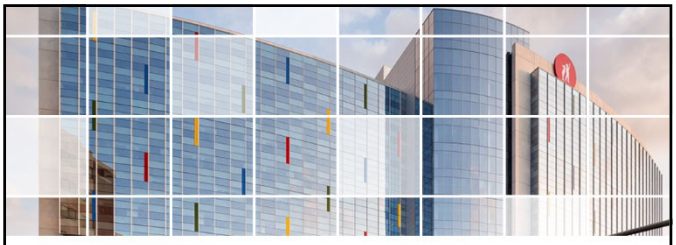

10 Questions you'd like to ask a Neonatologist

3rd Annual Practical Pediatrics Day 2022

February 5, 2022
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Neonatologist

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Disclosures

- No financial disclosures
- Non-scientific survey for source of questions
- Limited due to time constraints
- *Current* recommendations

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Objectives

- Brief background, recommendation(s), and caveats for 10 common questions asked of Neonatologists
- Make your life a little easier (hopefully!)

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1

Should I continue probiotics in the extremely preterm infant and for how long?

- **Background**:
  - Probiotics, defined by the World Health Organization (WHO) as "live micro-organisms which, when administered in adequate amounts, confer a health benefit on the host" & are one of the most studied preventive measures for NEC
  - Large meta-analyses of various study protocols have demonstrated the efficacy of multiple-strain probiotics in reducing necrotizing enterocolitis and all-cause mortality
  - However, there were numerous methodologic differences among study protocols (different strains and combination of therapy) and therefore the efficacy of single-strain probiotic preparations is less certain

1

Should I continue probiotics in the extremely preterm infant and for how long?

- **Background**:
  - Probiotic products in the US are available for use in the general category of dietary supplements, bypassing the US Food and Drug Administration (FDA) approval process in safety, efficacy, and manufacturing standards
  - Although there is good evidence that probiotic therapy reduces NEC, there remain challenges regarding the choice of agent, dosing, and duration of therapy and product safety
  - As a result, due to lack of consensus on optimal regiment and insufficient data for ELBW (<28wk), its use is not routinely recommended based on available data as stated in the most recent 2021 Clinical Report from the American Academy of Pediatrics (AAP)

Should I continue probiotics in the extremely preterm infant and for how long?

- **Recommendation**: Not routinely recommended, discontinue use at time of NICU discharge
- **Caveat(s)**:
  - Approximately 10% of extremely low gestational age neonates receive a probiotic preparation during their stay in the NICU
  - UAB RNICU discontinues use at 60 days, corrected 36wk gestation, or when baby is taking majority of their feeds PO due to difficulty to administer using feeding bottle (based on UAB and NRN NEC rates highest between 10 & 60d)
  - Other units either not use at all or discontinue at time of discharge

2

When should I think about herpes with emphasis on fever and pictures of rash?

- **Background**:
  - 1 out of every 3200 to 10,000 live births
  - Neonatal HSV accounts for 0.2% of neonatal hospitalizations and 0.6% of in-hospital neonatal deaths in the United States and leaves many survivors with permanent sequalae
  - Neonatal HSV has three distinct periods of acquisition:
    - **Intrauterine:** Intrauterine infection due to maternal primary infection vs Intrauterine infection due to ascending infection
    - **Perinatal:** 85%, type of maternal HSV infection (primary versus recurrent), maternal HSV antibody status, duration of ruptured membranes, use of fetal scalp monitors, and mode of delivery (cesarean versus vaginal)
    - **Postnatal:** 10%, exposure to caretaker with active lesions

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When should I think about herpes with emphasis on fever and pictures of rash?

Neonatal HSV Type	Proportion of Cases	Clinical Manifestations
SEM Disease • 1st wk of life	45%	• Characteristic vesicular lesions • Conjunctivitis, excessive tearing • Ulcerative lesions of the mouth, palate, and tongue
CNS Disease • 2nd or 3rd wk of life	30%	• Seizures • Lethargy • Irritability • Tremors • Poor feeding • Skin lesions are present in 60 to 70%
Disseminated • 1st wk of life	25%	• Sepsis syndrome • Fever or hypothermia • Hepatitis • Respiratory distress • DIC • Skin lesions are present in 60 to 80% • CNS involvement occurs in 60 to 75%

When should I think about herpes with emphasis on

Neonatal HSV Type
SEM Disease • 1st wk of life
CNS Disease • 2nd or 3rd wk of life
Disseminated • 1st wk of lfie

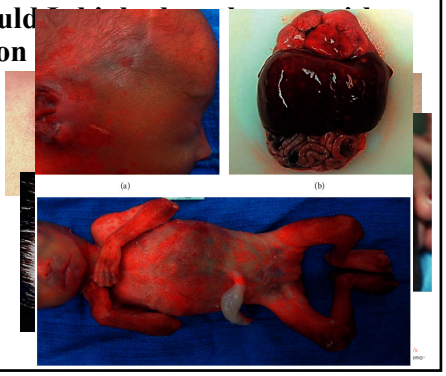


Table 3.23. Maternal Infection Classification by Genital HSV Viral Type and Maternal Type-Specific Serologic Test Results[a]

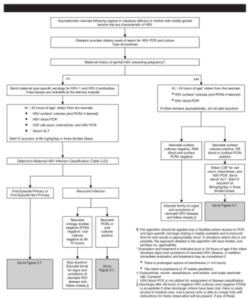
Classification of Maternal Infection	PCR/Culture From Genital Lesion	Maternal HSV-1 and HSV-2 IgG Type-Specific Antibody Status
Documented first-episode primary infection	Positive, either virus	Both negative
Documented first-episode nonprimary infection	Positive for HSV-1	Positive for HSV-2 AND negative for HSV-1
	Positive for HSV-2	Positive for HSV-1 AND negative for HSV-2
Assumed first-episode (primary or nonprimary) infection	Positive for HSV-1 OR HSV-2	Not available
	Negative OR not available[b]	Negative for HSV-1 and/or HSV-2, OR not available
Recurrent infection	Positive for HSV-1	Positive for HSV-1
	Positive for HSV-2	Positive for HSV-2

HSV indicates herpes simplex virus; PCR, polymerase chain reaction (assay); IgG, immunoglobulin G.

[a] To be used for women without a clinical history of genital herpes.

[b] When a genital lesion is strongly suspicious for HSV, clinical judgment should supersede the virologic test results for the conservative purposes of this neonatal management algorithm. Conversely, if, in retrospect, the genital lesion was not likely to be caused by HSV and the PCR assay result/culture is negative, departure from the evaluation and management in this conservative algorithm may be warranted.

Fig 3.6. Algorithm for the EVALUATION of asymptomatic neonates following vaginal or cesarean delivery to women with active genital herpes lesions


Asymptomatic neonate following vaginal or cesarean delivery to mother with visible genital lesions that are characteristic of HSV
Obstetric provider obtains swab of lesion for HSV PCR and culture
Type all positives
Maternal history of genital HSV preceding pregnancy?
no
yes
Send maternal type specific serology for HSV-1 and HSV-2 antibodies, if test assays are available at the delivery hospital
At ~ 24 hours of age* obtain from the neonate:
HSV surface† cultures (and PCRs if desired)
HSV blood PCR‡
CSF cell count, chemistries, and HSV PCR
Serum ALT
Start IV acyclovir at 60 mg/kg/day in three divided doses
Determine Maternal HSV Infection Classification (Table 3.23)
First Episode Primary or First Episode Non-Primary
Recurrent Infection
Go to Figure 3.7.
Neonatal virology studies negative (PCRs negative; viral cultures negative at 48-72 hours)
Neonatal PCRs or viral cultures positive
Stop acyclovir. Educate family for signs and symptoms of neonatal HSV disease and follow closely.§
Go to Figure 3.7.
At ~ 24 hours of age* obtain from the neonate:
HSV surface† cultures (and PCRs if desired)
HSV blood PCR‡
If infant remains asymptomatic, do not start acyclovir
Neonatal surface cultures negative, AND blood and surface PCRs negative
Neonatal surface cultures positive, OR blood or surface PCRs positive
Obtain CSF for cell count, chemistries, and HSV PCR. Send serum ALT. Start IV acyclovir at 60mg/kg/day in three divided doses.
Educate family on signs and symptoms of neonatal HSV disease and follow closely.§
Go to Figure 3.7.

¶ This algorithm should be applied only in facilities where access to PCR and type-specific serologic testing is readily available and turnaround time for test results is appropriately short. In situations where this is not possible, the approach detailed in the algorithm will have limited, and perhaps no, applicability.

* Evaluation and treatment is indicated prior to 24 hours of age if the infant develops signs and symptoms of neonatal HSV disease. In addition, immediate evaluation and treatment may be considered if:

- There is prolonged rupture of membranes (> 4-6 hours)
- The infant is premature (≤ 37 weeks gestation)

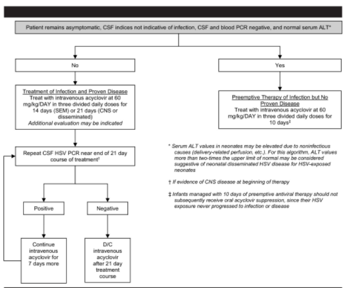
† Conjunctivae, mouth, nasopharynx, and rectum, and scalp electrode site, if present

‡ HSV blood PCR is not utilized for assignment of disease classification

§ Discharge after 48 hours of negative HSV cultures (and negative PCRs) is acceptable if other discharge criteria have been met, there is ready access to medical care, and a person who is able to comply fully with instructions for home observation will be present. If any of these conditions is not met, the infant should be observed in the hospital until HSV cultures are finalized as negative or are negative for 96 hours after being set up in cell culture, whichever is shorter.

Reproduced from Kimberlin DW, Baley J; American Academy of Pediatrics, Committee on Infectious Diseases. Guidance on management of asymptomatic neonates born to women with active genital herpes lesions. *Pediatrics*. 2013;131(2):e635-e646

Fig 3.7. Algorithm for the TREATMENT of asymptomatic neonates following vaginal or cesarean delivery to women with active genital herpes lesions


Patient remains asymptomatic, CSF indices not indicative of infection, CSF and blood PCR negative, and normal serum ALT*
No
Yes
Treatment of Infection and Proven Disease
Treat with intravenous acyclovir at 60 mg/kg/DAY in three divided daily doses for 14 days (SEM) or 21 days (CNS or disseminated)
Additional evaluation may be indicated
Preemptive Therapy of Infection but No Proven Disease
Treat with intravenous acyclovir at 60 mg/kg/DAY in three divided daily doses for 10 days‡
Repeat CSF HSV PCR near end of 21 day course of treatment†
Positive
Negative
Continue intravenous acyclovir for 7 days more
D/C intravenous acyclovir after 21 day treatment course

* Serum ALT values in neonates may be elevated due to noninfectious causes (delivery-related perfusion, etc.). For this algorithm, ALT values more than two-times the upper limit of normal may be considered suggestive of neonatal disseminated HSV disease for HSV-exposed neonates

† If evidence of CNS disease at beginning of therapy

‡ Infants managed with 10 days of preemptive antiviral therapy should not subsequently receive oral acyclovir suppression, since their HSV exposure never progressed to infection or disease

Adapted from Kimberlin DW, Baley J; American Academy of Pediatrics, Committee on Infectious Diseases. Guidance on management of asymptomatic neonates born to women with active genital herpes lesions. *Pediatrics*. 2013;131(2):e635-e646

When should I think about herpes with emphasis on fever and pictures of rash?

- **Recommendation**: High index of suspicion during 1st 6wk of life of any infant with new onset rash/lesion or nonspecific signs/symptoms, particularly if no history of HSV at all

- ~~**Caveat(s):**~~ **Myths**
  - Mode of delivery: vaginal or cesarean
    - ACOG recommendations
    - AAP recommendations

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3

When is irritation actually omphalitis?

- **Background**:
  - Umbilical/periumbilical cellulitis, often polymicrobial
  - 0.7% risk in US, up to 22% with at home births
  - 7-15% mortality, up to 75% mortality if complicated by necrotizing fasciitis
  - Clinical: purulent drainage from umbilical site or periumbilical erythema, edema, or tenderness
  - Risk factors: low birth weight, prolonged labor, prolonged rupture of membranes or maternal infection, nonsterile delivery, umbilical catheterization, and home birth
  - Complications: necrotizing fasciitis, peritonitis, umbilical peritonitis, sepsis
  - Risk factors for poor prognosis: Male sex, prematurity, septic delivery (including unplanned home delivery), and abnormal temperature are reported risk factors for poor prognosis in infants with omphalitis
- **Recommendation**: high index of suspicion, AAP supports dry cord care with topical antibiotics in 3rd world countries
- **Caveat(s):** none

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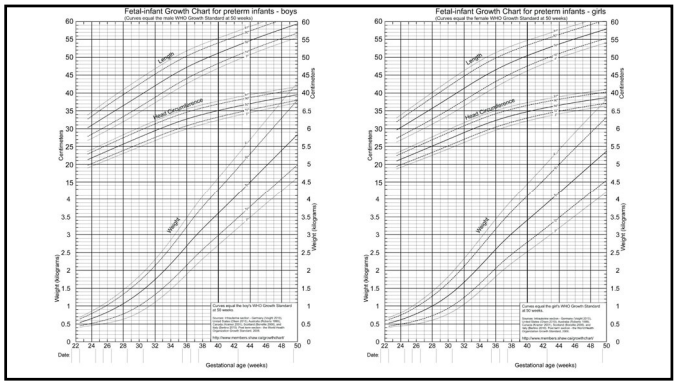
When is irritation actually omphalitis?

4 How long to follow NICU/fenton curves?

- **Background**:
  - Preterm infants are often significantly under weight at the time of hospital discharge
  - Preterm growth charts aim to mimic growth that occurs during a term pregnancy
  - Multiple preterm curves (Olsen, Bertino, Fenton)
  - If age is not corrected, the infant may appear to be growing suboptimally
  - Should be used in conjunction with term charts after 40 weeks
- **Recommendation**: Corrections for gestational age (GA) should be made for
  - head circumference through 18 months of age,
  - weight through 24 months of age,
  - stature through 40 months of age.
  - In general, utilize Fenton preterm infant growth chart until the infant is 44 to 48 weeks PMA
  - after which WHO growth curves for term infants can be utilized (~4-6wk post-term)
- **Caveat(s)**: more frequent monitoring for infants with BPD, history of GI comorbidities, and/or CKD



5 When take off fortified formula?

- **Background**: continuation from previous slide
- **Recommendation**: In general, formula-fed preterm infants should be fed enriched formula until *6mo of age* post-term or until they have achieved adequate catch-up growth
- **Caveats**: What about breastfed babies?
  - After hospital discharge, exclusively human milk-fed preterm infants are at increased risk for suboptimal growth compared with formula-fed infants
  - Human milk-fed preterm infants should also receive iron and vitamin D supplementation, as these two nutrients are inadequately supplied by human milk alone
  - Often fortified feeds are utilized

TABLE 21.12 ENTERAL NUTRITION COMPONENTS (PER LITER)

A. INFANT FORMULAS										
	Kcal/oz	**Protein (g)**	**Fat (g)**	**Carbs (g)**	**Na (mEq)**	**K (mEq)**	**Ca (mg)**	**P (mg)**	**Fe (mg)**	**Osmolality**
HUMAN MILK										
Term	20	11	39	72	8	14	279	143	0.3	286
Preterm	20	14	39	66	11	15	248	128	1.2	290
HUMAN MILK AND FORTIFIERS ANALYSIS										
Enfamil HMF Liquid + Preterm Human Milk (5 mL + 25 mL breast milk)	24	32	48	65	20	20	1150	650	15	322
Similac HMF + Preterm Human Milk (1 pkt/25 mL)	24	23	41	82	17	30	1381	777	4.6	N/A
PRETERM FORMULAS										
Enfamil EnfaCare	22	21	39	77	11	7.2	890	490	13.3	280
Enfamil Premature 20	20	20	34	74	17	17	1100	553	12	240
Enfamil Premature 24	24	27	41	88	25	21	1340	730	15	280
Enfamil Premature 24 High Protein	24	28	41	89	20	21	1340	670	15	300
Enfamil Premature 30	30	30	52	112	26	27	1670	840	18	300
Gerber Good Start Premature 20	20	20	35	71	16	21	1110	570	12	229
Gerber Good Start Premature 24 High Protein	24	29	42	79	19	25	1330	690	15	299
Gerber Good Start Premature 30	30	30	53	107	24	31	1660	860	18	341
Similac NeoSure	22	21	41	75	11	27	781	461	13.4	250
Similac Special Care 20	20	20	37	70	13	22	1217	676	12.2	235
Similac Special Care 24 High Protein	24	27	44	81	15	27	1461	812	14.6	280
Similac Special Care 30	30	30	67	78	19	34	1826	1014	18.3	325

6 Can I give rotavirus post-NEC?

- **Background**:
  - Rotarix (lives, monovalent human-attenuated vaccine given a 2 & 4mo)
  - RotaTeq (live, pentavalent human-bovine reassortment given at 2, 4, 6mo)
  - Contraindications: hypersensitivity to component, uncorrected congenital GI malformation (e.g., Meckel) that would predispose to intussusception, history of intussusception, and/or SCID
- **Recommendation**: Yes (maybe avoid post-surgical NEC)
- **Caveats**:
  - Most common late GI complications from NEC are stricture formation and short bowel syndrome
  - Post-surgical NEC:
    - Strictures – 24 percent (95% CI 17-31%t)
    - Intestinal failure – 13 percent (95% CI 3-15%)
    - Recurrent NEC – 8 percent (95% CI 7-19%)
    - Adhesion ileus – 6 percent (95% CI 4-9%)

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7 When should you worry when they don't pee in nursery?

- **Background**:
  - Although the time of the first void is variable, at least 50% of newborns void by 8hr of age with nearly all before 24 hours
  - Differentials: prerenal (shock, asphyxia, hypotension, RDS) and intrinsic (renal agenesis, hypoplastic, dysplastic, or polycystic kidneys), post-renal (neurogenic bladder, urethral stricture, posterior urethral valves, extrinsic compression)
- **Recommendation**:
  1. Verify void wasn't missed at delivery, review PO intake and daily weights, review diaper monitoring with parents (particularly female), verify no history of oligohydramnios, & palpate bladder
  2. sprinkle water, perform crede, and increase PO intake (supplementation)
  3. Obtain renal and pelvic US (often diagnostic & therapeutic), if concerning will expand workup in NICU
- **Caveats**:
  - Above applies to well-appearing infant

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8 When should you worry when they don't poop in nursery?

- **Background**:
  - Meconium passed within 24hr in 99% healthy, term infants; all by 48hr
  - Delayed passage of meconium ddx: duodenal atresia, malrotation, volvulus, atresia, meconium ileus, meconium plug, Hirschsprung's, imperforate anus, small left colon syndrome, hypothyroidism, maternal labor medications (MgS04)
- **Recommendation**: verify meconium wasn't passed at delivery, verify patent anus, rectal stimulation around 24hr of life, if imaging and exam reassuring follow with rectal suppository q2hr x3 and monitor response
- **Caveats**:
  - Above applies to well-appearing infant
  - Pre-term infant can have delayed passage

Day of Life	% of Infants
1	37%
2	68%
3	99%

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9

What to do with sacral dimples?

- **Background:**
  - Several large ultrasound studies have shown that the risk of significant spinal malformations in neonates with isolated sacral dimples or gluteal clefts, in otherwise healthy infants, is exceedingly low
  - When US is obtained for multiple cutaneous stigmata, infants are up to 6x more likely to have dysphrasim diagnosed than those imaged based on a single marker
  - MRI is more sensitive, with most diagnosed with filar abnormality (fatty filum and/or low conus medullaris), and is gold standard for diagnosis of occult spinal dysphrasim (OSD)
  - *When should I be concerned?*
    - Multiple dimples, dimple diameter larger than 5 mm, location greater than 2.5 cm above the anal verge, and/or association of the dimple with other cutaneous markers
    - Hypertrichosis, capillary hemangioma, atretic meningocele, subcutaneous mass (eg, lipoma), or a caudal appendage
    - Gluteal cleft anomalies other than dimples also have a weak association with milder forms of OSD and warrant further evaluation. (e.g. deviated or duplicate cleft)

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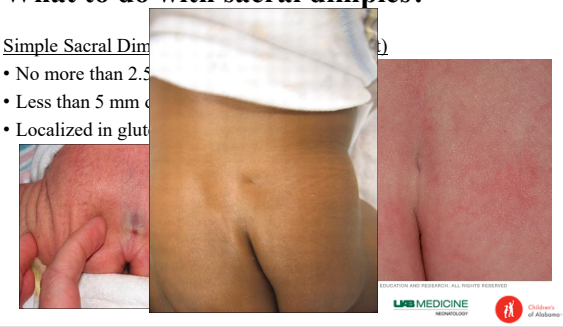
What to do with sacral dimples?

Simple Sacral Dim)

- No more than 2.5
- Less than 5 mm
- Localized in glut



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What to do with sacral dimples?

- **Recommendation**:
  - In general, simple cutaneous lumbosacral markings (such as simple sacral dimple or Y-shaped gluteal cleft) are unlikely to be associated with understudying occult spinal dysphrasim (OSD)
  - If covered completely by skin, otoscopic examination of the dimple often can determine if there is a bottom to the pit.
  - Although most lesions occur in the midline, eccentric lesions are not in themselves abnormal unless occurring in conjunction with other lesions or outside the sacral spine

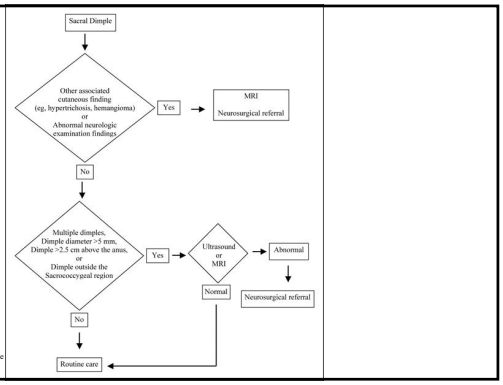


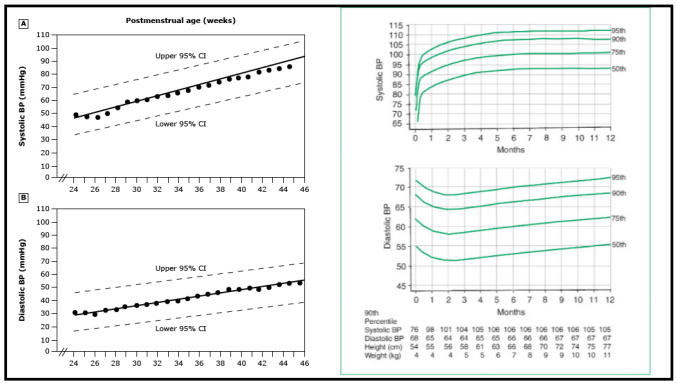
Figure 7. An algorithm for evaluation of dimples overlying the neural axis. MRI=magnetic resonance imaging. Pediatrics in Review . Volume 32, Issue 3 March 2011

What to do with sacral dimples?

- **Caveats**:
  - US vs MRI? Accessibility, radiology skill set, & physician preference
  - In general, if mild anomalies I consider spinal US and discuss with NSGY
  - If blatant, outpatient referral for spinal MRI by 2mo of life

10 What to do with AKI after NICU?

- **Background**:
  - Incidence of AKI in 20-40% infants in NICU
  - AKI incidence & severity increases with lower gestational age (GA)
  - Other high-risk neonatal groups include very preterm infants with the following:
    - Perinatal asphyxia
    - Congenital diaphragmatic hernia
    - Complex cardiac disease requiring cardiac surgery
    - Treatment with extracorporal membrane oxygenation (ECMO)
  - Infants with history of AKI are at risk for the development of chronic kidney disease (CKD)
- **Recommendation**: General pediatricians should consider neonates who have suffered AKI at increased risk for CKD and monitor blood pressure with consideration of further testing on a case-by-case basis
- **Caveats**: AKI diagnosis is poorly documented, high index of suspicion based on risk factors



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UAB MEDICINE NEONATOLOGY

Children's of Alabama

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b. Dimple is Less than 5 mm in diameter
c. Dimple is localized in the gluteal cleft
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Thanks!

Questions?