Sepsis: getting it right every time

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with thanks to Madhad Noursadeghi, UCL

The case history...

- 50y English man (Engineer)
  - Previously well
  - 2 week h/o of fever
  - Mild skin rash, but no other localising symptoms

- On examination
  - Looked unwell
  - Generalised truncal erythematous maculopapular rash
  - T 38.5, HR 110, RR 20
  - No other localising signs

Q1. What information would you like next?

1. HIV test
2. WCC
3. Travel history
4. Lactate
5. History of unwell contacts

A1. What information would you like next?

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2. WCC
3. Travel history
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5. History of unwell contacts

- Returned from China 3 weeks earlier
- Attended rural areas (exploring fresh water sources)
- Casual exposure to domesticated animals (Sheep & Goats)
- Otherwise born & brought up in the UK
- Previous holidays in the Far East & across Europe

Q2. What investigation will you do first?

1. FBC
2. Malaria film
3. Blood culture
4. HIV test
5. ABG

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- WCC 3 (otherwise N)
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- Blood & Urine sent
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Survival guide 1: fever in the returning traveller

- Always check for malaria
- Take prompts from localising features
- Most viral illnesses incubate <14 days
  - Rash
  - ALT ↑, L ↓, PLT ↓
  - Generally resolve within 7-10 days (exc. EBV / CMV / HIV)
- Typhoid (S. typhi / paratyphi) looks like a viral illness
  - ALT ↑, WCC ↓, PLT ↓
  - But with prolonged fever
- Typhus (Rickettsia)
  - Eschar & petechiae
- Consider the need for isolation
  - Respiratory viruses / Viral haemorrhagic fevers

Q3. What would you do next?

- ...our case
  - 2 week h/o of fever
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  - WCC 3
  1. Send him home
  2. Start antibiotics
  3. Admit him for observation
  4. Admit him to an isolation room

A3. What happened next?

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Severe sepsis is a major problem:

- 18m cases pa & 1,500 deaths per day

SIRS
Sepsis
Severe sepsis

Core temperature >38°C or <36°C
HR >90
RR >20 (Pa CO₂ <4.3kPa)
WCC >12 x10⁹/l or <4 x10⁹/l

Documented or suspected infection

Organ dysfunction
  - oliguria
  - hypoxia
  - lactic acidosis
  - ileus
  - altered mental state
  - shock

Crit Care Med 1992; 20:864-874
**Q4. Which antibiotic?**

- 2 week h/o of fever
- Looked unwell
- Maculopapular rash
- T 38.5, HR 110, RR 20
- No other localising signs
- WCC 3

- **Which regimen would you chose?**
  1. IV cefuroxime & metronidazole
  2. PO ciprofloxacin
  3. IV imipenem & vancomycin
  4. IV ceftriaxone
  5. IV augmentin & gentamicin

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**Survival guide 2: Empirical antibiotic choices**

- **cefuroxime**
  - E. coli
  - S. pneumoniae
  - S. aureus
  - S. pyogenes
  - Neisseria sp.
  - Salmonella sp.

- **Augmentin**
  - Covers everything that cefuroxime does
  - Upper GI anaerobes
  - Oraly active

- **gentamicin**
  - Gram negative sepsis

- **ceftriaxone**
  - Neurological features
  - Typhoid

- **benzylpenicillin & flucloxacillin**
  - Soft tissue infection

- **metronidazole**
  - Lower GI tract

**When you are worried about resistance...**

- glycopeptides → MRSA
  - Enterococci

- ciprofloxacin → *Pseudomonas sp.*

- **carbapenems**
  - Enterobacteriaceae (AmpC)
  - ESBL E. coli
Extended spectrum β-lactamases (ESBLs)

- Resistant *E. coli* & *K. pneumoniae*
  - Cephalosporins
  - Penicillins
  - Aminoglycosides
  - Quinolones
  - Trimethoprim

- Risk Factors
  - Previous ESBL isolates
  - Hospital acquired infection
  - Residential / nursing home exposure
  - Endemic geographical areas

**MRSA**

- Hospital Acquired (HA)
  - In-patient exposure
  - Elderly
  - Respiratory / urinary / blood stream
  - Multi-drug resistant

- Community Onset (CO)

-500 MAU admissions/month

72h later

- Still febrile, rash fading, otherwise clinically unchanged
- Blood & urine cultures showed no growth
- HIV test Negative
- FBC, Renal & Liver biochemistry were all normal

Q5. What would you do next?

1. Change antibiotics to vancomycin & meropenem
2. Stop antibiotics & send more blood cultures
3. Echocardiogram
4. CT scan
5. FDG-PET scan

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Survival guide 3: Pyrexia of unknown origin

- No satisfactory definition, but...
  - Time > 2 weeks (excludes most self-limiting infections)
  - Negative bacteriology
  - No treatment response

- The differential diagnosis
  - Infections
  - Vasculitis
  - Neoplasia (lymphoma, RCC)
  - Drugs (antibiotics)
Survival guide 3: Pyrexia of unknown origin

- Risk assessment for infection is mostly about exposure:
  - Lifetime travel history associated with endemic infection
    - TB, Malaria, Typhoid, Histoplasmosis, Leishmania, Leprosy
  - Animals
    - Q fever, Brucella,
  - Water
    - Leptospirosis, Schistosomiasis
  - Vectors (Arthropods)
    - Rickettsia, Borrelia, Trypanosomiasis, Bartonella
  - Sexual activity
    - HIV / EBV / CMV / Syphillis
- ...and a bit about host susceptibility
  - Immunological / Physical compromise

Survival guide 3: Pyrexia of unknown origin

- When you can’t grow the bug- talk to the lab.
  - Alternative samples
    - Stool samples / Throat swabs / Bone marrow biopsies
  - Culture for longer
    - ‘Culture negative endocarditis’
    - Brucella
  - Blood films
  - 16S PCR
  - Serology
    - Syphillis / Q fever / Brucella / Rickettsia / Bartonella
  - Mantoux skin test or IGRA

Survival guide 3: Pyrexia of unknown origin

- Often need a biopsy…..guided by imaging
  - CT
  - MRI
  - PET
  - Bone scan

Q6. What is the diagnosis?
1. TB
2. Syphillis
3. Q Fever
4. Sarcoidosis

Survival guide 3: Pyrexia of unknown origin

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  - CT
  - MRI
  - PET
  - Bone scan

A6. Doughnut granulomas are a feature of:
1. TB
2. Syphillis
3. Q Fever
4. Sarcoidosis

The Febrile patient

3 Survival guides
1. Sepsis syndromes
2. Choosing antibiotics
3. Pyrexia of unknown origin