兒科預防性投藥

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Antimicrobial Prophylaxis

- Practice of administering an antimicrobial agent or agents with the intent of preventing an infection
- Prevention, rather than treatment, always is prefered --- risk-benefit and cost-benefit ratios are acceptable

FEIGIN, et al. Textbook of Pediatric Infectious Diseases 2004;236:3029-3040.

General Principles of Prophylaxis

- Several factors that influence the efficacy
  - Potential pathogen
  - Prophylaxis agent
  - Host
  - Disease to be prevented
- Several factors will lead to ineffective prophylaxis
  - Overuse of antimicrobial agents
  - Promotion of resistant microorganisms
  - Economic waste
  - Risk of toxicity or side effects

FEIGIN, et al. Textbook of Pediatric Infectious Diseases 2004;236:3029-3040.

Factors influencing effective prophylaxis

- Single versus multiple potential pathogens
- Time of exposure to the pathogen
- Source of pathogens
- Severity of the disease to be prevented
- Targeted organ(s) that could become infected
- Spectrum of activity of the antimicrobial agent
- PK/PD of the selected agent
- Duration of chemoprophylaxis
- Cost, toxicity, side effects and acceptability of the agent
- Likelihood and consequences of emerging resistance

FEIGIN, et al. Textbook of Pediatric Infectious Diseases 2004;236:3029-3040.

The bacterial pathogen

- More effective : single pathogen
- Greater the number of targeted pathogens, less effective, more toxic, and more expensive the regimen
- Ideally, administered at the time of exposure to potential pathogen or shortly thereafter
- If exposure is prolonged or continuous, prophylaxis becomes less effective and less desirable

FEIGIN, et al. Textbook of Pediatric Infectious Diseases 2004;236:3029-3040.

The disease

- The severity of disease to be prevented
- The site of infection to be prevented
- Adequate concentrations of antimicrobials

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The antimicrobial agent

- Narrow spectrum
- Inexpensive
- Easily administered
- Well tolerated
- Minimal side effects
- Less frequently agent is given
- More reliable adherence (compliance) of patient
- Single administration of antimicrobial agent : ideal

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Prophylaxis in Newborn Infants

OPHTHALMIA NEONATORUM

- Against *Neisseria gonorrhoeae* and *Chlamydia trachomatis*
- Topical 1% silver nitrate solutions[1]
- 0.5% erythromycin ophthalmic ointment[1]
- 1% tetracycline ophthalmic ointment[1]
- Silver nitrate --- most effective against penicillinase-producing *N. gonorrhoeae* --- chemical conjunctivitis
- No topical regimen has proven efficacy against *Chlamydia* conjunctivitis[2]
- Do not eliminate *C. trachomatis* from nasopharyngeal and do not prevent pneumonia
- Administered as soon as possible after birth

1 Hammerschlag, et al. Pediatr. Infect. Dis. J.7:81-82, 1988.
2 Black-Payne, et al. Pediatr. Infect. Dis. J. 8:491-498, 1989.

Prophylaxis in Newborn Infants

GROUP B *STREPTOCOCCUS* INFECTIONS

- Prevention of early-onset neonatal group B Streptococcus (GBS) infections[1,2]
- Prophylaxis of early-onset GBS disease with penicillin G or Ampicillin soon after birth (post chemoprophylaxis) is ineffective[3]
  - In utero infection
  - Asymptomatic at or within a few hours after birth

1 American Academy of Pediatrics, 2000, p537.
2 American College of Obstetricians and Gynecologists, 1992.
3 FEIGIN, et al. Textbook of Pediatric Infectious Diseases 2004;236:3029-3040.

Prophylaxis in Newborn Infants

GROUP B *STREPTOCOCCUS* INFECTIONS

- Focus on targeting colonized woman[1,2]
- Selective intrapartum maternal chemoprophylaxis[1,2]
- AAP recommend[1]
  - Woman who have no prenatal GBS culture results
  - Woman who begin labor with an identified risk factor
  - Lower vaginal and anorectal (single swab) specimens for culture at 35 – 37 wks GA
  - Rapid antigen test or GBS culture

1 American Academy of Pediatrics, 2000, p537.
2 American College of Obstetricians and Gynecologists, 1992.

Risk factors for early-onset GBS infection

Maternal Risk Factors
Premature onset of labor of < 37 wks GA
PPOM at < 37 wks GA
ROM (> 18 hrs) at any GA
Maternal fever during labor
Multiple birth
High GBS genital inoculum
GBS bacteriuria
Low type-specific GBS capsular polysaccharide antibody
Maternal age < 20 yr
Black race
Diabetes mellitus
Infant Risk Factors
Low birth weight
Prematurity

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Intrapartum Antibiotic Prophylaxis for GBS INFECTIONS

- Previous delivery of an infant with invasive GBS disease, regardless of maternal colonization
  - Decrease incidence of maternal GBS postpartum endometritis
  - Decrease rate of invasive GBS disease 65%
  - Decrease rate of early-onset GBS infection 36%
- Treatment with woman with chorioamnionitis (Ampicillin + Gentamycin) reduces rate of GBS disease 86%

Ampicillin 2 g initially, then 1 to 2 g every 4 to 6 hrs or
Penicillin G 5 million U every 6 hrs until delivery
Penicillin allergic woman-clindamycin or erythromycin IV

*

* Catanzaro, F.J., et al. Am. J. Med.17:749-756, 1954.

Disease-Targeted Prophylaxis

RHEUMATIC FEVER

- Group A *Streptococcus* (GAS) infections of pharynx --- precipitating cause
- At least 1/3 of episodes of acute rheumatic fever result from inapparent streptococcal infections[1]
- Prevention of first attack (Primary Prevention)
  - Proper identification
  - Adequate antibiotic treatment
  - Eradication of *streptococcal* infection
- Continuous chemoprophylaxis to prevent recurrence (Secondary prevention)[2]
  - Very high risk for recurrence after subsequent GAS pharyngitis

1 Dajani, A. S. Pediatr. Infect. Dis. J. 10(Suppl.):25-27, 1991.
2 Dajani, A., et al. Pediatrics96:758-764, 1995.

Rheumatic fever

PRIMARY PREVENTION

- No single regimen eradicates GAS from pharynx in 100% of treated patients
- Penicillin --- Drug of choice for Rx of GAS[1]
- Start as long as 9 days after onset of acute illness[2]
- A brief delay (24 – 48 hrs) for processing the throat culture before initiation of antibiotic therapy --- not increase risk of rheumatic fever
- Noncontagious 24 hrs after initiation of therapy[3]

1 American Academy of Pediatrics, 1994.
2 Catanazaro, et al. Am. J. Med. 17:749-756, 1954.
3 Snellman, et al. Pediarics 91:1166-1170, 1993.

Rheumatic fever

PRIMARY PREVENTION

- Benzathine penicillin G is prefered to oral Penicillin*
  - Poor compliance to complete a 10-day course of oral Rx
  - Personal or family history of rheumatic fever, RHD
  - Other environmental factors
- Benzathine penicillin G 900,000 U + procaine penicillin G 300,000 U for most children --- less painful
- Penicillin V 10-day period is preferred to Penicillin G --- more resistant to gastric acid
- Broader-spectrum Penicillins, Ampicillin and Amoxicillin for treatment GAS pharyngitis --- no microbiologic advantage over penicillin

* Dajani, A., et al. Pediatrics96:758-764, 1995.

Rheumatic fever

PRIMARY PREVENTION

- Oral Erythromycin 10-day period --- allergic to penicillin
  - Some areas of the world --- strains of GAS resistant to erythromycin --- treatment failure[1]
- New macrolide Azithromycin[2]
  - Less GI side effects
  - Administered once daily and high tonsillar tissue concentrations
  - A 5-day course --- approved by FDA-USA
  - Second-line Rx for individuals 16 yrs or older
  - 500 mg PO single dose on first dose, followed by 250 mg once daily for 4 days

1 Seppala, et al. NEJM; 236:292-297, 1992.
2 Hooton, T.M. Am. J. Med. 91(Suppl.):23-30, 1991.

Rheumatic fever

PRIMARY PREVENTION

- A 10-day course of oral cephalosporin
  - acceptable alternative, particularly for penicillin-allergic individuals --- superior to a 10-day of oral penicillin[1]
  - Preferable --- narrower-spectrum cephalosporins such as cefadroxil and cephalexin[2]
  - Penicillin-allergic persons (<15%) are also allergic to cephalosporins
  - Not use in patients with immediate (anaphylactic-type) hypersensitivity to penicillin
  - Recent report[3,4] --- 5-day course of oral cephalosporin --- comparable to a 10-day course of oral penicillin --- regimens currently are not approved by FDA-USA

1 Block, et al. Pediatr. Infect. Dis. J. 11:919-925, 1992.
2 Dajani, A., et al. Pediatrics96:758-764, 1995.
3 Block, et al. Pediatr. Infect. Dis. J. 11:919-925, 1992.
4 Dajani, A. S. Pediatr. Infect. Dis. J. 14(Suppl.):7-11, 1995.

Rheumatic fever

SECONDARY PREVENTION

- Prevention of recurrent rheumatic fever --- continuous antimicrobial prophylaxis > recognition and Rx of acute episodes of *streptococcal* pharyngitis[1]
- Recommendation
  - Well-documented Hx of rheumatic fever (including cases manifested solely by Sydenham chorea)
  - Definite evidence of rheumatic heart disease
- Initialed as soon as Dx --- acute rheumatic fever or rheumatic heart disease
- 1,200,000 U of Benzathine penicillin G every 4 wks[2,3]
  - In country, high incidence of rheumatic fever --- high-risk e.g. residual rheumatic carditis --- Benzathine penicillin G every 3 wks

1 Dajani, A., et al. Pediatrics. 96:758-764, 1995. 3 Lue, et al. J. Pediatr. 125:812-816, 1994.
2 Lue, et al. J. Pediatr. 108:299-304, 1986.

Rheumatic fever

SECONDARY PREVENTION

- Benzathine penicillin G --- inconvenience and pain of injection --- causes discontinue prophylaxis
- Oral prophylaxis (penicillin V or sulfadiazine) --- depends primarily on patient's adherence --- risk of recurrence is higher than IM Benzathine penicillin G*
- Oral agents --- appropriate for patients at lower risk for rheumatic recurrence
- Some physicians --- switch Rx to oral prophylaxis --- late adolescent or young adults and remained free of rheumatic attacks for at least 5 yrs

* Feinstein, et al. N. Eng. J. Med. 260:697-702, 1959.

Rheumatic fever

SECONDARY PREVENTION

- Sulfonamides --- not effective in eradication of GAS --- do prevent infection
  - Contraindication in late pregnancy
    - transplacental passage
    - potential competition with bilirubin for albumin-binding sites
- Allergic to penicillin and sulfisoxazole
  - Erythromycin is recommended
- No data --- use of other penicillins, macrolides, or cephalosporins for secondary prevention of rheumatic fever

FEIGIN, et al. Textbook of Pediatric Infectious Diseases 2004;236:3029-3040.

Rheumatic fever

SECONDARY PREVENTION

- Appropriate duration of prophylaxis --- individual
- Patients who have had rheumatic carditis
  - Long-term ATB prophylaxis, perhaps for life
  - Continue, even after valve surgery, including prosthetic valve replacement
- Consider discontinuing prophylaxis after several years*
  - Patients who have had rheumatic fever without rheumatic carditis --- less risk of having cardiac involvement with a recurrence

* Berrios, et al. Intern. Med. 118:401-406, 1993.

Rheumatic fever

SECONDARY PREVENTION

- In general --- whichever is longer
  - Continue until 5 years has elapsed since last rheumatic fever attack
  - The age of 21 years
- Decision to discontinue prophylaxis or reinstate --- after discussion
  - Potential risks and benefits
  - Careful consideration of various epidemiologic risk factors

Dajani, A., et al. Pediatrics96:758-764, 1995.

Rheumatic fever

SECONDARY PREVENTION

- Individuals with increased exposure to streptococcal infections
  - Children and adolescents
  - Parents of young children
  - Teachers
  - Physicians
  - Nurses
  - Allied health personnel in contact with children
  - Military recruits
  - others living in crowded situations (economically disadvantaged populations

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Prevention of Rheumatic fever

Agent	Dose	Mode	Duration
Primary Prevention			
Benzathine penicillin G	600,000 U for pt ≤ 27 kg (60 lb)	IM	Once
	1,200,000 U for pt ≥ 27 kg (60 lb)	IM	Once
Penicillin V	Children :		
	250 mg 2 – 3 times daily	PO	10 days
	Adolescents and adults :		
	500 mg 2 – 3 times daily	PO	10 days
	For Individuals Allergic to Penicillin		
Erythromycin estolate	20 - 40 MKD 2 – 4 times daily (Max 1 g/D)	PO	10 days
Secondary Prevention			
Benzathine penicillin G	1,200,000 U every 3 – 4 wk or	IM	
Penicillin V	250 mg twice daily or	PO	
Sulfadiazine	0.5 g once daily for pt ≤ 27 kg (60 lb)	PO	
	1.0 g once daily for pt ≥ 27 kg (60 lb)	PO	
Erythromycin	For Allergic to Penicillin and Sulfadiazine		
	250 mg twice daily	PO	

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Disease-Targeted Prophylaxis

BACTERIAL ENDOCARDITIS

- IVDU and indwelling CVC are high-risk situations
  - Prophylaxis in these situations is not practical
- In general, dental or surgical procedures --- bleeding from gingiva or from mucosa surfaces of oral, respiratory, GI, and GU tracts --- bacteremia --- require prophylaxis
- Poor dental hygiene and periodontal or periapical infection --- bacteremia --- in absence of dental or oral procedures
- Maintenance of optimal dental care and oral hygiene is important --- prevent of IE in children with underlying cardiac disease --- optimal oral hygiene before cardiac Sx

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Disease-Targeted Prophylaxis

BACTERIAL ENDOCARDITIS

- Prophylaxis is most effective --- perioperatively
  - Starting shortly before a procedure
  - Maintained for approximated 10 hrs
- *Alpha-hemolytic streptococci**
  - most common cause of IE after dental, oral, upper respiratory tract, or esophageal procedures
  - Very susceptible to penicillin, ampicillin, or amoxicillin
- For penicillin-allergic patients
  - Clindamycin
  - Azithromycin and Clarithromycin --- alternatives

* Recommendations by AHA. J. A. H. A. 277:1794-1801, 1997.

Disease-Targeted Prophylaxis

BACTERIAL ENDOCARDITIS

- Enterococci endocarditis
  - after GI or GU tract surgery or instrumentation[1]
  - GI endoscopy is very rare in children[2,3]
  - More commonly after GU tract procedures
- Gram-negative bacilli endocarditis --- rare
- Receiving Penicillin prophylaxis
  - *Alpha-hemolytic streptococci* in their oral cavity, relatively resistant to penicillins
  - Clindamycin for endocarditis prophylaxis

1 Recommendations by AHA. 1997.
2 Byrne, et al. J. Pediatr. Gastroenterol. Nutr. 1:551-553, 1982.
3 El-Baba, et al. Gastrointest. Endosc. 44:378-381, 1996.

Disease-Targeted Prophylaxis

BACTERIAL ENDOCARDITIS

- Patients who undergo open heart surgery
  - *Staphylococcal aureus* and coagulase-negative staphylococci
  - A first generation cephalosporin or Vancomycin
  - Used only perioperatively and for no longer than 48 hours

FEIGIN, et al. Textbook of Pediatric Infectious Diseases 2004;236:3029-3040.

Relative Risk of Endocarditis for various conditions

High Risk
Prosthetic valves
Previous episode of endocarditis
Surgically constructed systemic artery-to-pulmonary artery shunts
Intravenous drug abuse
Indwelling central venous catheters
Complex cyanotic Congenital heart disease
Moderate Risk
Uncorrected patent ductus arteriosus
Ventricular septal defect
Uncorrected atrial septal defect (other than secondum)
Bicuspid aortic valve
Mitral valve prolapse with regurgitation and/or dysplastic leaflets
Rheumatic mitral or aortic valve disease
Other acquired valvular diseases
Hypertrophic cardiomyopathy

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Dental and Surgical procedures for which prophylaxis is recommended

- Dental procedures known to induce gingival or mucosal bleeding
  - Gingival surgery
  - Subgingival scaling or polishing
  - Subgingival orthodontic banding
  - Extractions
  - Matrix retainers and wedges
  - Periodontal surgery
  - Prophylactic teeth cleaning
- Tonsillectomy and/or adenoidectomy
- Bronchoscopy with a rigid bronchoscope
- Esophageal stricture dilatation
- Cystoscopy
- Urethral dilatation
- Urethral catheterization if urinary tract infection is present
- Urinary tract surgery if urinary tract infection is present
- Incision and drainage of infected tissue

FEIGIN, et al. Textbook of Pediatric Infectious Diseases 2004;236:3029-3040.

Recommended prophylaxis for dental, oral, respiratory tract, and esophageal procedures

Standard General Prophylaxis	
Amoxicillin	50 mg/kg (Max 2 g) PO 1 hr before procedure
Unstable to Take Oral Medications	
Ampicillin	50 mg/kg (Max 2 g) IV or IM within 1/2 hr before procedure
Penicillin-Allergic	
Clindamycin	20 mg/kg (Max 300 mg) PO 1 hr before procedure
or	
Azithromycin	15 mg/kg (Max 500 mg) PO 1 hr before procedure
or	
clarithromycin	
Penicillin-Allergic and Unstable to Take Oral Medications	
Clindamycin	20 mg/kg (Max 600 mg) IV within 1/2 hr before procedure

For patients in high-risk category for endocarditis, half dose may be repeated 6 hrs after initial dose (except for azithromycin, a second dose is not necessary)

Recommended prophylaxis for GU or GI tract procedure in children

High Risk	
Ampicillin	50 mg/kg (Max 2 g) IV or IM 1/2 hr before procedure
plus	
Gentamycin	1.5 mg/kg (Max 120 mg) IV or IM 1/2 hr before procedure
	(6 hrs) later, may use Ampicillin 25 mg/kg IV or IM, or amoxicillin 25 mg/kg PO
High Risk, Penicillin-Allergic	
Vancomycin	20 mg/kg (Max 1g) IV over a period of 1 hr.
plus	Complete infusion within 1/2 hr before procedure
Gentamicin	1.5 mg/kg (Max 120 mg) IV or IM
	Complete infusion/injection within 1/2 hr before procedure
Moderate Risk	
Amoxicillin	50 mg/kg (Max 2 g) PO 1 hr before procedure
or	
Ampicillin	50 mg/kg (Max 2 g) IV or IM 1/2 hr before procedure
Moderate Risk, Penicillin-Allergic	
Vancomycin	20 mg/kg (Max 1 g) IV over a period of 1 hr.
	Complete infusion within 1/2 hr before procedure

FEIGIN, et al. Textbook of Pediatric Infectious Diseases 2004;236:3029-3040.

Disease-Targeted Prophylaxis

RECURRENT OTITIS MEDIA

- *Streptococcus pneumoniae, Moraxella catarrhalis, and nontypable Hemophilus influenzae*
- Who has had ≥ 3 episodes of AOM in 6 months or 4 episodes within a years, last episode occuring during previous 6 months
- Benefit[1,2]
  - Younger 2 years
  - Out-of-home childcare
  - Native American children
- Amoxicillin 20 mg/kg, or sulfisoxazole 50 mg/kg
  - Period of 3 – 6 months or during the winter month

1 Klein, J.O. Pediatr. 11:44-60, 1994.
2 Paradise, J.L. Laryngol. 155:33-36, 1992.

Disease-Targeted Prophylaxis

RECURRENT OTITIS MEDIA

- Other measures
  - Eliminating smoking in the home
  - Reducing daycare attendance
  - Eliminating pacifiers
  - Administering influenza vaccine
- Fail to prevent recurrent infection
  - Referral to ENT for evaluation and possible tympanostomy tube placement or adenoidectomy, or both procedures

FEIGIN, et al. Textbook of Pediatric Infectious Diseases 2004;236:3029-3040.

Disease-Targeted Prophylaxis

RECURRENT URINARY TRACT INFECTION

- Female 5%, male 1 – 2%
- Recurrent UTI 30 – 50%, most recurrences within 3 months after initial episode
- 80% of recurrences
  - New infection --- different colonic bacterial species
  - Become resistant to recently administered ATBs
  - Recurrence rate is not altered by extending duration of treatment
- Complications of UTIs in children
  - Renal parenchymal infections
  - Renal scarring 10 – 15%
  - HT 10%
  - Renal insufficiency

Zelikovic, et al. An update. West. J. Med. 157:554-561, 1992.

Disease-Targeted Prophylaxis

RECURRENT URINARY TRACT INFECTION

- Vesicoureteral reflux (VUR) 30 – 50% of children with UTIs[1]
  - Directly related to number of UTI episodes
  - Inversely related to age
  - Higher incidence (30 – 60%) of pyelonephritic scarring
- > 90% of children with renal parenchymal scarring[2]
  - VUR and history of UTI
- Benefit from suppressive ATB Therapy[2]
  - ≥ 3 UTIs in a 12-month period
    - As long as 6 months to allow repair of instrinsic bladder defense mechanisms
  - Anatomical defects or reflux
    - As long as the underlying defect exists

1 McCracken, et al. Pediatr. Infect. Dis. J. 8:552-555, 1989.
2 Zelikovic, et al. An update. West. J. Med. 157:554-561, 1992.

Disease-Targeted Prophylaxis

RECURRENT URINARY TRACT INFECTION

- Methenamine mandelate (75 mg/kg divided every 12 hours)
- A pH of 5.5 or lower in urine
  - Ascorbic acid or other acidifying agents
- Trimethoprim-sulfamethoxazole (TMP-SMX)[1,2,3]
  - 2 mg/kg of TMP and 10 mg/kg of SMX in single daily dose or
  - 5 mg/kg of TMP and 25 mg/kg of SMX twice a week
- Trimethoprim (TMP)
  - Diffusing into vaginal and urethral fluids
  - Decreasing bacterial colonization of Enterobacteriaceae
  - Diminishing ascending reinfection

1 Brendstrup, et al. Acta Paediatr. Scand. 79:1225-1234, 1990.
2 McCracken, et al. Pediatr. Infect. Dis. J. 8:552-555, 1989.
3 Shapiro, E.D. Pediatr. Infect. Dis. J. 11:165-168, 1992.

Disease-Targeted Prophylaxis

RECURRENT URINARY TRACT INFECTION

- Nitrofurantoin
  - 1 – 2 mg/kg PO single dose at bedtime
  - Infants and children
- Nalidixic acid
  - 30 mg/kg divided every 12 hours
  - Not recommended for children
- Cephalosporin and amoxicillin-clavulanic acid
  - PO single dose at bedtime

Mangiarotti, et al. Review. J. Chemother. 12:115-123, 2000.

Postexposure Prophylaxis

PERTUSSIS

- Index case : standard & droplet precautions 5 days after Rx
- Erythromycin prophylaxis
- Close contact is effective in limiting secondary transmission
  - Household members
  - Attendees of childcare facilities
  - Other individuals who are in contact with index case for ≥ 4 hrs/day
- Chemoprophylaxis is recommended irrespective of age or vaccination status
  - Immunity after receiving pertussis immunization is not absolute
  - May not prevent infection
- 40 – 50 MKD (Max 2 g/D) PO in 4 divided doses for 14 D

American Academy of Pediatrics, 1994.

Postexposure Prophylaxis

PERTUSSIS

- Allergic to erythromycin or can not tolerate it
- TMP-SMX
  - 8 MKD of TMP and 40 MKD of SMX PO in 2 divided doses for 14 D
  - Efficacy --- has not been documented
- Persons who have been in contact
  - Monitored closely for respiratory symptoms for 2 weeks after last contact with index case
- Risk of contracting pertussis in adults providing medical care to children should be recognized

American Academy of Pediatrics, 1994.

Postexposure Prophylaxis

PERTUSSIS

- Pertussis Immunization
  - Close contacts < 7 years of age who are unimmunized or underimmunized should initiated or continued according to recommended schdule
- 4th dose
  - Children who received their third dose 6 mo or more before exposure
- 5th dose
  - Children who are < 7 years of age and received their fourth dose 3 or more years before exposure
- Booster Tdap vaccine
  - 11 – 18 years of age if they previously have not received Tdap

American Academy of Pediatrics, Red book 2006

Recommended Antimicrobial Therapy and Postexposure Prophylaxis for Pertussis in Infants, Children, Adolescents, and Adults

Age	Recommended Drugs: Azithromycin	Erythromycin	Clarithromycin	Alternative: TMP-SMX
<1 mo	10 mg/kg per day as a single dose for 5 days†	40–50 mg/kg per day in 4 divided doses for 14 days	Not recommended	Contraindicated at <2 mo of age
1–5 mo	See above	See above	15 mg/kg per day in 2 divided doses for 7 days	≥2 mo of age: TMP, 8 mg/kg per day; SMX, 40 mg/kg per day in 2 doses for 14 days
≥6 mo and children	10 mg/kg as a single dose on day 1 (maximum 500 mg); then 5 mg/kg per day as a single dose on days 2–5 (maximum 250 mg/day)	See above (maximum 2 g/day)	See above (maximum 1 g/day)	See above
Adolescents and adults	500 mg as a single dose on day 1, then 250 mg as a single dose on days 2–5	2 g/day in 4 divided doses for 14 days	1 g/day in 2 divided doses for 7 days	TMP, 300 mg/day; SMX, 1600 mg/day in 2 divided doses for 14 days

TMP indicates trimethoprim; SMX, sulfamethoxazole.
† Preferred macrolide for this age because of risk of idiopathic hypertrophic pyloric stenosis associated with erythromycin.

American Academy of Pediatrics, Red book 2006.

Postexposure Prophylaxis

MENINGOCOCCAL INFECTIONS

- Close contacts of patients with invasive Meningococcal disease (meningococcemia, meningitis, or both)
  - Higher risk for infection than general population
  - Attack rate for household contacts 0.3 – 1% (300 – 1000 times the rate in general population)
- Chemoprophylaxis should be administered as soon as possible, preferably within 24 hours of identifying index case
- Systemic ATB Rx does not eradicate nasopharyngeal carriage of *N. meningitidis*
  - Chemoprophylaxis should be administered to index patient before discharge from hospital

American Academy of Pediatrics, 1994.

Postexposure Prophylaxis

MENINGOCOCCAL INFECTIONS

- Rifampicin prophylaxis
  - Fails to eradicate *N. meningitidis* in 10 – 20%[1,2]
  - Not recommended for pregnant woman
- Side effects
  - Headache
  - Dizziness
  - GI symptoms
  - Discoloration of body secretions (saliva, tears, urine)
  - Staining of contact lenses
  - Hepatotoxicity

1 Munford, et al. J. Infect. Dis. 129:644-649, 1974.
2 Schwartz, et al. Lancet 1:1239-1242, 1988.

Postexposure Prophylaxis

MENINGOCOCCAL INFECTIONS

- A single IM of Ceftriaxone
  - 125 mg for children younger than 15 years
  - 250 mg for adults
  - Not recommended for routine prophylaxis
  - Safety in pregnancy
- For high-risk contacts ≥ 18 years
  - Ciprofloxacin 500 mg PO single dose

Schwartz, et al. Lancet 1:1239-1242, 1988.

Case Definitions for Invasive Meningococcal Disease

Confirmed
Isolation of *N. meningitidis* from a usually sterile site •Blood •Cerebrospinal fluid •Synovial fluid •Pleural fluid •Pericardial fluid •Petechial or purpuric lesions in a person with a clinical illness consistent with meningococcal disease or purpura fulminans
Presumptive
Gram-negative diplococci in any sterile fluid, such as cerebrospinal fluid, synovial fluid, or scraping from a petechial or purpuric lesion
Probable
A positive antigen test (ie,PCR) result for *N. meningitidis* in Cerebrospinal fluid in the absence of positive sterile site culture in a person with a clinical illness consistent with meningococcal disease or purpura fulminans

American Academy of Pediatrics, Red book 2006

High-risk : chemoprophylaxis recommended (close contact)
•Household contact, especially young children •Children care or nursery school contact during 7 days before onset of illness •Direct exposure to index patient's secretions through kissing or through sharing toothbrushes or eating utensils, markers of close social contact, during 7 days before onset of illness •Mouth-to-mouth resuscitation, unprotected contact during endotracheal intubation during 7 days before onset of illness •Frequently slept or ate in same dwelling as index patient during 7 days before onset of illness •Passengers seated directly next to the index case during airline flights lasting more than 8 hours
Low risk : chemoprophylaxis not recommended
•Casual contact : no history of direct exposure to index patient's oral secretions (eg, school or work) •Indirect contact : only contact is with a high-risk contact, no direct contact with the index patient •Health care professionals without direct exposure to patient's oral secretions
In outbreak or cluster
•Chemoprophylaxis for people other than people at high risk should be administered only after consultation with local public health authorities

American Academy of Pediatrics, Red book 2006

Age of Infants, children, And Adults	Dose	Duration	Efficacy %	Caution
Rifampicin				
< 1 mo	5 mg/kg, orally, every 12 hrs	2 days		
≥ 1 mo	10 mg/kg (Max 600 mg), orally, every 12 hrs	2 days	90 - 95	Can interfere with efficacy of oral contraceptives and some seizure prevention and anticoagulant medications; may stain soft contact lenses
Ceftriaxone				
< 15 yr	125 mg, IM	Single dose	90 – 95	To decrease pain at injection site, dilute with 1% lidocaine
≥ 15 yr	250 mg, IM	Single dose	90 - 95	
Ciprofloxacin				
> 18 yr	500 mg, orally	Single dose	90 – 95	Not recommended for people < 18 yr of age

American Academy of Pediatrics, Red book 2006

Postexposure Prophylaxis

HAEMOPLILUS INFLUENZAE TYPE b INFECTIONS

- Risk for secondary invasive disease with H. influenzae type b (Hib) is age-dependent[1]
  - Household contacts younger than 1 year = 6% (highest risk)
  - Children 4 years or younger = 2.1%
  - Children older than 6 years and adults = little or no risk
  - Children attending childcare centers may be increased but less than household contacts[2,3]
  - Exposed hospital personnel do not require antimicrobial prophylaxis

1 Band, et al. J. A. M. A. 251:2381-2386, 1984.
2 Murphy, et al. N. Eng. J. Med. 316:5-10, 1987.
3 Osterholm, et al. N. Eng. J. Med. 316:1-5, 1987.

Postexposure Prophylaxis

HAEMOPLILUS INFLUENZAE TYPE b INFECTIONS

- Peak incidence of meningitis and most other invasive Hib infections --- 6 to 18 months of age
- Patients with invasive Hib disease
  - Droplet precautions are recommended for 24 hours after initiation of parenteral antimicrobial therapy
- Conjugate Hib vaccines appear to decrease pharyngeal colonization --- reduce Hib transmission to unvaccinated children
- Rifampicin 20 MKD PO single dose (Max 600 mg) for 4 days --- efficacy 95%
  - Initiated as soon as possible because most secondary cases occur during first week after identification of index case

American Academy of Pediatrics, Red book 2006

Chemoprophylaxis Recommended

- For all household contact in the following circumstances :
- Household with at least 1 contact younger than 4 years of age who is unimmunized or incompletely immunized (spent ≥ 4 hr with index case for ≥ 5 of 7 days before admit)
- Household with a child younger than 12 months of age who has not received the primary series
- Household with a contact who is an immunocompromised child, regardless of that child's Hib immunization status
- For nursery school and child care center contacts when 2 or more cases of Hib invasive disease have occurred within 60 days
- For index case, if younger than 2 years of age or member of a household with a susceptible contact and treated with a regimen other than cefotaxime or ceftriaxone, chemoprophylaxis usually is provided just before discharge from hospital

Chemoprophylaxis Not Recommended

- For occupants of households with no children younger than 4 years of age other than the index patient
- For occupants of households when all household contacts 12 to 48 months of age have completed their Hib immunization series and when household contacts younger than 12 months of age have completed their primary series of Hib immunizations
- For nursary school and child care contacts of 1 index case, especially those older than 2 years of age
- For pregnant woman

American Academy of Pediatrics, Red book 2006

Postexposure Prophylaxis

TUBERCULOSIS

- The three goals of preventive therapy
  - Prevent asymptomatic (latent) infection from progressing to clinical (active) disease
  - Prevent recurrence of past disease
  - Prevent initial infection in individuals who have negative tuberculin skin tests
- Isoniazid (INH)
  - Only drug approved by FDA-USA
  - Dose 10 – 15 MKD (Max300 mg) PO once daily
  - Continued for a total of 9 months

FEIGIN, et al. Textbook of Pediatric Infectious Diseases 2004;236:3029-3040.

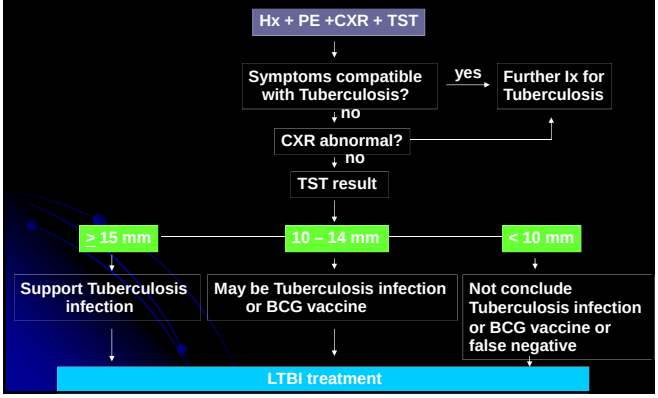
Guidelines for the investigation of contacts of persons with infectious tuberculosis

Source Case / Risk	Pulmonary, laryngeal, pleural TB CXR : cavity lesion or sputum AFB positive	Pulmonary, pleural TB CXR : abnormal consistent with TB NAA, sputum culture might be positive Sputum AFB positive	Suspected pulmonary TB CXR: abnormal not consistent with TB NAA, sputum culture negative
High	•Household contact •Contact index case eg. HIV or immunosuppressive drugs •Contact during bronchoscope, autopsy, sputum induction •Contact clouded persons eg. Classroom, apartment, car pool • Resident of narrow place/longtime	•Children less than 5 yr •Contact index case eg. HIV, immunosuppressive drugs therapy •Contact during bronchoscope, autopsy, sputum induction	
Moderate	•Children 5 – 15 yr •Residents of narrow place/shorttime	•Household contact •Contact clouded persons eg. Classroom, aparment, car pool •Residents of narrow place/shorttime	•Household contact •Children less than 5 yr •Contact index case eg. HIV or immunosuppressive drugs •Contact during bronchoscope, autopsy, sputum induction

CDC.MMWR 2005;54(RR15):1-37.

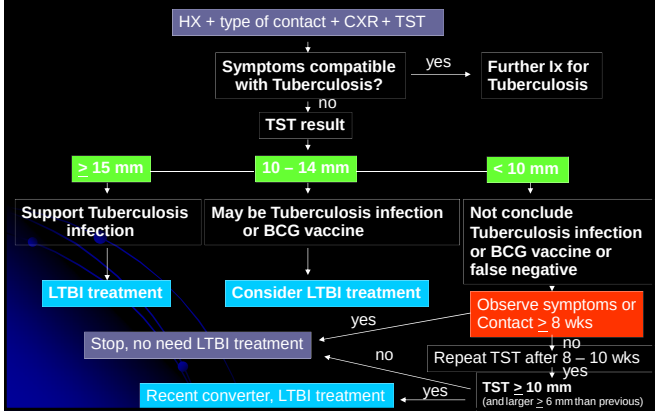
Thai PID Expert and TB NIH Meeting; 8 Feb 2007

Guidelines for the Investigations of contacts case < 5 yr with Index case sputum AFB +



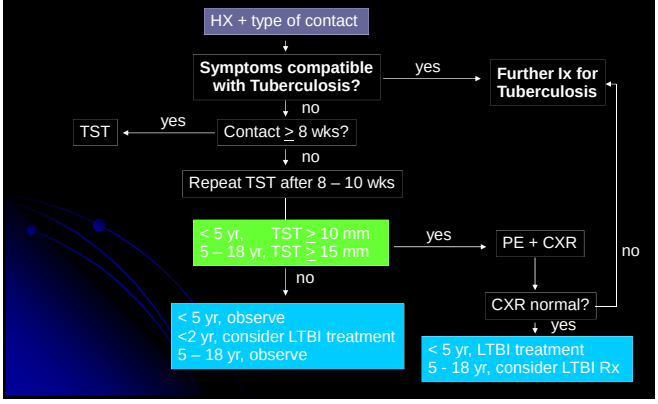
Thai PID Expert and TB NIH Meeting; 8 Feb 2007

Guidelines for the Investigations of contacts case 5 – 18 yr with Index case sputum AFB + or High or Moderately risks



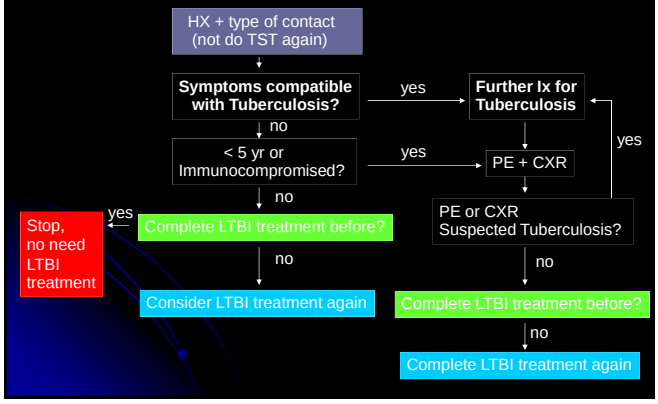
Thai PID Expert and TB NIH Meeting; 8 Feb 2007

Guidelines for the Investigations of contacts case with Index case Low risks (sputum AFB negative)



Thai PID Expert and TB NIH Meeting; 8 Feb 2007

Guidelines for the Investigations of contacts case with Index case and previous TST +



Postexposure Prophylaxis

LTBI treatment

- Isoniazid (INH)
  - 5 – 10 mg/kg/day (Max 300 mg/day) x 6 – 9 months
  - INH 2 days/wk + DOTs 15 mg/kg/day (Max 900 mg/day) x 6 – 9 months
- 2 months regimen (2RZ)
  - Rifampicin + Pyrazinamide
  - Severe hepatitis
  - Use in poor compliance for INH 6 – 9 months regimen
  - Need expert care
- Rifampicin 4 months
  - Easily developed drug resistant strains
  - Use in contact case with index case had INH monodrug resistant

PIDST. Update on Pediatric Infectious Diseases 2007;14:120-130.