Pandemic respiratory infections

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Major patterns of disease

- Endemic: a disease that exists permanently in a particular region or population. Eg. Malaria, diabetes.
- Epidemic: An outbreak of disease that attacks many peoples at about the same time and may spread through one or several communities. Defined by rate of growth of the epidemic curve. Eg. Influenza
- Pandemic: When an epidemic spreads throughout the world. Eg. Influenza
- Sporadic: few cases of disease that do not meet definitions above. Eg. Human cases of H5N1 avian influenza

The meaning of

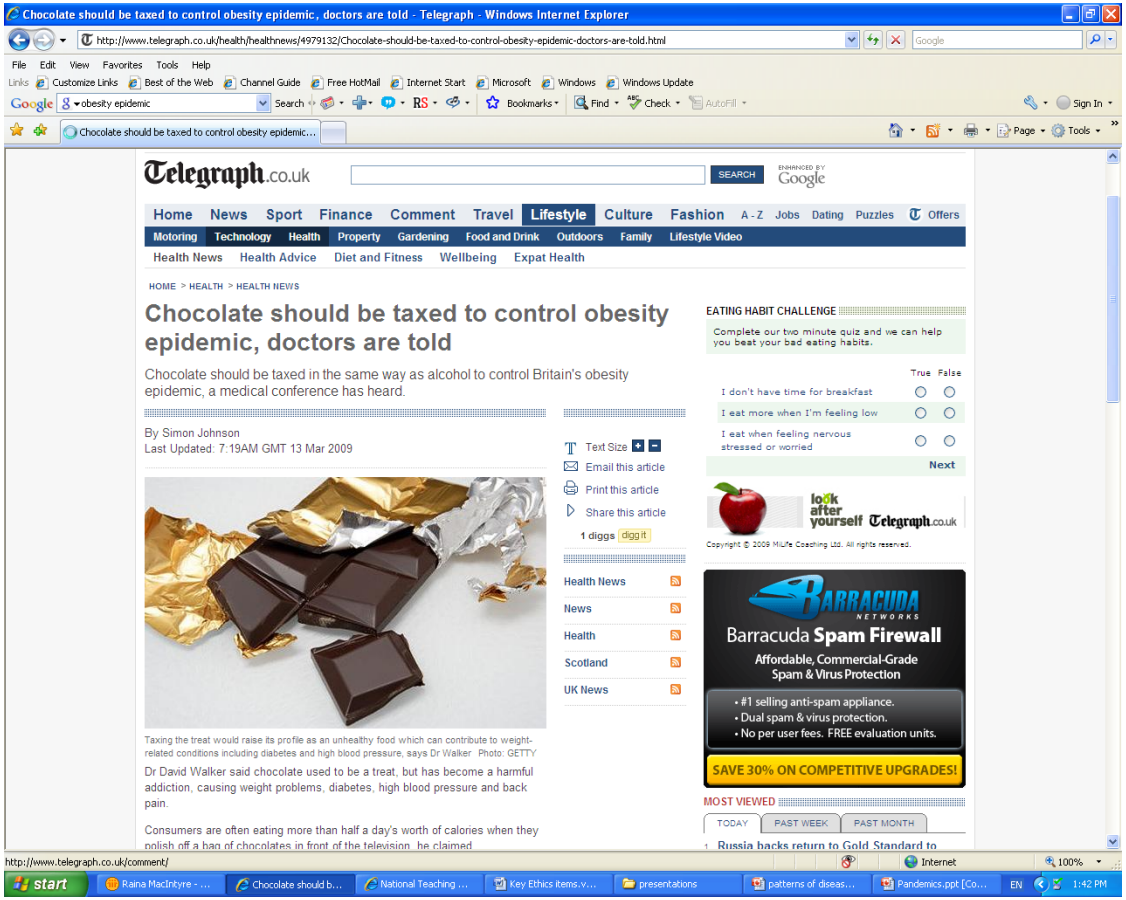
- R – the Reproductive Number

- the n of secondary cases generated from one index case
- The lower the Ro, the easier it is to eradicate or control a disease

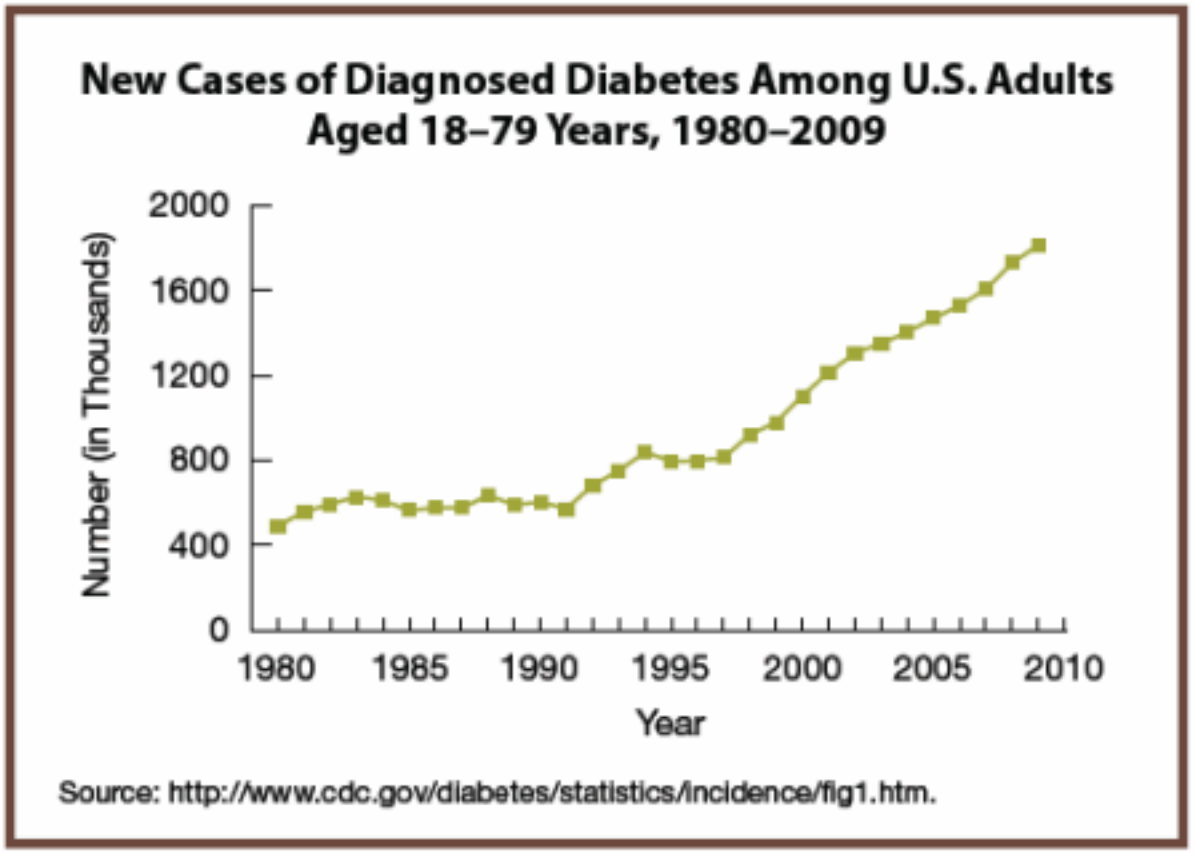
What is a pandemic?

- A global epidemic
- The epidemic threshold is R=1
- When R >1, epidemic (and pandemic) potential exists
- When R<1, epidemic conditions are not present.
- For disease control efforts aim to reduce R < 1

Epidemic vs endemic



NOT an epidemic – classic endemic disease



Not an epidemic

- Obesity
- Diabetes
- Heart disease
- Cocaine
- Malaria

Time scale - years

Image source: CC Pixabay

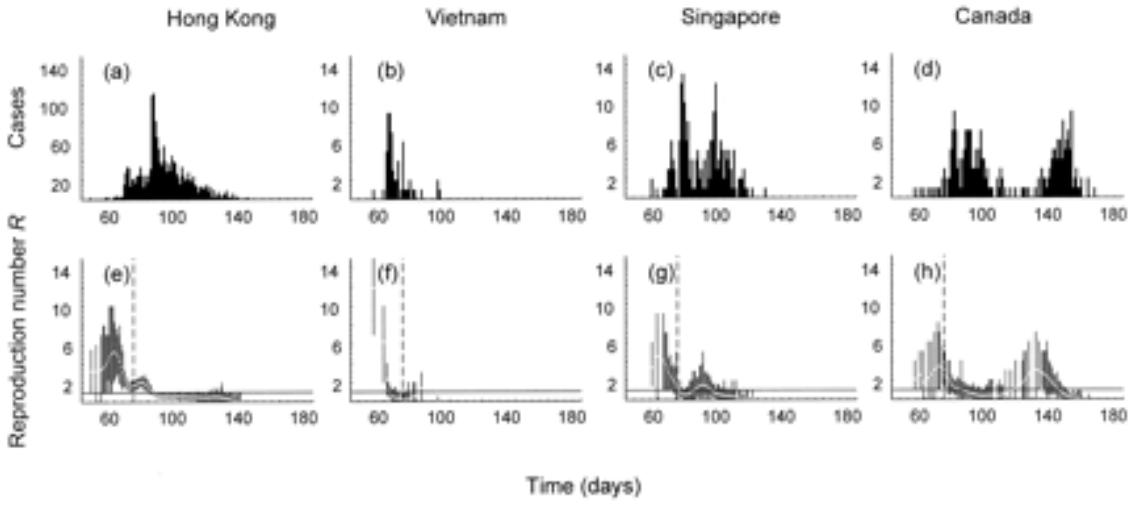
Epidemic defined by rate of rise/growth

- Mathematically, epidemics can be defined based on R
- Not by total number of cases
- Rapid rise over time (days to weeks, not years)
- Immediate surge capacity required

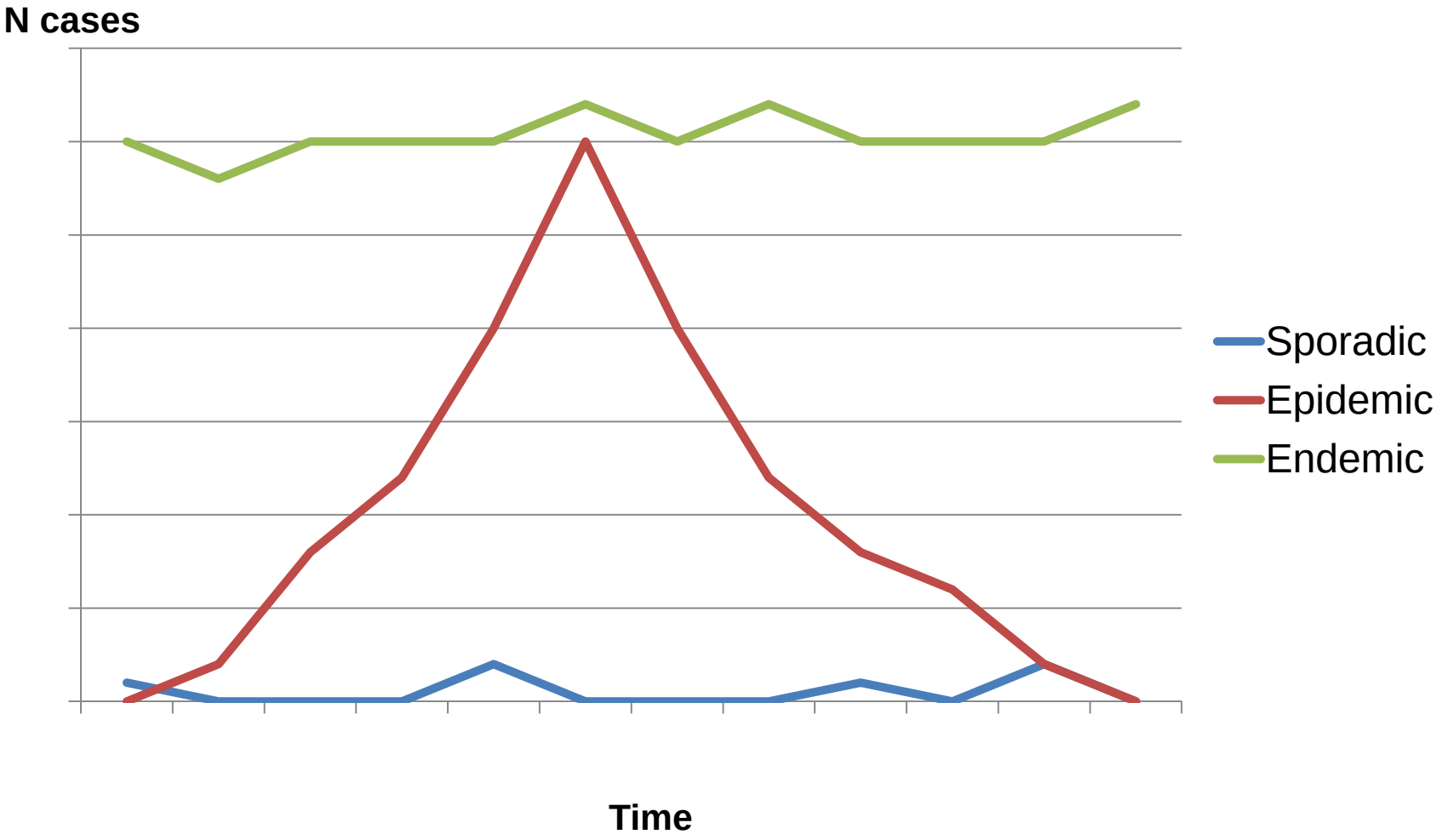
Image source. CC, http://betanews.com/wp-content/uploads/2014/07/Falling-sales-graph-e1431345307788.jpg

Classic epidemic pattern

American Journal of Epidemiology 2004 160(6):509-516;



Patterns of disease

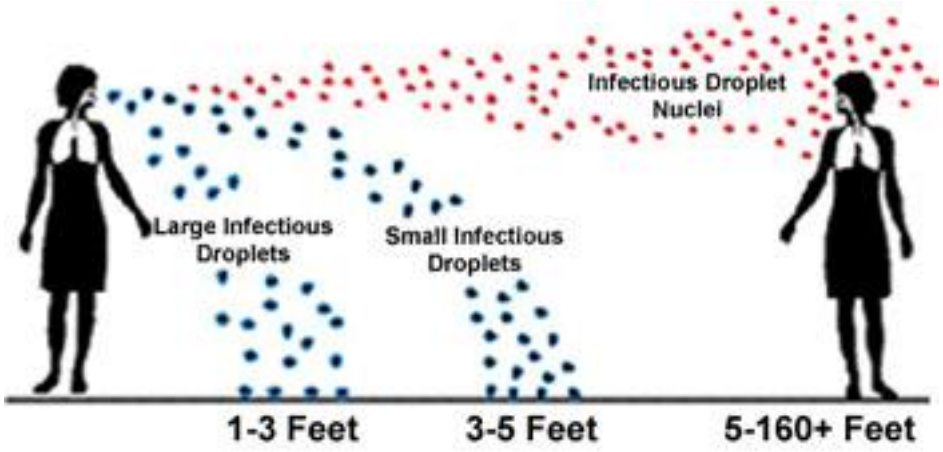


Routes of transmission of infection

- Person to person
- Vector (animal or insect) to person
- Soil/water/food to person

Routes of person to person transmission

- Respiratory (droplets, aerosol or airborne)
- Fomite or direct contact (hands, face)
- Blood borne
- Faecal/Oral
- Sexual
- Vertical (mother to baby)



Contact, droplet, airborne

- An artificial paradigm that has driven hospital infection control practice for >80 years.
- Belief that only large droplets are emitted close to the patient, and small droplet nucleii at a greater distance
- Based on experiments of aerobiologists from 1940's and 50's
- Newer research shows both small and large droplets can be present close to the patient*

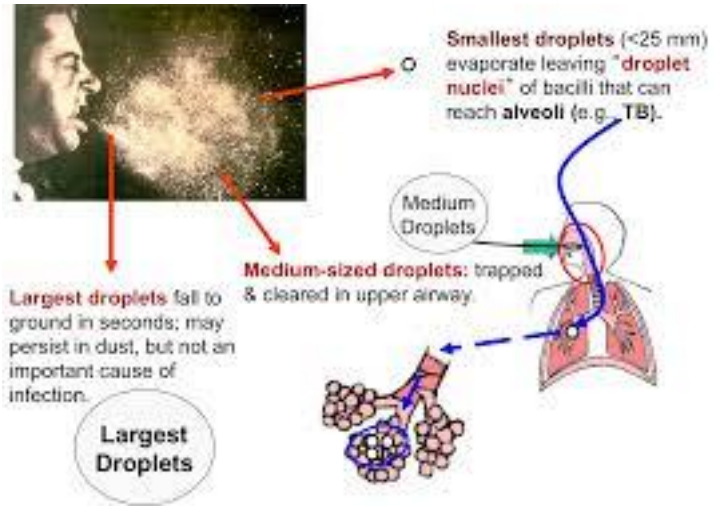
http://www.cidrap.umn.edu/news-perspective/2014/09/commentary-health-workers-need-optimal-respiratory-protection-ebola

Transmission

- Most pathogens have a predominant mode of transmission
- Transmission is not fully understood for many infections
- No infection is strictly unimodal - spread can usually occur by multiple modes
- Relative contribution of each mode difficult to quantify
- Aerosol is different from airborne transmission and can occur during high risk procedures with organisms that are normally transmitted by other routes
- Influenza – predominantly droplet, but numerous studies show airborne, contact and other transmission
- SARS – Airborne and droplet

Respiratory diseases with pandemic potential

- Influenza
- SARS
- Smallpox
- Plague
- Emerging new infections



- ?MERS
- ?TB
- ?Streptococcus pneumonia
- ?Ebola and other VHFs

Genesis of pandemic influenza

Wild birds with avian flu – migratory bird flyways

People or pigs with flu – farming practices

New pandemic strain – spread by international travel and trade

Genetic mixing – proximity of humans and birds/animals

Domestic birds get avian flu – poultry trade routes

R value of pandemic influenza

- Critical to the success of control strategies
- Many recent scientific papers suggest the R of an emergent pandemic will be 1.5 to 1.8.
- Some estimates as high as 6.7*
- If R > 3, all bets off
- If R <3…or 2, the cumulative impact of strategies may
  - Delay the impending pandemic arriving
  - Reduce the impact of the pandemic once it arrives

*Mathews JD, McCaw CT, McVernon J, McBryde ES, McCaw JM (2007) A Biological Model for Influenza Transmission: Pandemic Planning Implications of Asymptomatic Infection and Immunity. PLoS ONE 2(11): e1220. doi:10.1371/journal.pone.0001220

Predicted impact of a pandemic

- Rapid entry in Australia/NZ following overseas emergence
- 20-30% attack rate
- U or W shaped mortality curve
- High rates of work absenteeism
- Hospitals over capacity
- Two waves possible
- Transient but sharp economic impact

Economic impact

- Infectious epidemics have a unique capacity to cause major, almost instant economic disruption
- During SARS, near-bankruptcy of travel related industries
- US Anthrax letter bombs in 2001 – shut-down of the US Postal System
- Issues of law and order and public demand
- Major investments globally in planning for the health, economic and societal impacts of a pandemic

What can we do?

- Early surveillance and detection
- Communication with public and HCWs
- Pharmaceutical
  - Vaccines
  - Antivirals
  - Antibiotics and supportive care
- Non-pharmaceutical
  - PPE
  - Social distancing
  - Travel restrictions
  - Border control, screening, quarantine
  - Infection control measures

Challenges of vaccines

- Grown in embryonated hens eggs
- Slow, rate limited process
- Matched vaccine delay ~ 3-6 months to availability of vaccine
- Limited impact on a pandemic due to delay
- Supply may be limited even in countries with guaranteed manufacturing capacity

Advances in vaccines

- Novel adjuvants reduce the required antigen content (<4mcg)
- New vaccine manufacturing methods being developed (cell culture based, DNA vaccines etc)
- Other vaccines? Pneumococcal?

Prepandemic vaccines

- Not matched, but may provide some protection
- Choice of antigen (eg H5 or H7) driven by probabilities, but no guarantees

Antivirals

- H5N1 resistant to adamantanes
- Sensitive to neuraminidase inhibitors (NI) (oseltamivir and zanamivir)
- Increased WHO reports of primary NI resistance in seasonal flu
- Can be used as treatment or prophylaxis
- Modelling shows good impact if drug sensitive

When to use antivirals

- Early phase – “stamp out” – crucial first line defence before vaccine available
  - Focus on cases, contact tracing, prophylaxis
- Mid phase – “contain”
  - Focus on protection of front line responders (health care workers)

Antibiotics and supportive care

- Antibiotics for treatment of secondary complications (bacterial pneumonia)
- Critical care (Ventilation, ICU beds, HD, stepdown beds)
- ECMO
- Hospital capacity = limiting factor
- Alternative “clinics”, home care

Social distancing

- Closure of schools – modelling shows impact, mainly on transmission among children - only if done very early in the pandemic. Minimal impact if delayed.*
- Banning of mass gatherings
- Working from home arrangements
- Economic implications of these measures need to be considered

*Glass K, Barnes B. Epidemiology. 2007 Sep;18(5):623-8.

Travel restrictions

- Exponential rise in travel in the past decade
- International travel - limited impact, prolonged restrictions unfeasible
- Domestic travel - Limited impact, may benefit small towns
- Thermoscreening – no impact
- Quarantine – some role in “stamp out” phase

PPE and Infection control

- Hand washing – RCT

evidence of efficacy, a simple procedure available to entire population

Respirators and face masks

Other PPE

- Cohorting, isolation
- Cough etiquette
- Engineering controls (negative pressure rooms)

Limitations

- No single intervention is adequate - must be used together
- All estimates of efficacy of vaccines, antivirals, social distancing and travel restrictions are based on mathematical modelling
- Models show effectiveness where Ro is 1.7 or less
- If Ro >3, few interventions will have an impact

Facts *about* Ebola in the U.S.

You can't get Ebola through air

You can't get Ebola through water

You can't get Ebola through food

You can only get Ebola from:

- Touching the blood or body fluids of a person who is sick with or has died from Ebola.
- Touching contaminated objects, like needles.
- Touching infected animals, their blood or other body fluids, or their meat.

CDC

CS250580

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Kikwit Ebola outbreak

Table 1. Matched odds ratios (crude) of univariate analysis of a matched case-control (1:3) study comparing risk factors for infection in 44 patients without reported source of exposure to Ebola virus at the start of this investigation and 132 controls during the Ebola hemorrhagic fever (EHF) outbreak (Kikwit, Democratic Republic of the Congo, 1995).

Risk factor for infection	No. of patients with risk factor	No. of control subjects with risk factor	Matched odds ratio (crude)	95% confidence interval
Admission to hospital	15	7	9.9	3.1–41
Receipt of injection*	10	1	30.0	4.3–1302
Visit to ill friend†	23	11	10.6	3.8–36.3
Attended a funeral	17	25	3.0	1.2–7.6
Prepared a cadaver for burial	5	2	13.1	1.4–631
Physical contact with ill person at work or market†	8	1	24.0	3.2–1065
Health care worker	6	2	9.0	1.6–91.2

NOTE. All risk factors pertain to 3-week interval before onset of EHF in patients and same period for matched controls.

* 9 received injection during hospitalization; 1 as outpatient.

† Ill with fever and bleeding.

Roels T et al. Ebola Hemorrhagic Fever, Kikwit, Democratic Republic of the Congo, 1995: Risk Factors for Patients without a Reported Exposure
The Journal of Infectious Diseases 1999;179(Suppl 1):S92–7

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Non-contact transmission of Ebola

- Kikwit outbreak – 55 cases of Ebola without clear risk factor; risk factors found for all except 19 – 14/19 visited patient in the home and touched patient. 5/19 had no contact (Roels et al).
- A number of experimental studies in animals showed spread of Ebola without contact (Jaax 1995, Johnson 1995, Dalgard 1992, Kobinger 2011)
- Human studies also show Ebola virus in the lungs

Ebola transmission

✔Respiratory (aerosol or airborne) – *Kikwit DRC outbreak, animal studies, human autopsy studies*

✔Fomite or direct contact (hands, face, skin, droplets)

✔Blood borne - *contaminated needles – Kikwit DRC*

? Faecal/Oral

✔Sexual - *virus present in semen after recovery*

•✔Vertical

Summary

- Several known respiratory infections with pandemic potential
- R > 1 required for epidemic/pandemic potential
- Influenza is the most probable and most important of these infections
- Surveillance for SARI could identify newly emerged pandemic respiratory infections
- Control measures depend on the pathogen, and are either pharmaceutical or non-pharmaceutical.
- During a pandemic, multiple measures are required

Thank you

Image: Own photograph, NSW Quarantine Station

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