Using antibiotics wisely in General Practice

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42nd Annual Academic Sessions - College of General Practitioners
23rd October 2016
Bugs and treatment options!!!

- 2000 B.C.—Here, eat this root.
- 1000 A.D.—That root is heathen. Here, say this prayer.
- 1850 A.D.—That prayer is superstition. Here, drink this potion.
- 1920 A.D.—That potion is snake oil. Here, swallow this pill.
- 1945 A.D.—That pill is ineffective. Here, take this penicillin.
- 1955 A.D.—Oops . . . bugs mutated. Here, take this tetracycline.
- 2000 A.D.—The bugs have won! Here, eat this root.

Source: Anonymous, as cited by the World Health Organization, 2000
Correct Topic

HI, I'M MRSA "Superbug"

THAT WHICH DOES NOT KILL ME, MAKES ME STRONGER.

THE POST-ANTIBIOTIC ERA?
What is meant by the term wise?

- **Having or showing the ability to make good judgments, based on a deep understanding and experience of life**

  *Cambridge Dictionary*
Rational use of Medicine

• “Patients receive medicines appropriate to their clinical needs, in doses that meet their requirements, for an adequate period of time, and at the lowest cost to them and their country”

Evolution of terms!!

1. Rational use
2. Quality use
3. Appropriate use
4. Responsible use
5. Prudent use
6. Wise use
Successful treatment of an infection

1. Effective antibiotic

2. Adequate concentration of the antibiotic at the site of infection

3. Intact host’s immune mechanisms
Successful treatment of an infection

• **Effective antibiotic:**
  1. Discovery, development, availability, affordability
  2. Knowledge about:
     1. Pharmacodynamics of antibiotics
     2. Infectious agents
     3. Susceptibility of infectious agents to antibiotics
     4. Resistance pattern of the infectious agents (local, national, regional, global)
Successful treatment of an infection

- Adequate concentration of the antibiotic at the site of infection - Not only must inhibit the organism but also must remain below the level that is toxic to human cells!!

1. Dose, dosage form, dosing interval, route of administration
2. Bioavailability
3. Distribution
4. Penetration of barriers
5. Therapeutic index or therapeutic window
Bioavailability

• The amount (fraction or percentage) of unchanged drug and the rate at which the drug reaches the systemic circulation following any route of administration

• For orally administered medicines, bioavailability is affected by:
  • GIT absorption
  • Hepatic metabolism
Distribution

• Distribution is the process of reversible transfer of the chemical from the general circulation into the body tissues.

• Presence of any natural barriers such as blood brain barrier or acquired barrier such as abscess formation, fibrous tissue, caseation, etc will hinder distribution of antibiotic to the site of infection.
Minimum Inhibitory Concentration

• Lowest concentration of an antibiotic that will inhibit the visible growth of a bacteria after overnight incubation

• For serious infections like meningitis, the concentration of antibiotic in the CSF should be at least 8 times above the MIC
Therapeutic window

- Window bound by the lower margin of therapeutic threshold (MIC) and upper margin of therapeutic ceiling (MTC)
Key pharmacological parameters for successful treatment of an infection

The right antibiotic (E, S, Q, CE, A)
for the right patient
at the right time
with the right dose and
the right route, frequency and duration causing
the least harm to
the patient and future patients

Source: www/cdc.gov/getsmart/healthcare/inpatient-stewardship
Discovery void

Discovery void

ANTIBIOTIC PIPELINE HAS BECOME EXTREMELY DRY

Bitter Truth

• Only 2 new classes of antibiotics have emerged in the past 3 decades, namely, oxazolidinones (linezolid) and cyclic lipopeptides (daptomycin)

• No new antibiotic class active against MDR Gram-negative rods can be anticipated in near future

Carlet et al. Antimicrobial Resistance and Infection Control 2012, 1:11
http://www.aricjournal.com/content/1/1/11
Discovering and testing antibiotics take time and money.

Many pharmaceutical industries have abandoned the field.

Concentrating on drugs that will be in the market for a long time without losing effectiveness (antidepressants, Statins).
Beginning of the bar = Beginning of clinical use
Termination of the bar = Resistance has become a significant clinical issue
Antibiotic resistance

1. Gram-negative rods (e.g., Escherichia coli, Salmonella spp, Klebsiella spp, Pseudomonas aeruginosa, Acinetobacter spp) - Resistant to almost all currently available antibiotics in some settings
2014 – WHO Report

1. Very high rates of resistance have been observed in all WHO regions in common bacteria (*Escherichia coli, Klebsiella pneumoniae, Staphylococcus aureus*) that cause common health-care associated and community-acquired infections (UTIs, wound infections, septicaemia, and pneumonia)

2. Many gaps exist in information on pathogens of major public health importance (HIV, TB, Malaria)

*Source: Antimicrobial resistance: global report on surveillance: WHO: 2014*

- *Escherichia coli* in patients with UTI:
  - Resistance to ampicillin = 85%
  - Nalidixic acid = 58.5%
  - Trimethoprim/sulphamethoxazole = 47.1%
  - Ciprofloxacin = 46.2%
  - Norfloxacin = 43.7%
  - Amoxicillin /clavulanic acid = 36.3%,
  - Nitrofurantoin = 15%

Escherichia coli Resistant to Last resort antibiotic (Colistin): In USA – July 2016

.....End of the road isn’t very far away for antibiotics — that we may be in a situation where we have patients in our ICUs, or patients getting UTIs for which we do not have antibiotics”

Connection between antibiotic use and antibiotic resistance

More we use, more we lose

Antibiotics – Risks

1. **Adverse effects**
2. Antimicrobial resistance
3. Drug interactions
4. Super infections
5. Risks associated with intravenous antibiotics
6. Minor side-effects and impact on QoL
7. Teratogenecity
Antibiotics – benefits

- Most influential discoveries affecting human health
- Very effective, safe and relatively inexpensive
- Have saved millions of lives
- At least about 7 Nobel prizes had been awarded for discovery of antibiotics
- In cases for which antibiotics are indicated, the benefits outweigh the risks, including antibiotic resistance
Antibiotics – benefits

1. Significant decrease in the individual morbidity and mortality of classic infectious diseases

2. Catalysers in the development of modern Medicine, assuring a protective umbrella against infections
Antibiotic paradox

• Because of the selection of naturally emerging antibiotic-resistant bacteria, the extended use of antibiotics erodes its own action

• Antibiotic paradox

• How Miracle Drugs Are Destroying the Miracle
Two potential solutions

1. New antibiotics

2. To decrease excess or inappropriate consumption of existing antibiotics
Rational/ responsible/ quality/ Prudent/ appropriate/ Wise use of antibiotics
Using antibiotics wisely
IN GENERAL PRACTICE

1. General Practice handles the major bulk

2. Antibiotics are not required for majority of infections presenting in the primary care

3. Instant/reflex prescribing of antibiotics should be zero or minimal

4. Threshold to prescribe new antibiotics, broad spectrum antibiotics, antibiotics with the potential to produce serious AEs should be very high
Story 1
Three key conditions where irrational use of antibiotics is rampant!

1. Fever

2. AGE / Diarrhoea

3. Upper respiratory tract symptoms
Fever and antibiotics - 1

• Antibiotics ARE NOT antipyretics
• Most common complaint in patients presenting to GP
• Elevation of body temperature that exceeds the daily variation
• Self-limiting viral infections are the commonest infectious cause for fever and antibiotics have no role to play in their management, neither do “they shorten the duration of the illness” nor do they "prevent secondary infections".
Fever and antibiotics – 2

• Premature, presumptive and indiscriminate use of antibiotics in all cases of fever
  – Adds to the cost of therapy
  – Increase discomforts (SE, ADR, etc)
  – Contributes development of drug resistance
  – Mask the signs of bacterial infection
1. Urge to (reflex prescribing) prescribe antibiotics for all cases of fever should be curbed.
2. All attempts should be made to localize the site and type of the infection.
3. Empirical antibacterial therapy should be reserved only for emergencies.
4. Communicating with the patients is an art: Advice the patient/parents.
5. Should not give in to pressure from patients, parents, pharmaceutical industry, or peer practice.
6. Should keep the knowledge up to date and have access to unbiased information.
7. Algorithm.
Fever
- Demonstrable rise in temperature >99.9F

Clinical features suggesting severity
- Altered sensorium
- Hypotension: SBP <90
- Tachypnea: RR >24

If Present – Evaluate for SIRS / Sepsis

Urgent management of Sepsis

Exanthematous fever
Evaluate exanthem type

Look for Icterus
- Fever with Jaundice algorithm
  Malaria/ Hepatitis/Leptospirosis
  Drug induced hepatitis/hemolysis

C/F of localization to organ system
- Respiratory: Cough, Dyspnea
- CNS: Headache, Seizures, Stiff neck
- Urinary: Dysuria, Hematuria
- GIT: Abdominal pain, Diarrhea
- Skin: Abscess, furuncles

If Present – Manage specific syndrome
- Acute Respiratory infection (ARI)
- Acute encephalitis syndrome (AES)
- Acute meningitis
- Urinary tract infection (UTI)
- Acute GI infection
- Skin soft tissue infection etc

Acute undifferentiated Fever
Not suggestive of SIRS / Sepsis

1. Investigate for Malaria
   CBC, P/S, HRP-II, pv-LDH

   Positive for Malaria
   Pf or Pv
   Uncomplicated or Complicated
   Malaria treatment algorithm

   Negative for Malaria
   2. Investigate for Dengue
      NS-1, anti-den IgM

      Positive for Dengue
      Dengue evaluation algorithm
      Without warning signs
      With warning signs
      Severe Dengue

      Negative for Dengue
      If fever <3 days in duration
      Continue anti-pyretic drugs
Diarrhoea and antibiotics - 1

• In developing countries, less than 60% of children with acute diarrhoea receive necessary oral rehydration therapy yet more than 40% receive unnecessary antibiotics.

• Most cases are caused by a virus and do not respond to antibiotics.

Source: http://www/who.int/mediacentre/factsheets/fs338/en
Diarrohea and antibiotics - 2

• Indication for antibiotics are:
  – Suspected septicaemia (very ill with a high fever)
  – Small infants (under 1 month)
  – Severely malnourished children
  – Dysentery (blood in the stools)
  – Suspected cholera
• Routine antibiotics should not be used
• Ill infants with suspected septicaemia → IV antibiotics
• Dysentery (often due to Shigella) is usually treated with oral nalidixic acid
• Persistent diarrhoea (often due to Amoebae or Giardia) is treated with metronidazole
Check list for history and examination:

1. Age
2. Hydration
3. General well being (? Sick child or not)
4. Fever
5. Vomiting
6. Level of nutrition
7. Features of dysentery
8. Family / contact history
9. Past treatment
URTI and Antibiotics - 1

- Uncomplicated URIs account for 25 million visits to family physicians in USA
- Despite majority of URIs are viral, (90% of adults and 70% of children with pharyngitis – Viral), a high proportion is treated with antibiotics.
- A study from a large, outpatient ambulatory network of more than 52,000 cases of URI showed that antibiotics were prescribed in 65% of patients.

Source: Am Fam Physician. 2012;86(9):817-822
Table 1. Diagnostic Findings and Appropriate Treatments for Upper Respiratory Tract Infections

<table>
<thead>
<tr>
<th>Condition</th>
<th>Key diagnostic findings</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute bronchitis and tracheitis</td>
<td>Cough, possible phlegm production</td>
<td>Symptomatic treatment; antibiotics are not recommended&lt;sup&gt;3,4&lt;/sup&gt;</td>
</tr>
<tr>
<td>Acute otitis media</td>
<td>Acute onset of symptoms, presence of middle ear effusion, signs of middle ear inflammation</td>
<td>Amoxicillin, 80 to 90 mg per kg per day, in two divided doses (first-line treatment)&lt;sup&gt;5,6&lt;/sup&gt;</td>
</tr>
<tr>
<td>Acute rhinosinusitis</td>
<td>Nasal obstruction, anterior or posterior purulent nasal discharge, facial pain, cough, decreased sense of smell</td>
<td>Watchful waiting in mild cases; amoxicillin for severe or complicated bacterial rhinosinusitis&lt;sup&gt;7&lt;/sup&gt;</td>
</tr>
<tr>
<td>Common cold</td>
<td>Runny nose, cough, sore throat, sneezing, nasal congestion</td>
<td>Symptomatic treatment; antibiotics are not recommended&lt;sup&gt;8&lt;/sup&gt;</td>
</tr>
<tr>
<td>Epiglottitis</td>
<td>Dysphagia, voice change, tachycardia (heart rate &gt; 100 beats per minute), drooling, fever, subjective shortness of breath, tachypnea (respiratory rate &gt; 24 breaths per minute), stridor, respiratory distress, leaning forward</td>
<td>Intravenous combination of a third-generation cephalosporin and an antistaphylococcal agent active against methicillin-resistant &lt;i&gt;Staphylococcus aureus&lt;/i&gt; or intravenous monotherapy with ceftriaxone (Rocephin), cefotaxime (Claforan), or ampicillin/sulbactam (Unasyn)&lt;sup&gt;9-12&lt;/sup&gt;</td>
</tr>
<tr>
<td>Influenza</td>
<td>Abrupt onset of fever, headache, myalgia, malaise</td>
<td>Influenza vaccination for prevention; supportive care; initiation of antiviral therapy within 48 hours of symptom onset may decrease illness duration by one day&lt;sup&gt;13,14&lt;/sup&gt;</td>
</tr>
<tr>
<td>Laryngitis</td>
<td>Loss or muffle of voice, sore throat, cough, fever, runny nose, headache</td>
<td>Symptomatic treatment; antibiotics are unnecessary&lt;sup&gt;15&lt;/sup&gt;</td>
</tr>
<tr>
<td>Pharyngitis and tonsillitis</td>
<td>Sore throat, fever, absence of cough</td>
<td>Treatment based on modified Centor score (Table 2)</td>
</tr>
</tbody>
</table>

Information from references 3 through 18.
### SORT: KEY RECOMMENDATIONS FOR PRACTICE

<table>
<thead>
<tr>
<th>Clinical recommendation</th>
<th>Evidence rating</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin is the preferred treatment in patients with acute bacterial rhinosinusitis.</td>
<td>C</td>
<td>10</td>
</tr>
<tr>
<td>Short-course antibiotic therapy (median of five days’ duration) is as effective as long-course treatment (median of 10 days’ duration) in patients with acute, uncomplicated bacterial rhinosinusitis.</td>
<td>B</td>
<td>31</td>
</tr>
<tr>
<td>Antibiotic therapy should be considered for children six to 35 months of age with acute otitis media.</td>
<td>B</td>
<td>37, 38</td>
</tr>
<tr>
<td>Antibiotics should not be used in patients who have otitis media with effusion.</td>
<td>C</td>
<td>43</td>
</tr>
<tr>
<td>Penicillin should be used in patients with streptococcal pharyngitis to decrease the risk of rheumatic fever, alleviate symptoms, and decrease communicability.</td>
<td>B</td>
<td>45, 46, 49, 52</td>
</tr>
<tr>
<td>Antibiotics should not be prescribed for acute laryngitis.</td>
<td>A</td>
<td>18, 54</td>
</tr>
</tbody>
</table>

*A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to http://www.aafp.org/afpsort.xml.*
Table 2. Modified Centor Criteria for Pharyngitis and Tonsillitis

<table>
<thead>
<tr>
<th>Clinical finding</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absence of cough</td>
<td>1</td>
</tr>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>3 to 14 years</td>
<td>1</td>
</tr>
<tr>
<td>15 to 45 years</td>
<td>0</td>
</tr>
<tr>
<td>Older than 45 years</td>
<td>-1</td>
</tr>
<tr>
<td>Anterior cervical lymphadenopathy</td>
<td>1</td>
</tr>
<tr>
<td>Fever</td>
<td>1</td>
</tr>
<tr>
<td>Tonsillar erythema or exudates</td>
<td>1</td>
</tr>
</tbody>
</table>

NOTE: Patients with a score of 1 or less do not require further testing or treatment, although contact with a person who has documented streptococcal infection should be considered in patients with a score of 1, and testing should be performed in these cases. Those with a score of 2 or 3 should have rapid antigen detection testing and, if results are positive, should receive antibiotics; and those with a score of 4 or 5 should receive antibiotics.

Information from references 47 through 50.
Knowing is not enough; we must apply. Willing is not enough; we must do.
Using antibiotics wisely in GP

1. Antibiotics are not antipyretics
2. Common cold needs common sense not antibiotics
3. Majority of infections seen in GP is caused by viruses
4. Antibiotics are not effective against viral infections
5. For fever, diarrhoea, URTI, skin lesions, etc have your own algorithm/check list/wall chart
6. Counsel the patients, keep up to date, have access to unbiased information, avoid pressure from industry, patients, parents, peers
7. If you decide to use antibiotics:
   1. Prescribe “time tested”, “old”, narrow spectrum and “safe” ones
   2. Consider right dose, frequency, timing, duration, dosage form as well
   3. Dispensing – GDP
   4. Children are not small adults
   5. Give correct advices
8. (Not) writing a prescription is a science and reflects self-confidence
Unwise practices

1. Why amoxicillin is not seen in prescriptions?

2. Why erythromycin is not seen in prescriptions?

3. Why phenoxy methyl penicillin is not seen in prescriptions?
Unwise practices

1. Why co-amoxiclav?
2. Why cefixime?
3. Why ciprofloxacin?
Unwise practices

1. Why powders given to children?

2. Why packets given to children?

3. Why tablets given to infants and young children?
Unwise practices

1. Children, how dose is calculated?

2. Do we tell the parents that phlegm is excreted via the stools?

3. If medicines are dispensed in a doctor’s clinic– is Good dispensing Practice adhered?
Thank you!