaginialis (lateral to epigastric vessels)
    - Direct: weakness of inguinal floor medial to epigastric vessels
- Contents: omentum, small intestine; rarely large bowel, ovaries, fallopean tube
- Incarcerated = irreducible but good blood supply, may have pain or bowel obstruction
- Strangulated = irreducible with compromised blood supply/ischemia

Epidemiology

- Right sided > left sided > bilateral; M>F; common in preterm male infants up to 20% in lower GA

Presentation

- Asymptomatic - groin/scrotal swelling exacerbated by increased intra-abdominal pressure
- Symptomatic - tender or firm mass , irritability, vomiting, distension/obstruction, overlying skin changes, tachycardia, +/- leukocytosis

Management

- Asymptomatic - elective surgery
    - Immediate surgical consult or as soon as possible after diagnosis
    - Ideally within 14 days after diagnosis
        - At Sick Kids ~ 3 weeks for infants, 6 weeks for older children
    - If preterm, risk of OR/anaesthesia higher
        - Often wait until 50 weeks CGA for OR to minimize risk of post anaesthesia apnea
        - Individualized approach
- Symptomatic - call general surgery for manual reduction vs. surgery
    - Will attempt to reduce with analgesia
    - Surgical closure with closure of processus vaginalis within 24-48hr
    - Emergency OR if strangulated

Complications

- Incarceration
    - Occurs in 17% of right-sided, 7% of left-sided
    - >50% of incarcerations occur in the first 6 months of life (2/3rds within 1yr)
    - Premature infants x2 more likely to incarcerate
- Strangulation - obstruction, necrosis, perforation
- Reproductive structures may be affected - testicular/ovarian necrosis or atrophy, tubal stricture

11.12 - Undescended Testes (Cryptorchidism)

Key points

- ~80% of cryptorchid testes descend by third month of life
- Corrective surgery by 6-12 months of age
- Up to 50% of preterm infants <32 weeks GA, urology or general surgery will see for orchidopexy referral, should make the referral at or beyond 6 months corrected age.

Classification

- Undescended - failure to descend from retroperitoneal origin to scrotum
- Retractile - contraction of cremaster muscle pulls normally descended testis out of scrotum
- Ectopic - not in normal path of descent
- Absent/vanishing - no visible testis as a result of in utero event
- Ascended - previously confirmed to be in scrotum, now located above scrotum
- Entrapped - descent into scrotum blocked by scar tissue from previous operation

Presentation

- Scrotum may be underdeveloped
- Developed but empty scrotum (possibility for retractile or ascended testis)

- Milk groin from anterior superior iliac spine
    - Undescended testis will not reach scrotum
    - Retractile testis can be brought into scrotum (note - does not require orchidopexy unless evidence of testicular atrophy)

Where is the undescended testis?

- Superficial inguinal ring (44%), superficial inguinal pouch of Denis Bowne (26%), inguinal canal (20%), intra-abdominal (6%), absent or vanishing (3%), perineal (0.4%)

Investigations

- Imaging studies not helpful (cannot reliably find abdominal testis)
- Renal ultrasound - in patients with complete vasal atresia (atresia of the vas deferens), ipsilateral kidney may be absent

Management - orchiopexy surgery between 6-12 months of age

- Indications for surgery (orchiopexy) - HIS TESTIS
    - Hernia - patent processes vaginalis in 60-90% of children with undescended testes
    - Injury - orchiopexy helps avoid testicular trauma
    - Symmetry - cosmesis
    - Tumour - orchiopexy allows for examination of testis (eg. to identify testicular neoplasm)
    - Epididymo-orchitis - prevents epididymo-orchitis (prevents repeated trauma of testis when in inguinal canal)
    - Sterility - risk of infertility increased in abnormal testis
    - Torsion - prevents torsion caused by inadequate attachment of testis
    - Intersexuality - bilateral undescended testes and hypospadias (screen for disorders of sexual development)
    - Psychological considerations

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Chapter 12 – Gastroenterology

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12.1 - Necrotizing Enterocolitis (NEC)

- Pathophysiology- precise pathophysiology is unknown, but thought to be a multifactorial process including gut ischemia, bacterial translocation, and inflammation
- Risk factors include prematurity, feeding with formula and fortifiers, bacterial colonisation, PDA, congenital heart disease
- Incidence increases with decreasing gestational age at birth
- Full term infants rarely get NEC
    - Usually colonic, presents in the first few days of life and more commonly associated with HIE or CHD
    - Premature infants tend to develop NEC later than their full-term counterparts
- Clinical presentation
    - Local - abdominal distension, discoloration, and tenderness, bloody stools, emesis, increased volume gastric aspirates (can be bilious or hemorrhagic)
    - Systemic - apnea/bradycardia/desaturation episodes, tachycardia, hypotension
    - NEC usually occurs around 30 -32 weeks of postmenstrual age regardless of gestational age at birth

Table 12.1 - Modified Bell NEC Stages (adapted from Walsh, 1986)

<table>
<tr><th></th><th>Systemic manifestations</th><th>GI manifestations</th><th>Radiological findings</th><th>Comments</th></tr>
<tr><td>I</td><td rowspan="3">Apnea, bradycardia, desaturations, temperature instability, lethargy</td><td>Increasing gastric aspirates, mild abdominal distension, emesis, fecal occult blood</td><td>Normal or dilation, mild ileus</td><td rowspan="2">Non-specific</td></tr>
<tr><td>IB</td><td>Bloody stools (macroscopic)</td><td>Same as above</td></tr>
<tr><td>IIA</td><td>Same as above + diminished or absent bowel sounds with or without abdominal tenderness</td><td>Dilation, ileus, pneumatosis intestinalis</td><td>Specific. The absence of bloody stools is not infrequent in preterm infants <30 weeks</td></tr>
<tr><td>IIB</td><td>Same as above + mild metabolic acidosis and mild thrombocytopenia</td><td>Same as above + abdominal tenderness with or without abdominal wall cellulitis or right lower quadrant mass, absent bowel sounds</td><td>Same as above with or without portal vein gas, with or without ascites</td><td>Specific</td></tr>
<tr><td>IIIA</td><td rowspan="2">Same as above + hypotension, bradycardia, severe apneas, combined metabolic and respiratory acidosis, disseminated intravascular coagulation, neutropenia, anuria</td><td rowspan="2">Same as above + signs of generalized peritonitis, marked tenderness, distension of abdomen, and abdominal wall erythema</td><td>Same as above + definitive ascites</td><td>Specific</td></tr>
<tr><td>IIIB</td><td>Same as above + pneumoperitoneum</td><td>Pneumoperitoneum in the absence of other clinical systemic data points towards SIP</td></tr>
</table>

- Initial investigations
    - X-ray
        - Dilated, thickened bowel wall, fixed loops in serial x-rays, pneumatosis intestinalis, portal vein gas, or pneumoperitoneum in case of perforation (although concealed perforation can present without free air)
    - Ultrasound
        - Bowel wall (echogenic bowel loops, thinning, thickening, ileus, pneumatosis) and bowel loop dilation
        - Circulation - initial hyperperfusion evolving to hypoperfusion and finally avascular loops suggestive of necrosis
        - Peritoneal cavity - free air or ascites that can be simple or complex suggesting perforation
        - Liver - portal venous gas
    - Bloodwork
        - CBC- platelets (low), WBC (increased or decreased)
        - Biochemistry - CRP (increased), sodium (decreased), gas (metabolic, respiratory acidosis), glucose (hyperglycemia)
        - Microbiology – always take a blood culture!
- Management
    - Medical management
        - Broad spectrum antibiotics covering gram negative bacteria (aminoglycoside, cephalosporin), gram positive bacteria (ampicillin, vancomycin), and anaerobes (metronidazole). Anaerobic bacteria (metronidazole) in any case of proven/suspected perforation (triple antibiotics)
        - Standard duration of antibiotics - 7-10 days
        - Nil-per-os (NPO) for bowel rest. Standard duration NPO is 7-10 days
        - Gut decompression – NG tube connected to a low intermittent suction system (acute phase) or straight drainage (recovery phase)
        - Support – respiratory support (always invasive in confirmed cases with perforation), volume resuscitation (third spacing), inotropes/pressors, hydrocortisone (relative adrenal insufficiency), blood product transfusions
    - Surgical management
        - Resection of the necrotic sections and primary anastomosis or stoma creation (jejunostomy, ileostomy)
        - In case of resection the distal end might be brought to the skin (mucous fistula) or left intra-abdominal (clip and drop)
        - Occasionally a peritoneal drain is used if the patient is too unwell to tolerate a laparotomy. Most infants with a drain will require an operation at some point
- NEC associated complications
    - Death
        - Mortality rate of 20-30% and 50% in infants who require surgery
    - Sepsis
        - Around 1/3 of cases with have associated sepsis at presentation
    - Acute kidney injury during the acute episode
        - Usually oliguric, followed by a polyuric phase
    - Bronchopulmonary dysplasia
    - Neurodevelopmental impairment
        - White matter injury –cystic leukomalacia
        - Secondary to systemic inflammation
        - Consider screening HUS after recovery

    - Post-NEC stricture
        - Higher the risk with higher the CRP during the acute episode
        - Presents with feeding intolerance when a certain enteral volume has been reached, without systemic signs as there were during the first episode
- Postoperative surgical complications
    - Wound infection
    - Short bowel- malabsorption, growth impairment, need for prolonged parenteral nutrition, parenteral nutrition associated liver disease

12.2 - Blood in the Stool

- Differential diagnosis includes benign and life-threatening conditions (Table 12.2a)
- Life-threatening conditions should be ruled out in a timely manner
    - The general appearance of the baby is an important clue to the differential diagnosis, although close observation is required as this may change quickly

Table 12.2 - Causes for Blood in the Stool

Emergent/Urgent GI Causes	Other GI Causes	Coagulopathy	Others
Volvulus NEC Food Protein-Induced Enterocolitis Syndrome (FPIES) Spontaneous Intestinal perforation (SIP) Hirschsprung disease Intussusception Meckel's diverticulum	Anal fissure Cow milk protein allergy Infectious Vascular malformations	Vitamin K deficiency (neonatal hemorrhagic disease) Coagulation factors deficiency Liver dysfunction Maternal medications (warfarin, anticonvulsants, rifampicin, isoniazid)	Maternal swallowed blood (bloody tinged amniotic fluid)* Cracked nipples – not always visible*

* Alkali denaturation test (APT test) can help differentiate between fetal and adult hemoglobin

- Assessment
    - Physical exam
        - Vitals, general appearance, abdominal exam including auscultation and anal region
    - Imaging studies
        - 2 view abdominal x-ray, USS, and consideration for contrast GI studies after consultation with General Surgery
    - Bloodwork
        - Alkali denaturation test (APT test)
            - Helps to differentiate between fetal and adult hemoglobin by exposing the blood to an alkaline substance
            - Fetal blood will not denature while adult hemoglobin will
        - Depending on clinical assessment may consider- CBC, electrolytes, CRP, blood gas, coagulation profile, type and screen, liver panel

12.3 – Cow's Milk Protein Allergy/Food Protein-Induced Allergic Proctocolitis (FPIAP)

- Pathophysiology- non-IgE-mediated allergic reaction
    - Most commonly to milk
    - Other allergens include soy, egg, and corn
- Presents in the first 6 months of life
    - Typically, 1-4 weeks post delivery
- Symptoms
    - Slow intermittent onset hematochezia in an otherwise well infant and growing infant
- Can be in formula fed or breast-fed infants
- Investigations not indicated as this is a clinical diagnosis

- Management
    - Elimination of cow's milk from the diet by hydrolyzed formula or the mother going on a strict cow's milk free and soy free diet
    - Egg and corn can be removed if symptoms do not resolve with cow's milk and soy elimination
    - Rarely an amino acid-based formula is required
- Prognosis
    - Most infants will tolerate the reintroduction of cow's milk again around 12 months of age

12.4 – Food Protein-Induced Enterocolitis Syndrome (FPIES)

- Pathophysiology- non-IgE-mediated allergic reaction
    - Most commonly to milk
    - Other allergens include soy, grains, egg, meats, fish, vegetables, peanuts, and tree nuts
- Generally, presents between 2-7 months of age with introduction of formula or solids into the diet
- Symptoms
    - Profuse repetitive vomiting, often with pallor or lethargy, 1-4 hours after ingesting the trigger food
    - May be on first exposure or after a period of tolerance
    - In severe cases, infants may have hypotension, hypotonia, acidemia, loss of consciousness, or methemoglobinemia
- Investigations are not sensitive or specific for the diagnosis
    - May demonstrate a leukocytosis, neutrophilia, thrombocytosis, methemoglobinemia, or metabolic acidosis
- Management
    - In the acute setting, management includes fluid rehydration with fluid boluses
    - Consider ondansetron for patients >8 kg or IV corticosteroids
    - Long-term management includes eliminating the trigger food from the diet (relies largely on clinical history)
    - When an infant has cow's-milk FPIES, hydrolyzed formula can be considered
    - Children should be referred to an allergist who can offer oral food challenges
- Prognosis
    - High rate of spontaneous resolution
    - Reintroduction of trigger food should occur under medical supervision

12.5 – Conjugated Hyperbilirubinemia

- Cholestasis defined by bile flow impairment at any point from the hepatocyte to the duodenum
    - Conjugated hyperbilirubinemia is always pathologic!
    - Check a conjugated bilirubin in any baby with jaundice >2 weeks
- Clinical presentation
    - Jaundice, dark urine, pale (hypocholic or acholic) stools
- Differential diagnosis is broad
    - Biliary atresia
        - Presents at 2-6 weeks of life and requires early surgical treatment (portoenterostomy)
        - Liver USS cannot directly diagnose biliary atresia, but there are indirect signs that are highly suggestive - absence of gallbladder (although its presence does not rule the diagnosis), polysplenia
        - Nuclear medicine tests and biopsy are often required
    - Other forms of extrahepatic obstruction (i.e. choledochal cysts)
    - Metabolic diseases (i.e. galactosemia)
    - Infections and/or sepsis
        - Viral (i.e. CMV),
        - Bacterial (always send a urine dip and culture!)

    - Genetic conditions associated with cholestasis include
        - Alpha-1-antitrypsin deficiency
        - Cystic fibrosis
        - Trisomy 21
        - Alagille Syndrome - intrahepatic bile duct paucity. Associated with pulmonary stenosis/tetralogy of fallot, posterior embryotoxon (eye), distinctive facial features, and butterfly vertebrae
        - Progressive familial intrahepatic cholestasis. Will have normal GGT levels
    - Hypopituitarism (hypothyroidism most common)
    - Parenteral Nutrition Associated Liver Disease (PNALD) is a common cause of cholestasis in preterm and term infants with TPN dependent – GI diseases
        - It appears in cases when TPN is required for > 2 weeks. It may evolve to terminal liver disease if untreated, although this is now rare
- Investigations
    - Bloodwork- CBC, gas, electrolytes, pituitary hormones, microbiology, AST, ALT, alk phos, GGT, conjugated and unconjugated bilirubin, INR, PTT, albumin
    - Always send a urine dip and culture, consider urine CMV
    - Liver ultrasound
    - Consult GI, genetics and metabolics
    - Consider echo and ophtho exams
    - Consider nuclear medicine test- HIDA scan
    - Consider liver biopsy

12.6 – Gastroesophageal Reflux Disease (GERD)

- Pathophysiology - transient lower esophageal sphincter relaxation episodes and delay in gastric emptying
- Reflux is very common in the neonatal period
    - Only when it is associated with complications, such as poor weight-gain, is considered pathologic (gastro-esophageal reflux disease)
- Diagnosis is clinical
    - Irritability, desaturations, bradycardia, apnea episodes, worsening respiratory status pain with feeds, and arching
    - Fluoroscopy can identify reflux episodes, but is not linked consistently with symptoms
    - pH monitoring will miss non-acidic reflux episodes
    - Only multichannel intraesophageally impedance monitoring could detect, quantify, and grade GERD episodes
        - Symptoms depend on the volume and quality (pH) of the refluxed material. Commonly, symptoms of what was thought to be GERD have been proven not to be GERD related in most cases by esophageal impedance monitoring
- Management
    - Non-medical management
        - Postprandial prone or left lateral decubitus positioning, and head elevation
        - Reducing feeds volumes by increasing the frequency of feeds also reduces the number of GERD episodes, but increasing exposure to acid
        - Prolong feeds duration is also effective to reduce the number of episodes, however it may impair caloric delivery
        - There are no studies comparing transpyloric vs gastric feeds to reduce GERD
        - Use of thickeners have not proved to reduce the number of GERD episodes. They may increase the risk of NEC

- Medical management includes
  - Antacid drugs (Proton Pump Inhibitors, H2 blockers) - do not reduce the volume or frequency of GERD episodes but reduces the acidity of the gastric content. Consider only in case of esophagitis (pain) for a shorth period of time (4-8 weeks). Use is frequent in the NICU despite lack of evidence for efficacy. Antacids are associated with higher risk of NEC and candidemia in the preterm infant
  - Prokinetics (domperidone, erythromycin) although frequently used, have not proved to be effective in GERD and can have significant secondary effects

12.7 – Meconium Ileus and Meconium Plug

- Meconium ileus- located in the ileum
- Meconium plug- located in the colon
- Presentation
  - Signs of a bowel obstruction
  - Delayed passage of meconium (>48 hours)
- Associations
  - Hirschsprung's disease
  - Cystic fibrosis
  - Pancreatic atresia / pancreatic duct stenosis
  - Intestinal atresia
  - Maternal diabetes
  - Tocolysis with MgSO4
- Investigations
  - Meconium ileus
    - X-ray with no distal air, dilated bowel loops, soap bubble appearance
  - Meconium plug
    - X-ray with absence of rectal air
  - Diagnosis
    - Contrast rectal enema
- Management
  - Gastric decompression with NG
  - NPO until obstruction resolved
  - Contrast enema is often therapeutic!
  - Surgery if unsuccessful evacuation with enema or in case of complications

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Chapter 13 - Nephrology

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13.1 - Neonatal Hypertension

Screening

- Routine BP measurements are recommended for all infants in the NICU but are NOT required for healthy, term newborns

Epidemiology

- Incidence - 3% in NICU patients vs. 0.2% in healthy term newborns
- Greater prevalence in certain conditions (ie. BPD up to 43%)

Definition

- Persistent systolic and/or diastolic BP >95th percentile based on postmenstrual age (Figure 13.1a)

Measurement technique

- Non-invasive
    - Oscillometric (measures MAP, then estimates SBP/ DBP)
    - Appropriate size cuff - cuff width to arm circumference ratio = 0.45:0.55
    - Ideally performed when infant is calm or sleeping, prone or supine position, 90 minutes after feed or intervention, no pacifier, right arm, and 15 mins after cuff placement
    - Note - ideally obtain 3 readings q2mins (the 1st measurement is typically the least accurate)
- Invasive – intra-arterial catheter is most accurate

Risk factors for neonatal hypertension

- Maternal - hypertension, diabetes, BMI >30, heroin/cocaine use, antenatal steroids, and abnormal uteroplacental perfusion
- Infant - prematurity, low birth weight, UAC, specific diseases (see Figure 13.1.1), and severe illness

System-based approach to etiology & investigations (see Table 13.1.1)

- Most common causes - renovascular and renal parenchymal
- Most common non-renal causes - chronic lung disease and BPD

Physical Exam

- General - volume status, weight trend, dysmorphism (ie. syndromes)
- Cardiac - 4 limb BP, murmur, femoral and brachial pulses
- GU - abdominal mass, abdominal bruit, abdominal wall abnormalities, ambiguous genitalia, presence of UAC

Management

- Remove iatrogenic contributors eg. inotropes, steroids, hypercalcemia, fluid overload, pain
- Condition specific treatment - treat hypoxemia in BPD, surgery for coarctation, etc.
- Consultation with pediatric nephrology +/- pediatric cardiology
- Consider anti-hypertensive therapy for BP persistently >99th percentile to prevent LVH, encephalopathy, or retinopathy
- Calcium channel blocker such as amlodipine can be started, however it has a slow onset of action and prolonged duration
- Chronic lung disease - beta-blockers are relatively contraindicated, diuretics can be beneficial
- For acute, severe, symptomatic hypertension, consider IV infusions to prevent rapid reductions in BP and to allow easier titration (nicardipine, esmolol, labetalol, nitroprusside)
- Note - use of anti-hypertensive agents in neonates is off-label and based on expert consensus as there is no prior research for this use
- Consider home BP monitoring if discharged on anti-hypertensive therapy

Post-menstrual age		50th percentile	95th percentile	99th percentile
44 Weeks	SBP	88	105	110
	DBP	50	68	73
	MAP	63	80	85
42 Weeks	SBP	85	98	102
	DBP	50	65	70
	MAP	62	76	81
40 Weeks	SBP	80	95	100
	DBP	50	65	70
	MAP	60	75	80
38 Weeks	SBP	77	92	97
	DBP	50	65	70
	MAP	59	74	79
36 Weeks	SBP	72	87	92
	DBP	50	65	70
	MAP	57	72	71

Post-menstrual age		50th percentile	95th percentile	99th percentile
34 Weeks	SBP	70	85	90
	DBP	40	55	60
	MAP	50	65	70
32 Weeks	SBP	68	83	88
	DBP	40	55	60
	MAP	48	62	69
30 Weeks	SBP	65	80	85
	DBP	40	55	60
	MAP	48	65	68
28 Weeks	SBP	60	75	80
	DBP	38	50	54
	MAP	45	58	63
26 Weeks	SBP	55	72	77
	DBP	30	50	56
	MAP	38	57	63

Figure 13.1.1 – Neonatal blood pressure values. Estimated BP values by percentile after 2 weeks of age in infants from 26 to 44 weeks postmenstrual age (adapted from Dionne, 2012)

Table 13.1.1 – Approach to neonatal hypertension by system (Adapted from Dionne, 2012)

System	Causes		Investigations
Renovascular	- Renal artery thromboembolism - Renal artery stenosis or external compression - Mid-aortic coarctation - Renal venous thrombosis	- Idiopathic arterial calcification - Congenital rubella syndrome	- Urinalysis* - Quantitative Upr/cr, Ualb/cr* - CBC* - Electrolytes (incl. Ca2+), creatinine, urea* - Renal US with doppler* As indicated: - Plasma renin activity - Aldosterone - CT angiography
Renal Parenchymal	Congenital - Polycystic kidney - Bilateral cystic dysplastic kidney - Tuberous sclerosis - Ureteropelvic junction obstruction - Unilateral renal hypoplasia - Congenital nephrotic syndrome - Renal tubular dysgenesis	Acquired - Cortical or tubular necrosis - Interstitial nephritis - Hemolytic-uremic syndrome (rare in neonate) - Obstruction (stones, tumors)	- VCUG - Nuclear medicine scan
Neurologic	- Pain - Intracranial hypertension - Seizures	- Subdural hematoma - Familial dysautonomia	- Head US - Brain MRI
Endocrine	- Congenital adrenal hyperplasia - Hyperaldosteronism	- Hyperthyroidism - Pseudohypoaldosteronism type II	- Newborn screen, 17-OHP - TSH - Cortisol
Cardiac	- Thoracic aortic coarctation		- Echocardiogram - MR Angiogram
Pulmonary	- Bronchopulmonary dysplasia	- Pneumothorax	- Chest X-ray
Neoplastic	- Wilm's tumour - Mesoblastic nephroma	- Neuroblastoma - Pheochromocytoma	- Urine VMA/HVA - Abdo/ pelvis US - MRI
Medications	Infant - Corticosteroids (dexamethasone) - Adrenergic agents (bronchodilators, vasopressors) - Phenylephrine eye drops - Vitamin D intoxication - Theophylline - Caffeine - Pancuronium	Maternal - Cocaine - Heroin	
Other	- Hypercalcemia - TPN (with excess sodium, fluid overload, or hypercalemia) - Closure of abdominal wall defect	- Traction - ECMO - Birth asphyxia - Nephrocalcinosis - Adrenal hemorrhage	

* Investigations that should be completed in all newborns with hypertension

13.2 – Acute Kidney Injury (AKI)

Overview

- Defined as acute reduction in renal function impacting fluid balance, blood urea, and electrolyte dynamics
- Common finding in critically ill neonates especially in the first week of life
- Incidence of AKI in neonates varies (8-40%) due to lack of consensus definition
- Criteria for defining AKI in neonates limited by several factors:
    - Serum creatinine at birth reflects maternal creatinine
    - In preterm infants plasma creatinine may initially rise in the first 48 hours of life
    - Postnatal diuresis occurs in the first week of life in term infants (1 month in preterm) with an increase in glomerular filtraiton rate and subsequent fall in creatinine
    - Steady state of urine concentrating function of the kidney reached by approximately 1 year of age
- See Table 13.1.2 for the modified Neonatal AKI KDIGO Classification

Table 13.1.2 – Neonatal acute kidney injury diagnostic criteria (adapted from Modified KDIGO classification)

AKI Stage	Serum creatinine (SCr) criteria	Urine output criteria (hourly rate)
0	No change in SCr or SCr rise <0.3mg/dL >	≥0.5 ml/kg/h
1	SCr rise ≥ 0.3 mg/dL rise within 48 h or SCr rise ≥ 1.5-1.9 x baseline SCr	<0.5 ml/kg/h x 6-12 h
2	SCr rise ≥ 2.0-2.9 x baseline SCr	<0.5 ml/kg/h for >12 h
3	SCr rise ≥3 x baseline SCr or SCr ≥ 2.52.5 mg/dL or kidney support therapy use	<0.3 ml/kg/h for ≥24 h or anuria for ≥12 h

Pathophysiology

- Underlying pathology may be pre-renal, renal, or post-renal
    - Pre-renal: volume loss, sepsis, PDA leading to systemic steal phenomenon, CHD, NEC, ECMO
    - Renal: use of nephrotoxic medications commonly used in the NICU (i.e. antibiotics, PDA treatment), asphyxia with end organ dysfunction, renal anomalies
- Higher incidence of AKI in those with perinatal asphyxia and renal anomalies

Investigations

- Clinical examination including:
    - Volume status: skin turgor, urine output, edema, blood pressure, weight
    - Signs of sepsis or shock: vital sign abnormalities, poor perfusion, other signs of end organ dysfunction
- Laboratory investigations: electrolyte panel, creatinine, BUN, urinalysis, urine electrolytes, septic work up as indicated
- Imaging: renal ultrasound with doppler (assess for renal anomalies, kidney perfusion, thrombosis)

Management

- Supportive management with treatment of the underlying cause
- Monitor ins and outs, daily weights
- Monitor blood pressure and treat for hypertension if required
- Monitor for electrolyte imbalance and treat as required
- Fluid management: goal to maintain euvolemia
    - Fluid replacement with normal saline (bolus 10 ml/kg at a time)
    - Consider fluid balance incluing inputs (nutrition, medications) and outputs (urine, insensible and other losses)
    - If hypervolemic deficit gradually
- Avoid nephrotoxic agents and contrast (or minimize and monitor levels if required)
- Renal dosing of all medications
- Nephrology consultation

Outcomes

- Neonatal AKI is associated with high morbidity and mortality
- Potential for future risk of chronic kidney disease, therefore require long term monitoring of renal function, blood pressure, and proteinuria with counselling to minimize exposure to nephrotoic medications and future risks of AKI

13.3 – Renal Anomalies

Overview

- Congenital anomalies of the kidney and urinary tract (CAKUT) represents a spectrum of developmental abnormalities of the renal system
- Most common renal anomaly seen in newborns is antenatal hydronephrosis (see Chapter 5 Common Level 1 Consults)
- CAKUT include: (list adapted from the Paediatric Nephrology Resident Handbook)
    - Unilateral kidney agenesis
    - Hypoplastic kidney
    - Dysplastic kidney
    - Multicystic dysplastic kidney
    - Abnormalities of position
    - Hydronephrosis and related abnormalities including:
        - Pelviectasis, pelvicaliectasis, caliectasia, hydroureter/megaureter
        - Uretopelvic junction (UPJ) obstruction
        - Uretovesical junction (UVJ) obstruction
        - Vesicoureteral reflux
        - Posterior urethral valves
    - Prune belly syndrome
    - Kidney cysts
    - Genetic cystic kidney diseases including:
        - Autosomal dominant polycystic kidney disease (ADPKD)
        - Autosomal recessive polycystic kidney disease (ARPKD)
        - Nephronophthisis
        - Medullary cystic kidney disease

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Chapter 14 - Endocrinology

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14.1 - Neonatal Hypoglycemia

See Common Neonatal Consults

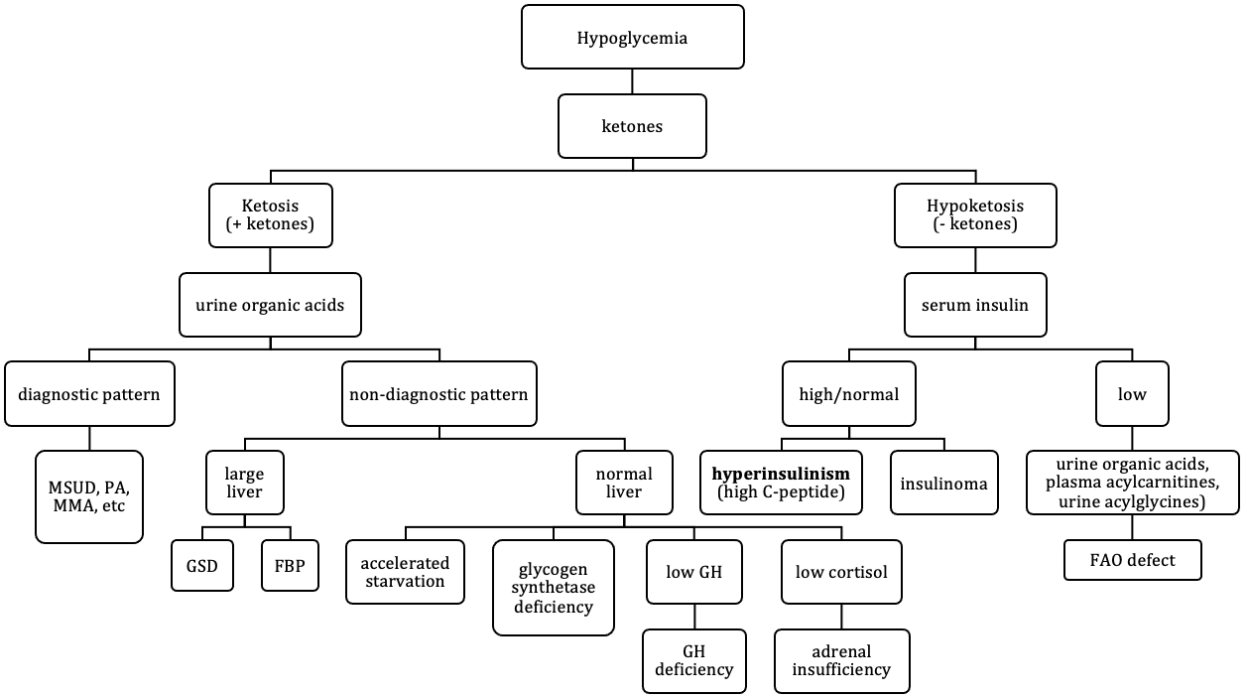
Table 14.1 - Hypoglycemia definition and critical sample threshold

	Birth to first 72 hours	After first 72 hours
Definition	< 2.6 mmol/L	< 3.3 mmol/L
Threshold for investigation	2.6 mmol/L	2.8 mmol/L

Glucose infusion rate (GIR) (mg/kg/hr) = $\frac{\text{rate (mL/h) x dextrose concentration (g/L)}}{\text{dosing weight (kg) x 60 (minutes/hr)}}$

Usual range of GIR in preterm and term infants: 5-8 mg/kg/hr

- Consider critical sample if persistent hypolycemia beyond 72 hours and/or requiring elevated GIR
- Critical sample investigations - serum glucose, insulin, ketones (serum beta-hydroxybutyrate and urine acetoacetate), C-peptide, free fatty acids (FFA), cortisol, growth hormone (GH), blood gas, lactate, ammonia, carnitine/acylcarnitine profile, electrolytes, urine organic acids
    - Priority (from Endocrine perspective) - serum glucose, insulin, cortisol, GH, ketones, FFA, C-peptide, lactate
    - If no serum sample - check urine
        - Presence of ketones is useful diagnostically
        - Absence of ketones non-diagnostic



Legend - MSUD = Maple Syrup Urine Disease; PA = Propionic Acidemia; Methylmalonic Acidemia = MMA; GSD = Glycogen Storage Disease; FBP = F-1,6-biphosphatase deficiency

Figure 14.1- Hypoglycemia algorithm in critical sample interpretation (adapted from Wolfsdorf J in Lifshitz F and Griese RF, 2003)

14.2 - Congenital Hyperinsulinism

Differential

- Transient - maternal diabetes, SGA/IUGR, asphyxia, perinatal stress, prematurity, IV glucose during labour/delivery, medications (propranolol)
- Permanent - Genetic (ABCC8, KCNJ11 mutations)
- Syndromes (Beckwith-Wiedemann Syndrome, Sotos Syndrome, Kabuki syndrome)
- Other classification methods
    - Congenital vs acquired
    - Diazoxide responsive vs unresponsive

Additional testing

- Glucagon stimulation testing - Δ glucose increase > 1.7 mmol/L suggests hyperinsulinemic hypoglycemia
    - Administer glucagon 0.03 mg/kg IM/IV/SC (max 1 mg) → baseline BG and monitor BG q10min for 40 minutes
- ^{18}F-DOPA PET CT scan of pancreas (currently not available in Ontario) – discriminate focal vs diffuse congenital hyperinsulism
- Genetic testing - Collect and send parental and child samples simultaneously

Management

- Glucose target - BG 3.3-6 mmol/L
- When TFI begins to increase over 120ml/kg/d in the first 24h or 160ml/kg/d after, consider increasing concentration to D12.5W and monitoring sodium and fluid balance
- High GIR (may require up to 15-25 mg/kg/min)

- Glucagon
    - Mechanism of action (MOA) - increase glucose release from liver (glycogenolysis, gluconeogenesis)
    - Consider when GIR >10-12 mg/kg/min
    - Dosing - 5-10 mcg/kg/hr
    - Side effects - nausea, vomiting, erythema necrolyticum migrans, poor stability/solubility, tachyphylaxis
- Diazoxide
    - MOA - opens K-ATP channel → limits membrane depolarization required for Ca^{2+}-mediated insulin release from beta cells
    - Dosing - 2.5-15 mg/kg/day divided BID
    - Anticipate response in 5 days, with dose titration q48h if ineffective
    - Side effects - fluid retention (may require hydrochlorothiazide with diazoxide dose ≥10 mg/kg/day), pulmonary hypertension, hypertrichosis (reversible), thrombocytopenia
- Other therapies if diazoxide non-responsive
    - Octreotide, lanreotide, sirolimus (mTOR inhibitor), focal or subtotal pancreactectomy
- Disposition planning - ensure 6-hour safety fast and education completed prior to discharge

Prognosis

- Perinatal stress hyperinsulinism - often responds well to diazoxide treatment, duration up to 6-12 months but resolves spontaneously

14.3 - Ambiguous Genitalia and Disorders of Sexual Differentiation (DSD)

Definition

- Disorders of sexual differentiation (DSD) - combination of differences in chromosomes, gonads, and genital phenotype
- When to consider - bilateral cryptorchidism, scrotal or perineal hypospadias, hypospadias with unilateral cryptorchidism, micropenis, clitoromegaly, posterior labial fusion, gonads palpable in labioscrotal folds, discordant genitalia/sex chromosomes
    - Micropenis - penis < 2 cm in length with full stretch in term infant
    - How to measure - dorsal surface from pubic ramus to tip of penis (excluding foreskin) after stretching penis to point of increased resistance

Sexual differentiation physiology

- Initial bipotential gonads and internal structures
    - Mullerian (paramesonephric) duct = precursor female internal genitalia
    - Wolffian (mesonephric) duct = precursor male internal genitalia
    - Y chromosome has Sex-determining Region Y gene (SRY) that is involved in production of anti-mullerian hormone (AMH) and testis development (testosterone production)
- Males
    - AMH degrades Mullerian duct → lack of female reproductive tract
    - Testosterone and dihydrotestosterone (DHT) promote internal and external male genitalia respectively
- Females
    - Absence of SRY → no AMH → permitting female reproductive tract to form
    - Lack of testosterone and androgens (DHT) → wolffian duct degeneration and formation of external female genitalia respectively

Workup and Investigations

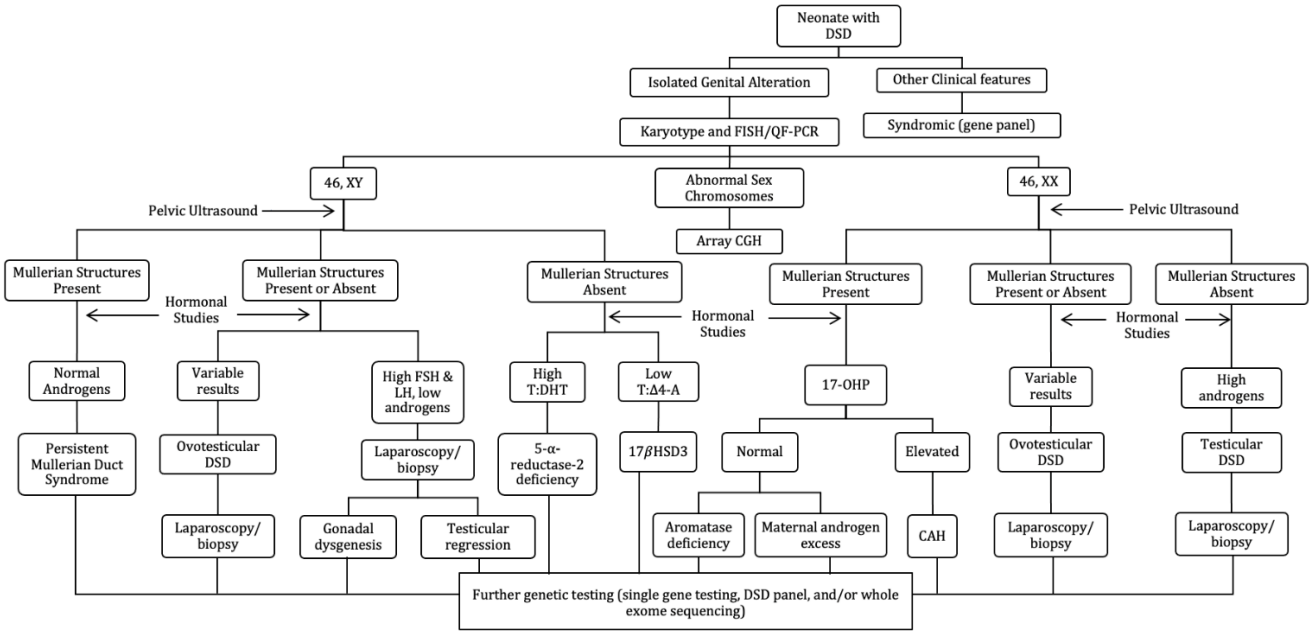
- Newborn screen - screens for 21-hydroxylase deficiency via 17-OH-PROGESTerone (17-OHP)
- Chromosome testing - QF-PCR or FISH for sex chromosomes, karyotype
- Cortisol, electrolytes, glucose, blood gas - assess for salt-wasting in congenital adrenal hyperplasia (CAH)
- Endocrine
    - 17-OHP, testosterone, estradiol, androstenedione, DHEAS, FSH, LH
    - DHT and AMH can be sent but are rarely done due to lack of reference ranges and long turnaround time

- Labs are most diagnostically useful when sent on DOL#1-3
- Beta-hCG stimulation testing for undervirilized male (rarely performed) - if appropriate increase testosterone, demonstrates presence of functional Leydig cells

- Imaging
  - Abdominal/pelvic US - internal Mullerian structures (uterus, vagina, fallopian tubes), ovaries vs testes

Management considerations

- Early involvement of multi-disciplinary team (including psychosocial support) to help guide decision making regarding gender assignment
- Until infant's sex of rearing has been determined, avoid gender terminology (refer to infant as "the baby" or "your child")
- Avoid presumptive conclusions about pending investigation results
- Counseling for parents - parents can tell others (family, friends) baby is doing well but in hospital for medical testing



Legend - CGH = comparative genomic hybridization; 17βHSD3= 17β-hydroxysteroid dehydrogenase-3 deficiency =; Δ4-A = Δ4-androstenedione; CAH = Congenital Adrenal Hyperplasia

Figure 14.3b- Algorithm for Ambiguous Genitalia (adapted from León et al, 2019)

14.4 - Adrenal Insufficiency

Table 14.4a- Differential diagnosis for adrenal insufficiency

Primary	Secondary
Congenital Adrenal Hyperplasia (CAH) Adrenal hypoplasia congenita (AHC) Transient, secondary to prematurity Maternal - high dose steroids, Cushing's Medications (ketoconazole) Peroxisome disorder (Neonatal adrenoleukodystrophy) Bilateral adrenal hemorrhage Aldosterone resistance Autoimmune polyglandular syndrome 1 or 2 Smith-Lemli-Opitz (undervirilized male) Infection and secondary hemorrhage (Waterhouse-Friderichsen syndrome)	Hypopituitarism Congenital - septic-optic dysplasia/optic nerve hypoplasia, pituitary aplasia/hypoplasia, agenesis corticotrophs, POMC, Holoprosencephaly/anencephaly Exogenous steroids, CNS trauma/surgery, radiation CNS tumour (craniopharyngioma)

Clinical signs and symptoms of adrenal insufficiency

- Lethargy/weakness, poor feeding, vomiting, dehydration, hypotension, shock, hypoglycemia
- Genitalia - virilization of female genitalia in CAH

Investigations

- Should be collected before starting a child on steroids
- Infants do not possess diurnal rhythm → no value to "8am cortisol"
- Random cortisol
    - <140 → possible AI
    - 140-250 → indeterminate
    - >250 → unlikely AI
- ACTH stim (cosyntrorpin test, gold standard) - baseline cortisol → administer cortrosyn (35 mcg/kg) IM/IV → repeat cortisol after 60 min
    - Plasma cortisol >415 nmol/L after 60 min → excludes AI
    - Low response in primary adrenal failure (or hypoalbuminemia)
    - Additional testing - 17-OHP (baseline and stimulated), autoimmunity screen
    - Not useful if recent or current steroid use
- Newborn screening for CAH (measure 17-OHP)
    - If suspected, send 17-OHP from serum

Table 14.4b- Primary versus secondary adrenal insufficiency

	Primary AI	Secondary AI
Metabolic/steroid	Hypoglycemia, ketosis, metabolic acidosis, low DHEAS	
Electrolytes	Low Na + high K	Normal
ACTH	High	Low
ACTH stim	Inadequate response	Low or Normal response
Renin, aldosterone	High renin, low aldosterone	Normal renin and aldosterone

Management

- Acute adrenal crisis
    - ABC, IV fluids (normal saline)
    - Treat hyperkalemia and hypoglycemia
    - Stress dose - 100 mg/m^2 IV bolus → 25 mg/m^2 IV q6h → taper
- Maintenance
    - Oral Hydrocortisone
        - Non-CAH, adrenal insufficient - 6-9 mg/m^2/day divided TID
        - CAH - 10-15 mg/m^2/day divided TID
    - Salt-wasting CAH
        - Fludrocortisone 0.05-0.2 mg/day divided daily-BID
        - +/- Oral NaCl supplementation
    - Medic alert bracelet and emergency plan for intercurrent illness
    - Stress dosing for known adrenal insufficiency
        - For fever, vomiting, or minor procedures - 40mg/m^2 IV /PO once → 40 mg/m^2 IV/PO div q8h (max 20mg) until clinical improvement
        - For sepsis, resuscitation, or major surgery - 100 mg/m^2 IV bolus → 25 mg/m^2 IV q6h

14.5 - Congenital Hypothyroidism

Congenital hypothyroidism

- Most common congenital endocrinopathy and most common preventable cause of intellectual disability worldwide

Etiology

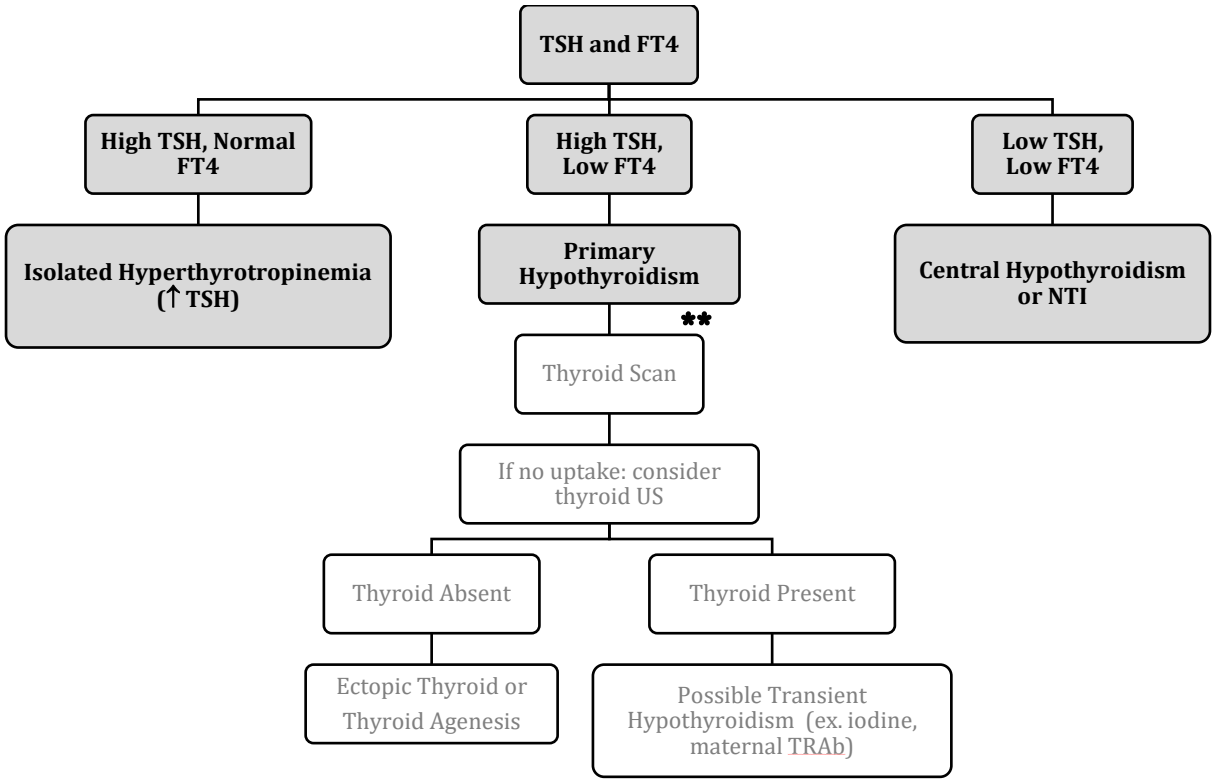
- Primary (more common, often sporadic and rarely inherited; high TSH, low Free T4 (FT4))
  - Thyroid dysgenesis (most common; ectopic > aplasia/hypoplasia/hemiagenesis)
  - Thyroid dyshormonogenesis (normal size & location, but impaired hormone synthesis)
  - Transient congenital hypothyroidism - maternal hypothyroidism, maternal Graves' disease [treated (transplacental anti-thyroid drugs) or untreated (transplacental blocking antibodies)], iodine excess or deficiency, maternal radioactive iodine therapy after 10 weeks gestational age
- Secondary (less common - low TSH & low FT4)
  - Congenital central hypothyroidism, hypopituitarism
- Consider non-thyroidal illness in unwell child (sick-euthyroid syndrome - low TSH, low FT4)
  - Recovers spontaneously

Presentation

- Generally asymptomatic at birth (protected by maternal thyroid)
- Early - hypothermia, macrosomia, coarse facial features, feeding difficulties, hypotonia, weak suck, prolonged jaundice and/or conjugated hyperbilirubinemia, mottling, umbilical hernia, protuberant abdomen, large anterior fontanelle, periorbital/peripheral edema
- Later (untreated) - poor suck, developmental delay, FTT, breathing difficulties, hoarse cry, myxedema, macroglossia, mottled/cool/dry skin
  - +/- goitre (if thyroid dyshormonogenesis)

Investigations

- Newborn screen
  - Ensure collected after 24 hr of life
    - High false positive rate if done early due to TSH surge at birth
  - Repeat required if <33 wk GA or BW <1.5 kg
  - LBW and preterm more likely to have low FT4 and normal TSH, which should normalize by 6 weeks of life
  - Measures TSH (in Ontario) → doesn't detect central hypothyroidism (false negative)
- Confirmatory test with thyroid function testing - TSH, FT4
  - If TSH 15-40 → repeat TSH + FT4
  - If TSH ≥ 40 → order repeat and start treatment pending results
- Additional testing (infrequently done)
  - Thyroid autoantibodies
  - Serum thyroglobulin concentration
  - Urinary iodine (if concern iodine excess/deficiency)
  - Thyroid US (helps to detect if ectopic thyroid)



Legend - NTI = non-thyroidal illness (sick-euthyroid syndrome); ** = Imaging is optional and doesn't impact need to treat

Figure 14.5 – Congenital hypothyroidism diagnostic algorithm

Treatment of primary or central hypothyroidism

- Levothyroxine
  - Dosing - 10-15 mcg/kg/day
  - Treat with crushed tablets dissolved in breast milk (do not prescribe liquid or suspension)
  - Target - TSH 0.5-5 mIU/L with FT4 upper half normal range
  - Close monitoring TSH + FT4 - 2-4 wk post initiation → q1-2 mo until 6 mo → q2-3 mo until 3 year → q6-12 mo until growth completed

Prognosis

- Most transient hypothyroidism resolves within first 1-6 months
- Depending on etiology, may trial off levothyroxine at 3 years old to see if ongoing hypothyroidism vs resolution and need for lifelong levothyroxine

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Chapter 15 - Hematology

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15.1 – Anemia

- Hemoglobin trends in the first few months of life
    - Transient increase after birth as plasma moves to the extravascular space
    - Nadir between 8-12 weeks (6 weeks if preterm) due to fall in reticulocyte counts (reduction of erythropoietin (EPO) production with the rise of PaO_2 after birth), shortened survival of neonatal erythrocytes, and rapid body growth
- Clinical Signs
    - Pale skin or mucous membranes, tachycardia, hypotension, respiratory distress, increase O2 requirement, delayed capillary refill, apnea, lethargy, feeding intolerance, failure to thrive, lactic acidosis
- Differential Diagnosis
    - Underproduction of RBCs
        - Anemia of prematurity - immature erythropoiesis and inappropriately reduced EPO production (production of hepatic EPO as seen in neonates, particularly preterm infants, is not as sensitive to hypoxia as renal EPO production)
    - Blood loss
        - Frequent blood draws (average newborn blood volume is 85ml/kg in term infants)
        - Antepartum hemorrhage - vasa previa
        - Feto-maternal hemorrhage - acute or chronic - placenta previa, subchorionic hemorrhage
        - Fetal hemorrhage - umbilical cord accidents, intraventricular hemorrhage (IVH), pulmonary hemorrhage
        - Twin-to-twin transfusion syndrome
    - Hemolysis
- Prevention
    - Maternal anemia management
    - Delayed cord clamping (30 - 180s) in all stable preterm infants
    - Reduce unnecessary blood draws
    - Iron supplementation
- Treatment
    - RBC transfusion
        - Indications – clinically significant anemia, acute blood loss, signs of shock, anemia of prematurity (see Table 15.1)
        - Transfuse 10-20ml/kg or determine the desired rise in Hb using
        - Irradiated blood in all infants to prevent graft versus host disease
        - 'CMV-safe' (pre-storage leukoreduced and/or CMV negative donor)
        - Slowly over 3-4 hours
        - Consider holding feeds for 4 hours if at increased risk of NEC

- Consider lasix for volume overload, chronic lung disease, hemodynamically significant PDA, renal failure
- Use higher volumes in preterm infants if can be tolerated to reduce exposure to different donors
- Risks
    - Transfusion-transmitted infections (especially CMV)
    - Effects of donor leukocytes (including immunomodulation, graft-versus-host disease, transfusion-related acute lung injury, and alloimmunization)
    - Acute volume overload
    - Blood group incompatibilities
    - NEC
    - Bacterial contamination/sepsis

Table 15.1 - Suggested hemoglobin and hematocrit thresholds for transfusing infants with anemia of prematurity (adapted from Whyte, 2014).

Postnatal Age	Respiratory Support* Hemoglobin, g/L (hematocrit, %)	No Respiratory Support Hemoglobin, g/L (hematocrit, %)
Week 1	115 (35)	100 (30)
Week 2	100 (30)	85 (25)
Week 3	85 (25)	75 (23)
*Respiratory support is defined as an inspired oxygen requirement in excess of 25% or the need for mechanical increase in airway pressure		

15.2 – Delayed Cord Clamping (DCC)

- Baby is held at or below the level of the introitus or at the level of the C-section for a period of time before the cord is clamped to increase neonatal blood volume
- Stabilization/resuscitation with an intact cord is feasible at certain centers with the equipment and expertise but the benefits and harms are still being studied
- Preterm: Recommended for 60-120s
    - Decreases mortality and morbidity and improves hematological outcomes
    - Maintain temperature by using warm towels or plastic bag/wrap
    - Umbilical cord milking (UCM) is currently not recommended in preterms because of risk of IVH
- Term: recommended for 60s
    - Improves hematological outcomes
    - Prolonged DCC beyond 60s can increase risk of hyperbilirubinemia requiring phototherapy
    - DCC is preferred to UCM in term infants
- Contraindications to DCC:
    - Absolute CI include fetal hydrops, need for immediate resuscitation of mother or baby, disrupted utero-placental circulation (ex. Vasa previa) and known TTTS or TAPS
    - Relative CI include infants at risk of hyperbilirubinemia, high maternal antibody titers, first infant of monochorionic twins

15.3 – Hemolytic Disease of the Newborn

- Clinical signs
  - Jaundice, pallor, and hepatosplenomegaly
- Laboratory abnormalities
  - Total serum bilirubin (TSB) at first signs of jaundice or within 24 hours. Consider earlier if concerning maternal antibodies.
  - If maternal blood type is O, determine baby's blood type. If they are discordant, send direct antiglobin test (DAT)
  - If TSB approaching phototherapy level consider CBC, reticulocyte count, G6PD, direct bilirubin
- Differential diagnosis
  - Immune hemolytic disease
    - DAT positive
    - Presentation - fetal anemia/hydrops may require intrauterine transfusion, early jaundice (<24h), severe jaundice in the first week of life, or prolonged jaundice
    - Differential
      - ABO incompatibility
        - Mother blood type O (Innate Anti-A and B Abs in type O mothers tend to be IgG and can thereby cross the placenta)
      - Rhesus incompatibility
        - Rare where Anti-D prophylaxis in pregnancy is available
        - Higher Anti-D titre → more severe anemia
        - PRBC often needed at birth (if not in-utero) and again at 4-8 weeks of age
        - Rh disease affects the reticulocytes so it is essential to ensure good follow up
      - Other blood groups (Kell)
    - Outcomes - late anemia occurs at 4-6 weeks, particularly in Rh disease and/or if babies receive IVIG
  - Non-immune hemolytic disease
    - DAT negative
    - Differential
      - Cell membrane defects - hereditary spherocytosis, elliptocytosis and others
      - Hemoglobinopathies – rare cause of hemolysis in the newborn, consider unstable hemoglobin (Heinz body + hemolytic anemia) and others
      - Enzyme defects - glucose-6-phosphate dehydrogenase (G6PD) deficiency and pyruvate kinase deficiency and others
      - Other - sepsis, DIC, congenital TTP, cephalohematoma
- Treatment
  - Treat jaundice following CPS guidelines
  - Consider repeat bilirubin at 4 to 6 hours after discontinuation of phototherapy due to risk of rebound in setting of hemolysis
  - Consider blood transfusion for anemia as above
  - If TSB is approaching or is over the exchange transfusion threshold
    - Start IV fluids at a minimum TFI 160cc/kg/d (monitor electolytes)
    - Triple phototherapy (ensure proper technique)
    - Consider IVIG (0.5 - 1g/kg) if immune hemolytic disease (DAT +)
    - Hold feeds
    - Transfer to tertiary centre for possible exchange transfusion
    - Consider insertion of UVC if there is time prior to transfer

15.4 – Polycythemia

- Overview
  - Polycythemia refers to the increase in blood viscosity that occurs as hematocrit rises, leading to reduced blood flow and oxygen delivery to tissues
- Clinical signs
  - Plethoric facies, lethargy, hypotonia, poor sucking, irritability, convulsions, tachypnea, cyanosis, hypoglycaemia, jaundice
  - Complications - cerebrovascular occlusion, renal vein thrombosis, NEC, myocardial ischemia, and thrombocytopenia
  - Risk factors- small for gestational age (SGA), maternal preeclampsia or other hypertensive or vascular disorder, IDM, large for gestational age (LGA), genetic conditions (Beckwith-Wiedemann syndrome, trisomy 21, 18, and 13)
- Investigations
  - Haemoglobin and hematocrit (arterial)
  - If the patient is a twin, check the other twin's CBC as they may be anemic (TTTS)
- Treatment
  - Patients require treatment if central venous or arterial hematocrit > 0.7, even if asymptomatic and central venous or arterial hematocrit > 0.65, if significant symptoms
  - Avoid umbilical catheterization (risk of NEC)
  - IV fluids at 1.5 to 2X maintenance
  - Hold feeds
  - Partial exchange transfusion if inadequate response to hydration

15.5 – Exchange Transfusion

- Exchange transfusion
  - Indications – TSB >= exchange threshold +- kernicterus (decreased LOC, irritability, arching, poor suck, hypotonia, lethargy), consider in severe anemia due to ABO incompatibility
  - Remove small aliquots of infant's blood and replace with donor pRBCs to rapidly reduce bilirubin and/or hemolytic antibodies
  - Risks – transfusion-related as above, infection, electrolyte disturbances, arrhythmia, hypotension, thrombocytopenia, dilutional coagulopathy, hypo or hyperthermia, death
  - Double volume exchange - 80ml x weight (kg) x 2
  - Hearing screen for all babies with TSB > 340 or required an exchange transfusion
- Partial exchange transfusion
  - Indications – polycythemia not adequately responsive to hydration
  - Remove small aliquots of infant's blood and replace with normal saline
    - Volume of partial exchange = ((actual HCT – desired HCT) x 80ml x weight (kg)) / actual HCT

15.6 – Thrombocytopenia

- Clinical signs
  - Petechial rash, ecchymosis, large cephalohematomas, intracranial, retroperitoneal, intraperitoneal, GI, and genitourinary bleeding may occur
- Differential
  - Decreased production
    - Prematurity
    - IUGR, placental insufficiency, maternal PIH
    - Wiskott Aldrich syndrome
    - Drug induced thrombocytopenia
    - Infant leukemia
    - Thrombocytopenia-absent radius syndrome
    - Amegakaryocytic thrombocytopenia
    - MYH9 - related macrothrombocytopenia
    - Liver failure

    - Both decreased production and increased destruction
        - Infections
            - Congenital - CMV, rubella, toxoplasmosis, herpes
            - Acquired after birth - bacterial - GBS, gram negative rods
    - Increased destruction
        - Neonatal Immune Thrombocytopenia
            - Etiology - Mother has immune thrombocytopenia and antibodies cross placenta. Antibody-sensitized platelets are prematurely destroyed in the spleen due to maternal antiplatelet antibodies transferred to the fetus
            - Platelet nadir is delayed to day 3-5 due to delayed splenic function in the neonate
            - Unlikely to cause bleeding
            - Treat severe thrombocytopenia with IVIG
        - Neonatal Alloimmune Thrombocytopenia (NAIT)
            - Etiology – infant inherits a platelet antigen of paternal origin that the mother does not have, most commonly HPA-1a antibody.
            - Mother develops antibodies to the infant's platelets in utero due to transplacental passage
            - Infants' platelets are rapidly destroyed and may result in thrombocytopenia in utero
            - Often occurs in first pregnancy, with worsening in successive pregnancies
            - Treat with random donor platelet (to avoid delay), +/- IVIG, antigen negative platelets if available (HPA1a most commonly), maternal washed platelets
        - Sepsis
        - Heparin induced thrombocytosis
        - Severe hemolytic disease of the newborn
        - Kasabach-Merrit syndrome
    - Increased consumption
        - Disseminated intravascular coagulation
        - Thromboembolic disease
            - Renal vein thrombosis (most common non-line associated clot)
            - May be associated with intravascular line
- Investigations
    - CBC
    - Peripheral smear
    - INR, PTT
    - Maternal CBC
    - Consider infectious work up, ultrasound of intravascular lines and renal vessels, genetic testing and less commonly bone marrow evaluation
- Treatment
    - Based on cause and stability of patient
    - If stable, otherwise well, consider CMV-safe, irradiated platelet transfusion when bleeding or when platelets <30,000 (thresholds vary)
    - If <30 weeks, mechanically ventilated, on ECMO, has indwelling UAC or UVC, is septic or otherwise unstable, consider CMV-safe transfusion when platelets <50,000

15.7 – Hemorrhagic Disease of the Newborn

- Overview
    - Due to low vitamin K stores from poor transplacental transport, decreased synthesis due to lack of bacterial colonization at birth, and lack of vitamin K in breastmilk
    - Risk factors include preterm infants, maternal coumadin use, certain antibiotics (cephalosporins), and some anticonvulsants
        - Preterm infants are particularly susceptible due to hepatic immaturity
- Three types of vitamin K deficient bleeding (VKDB)
    - Early onset (first 24 hours)
        - Usually from maternal medications that inhibit vitamin K activity (antiepileptics)
    - Classic (2 to 7 days)
    - Late onset (typically 2-12 weeks, up to 6 months)
        - Classic and late onset are associated with low vitamin K intake due to inadequate prenatal storage and low vitamin K content of breastmilk
- Clinical signs
    - Cutaneous bruising or bleeding from mucosal surfaces, the gastrointestinal tract, umbilicus or circumcision site, and intracranial hemorrhage
    - Laboratory findings
        - Elevated PTT and INR
    - Prevention
        - A single IM injection of vitamin K at birth effectively prevents VKDB
        - Oral vitamin K is less effective than IM vitamin K, but should be recommended to parents who decline IM vitamin K for their newborns
        - CPS Recommendations
            - All newborns should receive one IM dose of vitamin K within the first 6 hours after birth to prevent vitamin K deficiency bleeding
                - 0.5mg for infants weighing <1500g
                - 1.0mg for infants weighing > 1500g
            - If parents decline injection, they should be counselled on the serious risks of late VKDB including intracranial hemorrhage. If they still decline, PO vitamin K should be recommended
                - 2.0mg vitamin K at the first feeding, then again at 2-4 weeks and 6-8 weeks of age
            - In preterm infants in the NICU, there is insufficient evidence to recommend the routine use of IV vitamin K instead of IM dosing in this population
    - Treatment
        - If hemorrhagic disease of the newborn
            - Immediate treatment with parenteral vitamin K 1 to 2 mg IV or SC
            - Fresh frozen plasma or prothrombin complex concentration may be administered in addition to vitamin K

15.8 – Neutropenia

- Clinical signs
    - Increased secondary infections, fevers, aphthous ulcers, recurrent abscesses, failure of separation of the umbilical cord
- Differential
    - Decreased production
        - Infections (viral or bacterial)
        - Prematurity
        - Maternal hypertension
        - Reticular dysgenesis
        - Drug-induced
        - Inherited bone marrow failure syndromes (IBMFS) (genetic)

    - Increased consumption
        - Congenital acquired neutropenia – maternal lupus or drugs
        - Neonatal alloimmune neutropenia
        - Other stressors – infection, RDS or ICH
    - Neutrophil dysfunction (normal counts)
        - Chronic granulomatous disease
        - Leukocyte adhesion deficiency
- Investigations
    - CBC, differential, and reticulocytes to assess all cell lines
    - Peripheral smear to assess abnormal neutrophil morphology
    - Assessment for sepsis and other infection with appropriate investigations such as cultures and timely antimicrobial management
- Treatment
    - Consider G-CSF in IBMFS and some other causes (alloimmune neutropenia) in the context of severe infection

15.9 – Perinatal Transient Myeloproliferative Disorder (TMD) in Trisomy 21 (Down Syndrome)

- Overview
    - Occurs in 10-30% of infants with Trisomy 21 (T21)
    - Transient appearance of megakaryocytic blasts in the peripheral blood related to genetic changes in T21
- Clinical signs
    - Most cases occur by two months of age
    - Range of presentation from subclinical (blast cells detected on peripheral blood smears) to fulminant disease
    - Clinical signs include hepatosplenomegaly, rash, cardiac or respiratory failure, liver dysfunction, anemia, thrombocytopenia, or coagulopathy
- Laboratory findings
    - Peripheral smear and bone marrow exam - presence of blasts (typically megakaryoblasts)
    - Conjugated bilirubin elevation and ALT elevation
- Screening
    - At birth - CBC with differential
    - Infants with transient myeloproliferative disorders should be followed with a complete blood count and differential every 3 months until 3 years of age and then every 6 months until 6 years of age
- Treatment
    - If severe symptoms (heart failure, respiratory compromise, coagulopathy, or greater than 100,000/mL blast cells) consider cytarabine with rasburicase
- Prognosis
    - Early mortality up to 20%
    - Between 20-30% percent of children with TMD go on to develop AML

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Chapter 16 - Infectious Diseases

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16.1 – Neonatal Sepsis

See Early Onset Sepsis

- Background
    - Early onset - within first 7 days of life, vertical transmission, risk factors at time of birth such as PROM, maternal fever, previous infant with GBS sepsis or signs of chorioamnionitis
    - Late onset - vertical or horizontal transmission, risk factors at birth uncommonly associated, increased risk with invasive procedures
    - Most common bacterial organisms – Group B Streptococcus (GBS), gram negative bacilli (*Escherichia coli*), *Listeria monocytogenes*
    - Most common non-bacterial organisms – herpes simplex virus (HSV), enterovirus, parechovirus, *Candida* spp.
    - Clinical signs include respiratory distress, fever, temperature instability, poor perfusion, tachycardia, jaundice, poor feeding, hepatomegaly, signs of meningitis as below

Sepsis in the otherwise well term infant

- Diagnosis
    - All neonates with clinical signs of sepsis should receive a full septic work up (Blood - CBC, CRP, culture, consider viral PCR. Urine - urinalysis, culture. CSF - cell count, chemistry, culture, consider viral PCR). Urine testing may be deferred in early onset sepsis.
    - Consider chest x-ray if respiratory symptoms and other blood work to assess end organ function, blood glucose, and acid/base balance
- Management
    - Supportive management which can include fluid resuscitation, intubation and vasopressor support as indicated
    - Empiric antimicrobial coverage for early onset with ampicillin and aminoglycoside (gentamicin or tobramycin) when meningitis is not suspected
    - Empiric antimicrobial coverage as per meningitis management below if CSF is obtained
    - Empiric antiviral coverage for HSV as below

- Usual duration of IV antibiotic therapy for common microbes and typical susceptibility in bacteremia*
  - GBS - 10 days for an isolated bacteremia (will change if meningitis – see below). Antibiotic of choice - penicillin G or ampicillin
  - *E. coli* (and other gram negatives) - 14 days. Antibiotic of choice - based on susceptibility results
  - *Listeria monocytogenes* - 14 days. Antibiotic of choice - ampicillin
  - *Staphylococcus aureus* - 14 days. Antibiotic of choice – generally start with vancomycin if suspicion of MRSA and can switch to cloxacillin or cefazolin based on susceptibilities

Sepsis in already hospitalized infants

- Additional risk factors due to prematurity and hospitalization
  - Immunocompromised, immature epithelial/mucosal barrier, invasive devices
  - Increased risk for both early and late onset with lower gestational age / birth weight
  - Clinical signs as above as well as increased ventilator settings, apnea, feeding intolerance
- Common pathogens
  - Early onset most commonly GBS and *E. coli*
  - Late onset most commonly *coagulase negative staphylococci* (CoNS), other gram-positive bacteria (*Staphylococcus aureus*, enterococci, GBS), gram negative bacteria, *Candida* spp.
- Diagnosis
  - Neonates with clinical signs of sepsis should receive a septic work up (Blood - CBC, CRP, culture, consider viral PCR. Urine - urinalysis, culture. CSF - cell count, chemistry, culture, consider viral PCR). Urine testing may be deferred in early onset sepsis.
  - Some clinicians consider partial septic workup in hospitalized infants with some signs of infection that are not 'septic' (a blood culture and urine culture) since they are being so closely monitored
  - Consider chest x-ray if respiratory symptoms and other blood work to assess end organ function, blood glucose, and acid/base balance
- Management - as above
  - Empiric antimicrobial coverage for late onset in preterm depends on the suspected source of infection and the possible pathogens - consider including vancomycin if the baby had any central lines in the last 48-72 hours

* All antibiotic choices for definitive therapy should be made based on susceptibility of the given pathogen. The typical susceptibility patterns must be confirmed in each case.

16.2 – Bacterial Meningitis

- Background
  - Meningitis in neonates presents similarly to sepsis. Signs include temperature instability, lethargy, irritability, poor tone, seizures, feeding intolerance, apnea, vomiting and respiratory distress
  - Most common organisms - GBS, gram negative bacilli (E. coli), Listeria
- Diagnosis
  - Cerebrospinal fluid (CSF) analysis with culture is the gold standard for diagnosis
  - Gram stain can be helpful in identifying the most likely pathogen(s) prior to culture results
  - Bacterial PCR can aid diagnosis when cultures are negative (the child received antibiotics prior to the lumbar puncture)

Table 16.2 – Normal and abnormal CSF laboratory values (adapted from Dipchand, 2009).

Component	Normal Values		Abnormal Values	
	Neonate	>1 mo	Bacterial	Viral
WBC (× 10^6/L)	0–30	<5	50–5000	20–2000
%PMN	<60	0	95	<30
Protein (g/L)	<1.7	<0.3	>0.6	0.3–0.8
Glucose (mmol/L)	1.7–6.4	>2.8	<2.8	<3.3
Glucose (% of serum glucose)	45–125	>50	<40	<50

- Management
    - Empiric antibiotics (meningitis dosing)
        - 0-28 days - ampicillin + cefotaxime
        - 29-90 days - ceftriaxone* + vancomycin ± ampicillin
        - > 90 days - ceftriaxone* + vancomycin
        - *Ceftriaxone is contraindicated in premature infants up to 41 weeks corrected and term neonates up to 28 days of life because it can cause hyperbilirubinemia
    - Aminoglycosides can be added for suspected gram-negative meningitis pending culture sensitivity results.
    - Usual duration of IV antibiotic therapy for common microbes and typical susceptibility*
        - Group B Streptococcus (GBS) - 14-21 days, longer in case of cerebritis/ventriculitis. Antibiotic of choice - penicillin G or ampicillin
        - *Escherichia coli* (and other gram negatives) - 21 days, longer in case of cerebritis/ventriculitis. Antibiotic of choice - based on susceptibility results
        - *Listeria monocytogenes* - 21 days. Antibiotic of choice - ampicillin
        - *Neisseria meningitidis* - 5-7 days. Antibiotic of choice - penicillin G if confirmed susceptible, otherwise ceftriaxone/cefotaxime
        - *Haemophilus influenza* type B (Hib) - 7-10 days. Antibiotic of choice - ampicillin if beta-lactamase negative, otherwise ceftriaxone/cefotaxime
        - *Streptococcus pneumoniae* - 10-14 days. Antibiotic of choice - penicillin G if susceptible, otherwise based on susceptibility results

* All antibiotic choices should be made based on susceptibility of the given pathogen. The typical susceptibility patterns must be confirmed in each case.

    - Steroid therapy is not routinely recommended for meningitis (particularly in neonates given most common organisms), however can play a role in *cardiovascular* support of septic shock. Steroid treatment with dexamethasone should be considered in the following
        - Suspected pneumococcal or Hib meningitis by CSF gram stain
            - Pneumococcal - gram positive cocci or diplococci
            - Hib - gram negative bacilli or coccobacilli
        - Infants ≥ 6 weeks of age
        - First dose should be 2 hours prior the first dose of antibiotic up to 4 hours after
        - Dosing - dexamethasone 0.6mg/kg/day in 4 divided doses q6h
    - Repeat CSF sampling is usually not required for common pathogens. Consider repeat LP for
        - Clinical unresponsiveness to treatment
        - *S. pneumoniae*, repeat at 48h if the infant received steroid or resistant strain
        - GBS to confirm sterilization at 24-48h of therapy
        - Gram-negative enteric pathogens (*E coli*) within 24-48 hours of therapy
    - Brain imaging (MRI and/or US) is indicated if
        - Failure of CSF sterilization
        - Neurological symptoms (seizure or focal neurological deficit) develop during the course of treatment
        - Suspected complication - cerebritis, ventriculitis, or abscess formation

- Possible complications - syndrome of inappropriate antidiuretic hormone (SIADH), ventriculitis, hemorrhage, thrombosis, and infarction
- Careful monitoring for ins/outs, head circumference, and weight is recommended
- Hearing and vision evaluation should be done for all infants who develop meningitis

! Tips !

- Galactosemia should be considered if *E. coli* is the causative organism for late-onset meningitis
- About 15-50% of all infants with positive CSF bacterial cultures have negative blood cultures

16.3 – Urinary Tract Infection (UTI)

- Background
  - Indistinguishable from the signs of sepsis. Urine sampling for culture and analysis should be routinely part of the late-onset sepsis work up (>3 days of life)
  - Most common pathogens
    - Term infants - E. coli (up to 80%)
    - Other gram negative (Klebsiella, Enterobacter, Proteus and Citrobacter)
    - Consider Candida infection in extreme low birth weight infants (<1000g)
- Diagnosis
  - Sterile urine sampling for urinalysis and culture
  - In and out bladder catheterization is the standard method for collecting a sterile urine specimen, if contraindicated, suprapubic aspiration can be considered
  - Blood culture, CBC, CRP

Table 16.3a – Sterile urinalysis results with associated sensitivity and specificity for infection (adapted from Robinson, 2014).

Urinalysis Test	Sensitivity	Specificity
Leukocytes (LE)	83 (67–94)	78 (64–92)
Neutrophils (NT)	53 (15–82)	98 (90–100)
Either LE or NT positive	93 (90–100)	72 (58–91)
Microscopy, WBCs	73 (32–100)	81 (45–98)
Microscopy, bacteria	81 (16–99)	83 (11–100)
LE, NT or microscopy positive	99.8 (99–100)	70 (60–92)

Table 16.3b – Sterile urine culture type with associated minimum colony counts that are indicative of infection (adapted from Robinson, 2014).

Collection type	CFU*/mL	CFU*/L
Clean catch (midstream)	$\geq 10^5$	$\geq 10^8$
In and out catheter specimen	$\geq 5\times10^4$	$\geq 5\times10^7$
Suprapubic aspiration	Any growth	Any growth

* CFU = colony forming units

- Management
  - Empiric - ampicillin + aminoglycoside (tobramycin/gentamicin) OR ampicillin + cefotaxime
  - Duration of treatment is 7-10 days
  - Kidney US within 2 weeks of the first febrile UTI is recommended
  - Voiding cystourethrogram (VCUG) is indicated after a first UTI with abnormal renal ultrasound OR second UTI with normal kidney ultrasounds

! Tips !

- Urine nitrate is the least sensitive indicator for UTI in neonate, nitrite-producing bacteria needs the urine to be retained in the bladder for more than 4 hours to reduce nitrate to nitrite

16.4 – Ophthalmia Neonatorum (ON)

- Background
  - Conjunctivitis occurring within the first 4 weeks of life
  - The most serious (potentially vision threatening) infectious causes of ON are *N. gonorrhoeae* (GC) (<1%) and *C. trachomatis* (2 - 40%)
  - Other common infectious causes are staphylococci, streptococci, *Haemophilus,* and gram-negative bacterial species (30 - 50%). Viral infections are an uncommon cause.
  - The best prevention is GC and *C. trachomatis* screening and treatment of pregnant women
  - Prevention with topical antibiotics is mandated by Ontario law; however, parents can opt-out of prophylaxis if
    - Parents are well-informed about the treatment/consequences
    - No proven or serious risk factor for sexually transmitted infections in the mother
  - CPS does NOT recommend routine prophylaxis
- Diagnosis
  - Clinical evidence of purulent conjunctivitis, and swollen red eyelids occurring within the first four weeks of life
  - Eye swab for bacterial culture and nucleic acid amplification test for GC and *C. trachomatis*, respectively
- Management
  - *N. gonorrhoeae*
    - Exposure to GC antenatally, but clinically well
      - If mother is adequately treated with proven negative culture, no further action needed, unless the mother is considered high risk for re-infection
      - If mother was not treated, infants should have an eye swab for GC and *C. trachomatis* completed and receive a single dose of IM ceftriaxone
    - Clinically unwell in any way
      - Consultation with pediatric infectious diseases expert
      - Full sepsis work up with eye swab to confirm diagnosis and to rule out disseminated GC infection (sepsis, meningitis or arthritis)
      - Isolated gonococcal conjunctivitis
        - Single dose of ceftriaxone 50 mg/kg to a maximum of 125mg
        - Frequent saline eye irrigation until resolution of eye discharge
      - Suspected disseminated disease (sepsis, meningitis, or arthritis) or abscess
        - Ceftriaxone 25 to 50 mg/kg/dose once a day or cefotaxime 25 mg/kg/dose every 12 hours; for a total duration of 7 days
        - For newborns with suspected sepsis cefotaxime and ampicillin appropriate prior to availability of test results
    - If maternal GC status unknown, OR no follow up negative culture after GC treatment, OR high risk for GC exposure after negative screen
      - Test mother at delivery, treat accordingly
      - If planned for discharge and no available test result
        - Follow-up guaranteed – monitor for symptoms and follow up the test result
        - Follow-up not guaranteed – single dose of ceftriaxone (50 mg/kg to a maximum of 125 mg)
  - *C. trachomatis*
    - Exposure - Close monitoring for symptoms, treat if follow up is not guaranteed
    - Disease (conjunctivitis or pneumonia) - oral azithromycin (20 mg/kg as a single daily dose) for 3 days OR oral erythromycin (50 mg/kg/day in 4 divided doses daily) for 14 days

! Tips !

- Routine cultures should NOT be done in asymptomatic infants with risk factors for *C. trachomatis*
- Erythromycin is the only ophthalmic antibiotic eye ointment currently available in Canada for use in newborns

16.5 – Hepatitis B and C Prevention

16.5.1 – Hepatitis B (HBV) Prevention

- Newborns at risk
    - Born to mothers with positive hepatitis B surface antigen (HBsAg) and/or hepatitis B envelope antigen (HBeAg)
    - Household contact with HBV
- Management
    - Mother HBsAg positive
        - Newborn >2000g - HBV vaccine + HBIG (within 12 h of birth); 2nd and 3rd dose to be given at 1 and 6 months of age, respectively (3 doses)
        - Newborn <2000g - HBV vaccine + HBIG (within 12 h of birth); 2nd, 3rd and 4th dose to be given at 1, 2-3 and 6 months of age, respectively (4 doses)
        - Follow up on Hepatitis B surface antibody (HBsAb) and HBsAg around 9-12 months
            - HBsAb ≥ 10 mIU/mL - adequate immunization
            - HBsAb < 10 mlU/mL - needs booster or repeat vaccine series
            - HBsAg positive - Follow up and medical evaluation for chronic liver disease
    - Mother HBsAg unknown
        - Obtain mother's serology
        - Give HBV vaccine + HBIG if mother's serology will not be available within 12 h of birth or positive maternal HBsAg
    - Mother HBsAg negative
        - Newborn >2000g - Routine immunization
        - Newborn <2000g - delay first dose of HBV vaccine until 1 month of age if indicated in the routine schedule
        - No need to follow up on anti-HBs and HBsAg
- Special considerations
    - Household contact with positive HBsAg - vaccine series only (within 12h of birth), HBIG not required

! Tips !

- No form of postnatal prophylaxis is 100% effective; 3 doses of HBV vaccine + HBIG reduces the risk of transmission from 90% down to 10-15% and <1% for infants born to HBeAg+ and HBeAg– mothers, respectively
- HBsAg can be transiently positive for up to 18 days post HBV vaccination

16.5.2 – Hepatitis C (HCV) Prevention

- Background
    - Average transmission risk ~6%
    - Risk factors for transmission – HIV co-infection, higher HCV viral load, elevated ALT, cirrhosis
- Management
    - Avoid invasive procedures (scalp probe, instrumentation)
    - No evidence that caesarean section reduces transmission risk
    - Breastfeeding is NOT contraindicated. There is no evidence of transmission through breastmilk
    - Mother should temporarily interrupt breastfeeding if she has cracked or bleeding nipples
    - HCV serology at 18 months of age is recommended to exclude HCV infection. HCV PCR is not routinely recommended but may be considered after 2 months of age in select circumstances, such as where loss to follow-up is a significant concern
    - Consider vaccination for HBV

- Consider liver enzymes monitor every 6 months to screen for significant liver injury prior to serological testing

16.6 – Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoV-2)

- Background
  - Most affected neonates are infected postnatally (direct contact, respiratory droplet)
  - Clinical presentation is non-specific and may include fever, lethargy, rhinorrhea, cough, tachypnea, increased work of breathing, vomiting, diarrhea, and poor feeding
- Diagnosis
  - Nasopharyngeal / nasal swab PCR-testing for SARS-CoV-2
- Management
  - Asymptomatic newborns born to mother with confirmed or suspected SARS-CoV-2
    - Routine care
    - Screening should be done > 24-48h with PCR test
    - SARS-CoV-2 result is not mandatory for discharge
    - Mother should wear mask and comply with standard hand-hygiene technique
    - Criteria for discontinuing mother's precautions
      - ≥ 10 days passed from the onset of symptoms (up to 20 days in severe cases)
      - > 24 hours of the last fever
- Other symptoms have improved
  - Symptomatic newborns born to mother confirmed/suspected SARS-CoV-2
    - Supportive treatment as necessary and monitoring for any clinical deterioration
    - Consider steroid therapy and remdesivir with consultation of infectious diseases expert

! Tips !

- Early testing (<24h) for asymptomatic neonates will lead to false-positive or false-negative results
- The well-established benefits for mother-baby bonding outweigh the risk for neonatal SARS-CoV-2 transmission/infection

16.7 – Human Immunodeficiency Virus (HIV)

- Background
  - Majority of the HIV transmission occurs intrapartum or postnatally through breastmilk
  - Majority of infected infants are asymptomatic at birth
  - Elevated maternal viral load is the predominant risk factor for transmission
- Maternal Management
  - All women should have HIV testing in pregnancy
  - Women at high risk (intravenous drug use, unprotected sex with multiple partners) should be retested in 3rd trimester and at delivery (HIV antigen / antibody combo test)
  - Women with HIV should receive ART and viral suppression monitoring
  - Elective caesarean section if viral load > 1000 copies/mL near delivery
  - Intrapartum zidovudine is recommended for all women, from the onset of labour till delivery
- Infant Diagnosis
  - HIV serology should not be used to diagnose neonates or infants less than 18-24 months of age as maternal antibody persists for up to 18-24 months of age
  - HIV PCR is recommended for diagnosis in infants less than 18 months of age
  - Exclusion of HIV requires two negative molecular tests (one obtained at age ≥1 month and one at age ≥4 months) or negative HIV serology at ≥ 18 months. A positive molecular test should always be confirmed with a second molecular test

- Infant Management
    - Child should be bathed as soon as possible after birth (especially before vitamin K injection)
    - HIV PCR should be done within 48 hours of birth, 1-2 months of life, and 4-6 months of life (some experts recommend testing at 1 and 2 months of age as sufficient).
    - Zidovudine (ZDV) prophylaxis for 4 weeks is recommended for infants born to mothers who have good virologic control. ZDV should be started as soon as possible (within 6-12 h of age, utility is lost after 72h). For term neonates the standard ZDV dosing 2 mg/kg QID for 4 weeks
    - All children should be seen and followed by a pediatric HIV expert as an outpatient.
    - In the following high-risk scenarios, paediatric infectious diseases should be consulted early as treatment, rather than prophylaxis, may be considered
        - Mother did not receive ART consistently during the pregnancy
        - Mothers most recent viral load detectable or not documented within 4wks of delivery
        - Mother did not receive intrapartum prophylaxis when appropriate
    - Exclusive formula feeding is recommended
    - Monitor for short-term adverse effects of ZDV (anemia, neutropenia) while on ZDV
    - Long-term follow-up (general health, growth, development) of infants exposed to HIV and ART

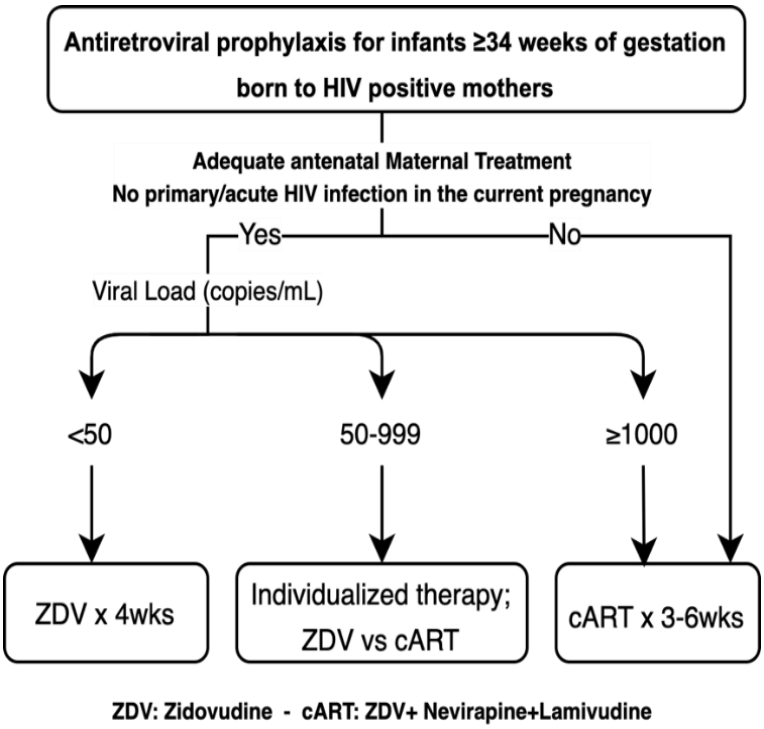


Figure 16.7– Antiretroviral prophylaxis for infants ≥34 weeks of gestation born to HIV positive mothers (Clinical Info, 2020)

! Tips !

- In resource-rich countries, breastfeeding should be avoided
- Combination antiretroviral therapy is warranted for infants born to mothers with poor virologic control (in consultation with pediatric HIV expert)

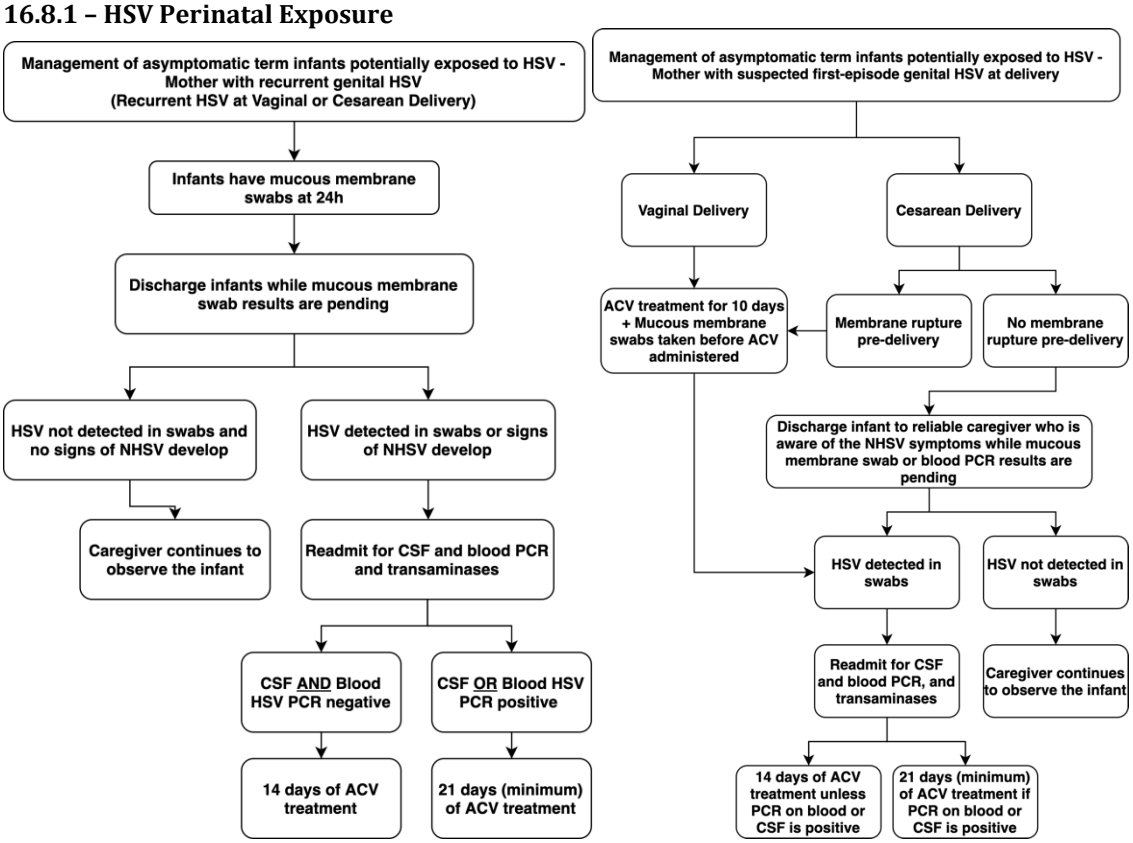
16.8 – Herpes Simplex Virus (HSV)

16.8.1 – HSV Perinatal Exposure
16.8.2 – HSV Encephalitis
16.8.3 – Disseminated HSV Disease
16.8.4 – HSV Skin and Mucous Membrane Infection

16.8 – Herpes Simplex Virus (HSV)

- Background
  - Neonatal HSV infection should be considered in neonates with vesicular skin or mucosal lesions or with signs of sepsis, particularly with liver dysfunction, irritability, seizure (often with bitemporal EEG changes), abnormal CSF (often with lymphocyte predominance)
- Risk factors for vertical transmission
  - Newly acquired HSV disease (first clinical episode)
  - Vaginal delivery
  - Rupture of membranes >6 hours
  - Intrapartum instrumentation
  - No antepartum prophylaxis
- Prevention
  - Caesarean delivery if mother has active lesions
  - Maternal prophylaxis with antiviral therapy in the third trimester (for women with recurrent genital lesions)

16.8.1 – HSV Perinatal Exposure



*Mucous membrane swabs – from conjunctivae, mouth, nasopharynx
Note - ACV treatment is via IV, oral route has low bioavailability

Figure 16.8.1 – Management of asymptomatic term infants potentially exposed to maternal genital HSV depending on first episode or recurrence (adapted from Allen, et al. 2020)

16.8.2 – HSV Encephalitis

- Diagnosis
  - Polymerase chain reaction (PCR) testing for HSV DNA in the CSF
  - CSF PCR might be negative for HSV early in the course of illness (<48h). Repeat of the lumbar puncture within 72h after starting the acyclovir is recommended if initial testing is negative and the index of suspicion for HSV disease is high
- Management
  - Intravenous acyclovir for 21 days
    - >32 weeks of gestation and ≥1200g - 60 mg/kg/day in three divided doses administered every 8 h, assuming the renal function is normal
    - ≤32 weeks of gestation and <1200g - 40mg/kg/day in two divided doses administered every 12h
  - Repeat lumbar puncture for HSV PCR testing should be done towards the end of the 3 weeks of empiric therapy. If the PCR is still positive, intravenous acyclovir should be continued and CSF retested weekly until negative
  - Oral acyclovir 300 mg/m2/dose three times a day should be commenced after completing the intravenous course of acyclovir and continued for total of 6 months

16.8.3 – Disseminated HSV Disease

- Diagnosis
  - Clinical signs of systemic involvement (severe sepsis syndrome, hepatitis, pneumonitis, disseminated intravascular coagulation, and/or thrombocytopenia), AND
  - ≥1 of the following - direct testing for HSV DNA in the CSF, blood, nasopharyngeal and vesicular skin lesions.
- Management
  - Full septic work-up and antibiotic coverage with the sepsis syndrome presentation
  - Similar to HSV encephalitis, if there is no evidence of CNS disease, suppressive oral therapy is not required but may be considered

16.8.4 – HSV Skin and Mucous Membrane Infection

- Diagnosis
  - Positive HSV PCR from the vesicular lesions and/or mucous membrane ≥24h of age
  - No clinical or microbiological evidence of CNS or disseminated disease
- Management
  - Intravenous acyclovir for 14 days
    - >32 weeks of gestation and ≥1200g - 60 mg/kg/day in three divided doses administered every 8 h, assuming the renal function is normal
    - ≤32 weeks of gestation and <1200g - 40mg/kg/day in two divided doses administered every 12 hours

! Tips !

- Majority (75-90%) of birthing women are asymptomatic but have positive serology, therefore, all infants must be considered to be at risk for neonatal HSV infection
- Absence of skin lesions and normal CSF count does not rule out HSV infection

16.9 – Varicella-Zoster Virus (VZV)

16.9 – Varicella-Zoster Virus (VZV)

- Timing of maternal VZV infection leads to different disease manifestations in the fetus and newborn
    - First and second trimester - fetal death or Congenital Varicella Syndrome characterized by
        - Limb hypoplasia
        - Cutaneous scarring
        - IUGR
        - Eye abnormalities (cataracts, chorioretinitis, Horner syndrome, microphthalmos, and nystagmus)
        - Central nervous system damage (cortical atrophy, seizures, and intellectual disability)
    - Third trimester - newborns usually asymptomatic; may develop herpes zoster in infancy or childhood
    - Perinatal (maternal rash onset from 5 days prior to 2 days after delivery) - disseminated neonatal varicella (pneumonia, encephalitis, thrombocytopenia, severe hepatitis)
- Management of neonates exposed to varicella
    - Indications for varicella immune globulin
        - Newborns of mothers who developed chickenpox with symptom onset (rash) within five days before to two days after delivery
        - Preterm infants ≥28 weeks of gestation with no evidence of maternal immunity who were exposed nosocomially/horizontally (shared room with positive case or face to face contact with a symptomatic person)
        - Preterm infants <28 weeks of gestation at the time of delivery or preterms <1000g who were exposed nosocomially/horizontally (shared room with positive case or face to face contact with a symptomatic person)
    - Neonates exposed to varicella who fulfill the above criteria should receive varicella immunoglobulin up to 10 days after the exposure
    - Airborne and contact precautions for the exposed neonate until 21 days after last exposure (28 days after exposure if varicella immunoglobulin was given)

16.9.1 – Congenital VZV Infection

- Exposure – first or second trimester
- Presentation – congenital varicella syndrome
- Management
    - Supportive care targeted towards symptoms, close neurodevelopmental follow up

16.9.2 – Neonatal VZV Infection

- Exposure – perinatal or neonatal
- Presentation – rash, disseminated disease
- Management
    - FSWU
    - Acyclovir (20 mg/kg/dose q8h) for 10 days
    - Varicella immunoglobulin not indicated
    - Contact and airborne precautions until all lesion are dry and crusted

16.10 – Congenital Cytomegalovirus (CMV)

- Background
  - CMV is the most common congenital infection
  - Vertical transmission is much more likely in primary vs non-primary maternal infection
  - 90% of infected newborns are asymptomatic
- Features of neonatal CMV (Table 16.10)

Table 16.10– Features of symptomatic neonates (adapted from Barton et al., 2020)

	Physical Exam Findings	Laboratory Abnormalities	Head Imaging Abnormalities
Sufficient to trigger testing*	Microcephaly	Transaminitis**	
	Hydrops	Thrombocytopenia**	
	Petechiae	Hyperbilirubinemia**	
	Hepatosplenomegaly		
	Chorioretinitis		
	Hearing loss		
Clinically significant CNS disease*	Seizures		Ventricular / periventricular calcifications
	Cortical visual impairment		Ventriculomegaly +- atrophy
			Cerebellar/ ependymal / parenchymal cysts
			Polymicrogyria
			Lissencephaly, porencephaly, schizencephaly, extensive encephalopathy
Other features	SGA		Lenticulostriate vasculopathy***
	Jaundice		
	Pneumonitis		
	Poor suck, hypotonia, lethargy		
	Optic atrophy, microphthalmia, retinal scars, strabismus		

* Presence of these features in isolation, or in conjunction with other findings, are sufficient to trigger testing of infant's urine or saliva for CMV. Clinically significant CNS disease, particularly compatible head imaging findings, should trigger testing. Isolated 'other features' have a low positive predictive value and so should not automatically trigger testing.
**Non-transient elevations in transaminases (>2x normal), bilirubin (> 1-2x normal), platelets < $100x10^9$/L
***Common finding of questionable clinical significance. Presence in isolation is not sufficient to classify as moderate / severe

- Prevention – decrease the risk of vertical transmission by reducing the maternal exposure to CMV
  - Avoid contact with body fluids
    - Sharing toothbrushes, putting child pacifiers in own mouth, sharing food, drink or utensils used by young children, contact with saliva when kissing children
    - Avoid new sexual partners
  - Keep hands and surfaces clean
    - Hand hygiene after diaper change / toileting, nose wiping, contact with toys/ surfaces, handling child's dirty laundry
    - Regular cleaning of fomites by cleaning diaper change area after each use, regularly washing toys, wiping surfaces that young children touch
- Indications for testing in the newborn infant
  - Antenatal risk factors - confirmed primary maternal CMV infection in pregnancy, placental pathology, fetal u/s findings in keeping with CMV
  - Failed newborn hearing screen
  - Newborn with features of symptomatic CMV infection (Table 16.7.1)
- Diagnosis
  - Direct PCR testing for CMV in newborn's body fluids (urine gold standard) within the first 3 weeks of life. Prenatal diagnosis can be made by PCR testing of the amniotic fluid

- Work up
    - Blood (CBC, differential, bilirubin, transaminases)
    - CSF (if seizures / sepsis)
    - Imaging (HUS unless neurologic concerns or HUS abnormal, then MRI)
    - Hearing and ophthalmologic evaluation
- Management
    - Asymptomatic or mildly symptomatic (1 or 2 isolated, transient, mild features without chorioretinitis or CNS involvement) +- SNHL
        - If SNHL OR symptomatic – refer to ID specialist
        - Close monitoring of hearing until school age
        - Routine developmental follow-up
    - Moderate to severely symptomatic (multiple manifestation or CNS involvement)
        - Very sick neonates may be treated with IGanciclovir (6mg/kg/dose IV BID) for 2 to 6 weeks before transitioning to valganciclovir
        - Treatment initiated within the first month of life with valganciclovir (16 mg/kg/dose administered orally twice daily) for 6 months
        - Close monitoring for neutropenia on weekly bases for 4 weeks, then alternate weeks for 8 weeks, then monthly for the duration of therapy
        - Monthly liver enzymes for the duration of therapy
        - Hearing, vision and developmental follow-up on a regular basis

! Tips !

- Preterm infants are more at risk of disseminated disease (pneumonitis, hepatitis)

16.11 – Congenital Rubella

- Background
    - Classic triad of cataract, patent ductus arteriosus (PDA), and sensorineural hearing loss
    - First trimester infection leads to abortion in 20% and multiple congenital anomalies in 80%. Congenital anomalies are uncommon after 16 weeks gestation
    - Rubella is no longer endemic in Canada following vaccination program
    - Risk factors
        - Unvaccinated or vaccinated women with low rubella titers returning from travel to endemic region
        - New immigrant and refugee women of child-bearing age

Table 16.11 – Clinical manifestations of congenital rubella (Adapted from Desai and MacDonald, 2019)

Transient early manifestations	Low birth weight
	Hepatosplenomegaly, lymphadenopathy
	Blueberry muffin rash
	Hemolytic anemia, thrombocytopenia
	Bone lucencies
Permanent defects	Sensorineural hearing loss
	Cataract, salt & pepper retinitis, microphthalmia, glaucoma
	PDA, peripheral pulmonary stenosis, pulmonary valvular stenosis, VSD, myocarditis
	Global developmental delay, language defects, behavioral disorders, seizures
	diabetes, thyroid disease, growth hormone deficiency

- Diagnosis
    - Serological detection of rubella-specific IgM within 6 months of life and/or IgG increase over the first 7 to 11 months of life
    - Detection of rubella by PCR in respiratory, urine or other body fluids or tissues

- Management
    - Audiology and ophthalmology follow ups
    - Contact isolation for at least 1 year of age, or until two consecutive samples (throat swab or urine) obtained one month apart and after 3 months of age test negative by PCR
    - Pregnant women with low vaccine titres should be provided MMR booster after birth

! Tips !

- Serology testing is not useful for diagnosis after a child's first birthday if received the MMR vaccine

16.12 – Congenital Syphilis

- Background
    - Sexually transmitted bacterial infection
    - Risk for congenital infection by maternal infection stage without treatment
        - Primary syphilis - 60-100%
        - Early latent (less than 12 months of the primary infection) – 40%
        - Late latent (more than 12 months of the primary infection) – 10%
    - Clinical features - Majority of newborns are asymptomatic at birth (Table 16.11)

Table 16.12 – Clinical features of congenital syphilis (adapted form Robinson, 2018)

Feature	Usual timing
Spontaneous abortion/ stillbirth/ hydrops fetalis	Any gestation
Necrotizing funisitis	At birth
Rhinitis and/or snuffles	Often first manifestation
Rash	Onset in first eight weeks
Hepatomegaly/splenomegaly	Onset in first eight weeks
Neurosyphilis	Can be present at birth or can be delayed
Musculoskeletal involvement	Onset in first week with permanent bony changes eventually developing
Hematological abnormalities	Present at birth or can be delayed
Interstitial keratitis	Age 2-20 years
Hutchinson's teeth	When permanent dentition erupts
Mulberry molars	Age 13-19 months
SNHR	Age 10-40 years
**Rare features are meningitis, chorioretinitis, nephritic syndrome, and paroxysmal cold hemoglobinuria*	

- Inadequate maternal treatment during pregnancy is defined as one or more of following
    - No treatment
    - Less than 4-fold drop of the rapid plasma reagin (RPR)
    - Treatment not documented
    - Treatment not completed at least 1 month before delivery
    - Treatment given, but with non-penicillin regimen
    - Evidence of maternal reinfection or recent infection in partner
- Diagnosis
    - Darkfield visualization of the *Treponema pallidum* in the fetal or placental tissues/lesions
    - A presumptive diagnosis of congenital syphilis is warranted when the infant has clinical manifestations consistent with congenital syphilis or if the non-treponemal titer of the infant is 4-fold or higher than that of the mother (concurrently taken samples)
- Management of well newborns (normal physical examination) of mothers who were appropriately treated in pregnancy with no concern for relapse or reinfection
    - Syphilis serology in peripheral blood of infant and mother (taken concurrently)
        - If infant non-treponemal titre same or lower than the maternal titer, no further acute care management needed
        - If infant non-treponemal titer 4-fold or greater than maternal titre, consult infectious disease and initiate work up below and treatment

- Management of newborns of mothers who were inadequately treated (as defined above)
    - Routine investigations
        - CBC, liver function tests, creatinine
        - Long bone x-rays
        - Ophthalmologic exam
        - Hearing screen
        - Lumbar puncture with CSF parameters and syphilis serology
        - Syphilis serology in peripheral blood
    - Empiric treatment with a 10-day course of Penicillin G 50,000 units/kg, frequency of the medication as follows
        - Every 12 hours for infants <7 days
        - Every 8 hours for infants 1-4 weeks
        - Every 6 hours for older infants >4 weeks
- Follow up serologic testing and disease monitoring is dependent on the specific clinical scenario and is outlined here

! Tips !

- Newborns with no maternal screening for syphilis should NOT leave the hospital without testing maternal serology for syphilis

16.13 – Congenital Toxoplasmosis

- Background
    - Classic triad of hydrocephalus, intraparenchymal cerebral calcifications, and chorioretinitis
    - Other manifestations include microcephaly, seizures, cognitive impairment, hepatosplenomegaly, anemia, jaundice, thrombocytopenic purpura, lymphadenopathy, myocarditis, and pneumonitis
    - First and early second trimester infections often associated with moderate-to-severe symptomatic disease. Most newborns infected following third trimester maternal infection are asymptomatic at birth but are at risk of subsequent eye disease
    - Parasitic infection, felines are the definitive host. Humans are infected by consumption of raw or undercooked meat, raw shellfish, unpasteurized goat's milk, accidental ingestion from soil or contaminated water
- Diagnosis
    - Newborn diagnostic tests should include serology (IgG and IgM), and PCR on body fluids where appropriate
    - The combination of IgA and IgM antibody to *T gondii* in fetal or newborn blood, can be helpful diagnostically. However, IgA serology is not routinely available in Canada. False negative IgM and IgA can occur
- Management of confirmed congenital infection
    - Medications
        - Pyrimethamine 1 mg/kg (max 25 mg/dose)
            - Twice a day for 2 days
            - Then, once daily for 6 months
            - Then, three times weekly to complete 12 months
        - Sulfadiazine 50 mg/kg (max 4 g/day), twice daily for the course of therapy
        - Leucovorin (Folinic acid) 10 mg three times per week and up to 1 week after completion of Pyrimethamine
        - Severe disease (hydrocephalus and chorioretinitis)
            - Prednisone 0.5 mg/kg twice daily (max 40 mg/day), with rapid taper
    - Treatment duration
        - Asymptomatic - 3 months
        - Symptomatic - 12 months

- Frequent monitoring of neutrophil count
- VP shunt for hydrocephalus
- Long term ophthalmologic follow-up due to risk of recurrent eye disease

! Tips !

- Outcome improved with therapy (normal cognitive, neurologic, auditory outcome in 70% with moderate or severe disease at birth)

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Chapter 17 - Congenital Malformations, Syndromes, and Inherited Metabolic Disorders

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17.1 - Prenatal Genetic Testing

17.2 - Dysmorphic Features

17.3 - Workup of Genetic Conditions

- Karyotype
  - Rarely used as a first-line test in high income countries
  - Identifies abnormalities in the number and structure of chromosomes
  - Rapid test to identify genetic conditions that are caused by aneuploidies, translocations inversions, large deletions, or large duplications
  - Examples of conditions can be diagnosed by karyotyping*
    - Aneuploidies - T21 (Down syndrome), T18 (Edward syndrome), T13 (Patau syndrome), 45,X (Turner syndrome), and 47,XXY (Klinefelter syndrome)
    - Large deletions - 5p deletion (Cri-du-Chat)

      *Note - microdeletions and microduplications (e.g., 22q11.2 deletion syndrome) cannot be routinely detected by karyotyping
- Fluorescence in situ hybridization (FISH)
  - Identifies the presence, absence, or rearrangement of specific DNA segments and is performed with gene or region-specific DNA probes
  - Main advantage of FISH compared to other genetic tests is speed
    - Results as early as 48h for aneuploidy
  - Uses a unique known DNA sequence or probe labeled with a fluorescent dye that is complementary to the studied region of disease interest. The labeled probe is exposed to the DNA on a microscope slide and when the probe pairs with its complementary DNA sequence, it can be then visualized by fluorescence microscopy
    - Location of each probe copy can be documented and the number of copies (deletions, duplications) of the DNA sequence as well
- Microarray
  - Detects submicroscopic chromosome imbalances (microdeletions and microduplications)
    - In contrast, FISH requires clinical knowledge and tests only one area at a time
    - Microarray can detect single and contiguous gene deletion syndromes
- Whole exome sequencing (WES)
  - Allows for sequencing of most exons of most protein-coding genes in a single experiment
  - See link for more details

- Short tandem repeat tests
    - Accordion-like stretches of DNA containing core repeat units of between two and seven nucleotides in length that are tandemly repeated from approximately a half dozen to several dozen times
- Multiplex ligation-dependent probe amplification (MS-MLPA)
    - A PCR-based technique that can identify gains, amplifications, losses, deletions, methylation and mutations of up to 55 targets in a single reaction
    - Requires only small quantities of DNA
- Gene panel tests
    - Off-the-shelf
        - Designed by a laboratory to include genes commonly associated with a broad phenotype or a recognizable syndrome with mutations at two or more genetic loci that produce the same or similar phenotypes
    - Custom designed
        - Includes genes selected by a clinician for analysis by sequencing

17.4 - Genetic Syndromes

17.4.1 - Aneuploidies

- Trisomy 21, Down syndrome
    - Incidence in live births is approximately 1/733
        - The incidence at conception is more than twice that rate, with the difference accounted by early pregnancy losses
    - In approximately 95% of cases there are 3 copies of chromosome 21
        - Extra chromosome 21 is maternal in 97% of patients due to errors in meiosis-occurs in maternal meiosis I (90%)
    - Approximately 1% of persons with T21 are mosaics, with some cells having 46 chromosomes, and another 4% have a translocation involving chromosome 21
        - Most translocations are fusions at the centromere between chromosomes 13, 14, 15, 21, and 22; known as Robertsonian translocations
        - Translocations are de novo or inherited
        - It is not possible to distinguish the phenotypes of persons with T21 and 3 copies of chromosome 21 and those with a translocation
    - FISH is typically the confirmatory test because the results are rapidly available, and it will also detect mosaicism
    - Karyotype is then performed as it shows chromosomal structure and rules out translocations
    - T21 is associated with congenital anomalies and characteristic dysmorphic features (see table below)
        - Constellation of phenotypic features is consistent and permits clinical recognition of T21
        - T21 is associated with heart defects (50%), congenital and acquired gastrointestinal abnormalities
        - Other medical conditions include megakaryoblastic leukemia, immune dysfunction, diabetes mellitus, celiac disease, and problems with hearing and vision

Table 17.4.1a – T21 features

Central nervous system	Hypotonia
	Poor Moro reflex
Craniofacial	Upward slanted palpebral fissures
	Epicanthal folds
	Speckled irises (Brushfield spots)
	Small nose, flat nasal bridge
	Macroglossia, open mouth
Cardiovascular	Endocardial cushion defects
	Ventricular septal defect
	Atrial septal defect
	Patent ductus arteriosus
	Tetralogy of Fallot
	Aberrant subclavian artery
	Pulmonary hypertension
Musculoskeletal	Short neck, redundant skin
	Short 5th digit with clinodactyly
	Single transverse palmar creases
Gastrointestinal	Duodenal atresia
	Tracheoesophageal fistula
	Hirschsprung disease
	Imperforate anus

- Trisomy 13, Patau syndrome
  - Incidence is 1/10,000 births
    - Early lethality in most cases, with a median survival of 7 days; ~91% die by 1 year; only 5% live >6 years
  - Results from the presence of three copies of chromosome 13 in all cells of the body
  - T13 is less commonly caused by translocation of chromosome 13 and is rarely mosaic
  - Survivors have significant neurodevelopmental delay

Table 17.4.1b – T18 features

Head and face	Scalp defects (e.g., cutis aplasia)
	Microphthalmia, corneal abnormalities, ocular hypotelorism
	Cleft lip and palate in 60%-80% of cases (midline)
	Microcephaly
	Sloping forehead
	Holoprosencephaly
	Capillary hemangiomas
	Low-set, malformed ears, deafness
Chest	Congenital heart disease (e.g., vsd, pda, and asd) in 80% of cases
	Thin posterior ribs (missing ribs)
Extremities	Overlapping of fingers and toes (clinodactyly)
	Polydactyly (postaxial)
	Hypoplastic nails, hyperconvex nails
General	Severe developmental delays and prenatal and postnatal growth restriction
	Renal abnormalities
	Visceral and genital anomalies

- Trisomy 18, Edward syndrome
  - Incidence is 1/6,000 births
    - ~92% of children die in the first year without medical intervention/supportive management; only 5% live >1 year
  - Trisomy 18 is the presence of three copies of chromosome 18
    - About 5% of cases are mosaic T18. In this case, the severity depends on the number and type of the affected cells
  - Survivors have significant neurodevelopmental delay

Table 17.4.1c – T18 features

HEAD and NECK	Small and premature appearance
	Tight palpebral fissures
	Narrow nose and hypoplastic nasal alae
	Narrow bifrontal diameter
	Prominent occiput
	Micrognathia
	Cleft lip or palate
	Microcephaly
Chest	Congenital heart disease (e.g., vsd, pda, asd)
	Short sternum, small nipples
Extremities	Narrow hips with limited hip abduction
	Clinodactyly and overlapping fingers; index over 3rd,
	5th over 4th; closed fist
	Rocker-bottom feet
	Hypoplastic nails
General	Low birth weight
	Severe developmental delays and prenatal and postnatal growth restriction
	Premature birth, polyhydramnios
	Inguinal or abdominal hernias

- 45X, Turner syndrome
    - Incidence is 1/5,000 female births
        - 95-99% of 45,X conceptions are miscarried
    - Characterized by complete or partial absence of one of the of the X chromosomes
        - Half of the patients with Turner syndrome have a 45,X set and the other half exhibit mosaicism
        - Lost chromosome is usually of paternal origin
    - Turner syndrome has a wide spectrum of phenotype and many are phenotypically normal
        - Newborns are frequently small size for gestational age, have webbing of the neck, protruding ears, and lymphedema of the hands and feet
        - Children have short stature, cubitus valgus, widely spaced nibbles, a shield chest, and a low posterior hairline
        - Congenital heart defects (40%, bicuspid aortic valves, coarctation of the aorta, aortic stenosis, and mitral valve prolapse) and structural renal anomalies (60%, horseshoe kidneys) are common
        - The gonads are generally streaks of fibrous tissue (gonadal dysgenesis) and older children commonly have primary amenorrhea and lack of secondary sex characteristics

17.4.2 - Deletions and Microdeletions

- 5p Deletion, Cri-du-chat syndrome
    - Main features
        - Hypotonia, short stature, characteristic shrill cry (cat-like cry) in the first few weeks of life, microcephaly with protruding metopic suture, hypertelorism, bilateral epicanthic folds, high arched palate, wide and flat nasal bridge, and intellectual disability
- 22q11.2 Microdeletion, DiGeorge syndrome
    - Main features
        - Conotruncal cardiac anomalies, cleft palate, velopharyngeal incompetence, hypoplasia or agenesis of the thymus and parathyroid glands, hypocalcemia, hypoplasia of auricle, learning disabilities, and psychiatric disorders

- 15q11-q13 (Paternal) Microdeletion, Prader-Willi syndrome
    - Main features
        - Small for gestational age, severe hypotonia, and feeding difficulties at birth, voracious appetite and obesity in toddler years, short stature (responsive to growth hormone), small hands and feet, hypogonadism, and intellectual disability
    - ~30% of Prader-Willi syndrome is caused by a different type of genetic change, therefore need MS-MLPA testing if strongly suspected!
- 20p12 Microdeletion, Alagille syndrome
    - Main features
        - Bile duct paucity with cholestasis (conjugated hyperbilirubinemia), heart defects (particularly pulmonary artery stenosis), ocular abnormalities, skeletal defects such as butterfly vertebrae, and long nose
- 11p13 Contiguous Deletion, WAGR syndrome
    - Main features
        - Wilms tumor, aniridia, male genital hypoplasia of varying degrees, gonadoblastoma, long face, upward slanting palpebral fissures, ptosis, beaked nose, low-set poorly formed auricles, and intellectual disability

17.4.3 - Imprinting Genetic Disorders

- Beckwith-Wiedemann syndrome
    - Incidence 1/14,000 births, equal in males and females
    - Caused by genetic disruptions affecting 11p15.5 region including gene duplication, loss of heterozygosity, and relaxation or loss of imprinting that requires targeted genetic testing
        - Genes involved include IGF2, the gene H19, which is involved in IGF2 suppression, as well as WT-1 (the Wilms tumor gene), and others affecting metabolic cycles and/or channels
    - Selected features
        - Macrosomia, macroglossia, hemi-hypertrophy, and omphalocele
        - Hypoglycemia, especially early in life, secondary to hyperinsulinemia from pancreatic β-cell hyperplasia
        - Predisposed to embryonal tumors including Wilms tumor, hepatoblastoma, neuroblastoma, and adrenocortical carcinoma
    - Primary issues during the neonatal period revolve mainly around the management of omphalocele, airway issues due to macroglossia, and hypoglycemia
    - At high risk of embryonal tumors
        - Requires regular surveillance with abdominal ultrasounds and α-fetoprotein monitoring

17.4.4 - CHARGE syndrome

- Incidence 0.1-1.2/10,000 births
    - CHARGE- Coloboma, Heart anomaly, Choanal atresia, Retardation, Genital and Ear Anomalies
    - 60-65% have CHD7 gene mutations on chromosome 8q12.2
        - Autosomal dominant pattern of inheritance
    - 20% of patients with choanal atresia are found to have CHARGE

17.5 - Congenital Disorders

- Neural Tube Defects (NTD)
    - Incidence 1-5/1,000 births
    - Most common congenital CNS anomaly

- Develops when the neural tube does not close at 5-6 weeks of gestation
  - Periconceptual folate supplementation helps prevent the occurrence of NTDs
  - Medications such as carbamazepine and valproate increase the risk for open NTDs
  - Hyperthermia (febrile illness, hot tubs, saunas etc) have also been shown to increase the risk for open NTD
  - Other risk factors include diabetes and obesity
- NTDs can be open or closed
  - Open NTDs are only covered by a membrane and account for 80% of NTDs
    - Myelomeningocele (spina bifida), meningocele, myelocele
  - Closed NTDs are covered by skin
    - Concerning features on exam include a hairy patch, dermal sinus or cyst, dimples that are >5 mm deep or >2.5 cm from the anal verge, have overlying skin appendages, vascular lesions, or subcutaneous masses
    - Include lipomyelomeningocele and lipomeningocele
- Screening and diagnosis
  - Second trimester fetal anatomy USS
  - The level of the lesion on ultrasound may also predict prognosis
- Follow-up testing after birth for myelomeningocele
  - Kidney and bladder USS 3 days following birth (accounts for physiologic diuresis) to assess bladder wall thickness, volume, and hydronephrosis
  - If neurogenic bladder diagnosed, requires Urology consult and intermittent catherizations to decrease risk of UTIs, VUR, and hydronephrosis

- VACTERL Association
  - Incidence 1/10,000-40,000 births
    - Sporadic inheritance pattern
  - VACTERL- Vertebral defects, Anal atresia, Cardiac defects, Tracheo-esophageal fistula, Renal anomalies, and Limb abnormalities
    - Diagnosis usually requires at least three of these characteristics
    - Diagnosis of exclusion
    - Disruption to fetal development likely occurs early in development, resulting in birth defects that affect multiple body systems

17.6 - Inherited Metabolic Disorders

- Majority of inherited metabolic disorders (IMDs) are caused by single gene that results in altered structure or function of specific proteins
- Most are inherited in an autosomal recessive pattern
  - A history of consanguinity or unexplained neonatal death in the family may exist
  - Mutations are variable from family to family, therefore the phenotype is highly variable
- Important to identify these conditions early, as many of them can be controlled, before irreversible damage to organs occurs
  - Currently achieved by newborn screening of some IEMs (see chapter *** for more details)
- Presentation
  - Feeding intolerance
  - Emesis
  - Liver dysfunction/failure
  - Lethargy
  - Seizures not responding to treatment
  - Coma/encephalopathy
- Initial work-up
  - Basic
    - CBC, electrolytes, glucose, liver enzymes, blood gas, ammonia, lactate, urate, and urine dip (for ketones)

        - Advanced
            - Acylcarnitine profile, total and free carnitine, plasma amino acids, homocysteine, and urine organic acids
            - Elevated ammonia and a normal anion gap suggests a urea cycle defect
            - Elevated or normal ammonia with a raised anion gap metabolic acidosis, and lack of ketones suggests fatty acid oxidation disorder
            - Elevated or normal ammonia with a very raised anion gap metabolic acidosis suggests organic acidemias
- Treatment
    - Can be difficult and often requires a multidisciplinary approach that is individualized to each patient
    - The general emergency management includes
        - Stop catabolism- stop all protein intake and start D10W at 1.5 X maintenance
        - STAT bloodwork (as above)
        - Follow care plan if available and consult metabolics
    - Long term management
        - Stop accumulation of toxic substrates
            - Dietary changes tailored to the pathophysiology of the condition and the patient
        - Eliminate toxic substrates
            - May include peritoneal or hemodialysis for removal of accumulated noxious compounds in the acute phase
        - Replace the deficient product
            - Administration of the deficient metabolite or enzyme
            - Administration of the cofactor or coenzyme to maximize the residual enzyme activity
            - Activation of alternate pathways to reduce the noxious compounds accumulated because of the genetic mutation
            - Bone marrow or liver transplantation

17.7 - Teratogens

- Several factors influence the normal intrauterine development of the fetus
    - Includes environmental, maternal, infectious, and genetic factors
- Any factor that results in an abnormal fetal intrauterine development is a teratogen
    - Abnormal development includes fetal growth, abnormal development of organs and anatomic structures, impaired physical function and postnatal development (cognitive, behavioural and emotional regulation)
    - This also encompasses miscarriage, preterm delivery, neonatal withdrawal and neonatal toxicity

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Chapter 18 - End of Life Care

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18.1 – General Approach to Perinatal Loss

- Communicating with families
    - Compassionate, honest, respectful communication with information provided in clear, timely and sensitive ways
    - Ensure all decision makers are present if possible
    - No matter how dire the situation, families will have difficulty accepting their child's death. Discussions should occur over time rather than in one sitting.
- Palliation vs termination of pregnancy
    - Many anomalies are detected antenatally - accurate medical information must be provided to parents to allow for informed decisions
    - Newborn palliative care – some families will choose to carry a pregnancy to term despite a lethal / serious diagnosis with the intention to focus care on palliation
    - Newborn palliative care should be given equal validity to termination of pregnancy in instances of life-limiting conditions
- Withdrawing or withholding life support
    - Decisions are often made using a shared-decision making model with parents
    - Placing the sole onus on parents to decide to withhold or withdraw lifesaving support ignores the complex moral and emotional burden families feel with the decision
    - Rather, when interventions are highly unlikely to achieve the therapeutic goal or withdrawal of life support reflects the values of the family, the physician should recommend withholding or withdrawing life support while allowing for respectful disagreement
    - If disagreement arises, continued and regular discussion is key and mediation should be pursued
    - Healthcare providers should prepare parents for the dying process, focusing on how the infant will be cared for
- Supporting parenting and grieving
    - Supporting parental bonding helps with grieving and allows parents to build a sense of their child's identity
    - Allow time for the family to remain with their deceased child if they wish
    - Consider legacy building (photos, hand/foot prints, molds, other mementos), spiritual care and ceremonies
- The grieving process
    - Perinatal loss is as painful as other bereavement but often also has a sense of biological failure, loss of identity, lack of shared memories, post-traumatic stress symptoms
    - Parents experience conflicting emotions when they have a healthy child
- Siblings
    - Young children may not understand the permanence of death but may understand their world is less secure
    - The 4 C's - ensure children know that they did not CAUSE their sibling's illness or death, there is no CURE for their sibling's illness, their illness is not CONTAGIOUS, and that they will continue to be loved and CARED for
- Bereavement support
    - Peer support, grief support, death review by parents 2-3 months after the loss

18.2 - Goals of Care

- Goals of care refer to the overarching aims of medical care that are informed by a family's underlying values and priorities, and are established within the existing clinical context
- Goals often change over time as a family learns more about their child's illness or as their child's illness changes
- An approach to a goals of care discussion (adapted from SICG and SHS frameworks)
    1) Prepare yourself
        - Become the medical expert on your patient, discuss with specialists about prognosis and what prior conversations have occurred
    2) Assess illness understanding
        - Assess both understanding of the child's current state of illness and what is expected in the future
        - If family's understanding differs from yours, pause on step 2 and 3
    3) Inform of prognosis ('wish, worry, wonder' approach)
        - 'I wish' / 'I hope' – allows for alignment with the family's hopes
        - 'I worry' – allows for being truthful while sensitive
        - 'I wonder' – a subtle way to make a recommendation or ask a difficult question
    4) Ask about values / goals of care
        - Given their child's current medical status, what is most important to the family, what are they hoping for, and what are they most worried about
        - If their child were to become sicker, what would be most important?
        - Where does the family find strength?
        - Goals of care tend to fall within three categories - prolong life, prolong life while of good quality, and comfort care only
    5) Make a plan
        - Provide recommendations for ongoing care and relate your plan back to the family's goals
        - Try to focus on what you will do rather than you won't

18.3 – End-of-Life Care

- Tailor interventions (blood work, diagnostic investigations, procedures, care setting, spiritual care / ceremonies) to the family's goals
- Vital signs and respiratory support may be modified / weaned to support the family's goals and patient's comfort
    - Monitors may increase anxiety and distract parents from focusing on the infant but, for some families, removing monitors may increase anxiety because they have become familiar with using them as a tool to assess their child
- Supportive care can help with many symptoms (skin to skin, massage, music, dim lighting, swaddling)
- Consider holding or reducing feeds or fluids for ileus, edema, pulmonary congestion, excess secretions, feeding intolerance
- Assess the value of each prescribed medication in achieving the family's goals. When care is comfort-focused, medications that are not contributing to comfort may be discontinued.
- Determine appropriate medication route (enteral, sublingual, subcutaneous, intravenous)
- See Table 18.3 for symptom-specific management
- Seek support from paediatric palliative care specialists if needed (supportive care for serious illness, decision-making support, transition to community, symptom management, grief / sibling support, etc.)
    - See Boston Children's Hospital pain and symptom management guide

Table 18.3 – Common comfort-focussed treatments in neonatal end-of-life care (adapted from The Hospital for Sick Children Formulary)

Symptom	Treatment	Starting dose / route	Comments
Pain	Sucrose (24% solution)	0.1mL PO/SL as needed	Monitor for choking in neonates with neurologic impairment. Will not significantly prolong life in those whom ANH is withdrawn
	Morphine	0.1 to 0.5mg/kg PO q2-4h 0.05 to 0.1mg/kg IV/SL/SC q2-4h 5 to 40mcg/kg/hr IV/SC infusion	
	Hydromorphone	0.04 to 0.08mg/kg PO q2-4h 0.01 to 0.02mg/kg IV/SC/SL q2-4h 2 to 8 mcg/kg/hr IV/SC infusion	
	Fentanyl	0.5 to 1mcg/kg q2-4h IV/SL/SC 0.5 to 2mcg/kg/hr IV/SC infusion	
Shortness of breath	Oxygen	Titrate up based on appearance of comfort to max 2L/min	To target comfort and shortness of breath, not oxygen saturations. Will not prolong life.
	Opioids	As above	Typically requires lower end of starting dose as compared to pain dosing.
	Lorazepam	0.03 to 0.1mg/kg IV/SL/PO q4-6h	
	Midazolam	0.05 to 0.1mg/kg IV/SC q2-4h 0.5 to 4mcg/kg/min IV/SC	
Seizures / agitation	Benzodiazepines	As above for IV/SC/SL. IN/PR may be used for seizures / agitation. Lorazepam 0.1mg/kg PR Midazolam 0.2-0.5mg/kg IN	
	Baseline seizure medications		Many seizure medications can be given IV/SC/PR if enteral route is lost. Consult with pharmacy
Secretions	Suctioning / positioning		If secretions are obstructing or uncomfortable, suctioning can be used. Side positioning can sometimes allow secretions to drain without obstructing
	Decrease or stop fluid intake	Initial reduction may be to ~70% TFI	Consider reducing until improvement in secretions
	Atropine (1% ophtho drops diluted to 0.5%)	1 to 2 drops SL Q4-6h	May thicken secretions making them difficult to suction / causing obstruction. Limited evidence for terminal secretions.
	Glycopyrrolate	40 to 100 mcg/kg PO TID or QID 4 to 10 mcg/kg IV/SC q2-4h	May thicken secretions making them difficult to suction / causing obstruction. Limited evidence for terminal secretions.

Notes

1) All of the listed medications are as needed and can be titrated to symptoms both in dose and frequency
2) All of the listed doses are recommended starting doses. Dosing can be titrated to desired effect.
3) For pervasive symptoms, consider around the clock dosing or infusion
4) Where possible, consider parent / nurse controlled device (PCA or CADD pump) for ease of administration, rapid symptom relief, and to involve parents in care

18.4 – Withdrawal of Artificial Nutrition and Hydration

- Artificial Nutrition and Hydration (ANH) = 'medically assisted' nutrition or hydration (feeding tubes, TPN, IV fluids, etc)
    - ANH indications - neurologic impairment (risk of aspiration, inability to feed orally), malnutrition, malabsorption, support of chronic diseases
    - Potential benefits of ANH - enhance health and nutrition
    - Potential risks of ANH - procedural interventions, financial burden, aspiration, feeding intolerance

- Withdrawal of ANH
    - Represents the withdrawal of a life-sustaining medical intervention
    - Consideration for withdrawal of ANH occurs when ANH is no longer felt to be in the child's best interests such as when it will prolong survival without improving quality of life, or when it is actively contributing to suffering
    - Situations where withdrawal of ANH is considered
        - If the child lacks awareness or is unable to interact with their environment
        - When ANH prolongs or adds morbidity to the process of dying
        - Enteral feeding is not tolerated for a variety of reasons
    - Children who are able to eat or drink safely by mouth SHOULD be offered food / fluid as tolerated
    - Death following withdrawal of ANH is generally peaceful with no added suffering as a result
- Parents should
    - Be involved in shared decision-making
    - Support the decision for withdrawal of ANH
    - Be informed of the course of events following withdrawal of ANH
        - Newborns may live for weeks following withdrawal of ANH
        - Newborns will change in physical appearance
        - HCP can offer to change and bathe infants for parents if this is distressing
    - Be reassured that measures will be taken to keep their child comfortable

18.5 - Pronouncing a Death

- Collect yourself, ensure you know the baby's and family members names
- In the room
    - Introduce yourself, explain that you have been asked to examine the child and prepare them that you will be listening and feeling for what seems like a long time
    - Ensure everyone is comfortable
    - For 2 MINUTES**,** auscultate the heartbeat/breath sounds, watch for chest rise, feel for pulse
    - If they are detected, tell parents the child is still alive, that you will come back periodically to check on their child and ask if there is anything else you can do
    - If none are detected after two minutes, state that you did not detect breathing or a heartbeat, and that you are very sorry that their child has died
        - Use the word 'died' rather than euphemisms like 'passed away' as they can be ambiguous and some families may not understand
    - Offer to answer questions, offer them alone time with their child
    - Discuss parental wishes for autopsy and organ / tissue donation if applicable (if not previously documented)
- After pronouncing a death
    - Write a 'Death Note' in the chart including your exam, the date and the time
    - Complete the death certificate and other paperwork (often there will be a 'death package')
    - Document parental wishes for autopsy and eligibility for organ / tissue donation (Trillium Gift of Life 24h 1-877-363-8456 in Ontario)
    - Offer family grief support resources, legacy building, and assistance with funeral planning

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