Life-threatening infections

Frank Bowden
October 5, 2018
“Evidence Based Medicine is the integration of best research evidence with clinical expertise and patient values.”
The Golden Rules of Infectious Diseases
The 28 Golden Rules of Infectious Diseases

1. Recurrent rigors are most likely to be caused by bacterial infections.
2. Severe muscle pain may be a symptom of sepsis, even in the absence of fever.
3. Fever in the elderly is rarely caused by a viral infection.
4. Sepsis in the elderly may not present with fever: the older the colder.
5. Hypothermia in a septic patient is a medical emergency.
6. ‘When a patient has a fever postoperatively, it is usually related to the surgical procedure’ (Petersdorf’s law).
7. Jaundice in a febrile patient is rarely caused by viral hepatitis.
8. Early meningococcaemic rash may resemble a non-specific viral rash.
9. Generalised rashes that involve the palms and soles - consider drugs, viral infections, rickettsial infections or syphilis.
10. Malaria must be excluded in a febrile traveller returning from a malaria endemic area.
11. An elderly patient from a TB endemic setting with fever and multisystem disease has disseminated TB until proven otherwise.
12. *Staph aureus* in the urine is a sign of staphylococcal bacteraemia until proved otherwise.
13. Never underestimate a *Staph aureus* bacteraemia - look into the heart and at the bone.
14. Staph aureus meningitis without preceding CNS instrumentation indicates the presence of endocarditis until proved otherwise.
15. A movable joint does not exclude septic arthritis
16. More than one infection may be present in an adult patient, particularly the elderly, the immunosuppressed and the returned traveller.
17. Think of acute bacterial epiglottitis in an adult patient with a normal looking throat who is complaining of acute sore throat, pain on swallowing and/or hoarse voice.

18. Infection in a diabetic patient will flourish until the diabetes is controlled.


20. Consider common bacterial infections and not just opportunistic infections, in febrile patients with advanced HIV infection.

21. Specific IgM antibodies are a useful but unreliable marker of infections in pregnancy, thus clinical decisions should not be based solely on a positive IgM.

22. Not everyone with aseptic meningitis has viral meningitis; unless confirmed by PCR viral meningitis is a diagnosis made after the patient has recovered.
23. Avoid the term ‘atypical pneumonia’ in children, adults over the age of 50, the immunocompromised, the severely ill or patients with diffuse bilateral interstitial pulmonary infiltrates.

24. Remember that *Listeria monocytogenes* encephalitis can masquerade clinically as herpes simplex encephalitis.

25. Bacterial aortitis needs to be excluded in a patient who develops abdominal or back pain within weeks of an episode of diarrhoea.


27. When you suspect bacteraemia do not wait for the patient’s temperature to go up before doing blood cultures.

28. In community-acquired infections, resistant organisms do not cause more severe illness than their sensitive counterparts. The only reason for using broader than usual therapy is when you (and the patient) cannot afford to be wrong!
Choose Wisely

Which would you rather have?

A heart attack or a penicillin-sensitive *Staph aureus* bacteraemia?
<table>
<thead>
<tr>
<th>Condition</th>
<th>1 year Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>E. coli</em> bacteraemia</td>
<td>5 - 30%</td>
</tr>
<tr>
<td><em>Staph aureus</em> bacteraemia</td>
<td>20%</td>
</tr>
<tr>
<td>Septic shock</td>
<td>30 - 50%</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>3-5%</td>
</tr>
</tbody>
</table>
SEPSIS IS A MEDICAL EMERGENCY

Any Kind of Infection Can Lead to Sepsis

Some common infections that can lead to sepsis include:

- Urinary Tract Infections (UTIs)
- Strep Throat
- Influenza
- MRSA

- Sepsis is your body’s lifethreatening response to an infection.
- Sepsis is usually easy to treat if it is detected early.
- Sepsis kills 236,000 people each year in the U.S.

If you have had an infection or suspect an infection, and develop a combination of these symptoms, seek medical attention right away:

- Fever or chills
- Extreme pain or discomfort
- Pale or discolored skin
- Sleepiness or confusion
- Shortness of breath

Get involved and join the fight at sepsis.org

SEPSIS ALLIANCE

SEPSIS KILLS

RECOGNISE • RESUSCITATE • REFER
Eurosepsis
Recognition of sepsis

Early antibiotics

Early fluids
Vaccination
Back to basics
Clinical features of severe sepsis: qSOFA

<table>
<thead>
<tr>
<th>qSOFA</th>
<th>Other clinical features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory rate ( \geq 22/ ) minute</td>
<td>Severe muscle pain, esp in thighs</td>
</tr>
<tr>
<td>Altered mentation</td>
<td>Hypothermia in elderly</td>
</tr>
<tr>
<td>Systolic BP ( \leq 100 \text{ mmHg} )</td>
<td>Typical rash</td>
</tr>
</tbody>
</table>
Principles of infectious diseases
<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Normal host</th>
<th>Immunocompromised</th>
</tr>
</thead>
</table>
| Pneumonia                        | *Streptococcus pneumoniae*  
*Haemophilus influenzae*  
*Staphylococcus aureus*  
*Legionella pneumophila*  
*Influenza A*           | *Enterobacteriaceae*  
*Pneumocystis jirovecii*  
*Aspergilus sp.*  
*Moulds*                |
| Meningitis                       | *Streptococcus pneumoniae*  
*Neisseria meningitidis*  
*Haemophilus influenzae* | *Listeria monocytogenes*                                                  |
| Bacteraemia                      | *Staphylococcus aureus*  
Gram negatives                     | *Pseudomonas aeruginosa*                              |
| Soft tissue infections           | *Staphylococcus aureus*  
*Streptococcus pyogenes*  
*Clostridia sp*  
*Mixed anaerobes*         |                                                                                 |
| Intra-abdominal sepsis           | Gram negatives and anaerobes                                          |                                                                                 |
| Urinary tract infections         | Gram negatives                                                           |                                                                                 |
| Others                           | Malaria  
Dengue  
Typhoid  
Viral haemorrhagic fevers  
SARS/MERS |                                                                                 |
The Big Three

- *Streptococcus pyogenes*
- *Streptococcus pneumoniae*
- *Neisseria meningitidis*
18 yo man with chills and fever, back pain, severe lower limb muscle pain

Moderate headache but no neck stiffness

No sick contacts
The 28 Golden Rules of Infectious Diseases

1. Recurrent rigors are most likely to be caused by bacterial infections.

2. Severe muscle pain may be a symptom of sepsis, even in the absence of fever.

3. Fever in the elderly is rarely caused by a viral infection.

4. Sepsis in the elderly may not present with fever: the older the colder.

5. Hypothermia in a septic patient is a medical emergency.

6. ‘When a patient has a fever postoperatively, it is usually related to the surgical procedure’ (Petersdorf’s law).

7. Jaundice in a febrile patient is rarely caused by viral hepatitis.

8. Early meningococcaemic rash may resemble a non-specific viral rash.

9. Generalised rashes that involve the palms and soles - consider drugs, viral infections, rickettsial infections or syphilis.
Meningococcal disease notifications
Necrotising fasciitis
Types of necrotising fasciitis

Type 1 - polymicrobial

Type 2 - monomicrobial
Type 1

Combination of

Anaerobes
e.g. *Bacteroides*, *Clostridium*, or *Peptostreptococcus*

Facultative anaerobic streptococci
(apart from GAS)

Enterobacteriaceae
e.g. *Escherichia coli*, *Enterobacter*, *Klebsiella*, *Proteus*
Type 1 Risk factors

- Diabetes
- Peripheral vascular disease
- Immune compromise
- Recent surgery
  - Including minor procedures such as circumcision in newborn infants.
Type 1 - Head and neck

- *Fusobacteria* sp
- Anaerobic streptococci
- *Bacteroides* sp
- Spirochetes
Type 1 - Fournier’s gangrene of the perineal region

- E. coli
- Klebsiella sp
- Enterococci

Plus

- Bacteroides
- Fusobacterium
- Clostridium

Plus

- anaerobic or microaerophilic streptococci
Type 2

- **Monomicrobial**
  - most commonly Group A strep
- **Often healthy individuals with no past medical history, in any age group**
- **Predisposing factors**
  - history of laceration or burn, blunt trauma, recent surgery, childbirth, injection drug use, and varicella infection (chickenpox)
Type 2 - Group A Streptococcus

- **M protein**
  - Virulence determinant anchored to the cell membrane
  - Antiphagocytic properties
  - Types 1 and 3 most common and associated with streptococcal toxic shock syndrome in about 50 percent of cases
Why so sick in GAS?

- Pyrogenic exotoxins
  - superantigens that cause rapid proliferation of T cells
  - production of TNF-alpha, IL-1, IL-6 and lymphokines IL-2 and TNF-beta
Type 2 - water exposure

- *Aeromonas sp*
- *Vibrio vulnificus*
  - Gram negative bacilli
  - Environmental
The most effective antibiotics for necrotising fasciitis
Empirical therapy

For empirical therapy, if diagnosis is uncertain, until the results of tissue and blood cultures are available, use:

meropenem 1 g (child: 25 mg/kg up to 1 g) IV, 8-hourly

PLUS

vancomycin IV; see Appendix 2,3 for dosage and principles of use

PLUS

clindamycin 600 mg (child: 15 mg/kg up to 600 mg) IV, 8-hourly [Note 7].
**Streptococcus pyogenes** necrotising fasciitis

For *S. pyogenes* necrotising fasciitis, in combination with surgical debridement, use:

- Benzylpenicillin 1.8 g (child: 50 mg/kg up to 1.8 g) IV, 4-hourly

PLUS

- Clindamycin 600 mg (child: 15 mg/kg up to 600 mg) IV, 8-hourly [Note 8]

PLUS (consider after expert advice)

- Normal immunoglobulin (adult and child) 1 to 2 g/kg IV, for up to 2 doses during the first 72 hours.

For patients hypersensitive to penicillins (excluding immediate hypersensitivity, see Antimicrobial hypersensitivity), replace benzylpenicillin in the above regimen with:

- Cephalzin 2 g (child: 50 mg/kg up to 2 g) IV, 8-hourly.
Using oxygen at high pressure (in a compression chamber) for the treatment of individuals with severe soft tissue infection (necrotizing fasciitis)

Published: 15 January 2015
Authors: Levett O, Bennett MH, Millar I
Primary Review Group: Anaesthesia, Critical and Emergency Care Group

Severe soft tissue infection (necrotizing fasciitis) is life threatening, is associated with prolonged hospital stay and carries high risk of long-term loss of function. Routine treatment consists of immediate surgical removal of infected tissue and administration of antibiotics. Use of hyperbaric oxygen therapy, or HBOT, in addition to surgery and antibiotics has been suggested as a way to minimize tissue loss, decrease the number of limb amputations and reduce death. The aim of HBOT is to increase the supply of oxygen to the site. This approach may be toxic to bacteria, may improve the effectiveness of antibiotics and can improve healing.

We searched the databases to September 2014. This Cochrane review found no high-quality trials to support or refute the use of HBOT in the treatment of individuals with necrotizing fasciitis. It should be noted that HBOT may very rarely result in serious adverse effects. Further studies are required to address the effectiveness of HBOT because currently it is provided as routine practice in some centres.

Authors’ conclusions:

This systematic review failed to locate relevant clinical evidence to support or refute the effectiveness of HBOT in the management of necrotizing fasciitis. Good quality clinical trials are needed to define the role, if any, of HBOT in the treatment of individuals with necrotizing fasciitis.
The pneumococcus
**Streptococcus pneumoniae**

- Invasive disease peaks in childhood and elderly
- Invasive disease
  - Meningitis
  - Bacteraemia
  - Pneumonia
- Non-invasive disease
  - Sinusitis
  - Otitis media
- Usually penicillin sensitive in Australia but changing
Overwhelming sepsis following splenectomy

- *Strep pneumoniae*
- *Haemophilus influenzae*
- *Neisseria meningitidis*
- *Capnocytophaga sp*
Staph aureus
Echocardiogram

Lens Temp: 39.2°C

46 fps / 120 mm
77 bpm / General
H5.5MHz / -9 dB
DR: 79 dB
1051 / 1052

1 Distance = 1.98 cm
2 Distance = 0.96 cm
**FINAL Urine MC&S MUrine**

**SPECIMEN:** URINE  

**MICROSCOPY:**
- Leucocytes: $> 100 \times 10^6/L$  
- Erythrocytes: $< 10 \times 10^6/L$  
- Squamous Epithelial Cells: $< 10 \times 10^6/L$

A squamous epithelial cell count of $>10 \times 10^6/L$ is suggestive of improper collection.

**DIPSTICK CHEMISTRY:**
- pH: 5  
- Protein: Negative  
- Glucose: Negative  
- Nitrite: Positive

Normal value 4.5 - 8.0  
Normal value $< 0.3$ g/L  
Normal value $< 2$ mmol/L

**COLONY COUNT:**
$> 10^8/L$

Normal MSU values for:
- Males $<10^6/L$
- Asymptomatic Females $<10^8/L$
- Symptomatic Females $<10^5/L$

**CULTURE:**
- *Staphylococcus aureus*

**SENSITIVITIES:**
- Amp/Ampicillin: R  
- Cephalexin: S  
- Cotrimoxazole: S  
- Flucloxacillin: S  
- Nitrofurantoin: S
SPECIMEN: BLOOD CULTURES
BLOOD CULTURE RESULT:
Aerobic Bottle: POSITIVE after 18 hours incubation
Anaerobic Bottle: POSITIVE after 13 hours incubation

GRAM STAIN COMMENT:
Gram positive cocci resembling Staphylococcus.

CULTURE
1. Staphylococcus aureus

*Staphylococcus aureus* bacteremia (including Methicillin Resistant Staphylococcus Aureus) should **ALWAYS** be considered significant and be treated with a **minimum of 2 weeks** of intravenous therapy. This aims to prevent metastatic disease developing (eg endocarditis, osteomyelitis, abscesses). Many require further prolonged therapy if deep seated infection is found or prosthetic material is present.

Infectious Diseases input should be sought for all cases of *Staphylococcus aureus* bacteremia.

If you have any queries about this result please phone a specialist Microbiologist, or a Registrar or Senior Scientist at The Canberra Hospital Microbiology Laboratory on 62442514.

SENSITIVITIES: R
- Penicillin
- Flucloxacillin
- Cefazolin
- Clindamycin
- Erythromycin
- S
Staph aureus

- Second commonest cause of bacteraemia in most hospitals
- high morbidity and mortality
- long hospital stays
- Bacteraemia needs
  - 2 weeks IV antibiotics
  - transthoracic echo
- S. aureus in urine may mean S. aureus in blood
Fever in the returned traveller
Returned traveller from PNG

Returned 1 week ago from the Kokoda Trail.

Headache, diarrhoea, nausea and vomiting

3 rigors

Temp to 39.5 °C

No rash or splenomegaly

Crackles at left base
Also consider:
Typhoid
Dengue
Hantavirus
Leptospirosis
Is resistance a distraction?

The Big Three are almost always sensitive to penicillin!

Never withhold broad spectrum antibiotics in the critically ill.

Incorrect antibiotic choice is as important as antibiotic delay.
Antibiotic choices *a la carte* for community-acquired sepsis#

<table>
<thead>
<tr>
<th>Likely source of sepsis</th>
<th>Antibiotic regimen</th>
<th>What’s missing?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unknown source</td>
<td>Flucloxacillin <em>plus</em> gentamicin</td>
<td>Anaerobes and MRSA</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>Ampicillin <em>plus</em> gentamicin</td>
<td>Staph</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>Penicillin <em>plus</em> azithromycin <em>plus</em> gentamicin OR</td>
<td>Staph PCP Fungal Viral</td>
</tr>
<tr>
<td></td>
<td>Ceftriaxone <em>plus</em> azithromycin</td>
<td></td>
</tr>
<tr>
<td>Meningitis</td>
<td>Corticosteroids PLUS Ceftriaxone +/- penicillin +/- vancomycin</td>
<td>Staph ESBL</td>
</tr>
<tr>
<td>Intra-abdominal</td>
<td>Ampicillin <em>plus</em> gentamicin <em>plus</em> metronidazole</td>
<td>Staph Candida</td>
</tr>
<tr>
<td>Necrotising fasciitis</td>
<td>Meropenem <em>plus</em> vancomycin <em>plus</em> clindamycin</td>
<td>Hardly anything</td>
</tr>
</tbody>
</table>

# does not apply to tropical Australia
Examination
1. Recurrent rigors are most likely to be caused by bacterial infections.
2. Severe muscle pain may be a symptom of sepsis, even in the absence of fever.
3. Fever in the elderly is rarely caused by a viral infection.
4. Sepsis in the elderly may not present with fever: the older the colder.
5. Hypothermia in a septic patient is a medical emergency.
6. Early meningococcaemic rash may resemble a non-specific viral rash.
7. Malaria must be excluded in a febrile traveller returning from a malaria endemic area.
8. *Staph aureus* in the urine is a sign of staphylococcal bacteraemia until proved otherwise.
9. More than one infection may be present in an adult patient, particularly the elderly, the immunosuppressed and the returned traveller.
10. Think of acute bacterial epiglottitis in an adult patient with a normal looking throat who is complaining of acute sore throat, pain on swallowing and/or hoarse voice.
11. When you suspect bacteraemia do not wait for the patient’s temperature to go up before doing blood cultures.
Take home messages

Consider life-threatening sepsis

History is crucial

Examination can be (very) helpful

Culture early

Antibiotics early

(Fluid early)

Inotropes early

Resistance is an important distraction
Any questions?