Principles of infectious disease transmission

Short course on Infectious Diseases in Humanitarian Emergencies
London, 30 March 2009

Francesco Checchi
Disease Control in Humanitarian Emergencies (DCE)
Department of Epidemic & Pandemic Alert and Response (EPR)
Infectious diseases

- Most crisis-attributable indirect morbidity and mortality

- Prions
-Viruses
- Bacteria
- Fungi
- Protozoa
- Multicellular parasites

- Infectious or communicable?
How does transmission take place?

- **Route of transmission**
  - Much more important than whether pathogen is a virus, bacterium, or anything else
  - Several routes possible for one pathogen

- **Transmission cycle**
  - Most complex for vector-borne infections

- **Reservoir**
  - Organism or habitat in which pathogen does not go extinct
  - Primary vs. secondary reservoir
  - Is disease...Anthroponosis? Zoonosis? Neither?
<table>
<thead>
<tr>
<th>Transmission route</th>
<th>Main diseases</th>
<th>How transmission occurs</th>
</tr>
</thead>
</table>
| **Air droplet** (i.e. pathogens are breathed, sneezed or coughed out of the respiratory system of the infected person, and enter the respiratory system of another) | Tuberculosis  
Measles  
Whooping cough  
Most other respiratory diseases, including those caused by:  
*Common flu/cold viruses*  
*Streptococcus pneumoniae*  
*Haemophilus influenzae B*  
Pandemic influenza  
Meningitis  
Trachoma | Inhalation of or eye contact with droplets containing pathogens as a result of close interaction with infectious person  
Especially likely if infectious person sneezes or coughs |
| **Faecal-oral** (i.e. pathogens are excreted from the gut of an infected person, and enter the gut of another person through his/her mouth) | Diarrhoeal diseases, including:  
*Cholera*  
*Shigella* (bacterial dysentery)  
*Salmonella*  
*Escherichia coli*  
*Rotavirus*  
*Amoebiasis*  
*Giardiasis*  
*Typhoid*  
Most intestinal worms  
*Hepatitis A*  
*Hepatitis E*  
*Polio* | Ingestion of faecal matter (see Chapter 3: Poor water, sanitation and hygiene conditions) |
<table>
<thead>
<tr>
<th>Disease Category</th>
<th>Pathogens</th>
<th>Transmission Route</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sexual</strong></td>
<td>HIV, Syphilis, Chlamydia, Gonorrhoea, Hepatitis B</td>
<td>Unprotected sex (anal sex particularly hazardous)</td>
</tr>
<tr>
<td><strong>Vector-borne</strong></td>
<td>Malaria, Dengue fever, Japanese encephalitis, African sleeping sickness, Leishmaniasis/kala azar, River blindness, Schistosomiasis, Typhus, Relapsing fever</td>
<td>Mosquito bite (night-biting), Mosquito bite (day-biting), Tsetse fly bite, Sand fly bite, Black fly bite, Fresh-water snail, Bites of lice, fleas, mites, Bites of lice and ticks</td>
</tr>
<tr>
<td><strong>Blood</strong></td>
<td>HIV, Hepatitis C, Hepatitis B</td>
<td>Unsafe injections, Transfusions with unsafe blood</td>
</tr>
<tr>
<td><strong>Unclean wound</strong></td>
<td>Tetanus</td>
<td>Deep cuts, Infection of umbilical cord after birth</td>
</tr>
<tr>
<td><strong>Mother to child (vertical)</strong></td>
<td>HIV, Hepatitis B, Syphilis</td>
<td>During childbirth, Breast milk</td>
</tr>
</tbody>
</table>
Transmission cycle and reservoir: examples

- **Most airborne-droplet diseases** (e.g. ARI, measles, meningococcal meningitis):
  - Humans are reservoir
  - Cycle is direct human to human transmission
  - For ARI specifically: colonisation of upper airways

- **Faecal-oral diseases**:
  - Cholera vs. polio: what can vaccination achieve?

- **Tetanus** (e.g. post-tsunami “epidemic” in Aceh)

- **Not homogeneous processes**
  - Chronic carriers and “super-shedders”
Transmission cycle of Rift Valley Fever virus

- Zoonosis
- Each sub-cycle is one “epidemiological system”
- Where is the reservoir?
How much transmission is occurring?

- Natural progression parameters
  - Incubation period, duration of infectiousness, serial interval

- Reproductive ratio
  - Determinants
  - Implications

- Transmission level and transmission rate

- Endemic versus epidemic
Illustration of incubation period, duration of infection and serial interval

- **Primary case**
  - Incubation period
  - Symptoms
  - Onset of symptoms in primary case

- **Secondary case**
  - Incubation period
  - Symptoms
  - Onset of symptoms in secondary case

- **Duration of infection**
  - Infectious period (d)
  - Transmission from primary to secondary case

- **Serial interval**
  - Start of infectiousness
  - End of infectiousness
  - End of infection

**Time**
Example: A patient (A) with meningitis who remains infectious for 4 days

Day 1 (first day of infectiousness): A still feels well; he comes into close contact with 8 susceptible people, of whom he infects 1.

Day 2: A is still well and attends a gathering, where he comes into contact with 18 susceptibles, of whom he infects 4.
Reproductive ratio (continued)

Day 3: A feels sick and restricts his movement. He comes into contact with 4 susceptible people, and infects 0.

Day 4: (last day of infectiousness) A is bed-ridden, only coming into contact with 2 susceptible relatives, of whom he infects 1. He is then hospitalised and treated, following which he is no longer infectious.
What determines the level of transmission?

- **Reproductive ratio (R)**
  - average number of infections arising from one infection
  - ever-changing quantity across time and space (i.e. context-specific)
  - Basic reproductive ratio \( R_0 \): everyone is susceptible and there is no control (= maximum value that R can take = transmission potential)

- **One unique R value...**
  - ...for each route of transmission: e.g. R for HIV = R(vaginal) + R(anal) + R(transfusion)...
  - ...for each “epidemiological system”

- **Implications:**
  - R>1: transmission is increasing
  - R<1: transmission is decreasing, and the disease is on the way to extinction
  - R≈1: transmission is stable, humans are a reservoir
**What determines the reproductive ratio?**

**Components of the reproductive ratio of an infectious disease**

\[ R = c \times p \times d \]

where:
- \( c \) = average number of susceptible people (i.e. who are not infected and can contract the infection) an infectious person comes into contact with, per unit time (e.g. per day)
- \( p \) = average probability that transmission will take place, per unit contact
- \( d \) = average duration of infectiousness, or infectious period (e.g. in days)

Note that these our symbols do not reflect any standard notation.

Any increase in \( c \), \( p \) or \( d \) will result in an increase in \( R \).

- “\( c \)” represents contact, very context-specific:
  - **Faecal-oral**: contacts with faecal matter
  - **Vector-borne**: bites of susceptible vectors on infectious humans \( \times \) bites of infectious vectors on susceptible humans
  - Crucially dependent on % susceptible

- “\( p \)” greatly dependent on pathogen **virulence**

- “\( d \)” affected by host-pathogen interactions
  - Immune response, CFR
“Stop TB” targets: >70% detected, >80% cured – why?
What determines the rate of transmission?

- We know R determines the level of transmission, but how fast will new infections occur?
- Depends on
  - R
  - Serial interval

Imagine two diseases of equal R but different serial interval, in a population of 1000 people:

- R = 5, serial interval = 10 d
  - Start with 1 infection: after 10d, 5 new infections; 10d later, 5x5=25; 10 d later, 25x5 =125; total (1+5+25+125)/30d = 156/(1000 people x 30d) = 5.2/1000 person-d

- R = 5, serial interval = 30 d
  - Start with 1 infection: after 30d, 5 new infections; total (1+5)/(1000 people x 30d) = 6/30d = 0.2/1000 person-d
## The basic parameters for some diseases

<table>
<thead>
<tr>
<th>Disease</th>
<th>$R_0$</th>
<th>Incubation period (days)</th>
<th>Serial interval (days)</th>
<th>CFR if untreated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholera</td>
<td>4–15</td>
<td>2–3</td>
<td>7–10</td>
<td>up to 50%</td>
</tr>
<tr>
<td>Shigella (bacterial dysentery)</td>
<td>unknown</td>
<td>1–3</td>
<td>unknown (a few days)</td>
<td>up to 10%</td>
</tr>
<tr>
<td>Malaria</td>
<td>Low-transmission areas: ~1–10 High-transmission areas: ~100–1,000</td>
<td>9–13</td>
<td>~60–120</td>
<td>30–50% of severe episodes ~1% of all episodes in non-immunes</td>
</tr>
<tr>
<td>Measles</td>
<td>Rural: 5–6 Urban or crowded: &gt;12</td>
<td>10–12</td>
<td>~15</td>
<td>3–5% (developing countries) 10–30% (displaced populations)</td>
</tr>
<tr>
<td>Meningococcal meningitis</td>
<td>unknown</td>
<td>3–4</td>
<td>unknown (a few days)</td>
<td>up to 50%</td>
</tr>
<tr>
<td>Pandemic influenza (based on 1918 Spanish flu)</td>
<td>3</td>
<td>2</td>
<td>unknown (a few days)</td>
<td>2% (depends on age and previous exposure to related strain)</td>
</tr>
</tbody>
</table>
From transmission to disease and death

Simplified framework of the dynamics of disease in a population
Relationship between infection, progression to disease, case-fatality ratio, incidence rate and mortality due to a given disease

\[ MR \text{ due to disease } X = TR \times Pr \times CFR \]

[lag time: incubation period + duration of disease before death]

where

- **MR due to disease** \( X \) = specific mortality (or death) rate due to a given disease
- **TR** = transmission rate, i.e. rate at which the population is becoming infected with the pathogen responsible for the disease
- **Pr** = probability an infected person will actually develop the disease†
- **CFR** = case-fatality ratio of the disease, including treated and untreated cases†

and

\[ IR \text{ of disease } X = TR \times Pr \]

[lag time: incubation period]

where

- **IR due to disease** \( X \) = incidence rate of a given disease

so that

\[ MR \text{ due to disease } X = IR \times CFR \]

Note that:
- If TR, Pr or CFR increase, so will MR.
- The lag time between infection (TR) and death (MR), namely the sum of the incubation period (how long it takes to progress to disease) and the duration of the disease before death, varies widely (compare ebola with HIV).
Endemic versus epidemic diseases

- Somewhat outdated, rarely clear-cut
  - Depends on context: e.g. malaria

- Epidemic ("epidemic-prone" disease):
  - Disease “usually absent” (low exposure = high susceptibility = if a case is introduced, $R \approx R_0$), or
  - Incidence in excess of expected range ($R \gg 1$)

- Endemic:
  - Disease “always present”
  - Stable incidence over relatively long time interval (excluding seasonality)
  - Two possibilities:
    - $R \approx 1$
    - $R < 1$, but constant spillover to humans from reservoir
Transmission cycle of Rift Valley Fever virus

- **Sylvatic cycle**
  - Wildlife
  - Aedes/Culex
  - Transovarial transmission

- **Domestic cycle**
  - Birds? Rats? Rodents?
  - Aedes/Culex
  - Transovarial transmission

- **Human cases**
  - Mosquitoes
  - Peri-urban mosquitoes?
  - Zoonoses

**Transmission rates**:
- $R \approx 1$ always (endemic)
- $R > 1$ sometimes (epizootic)
- $R < 1$ always (zoonosis due to epizootic)
How do we know an epidemic is happening?

- Arbitrary definitions
- Epidemic thresholds:

<table>
<thead>
<tr>
<th>Disease</th>
<th>Context</th>
<th>Outbreak/epidemic threshold</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measles</td>
<td>Camp</td>
<td>1 case</td>
</tr>
<tr>
<td>Cholera</td>
<td>Overcrowded community</td>
<td>1 case</td>
</tr>
<tr>
<td></td>
<td>Rural community</td>
<td>Significant increase from expected</td>
</tr>
<tr>
<td>Meningococcal meningitis</td>
<td>Community of &lt;30,000 people</td>
<td>5 cases in 1 week or doubling of cases in 3-week period or decision on a case-by-case basis</td>
</tr>
<tr>
<td></td>
<td>Community of ≥ 30,000 people</td>
<td>10 cases per 100,000 people per week if no epidemic in last 3 years and vaccination coverage ≥80% or alert threshold crossed early in dry season; otherwise, 15 cases per 100,000 people per week</td>
</tr>
</tbody>
</table>

(Will talk more about epidemic/outbreak thresholds later)