Case 1

- Day 8 , started jaundice
- Bilirubin total : 13.9 and direct : 2.1 , retics 1,6%
- ALT 36 , AST 52
- Ultrasound normal liver, normal gall bladder , urinary bladder 5 mm wall thickness, normal kidneys
- Jaundice persisted till day 16 , where stoppage of breastfeeding and artificial formula for 48 hrs
- Partial improvement of Jaundice , then recurred again
- G6PD normal

- Differential diagnosis ?

Case 2

- Preterm, incubated for weight gain and mild RD
- Day 6 started to develop apnea , not adequately improving on caffeine
- Normal cranial US
- Blood culture no growth

- Differential diagnosis ?

Case 3

- Breastfed newborn
- Failure to gain weight
- Changed to artificial formula
- Still poor appetite and failure to thrive
- Diagnosed as cow's milk intolerance
- Shifted to a.a. formula with no improvement

Case 4

- Feverish 2 weeks old neonate without a focus
- diagnosed first as dehydration fever
- Then a second opinion treated it as pharyngitis !!

- Would you include in your diagnosis :

Neonatal urinary tract infection

Case 1

- Day 8 , started jaundice
- Bilirubin total : 13.9 and direct : 2.1 , retics 1,6%
- ALT 36 , AST 52
- Ultrasound normal liver, normal gall bladder , urinary bladder 5 mm wall thickness, normal kidneys
- Jaundice persisted till day 16 , where stoppage of breastfeeding and artificial formula for 48 hrs
- Partial improvement of Jaundice , then recurred again
- G6PD normal

- Differential diagnosis ?

Case 1

- *Urinary tract infections (UTI) are attributed as **the main reason for prolonged jaundice**, and it is well known that UTI can occur without apparent signs, and **jaundice is an important and sometimes the presenting feature of UTI** .*

Bilgen H, et al. Urinary tract infection and hyperbilirubinemia. Turk J Pediatr. 2006

Case 1

Conclusion :

- We recommend that testing for a UTI be part of the diagnostic evaluation of asymptomatic jaundiced newborns especially when no other obvious reason of jaundice is found. This may lead to early detection and treatment of these newborns leading to lesser long term complications of the kidneys.

Bilgen H, et al. Urinary tract infection and hyperbilirubinémie. Turk J Pediatr. 2006

Neonatal UTI may cause apnea in preterms

- Preterm, incubated for weight gain and mild RD
- Day 6 started to develop apnea , not adequately improving on caffeine
- Normal cranial US
- Blood culture no growth

- Differential diagnosis ?

Arshad and Seed, Clin Perinatol. 2015 .

Neonatal UTI is an important cause of failure to thrive

- Breastfed newborn
- Failure to gain weight
- Changed to artificial formula
- Still poor appetite and failure to

Very common cause of neonatal FUO

- Feverish neonate without a focus
- diagnosed as dehydration fever
- or pharyngitis !!

Urinary Tract infection in Neonates

SAMUEL MAKAR , MD

PROF OF PEDIATRICS AND PEDIATRIC NEPHROLOGY ,CAIRO UNIVERSITY

Neonatal urinary tract infection is peculiar :

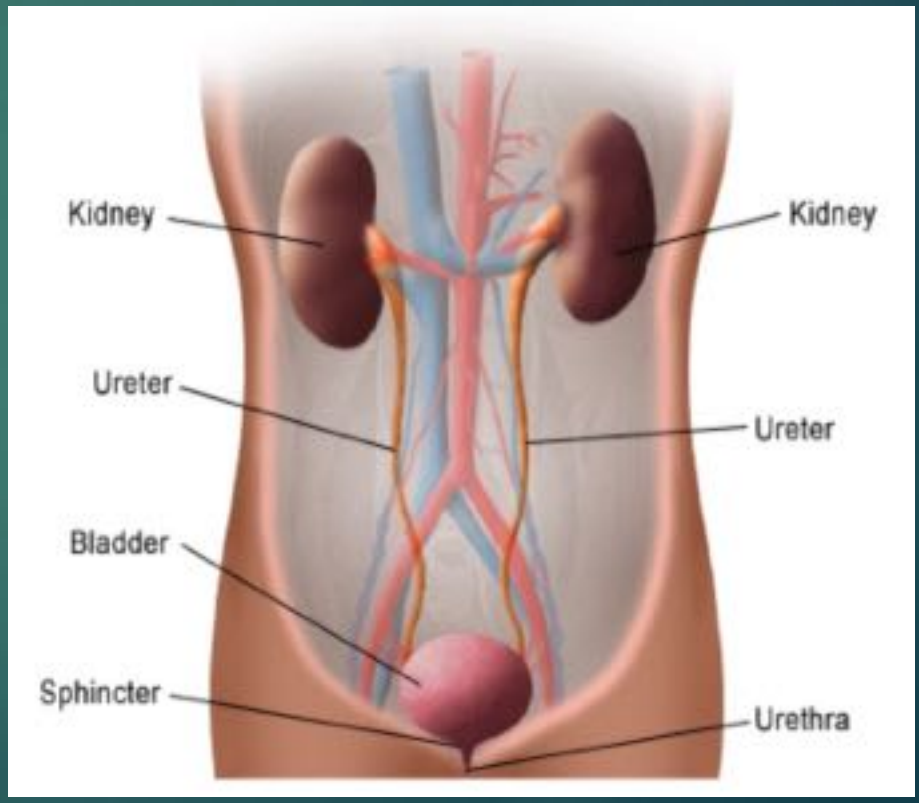
- Peculiar in its presentation
- Peculiar predisposing factors
- Peculiar presence of concomitant morbidity
- Peculiar drugs pharmacokinetics

Introduction

Urinary tract infections (UTIs) can affect the whole urinary tract including :

- urethra (urethritis)
- bladder (cystitis),
- kidneys

(Pyelonephritis or upper tract infection)



Introduction : **PN or Cystitis**

- Unfortunately ,UTIs in neonates is mostly pyelonephritis rather than cystitis
- In FT , UTI is mostly due to ascending infection rather than hematogenous spread
- In Preterm it is mostly due to hematogenous spread as part of sepsis

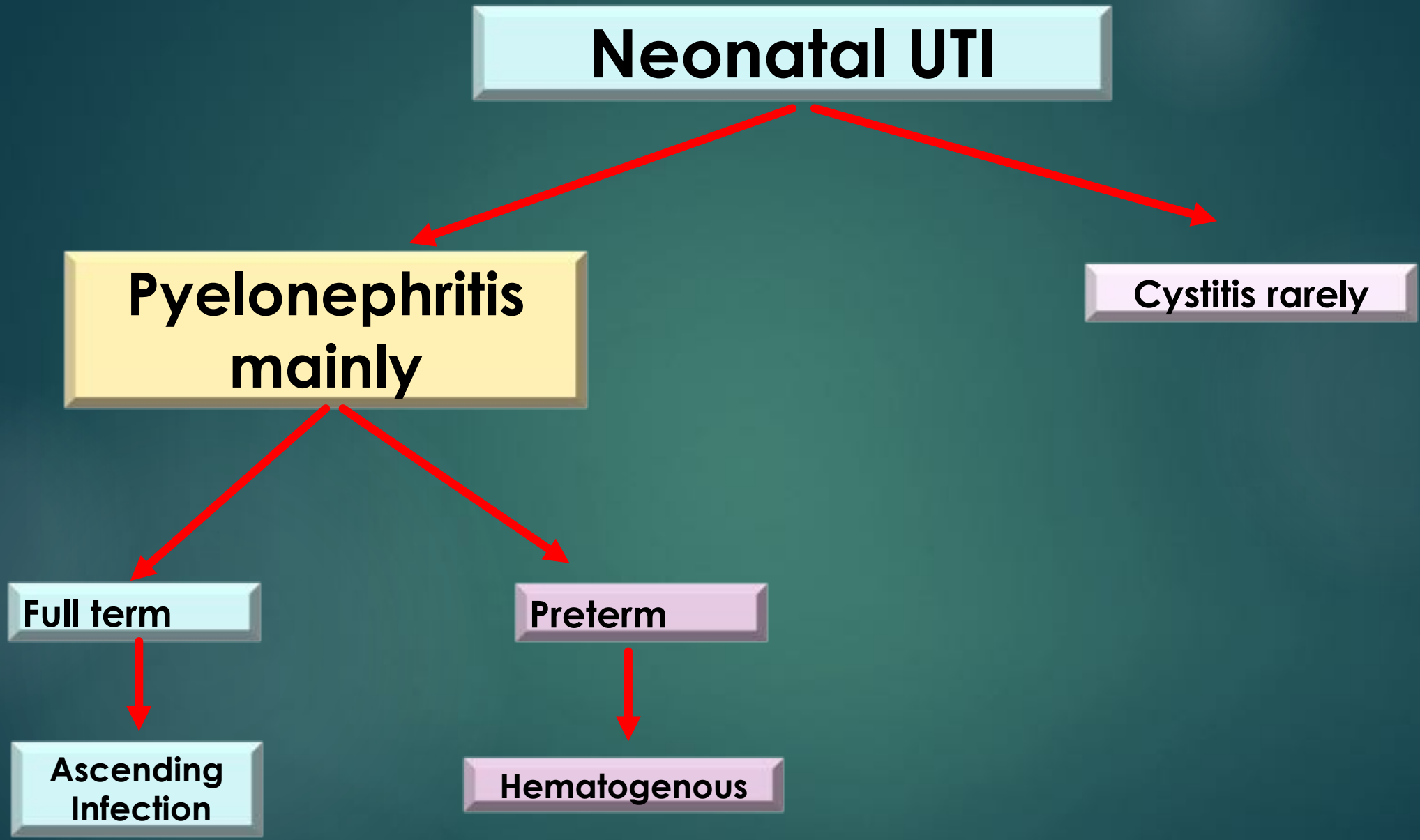
Introduction : **Full term vs Preterm**

In Full trerm :

- Escherichia coli most common pathogen (80 % of cases)
- Other gram-negative bacterial include
  - Klebsiella, Proteus, Enterobacter, and Citrobacter.
- Gram-positive pathogens include
  - Staphylococcus coagulase-negative species, Enterococcus, and, **rarely**, **Staphylococcus aureus**.

In Preterm:

- Coagulase-negative Staphylococcus and Klebsiella are more likely causes of UTI in hospitalized preterm infants, and E. coli is less commonly seen


Neonatal UTI
Pyelonephritis mainly
Cystitis rarely
Full term
Preterm
Ascending Infection
Hematogenous

Introduction : **Incidence**

Febrile neonate :

- Rates of UTI vary from **10 to 20 %** in cases presenting with febrile episode in the neonatal period (full term)
- Risk increases with decreasing gestational age and birth weight.
- UTI is uncommon in the first few days of life even in neonates with bacteremia. **(<1 % of such patients)**
- Thus,urine cultures are not routinely included in the evaluation for early-onset sepsis in term neonates

Bonadio W, et Maida G. Pediatr Infect Dis J 2014

Introduction : **Incidence**

- It affects 3% of preterm
- 0.7% of term infants at some point in the first 3 months of life.

- After first episode of PN :
  - 2.8–16% of individuals may develop kidney scarring ,
  - 8.4% of these developing hypertension,
  - and a small proportion progressing to kidney failure

Introduction : **Predisposing Factors**

- congenital urinary tract abnormalities, (vesicoureteral reflux (VUR) and others) ,
- male sex,
- uncircumcised penises.
- preterm delivery

HOST FACTORS : **Male infants**

- 75 % of neonates and young infants (<3 months of age) with UTIs are males

- higher incidence of urinary tract anomalies in males
- Increased risk of UTI in uncircumcised males.

HOST FACTORS : **Circumcision**

- The incidence of UTI is 10-fold greater in uncircumcised versus circumcised males.
- The higher incidence of UTI in uncircumcised males is related to an increased rate of bacterial colonization and enhanced bacterial adherence

Wiswell TE and Geschke DW , Pediatrics 1989

HOST FACTORS : **Prematurity**

- Relatively immunocompromised status
- The use of invasive devices (eg, urinary catheters)

HOST FACTORS: **UT Abnormalities**

- They are seen on ultrasound in **35 to 50 %** of neonates and young infants (<3 months of age) with UTI.
- Most common pelviectasis and mild hydronephrosis .
- Major renal or urologic abnormalities (eg, high-grade VUR) in 5 to 10 % of infants

Sastre JB,et al , Pediatr Nephrol 2007

HOST FACTORS: **UT Abnormalities**

Others as obstructive lesions ncluding:

- ureteropelvic junction obstruction (PUJ)
- ureterovesical junction obstruction
- posterior urethral valves (PUV)

CLINICAL FEATURES :

- The signs and symptoms of UTI in neonates are nonspecific.
  - lethargy,
  - Irritability,
  - Tachypnea
  - Cyanosis and may appear acutely ill.

Clinical Picture

Full term

- Fever (20 - 40 %)
- F T T (15-43 %)
- Jaundice (3 – 41 %)
- Vomiting (9 - 41 %)
- Loose stools (3 - 5 %)
- Poor feeding (3 - 5 %)

Preterm

- Feeding intolerance (62 %)
- Apnea and bradycardia (45 %)
- Lethargy (30 %)
- Tachypnea (30 %)
- Abdominal distension (12 %)
- Hypoxia with O2 desaturation (12 %)

Donough J O'Donovan, uptodate 2022

Clinical Picture

Full term

- Fever (20 - 40 %)
- F T T (15-43 %)
- Jaundice (3 – 41 %)
- Vomiting (9 - 41 %)
- Loose stools (3 - 5 %)
- Poor feeding (3 - 5 %)

Direct , or

Indirect ?

Preterm

- Feeding intolerance (62 %)
- Apnea and bradycardia (45 %)
- Lethargy (30 %)
- Tachypnea (30 %)
- Abdominal distension (12 %)
- Hypoxia with O2 desaturation (12 %)

Donough J O'Donovan, uptodate 2022

CLINICAL FEATURES : **Jaundice**

- The hyperbilirubinemia that occurs with UTI **typically is conjugated**
- Jaundice may be the first sign of UTI in some infants.
- In one report, UTI was diagnosed in 12 (**7.5%**) of 160 asymptomatic jaundiced infants less than eight weeks of age who presented to an emergency department .
- In this cohort, infants with the onset of conjugated jaundice after eight days of age were more likely to have a UTI.

Garcia FJ and Nager . Pediatrics 2002

Clinical Picture

Full term

- Fever (20 - 40 %)
- F T T (15-43 %)
- Jaundice (3 – 41 %)
- Vomiting (9 - 41 %)
- Loose stools (3 - 5 %)
- Poor feeding (3 - 5 %)

Direct , or

Original Article

Urinary tract infection and indirect hyperbilirubinemia in newborns

Chamdine Omar, Shadi Hamza, MD., Abou Merhi Bassem, Rajab Mariam

Department of Pediatrics, Makassed General Hospital, Beirut, Lebanon.

Citation: Omar C, Hamza S, Bassem AM, Mariam R. Urinary tract infection and indirect hyperbilirubinemia in newborns. **North Am J Med Sci** 2011; 3: 544-547.
doi: 10.4297/najms.2011.3544

Abstract

Background: Jaundice is a common problem during the neonatal period. About 60% of the full term and 80% of premature infants develop jaundice. It can be associated with serious illnesses such as Urinary tract infections. **Aims**: The aim of this study is to evaluate the incidence and prevalence of urinary tract infection in newborns with indirect hyperbilirubinemia and to find a relationship with prolonged jaundice. **Patients and Methods**: We retrospectively evaluated asymptomatic, jaundiced neonates for evidence of a urinary tract infection. Data reviewed including demographic and historical data were included with data of blood studies, radiological evaluation and treatment. **Results**: 32 neonates of 152 cases had urinary tract infection. Most commonly isolated organisms were Klebsiella and Escherishia coli. Maximum duration of phototherapy was 4 days in the urinary tract infection group versus 7 in the non-urinary tract infection group. Intensive phototherapy was used in 18.7% in the urinary tract infection group versus 29.16% in the non-urinary tract infection group. None of the newborns in the urinary tract infection group underwent exchange transfusion therapy. **Conclusion**: Urinary tract infection can occur in asymptomatic, jaundiced newborns. Thus, it may be the first in these babies before other signs become evident.

Clinical Picture

Full term

- Fever (20 - 40 %)
- F T T (15-43 %)
- Jaundice (3 – 41 %)
- Vomiting (9 - 41 %)
- Loose stools (3 - 5 %)
- Poor feeding (3 - 5 %)

Jaundice (3 – 41 %) →

- Direct , or
- Indirect

Jaundice: *direct or indirect ?*

- In Both types UTI should be considered
- And included in the workup if the clinical picture suggests

CLINICAL FEATURES : *Preterm infants*

- Feeding intolerance (62 %)
- **Apnea and bradycardia (45 %)**
- Lethargy (30 %)
- Tachypnea (30 %)
- Abdominal distension (12 %)
- **Hypoxia with documented oxygen desaturation (12 %)**

Diagnosis

Urine analysis

- Leukocytes esterase
- Nitrites
- Bacteruria

Urine culture

- Single uropathogenic Organism
- Colony count (CFU/ml)
- Method of sample collection

Diagnosis

- NICE (UK)
- AAP (USA)
- Other countries

Dipstick testing for UTI : Leucocyte esterase

- Leucocyte esterase (LE) is an enzyme produced by white cells and is found in urine where **white cells have been active (pyuria)**, such as when there is active infection

- Should be taken in the context of the clinical picture

Price E, et al J Antimicrob Chemother 2010 (NICE)

Dipstick testing for UTI : Leucocyte esterase

High rate of false negatives in:

- Neutropenic patients

and in

- younger children whose frequent voiding reduces LE accumulation in stored urine

Price E, et al J Antimicrob Chemother 2010 (NICE)

This is typically in neonates , so don't depend on LE negative in neonates

Dipstick testing for UTI : Nitrite

- Nitrite is produced from dietary nitrate in the bladder through metabolism by bacteria.

- Nitrite is not associated with all organisms as it is not produced by:
  - Pseudomonas species
  - gram-positive organisms such as Enterococcus

Dipstick testing for UTI : Nitrite

- Nitrite testing is also impacted by age, as the more frequent voiding of younger children allows less time for nitrite to accumulate prior to sampling

Price E, et al J Antimicrob Chemother 2010 (NICE)

- Original studies quote a dwell time of 4 h in the bladder to convert dietary nitrates to nitrites (controversial).

Dipstick testing for UTI : Nitrite

- Therefore neonates with pseudomonas or enterococci may have nitrites negative
- as well as negative LE !!
- **Therefore a urine culture is always mandatory , not only if urinalysis is positive for pus cells or LE or nitrite**

- Some centers , for well appearing febrile infants, perform urinalysis as the initial test and only perform culture if the urinalysis is positive (ie, reflexive testing).

- The advantage of performing both tests up front is that it has greater likelihood of identifying all affected neonates (ie, fewer false negatives).

- In addition, culture results and susceptibility testing may be available earlier, allowing for appropriate tailoring of antibiotic therapy.

Diagnosis : ***Positive urine culture***

- ***A positive result is based on identifying a single uropathogenic bacteria and reaching a threshold of number of CFU that grow on the culture medium.***

- ***The number of CFU defining a positive urine culture varies based on the method of collection***

Method of urine sample collection

- Clean Catch (CCU)
- Catherization
- Suprapubic aspiration
- Bag
- Pad

Methods of Collection : **Clean Catch Urine (CCU)**

- Clean catch urine (CCU) samples are obtained by holding a sterile container beneath the urethra with the nappy off, until a void begins, with care taken to avoid any skin contact with the specimen container.

- Voiding can be stimulated by different methods

Stimulation of voiding

- hold the baby upright under both armpits with the legs dangling
- tap the abdomen suprapubically at 100 taps/min for 30 s
- followed by circular lumbosacral massage for 30 s
- alternating for up to 5 min.

Fernández ML,et al. Arch Dis Childn(2013)

Stimulation of voiding

- This has been shown to promote voiding, especially if performed 30 min post feeding . Using this technique in those < 7 days old led to voiding within 5 min in 90% of infants .
- The effectiveness of the technique declines with age and weight of infants

Fernández ML,et al. Arch Dis Childn(2013)

Methods of Collection : Clean Catch Urine (CCU) ***the Quick-Wee method***

In Australia , single-center RCT compared 2 methods for obtaining a clean-catch urine sample within 5 minutes:

- ***the Quick-Wee method*** (suprapubic stimulation with gauze soaked in cold fluid)

Or

- Usual care (waiting for spontaneous voiding with no stimulation).
- 354 infants (ages 1-12 months) who required urine sample collection were randomized in a 1:1 ratio
- Infants with anatomic or neurologic abnormalities and those needing immediate antibiotic therapy were excluded.

Methods of Collection : Clean Catch Urine (CCU)

Results :

- 31% of the patients in the Quick-Wee group voided within 5 minutes, compared with 12% of the usual-care patients.
- Similarly, 30% of patients in the Quick-Wee group provided a successful clean-catch sample within 5 minutes compared with 9% in the usual-care group (*P*<.001; number needed to treat=4.7; 95% CI, 3.4-7.7).
- Both parents and clinicians were more satisfied with the Quick-Wee method than with usual care

Kaufman J, et al. Faster clean catch urine collection (Quick-Wee method) from infants: randomized controlled trial. BMJ. 2017

Methods of Collection : Clean Catch Urine (CCU) ***the Quick-Wee method***

Kaufman J, et al. Faster clean catch urine collection (Quick-Wee method) from infants: randomized controlled trial. BMJ. 2017

Urine sampling :*In-out catheterization*

Urine sampling :*In-out catheterization*

- Temporary insertion of a urinary catheter to obtain a sample, with the catheter then being removed.

- Theoretical benefits are that this avoids some contamination from colonizing bacteria in the distal urethra compared with voided samples and may be less likely to lead to complications than suprapubic aspiration.

Urine sampling :*In-out catheterization*

- Best practice is to discard the initial few drops of urine which are thought to have a higher likelihood of contamination from urethral bacteria
- A randomized comparison of early sampling or late sampling found significantly higher sample contamination if the first drops of urine collected were cultured

Urine sampling :*In-out catheterization*

- Catheterisation procedure reports a 92.3% to 100% success rate .
- Significant complications are rarely described, with transient microscopic haematuria in 17% .

- One study found that previous catheterisation was a risk factor for septicaemia in neonates

Schroeder AR et al,. Arch Pediatr Adolesc Med 2005

Urine sampling : ***Suprapubic sampling***

Urine sampling : ***Suprapubic sampling***

- Suprapubic aspiration is undertaken through the insertion of a 22G needle through the anterior abdominal wall and into the bladder, usually aided by ultrasound guidance, with urine aspirated into a syringe.

- Suprapubic sampling is often described as the gold standard for urine sampling due to the theoretical minimal likelihood of contamination , avoiding bacteria which colonise the distal urethra as normal flora .

Diviney & Jaswon, Pediatric Nephrology (2021)

Urine sampling : ***Suprapubic sampling***

- Any growth on urine cultured from SPA may be taken as significant given the sterile nature of the procedure
- However, SPA is also considered the most invasive and painful method by practitioners and parents .
- Reported success rates in unguided attempts were 46% - 64%.
- Under sonar guidance success improves from 79% to 90% .

Ozkan B, et al. Clin Pediatr (2000)

Urine sampling : ***Suprapubic sampling***

- Patient selection and preparation are also important.
- Sonar guided or not

- In one study , there was no difference in success noted with or without sonar guidance in if the patients were prehydrated and had identifiable dullness on suprapubic percussion

Urine sampling : ***Suprapubic sampling***

- Complications are rare, occurring with a rate of only 0.22% of 4985 SPAs performed in one study

Hildebrand WL,et al Am Fam Physician (1981)

- However, other studies have noted aspiration of gut lumen contents in 1 in 140 aspirations .

- Microscopic haematuria has been seen for 24 h post aspiration in 3.6% of patients .

Ozkan B, et al. Clin Pediatr (2000)

Urine sampling : ***bag***

Urine sampling : ***bag***

- Actively recommended ***AGAINST*** by the AAP

- Still remains a highly utilised method of sampling, especially in the community.

- It is the preferred method of collection in Europe by pediatricians

Hadjipanayis A, et al , Arch Dis Child

Urine sampling : ***bag***

The AAP guideline states that bag cultures have “an unacceptably high false-positive rate and are valid only when they yield negative

results”, stating that the rate of false positives range from 88 to 99% of tests

Urine sampling : ***Pad***

- Pad sampling involves the insertion of an absorbent material into the child's nappy from which urine is later aspirated after voiding.
- There are custom designed pads for this purpose, such as the ***Newcastle urine collection pad (UCP).***
- The main advantages of the pad collection are that the process is passive and requires less parental effort with less disruption to the child.
- There is decreased likelihood of missing a sample compared with clean catch collection, with overall sampling success of 96%.
- It is the preferred collection method of parents but with high risk of contamination

Urine sampling ***(perineal cleaning)***

- Practice differs between centres as to if and how the perineum should be cleaned before a clean catch sample is collected, with some centres using saline, soap or chlorhexidine

Urine sampling *(perineal cleaning)*

Randomized Controlled Trial > Pediatrics. 2007 Jun;119(6):e1288-93.
doi: 10.1542/peds.2006-2392. Epub 2007 May 14.

To clean or not to clean: effect on contamination rates in midstream urine collections in toilet-trained children

Suzanne Vaillancourt [1], David McGillivray, Xun Zhang, Michael S Kramer

Affiliations + expand

PMID: 17502345 DOI: 10.1542/peds.2006-2392

Abstract

Objective: Urinary tract infection is one of the most common bacterial infections among children. Difficulty in specimen collection and interpretation of inadequately collected specimens may contribute to misdiagnosis of urinary tract infection. Our objective was to assess the effect of perineal/genital cleaning on bacterial contamination rates of midstream urine collections in toilet-trained children.

Methods: We conducted a randomized trial in toilet-trained children who presented to a tertiary care pediatric emergency department between November 1, 2004, and October 1, 2005. All toilet-trained children who were between the ages of 2 and 18 years and had a midstream urine sample requested were eligible. Those whose parents consented were cluster-randomized by week to either cleaning or not cleaning the perineum with soap. The risk for a contaminated urine culture (defined as growth of < 10(8) colony-forming units per liter [< 10(5) colony-forming units per milliliter] of a single organism or a mix of > or = 2 organisms) and the risk for a positive urinalysis (defined as a positive leukocyte esterase and/or nitrites on dipstick or > or = 5 white blood cells per high-powered field on a standard microscopic examination) were analyzed by intention to treat.

Results: A total of 350 children were enrolled. The rate of contamination in the cleaning group was 14 (7.8%) of 179 vs 41 (23.9%) of 171 in the noncleaning group. Children who were randomly assigned to cleaning were less likely to have a positive urinalysis (37 of 179 [20.6%]) than those in

Urine sampling ***(perineal cleaning)***

- A randomised trial of cleaning with soap vs. not cleaning in 350 patients found significantly lower contamination rates in the cleaning group (7.8%) vs. the non-cleaning group (23.9%)

Vaillancourt S et al, Pediatrics (2007)

Urine sampling ***(UK NICE)***

1) **Clean catch urine (CCU)** sampling is the recommended methodology

2) If CCU is unobtainable, then other **non-invasive** methods such as a urine collection pad (but not gauze, cotton wool or sanitary towels) should be used.

3) Where it "is not possible or practical" to collect urine non-invasively then **catheter sampling or suprapubic aspiration (SPA)** should be used.

4) If SPA is used, then an ultrasound should be performed first to confirm urine in the bladder.

NICE (2007) Urinary tract infection in under 16s: diagnosis and management

Urine sampling : ***The American Academy of Paediatrics (AAP)***

- for diagnosis of UTI if **antibiotics are to be given**, then the "specimen needs to be obtained through
  - *Catheterization or SPA*

- because the diagnosis of UTI cannot be established reliably through culture of urine collected in a bag."

Urinary tract infection: clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2 to 24 months. Pediatrics (2011)

Urine sampling : ***The American Academy of Paediatrics (AAP)***

If immediate antibiotics are not required, then there are two options:

1) Either "to obtain a urine specimen through catheterization or SPA

- for culture and
- urinalysis"

Or

2) "to obtain a urine specimen through the most convenient means and to perform a urinalysis."

Urinary tract infection: clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2 to 24 months. Pediatrics (2011)

Urine sampling : ***The American Academy of Paediatrics (AAP)***

If the urinalysis results suggest a UTI (positive leucocyte esterase or nitrite test or microscopic analysis positive for leucocytes or bacteria), then

a urine specimen should be obtained through catheterization

or SPA and cultured.

They do not recommend clean catch, pad or bag sampling.

Urinary tract infection: clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2 to 24 months. Pediatrics (2011)

Urine sampling *(other countries)*

Other international guidelines from

- Australia,
- Canada,
- The European Society for Paediatric Urology,
- Italy
- New Zealand

Well children :

use of bag sampling :

if dipstick from bag samples suggestive of infection >> alternate method of collection required (clean catch, catheter or SPA)

Unwell children, : catheter or SPA sampling is recommended

Diviney & Jaswon, Pediatric Nephrology (2021)

Diagnosis

- Urine specimens should be transported on ice and must be processed expeditiously to avoid further growth of organisms in the urine specimen.

- If the specimen cannot be processed quickly, it should be refrigerated.

Diagnosis

SPA

Any growth of a urinary pathogen is significant.

SPA of the bladder urine is the most reliable technique to identify bacteriuria; however, it is rarely necessary

Diagnosis

Bladder catheterization :

growth of a single uropathogenic pathogen with :

- colony count of ≥50,000 CFU/mL

  or

- colony count between 10,000 and 50,000 CFU/mL with associated **pyuria** detected on urinalysis

Methods of Collection : contamination rates

Method Contamination	rates reported
Clean catch	4.5- 38 %
Bag	18- 88%
Pad	9.1- 80 %
Catheterization	9- 28%
Suprapubic aspiration	0-9.1%

Diviney & Jaswon, Pediatric Nephrology (2021)

Differential Diagnosis

- Because the signs and symptoms of neonatal UTI are nonspecific (several other disorders may present with similar findings
- Other infectious conditions including sepsis and meningitis – Cultures of urine and other body fluids (eg, blood, cerebrospinal fluid) distinguish UTI from these other infectious diseases
- Inborn errors of metabolism

FURTHER EVALUATION- **Laboratory**

Sepsis evaluation :

- A blood culture should be obtained in all neonates with suspected or confirmed UTI.

- The risk of concurrent bacteremia in neonates with UTI varies from **4** to **7 %** in term infants and as high as **14 %** in preterms .

- A positive blood culture does not alter initial management in the vast majority of patients (usually the same organism as from urine) but it may ***alter the duration of therapy***.

Downey LC, J Perinatol (2013)

FURTHER EVALUATION- **Laboratory**

- In addition, clinicians should have a **low threshold to perform a lumbar puncture** as approximately **1 to 3 %** of infants with UTI have bacterial meningitis , in particular in ill-appearing infants or those with neurologic findings (irritability, bulging fontanel)

Downey LC, J Perinatol (2013)

FURTHER EVALUATION -**Radiographic**

- Because of the high prevalence of urinary tract abnormalities, all neonates with UTI should undergo we radiographic evaluation .

- The first step of this evaluation is renal ultrasonography to identify structural abnormalities.

FURTHER EVALUATION –**Renal ultrasound**

- 30 - 50 % of neonates with UTI have abnormalities on renal ultrasound, most commonly pelviectasis or mild hydronephrosis.
- However, a normal ultrasound examination does not exclude VUR or renal scarring .

FURTHER EVALUATION –**Renal ultrasound**

Timing :

- Obtained after initiation of antibiotic treatment and stabilization of the patient is initiated and the infant's clinical condition has stabilized.
- Very early (first few days of life) could be misleading (falsely normal) due to inadequate hydration of the neonate (may repeat at day 7)

- Antenatal Ultrasound is informative, but the urinary tract is fully developed by 30- 32 weeks of gestation , therefore prenatal US prior to this may not give adequate information (those done later are adequately informative)

FURTHER EVALUATION –**Renal ultrasound**

- size
- position of the kidneys
- appearance of the collecting system, including
- size and thickness of the bladder.
- structural abnormalities (eg, solitary kidney, multicystic dysplasia, duplex collecting system)
- Stones

FURTHER EVALUATION – **Voiding cystourethrogram**

- VCUG should be performed in neonates with ***abnormal*** ultrasound findings.

- Rational practice for most neonates with first-time UTI and normal renal ultrasound is to "***wait and watch***."

FURTHER EVALUATION – **Voiding cystourethrogram**

- Do VCUGs only in neonates with
  1. abnormal renal ultrasound
  2. non-E. coli pathogen
  3. or recurrent UTI.

- Some centers routinely perform VCUGs in all neonates with first-time febrile UTI.(controversial)

FURTHER EVALUATION – **Voiding cystourethrogram**

In a retrospective study that included 122 infants (<3 months old) with first febrile UTI, The probability of high-grade VUR was

- 3% in the presence of urinary *E. coli* infection.
- Adding a normal renal US finding decreased this probability to 1%.

- However, in the presence of non-*E. coli* bacteria, the probability of high-grade VUR was 26%,
- and adding an abnormal US finding increased further this probability to 55%.

Pauchard JY et al. , Arch Dis Child 2017

FURTHER EVALUATION – **Renal cortical scintigraphy**

- Renal cortical scintigraphy (with Tc99m-dimercaptocuccinic acid [DMSA]) may be used to identify renal scarring and acute changes due to pyelonephritis.

- It is not generally helpful in the acute setting but may be obtained as part of follow-up evaluation, particularly if renal damage is suggested by ultrasonography.

- Although computed tomography also can identify these findings, it is not suggested for routine use, because of the exposure to radiation

Treatment

- IV broad-spectrum antimicrobial agents should be initiated as soon as cultures of urine, blood, and cerebrospinal fluid (if indicated) have been obtained.
- The effectiveness of antimicrobial therapy for pediatric UTIs is demonstrated by the change in mortality between the pre- and post-antibiotic eras.
- The mortality of UTI was as high as **20 %** in the pre-antibiotic era. In contrast, when UTIs are appropriately treated with antibiotics, acute complications (eg, renal abscess, death) are uncommon.

Treatment

- Initial (Emperical)
- Specific

Treatment – **Empiric initial**

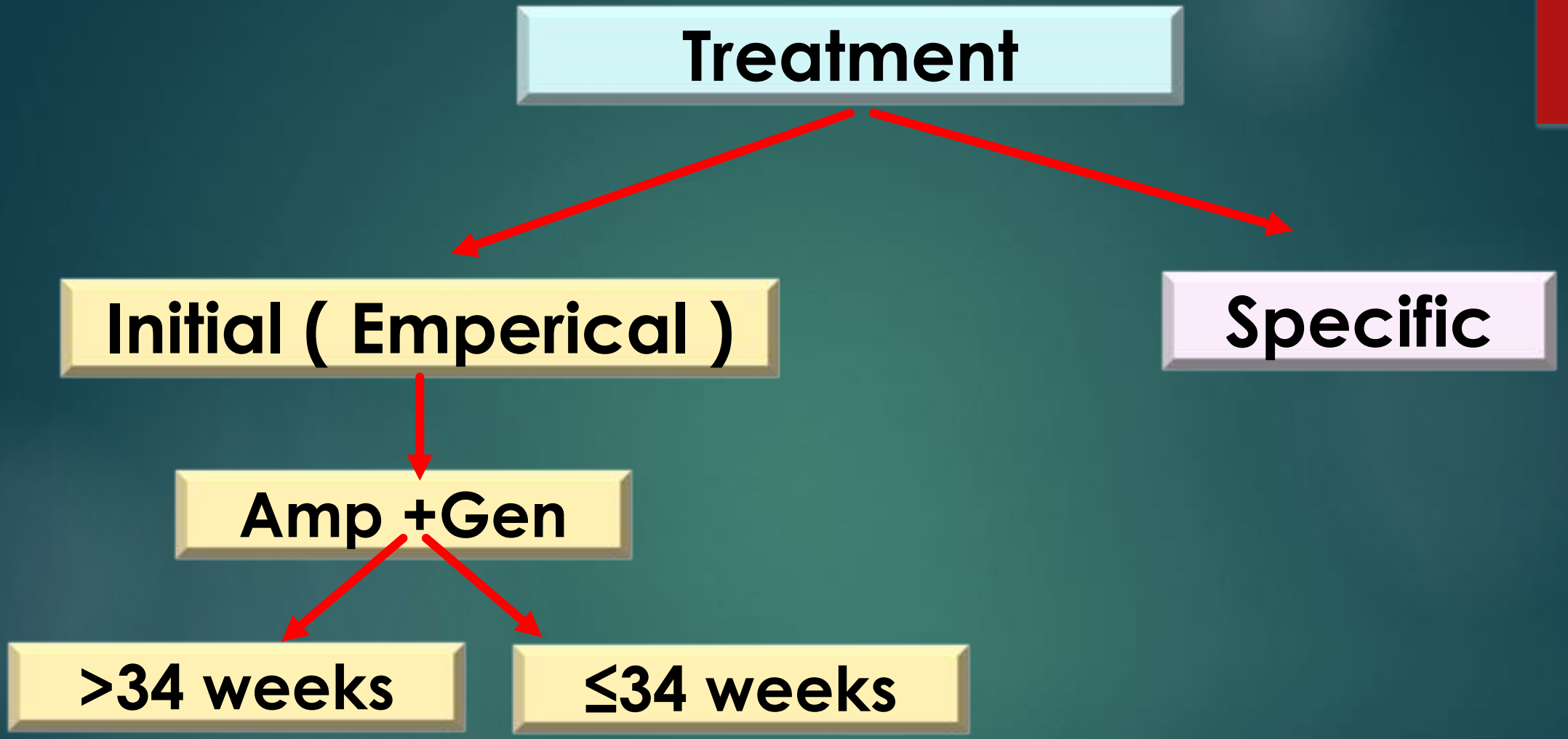
- The choice and dosing of empiric antibiotic therapy is generally the same as for the treatment of **neonatal sepsis.**

- This is because the causative agents are similar in neonatal sepsis and UTI, it is difficult to differentiate between the two based on presentation, and there is risk of concurrent infection

Treatment – **Empiric initial**

The combination of parenteral **ampicillin and gentamicin** provides coverage for the most common bacterial pathogens.

Doses are dependent on the weight and chronologic age of the infant:


Treatment
Initial (Emperical)
Specific
Amp +Gen
>34 weeks
≤34 weeks

Treatment – **Empiric initial**

- **Gestational age >34 weeks**:

Ampicillin :

≤7 days old : 50 mg/kg per dose IV every 8

>7 days old : 50 mg/kg per dose IV every 6 hours.

- Gentamicin :

≤7 days old : 4 mg/kg per dose IV every 24 hours

>7 days old : 5 mg/kg per dose IV every 24 hours.

Treatment – **Empiric initial**

Gestational age ≤34 weeks:

Ampicillin :

≤7 days old : 50 mg/kg per dose IV every 12 hours

>7 days old with community-acquired UTI: 50 mg/kg per dose IV every 8 hours.

However, most late UTIs in low birth weight neonates are hospital acquired and vancomycin is suggested rather than ampicillin in this setting

Treatment – **Empiric initial**

Gestational age ≤34 weeks:

Gentamicin –**30 to 34 weeks gestation**

≤14 days old : 5 mg/kg per dose IV every 36 hours

>14 days old: 5 mg/kg per dose IV every 24 hours.

For neonates **<30 weeks gestation**

≤14 days old :5 mg/kg per dose IV every 48 hours

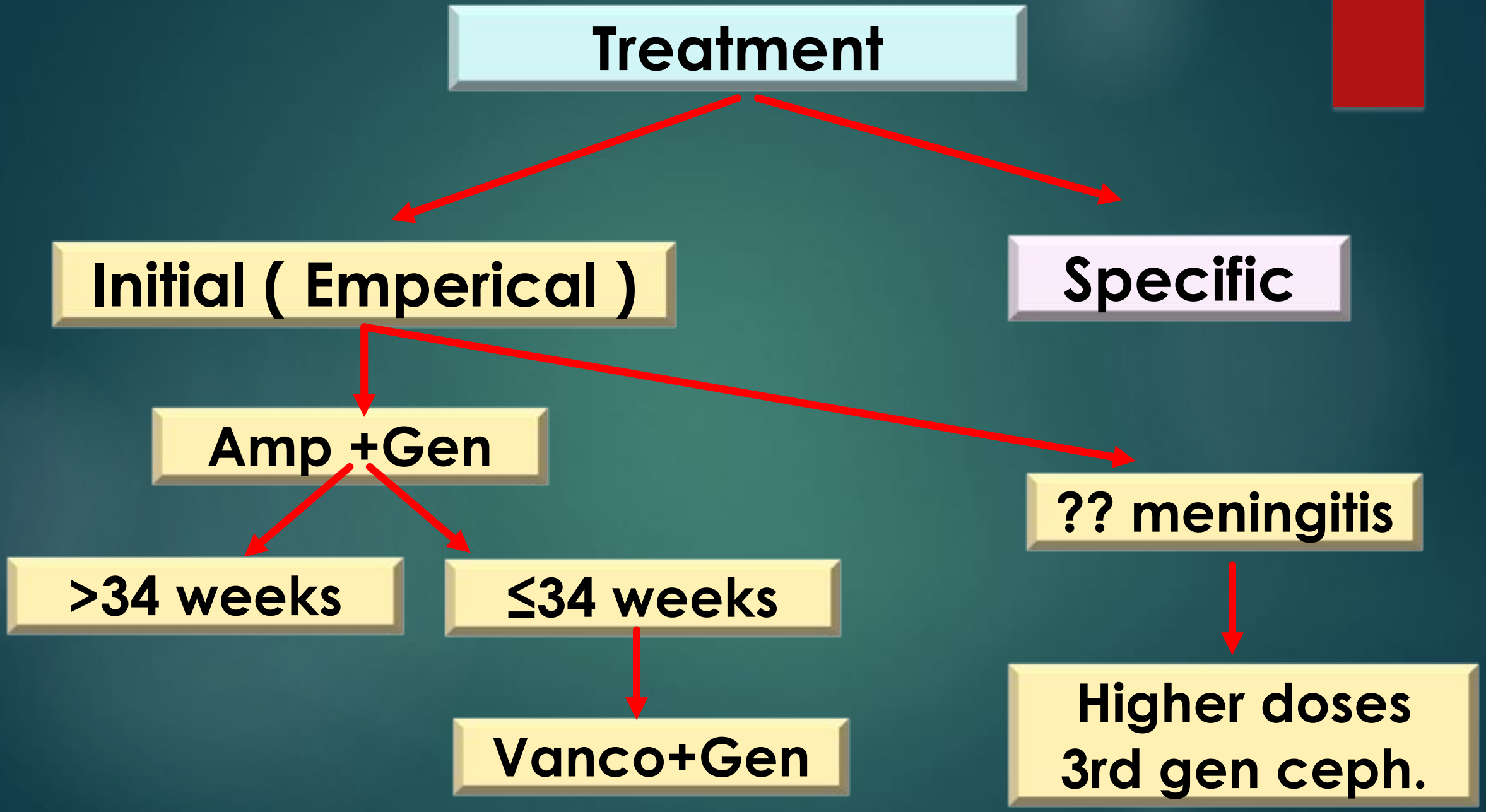
>14 days old :5 mg/kg per dose IV every 36 hours.

Treatment – **Empiric initial**

- For hospital-acquired infections, vancomycin is substituted for ampicillin since the predominant organisms include coagulase-negative staphylococci, S. aureus, and Enterococcus species.

- If meningitis is also suspected, higher doses of antibiotics must be used. In infants >7 days old, a third-generation cephalosporin is added, pending culture results

Kimberlin DW et al,. American Academy of Pediatrics, 2021


Treatment
Initial (Emperical)
Specific
Amp +Gen
?? meningitis
>34 weeks
≤34 weeks
Vanco+Gen
Higher doses
3rd gen ceph.

Treatment – **Organism-specific therapy**

Antimicrobial therapy is altered based upon the isolation of a pathogen, its pattern of antimicrobial susceptibility, and if there are concurrent infections (eg, sepsis or meningitis).

Treatment – **Duration of therapy**

- Usually the duration of antibiotic therapy is **10 to 14 days** for neonates with **uncomplicated bacterial UTI** (ie, susceptible E. coli isolate in a patient with a normal renal ultrasound).

- Usually it is better to complete the treatment course in neonates with a course of IV antibiotics, although older infants with uncomplicated UTIs can be switched to oral antibiotics after clinical improvement based on the judgement of the clinician.

Treatment – **Duration of therapy**

- If the radiologic procedure is delayed, some centers prescribe , antibiotic prophylaxis with low-dose, orally administered **amoxicillin (15 to 20 mg/kg per day)** is started until radiographic evaluation has been performed to for urinary tract abnormalities.

- Continuation of this prophylaxis depends upon the results of imaging studies

OUTCOME

- Infants who have had UTI during the neonatal period are at risk for developing renal parenchymal scarring .
- The risk is increased among patients with vesicoureteral reflux (VUR).

- Renal parenchymal scarring is associated with an increased risk for hypertension and chronic kidney disease.
- Long term follow up is recommended and false reassurance should not be provided carelessly to the parents

Take Home messages :

Remember well the non traditional presentation of neonatal UTI :

- in any prolonged jaundice
- In Febrile neonate without symptoms
- In failure to gain weight

Take Home messages :

- Urine sampling should be done carefully using perineal cleaning and the least invasive but still accurate methods
- Neonatal UTI is mainly PN and should be addressed promptly
- Duration and route of antibiotics is important
- Check for comorbidities (bacteremia, meningitis)

- VCUG should be done in abnormal ultrasound , non E coli pathogens and repeated UTI
- Long term follow up is mandatory

Thanks

1) Choose the most correct answer:

a) Preterms present mainly by UTI through ascending infections
b) Full term babies show klebsiella as the main pathogen except if they have VUR where the organism is mainly CONS
c) LE and nitrite can be falsely negative in neonates and shouldn't cancel the possibility of UTI
d) None of the above

2) Choose the most correct answer:

a) UTI is diagnosed only if colony count is more than 50.000 CFU/ml in SPA
b) The AAP highly encourages clean catch urine for diagnosis of UTI to start antibiotics
c) Antibiotics should continue for at least 5 to 7 days in neonatal UTI
d) NICE recommendations suggest to collect urine with clean catch urine when possible

3) Choose the most correct answer:

a) Direct jaundice could be the presenting signs of UTI especially if developing after the 8th day
b) Apnea can be caused by a UTI in a preterm
c) VCUG is done if non E- coli pathogen is diagnosed in neonatal UTI
d) All of the above

Take Home messages :

Diagnosis

Diagnosis of UTI is based upon a positive urine culture from a specimen of urine that is either collected by bladder catheterization or SPA.

Clean voided" bag urine samples ***should not*** be used for culture, as there is a high rate of false-positive results. Despite efforts to improve the ability to obtain a midstream clean catch specimen in neonates , it remains an impractical and unreliable technique as there remains a high rate of contamination.

Donough J O'Donovan, uptodate 2022

Diagnosis

Urine specimens should be transported on ice and must be processed

expeditiously to avoid further growth of organisms in the urine specimen. If the

DIFFERENTIAL DIAGNOSIS

specimen cannot be processed quickly, it should be refrigerated.

Diagnosis

Bladder catheterization is a reliable method for detection of UTI in neonates.

Specimen contamination is more likely with bladder catheterization than with SPA; however, this can be mitigated by discarding the initial stream and culturing the subsequent urine stream during catheterization.

Many practitioners and parents also prefer bladder catheterization because they view SPA as much more invasive and painful.

Diagnosis

SPA

Any growth of a urinary pathogen is significant.

SPA of the bladder urine is the most reliable technique to identify bacteriuria; however, it is rarely necessary

Urine sampling (UK NICE)

1) **Clean catch urine (CCU)** sampling is the recommended methodology

2) If CCU is unobtainable, then other **non-invasive** methods such as a urine collection pad (but not gauze, cotton wool or sanitary towels) should be used.

3) Where it "is not possible or practical" to collect urine non-invasively then **catheter sampling or suprapubic aspiration (SPA)** should be used.

4) If SPA is used, then an ultrasound should be performed first to confirm urine in the bladder.

NICE (2007) Urinary tract infection in under 16s: diagnosis and management

Urine sampling : The American Academy of Paediatrics (AAP)

- for diagnosis of UTI if **antibiotics are to be given**, then the "specimen needs to be obtained through
  - *Catheterization or SPA*

- because the diagnosis of UTI cannot be established reliably through culture of urine collected in a bag."

Urinary tract infection: clinical practice guideline for the diagnosis andmanagement of the initial UTI in febrile infants and children 2 to 24 months. Pediatrics 128:595–610

Urine sampling : The American Academy of Paediatrics (AAP)

If immediate antibiotics are not required, then there are two options:

1) Either "to obtain a urine specimen through catheterization or SPA

- for culture and
- urinalysis"

Or

2) "to obtain a urine specimen through the most convenient means and to perform a urinalysis."

Urinary tract infection: clinical practice guideline for the diagnosis andmanagement of the initial UTI in febrile infants and children 2 to 24 months. Pediatrics 128:595–610

Urine sampling : The American Academy of Paediatrics (AAP)

If the urinalysis results suggest a UTI (positive leucocyte esterase or nitrite test or microscopic analysis positive for leucocytes or bacteria), then

a urine specimen should be obtained through catheterization

or SPA and cultured.

They do not recommend clean catch, pad or bag sampling.

Urinary tract infection: clinical practice guideline for the diagnosis andmanagement of the initial UTI in febrile infants and children 2 to 24 months. Pediatrics 128:595–610

Urine sampling (other countries)

Other international guidelines from

- Australia,
- Canada,
- The European Society for Paediatric Urology,
- Italy
- New Zealand

Well children :

use of bag sampling :

if dipstick from bag samples suggestive of infection >> alternate method of collection required (clean catch, catheter or SPA)

Unwell children, : catheter or SPA sampling is recommended

Diviney & Jaswon, Pediatric Nephrology (2021)

Methods of Collection : Clean Catch Urine (CCU)

Clean catch urine (CCU) samples are obtained by holding a sterile container beneath the urethra with the nappy off, until a void begins, with care taken to avoid any skin contact with the specimen container.

Voiding can be stimulated as described later

Methods of Collection : Clean Catch Urine (CCU)

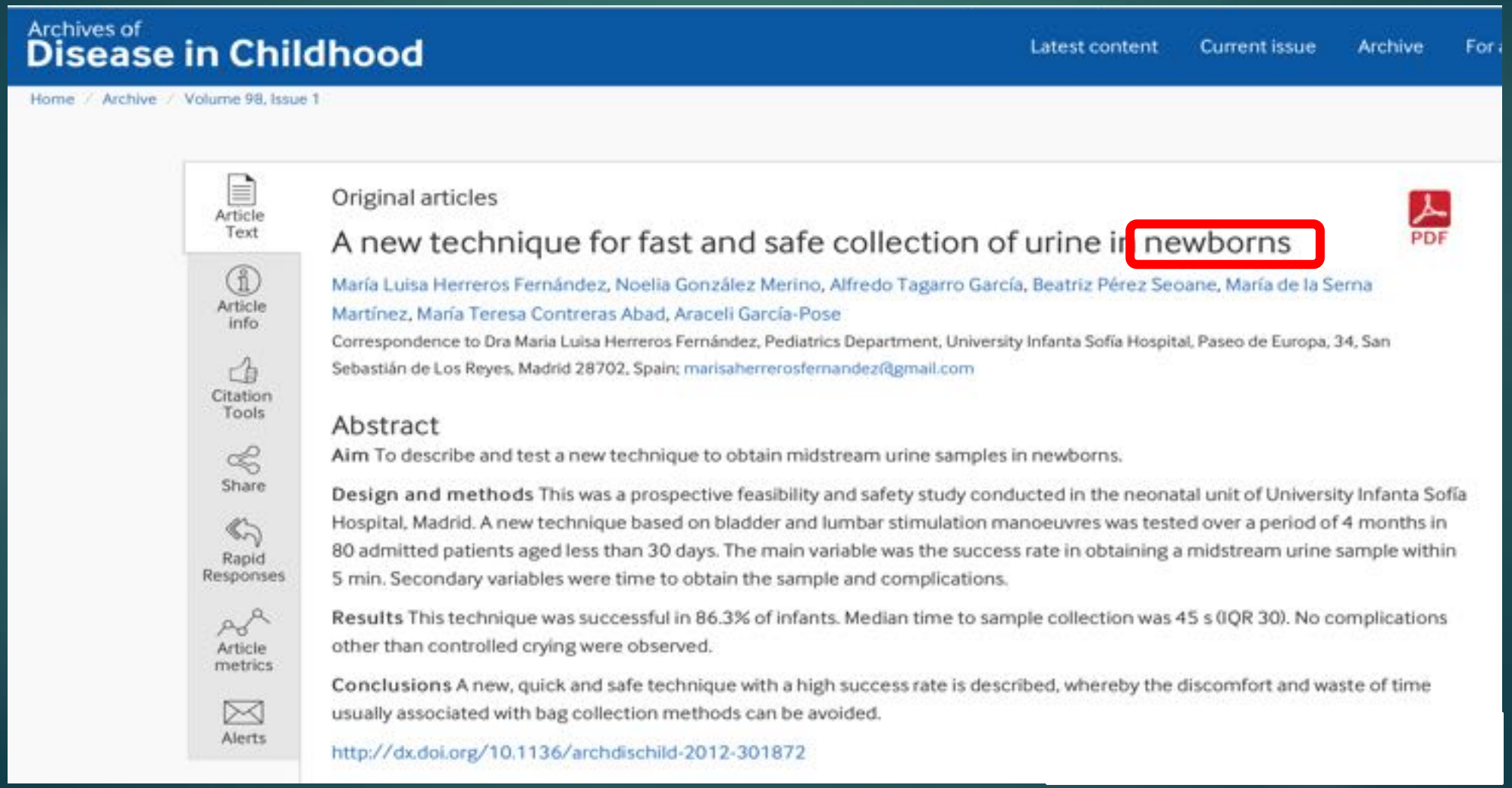
NICE recommends clean catch sampling and SPA as the most diagnostically accurate sampling methods

clean catch compares well to catheter sampling with a contamination rate of 5%, compared with 8% for catheter samples

A randomised trial of cleaning with soap vs. not cleaning in 350 patients found significantly lower contamination rates in the cleaning group (7.8%) vs. the non-cleaning group (23.9%).

Vaillancourt S et al , Pediatrics (2007)

Methods of Collection : Clean Catch Urine (CCU)



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A new technique for fast and safe collection of urine in newborns

PDF

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Abstract

Aim To describe and test a new technique to obtain midstream urine samples in newborns.

Design and methods This was a prospective feasibility and safety study conducted in the neonatal unit of University Infanta Sofía Hospital, Madrid. A new technique based on bladder and lumbar stimulation manoeuvres was tested over a period of 4 months in 80 admitted patients aged less than 30 days. The main variable was the success rate in obtaining a midstream urine sample within 5 min. Secondary variables were time to obtain the sample and complications.

Results This technique was successful in 86.3% of infants. Median time to sample collection was 45 s (IQR 30). No complications other than controlled crying were observed.

Conclusions A new, quick and safe technique with a high success rate is described, whereby the discomfort and waste of time usually associated with bag collection methods can be avoided.

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-

Methods of Collection : Clean Catch Urine (CCU)

- A recent prospective cohort study examined a noninvasive alternating lumbar-bladder tapping method to stimulate voiding in infants ages 0 to 6 months.[7] Within 5 minutes, 49% of the infants provided a clean-catch sample, with contamination rates similar to those of samples obtained using invasive methods.[7]Younger infants were more likely to void within the time all

Labrosse M, et al. Evaluation of a new strategy for clean-catch urine in infants. Pediatrics.2016