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Zoonoses and Meliodosis

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Conflicts of interest

• I have no conflicts of interest related to this presentation

• I am humbled and concerned to have to talk about meliodosis in Thailand!
Pulmonary Zoonoses

• Viruses
  – Hanta virus, MERS, Avian Influenza

• Bacterial
  – Q Fever, Chlamydia spp (inc Psittacosis), Mycoplasma spp.,
  – Brucella, Leptospira, Tularemia, Yersinia, Streptococcus zooepidemicus

• Protozoa
  – More of a problem in solid organs (Trypanasoma cruzi, Toxoplasma gondii etc)
Question 1

- Spending 24 hours in an enclosed space with which of the following would not put you at risk of a zoonoses causing pneumonia?
  - A – a chicken
  - B – a pig
  - C – a chimpanzee
  - D – a camel
  - E – a bat
  - F – all of the above
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COMMONLY PERCEIVED BIOTERRORISM THREATS

• CDC category A
  – Easily transmitted or high person to person
  – Likely high mortality
  – High social impact/potential for panic
  – Anthrax, plague, smallpox, tularemia
  – Botulism, Ebola, Marburg, Lassa, other South American haemorrhagic fevers
COMMONLY PERCEIVED BIOTERRORISM THREATS

- CDC category B
  - Brucellosis
  - Ricin
  - Glanders (*Burkholderia mallei*)
  - Melioidosis (*Burkholderia pseudomallei*)
  - Psittacosis
  - Staph enterotoxin B
  - Q fever
  - Viral encephalitis
Why zoonoses so scary?

• No herd immunity
• High pathogenicicity in “first pass” transfer
Hanta Virus

- Hantaviruses are tri-segmented negative sense single-stranded RNA
- Worldwide
- Two syndromes
  - Haemorrhagic fever with renal syndrome
  - Hantavirus cardiopulmonary syndrome
- Humans contract infection through inhalation of aerosols from the saliva or urine of infected animals (rodents, shrews, moles and bats)
- Different hantaviruses have different manifestations
  - Andes virus typically causes severe cardiopulmonary syndrome
  - Prospect hill virus doesn’t cause disease in humans
  - “New World” hantaviruses – Cardiopulmonary, “Old World” hantaviruses – Haemorrhagic fever
- Estimation 20000 cases per year, most in Asia (Jiang et al Virologica Sinica 2017)
<table>
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<th>Virus Isolate or Strain</th>
<th>Abbreviation</th>
<th>Associated Disease</th>
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<th>Geographic Distribution</th>
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<td>Sin Nombre virus (Bolton et al., 2014)</td>
<td>SNV</td>
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Figure 1. Geographical representation of approximate incidence of hantavirus cardiopulmonary syndrome (HCPS) and hemorrhagic fever with renal syndrome (HFRS) by country per year (data updated to 2016).
Hanta virus

• Primary infect vascular endothelial cells
• Leads to endothelial dysfunction in capillaries and small vessels
• Cardiopulmonary syndrome first described in 1993
• Initial symptoms dry cough, increasing dyspnoea
• Rapidly evolving bilateral interstitial odema
• Common to have renal failure, thrombocytopenia, haemorrhage, vomiting, diarrhoea, shock
Hanta diagnosis

• Clinical syndrome
  – Very easy to misdiagnose as influenza
• History of exposure
• Serology may be negative early on (<1 week) and is not readily available
• PCR assays unreliable
Hanta virus treatment

- Supportive care including ECMO
- Human immune plasma?
  - Vial et al Antivir Ther 2015
  - 32 cases, non significant trend to benefit
- Corticosteroids don’t help
  - Vial et al Clin Infect Dis 2013
Hantavirus CPS outcome

• Up to 35% mortality rate in hospitalised cases
  – Vial et al Clin Infect Dis 2013

• True mortality rate unknown but obviously much lower

• There are no reports of long term adverse outcomes in survivors
Coronaviruses

• Zoonoses that can make the leap to human-human
• SARS
• MERS
• More emerging
  – HKU1 in Thailand from bats
  – Joyjinda et al Microbiol Resour Announc 2019
Q-fever

- Coxiella burnetti – obligate intracellular Gram-negative bacteria
- Initially Rickettsia burnetti, now reclassified as a Legionellales
- Worldwide (except New Zealand)
- Cattle, goats, sheep, birds
- Urine, saliva, faeces, milk, especially birth products
- Animals are usually asymptomatic
- Can cause both acute (e.g. pneumonia) and chronic infection (2-5%)
- Is a vaccine (inactivated whole cell) but not widely available outside Australia.
- Cellular response in 60-90% for 5-years, failures have been reported especially with high exposure (Bond et al Vaccine 2017)
Q-fever pneumonia

- Male:Female 5:2
- Usually a mild disease
  - 60% of serological converters are asymptomatic
  - Only 2-4% hospitalised
  - Raoult et al Lancet Infect Dis 2005
- Presents as a flu-like illness 14-40 days post exposure
- High fever is usual (>38.5 °C)
- Pleuritic chest pain not unusual
- Rash 5-20%, punctiform or maculopapular, rarely erythema nodosum
- Hepatosplenomegaly common
- CXR is non specific, typically round opacities +/- pleural effusion, upper lobes>lower
- Can get meningitis/encephalitis, endocarditis, pericarditis, myocarditis
Q-fever pneumonia

- **Diagnosis**
  - **Exposure**
  - Serology (IFA) is the reference method
    - IgM and IgG detected
  - PCR assays now also available
  - Persistent high elevation (1:800) of Ab levels at 6 months = chronic infection
Q-fever pneumonia

• Treatment
  – Doxycycline 100mg BD 15 days drug of first choice
  – Clarithromycin, roxithromycin, azithromycin
  – Fluroquinolones (Ciprofloxacin, moxifloxacin, levofloxacin)
  – Cotrimoxazole and rifampicin if desperate due to allergy or contraindications
  – Need to follow up serology for 3-6 months
  – If have a valvular lesion follow up echocardiography to 12 months is advised
Cutaneous Anthrax
Early pulmonary anthrax
Tularemia

- Aerosolization
  - Primary pneumonic Tularemia
  - Typhoidal Tularemia
  - Oculoglandular Tularemia
  - Ulceroglandular Tularemia
  - Oropharyngeal Tularemia
Tularemia

- Following inhalation
  - Granuloma formation at entry and lymph nodes
  - 3-5 day incubation
  - Fever, chills, headache
  - Non productive cough and chest pain +/- pneumonia (50% have abnormal CXR)
  - Sore throat common and may be severe
  - May see ulcerative respiratory tract lesions
  - Septic shock and ARDS if not treated

- Mortality 35% without therapy, <5% with
Tularemia

- Treatment
- Gentamicin
- Ciprofloxacin, Doxycycline, or chloramphenicol
- Prophylaxis
  - Doxy 100mg bd or cipro 500mg bd
What’s the message

- There is no zoonose that is characteristic enough to diagnose every time or even most of the time
- An accurate history is critical
- Need to always be on the alert for emerging infections
Meliodosis

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Organism

• *Burkholderia pseudomallei*
  – Aerobic, gram-negative motile bacillus
  – Found in water and moist soil
  – Opportunistic pathogen
  – Produces exotoxins
  – Can survive in phagocytic cells
    • Latent infections common
History

• 1912, Burma
• Alfred Whitmore
• Organism isolated in humans
  – Glanders-like disease
    • Colony growth differed
  – No equine exposure
  – “Whitmore” disease
History

• 1913, Malaysia
• Stanton and Fletcher
• “Distemper-like” outbreak in animals
  – Isolated *B. pseudomallei*
• Pioneered serological tests for diagnosis
Transmission

- Wound infection
  - Contact with contaminated soil or water
- Ingestion
  - Contaminated water
- Inhalation
  - Dust from contaminated soil
- Rarely
  - Person-to-person
  - Animal-to-person
Epidemiology

- Clinical disease uncommon
  - In endemic areas
    - Antibodies in 5 to 20% of agricultural workers
    - No history of clinical disease
- Wet season
  - Heavy rainfall
  - High humidity temperature
Human Disease

• Incubation period: <1 day to years
  – Latent infection (~4% of presentations are reactivation)
• Most infections asymptomatic
• Clinical forms
  – Acute pulmonary infection
    • Most common
  – Focal infection
  – Septicemia
  – Neurological (rare)
• Alcoholism has a high association with mortality
Acute Pulmonary Infection

- Most common form
- High fever, headache
- Dull aching chest pain
- Cough, tachypnea, rales
- Chest X-rays
  - Upper lobe consolidation
  - Nodular lesions
  - Pleural effusion
Chronic Pulmonary Infection

- Easily misdiagnosed as tuberculosis
- ~10% of all cases of melioidosis reported
- Dull aching chest pain
- Cough, tachypnea, crackles
- Chest X-rays
  - Upper lobe consolidation
  - Nodular lesions
  - Pleural effusion
Melioid antibiotic resistance

• Efflux pumps
  – Aminoglycoside and macrolide resistance
  – Trimethoprim resistance

• Reduced outer membrane permeability
  – Polymyxin resistance

• Enzymatic breakdown
  – Beta-lactamases
Question 2

- For meliodosis, which of the following has been proven in a randomised controlled clinical trial
- A – meropenem is superior to imipenem
- B – meropenem is superior to ceftazidime
- C – ceftazidime is superior to cotrimoxazole
- D – imipenem is superior to cotrimoxazole
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Diagnosis and Treatment

• Diagnosis
  – Isolation of organism (Blood cultures positive in up to 55% in some series)
  – Various serological tests

• Treatment
  – Initial Systemic antibiotics 10-14 days, 28 days if extensive/severe disease
    • Ceftazidime – RCT vs chlor/doxy/cotrimoxazole 37% vs 74% White et al Lancet 1989
    • Trimethoprim sulfa
  – Surgical drainage of skin wounds
  – Subsequent oral eradication with cotrimoxazole or coamoxyclav from 3 months (Australia) up to 5 months (Thailand)

• No vaccine available – proving difficult

Center for Food Security and Public Health, Iowa State University, 2011
Meliodosis summary

• Know your local epidemiology
• High suspicion in right area
• Need to take a good history in all patients with pneumonia!
Thank you!

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