# Addressing Confusions IN URINARY TRACT INFECTION

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# CLINICAL SCENARIO

2 y/o girl was brought for consultation cause of 4 days fever (39.80, associated th chills and vomiting). On examination, she pears dehydrated and has no identifiable urce of fever.

boratory results:

### inalysis:

PMN 6 hpf RBC 0-4/ hpf Bacteria- 2/hpf Specific gravity: 1.030

### **Urine dipstick**

(+) leucocyte esterase

(-) nitrite

Urine culture 48 hrs: 50,000 cfu of E. Coli

**IMPORTANT** details:

1) AGE : 2 y/o

2) 4 days fever and chills and vomiting

3) pmn: 6 /hpf : rbc: 0-4

specific grav: 1.03

6) (+) leucocyte esterase

(-) nitrite test

7) urine culture and sensitivity: 50,0000 cfu

# Why confusion?

• FEVER

- VOMITING
- CHILLS

NON specific signs and symptoms

### URINALYSIS SUSPICOUS RESULTS

- PMN 6 hpf
  - RBC 0-4/ hpf
  - Bacteria- 2/hpf
  - Specific gravity: 1.030



### URINE CULTURE OF 50,000 CFU

### **PRESIDENTIAL CONFUSIONS**



## AREAS of CONFUSION in UTI

AGE: when to be more aggressive Symptomatology: is it UTI? Interpretation of results How to Diagnose? Treatment: DRUG of choice ROUTE of CHOICE FOR HOW LONG?



Other Diagnostic tests: HOW FAR should we go Why is it important to treat UTI

## **AREAS of CONFUSION in UTI**

AGE: when to be more aggressive

Symptomatology: is it UTI?

Interpretation of results

Treatment: DRUG of choice ROUTE of CHOICE FOR HOW LONG?

Other Diagnostic tests: HOW FAR should we go

• AGE : our patient is a 2y/o

**Recommendation:** 

In any child with fever with no clear focus in a child = or < 2 : UTI should be considered

AAP (2011) PNSP (2015)

## AGE

- Initially cut off is 5 but it was lowered to 2 because of the ability of the child to VERBALIZE the complaint
- Any complaint referable to the Urinary Tract like dribbling, frequency, dysuria, flank pain→ very high index of suspicion for UTI
- FEVER and CHILLS  $\rightarrow$  UTI
- FEVER and smelly urine  $\rightarrow$  UTI



## Clinical Manifestations of UTI (NICE guidelines)

Presenting symptoms and signs in infants and children with UTI

Age group Infants younger than 3 months		Symptoms and signs Most common		Least common	
		Fever Vomiting Lethargy Irritability	Poor feeding Failure to thrive	Abdominal pain Jaundice Haematuria Offensive urine	
Infants and children 3 months or older	Preverbal	Fever	Abdominal pain Loin tenderness Vomiting Poor feeding	Lethargy Irritability Haematuria Offensive urine Failure to thrive	
	Verbal	Frequency Dysuria	Dysfunctional voiding Changes to continence Abdominal pain Loin tenderness	Fever Malaise Vomiting Haematuria Offensive urine Cloudy urine	

# Clinical Manifestations & Classification

#### BACTERURIA **PYELONEPHRITIS CYSTITIS** • [+] urine culture abdominal pain without manifestations bladder involvement of infection flank pain • dysuria most common- girls fever urgency incidence malaise frequency 1-2 % - pre-school & suprapubic pain nausea school girls vomiting incontinence diarrhea malodorous urine 0.03%- boys Newborn – poor no fever benign feeding, irritability, does not cause renal does not result in weight loss injury except in renal injury pregnant women complication : renal take detailed history abscess [day/night incontinence or perineal discomfort]

## **AREAS of CONFUSION in UTI**

AGE: when to be more<sup>2</sup> aggressive Symptomatology: is it UTI?

Interpretation of results

How to Diagnose?

Treatment: DRUG of choice ROUTE of CHOICE FOR HOW LONG?



Other Diagnostic tests: HOW FAR should we go Why is it important to treat UTI

# SYMPTOMOLOGY .... When to think of UTI?



- All infants and children =/< 2 yrs with unexplained fever =/> 38.5 C
- Infants and children with alternate sites of infection who remain unwell
- Infants and children with symptoms and signs suggestive of UTI
- AAP and IAP recommendation 2011
- Pediatric Nephrology on the Go 2015

Courtesy of: Kanitkar 2015 PNSP Convention

## **AREAS of CONFUSION in UTI**

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How to Diagnose?

Treatment: DRUG of choice ROUTE of CHOICE FOR HOW LONG?



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# Interpretation of results

## **Urine dipstick**

(+) leucocyte esterase(-) nitrite



### **Urine dipstick**

(+) leucocyte esterase(-) nitrite

## Can we use Dipstick for diagnosing U

Gram staining of urine has good Sensitivity and specificity





Useful for screening in office practice, equivalent to a microscop Good supportive evidence in case of low bacterial counts in U

Sensitivity & Specificity of rapid urine tests.Pediatric Nephrology 2011\*Low urinary bacterial count, do they count?Pediatric Nephrology 2015

Courtesy of: Kanitkar 2015 PNSP Convention



alysis Interpretation Using the Dipstick Method (refer to Figure 1)

 If both nitrite and leukocyte esterase are positive on urinary dipstick (sensitivity 45%; specificity 98%), the child should be regarded as having UTI, urine specimen should be sent for culture and antibiotic treatment should be started. (Level 1c) If nitrite is positive and leukocyte esterase is negative [sensitivity 49% (range 41-57%); specificity 98% (range 96-99%)], urine specimen should be sent for culture and antibiotic treatment should be started. (Level 1c)



 If nitrite is negative and leukocyte esterase is positive (sensitivity 79%; specificity 87%), urine sample should be sent for microscopy and culture. Antibiotic treatment for UTI should be started only if there is good clinical evidence of UTI. (Level 1c)



 If both leukocyte esterase and nitrite are negative, the child should not be regarded as having UTI. Antibiotic treatment for UTI should not be started, and a urine sample should not be sent for culture. Other causes of illness should be explored. (Level 1c)



# Interpretation of results

## **Urinalysis:**

PMN 6 hpf RBC 0-4/ hpf Bacteria- 2/hpf Specific gravity: 1.030

- = HMMMM..
  - PMN of 6/hpf
  - RBC 0-4/hpf
  - High specific gravity

## URINALYSIS:

- Pus cells of greater than
   5 of centrifuged sample is considered significant
- (+) symptomatology→UTI

# agnosing UTI by Urinalysis Interpretation **rine Microscopy**

	Pyuria (+)*	Pyuria (-)
cteriuria (+)	Send for urine CS Treat as UTI Start antibiotics	Send for urine CS Treat as UTI Start antibiotics
cteriuria (-)	Send for urine CS Start antibiotics if with symptoms	Not UTI
end:		NICE guidelines 2007

vuria (+) – WBC >5/HPF in centrifuged urine

- WBC >10/uL in uncentrifuged

	Sensitivity	Specificity
ram stained bacteria	91% (95% CI 80–96)	96% (92–98),
nstained bacteria	88% (75–94)	92% (84–96),
rine white cells	74% (67–80)	86% (82–90),
ucocyte esterase or nitrite positive	88% (82–91)	79% (69–87),
pstick		
trite-only positive dipstick	49% (41-57)	98% (96–99)
ukocyte only positive dipstick	79%	87%
oth leukocyte esterase and nitrite	45%	98%
	ODDS ratio	
icroscopy for bacteria with gram stain compare with bacteria without Gram ain	8 ·7 (95% CI 1 ·8–41 ·1)	
icroscopy for bacteria with gram stain compare with white cells	14.5 (4.7–44.4),	
icroscopy for bacteria with gram stain compare with nitrite	22.0 (0.7-746.3).	
Williams et al, 2010. Absolute and	relative accuracy of rap	id urine tests

for UTI in children: a meta-analysis 95 studies with 95,703 children

# Position Statement 4: Urinalysis Interpretation

Urinalysis findings positive for nitrites, leukocyte esterase, pyuria or bacteriuria may suggest urinary tract infection in children

## Which guideline to follow?



## **PNSP Consensus of UTI 2016**

- A Philippine stand on UTI
- Reviewed all pertinent literature
- Considered local practice and circumstances
- Incorporated all local available searchable data and other national concensus in the world
- SOON to come ,,,
- This is just a preview...



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**IMPORTANT** details:

1) AGE : 2 y/o

2) 4 days fever and chills and vomiting

3) dehydrated

5) 6 /hpf : PMN,specific grav: 1.03

6) (+) leucocyte esterase

7) urine culture and sensitivity: 50,0000 cfu

## Interpretation of Urine Culture is based on Manner of Collection



BAG vs Cathether: **4 to 5x** more likely to have unnecessary treatment and radiological investigation **12x** more likely to have unnecessary hospitalization **PNSP** Consensus on the Definition of Urinary Tract Infection

- Acute pyelonephritis is to be defined as:
- Clinical symptomatology and urinalysis findings\* referable to UTI and Jrine culture which is either:
  - Any growth of a single uropathogen collected via suprapubic aspiration

  - Growth of ≥ 100,000 single uropathogen collected via midstream/clean catch
- Recommended Approach: If the above criteria are met
  - Request for a Kidney Urinary Bladder (KUB) ultrasound and
  - If KUB ultrasound is abnormal, REFER to a pediatric nephrologist for further work up



## To diagnose UTI-Use Gold Standard Culture a must!!!

- Culture of urine required
  - Plate within hour/refrigerate 4°C upto 24 h
- Method of collection important
  - clean catch midstream
  - catheterization
  - suprapubic aspiration
  - bag??

### How can we make a diagnosis in office quickly?



Courtesy of: Kanitkar 2015 PNSP Convention



# FOR CONFUSING UTI? Are there other ways?

DIAGNOSIS

CLINICALDMSA?BLOOD TESTS?



## DMSA

- How does a scan in acute infection help?
  - It is sensitive and specific for the diagnosis of acute pyelonephritis
  - Can differentiate cystitis and pyelonephritis
  - Helps in the need of the VCUG to diagnose VUR

The reality It is expensive :				
	SLMC	ТМС	MMC	Cardina
	6,995	5.965	6,300	7,437

- Requires infrastructure that is i found anywhere
- It requires a still child → or else needs an anesthesiologist to se
- May delay treatment
- Radiation
- Can not always differentiate between acute pyelonephritis a old scar









Normal kidney

Acute PNA

Renal scars

F

# Position Statement 5: Serum Markers

Acute Phase Reactants such as C-reactive protein, Erythrocyte Sedimentation Rate and White Blood Cell count are non-specific but may help in the diagnosis of Urinary Tract Infection.

Procalcitonin promises to be a stronger predictor in the diagnosis of Acute Pyelonephritis

## BLOOD TEST Clinical and Laboratory test that may aid in the diagnosis of UTI

		Sensitivity	Specificity	
Neutrophil		50%(41.94-58.08	70.45% (63.1-	77.81)
White Blood Cell count		50%(41.94-58.08)	70.93%(63.61	-78.25)
Absolute Neutrophil Count		59.26%(51.32-67.3)	75.27%(68.29	-82.24)
C Reactive Protien		49.32%(41.26-57-37)	73.33%(66.21	-80.46)
Procalcitonin		100%	100%	

Acta Pediatrica 2014 103 pp e404-e409

# What is procalcitonin?

### Procalcitonin- A marker for APN?



- Only 6 studies for PCT
- Heterogeneity of studies
- Focussed on a cut off of 0.5ng/ml
- Studies with higher cut-offs had higher specificity
- NO CONCLUSIVE RECOMMENDATIONS



- It is a precursor of calcitonin without hormonal activity
- Virtually undetectable in physiological conditions
- Rises quickly and in proportion to bacterial infection and not viral
- Elevation from 2h after the onset of infection peaks at 12h and normalizes with in 2-3 days when subsides
- Cochrane focused on a cut off 0.5 ng/ml
- High cut offs had higher specificity
- NO CONCLUSIVE RECOMMENDATIONS
- The Cochrane Collaboration published in *The Cochrane Library*2015, Issue 1

## Role of PCT



- PCT is not meant to replace DMSA scan
- PCT can be used as an intermediate strategy since
  - Based on a single biomarker
  - Easier to set up than a nuclear imaging process
  - Can help discriminate between cystitis and APN
  - Useful to predict scars when DMSA not available
- PCT may therefore be helpful when choosing between oral or intravenous antibiotic treatments

ТМС	SLMC	MMC
4200	3605	2000

## **AREAS of CONFUSION in UTI**

AGE: when to be more aggressive Symptomatology: is it UTI? Interpretation of results How to Diagnose? Treatment Route of Choice FOR HOW LONG? Drug of Choice



Other Diagnostic tests: HOW FAR should we go Why is it important to treat UTI

# Treatment

- Goals of Treatment:
- •Elimination of infection and prevention of urosepsis
- •Relief of acute symptoms (eg, fever, dysuria, frequency)
- •Prevention of recurrence and longterm complications including hypertension, renal scarring, and impaired renal growth and function



## Treatment



Early and aggressive antibiotic therapy  $\rightarrow$  (within 72 hours of presentation) is necessary to prevent renal damage.

Delayed therapy:

- 1) increased severity of infection
- greater likelihood of upper tract disease
- 3) Higher risk of renal damage

Fernandez PN 2003 18:115

# TREATMENTS

- Empiric antimicrobial therapy  $\rightarrow$  initiated immediately **after** appropriate <u>urine collection in children</u> with suspected UTI and a positive urinalysis).
- HIGH INDEX of suspicion on the following subsets of patient:  $\rightarrow$  increased risk for renal scarring if UTI is not promptly treated
- Fever (especially >39°C [102.2°F] or >48 hours)
- III appearance
- Costovertebral angle tenderness
- Known immune deficiency
- Known urologic abnormality



# Antibiotics

oral

- Children older than 2 mos can be effectively treated
- Close contact with family
- Infants less than 2 mos
- immunocompromised
- Poor oral intake
- Organism with resistant to oral antibiotic
- Atypical or complicated UTI
  - Atypical means: seriously ill, poor urine flow, abdominal or bladder mass, raised creatinine. Septicimia, failure to respond to treatment within 48 hours or infection with Non-E coli organism, dilatation of the PCS on US

# Choice of Agent : based on Etiology

- Escherichia coli most common→ 80% of UTI in children
- Gram-negative bacterial pathogens
  - Klebsiella
  - Proteus
  - Enterobacter
  - Cittrobacter

Gram positive bacterial pathogens:

- Gram-positive bacterial pathogen
- Staphylococcus saprophyticus
- Enterococcus
- Staphylococcus aureus.



- Infection with an organism other than E. coli is associated with a higher likelihood of renal scarring.
- Viral UTI are usually limited to the lower urinary tract.
- Risk factors for fungal UTI include immunosuppression and long-term use of broad-spectrum antibiotic therapy, and indwelling urinary catheter

# Based the treatment on the sensitivity of the community→guided by Resistance Pattern

**RESEARCH** base Recommendation:

A. Children greater than 2 mos: orally can be given as long contact with family and education is very important

Suggestion: Cefixime for 14 days is equal to cefotaxime for days then shifted to oral based on: mean time of deferves (24 hrs), sterilization of urine (100%), reinfection rate and r scarring (9.8 and 7.2%) (RCT 3306 children)

Cefixime, cefdinir, and ceftibuten are dosed as follows:

 <u>Cefixime</u> (16 mg/kg by mouth on the first day, followed by mg/kg once daily to complete therapy)

- •<u>Cefdinir</u> (14 mg/kg by mouth once daily)
- •<u>Ceftibuten</u> (9 mg/kg by mouth once daily)



<u>Amoxicillin</u> and <u>Ampicillin</u> are not routinely recommended f empiric therapy  $-\rightarrow$  High rate of resistance of *E. coli*.

Similarly, <u>amoxicillin-clavulanate</u>, first-generation cephalos (eg, <u>cephalexin</u>), and TMP-SMX should be used with caution because of the increasing rates of resistance to these drug some communities

### Ciprofloxacin:

- NOT routinely used as 1<sup>st</sup> line
- used for Pseudomonas or Multidurg resistant

## Nalidixic and Nitrofurantoin:

- oral agents that are excreted in the urine but do not achie therapeutic concentrations
- Should NOT be used in febrile UTI in whom renal involve likely because parenchymal and serum concentrations is insufficient to treat UROSEPSIS and PYELONEPHRITIS



## DURATION OF TREATMENT

### NO ROLE FOR SHORT COURSE IN CHILDREN with Upper UTI

(AAP, COCHRANE DATA BASE)

### Role of Short course only on Lower UTI

- 10-14 DAYS
- 10 DAYS

COMPLICATED Upper UTI UNCOMPLICATED Upper UTI

3-7 DAYS

Lower UTI

PERSISTENT BACTERIURIA NOTED IN:

24%  $\rightarrow$  short course

 $1\% \rightarrow$  if 10 day course

 Serial cultures not required if clinical improvement is noted with in 2-3 days

gerald: hrane

abase Syst Published uary 1, 2012. ume 8, Issue ; jes 006857



# Other considerations...



# When to do KUB?

- Children younger than 2 years of age with first febrile UTI
- Children of any age with recurrent febrile UTI
- Children of any age wit a UTI with a family history of renal or urologic disease, poor growth or hypertension
- Those who do not respond to the initial antibiotics

- Timing:
- IF unusually severe illness or failure to improve as expected after initiation of antimicrobial therapy
- → do it in the acute phase of illness
- If response is favorable → may do it after the acute phase to reduce risk of fase positive due to renal inflammation

# VCUG

- Children of any age with 2 or more febrile UTI
- Child of any age with first febrile UTI and any anomalies on renal ultrasound
- High temp of 39 and a pathogen other than E. Coli
- Poor growth and hypertension





# CIRCUMCISION

umcised penis Circumcised penis Glans

Uncircumcised male infants  $\rightarrow$  4-8X higher prevalence of UTI

Two mechanisms:

 The mucosal surface of the uncircumcised foreskin→binds uropathogenic bacterial species than keratinized skin on a circumcised penis

•Partial obstruction of the urethral meatus 85 versus 42% The tightness of the foreskin diminishes with time and is an infrequent finding after one year of age

111 circumcisions would be needed to prevent one UTI

FOR MEDICAL EDUCATION AND RESEARCH. ALL RIGHTS RESERVED.

# **lenal Scarring**

- Seen in 15.5% of children with UTI
- **/UR** VUR, especially high-grade VUR, was associated with the velopment of renal scars (Grade I and II [odds ratio (OR) = 1.8, % CI 1.2–2.8] and Grade IV and V VUR [OR 22.5, 95% CI 11.3-.8])
- Abnormal **renal bladder ultrasonography** (OR 3.8, 95% CI 2.6-5)
- nflammatory markers including a **high C-reactive protein** of >40 g/L (OR 3.0, 95% CI 2.0-4.6), or a polymorphonuclear cell count 0 percent (OR 1.9, 95% CI 1.3-2.8); only children who have elonephritis are at risk for the development of renal scarring
- **Temperature ≥39°C** (102.2°F) (OR 2.3, 95% CI 1.6-3.3)
- JTI caused by organism **other than** *E. coli* (OR 2.2, 95% CI 1.3-6)



Normal kidney Acute PNA

R



## **Global Burde**

Overall prevalence among febrile infants: 7% Prompt and accurate diagnosis of childhood UTI maybe the only clue in the recognition of urologic abnormalities

Cognizant of the prevalence of UTI in childhood: a meta-analysis (Shaikh, 2008)

### Need to focus on the:

- Diagnosis
- Treatment
  - Urologic work-up

May lead to renal scarring and chronic kidney disease (CKD)

2010 Global Burden of Disease (GBD) CKD ranked 18th

Prevent complications Urologic abnormalities remain as the leading causes of pediatric CKD requiring KT

Simangan, Lorna pps 2015

## Which guideline to follow?



SP is coming up with a concensus that will truly fit the Filipino experience- ready by Nov 2

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ROUTE of CHOICE FOR HOW LONG?



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