

## Week 9: Respiratory Infections and Non-Respiratory Infections Spread by Aerosols

### **Breathing and Cough/Sneeze Physiology**

- Humans breathe: 6-10L/min
- Inhalation and expiration are not a one-way flow
  - o Contain millions of bacteria
- Coughing:
  - o Follows irritation of trachea and large bronchi
  - o Is an innate immune defense
    - Removes particles in trachea and lungs to prevent build up
  - o Particle travel up to – 1000kmph; slow down quickly
  - o ∴ local organisms/viruses are aerosolised = spread
- Sneezing:
  - o Results from nasal irritation
  - o Outrush of air similar to cough
  - o Mobilises aerosols from nose in addition to rest of respiratory tract

### **Considerations on Aerosol and Droplet Transmission**

- Coughs and sneezes can release ~ 20,000 particles
- Projectile vomiting also yields aerosols
  - o E.g. norovirus aerosols
- Effective range up to 3-4 meters
- Spoken 'plosives' in English also produce aerosols (p, t, s, f)

### **Aerosols**

- Infective range of bacteria and viruses depends on the size of particle they're in and if they have a short or longer range
- Larger droplet particles:
  - o Dry out slower
  - o Sink quickly
  - o Have a short range
- Small aerosols (~10um):
  - o Dry quickly → if humidity is low and warm
    - Some organisms are susceptible to drying
  - o Encapsulation in mucus may slow desiccation
  - o Remain aloft for ~ 20 minutes in still air
    - Can walk though this after they've moved on
  - o Can reach deeper in the respiratory tract
- ∴ aerosol transmission is most efficient when people gather indoors in cool weather
- Enable protected and direct transmission between respiratory tracts
- Also land on + contaminate surfaces → picked up by hands
- Large number of bacteria and fungal spores are present in air normally
  - o ~10000 bacteria and 15000 fungal spores inhaled daily
  - o Varies greatly depending on location + weather
- Saliva:
  - o Can transmit EBV, HSV, meningococcus
  - o 1L/day → may contain pharyngeal bacteria and viruses
  - o Exchanged by kissing, shared utensils, cups, cigarettes, etc.

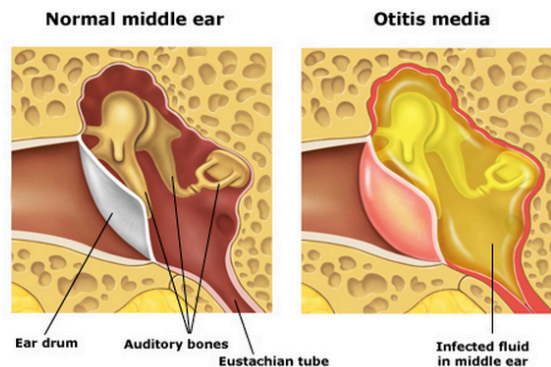
### **Infections of the Respiratory Tract**

- URTI (upper respiratory tract infection)

- Sinusitis
- Pharyngitis
- Rhinitis
- Otitis
- Diphtheria
- LRTI (lower respiratory tract infection)
  - Whooping cough (pertussis)
  - Bronchitis
  - Bronchiolitis
  - Pneumonia

## Otitis

- Otitis externa:
  - “Swimmers ear”
  - Outer ear → auditory canal
  - Opportunistic:
    - *S. aureus*, *Pseudomonas aeruginosa*, *Candida albicans*
- Otitis interna:
  - Inner ear → vestibule + semicircular canals
  - Can lead to severe nausea, and balance issues such as vertigo
- Otitis media:
  - Middle ear infection → “acute otitis media” AOM
  - Viral and bacterial cause
    - Prior viral URTI may predispose for bacterial AOM
  - Bacterial pathogens are nasopharyngeal colonisers
    - *S. pneumonia*, *Haemophilus influenza*, less commonly *S. aureus*
    - Most common in children
    - Inflammation, pain, fluid accumulation → impairs hearing and learning, chance of chronicity and discharge
      - Chronic = antibiotics may be needed
    - Usually self-limiting (24 hours), analgesia



## Sinusitis

- Inflammation of the paranasal sinus mucosa, facial pain, congestion, tenderness
  - Pus and discharge in sinus → localised inflammation
- Viral, fungal and bacterial causes
  - *S. pneumonia*, *Haemophilus influenza*
    - These are nasopharyngeal commensals
- Usually self limiting → antibiotics for persistent sinusitis

## Pharyngitis

- Sore throat
- Mostly viral:
  - o Saliva transmitted → EBV, herpes simplex virus 1 and 2
  - o Aerosol → adenovirus + enterovirus
  - o Faecal-oral → coxsackie + enterovirus
  - o Localised inflammation + pain
  - o Neck lymphadenopathy → swelling of lymph nodes
  - o Ulceration with Herpes Simplex Virus
  - o Persistent, generalised malaise and increase LFT (liver function tests?) with EBV → 'infectious mononucleosis/glandular fever'
- Bacterial pharyngitis:
  - o Streptococcus pyogenes (Group A B-haemolytic Strept. 'GABHS'/'GAS')
  - o Droplet and contact spread → 2-25% population are colonised
  - o Symptoms: inflammation, swollen throat with discharge and pus, pain on swallowing, cervical nodes raised
    - Headache and fever may be present
  - o Streptococcal pharyngitis may not need antibiotic treatment unless severe, prolonged, or in special risk groups (immunocompromised, children, elderly)
- Chronic = nodules, may remove tonsils

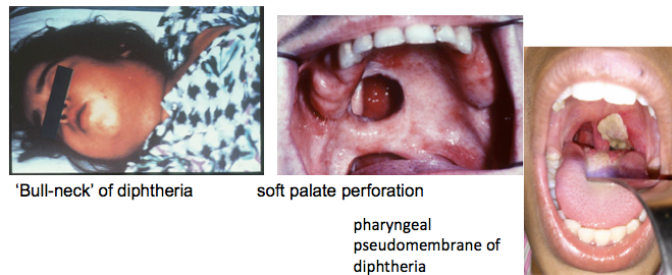
Streptococcal pharyngitis



Chronic pharyngitis

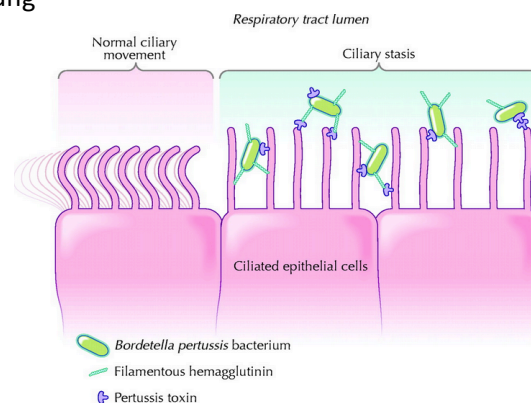
## Diphtheria

- Toxigenic strains of *Corynebacterium diphtheria*
  - o GPR, club shaped, catalase +
- Lysogenic bacteriophage encodes diphtheria toxin
  - o AB dipeptide toxin = B component bind to cell, allows A component to enter cell = inhibits protein synthesis
- Spread by aerosol → nasopharyngeal coloniser
- Toxin synthesised and diffuses to underlying tissue → death of epithelia and PMN (polymorphonuclear leukocytes) → necrotic ulceration → exudate of fibrin + debris → pseudomembrane over pharynx
  - o Membrane blocks windpipe
- Lymphadenopathy and edema gives rise to 'bull-neck'
  - o Characteristic of diphtheria
- Risk of hearing and neural problems
- Preventable: diphtheria toxoid vaccine
  - o Toxoid = inactivated toxin which retains its antigenicity
    - Recognised by immune system = generates response
  - o Antibiotics?
- Only 1 case in Australia between 1992-2010
- High fatality rate → 1 death in 2011, 6 cases in 2016 bc ↑ travel + ↓ vaccination rates



### Whooping Cough (Tracheobronchitis)

- Caused by *Bordetella pertussis*
  - o Small GNR
- Aerosols spread from person to person
- Very infectious
- Vulnerable = young, frequently acquire from older siblings and close family
  - o Esp. babies too young for vaccinations
  - o Could be prevented by vaccinating mother = passive immunity
  - o Vaccinating anyone in contact with baby
  - o Keep vaccination % high within the community
  - o Adults are still susceptible, it is just not as severe
- 100 day cough affects all ages, but most severe in young children
- Initially mild respiratory symptoms develop into a violent paroxysmal (sudden, uncontrollable) cough → struggle for breath
- Characteristic 'whoop' inhalation sound in young children
  - o Absent from older children and adults
  - o Affects diagnosis, bc doctors listen for 'whoop'
- Organism binds to cilia via pili and releases toxin
  - o Tracheal cytotoxin paralyzes + kills epithelial cells
  - o Pertussis toxin promotes hypersecretion and lymphocytosis
  - o Toxins can cause epithelial and tissue necrosis
- Complications incl.: exhaustion, cerebral anoxia, seizures, conjunctival haemorrhage, vomiting, secondary pneumonia
  - o Bc ↓ oxygen, struggling for breath
- Occasional deaths, and hospitalisation for young
- Vaccine preventable (acellular pertussis vaccine) → universal vaccination
  - o Boosters for parents, child carers, health-care workers, others to ↓ risk of transmission to vulnerable young
- Notified cases:
  - o 1997 = 10,900
  - o 2006 = 11,000
  - o 2007 = 5,345
  - o 2008 = 14,516 (start of epidemic)
  - o 2009 = 29,736 (2 deaths)
  - o 2011 = 38,500 (5 deaths)
  - o 2015 = 23,000



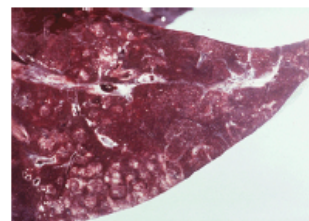
- Remains high in Australia bc ↓ vaccine rates + new vaccine does not last as long ∴ need boosters

## Pneumonia

- Inflammation of the lung with exudate in alveolar, or airway spaces
  - o Exudate released by cells due to infections
- Symptoms: shortness of breath, cough, fever, resp. distress, increases blood pressure, chest pain, confusion, purulent sputum (may present silently in elderly)
- Complications if spreads:
  - o Septicaemia
  - o Meningitis
  - o Empyema → pleural space effusion with pneumococcus
- Bacterial, viral and fungal causes
  - o Viral pneumonia is usually less severe
- Many causes of pneumonia, most common is *S. pneumonia* = 'classical' cause
  - o 25-60% of cases
  - o Mostly lobar pneumonia
  - o Pharyngeal coloniser in  $\leq 5\%$  adults, 15% in children
- Primary atypical pneumonia:
  - o i.e. non-pneumococcal
  - o *H. influenza* → 5-15%
  - o *S. aureus* → rare
  - o *Klebsiella pneumoniae* → vagrants and hospital-acquired
  - o *Legionella* → contaminated air-conditioning, potting mix aerosols, spa-baths, carwashes
    - Not spread from person to person → water associated acquisition
- Viral pneumonia:
  - o Influenza, measles, adenovirus, cytomegalovirus (CMV), respiratory syncytial virus (RSV) in children (RSV occ. in adults)
- Antibiotics for bacterial cause
- Vaccines → pneumococcus, pertussis, influenza, measles, Hib
- 'Lobar' pneumonia
  - o Exudate consolidates between alveoli → lobar appearance on x-ray
  - o Affects 1 or more sections/lobes of the lung
- Bronchopneumonia → inflammation of the lungs arising from the bronchi or bronchioles
  - o Involves diffuse foci of consolidation along smaller airways → patch consolidation on x-ray
  - o Can be mild or severe



Bilateral lobar pneumonia with air bronchogram (left middle field)



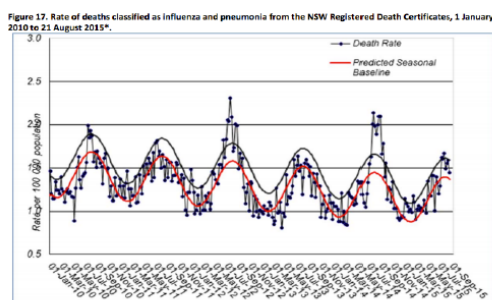
Bronchopneumonia (nb. peribronchial inflammation)

## Influenza

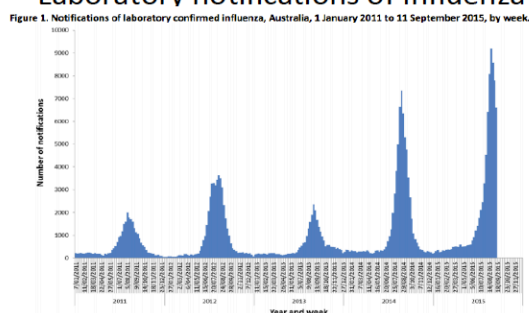
- Notified cases: 2008 = 9,137, 2009 = 58,562, 2015 = 82,000
  - o H1N1 swine flu pandemic
  - o Flu kills thousands every year in Australia, 3,000-4,000 esp. elderly
- Enveloped RNA virus
- Highly transmissible by respiratory aerosol + contagious

- 3 types (A, B, C):
  - o A is the most important, then B
  - o Influenza A are bird viruses (esp. water birds)
- Flu A strains exhibit multiple envelope haemagglutinin + neuraminidase (H + N) Ags
  - o All H and N types circulate in water birds
  - o Only a few are able to circulate in human populations
    - E.g. H5N1 'bird flu' poorly transmits from birds to humans, or human to human, but when it does, case fatality is 60%
- Human flu A strains contain H1, H2 or H3, N1 or N2
  - o Many variants of these exist
  - o Transmit human to human
- H and N antigens also 'shift and drift' in their structure
  - o Shift = major change in the Ag structure
    - To new antigen not previously seen
    - No antibody exists in population
    - Potential new pandemic strain
  - o Drift = minor change in Ag structure
    - E.g. point mutations
    - Poorer coverage by existing vaccine
    - Poorer recognition by existing antibody
- Symptoms: chills, fever, myalgia, headache, malaise, dry cough, prostration, tachycardia (↑ HR), vomiting, diarrhoea
  - o Risk of pneumonia, or secondary bacterial pneumonia
- Prevention: vaccine
  - o Different each season due shift and drift
- Also prevent by isolation and limiting contact
- Anti-virals are yet to show a major effect of preventing contraction of disease and reducing severity of disease
  - o But still can reduce the duration and lessen the symptoms
  - o Rx: amantadine for pneumonia, neuraminidase inhibitors (oseltamivir "Tamiflu" & zanamivir "Relenza") for early disease
- Rate of death from influenza was higher than predicted in 2012 + 2014 → peaks
- Increases in notification numbers, almost double in recent years

### Seasonal death rate for Influenza



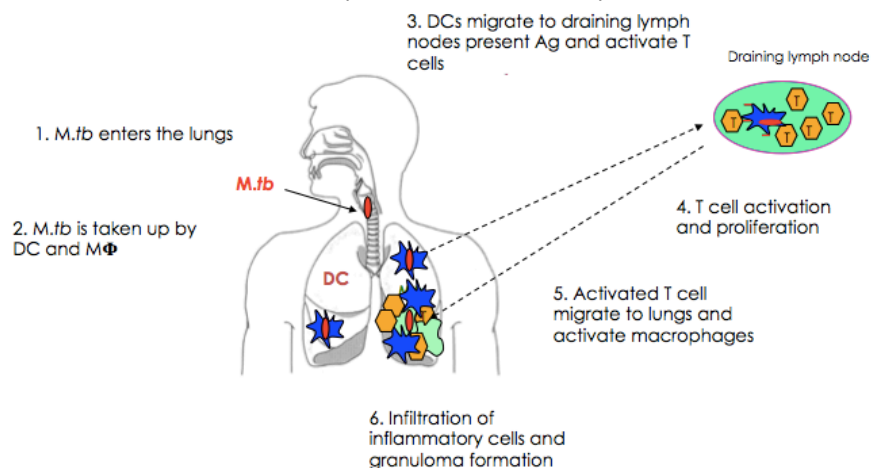
### Laboratory notifications of Influenza



### Tuberculosis

- *Mycobacterium tuberculosis* is primary cause
  - o Bacilli is acid fast, not typical GN/GP → stained by Zhiel-Neelsen Stain
    - Sometimes said to be GP
- WHO estimates 2 billion individuals have latent TB infection
  - o Only 5-10% of individuals who get infected, develop disease
- 9 million new cases each year + 1.5 million deaths

- Australia rates are very low at around ~1,400 yearly
  - o  $\therefore$  ~5 cases per 100,000
  - o Other areas such as Africa can have ~500 cases per 100,000
- Growing drug resistance is a major problem
  - o Estimated 550,000 cases of multi drug-resistant TB last year
  - o Causes death
- Treatment for TB requires 4 antibiotics for first 2 months + 2 antibiotics for 6 months
  - o Slow treatment
  - o Side effects e.g. liver toxicity
  - o Difficult for patients to stay on antibiotics for that long
    - May begin to feel better in first few weeks bc bacteria being killed rapidly = stop antibiotics = resistance
- WHO recommends 'DOTS' strategy  $\rightarrow$  'Directly Observed Therapy Shortcourse'
  - o Health care workers watch patients swallow their drugs
- Very low infectious dose ~ 10 bacilli
  - o TB bacteria reside within macrophages
    - $\therefore$  Abs are not protective bc cannot penetrate and reach bacteria



pulmonary macrophages are infected with

- When taken up by alveolar macrophages, the macrophage is unable to digest it + eradicate it bc the cell wall prevents the fusion of the phagosome with the lysosome
  - o  $\therefore$  the bacteria resist phagocytosis + multiply within the macrophage
- TB induces **cell-mediated** immune response
  - o Cell-mediated immunity contains infection for decades, or life
  - o Of those with latent TB  $\rightarrow$  over 90% will never develop active disease
    - Latent TB is non-infectious only infectious in active disease
  - o CD4<sup>+</sup> T cells are essential
    - Major reason why individuals with HIV are highly susceptible to TB
      - HIV kills off CD4<sup>+</sup> T cells
- T-cells are important  $\rightarrow$  release cytokines to recruit other cells to site of infections = granulomas build 'wall' around macrophages = stop spread
- TB infection induces granulomas  $\rightarrow$  inflammation and cellular accumulation within the infected site, most commonly the lung
- Granulomas/tubercles
  - o May become necrotic = caseating necrosis = hole in lung
  - o Fibrotic or calcified
  - o Lead to a cavitation (void) in the lung tissue
- Symptoms: fever, cough, night sweats, unexplained weight-loss, loss of appetite, chest pain

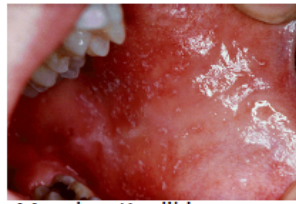
- Can occur in any organ of the body if it spreads e.g. meningitis
- Re-activation may occur due waning immunity e.g. in elderly
  - o Don't have method of predicting who will reactivate bc unaware of cause
- TB granulomas appear as dark purple lesions surrounded by alveoli structures
  - o Pink = macrophages
  - o TNF is essential for controlling inflammation
  - o Wild-type mice, like humans develop granulomas in the lung, these are composed primarily of macrophages and lymphocytes (T cells)
  - o If the mice lack TNF the inflammation is uncontrolled and lesions are larger, with more necrosis (similar to response seen in humans)
- Sputum test = smear microscopy with special stain
- If suspected case of TB = Mantoux test
  - o 'Tuberculin skin test'
  - o Test for immunity to TB using intradermal injection of tuberculin (Ag)
  - o Positive = person is infected with TB but does not mean they have disease and are infectious
    - Further testing to look for signs of active disease
      - E.g. X-ray + physical examination
- BCG TB vaccine to prevent disease
- In the case of a public health notification
  - o Increase vaccinations
  - o Screen at risk populations e.g. HIV patients

Some infections spread *via* aerosols but only involve mild respiratory disease but more severe disease in other body systems

### Measles

- Very contagious, enveloped RNA virus
- 1-2 week incubation, average 10 days
- Symptoms: early symptoms like the flu-fever, cough, malaise, aches, then skin rash
  - o Infectious before skin rash develops ~ 4 days
- Complications:
  - o Pneumonia (9%)
  - o Encephalomyelitis (~ 0.1%, death in 10-15% or permanent neurological deficit in 15-40%)
    - Inflammation + swelling of the CNS
  - o Subacute sclerosing panencephalitis (SSPE, ~ 1 in 100,000 – always fatal)
    - Brain swelling in patients with measles
- Developed world ~ 20 million cases a year
- 146,000 deaths in 2014
- 5<sup>th</sup> highest cause of illness and death in children
- Australia → declared measles eliminated, cases now imported
  - o No longer have endemic measles
- April 2015 outbreak Queensland university, student returning from overseas with disease
- Australian notified 2014 = 340 (16 year high school) incl. 62 children under 5
- Vaccine-preventable (MMR)
- Infectious 4 days prior first fever/malaise until 4 days post appearance of rash
- WHO estimates the measles vaccine saved 15.6 million lives from 2000 – 2013





Measles: Koplik's spots



& rash.

## Mumps

- Enveloped ssRNA virus
- Saliva/droplet transmission as an aerosol
- Less communicable than measles, not as infectious
  - o Requires more contact with infected individuals
- Peak incidence pre-vaccine in 5-9 year olds
- Virus-tropism for glandular tissue → swollen salivary glands, testis pancreatitis (can lead to sterility in males, painful) and inflammation of other secretory organs
- Swelling to face and jawline, malaise, fever, anorexia
- Infectious ~ 6 days prior swelling to 9 days after onset
- Complications:
  - o Encephalitis = 1 in 200 cases, fatal in ~1 of these
  - o Neurosensory deafness (rare)
- Notifies cases 2013 = 218, 2015 = 1,005 (current outbreak in WA/NT in vaccinated individuals, esp. Indigenous populations bc do not recognise new variant ∴ modification of vaccine for Indigenous population)
- Vaccine preventable (MMR)

## Rubella (German Measles)

- Enveloped RNA virus
- Aerosol transmission but not highly contagious
- Mild febrile (having or showing symptoms of fever) illness + rash, 50% asymptomatic
- MMR vaccine → prevent infection during pregnancy
- Congenital rubella syndrome:
  - o Infection during first trimester of pregnancy, first 8-10 weeks
  - o Large issue if crosses placental barrier
    - Transplacental, foetus infected
  - o Low contagiousness may delay exposure till adult life
  - o Congenital abnormalities in 90% infants
  - o Neurosensory deafness, blindness, cataracts, heart abnormalities, retardation
  - o Notified cases 2015 = 21, 1 case of congenital rubella

## Varicella Zoster (Chickenpox + Shingles)

- Enveloped DNA herpes virus
- Transmission via respiratory secretions and pox vesicle fluid contact
- Readily transmissible, most will develop chickenpox in childhood
- Symptoms = vesicular/crusting rash, pruritus (itchiness), fever and lethargy
- Complications:
  - o Pneumonitis (esp. in pregnant women) = inflammation of the alveoli
  - o Encephalitis (0.001%)
  - o Reye's syndrome = swelling in the liver + brain
  - o Latent infection in nerve ganglia → may reactivate, as zoster (shingles)

- Reactivation due to stress, reduced immune system
- Painful, crusting vesicular skin lesions along affected nerves
  - May affect facial or trunk nerves
  - Often treated with antidepressants to suppress nerve function
  - Can have shingles without any presentation of rash
- Notified cases in 2013 = 2,121 (chickenpox) + 5,034 (shingles)
- New vaccine
  - Most people infected with chicken pox before vaccine ∴ chance of shingles



chickenpox



shingles

### **Cytomegalovirus (CMV)**

- Enveloped DNA herpesvirus
- Transmitted via saliva, semen, breast milk, vaginal secretions, blood + organ transfusions
- CMV primary, and life-long latent infections, can recur
  - Generally mild or asymptomatic
- Severe disease in special circumstances:
  - Primary infection of pregnant women
    - Risk of stillbirth/congenital abnormalities → deafness, microcephaly
    - Hepatosplenomegaly = swelling of liver + spleen
    - Jaundice
    - Respiratory distress
  - In blood + organ recipients = hepatitis, pneumonitis or mononuclear syndrome
  - In AIDS patients = retinitis, pneumonitis and others
- Treat with antiviral → ganciclovir and antibody preparations (no vaccine)

### ***Neisseria meningitidis* (Meningococcal Disease)**

- Small, gram negative diplococcus (GNdC)
- Nasopharyngeal commensal → up to ~ 20% of population
  - Doesn't usually cause infection in these individuals
- 13 capsular serotypes → A, B, C, W-135, Y are most common
- Capsules important for invading immune system:
  - Anti-phagocytic + anti-complement
- Other virulence factors = pili, IgA (mucosal Ab) protease and lipooligosaccharide (endotoxin)
- Transmitted by saliva, and aerosols from carrier
- Risk factors for colonisation and invasive disease
  - Highest rate in < 5 year old
- 149 notifications 2013
- Disease is sporadic, or involves outbreaks in groups, winter/early spring peak
- Early petechial rash, later purpuric haemorrhagic rash and peripheral gangrene of meningococcal
  - Petechial = red or purple spot on the skin, caused by a minor bleed from broken capillary
  - Gangrene = death of tissue
  - Risk of amputation, extensive debridement
  - Early rash may be non-specific and blanching
- Complications (can have both):

- Meningitis:
  - Children and young adults more affected
  - Headache, nausea, vomiting, stiff neck, temperature, irritability, malaise, (rash), altered sensory perception
  - Risk of progressive neurological dysfunction and coma
- Meningococcal septicaemia can spread to multiple organs = multiple organ failure and death
- Vaccine for type B and C, part of the vaccine schedule = greatly reduced disease
- Vaccination for at-risk individuals
  - Travellers going to endemic areas in the summer months + Hajj pilgrims
    - Parts of Africa and Middle East
  - Multivalent vaccine now a visa requirement for Hajj pilgrims



### **Legionnaire's Disease: Tutorial**

- Legionella bacteria
  - Causes a pneumonia-type illness
  - Grows best in warm water
- Usually acquired through aerosols released from cooling towers, spas, potting mix, etc.
- Spread by mist/vapour associated with the bacteria from these sources
- Aerosols from person to person are not likely
  - Not usually transmitted this way
  - Water acquisition
- No vaccine
- Prevent by maintaining and treating of artificial water systems
  - Spa baths
  - Warm water systems
  - Decorative fountains
  - Cooling towers
- Take care with potting mix