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The basics of rational and prudent antibiotic use for common childhood infections in ambulatory care

ARPEC Educational Group

Julia Bielicki
Giangiacomo Nicolini
Marta Romanengo
Francois Dubos
Rebecca Lundin



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INTRODUCTION

The role of microorganisms in the human body

- 500-600 different kinds of bacteria thrive on mucus and food remnants in the mouth (*Streptococcus, anaerobes*).
- Some microorganisms live on the external ear and skin and constitute its normal flora (*Propionibacterium acnes, Staph epidermidis, Micrococcus*).
- A normal flora lives on the lower part of the urethra and the female genital tract (*Lactobacilli*).
- The colon is a holding tank for bacteria (10^{12} - 10^{13} /ml) that participate in the end stages of food digestion.

Microorganisms and their treatments

Viruses



Antivirals

Most often used in the community and the focus of these slides

Bacteria



Antibacterials (also called antibiotics)

Antimycobacterials (specifically active against mycobacteria)

Fungi



Antifungals

Parasites



Antiparasital drugs (active against malaria and other parasitic infections)

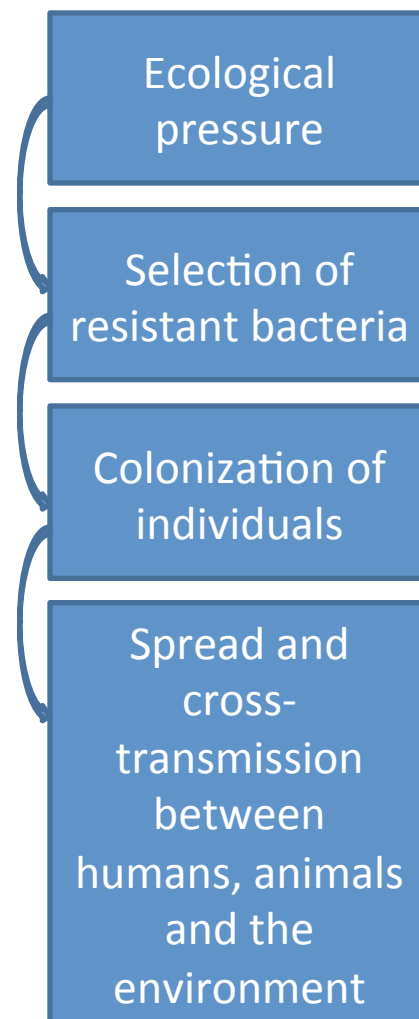
Antimicrobial resistance is the ability of a microorganism to resist the actions of antimicrobial agents. It is a characteristic of microorganisms, not patients, and may or may not be seen in conjunction with disease in a patient. Resistance may also be found when surveillance or environmental samples are analysed.

Not all infections require specific treatment

- Most infections seen in ambulatory care are viral in nature (e.g. common cold, pharyngitis, acute otitis media, flu)
- Most of these infections do not require specific treatment (indeed, often this is not available)
- The key decision is whether the patient is presenting with an infection that is (a) likely to be bacterial and (b) likely to benefit from antibiotic treatment

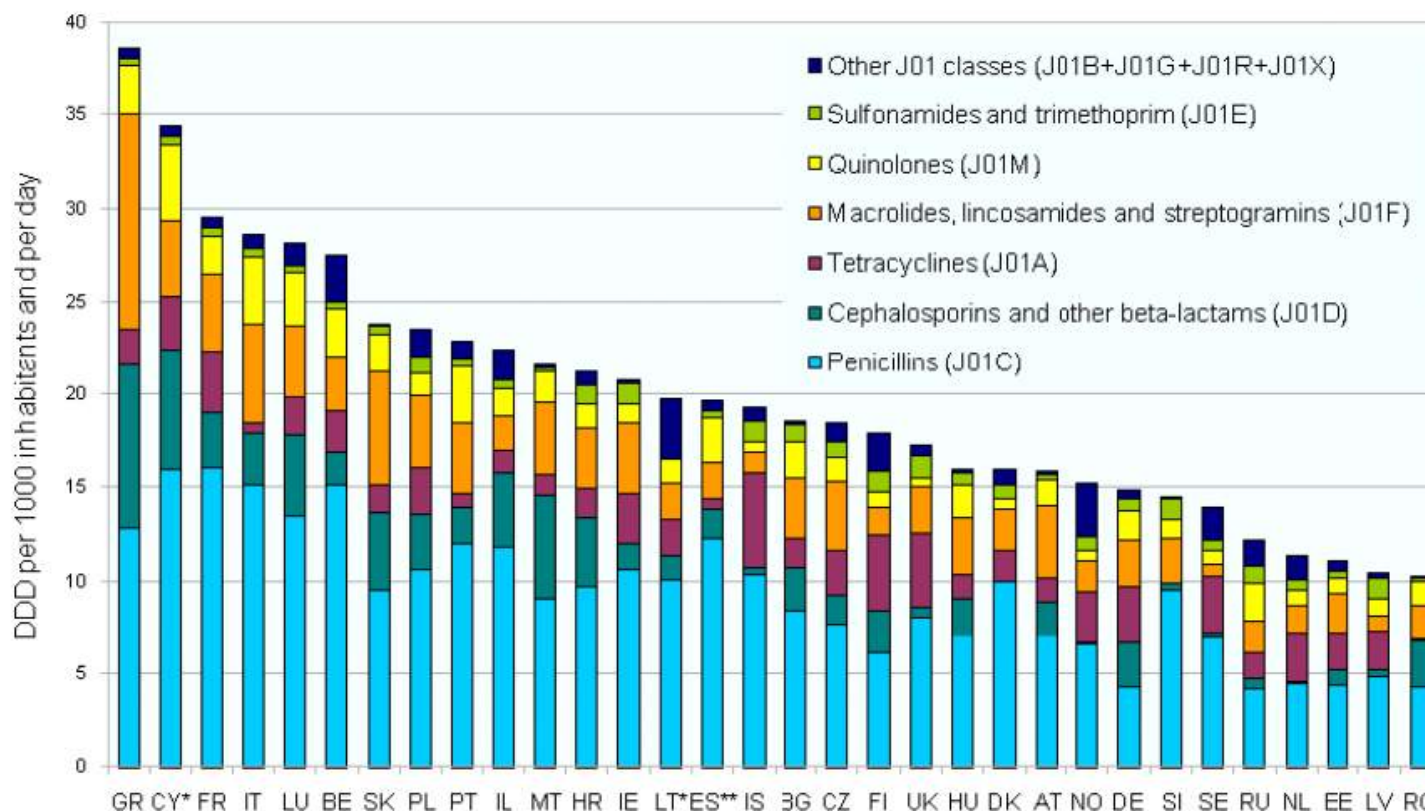
What antibiotics do...

- If there is a bacterial infection caused by a microorganism susceptible to the chosen antibiotic, the infection may be treated with the correctly administered antibiotic
- The normal human flora will also be modified, resulting in some well-known side-effects such as diarrhoea
- Groups of resistant bacteria may be selected and persist as colonizing organisms
- These can cause infection in the same patient or in other contacts of that patient later



European outpatient antibiotic use

Figure 3.4: Outpatient antibiotic (J01) use in 2009 subdivided into the major antibiotic classes according to ATC classification (N=32 countries)



ESAC Year book 2009, accessible at [ESAC-Net website](http://ESAC-Net.org) through ECDC. Reproduced with permission.

Antibiotics are used very frequently in ambulatory healthcare & very variably across Europe

Relationship between antibiotic resistance and antibiotic use

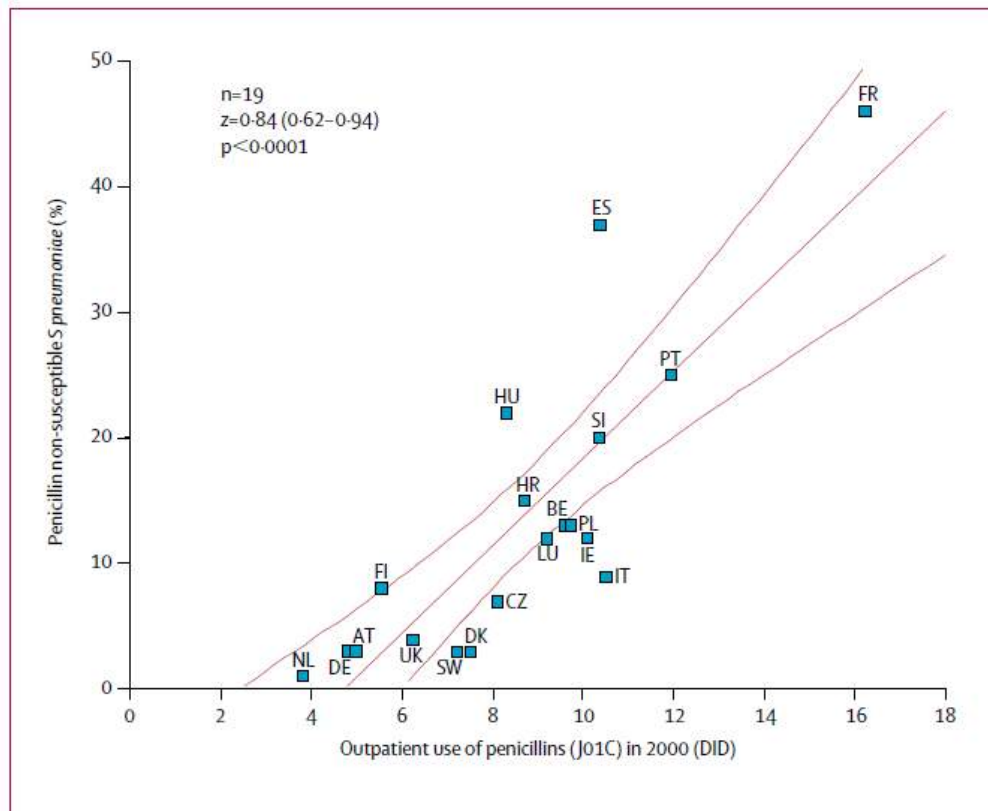


Figure 6: Correlation between penicillin use and prevalence of penicillin non-susceptible *S. pneumoniae*
AT, Austria; BE, Belgium; HR, Croatia; CZ, Czech Republic; DK, Denmark; FI, Finland; FR, France; DE, Germany;
HU, Hungary; IE, Ireland; IT, Italy; LU, Luxembourg; NL, The Netherlands; PL, Poland; PT, Portugal; SI, Slovenia;
ES, Spain; UK, England only.

Study of the relationship between penicillin use and prevalence of penicillin non-susceptible *S. pneumoniae* in Europe:

High observed levels of antibiotic resistance are associated with more intensive antibiotic use

The landscape of antibiotic resistance in Europe: *E.coli*

Figure 4.1: *Escherichia coli*: percentage (%) of invasive isolates with resistance to third-generation cephalosporins by country, EU/EEA countries, 2011



Note variation in resistance to third-generation cephalosporins amongst *E.coli* bloodstream and cerebrospinal fluid isolates → In some countries the utility of cephalosporins in treatment of *E.coli* infection may already be limited

Aspects of rational antibiotic prescribing in outpatient care

- It is in the interest of patients to preserve currently available antibiotics for future use
- Patients must receive antibiotics that they need at the right time, dose and duration
- A given antibiotic should be prescribed if
 - the infection is most likely caused by bacteria
 - the causative bacteria are likely to be susceptible to the antibiotic of choice
 - antibiotic treatment is the only safe option to manage the patient
- Gathering all relevant information to address the above points at each patient encounter is critical

Further information: Relevant antibiotic prescription guidelines

Potentially relevant guidelines in English may be found at:

- The National Guideline Clearinghouse run by the US Department of Health and Human Services and the Agency for Healthcare Research and Quality (<http://guideline.gov/>)
- The Clinical Guidelines Portal run by the National Health and Medical Research Council, Australia (<http://www.clinicalguidelines.gov.au/>)
- Clinical Guidelines provided by the National Institute for Clinical Excellence (NICE) ([#http://guidance.nice.org.uk/CG](http://guidance.nice.org.uk/CG))
- The Scottish Intercollegiate Guidelines Network run by Healthcare Improvement Scotland (<http://www.sign.ac.uk/guidelines/published/index.html>)
- The Cochrane Reviews provided by the Cochrane Collaboration (<http://www.cochrane.org/>)

In addition, you may be able to find guidelines for the treatment of the common infections discussed in this slide set through your national paediatric or paediatric infectious diseases society.

Further information: Country specific antibiotic use and resistance

EU country specific data on antibiotic use and resistance may be found at:

- The European Antimicrobial Resistance Surveillance Network (EARS-Net) run by the European Centre for Disease Prevention and Control (ECDC)

(
<http://ecdc.europa.eu/en/activities/surveillance/EARS-Net/database/Pages/database.aspx>)

- The European Surveillance of Antimicrobial Consumption Network (ESAC-Net), also run by the European Centre for Disease Prevention and Control (ECDC) (

<http://www.ecdc.europa.eu/en/activities/surveillance/ESAC-Net/database/Pages/database.aspx>)

In addition, you may be able to find information on national, regional, or hospital level antibiotic use and resistance through your national or regional public health authority or laboratory or pharmacy departments within individual hospitals.



The basics of rational and prudent antibiotic use for common childhood infections in ambulatory care

DEALING WITH COMMON CHILDHOOD INFECTIONS PRESENTING TO AMBULATORY CARE PROVIDERS

Introductory remarks

- This slide set includes discussions on the management of specific common childhood infections in ambulatory care
- Whenever a specific guideline is cited, this is as an example of a structured approach rather than as an endorsement of that particular recommendation
- Users of this slide set should be encouraged to adhere to local guidelines, wherever these exist
- Recommendations for specific antibiotic treatments included in this slide set are used only as examples, because rational antibiotic choices may vary according to local epidemiology

Common childhood infections presenting to ambulatory care providers

Infections covered in slide set

- Pharyngitis
- Acute otitis media
- Community acquired pneumonia
- Sinusitis
- Urinary tract infection
- Skin and soft tissue infection

Structured approach

Broadly, for each infection the slide set contains information on

- Case outline
- Background information
- Clinical assessment
- Benefit of laboratory testing
- Choosing a treatment strategy
- Risk-benefit considerations for antibiotic treatment
- Proposed approach



Basic knowledge on good clinical practice in common infectious diseases in children

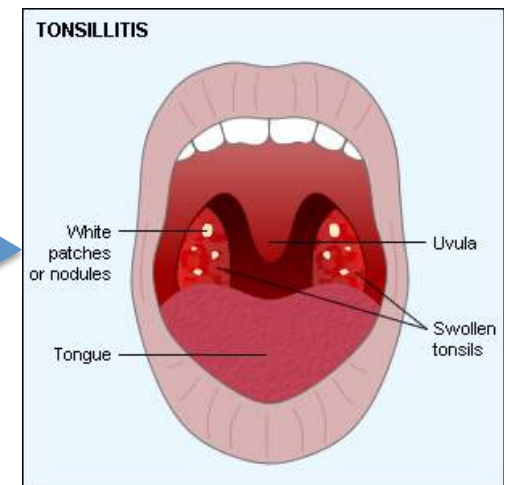
PHARYNGITIS

David can't eat today...

“David, my 5 year old son attending pre-school, was always healthy before nephrotic syndrome was discovered about 2 months ago. For about three days he has had a bad sore throat, especially when he swallows, and I wonder if this can be related to his kidneys, as he has been taking steroids for nearly 2 months. His fever was 38.5°C this morning. He is not eating much”

Ever seen these?

On clinical examination David is hot and you can feel his cervical lymph nodes. He has no signs of toxicity or respiratory distress. His throat is very red, with big tonsils with exudate and erythema.



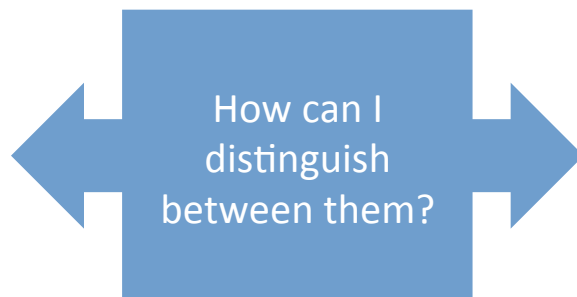
Background information: Pharyngitis

Viral aetiology

The most common (60-80%) associated features:

- Conjunctivitis
- Rhinitis
- Hoarseness
- Cough
- Diarrhoea
- Exanthema

Rhinovirus, adenovirus, EBV, Enterovirus, HSV, influenza virus, RSV, parainfluenzae virus, coronavirus, metapneumovirus



Many symptoms are similar; it is not easy to distinguish bacterial from viral streptococcal infection only on clinical grounds

Bacterial aetiology

***S. pyogenes* = Group A Strep** (20-30% children)

- Gram positive cocci
- May be present in the normal pharyngeal flora in children
- Several factors of virulence

• Other rare bacteria






- *Fusobacterium* (adolescents)
- *Neisseria*
- *Corynebacteria*

Clinical criteria more frequently met in bacterial infection

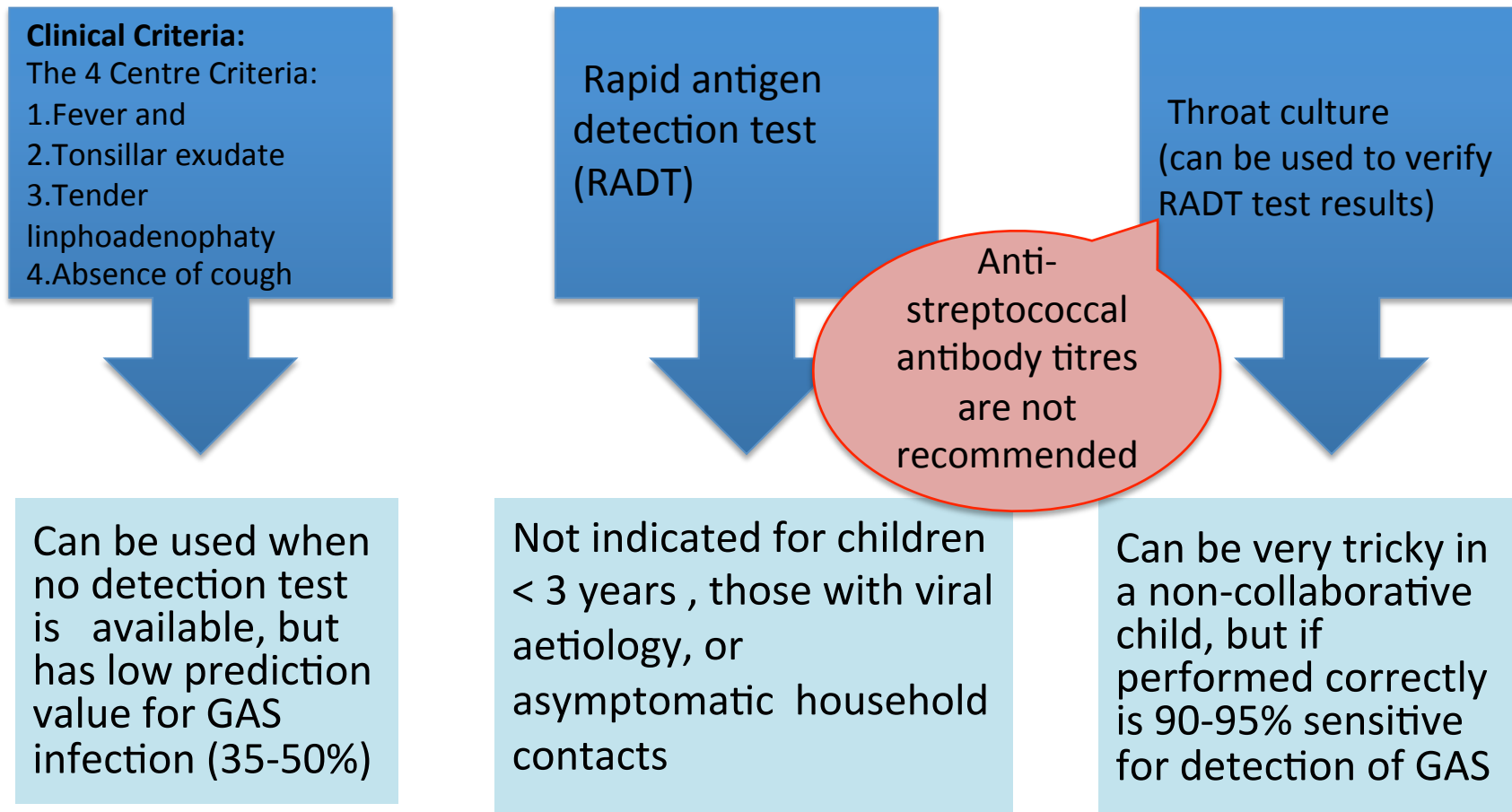
Epidemiological	Onset	Pharyngeal appearance	Associated symptoms
<ul style="list-style-type: none"> -Rare in children < 3 years -Older age 5-15 years -Winter-early spring 	<ul style="list-style-type: none"> -Sudden onset sore throat -Pain on swallowing -Presence of fever -Absence of cough 	<ul style="list-style-type: none"> -Tonsillo-Pharyngeal erythema (dark red) -Patchy exudate on tonsils -Soft palate petechiae -Tender anterior adenitis 	<ul style="list-style-type: none"> -Headache -Nausea, vomiting, abdominal pain -Cervical adenitis -Scarlatiniform rash

Specific considerations with Group A *Streptococcus*

Accurate identification of streptococcal pharyngitis followed by AB therapy can be important for improving clinical symptoms and for prevention of complications, but several facts should be considered

-  GAS pharyngitis is a self-limited illness even without AB treatment
-  Transmission: GAS Pharyngitis is transmitted by droplets from person to person, AB treatment can stop transmission.
-  Purulent complications: Retropharyngeal abscesses, peritonsillar abscesses, (quinsy), Lamierre's Syndrome are very rare (< 1%)
-  Carriers: GAS carriers should not be treated with antimicrobial therapy, they are unlikely to spread GAS pharyngitis or develop complications.
-  Non purulent complications
 - Scarlet fever
 - Acute post-streptococcal Glomerulonephritis (it is not prevented by antimicrobial therapy!)
 - Rheumatic fever (ARF) (still leading cause of acquired heart disease in children in parts of the world)
 - Post-streptococcal reactive arthritis

Possible diagnostic approaches towards acute Pharyngitis

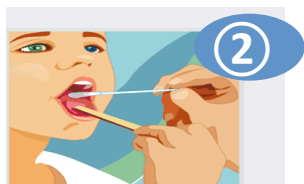


How can I make an informed decision on the use of antibiotics in children with acute pharyngitis?

Group A Strep-rapid test (RADT)



①



②

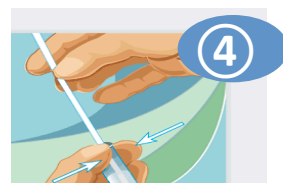
Detect the membrane group A specific carbohydrate antigens.



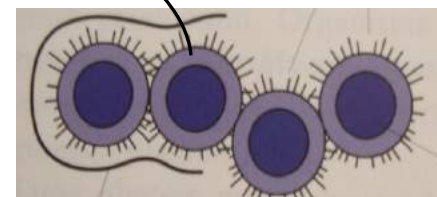
③

1 min

10x



④



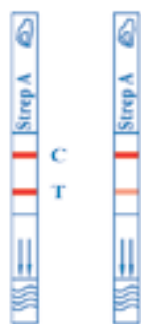
⑤

5 min

The performance of the test depends on the quantity of antigen in the swab. A swabbing with high charge of pus is important.

AB treatment can be proposed

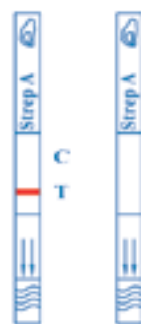
- Amoxicillin susceptibility: 100%
- Macrolide resistance: 2-20% by an **efflux pump mechanism**



Positive



Negative



Invalid

This is GOOD practice, we can avoid inappropriate administration of AB!

No Antibiotics

- Symptomatic treatment

Benefits & Risks of AB in Pharyngitis

Risks of AB Rx in pharyngitis

- Adequate AB treatment should follow bacteriological confirmation with RADT or swab.
- Clinical criteria for GAS pharyngitis are not certain
- Inappropriate AB Rx for large numbers of non-GAS pharyngitis
- Natural history of symptoms is towards a spontaneous resolution
 - Development of antimicrobial resistance among common pathogens
 - Risk for AB side-effects
 - Rash
 - Diarrhoea
 - Excessive diagnoses of allergy

Benefits of AB in pharyngitis

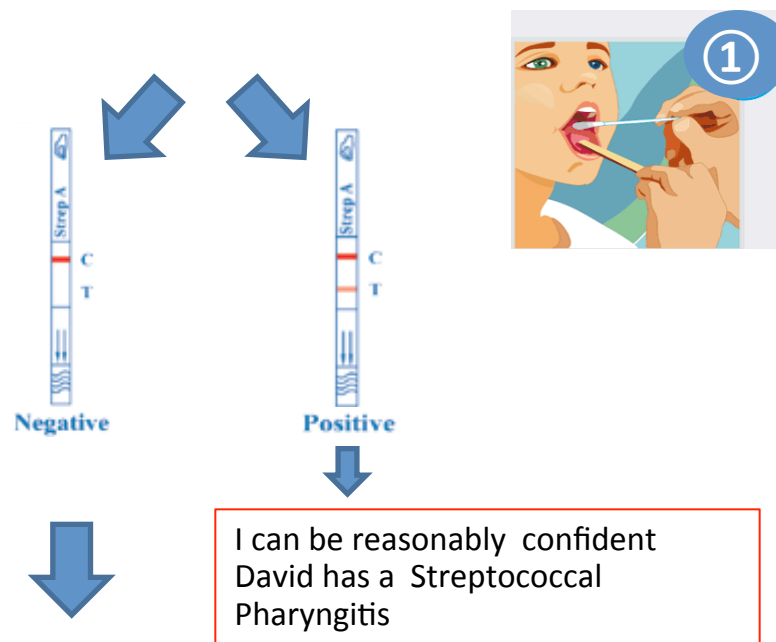
- AB are an effective treatment for bacterial Pharyngitis caused by GAS
- Positive RADT are highly specific for GAS and allow targeted Rx .
- Reduction of contagiousness from 6-14d to 24h for Strep A pharyngitis
- Reduction of complications
 - the greatest burden of disease, particularly invasive disease and post-streptococcal sequelae, is in children in resource-poor areas.
- Reduction of inflammatory complications not different between delayed or immediate AB treatment
- Antimicrobial therapy is of no proven benefit as treatment due to organisms other than GAS
- Family & Physician reassurance

A reasonable approach to David's sore throat...

Considering David's symptoms, age, and examination results, I must consider a possible GAS infection. What are my next steps?

- ✓ David is febrile and mum is worried
- ✓ David has just had a long treatment with steroids for GN
- ✓ You do not want to prescribe unnecessary treatment to him
- ✓ You need a quick answer for mum and a solid plan for his discharge

→ **You can use a RADT test !**



- You can perform a throat swab for culture for patients with underlying conditions if strep A test is negative
- Give antibiotics in case of positive *culture*

Antibiotic Regimens recommended for Group A Streptococcal Pharyngitis

If you decide to prescribe antibiotics you should follow your local guidelines.

Table 2. Antibiotic Regimens Recommended for Group A Streptococcal Pharyngitis

Drug, Route	Dose or Dosage	Duration or Quantity
For individuals without penicillin allergy		
Penicillin V, oral	Children: 250 mg twice daily or 3 times daily; adolescents and adults: 250 mg 4 times daily or 500 mg twice daily	10 d
Amoxicillin, oral	50 mg/kg once daily (max = 1000 mg); alternate: 25 mg/kg (max = 500 mg) twice daily	10 d
Benzathine penicillin G, intramuscular	<27 kg: 600 000 U; ≥27 kg: 1 200 000 U	1 dose
For individuals with penicillin allergy		
Cephalexin, ^b oral	20 mg/kg/dose twice daily (max = 500 mg/dose)	10 d
Cefadroxil, ^b oral	30 mg/kg once daily (max = 1 g)	10 d
Clindamycin, oral	7 mg/kg/dose 3 times daily (max = 300 mg/dose)	10 d
Azithromycin, ^c oral	12 mg/kg once daily (max = 500 mg)	5 d
Clarithromycin, ^c oral	7.5 mg/kg/dose twice daily (max = 250 mg/dose)	10 d

Antibiotic Regimens recommended for GAS Pharyngitis

- A course of 10 days of oral penicillin V is recommended in view of rheumatic fever prevention but compliance is very low
 - Benzathine Penicillin G Intramuscular can be used in those patients unlikely to complete a full course of treatment, but is very rare approach in western Countries.
 - Alternative regimens with comparable effectiveness are high dose amoxicillin twice a day or narrow spectrum cephalosporins for 5-6 days.
-
- You decide to initiate antibiotic treatment with high dose Amoxicillin a day for David for a week.
 - David's mum rings you after 2 days. He is much better and has been afebrile for a full day today. His appetite has come back and he is much happier.

References

- Shulman ST et al. Clinical Practice Guideline for the diagnosis and management of group A streptococcal pharyngitis: 2012 update by the Infectious Diseases Society of America. *Clin Infect Dis* 2012 Nov 15;55(10): 1279-82.



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ACUTE OTITIS MEDIA

James has a fever and is refusing food...

James's mother brings her nine month-old son to your office early on Monday morning. His fever spiked in the previous afternoon but later he had a good meal. He woke up at 2 am crying and little could be done to calm him. He finally could go back to sleep after being given a dose of 5 mL Paracetamol. In the morning he refused his milk and appeared restless and possibly hot again.

You know James, he has no previous medical problems. His mum reports that he was recently introduced into a day care nursery for three half-days a week.

Examination

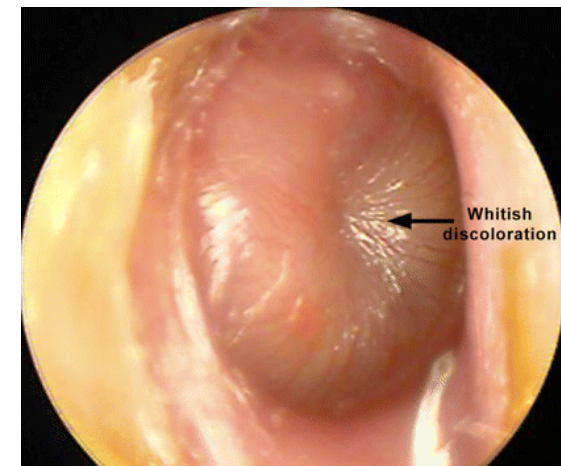
Irritable, with normal consciousness, not smiling.

Signs of upper airway infection.

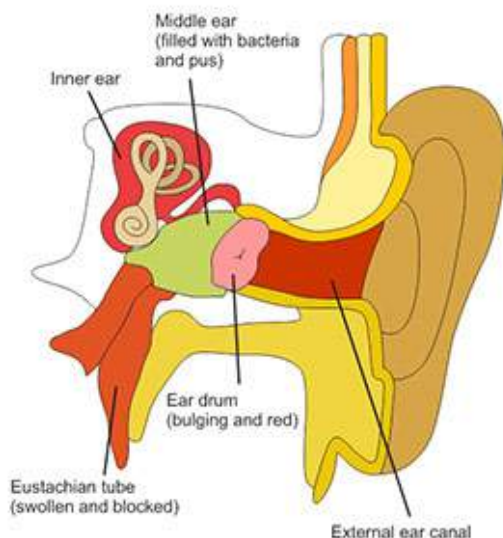
$T^{\circ}=38.9^{\circ}\text{C}$

No respiratory signs, normal general examination.

Mum helps you and you manage to check his ears. This is what you see: (left otoscopy)



Background information: acute otitis media



Highest incidence among children between 6 months and 2 years of age

By 3 years of age, 80% of children have had at least one episode of acute otitis media

Episodes of upper respiratory viral infection (adenovirus, rhino, influenza, RSV) often precede or are concurrent with development of AOM

Middle ear fluid pathogens in AOM:
Streptococcus pneumoniae & *Hemophilus Influenzae* (80-85%)
Moraxella Catarrhalis (5-10%)
Streptococcus Pyogenes (5%)

What should I consider in the approach to a child with suspected acute otitis media?

- AOM is the most commonly reported indication for antibiotic treatment in children
- ➔ There is serious problem with over-diagnosis and overprescribing of AB for AOM in children
- Precise microbiologic diagnosis requires a sample of middle ear fluid
- ➔ Middle ear fluid sampling is not possible
- Natural history of the majority of AOM episodes is a spontaneous resolution of pain and fever in 5-7 days
- ➔ Is antibiotic treatment necessary?
- Rare but serious suppurative complications of AOM can occur (mastoiditis, hearing loss, meningitis)
- ➔ Incidence in children is not influenced by initial treatment with antibacterial agents

How can I make an informed decision on the use of antibiotics in children with suspected acute otitis media ?

A possible strategy for treating James...

1) How likely is this to be a real acute otitis media?

Focus on TM: must be cloudy, bulging with impaired mobility

1. Check history of acute onset

- **Otalgia**
- **Irritability**
- **Fever**
- **Excessive crying**

The symptoms are often aspecific

2 Check tympanic membrane for signs of:

Middle-ear effusion (MEE)

- Fullness or bulging of TM
- Limited or absent mobility of TM
- Air-fluid level behind the TM
- Otorrhea

Middle-ear inflammation

- Distinct erythema of TM
- Distinct otalgia

Can you differentiate AOM from OME ?

3. Assess and check for sign of severe illness or presence of suppurative complications

If this is present, refer the child accordingly

4. Treat pain with Paracetamol or Ibuprofen following local guidelines for pain management, adequate dose and age appropriate indications

This is what James' mum has reported

OME (Otitis Media with Effusion) is a sterile inflammatory state of the middle ear that resolves spontaneously; AB are not appropriate or beneficial in this case

A possible strategy for treating James...

2) I am reasonably confident James has AOM, should I prescribe an antibiotic?

→ Observation without use of antibacterial agents (or delayed AB prescribing) is an option for selected children with uncomplicated AOM

But it is important to consider and weight the presence of other factors that might influence your decision how to treat the AOM:

- ✓ **How old is the child?** Young child (< 6 months or < 2 years) or bilateral AOM, otorrhea
- ✓ **Has pain and fever been assessed?** and adequately treated?
- ✓ **Can the child be adequately supervised?** Inform the parents regarding the treatment plan and expected illness progression
- ✓ **Has adequate follow up appointment been agreed upon?**

Antibiotic choice for AOM

If you decide to prescribe antibiotics you should follow your local guidelines.

The following tables are the recommended antibacterial agents in the AAP Guidelines for AOM published in 2013.

Recommended Antibiotics for (Initial or Delayed) Treatment and for Patients Who Have Failed Initial Antibiotic Treatment

Initial Immediate or Delayed Antibiotic Treatment		Antibiotic Treatment After 48–72 h of Failure of Initial Antibiotic Treatment	
Recommended First-line Treatment	Alternative Treatment (if Penicillin Allergy)	Recommended First-line Treatment	Alternative Treatment
Amoxicillin (80–90 mg/kg per day in 2 divided doses)	Cefdinir (14 mg/kg per day in 1 or 2 doses)	Amoxicillin-clavulanate ^a (90 mg/kg per day of amoxicillin, with 6.4 mg/kg per day of clavulanate in 2 divided doses)	Ceftriaxone, 3 d Clindamycin (30–40 mg/kg per day in 3 divided doses), with or without third-generation cephalosporin
or	Cefuroxime (30 mg/kg per day in 2 divided doses)	or	Failure of second antibiotic
Amoxicillin-clavulanate ^a (90 mg/kg per day of amoxicillin, with 6.4 mg/kg per day of clavulanate [amoxicillin to clavulanate ratio, 14:1] in 2 divided doses)	Cefpodoxime (10 mg/kg per day in 2 divided doses)	Ceftriaxone (50 mg IM or IV for 3 d)	Clindamycin (30–40 mg/kg per day in 3 divided doses) plus third-generation cephalosporin
	Ceftriaxone (50 mg IM or IV per day for 1 or 3 d)		Tympanocentesis ^b Consult specialist ^b

IM, intramuscular; IV, intravenous.

^a May be considered in patients who have received amoxicillin in the previous 30 d or who have the otitis-conjunctivitis syndrome.

^b Perform tympanocentesis/drainage if skilled in the procedure, or seek a consultation from an otolaryngologist for tympanocentesis/drainage. If the tympanocentesis reveals multidrug-resistant bacteria, seek an infectious disease specialist consultation.

^c Cefdinir, cefuroxime, cefpodoxime, and ceftriaxone are highly unlikely to be associated with cross-reactivity with penicillin allergy on the basis of their distinct chemical structures. See text for more information.

Risks & benefits of antibiotic use in AOM

Risks

- Antibiotic treatment has no effect for :
 - Reducing pain on day 1
 - Preventing suppurative complications
 - Accelerating resolution of middle ear fluid
 - Unwanted AB side-effects
 - Diarrhoea
 - Vomiting
 - Rashes
 - Allergy/Anaphylaxis
 - Increased AB resistance in community
 - Higher rate of treatment failure
 - Use of low dosage dose or incorrect course

Benefits

- The treatment is always empirical
- Family reassurance
- Can be safe to prescribe empirically even among infants and children < 2 years

1-Rosenfeld, Laryngoscope 2003

2-Little P, Br J Gen Pract 2006

3-Spiro DM, JAMA 2006

4-Coker, JAMA 2010

A reasonable approach to James's problem...

You consider James is only 9 months old, his temperature is 38.5°C now and his mum appears very concerned for his distress. You are certain that James has AOM but at present his condition is not severe and you have time to observe the situation. You reassure and explain to his mum what you think and that she needs to give him Paracetamol regularly. Nevertheless, you decide to discharge him with an antibiotic prescription (Amoxicillin at 80 mg/kg/24 hours) and instruct his mum that if symptoms do not improve within 2 days, she can call you and a different treatment can be agreed upon.

You review James 2 days later. He is much better and has been treated with only Paracetamol for about 24 hours and his distress has disappeared.

James mum asks if anything can be done to prevent further episodes of AOM, can you advise her on this?

References

- The diagnosis and management of acute otitis media. American Academy of Pediatrics subcommittee on management of acute otitis media. *Pediatrics*. 2013 February; DOI: 10.1542/peds.2012-3488
- Respiratory tract infections – antibiotic prescribing. NICE clinical guidelines 69, issued July 2008
- Wald ER. Acute otitis media and acute bacterial sinusitis. *Clin Infect Dis* 2011 May;52(Suppl 4):S277-83.
- Wald ER, Demuri GP. Antibiotic Recommendations for Acute Otitis Media and Acute Bacterial Sinusitis in 2013 - The Conundrum. *Pediatr Infect Dis J* 2013 Jan 21. [Epub ahead of print]



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COMMUNITY ACQUIRED PNEUMONIA

Albert has a bad cough...

Albert's father brings his 12 years old boy to your attention. He wants Albert to be assessed because he has been coughing for five days now. He was originally diagnosed with a viral infection by his regular doctor, who suggested salbutamol and steroid inhalers, which Albert has needed before. Albert has many allergies, mostly to foodstuffs and pollen. He likes to play football, and he had continued to be able to play until yesterday, when he developed a high fever and the cough got worse, on 2 occasions resulting in Albert having to throw up.

You examine Albert, who is attentive and able to co-operate with the examination. However, you note that his respiratory rate is 32/min and he is slightly out of breath after undressing. He also has a temperature of 39.2°C. You hear crackles over the right lung and find Albert's oxygen saturation to be 93% in room air. His throat is normal and he does not have a cold. You feel Albert has community-acquired pneumonia (CAP).

Background information: Community acquired pneumonia

In children, CAP is most commonly due to viral infection, but can be bacterial with different pathogens important at different ages

Viruses (20-45%)

- Influenza virus
- Parainfluenzae virus
- RSV
- Rhinovirus
- Adenovirus
- Coronavirus
- Enterovirus
- Bocavirus
- Metapneumovirus

Bacteria

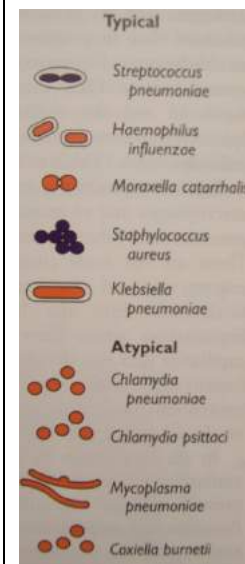
Typical

- *Streptococcus pneumoniae*
- *Streptococcus group A*
- *Staphylococcus aureus* (*H. influenzae* & *M. catharralis*)

Atypical

- *Mycoplasma pneumoniae*
- *Chlamydia pneumoniae*
- *Bordetella pertussis*

Curr Opin Pulm Med 2005



A microorganism is identified in less than 10% of cases

neonates	1m-3m	4m-5y	5y-15y
Strep B Gram neg bacilli (E. coli)	Chlamydia trachomatis Streptococcus pneumoniae Viruses Bordetella pertussis	Viruses Streptococcus pneumoniae Mycoplasma pneumoniae	Mycoplasma pneumoniae Streptococcus pneumoniae Chlamydia pneumoniae Viruses

What is pneumonia?



In some studies, viral aetiologies of CAP have been documented in up to 80% of children younger than 2 years.

The distinctions between typical – bacterial, atypical – bacterial and viral cases are difficult. Laboratory tests and chest radiography could help but are not conclusive.

Pneumonia is an acute or chronic inflammation of the lung caused by infection. Bacteria, viruses, fungi or parasites can cause pneumonia.

The most important criteria for diagnosis are clinical signs and symptoms

Pneumonia definitions:

-  very sensitive: e.g. fever and cough → for epidemiologic considerations
-  very specific: e.g. clinical symptoms and signs + radiologic documentation / microbiologic confirmation → defined by government regulatory agencies for approval of antimicrobials to treat pneumonia

Lower respiratory tract infection (LRTI) can be synonymous with CAP when defined in a way that is clinically oriented, to assist practitioners with diagnosis and management.

How likely is this to be a community acquired pneumonia?

Signs of Respiratory Distress

1. Tachypnea, respiratory rate, breaths/min^a

Age 0–2 months: >60

Age 2–12 months: >50

Age 1–5 Years: >40

Age >5 Years: >20

2. Dyspnea

3. Retractions (suprasternal, intercostals, or subcostal)

4. Grunting

5. Nasal flaring

6. Apnea

7. Altered mental status

8. Pulse oximetry measurement <90% on room air

^a Adapted from World Health Organization criteria.

Albert has some signs of distress; By definition he suffers from CAP.

CAP in children is defined as the presence of signs and symptoms of pneumonia in a previously healthy child caused by an infection that has been acquired outside of the hospital.

More directly relevant to evaluating severity of disease in CAP is the simple measurement of oxygen saturation by pulse oximetry.

Diagnostic approach towards CAP

CAP is a clinical diagnosis, therefore no further testing is required to identify CAP. However, some further evaluation and tests may be helpful to determine appropriate CAP management

Patient will be managed as outpatient

Consider

- 🌐 Influenza virus and other viral test, tests for *Mycoplasma* (depending on age and clinical signs) → to help delineate aetiology
- 🌐 Pulse oximetry → rule out need for hospitalisation

Probably not necessary

- 🌐 Blood cultures
- 🌐 Sputum → children are rarely able to expectorate
- 🌐 Pneumococcal urinary antigen → often false – positive
- 🌐 Complete blood cell count and acute –phase reactants
- 🌐 Routine chest radiographs

Patient will be managed in hospital

Consider

- 🌐 Influenza virus and other viral test, tests for *Mycoplasma* (depending on age) → to help delineate aetiology
- 🌐 Pulse oximetry → confirm need for hospitalisation
- 🌐 Blood cultures → higher rates of bacteraemia if unwell
- 🌐 Sputum → if child is able to expectorate
- 🌐 Complete blood cell count and acute –phase reactants → to assess response to therapy
- 🌐 Routine chest radiographs or ultrasound → to assess for pleural effusion

Probably not necessary

- 🌐 Pneumococcal urinary antigen → often false – positive

Does this child with CAP require hospital admission?

There are some situations when admission to hospital should be considered in a child with CAP.

1. Children and infants who have moderate to severe CAP, as defined by several factors, including respiratory distress and hypoxemia (sustained peripheral oxygen saturation $\leq 90\%$ at sea level) should be hospitalized for management in a setting where skilled paediatric nursing care can be provided.
2. Infants less than 3–6 months of age with suspected bacterial CAP (but also frequently those with viral aetiology) are likely to benefit from hospitalization, especially when there are feeding problems.
3. Children and infants with suspected or documented CAP caused by a pathogen with increased virulence, such as community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) should be hospitalized. These children will be generally very unwell and remain so despite treatment with antibiotics.
4. Children and infants for whom there is concern about careful observation at home or who are unable to comply with therapy or unable to be followed up should be hospitalized.

It looks like Albert can be managed at home. The most common reasons for admission are hypoxaemia and feeding difficulties/refusal to drink.

CAP – a strategy to determine whether treatment is required

Decide on where to manage the patient: based on clinical severity of symptoms and patient characteristics

Choice of diagnostic test: if you decide to manage patient at home possibly 1) no blood sample, 2) viral antigen, 3) no X-ray.

If bacterial aetiology is felt likely (see next slide) and viral antigen testing (if relevant in your area) is negative, antibiotic treatment should be given

- *S.pneumoniae* continues to be the most common cause of bacterial pneumonia and therefore should be covered
- In some patients may need to consider a macrolide if atypical bacteria are suspected

Route of treatment: oral

Duration of treatment should be between 7 to 10 days, but local guidelines may vary

Follow-up:

- If possible review patient on antibiotic treatment within 48-72 hours
- Change treatment and refer to hospital if worsening

Limited role for blood tests in screening (CRP, PCT, WBC, ESR) but if all or most of these are elevated bacterial aetiology is highly probable

Albert can be managed at home.
You take a full blood count and CRP, both of which are elevated.
Testing for influenza is negative.
You are not able to perform an X-ray at your practice.

On the basis of his clinical signs
Albert is most likely to have disease caused by typical bacteria.
Therefore the treatment should cover these first and foremost.

IDSA CAP guideline, 2011

Differentiation of bacterial and viral CAP in children, Don et al. Pediatr Int. 2009

Antibiotic choice for CAP – a strategy

Presentation

- Bilateral pneumonia, well child with signs of viral infection (pharyngitis, runny nose, wheezing, diarrhoea etc.)
- Bilateral pneumonia, moderately unwell
- Bilateral pneumonia, severely unwell
- Lobar/segmental pneumonia, mild
- Lobar/segmental pneumonia, moderate to severe

Most probable cause

- Viruses
- Investigate for *Mycoplasma*, *Influenza A/B*, *S. pneumoniae*
- *S. pneumoniae*, *S. pyogenes*, consider *S. aureus* in case of necrotizing pneumonia/abscess
- *S. pneumoniae*, *S. pyogenes*
- *S. pneumoniae*, *S. pyogenes*

First line AB treatment

- No AB therapy required + strict follow-up (even with viral infection children can get unwell)
- Amoxicillin or equivalent; consider macrolide first if >5yo
- Requires hospitalisation
- Amoxicillin or equivalent
- Consider assessment in hospital

Duration of treatment must be of 7 – 10 days

Risks & Benefits of antibiotic use in CAP

Risks of AB in CAP

- Unnecessary AB treatment in children with viral CAP
- Unnecessary broad-spectrum antibiotic treatment in children most likely to have *S.pneumoniae* infection responsive to penicillin
- Prescribing errors resulting in inadequate treatment
- Unwanted AB side-effects
 - Diarrhoea
 - Vomiting
 - Rashes
 - Allergy/Anaphylaxis
- Selection of resistant bacteria
 - Risk of re-consultation for an infection caused by a resistant microorganism

Benefits of AB in CAP

- In bacterial CAP AB are effective treatment. There are no benefits in case of viral CAP, but distinguishing viral and bacterial CAP can be difficult.
- In typical *S.pneumoniae* lobar pneumonia AB treatment may prevent suppurative complications
- Family & Physician reassurance, however review is important to monitor progress

A reasonable approach to Albert's problem...

You explain to Albert and his father that you suspect CAP. You feel that Albert would benefit from antibiotics and that the symptoms and signs are not severe enough to require an admission to hospital. When you perform a rapid screen for influenza, the test comes back negative. Luckily, and despite his many allergies, Albert's father confirms that he has had penicillin antibiotics previously without any symptoms suggestive of allergy. Therefore you propose to start an oral antibiotic treatment, choosing as first line amoxicillin. You also suggest to discontinue the inhalations for now. You warn Albert that he may experience some diarrhoea, but that he should hopefully feel better within a few days. You ask to see Albert again in a couple of days to assess his progress and to review your treatment.

You review Albert 2 days later. He is much better and has been afebrile for a day although still coughing. There is no wheezing on auscultation. You propose to go on with antibiotic treatment for another 5 days. You ask Albert's father to contact you if he get worse again and you reassure both that the cough should eventually settle down.

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The basics of rational and prudent antibiotic use for common childhood infections in ambulatory care

ACUTE RHINOSINUSITIS

Sophia has rhinorrhoea, headache and cough...

Sophia's mother brings her 8 year old daughter to your attention. Sophia has been complaining about persistent, thick nasal discharge, nasal congestion, headache and cough for 13 days now. The cough is worse at night but there is no wheezing. Every day, in the afternoon, she has a temperature spike of 38.2°C. She doesn't vomit and has no rashes or other symptoms. There are no signs of referred nasal foreign bodies. No allergy or other illnesses are mentioned by Sophia's mother.

You examine Sophia, who is breathing well, without signs of dyspnoea; no fever at the moment. You don't find any eye abnormalities, her tympanic membranes are clear. She has nasal congestion with thick yellow purulent mucus in the posterior nasal pharynx. She has mild tenderness to palpation of her maxillary sinuses. Her oral pharynx is non erythematous. Her breath is malodorous. She has no obvious dental caries or pain on tapping of her teeth. You feel Sophia has an acute sinusitis.

What is sinusitis?

Acute rhinosinusitis is defined as an inflammation of the mucosal lining of the nasal passage and paranasal sinuses lasting up to 4 weeks.

It can be caused by various inciting factors including allergens, environmental irritants, and infection by viruses, bacteria, or fungi.

A viral aetiology associated with a upper respiratory tract infection (URI) or the common cold is the most frequent cause of acute rhinosinusitis

Background information: acute sinusitis

Approximately 80% of episodes of acute bacterial sinusitis are preceded by a viral URI

The prevalence of a bacterial infection during acute rhinosinusitis (ABRS) is estimated to be 2%–10%, whereas viral causes account for 90%–98%

Aetiologies of ABRS:

S. pneumoniae (20-30%)

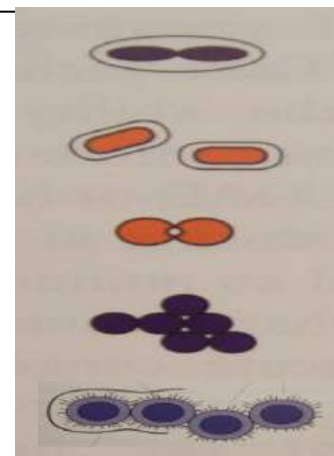
H. Influenzae (30%)

M. catarrhalis (8-11%)

Less commonly also:

S. aureus, *S. pyogenes*

No growth in 30%



Antibiotics are frequently prescribed for patients presenting with symptoms of acute rhinosinusitis, being the fifth leading indication for antimicrobial prescriptions by physicians in office practice

To decide whether to treat Sophia for sinusitis, further evaluation needs to take place

How likely is this to be a ABRS?

Clinical Criteria for the Diagnosis of ABS: 3 patterns of onset

Persistent symptoms

Nasal congestion, rhinorrhea, or cough ≥ 10 days' duration without improvement

Severe symptoms

Temperature $\geq 38.5^{\circ}\text{C}$ for 3–4 days
Purulent rhinorrhea for 3–4 days

Worsening symptoms

Return of symptoms after initial resolution
New or recurrent fever, increase in rhinorrhea, or increase in cough

Sophia has persistent symptoms. It seems to be a bacterial infection

Overprescription of antibiotics is a major concern in the management of acute rhinosinusitis, largely due to the difficulty in differentiating ABRS from a viral URI (upper respiratory infection)

Imaging studies cannot distinguish inflammation caused by viruses from that caused by bacteria

Diagnostic approach towards Sinusitis

The diagnosis of Acute bacterial sinusitis in children is clinical and based on history, with the use of the criteria listed in the previous slide

Imaging studies (plain-film radiography, computed tomography, magnetic resonance imaging MRI, and ultrasonography) show signs of sinus inflammation but are not recommended in patients with uncomplicated infection, given the low specificity of these studies. Cultures are not indicated.

Imaging may be useful in ruling out a diagnosis of sinusitis when the findings are normal. CT or MRI is warranted in patients with symptoms or signs suggesting complicated sinusitis (e.g., severe headache, seizures, focal neurologic deficits, peri-orbital oedema, or abnormal intraocular muscle function) and may show drainable fluid collections within the cranium or the orbit



You don't need any further tests to confirm Sophia's sinusitis.

Sinusitis – a strategy to determine whether treatment is required

Diagnostic approach: in uncomplicated cases, we don't perform radiological imaging or microbiological test.

- The role of antibiotic therapy in acute bacterial sinusitis is controversial, with few studies providing discordant results. Antibiotics to be suggested if strong suspect of bacterial aetiology
- Nasal saline washes or sprays don't provide substantial relief from symptoms
- Intranasal glucocorticoids provide only slight relief
- Antihistamines and decongestants have been shown to be of no benefit

Route of treatment: oral

First line treatment: Amoxiclavulanate

Duration of treatment : 10 – 14 days

Follow-up:

Sophia can be managed at home.
You don't need to perform any further test, including nasal swab culture or CT or MRI

On the basis of her clinical signs
Sophia is most likely to have disease caused by usual bacteria.
Therefore typical first-line antibiotic treatment should be suggested.

Risks & Benefits of antibiotic use in Sinusitis

• Risks of AB: important individually and for the community

- Use of unnecessary AB for the treatment of non bacterial infection
- Risk for AB side-effects
 - Rash, Diarrhoea, Excessive diagnoses of allergy
- Selection & dissemination of AMB resistance
- Re-consultations for side-effects and resistant bacteria related infections
- Unnecessary costs
 - It is estimated that unnecessary AB treatments in acute sinusitis cost ...
- Among patients with acute rhinosinusitis, a 10-day course of amoxicillin compared with placebo did not reduce symptoms at day 3 of treatment.¹
- Adult patients in general practice with clinically diagnosed acute rhinosinusitis experienced
 - no advantage with amoxicillin-clavulanate
 - more likely to experience adverse effects.²
- In a meta-analysis of 9 randomized controlled trials (n=2547):
 - the mean NNT* patients with AB was 15 (95% CI, 7 to 190) before one additional patient benefits from AB treatment.³
 - **64 to 80% of patients were cured at 14 days even without antibiotic treatment.**^{3,4}
- Moderate symptom severity does not distinguish a bacterial from a viral infection

• Benefits of AB: Small AB efficacy demonstrated on appropriately identified patients^{5,6}

- Persistent symptoms (nasal discharge or cough for ≥ 10 days without improvement),
- OR acutely worsening symptoms (nasal discharge or daytime cough worsening after 5-6 days with new onset fever, headache or worsening in nasal discharge after transient improvement),
- OR severe symptoms (temperature $\geq 39^{\circ}\text{C}$ and purulent nasal discharge or facial pain for at least 3-4 consecutive days).
- In those cases AB are thought to decrease both the duration and the severity of symptoms and potentially prevent suppurative complications
 - First-line treatment⁶
 - Amoxicillin/clavulanate 10 days
 - Amoxicillin 10–14 days
 - Second-line agents
 - Clarithromycin 14 days
 - Azithromycin 3 days
 - Trimethoprim–sulfamethoxazole 10 days
 - Clindamycin + C2G or C3G (for Pen allergy)

1-Garbutt, JAMA 2012

2-Bucher, Arch Intern Med 2003

3-Young, Lancet 2008

*NNT, number needed to treat

4-Ahovuo-Saloranta, Cochrane 2008

5-Curr Opin Infect Dis 2012

6-IDSA, Clin Infect Dis 2012

A reasonable approach to Sophia's problem...

You explain to Sophia and her mother your diagnosis of sinusitis and its suspected bacterial origin. You feel that Sophia would benefit from antibiotics and that she can be treated at home. You explain that it's not useful to perform an x-Ray or a CT scan for a better diagnosis. You ask Sophia's mother about any allergy to antibiotics and you propose to start an oral antibiotic treatment, choosing as first-line high dose amoxicillin plus clavulanic acid. You also suggest not to give steroids, nasal washes, decongestants or other drugs. You warn Sophia that she may experience some diarrhoea, but that she should hopefully feel better within a few days. You ask to see Sophia again in ten days to assess her progress.

You review Sophia 10 days later. She is much better and has been without cough, rhinorrhea and headache for 2 days. You propose to stop with antibiotic treatment.

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The basics of rational and prudent antibiotic use for common childhood infections in ambulatory care

URINARY TRACT INFECTION

Suzie is attending with a fever...

Suzie's mother brings 7 month-old Suzie to your office. She has come to see you, because Suzie has had a fever up to 39.5 °C for the last 2 days. She is refusing her feeds and has vomited several times. Her mother has not noted any diarrhoea, which she was expecting because Suzie's older sister had a bad tummy the previous week. Suzie has not been quite herself those last two days. Despite having occasionally wanted to play a little, she seemed fretful and clingy. The family went to see an emergency office physician when the vomiting started. He was unable to find a source for the fever, but found Suzie to be quite well in herself. He suggested Paracetamol and frequent intake of sips of electrolyte solution, thinking that this might be a vomiting bug. Suzie's mother is bringing her in, because she worries as things are not improving.

You examine Suzie and find her attentive, but not very playful. She has a temperature of 38.8°C, pulse rate of 148/min and respiratory rate of 25/min. Her hands and feet are warm and she looks pink. There are no signs of dehydration and Suzie's fontanel is soft and level. The rest of the examination is normal. You suspect Suzie has a urinary tract infection.

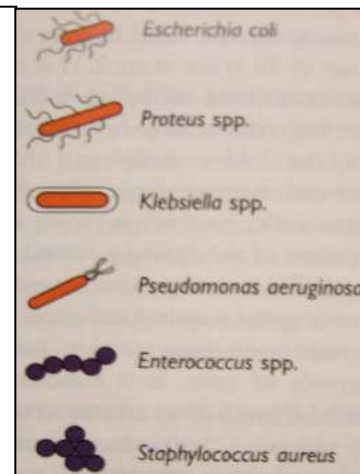
Background information: community-acquired urinary tract infection

In previously healthy children, UTI is a bacterial disease most commonly due to infection by Gram-negative bacilli

Escherichia coli (80-85%)
Proteus mirabilis (5-10%)
Klebsiella pneumoniae (5%)

Less commonly also:

Enterococcus spp
Enterobacter spp
Pseudomonas aeruginosa
Staphylococcus aureus



Relevant bacteriological information for treatment

Many enterobacteriaceae isolates (*E. coli*, *Klebsiella spp.*, *Enterobacter spp.*) are now resistant to commonly used antibiotics. For example, resistance of *E. coli* to

- amoxicillin is mostly too high (40-60%) to recommend this AB as a first line UTI treatment.
- co-amoxiclav varies from 0 to 30 %.

ESBL producing enterobacteriaceae are increasingly isolated driven by but also limiting the usefulness of cephalosporins.

Enterococci are naturally resistant to all cephalosporins.

To decide whether to treat Suzie for UTI, further evaluation needs to take place

How likely is this to be urinary tract infection?

Individual Risk Factors: Girls

White race
Age < 12 mo
Temperature $\geq 39^{\circ}\text{C}$
Fever ≥ 2 d
Absence of another source of infection



Individual Risk Factors: Boys

Nonblack race
Temperature $\geq 39^{\circ}\text{C}$
Fever > 24 h
Absence of another source of infection



Suzie has several risk factors for UTI

When young children remain febrile without developing symptoms strongly suggestive of an alternative diagnosis, UTI should be considered and ruled out

Consider the diagnosis of febrile UTI (which can be pyelonephritis) in case of:

-  unexplained sepsis, particularly in children less than 24 months
-  unexplained fever for >48h

Consider the diagnosis of cystitis in case of:




-  Incontinency, haematuria, urgency of micturition
-  Low weight gain, vomiting, decreased feeding in babies

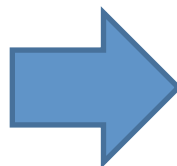
This applies to Suzie.

Diagnostic approach towards suspected UTI

To assess whether a UTI is present collect an uncontaminated urine sample

OPTIONS for appropriate urine sampling

-  Clean-catch → usually acceptable, requires patience and must be clean catch!
-  Supra-pubic aspiration or In-out bladder catheterization → may not be acceptable to parents, can be difficult if provider has little experience of procedure
-  A urine bag should be a last resort → results may not be interpretable



And then?

1. Urine dipstick → Leukocyte esterase (LE) and nitrite testing helps to identify UTI
2. Urine microscopy → Pyuria and bacteriuria are suggestive of UTI
3. Urine culture → will confirm UTI, identify causative organism and allow for antibiotic therapy to be adapted accordingly

Suzie's urine dipstick is positive for LE but negative for nitrite, you are unable to perform urgent microscopy in your practice.

What constitutes a UTI?

To confirm UTI the combination of 1) symptomatic child, 2) abnormal urine dipstick/microscopy and 3) a positive culture is required

What constitutes a positive urine culture?

Different cut-offs for growth are applied

🌐 AAP: $\geq 50,000$ cfu/ml

🌐 NICE: $\geq 100,000$ cfu/ml

Different cut-offs may be in use for different types of urine sample

Growth should involve a uropathogen (see background)

The accurate diagnosis of UTI may prevent renal complications and will reduce overtreatment. In some settings in Europe it may not be felt necessary to obtain urinary culture for certain age groups if LE and nitrite are positive on dipstick.

Suzie's urine results are suggestive for UTI. Taking a urine culture will help you to confirm or rule out the diagnosis of UTI.

UTI treatment – a strategy for choosing treatment

Once UTI is highly likely or is confirmed, antibiotic treatment is necessary while awaiting cultures

Despite a nitrite negative dipstick you may want to start Suzie on antibiotics empirically, because she has been unwell for a little while.

Deciding on need for referral: if serious illness is suspected or the patient is very young (e.g. <3 months) referral to secondary care should be considered

Determine location: Clinical evaluation to differentiate cystitis and upper urinary tract infection (pyelonephritis) - generally with fever and loin pain indicating upper urinary tract infection

Choice of antibiotic: This is determined by 1) common pathogens, 2) local resistance patterns (if available) and 3) availability of local guidelines

Route of treatment: Oral and intravenous are equally efficacious, but may be of different benefit clinically

Duration of treatment should be between 7 to 14 days for upper UTI and 3 to 5 days for lower UTI

Antibiotic choice for UTI– a strategy

Some treatment choices...

<u>Oral</u>	<u>Intravenous</u>
Amoxicillin-clavulanic acid	Ceftriaxone
Trimethoprim-sulfamethoxazole	Cefotaxime
Cefixime	Ceftazidime
Cedpodoxime	Gentamicin
Cephalexin	Tobramycin
Cefuroxime axetil	Piperacillin

For Suzie may want to consider Amoxicillin – clavulanic acid in areas of low resistance or an oral cephalosporin

Benefits & Risks of antibiotic use in UTI

Risks of AB in UTI

- Unnecessary AB treatment if UTI not formally diagnosed
- Unnecessary broad-spectrum antibiotic treatment when a urinary culture has not been performed
- Prescribing errors resulting in inadequate treatment
- Unwanted AB side-effects
 - Diarrhoea
 - Vomiting
 - Rashes
 - Allergy/Anaphylaxis
- Selection of resistant bacteria
 - Risk of re-consultation for an infection caused by a resistant microorganism

Benefits of AB in UTI

- Simple screening tests are available with good sensitivity for UTI
- A microbiological diagnosis and therefore identification of clear indication for treatment can usually be made
- AB are an effective treatment for UTI and may avoid suppurative complications of the disease
- Long-term renal damage may be reduced if UTIs are promptly and aggressively treated
- Family & Physician reassurance, but with option to discontinue if diagnosis is not confirmed

A reasonable approach to Suzie's problem...

It is agreed to evaluate Suzie for possible UTI. The options for obtaining a urine sample are discussed with Suzie's mum. You feel that a UTI is quite likely. Therefore you suggest to Suzie's mother to perform an in-out catheter. Urine dipstick is positive for LE but negative for nitrite. You therefore send off a sample for culture and decide to start Suzie on oral antibiotic treatment, choosing the antibiotic according to your local guidelines for treatment of UTI. You ask to see Suzie again in a couple of days to assess her progress and to review your treatment with culture and sensitivity results. You arrange for further imaging according to your national UTI guidelines. You instruct Suzie's mother to contact you or her local emergency department immediately in case of persistent vomiting or any deterioration.

You review Suzie 3 days later. She is much better and has been afebrile for around 36 hours. Her urine culture has shown 1,000 cfu/ml mixed growth. You therefore decide to stop antibiotic treatment at this point. You ask Suzie's mother to contact you should she get worse again over the course of the next days.

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The basics of rational and prudent antibiotic use for common childhood infections in ambulatory care

SKIN AND SOFT TISSUE INFECTION

Tom has a rash...

Tom's dad brings 3 year-old Tom to your office. He and Tom have come to see you, because Tom has developed a rash over the last 2 days. This has started with some reddish spots around Tom's mouth which have gradually enlarged and become crusty. Tom's parents have also noticed additional spots and crusting on his tummy. Tom is otherwise healthy and has no known allergies. Tom's dad is worried, because although he is very well, the lesions are spreading. The family have applied a basic cream without any improvement. When specifically asked whether Tom has complained of pain or itching, Tom's father says he has noticed Tom is picking at the rash, but does not seem to be otherwise bothered by it.

When you examine Tom,
this is what you see:



Background information: community-acquired skin & soft tissue infection

Skin rashes are a frequent problem in neonatal and paediatric patients. Most of them are benign and self-limiting.

Bacterial aetiology



Group A
streptococcus

Impetigo, ecthyma, erysipelas, cellulitis,
paronychia



*Staphylococcus
aureus*

Impetigo, folliculitis, carbuncles, cellulitis,
paronychia

Commonly: *Streptococcus pyogenes* or
Staphylococcus aureus

Rarely: *H. influenzae*, *P. aeruginosa*,
Anaerobes and others

Non-bacterial aetiology

1. Non-specific rashes, e.g. maculopapular eruptions, urticaria

2. Viral rashes

Chickenpox (vesicles)

Parvovirus B19

HPV (warts, verrucae)

Poxvirus (Molluscum)

Measles

Mumps

HHV5/HHV6

Coxsackievirus (HFV)

3. Fungal rashes

Tinea corporis

Tinea pedis

Tinea capitis

Pityriasis rosacea

4. Rashes related to parasite infestations

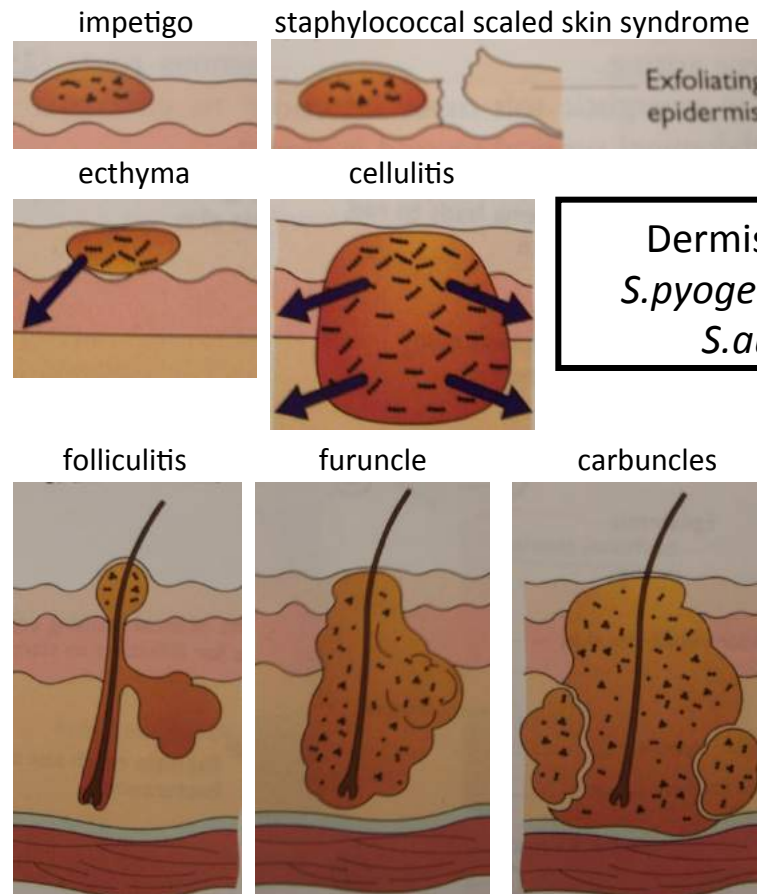
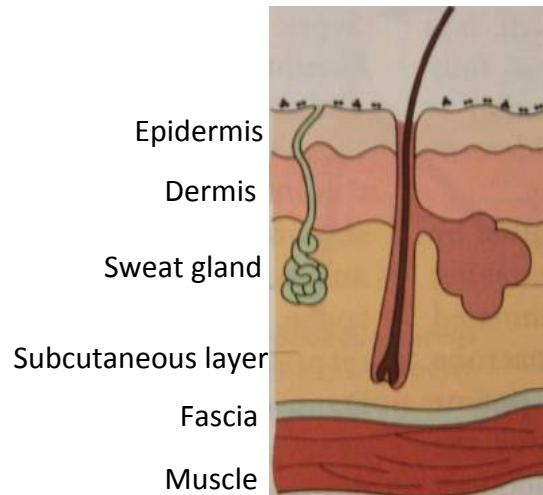
Headlice

Scabies

How likely is this to be bacterial SSTI?

To define whether a skin infection is likely to be due to bacteria, the rash must be classified further on the basis of clinical features including distribution and associated symptoms

Basic anatomy of skin structures



Epidermis: mainly
S.pyogenes, some
S.aureus

Dermis: mainly
S.pyogenes, some
S.aureus

Deeper skin
structures: mainly
S.aureus, some
S.pyogenes

Diagnostic approach towards SSTI

Because aetiological diagnosis in suspected bacterial SSTI is generally difficult and unnecessary in children with mild symptoms, the key to management is assessment of disease severity

Indicators of severe/systemic disease

Note: Consider whether features of toxic shock are present → if so, immediate referral to hospital is warranted






Need for further evaluation & hospital admission must be carefully considered

Patient will be managed as outpatient



Consider

-  Local resistance patterns to define choice of antibiotic
-  Swab if there is pus or any exudate that is easily accessible
- Probably not necessary
-  Any further testing

Tom appears well and can probably be managed as an outpatient

Unusual SSTI

In certain situation SSTI can be caused by unusual organisms and caution is necessary in deciding on further management and treatment

IDSA classification of SSTI



Superficial, uncomplicated infection (includes impetigo, erisipelas and cellulitis)



Necrotising infection; infections associated with bites and animal contact; surgical site infections



Infections in the immunocompromised host.

Infection likely to involve unusual organism and require inpatient treatment

Red flags in SSTI



Systemic symptoms and signs especially fever, tachycardia, hypotension



Severe pain



SSTI in association with animal or human bites (Tetanus status must be checked!)



History of travel



Surgical site infections








Immunocompromised host

Tom does not have any red flags and is unlikely to have unusual SSTI

Specific considerations when treating superficial SSTI

Once SSTI is deemed highly likely to be bacterial, antibiotic treatment is necessary, but a few additional considerations are required to determine treatment choice




-  Type of SSTI: Impetigo may be treated topically, cellulitis and erysipelas will need systemic treatment
-  Abscess formation: Abscesses, furuncles and carbuncles may need incision and drainage and can subsequently usually be managed without antibiotics
-  Location: Impetiginous lesions on the eyelids or near the mouth may be difficult to treat topically
-  Extent of disease: more extensive disease that needs to be rapidly controlled requires systemic treatment
-  Local resistance prevalence: Where MRSA is common, treatment choices may have to be adapted accordingly

Tom has multiple lesions...




Choosing antibiotics for SSTI – considerations of bug/drug combination

Relevant bacteriological information for treatment

S.pyogenes

-  100% penicillin sensitive
-  Macrolide resistance: 2-20% by an efflux pump mechanism
-  Associated toxin production possible can be interrupted using clindamycin or rifampicin

S.aureus

-  Penicillin is ineffective since most *S.aureus* are penicillinase producers
-  Penicillinase resistant beta-lactams such as Flucloxacillin are usually effective in community acquired SSTI in Europe
-  MRSA is rare in Europe and should be considered only for patients coming from countries with high CA-MRSA incidence

The most common bacterial pathogens in SSTI (*S.pyogenes* and *S.aureus*) must be considered when choosing antibiotics for SSTI

SSTI – choosing antibiotic treatment

Disease	Antibiotic	Comment
Impetigo	Penicillinase-resistant AB, such as Flucloxacillin Macrolides, such as Erythromycin Clindamycin	<p>These are the antibiotics that one may want to consider for Tom.</p> <p>S.pyogenes and S.aureus may be resistant Often active against MRSA, potential of resistance in erythromycin-resistant strains, inducible resistance in MRSA is a risk</p>
	Amoxicillin/Clavulanic acid Mupirocin (topical)	
Cellulitis/ Erysipelas	Pencillin Penicillinase-resistant AB, such as Flucloxacillin Clindamycin	Only if classical erysipelas
	Amxocillin/Clavulanic acid Tetracyclines, such as Doxycycline	See above Not in persons <8 years of age, may be considered in MRSA

Choice of antibiotic depends on the type of SSTI, its distribution and spread, availability of different antibiotics and formulations, likely causative organisms and known local resistance patterns

Benefits & Risks of antibiotic use in SSTI

Risks of AB in SSTI

- Unnecessary AB treatment , e.g. for localised abscesses/furuncles
- Unnecessary broad-spectrum or oral antibiotic treatment
- Treatment of rashes that are not in fact due to bacterial infection (e.g. fungi, other aetiology)
- Unwanted AB side-effects
 - Diarrhoea
 - Vomiting
 - Rashes
 - Allergy/Anaphylaxis
- Selection of resistant bacteria
 - Risk of re-consultation for an infection caused by a resistant microorganism

Benefits of AB in SSTI

- A clinical diagnosis is usually possible
- Often topical treatment is appropriate
- Treatment with antibiotics may prevent spread of contagious SSTI, e.g. impetigo, to others
- AB are an effective treatment for bacterial SSTI
- Family & Physician reassurance

A reasonable approach to Tom's problem...

You explain to Tom's dad that you feel the rash is typical of impetigo, a bacterial infection of the skin. Because you feel confident in your diagnosis and you know that MRSA is rare in your area, you decide not to take a swab. You propose to treat Tom with oral amoxicillin/clavulanic acid on account of multiple lesions. You advise Tom's dad that he should not attend day care or any other childhood group activities for at least 24 hours after the start of treatment. Tom's father will contact you in case of lack of improvement, difficulty in administering the medication or any worsening in Tom's condition.

You next see Tom for a regular vaccination appointment. His mother tells you the rash quickly disappeared after starting antibiotics, but that Tom had developed a bit of diarrhoea during antibiotic treatment. This stopped after the course was finished.

References

- Stevens DL et al. Practice Guidelines for the diagnosis and management of skin and soft-tissue infections. *CID* 2005 Nov; 41: 1373 -1406

At the end ...

... when parents demand antibiotics

- **Provide educational materials**

- share your treatment rules to explain ABs risks and benefits.
- Offer educational materials on the differences between viruses and bacteria.

- **Ask parents why they feel their child need an AB**

- **Delayed prescription**

- Ask your patients to wait some time without a prescription, and to call back after that time if they are still experiencing symptoms

- **Explain that unnecessary ABs can be harmful**

Tell parents that unnecessary antibiotics CAN be harmful, by promoting resistant organisms in their child and the community.

- Side effects
- Selection of secondary resistant organisms
- Do not decrease the length of the disease
- Is not active on pain or on a virus-related fever

- **Share the facts: spend some time educating your patients about why ABs are not helpful against viruses**

- bacterial infections can be cured by antibiotics, but viral infections never are
- treating viral infections with antibiotics to prevent bacterial infections does not work.

- **Build cooperation and trust**

- **Encourage active management of the illness**

- plan treatment of symptoms with parents.
- describe the expected normal time course of the illness and tell parents to come back if the symptoms persist or worsen.

- **Be confident with the recommendation to use alternative treatments**

- Prescribe analgesics and decongestants, if appropriate.
- Emphasize the importance of adequate nutrition and hydration.
- Consider providing “care packages” with non-antibiotic therapies.

- **Talk about antibiotic use at mandatory well child visits**

- **Start the educational process in the waiting room**

Videotapes, posters, and other materials are available.

- **Involve office personnel in the educational process**

- **Use the CDC/AAP pamphlets and principles to support your treatment decisions**

Further information: Relevant antibiotic prescription guidelines

Potentially relevant guidelines in English may be found at:

- The National Guideline Clearinghouse run by the US Department of Health and Human Services and the Agency for Healthcare Research and Quality (<http://guideline.gov/>)
- The Clinical Guidelines Portal run by the National Health and Medical Research Council, Australia (<http://www.clinicalguidelines.gov.au/>)
- Clinical Guidelines provided by the National Institute for Clinical Excellence (NICE) ([#http://guidance.nice.org.uk/CG](http://guidance.nice.org.uk/CG))
- The Scottish Intercollegiate Guidelines Network run by Healthcare Improvement Scotland (<http://www.sign.ac.uk/guidelines/published/index.html>)
- The Cochrane Reviews provided by the Cochrane Collaboration (<http://www.cochrane.org/>)

In addition, you may be able to find guidelines for the treatment of the common infections discussed in this slide set through your national paediatric or paediatric infectious diseases society.

Further information: Country specific antibiotic use and resistance

EU country specific data on antibiotic use and resistance may be found at:

- The European Antimicrobial Resistance Surveillance Network (EARS-Net) run by the European Centre for Disease Prevention and Control (ECDC)

(
[http://ecdc.europa.eu/en/activities/surveillance/EARS-Net/database/
Pages/database.aspx](http://ecdc.europa.eu/en/activities/surveillance/EARS-Net/database/Pages/database.aspx))

- The European Surveillance of Antimicrobial Consumption Network (ESAC-Net), also run by the European Centre for Disease Prevention and Control (ECDC) (

[http://www.ecdc.europa.eu/en/activities/surveillance/ESAC-Net/
database/Pages/database.aspx](http://www.ecdc.europa.eu/en/activities/surveillance/ESAC-Net/database/Pages/database.aspx))

In addition, you may be able to find information on national, regional, or hospital level antibiotic use and resistance through your national or regional public health authority or laboratory or pharmacy departments within individual hospitals.