Orthomyxovirus
- Diameter ~100 nm
- RNA: 8 genome strands
- M1 matrix capsid
- Lipid envelope
  - Haemagglutinin (HA)
  - Neuraminidase (NA)
Types

- Influenza A
  - Animal & human hosts
  - High antigenic variability (hence epidemics)
- Influenza B
  - Human hosts only
  - Some antigenic variability (some epidemics)
- Influenza C
  - Swine & human hosts
  - Antigenic stability
  - Mild disease
Subtypes

- Most antigenic variability lies in HA and NA glycoproteins
- 15 HA subtypes
- 9 NA subtypes
- HA spike is complex folded structure
  - HA1 & HA2 subunits
  - attaches virus to host cell sialic acid
- NA is tetramer of identical units
  - sialidase
  - facilitates release & prevents self-aggregation
Nomenclature

- Type/host/geographic/strain/year(HxNy)
  - A/swine/Iowa/15/30(H1N1)
  - A/California/7/2009(H1N1)
Nuts and Bolts

- Spread
  - droplet
  - contaminated surfaces (includes hands)
- Defence
  - cough
  - mucus: IgA & non-specific inhibitors
- Incubation 1 – 4 days
- Shedding
  - from day *before* onset of symptoms
  - peak at 24/24, plateau 1 – 2/7, rapid decline
Nuts and Bolts

- **Infection**
  - virus infects respiratory tract mucosa
  - protease necessary to cleave HA1 & HA2
  - NA reduces viscosity of mucus

- **Pathology**
  - cell death and desquamation of respiratory mucosa
  - decreased resistance to secondary infection
  - complete repair takes 1 month
Clinical

- Uncomplicated infection
  - fever, headache, myalgia, malaise, anorexia: 3/7
  - dry cough: 7/7
  - may persist with weakness: 1 – 3/52

- Type C causes mild infection only
- Children: higher fever
  - more GIT symptoms
  - OM (12%)
  - croup (under 1’s)
Clinical

- Pneumonia
  - Old, debilitated, chronic disease
  - Viral and/or secondary bacterial
  - Pathogenesis: damaged mucosa
    mucus carries pathogens
    exudate acts as growth medium
    decreased ciliary escalator function
    phagocyte dysfunction
    some *S aureus* secrete HA protease
Reye’s syndrome
- Acute encephalopathy of 2 – 16 year olds
- 10 – 40% mortality
- Complication of influenza A & B and varicella
- ?linked to salicylates
**Immunity**

- Mediated by antibody to HA and/or NA
- Anti-HA confers resistance to infection
- Anti-NA decreases severity
  reduces transmission
- There are shades in between:
  - incomplete immunity
  - viral point mutations
Epidemiology

- Regular epidemics of type A and B influenza
- Due to antigenic
  - drift (point mutations)
  - shift (gene reassortment): type A only
- Probably avian reservoir
- Pigs act as reassortment vessels
Pandemics

- Global epidemic
  - 1918: H1N1 (40 – 50 million deaths)
  - 1957: H2N2 (less severe)
  - 1968: H3N2 (mild)
- Herald wave
- School-age children predominant vector
Treatment

- Adamantanes
  - amantadine
  - rimantadine

- Neuraminidase inhibitors
  - Oseltamivir (Tamiflu)
  - Zanamivir (Relenza)

- Inhibit M2 ion channel
  - decreased infection
  - decreased budding
  - effective against A only

- Effective against A & B
This H1N1 thing...

- ...is a new thing
- WHO assessment (11 May):
  - higher secondary attack rate (22-33% v 5-15%) 
  - mild disease outside Mexico 
  - deaths outside Mexico in chronically ill patients 
  - more severe cases in younger people (Mexico & USA) 
  - is sensitive to both NA inhibitors, but not amantadanes
This H1N1 thing... in May

New Influenza A (H1N1),
Number of laboratory confirmed cases and deaths as reported to WHO

Status as of 13 May 2009
06:00 GMT

Total: 5728 cases
61 deaths

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

Map produced: 13 May 2009 06:30 GMT

Data Source: World Health Organization

Map Production: Public Health Information and Geographic Information Systems (GIS) World Health Organization

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Pandemic

- WHO phase 4 plan
  - containment
- WHO phase 5-6 plan
  - surveillance
  - isolate/cohort cases
  - reduce opportunities for spread
  - antivirals & vaccines
  - adjust triage
  - boost infection control
  - PPE
  - corpse management
  - **no** masks for well
PPE – droplet precautions:
- Medical mask if within 1 m
- Hand hygiene
PPE – risk of splashes:
- goggles or mask with visor
- gown and gloves
PPE – aerosol generating procedures:
- FFP2/N95 facial particulate respirator
- ventilated room (>12 air changes/hour)
- limit access to room
Several countries no longer routinely testing
Median age 12 – 17; mean drifting up
Majority mild symptoms recovering within 1 week
Most severe cases in people with comorbidities
Isolated severe cases in healthy people:
  - rapid progression
  - pneumonia & multi-organ failure
  - no predictors identified
This H1N1 thing...now
This H1N1 thing... in Europe

- Widespread activity in Austria, England, Malta, Wales
- In the UK:
  - activity decreasing (est. 30,000 v 110,000 cases)
  - 40 deaths to date
  - highest admission rate in under 5s
  - on 4 Aug, 576 inpatients (55 in ICU)
  - no antiviral resistant strains
This H1N1 thing... in the UK

Figure 1: GP weekly consultation rates for influenza/ILI in the UK national sentinel influenza schemes, 2008/09.
This H1N1 thing...in the UK

Figure 5: Daily number of assessments, antivirals authorised and collected by NPFS.
This H1N1 thing...Vaccination

WHO

1. Identify virus
2. Prepare vaccine strain
3. Vaccine strain verification
   Distribution to manufacturers
4. Prepare reference reagents

MANUFACTURER

1. Optimise growth conditions
2. Bulk manufacture:
   ▪ Incubation in eggs
   ▪ Isolation & killing
   ▪ Ag extraction
3. Quality control
4. Vial production, testing & release for distribution
This H1N1 thing...

- The future?
  - further mutation?
  - interaction with southern hemisphere seasonal influenza?
  - winter pressures
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Don’t forget bird flu
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