The Waze of Childhood Leptospirosis

Outsmarting Leptospirosis Together

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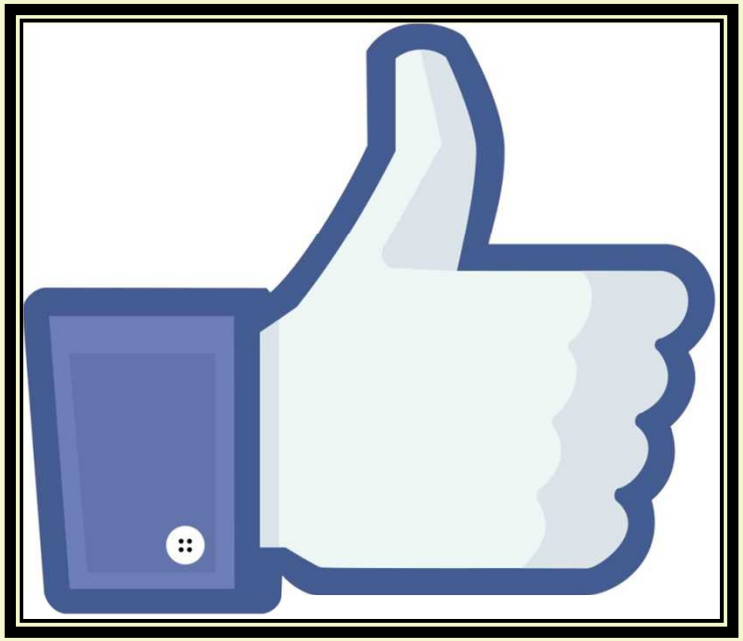
THE CLINICAL PRACTICE GUIDELINES ON CHILDHOOD LEPTOSPIROSIS

CORE GROUP RECOMMENDATION

- Diagnosis
- Treatment
- Prevention



Disclosure of Interest

Medical Affairs Manager

GlaxoSmithKline
Philippines

Leptospirosis is here to STAY!

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OUTBREAKS !

Top Ten Health Stories of the Year 2013

210 cases and 6 deaths in 48 hours

A. Diagnosis

WHO Assessment

Strength of Evidence

- High: further research is very unlikely to change confidence in the estimate of the effect
- Moderate : Further research is likely to have an important impact
- Low: further research is vey likely to have an estimate of effect and likely to change estimate
- Very low: any estimate of effect is uncertain

Strength of Recommendation

- Strong: panel is confident that the desirable effects of adherence to recommendation outweigh the undesirable effects
- Conditional /Weak: desirable effects of adherence to the recommendation probably outweighs the undesirable effect; only applicable to a specific group, or changes the balance of risk, benefits may not warrant the cost or resource
- No recommendation: further research is required

What clinical manifestations should make one suspect leptospirosis in children?

- 98 studies, included only are 5 studies done exclusively on children and 3 studies on adults and children

Top 4 SYMPTOMS found in leptospirosis confirmed patients:
• Fever • Abdominal pain • Myalgia and/or joint pain • headache

Top 3 SIGNS found in leptospirosis confirmed patients:
• calf tenderness • jaundice • hepatomegaly

WHO Criteria for the Diagnosis of Leptospirosis

Faine's Criteria

- Part A : Clinical Data
- Part B: Epidemiologic Factors : Contact with animals or contact with known contaminated water (collectively 10 points)
- Part C: Bacteriologic Factors and Lab findings

Modified Faine's Criteria

- Part A : Clinical Data
- Part B: Epidemiologic Factors : Rainfall, contact with contaminated environment, animal contact (specific scores for each)
- Part C: Bacteriologic Factors and Lab findings

Faines Criteria		Modified Faines Criteria	
Part A : Clinical Data		Part A : Clinical Data	
Question	Score	Question	Score
Headache	2	Headache	2
Fever	2	Fever	2
Temp > 39°C	2	Temp > 39°C	2
Conjunctival suffusion	4	Conjunctival suffusion	4
Meningism	4	Meningism	4
Muscle pain	4	Muscle pain	4
Conjunctival suffusion + Meningism + Muscle pain	10	Conjunctival suffusion + Meningism + Muscle pain	10
Jaundice	1	Jaundice	1
Albuminuria/Nitrogen Retention	2	Albuminuria/Nitrogen Retention	2
Total score		Total score	

Pediatric Locally Modified Criteria:

Muscle pain And Conjunctival Suffusion = 10 points

Presumptive diagnosis = 26 points or more from part A or Part A and B or 25 or more from Part A, B, C

Tests		Validity results	
Combination of Clinical, epidemiologic criteria and serology	Id# /Study title/study type	Sensitivity	Specificity
1) World Health Organization Faine's Criteria	Validation of the World Health Organization Criteria using the Microscopic Agglutination Test (MAT) as the Gold Standard in the Diagnosis of Leptospirosis	33	65
2.)Modified Faine's criteria	Validation of the Modified Faine's Criteria in the Diagnosis of Leptospirosis in Children Using the Microscopic Agglutination Test as the Gold Standard; diagnostic validity	60	73
3.) Pediatric Locally Modified Criteria	Validation of the Modified Faine's Criteria in the Diagnosis of Leptospirosis in Children Using the Microscopic Agglutination Test as the Gold Standard; diagnostic validity	80	73

Diagnostic Tests

- Microscopic agglutination tests (MAT) is the Gold standard test, but it is complicated and less sensitive compared to some rapid diagnostic tests (ELISA and SAT)
  - **The antibody titers rise and peak only in 2nd or 3rd week, making it a less sensitive test.**
  - **The high titers of past infection persist for a long time (1-5 years) and therefore interfere with the diagnosis of current leptospirosis.**
  - **A positive titer may represent a rising titer of current infection or declining titer of past infection.**

Which among the rapid leptospirosis diagnostic tests is/are most useful in establishing the diagnosis of leptospirosis in children?

Test	Sensitivity/Specificity	Remarks
Elisa IgM Test	Sensitivity :98.96%. Specificity : 54-100%	the most studied
Slide agglutination test	Sensitivity: 99% Specificity: 99%	
Lepto Dipstick Test	Sensitivity: 79-80%	
Lepto agglutination test	Sensitivity: 82-89% Specificity: 90-94%	

FYI:Available tests

Diagnostic test	PGH	RITM	St. Lukes	NKTI	TMC
Lepto MAT	PGH MRL Lab (554-8400 loc. 3232) Walk in –P520 ; Charity - P245 Pay – P555	P2800			
Lepto Culture	PGH MRL Lab (554-8400 loc. 3232) Walk in –P775; Charity – P650 Pay – P820	P2800			
Leptospira IgG/IgMTest					780
Rapid test by immunochromatography				1320	
Leptospiral Antigen Test			P1234		

What clinical manifestations should make one suspect leptospirosis in children?

Statement	Recommendation
In patients presenting with fever, abdominal pain, myalgia and/or joint pain, headache associated with calf tenderness, jaundice and hepatomegaly, lepospirosis should be clinically suspected	Moderate evidence; Strong recommendation

Clinical Questions on Diagnosis

Which among the leptospirosis diagnostic tests is most useful in establishing the diagnosis of leptospirosis in children?

CORE GROUP RECOMMENDATION

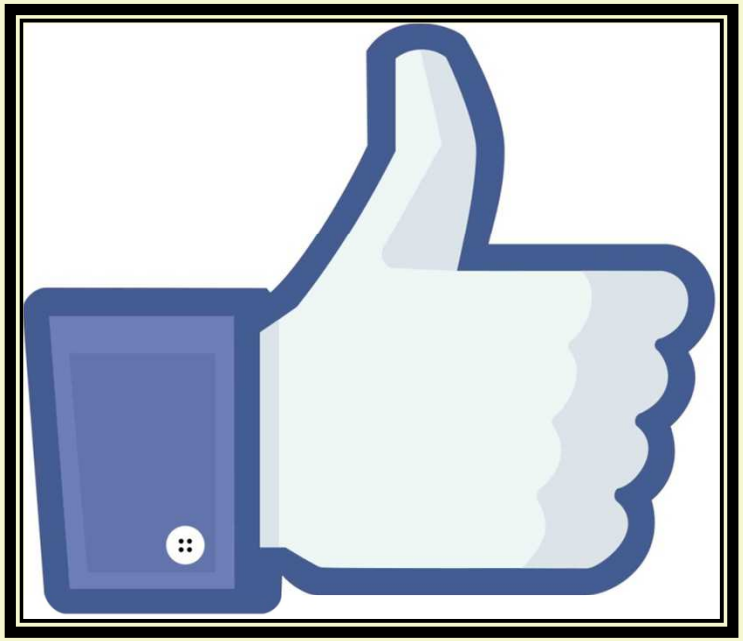
Test	Strength of recommendation
Rapid IgM tests – may be used for early diagnosis (< 1 week; at least 5 days)	Strong evidence; Strong recommendation
MAT – although the gold standard for diagnosis , have a lot of limitations; used for epidemiologic studies/purpose; - Not recommended as a ROUTINE diagnostic test	Strong evidence; Strong recommendation

Clinical Questions on Diagnosis

Which among the leptospirosis diagnostic tests is most useful in establishing the diagnosis of leptospirosis in children?

CORE GROUP RECOMMENDATION

Statement	Recommendation
There is NO need to wait for laboratory test results prior to treatment initiation for clinically suspected leptospirosis	Strong evidence Strong recommendation



In Children with leptospirosis, what are the signs and symptoms predictive of disease severity?

Four studies showed the following to be signs and symptoms predictive of severity/mortality:

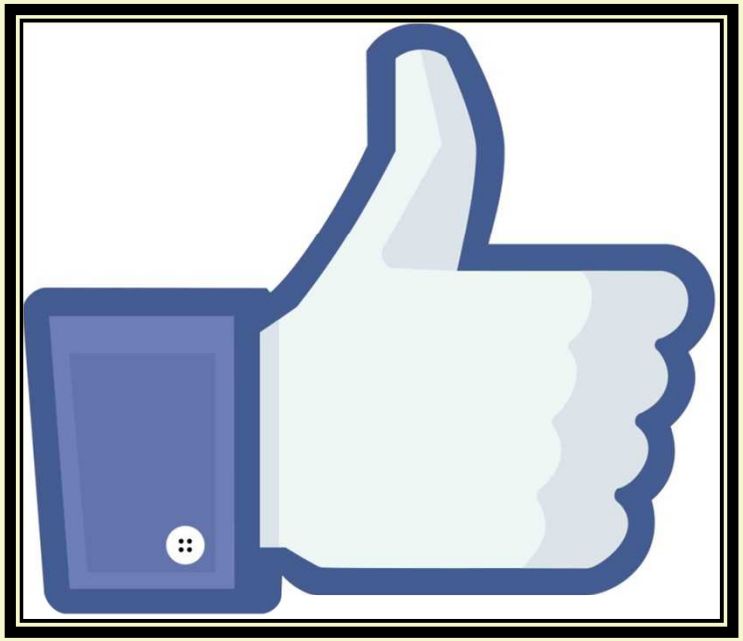
- Pulmonary symptoms
- Shock
- Altered Mental Status
- Signs of Bleeding

What ancillary laboratory tests should be requested in children with leptospirosis to predict possible complications?

Laboratory Tests	Results	Study Title
Platelet Count ≤50,000/µl	OR=6.36 [CI 1.79-22.62]	Risk factors and predictors of severe leptospirosis in New Caledonia
Serum Creatinine >200 Mm	OR=5.86 [CI 1.61-21.27]	
Serum Lactate >2.5 Mm	OR=5.14 [CI 1.57-16.87]	
Serum Amylase >250 UI/L	OR=4.66 [CI 1.39-15.69]	
Leptospiremia >1000 Leptospires/Ml	OR=4.31 [CI 1.17-15.92]	
Serum Potassium (Mmol/L)	OR = 2.6; 95% CI = 1.1-5.9	Early identification of leptospirosis-associated pulmonary hemorrhage syndrome by use of a validated prediction
Serum Creatinine (Micromol/L)	OR=1.2; 95% CI=1.1-1.4	
Haemoglobin Concentrations, Haematocrits, Counts Of Erythrocytes, Leucocytes, Neutrophils And Platelets		Haemotological and clinical-chemistry markers in patients presenting with leptospirosis: a comparison of the findings from uncomplicated cases with those seen in the severe disease
Urea, Protein And Albumin		

What ancillary laboratory tests should be requested in children with leptospirosis to predict possible complications?

	Recommendation
A low platelet count , high serum creatinine , abnormalities in potassium are the more practical/available tests to obtain to predict possible complications	Strong evidence; Strong recommendation



B. Treatment

What antibiotics are recommended for suspected leptospirosis in children?

There are no randomized controlled trials done exclusively in pediatric patients that have studied the efficacy of antibiotics as treatment for leptospirosis.

What antibiotics are recommended for suspected leptospirosis in children?

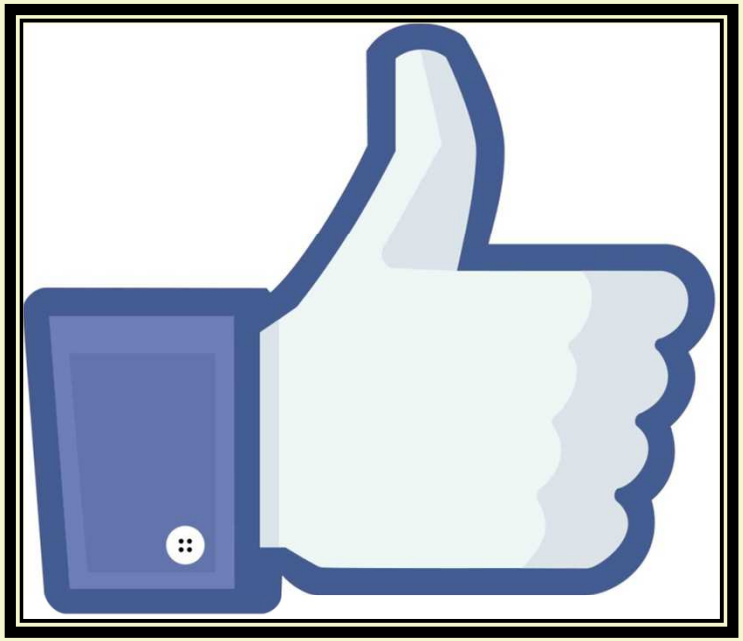
CORE GROUP RECOMMENDATION

	Drug and dose	Strength of recommendation
Uncomplicated Leptospirosis		
1st line	Doxycycline – 2-4 mg/kg/day x 7days Max dose: 200 mg /day	Moderate evidence; strong recommendation
2nd line	Amoxicillin - 50 mg/kg day q 8 hours for 7 days Azithromycin- 10 mg/kgday	Moderate evidence; strong recommendation

What antibiotics are recommended for suspected leptospirosis in children?

CORE GROUP RECOMMENDATION

	Drug and dose	Strength of recommendation
Moderate to severe		
1st line	Penicillin – 250,000-400,000 iu div 4-6 doses x 7days Ampicillin – 100 mg/kg/day q 6 hrs x 7days	Moderate evidence; strong recommendation
Alternative	Cefotaxime- 100-150 mg/kg in 3-4 divided doses; Ceftriaxone – 80-100 mg/kg/day once daily (max 2 g,s)	Moderate evidence; strong recommendation



C. PREVENTION

Clinical Questions on Prevention
What are the recommended pre and postexposure prophylaxis for children?

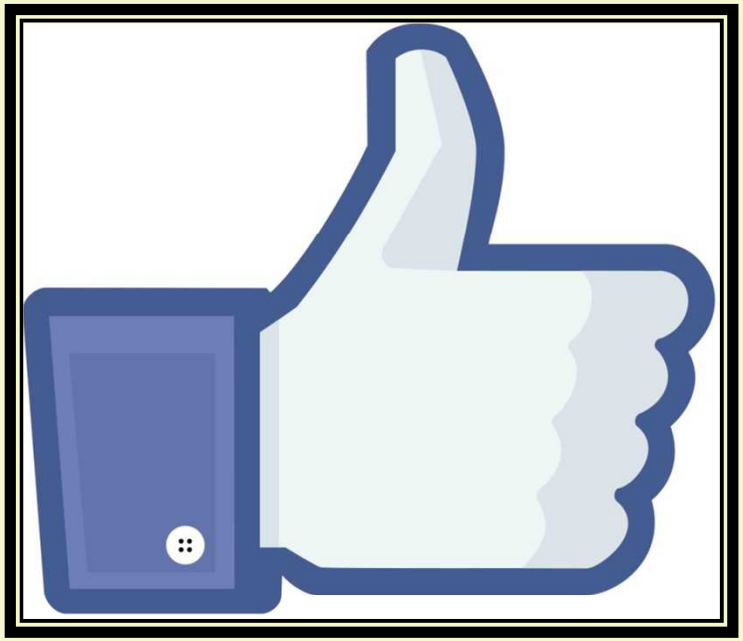
- Based on a single RCT that found no permanent yellowish discoloration of developing teeth after using Doxycycline in treating 31 asthmatic children below 8 yrs of age for atypical pneumonia, short-term use of Doxycycline may be considered as chemoprophylaxis against leptospirosis for children below 8 yrs of age

What are the recommended pre and postexposure prophylaxis for children?

CORE GROUP RECOMMENDATION

	Drug	Strength of recommendation
1st line	Doxycycline - 4 mg/kg single dose; Max. Dose: 200 mg (regardless of age)	Moderate evidence Strong recommendation
Alternative	Amoxycillin – 50 mg/kg/day g 8 hours for 3 -5 days ; Max dose: 500 mg q 8 hrs.	Low evidence Strong recommendation
	Azithromycin – 10 mg/kg single dose; Max dose: 500 mg	Low evidence Conditional recommendation

If children are exposed for more than 7 days, the dose should be repeated after 1 week



General Guidelines for the Prevention of leptospirosis

- Parents should instruct their children not to wade or swim in flood waters
  - If unavoidable, protective gear such as boots, goggles, overalls and rubber gloves should be used
- All food and drinking water should be protected against contamination. Fresh vegetables and fruits should be washed in previously boiled or clean water and then cooked or peeled
- Boil drinking water for at least 10-15 minutes
- Food should be protected against rodent attack or contamination

General Guidelines for the Prevention of leptospirosis

- If children are exposed to flood waters, antibiotic prophylaxis may decrease occurrence of clinical disease and mortality
- Exposure to animal farm water runoff should be avoided
- Vaccination of domestic and farm animals can only provide variable levels of protection
- There is NO human vaccination available to date

Top 3 Recommendations

Diagnosis:

- MAT is NOT routine: Rapid diagnostic tests may be helpful early (> 5days) in the course

Treatment:

- Uncomplicated : Doxycycline
- Severe: Penicillin

Prevention:

- Doxycycline
- Alternatives: amoxycillin , azithromycin

Clinical Practice Guideline on Leptospirosis in Children

Technical Working Group

Over-all Chair:		**Gyneth Lourdes G. Bibera, MD**
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Thank
You!