Neonatal Pharmacotherapy

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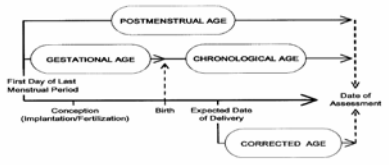
Neonatal Terminology

- Neonate: <1 month of life
- Preterm: <37 weeks gestation
- Birth Weight:
  - LBW: <2500 g
  - VLBW <1500 g
  - ELBW: <1000g



American Academy of Pediatrics, Committee on Fetus and Newborn. Age Terminology During the Perinatal Period. *Pediatrics. 2004;114:1362-1364*

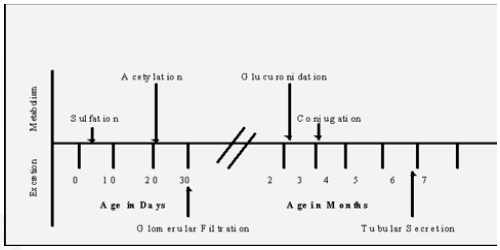
Pharmacology and Pharmacokinetics

- Gestational age & postnatal age affect:
  - Absorption
    - IV, Oral, IM, SQ, transdermal, rectal
  - Distribution
    - Body composition, protein binding, disease state
  - Metabolism
    - Hepatic phase I and II
  - Elimination

Elimination

- GFR & tubular secretion
  - Schwartz equation
  - Scr reflective of mother's value for up to 2 weeks
  - Limited muscle mass → dec SCr and overestimation of ClCr
- Drugs requiring renal adjustment
  - Aminoglycosides (amikacin, gentamicin, tobramycin)
  - Vancomycin
  - Digoxin
  - Penicillins/cephalosporins
  - Theophylline (neonatal period)
  - Caffeine (neonatal period)
  - Phenobarbital (neonatal period)
- Steady state ~5 $T_{1/2}$'s

Metabolism and Elimination



Reiter, PD. Neonatal Pharmacology and Pharmacokinetics. *NeoReviews. 2002*;3:e229-e236

Common Disease States

- Apnea of Prematurity
- Bronchopulmonary Dysplasia
- Patent Ductus Arterious (PDA)
- Sepsis
- Necrotizing Entercolitis

Apnea of Prematurity

Definition:

- Apnea: Pause in breathing > 20 sec duration or apnea < 20 sec if it is accompanied by bradycardia or oxygen desaturation
  - Bradycardia: HR slows at least 30 beats per minute (bpm) from the resting heart rate
  - Desaturation: oxygen saturation <85% for at least 5 seconds
- Apnea classification:
  - Central, obstructive, or mixed
- Inversely associated with gestational age and birth weight

Pharmacotherapy of Apnea

Caffeine

- Mechanism of action
  - Relaxes smooth muscles of the bronchi
- Dosing
  - Loading dose: 20 - 40 mg/kg/dose IV or PO
  - Maintenance doses: 5 - 8 mg/kg/dose IV or PO q24h
- Half Lives:
  - Preterm: >50 hours
  - 2 months: ~26 hours
- Therapeutic troughs: 5-25 mcg/ml
- Toxicity: >40 mcg/ml
  - CNS stimulation and GI effects, monitor HR
- Caffeine citrate 20mg/ml = Caffeine base 10 mg/ml
  - Caffeine citrate is not interchangeable with caffeine sodium benzoate

Bronchopulmonary Dysplasia

- Chronic Lung Disease (CLD)
- Presentation:
  - tachypnea/dyspnea, hypoxemia, radiologic changes, hypercarbia
- Risk Factors:
  - RDS, PDA, prematurity, low birth weight, white race, male, ventilatory and oxygen support, poor nutrition

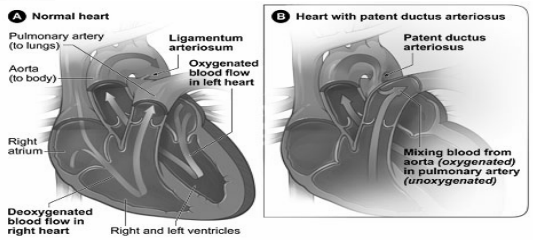
Pharmacotherapy of BPD

- Diuretic
  - furosemide/chlorothiazide
- Bronchodilators
  - albuterol/ipratropium
- Steroids
  - Dexamethasone
    - High dose v. low dose, adverse effects
- Nutrition
  - Vitamin A 5000 unit IM 3x weekly

Committee on Fetus and Newborn. Postnatal corticosteroids to treat or prevent chronic lung disease in preterm infants. *Pediatrics.* Vol 109:2, 2002.

Patent Ductus Arterious (PDA)

- Definition: condition when the ductus arteriosus, a blood vessel that allows blood to bypass the baby's lungs before birth, fails to normally close after birth
- Inversely proportional to age



Treatment of PDA

- Control Pulmonary Edema
  - Fluid Restriction
  - Diuretics
    - Concurrent use of furosemide may increase PG production, esp. with reduced renal function or dehydration
- Closure
  - Wait for spontaneous closure, esp. if asymptomatic
  - Indomethacin IV
  - Ibuprofen IV
  - PDA Ligation (Surgery)
- Alprostadil can be used to keep DA open
  - MOA: vasodilates vascular and DA smooth muscle

Pharmacotherapy of PDA

- Indomethacin
  - MOA: NSAID prevents formation of prostaglandins
  - Contraindications: High BUN/Cr, IVH, NEC, High Bilirubin, Low platelets
  - Give 3 doses at 12 – 24 hour intervals
  - Possibly most efficacious if administered during the first days after birth
    - May be useful in preterms at risk for grade III/IV intracranial hemorrhage & pulmonary hemorrhage

Age at 1st dose	1st dose	2nd dose	3rd dose
<48 hours	0.2 mg/kg	0.1 mg/kg	0.1 mg/kg
2-7 days	0.2 mg/kg	0.2 mg/kg	0.2 mg/kg
>7 days	0.2 mg/kg	0.25 mg/kg	0.25 mg/kg

Sepsis

- Early onset Sepsis
  - *Group B Streptococcus (GBS)*
  - *Listeria monocytogenes*
  - *Escherichia coli*
  - *Chlamydia*
  - *Mycoplasma and Ureaplasma*
- Late onset Sepsis
  - Coagulase-negative *staphylococci*
  - Gm (-) bacilli
    - *Kiebsiella pneumoniae, E. Coli, Salmonella, Campylobacter, Enterobacter, Citrobacter, Pseudomonas aeruginosa, Serratia*
  - *Enterococci*
  - *Staphylococcus aureus*
  - *Candida*

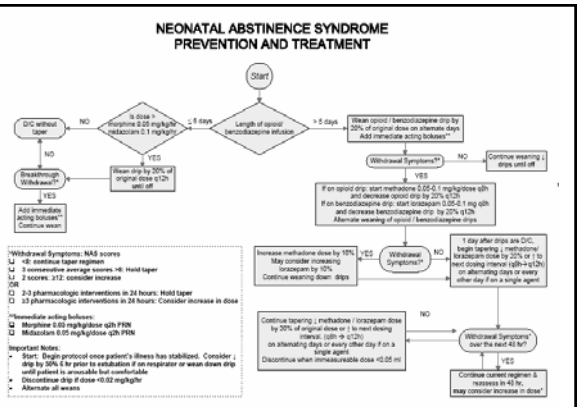
Pharmacotherapy of Sepsis

- Empiric treatment for Early onset sepsis
  - Ampicillin and gentamicin
  - May use 3rd generation cephalosporin instead of aminoglycoside
- Empiric treatment for Late onset sepsis
  - Vancomycin and gentamicin
  - May use 3rd generation cephalosporin instead of aminoglycoside
- Do not use ceftriaxone in neonates
  - hyperbili & risk of precipitation with calcium
- Duration 7-10 days after negative cultures or clinical response

Necrotizing Entercolitis

Staging of NEC

- Bell stage I - Suspected disease
  - Treatment is NPO with antibiotics for 3 days.
- Bell stage II - Definite disease
  - Treatment includes NPO and antibiotics for 10-14 days with bicarbonate for metabolic acidosis
- Bell stage III – Advanced NEC (possible bowel perforation)
  - Treatment involves NPO for 14 days, fluid resuscitation, inotropic support, ventilator support, and paracentesis. May require surgical treatment.
- Antibiotics
  - Ampicillin, gentamicin, and metronidazole or clindamycin



Vaccination Table

Age	Vaccine	Description	Product	Dose	Route	Notes
Birth	Hep B #1	Hepatitis B Recombinant	ENGERIX B	0.5ml	IM	0-19 years Preservative free
1 month OR 2 months	Hep B # 2	Hepatitis B Recombinant	ENGERIX B	0.5ml	IM	0-19 years Preservative free
2 Months	Rota #1	Rotavirus	ROTATEQ	2ml	ORAL	6 weeks-8 months Preservative free
	DTaP # 1/Hepatitis B # 2/ IPV # 1	Diptheria and tetanus toxoids and acellular pertussis adsorbed, recombinant hepatitis B and inactivated poliovirus	PEDIARIX	0.5ml	IM	6 weeks – 7 years Preservative free
	Hib # 1	Haemophilus influenzae Type B conjugate	ACTHIB	0.5ml	IM	2-18 months preservative free
	PCV # 1	Pneumococcal conjugate	PREVNAR	0.5ml	IM	6 weeks to 10 yrs
4 months	Rota # 2	Rotavirus	ROTATEQ	2ml	ORAL	6 weeks-8 months Preservative free
	Hib # 2	Haemophilus influenzae Type B conjugate	ACTHIB	0.5ml	IM	2-18 months preservative free
	PCV # 2	Pneumococcal conjugate	PREVNAR	0.5ml	IM	6weeks to 10 yrs
	DTaP # 2 /Hepatitis B # 3/ IPV # 2	Diptheria and tetanus toxoids and acellular pertussis adsorbed, recombinant hepatitis B and inactivated poliovirus	PEDIARIX	0.5ml	IM	6 weeks – 7 years Preservative free
6 months	Rota # 3	Rotavirus	ROTATEQ	2ml	ORAL	6 weeks-8 months Preservative free
	DTaP # 3 / Hep B #4/ IPV # 2	Diptheria and tetanus toxoids and acellular pertussis adsorbed, recombinant hepatitis B and inactivated poliovirus	PEDIARIX	0.5ml	IM	6 weeks – 7 years Preservative free
	Hib # 3	Haemophilus influenzae Type B conjugate	ACTHIB	0.5ml	IM	2-18 months preservative free
	PCV # 3	Pneumococcal conjugate	PREVNAR	0.5ml	IM	6 weeks to 10 yrs
	Influenza	Influenza virus	FLUZONE	0.25 ml	IM	Pink syringe 6 mo-1.5 yrs Preservative free (Yearly)

References

- Young TE & Mangum B. *Neofax 2006.* 19th Edition. Acorn Publishing Inc.
- American Academy of Pediatrics, Committee on Fetus and Newborn. Age Terminology During the Perinatal Period. *Pediatrics. 2004;114:1362-1364*
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- Gumpper, Karl. Neonatal Pharmacotherapy. PowerPoint Presentation.
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- Additional References available upon request