Concepts for the prevention and control of microbial threats – 2

Center for Infectious Disease Preparedness
UC Berkeley School of Public Health
URL: http://www.idready.org

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Learning objectives: Particpants will be able to ...

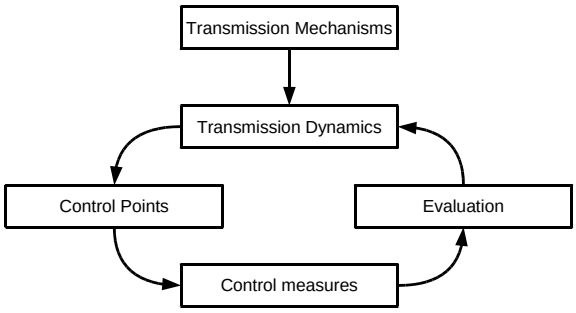
- Describe the characteristics of infectious cases that promote microbial agent transmission to susceptible hosts;
- Describe the characteristics of susceptible hosts that promote microbial agent transmission to them;
- Describe six control strategies for interrupting transmission of a microbial agent;
- Design comprehensive control measures based on the the six control strategies

Infectious disease epidemiology concepts – Overview

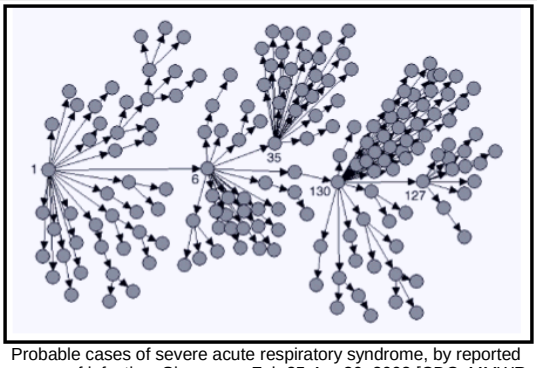
- Mechanisms (Part 1)
  - Chain model of infectious diseases
  - Natural history of infection/infectiousness
  - Convergence model for human-microbe interaction
- Dynamics (Part 2)
  - Reproductive number (R)
  - Conditional infection rate (I)
  - Generation time (T)
- Control points and Control measures

Notes:

Epidemiologic concepts for the control of microbial threats



Reproductive number & conditional infection rate



Probable cases of severe acute respiratory syndrome, by reported source of infection, Singapore, Feb 25-Apr 30, 2003 [CDC. MMWR 2003;52(18):405.]

The reproductive number

- Basic reproductive number (R_0)
  - Average number of secondary infectious cases produced by an index case in a susceptible population in the absence of control measures
- Effective reproductive number (R)
  - Average number of secondary infectious cases produced by infectious cases
- Control reproductive number (R_c)
  - The effective reproductive number in the presence of control strategies

Notes:

Basic reproductive number (R_0) (perspective of infectious case)

DEFINITION
The average number of secondary infectious cases that are produced by a single index case in a completely susceptible population in the absence of control strategies

$$R_0 = c\ p\ d$$

- c: number of contacts per unit time
- p: transmission probability per contact
- d: duration of infectiousness

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Effective reproductive number

$$R(t) = R_0\, x(t)$$

$x(t)$: Fraction of population that is susceptible to infection

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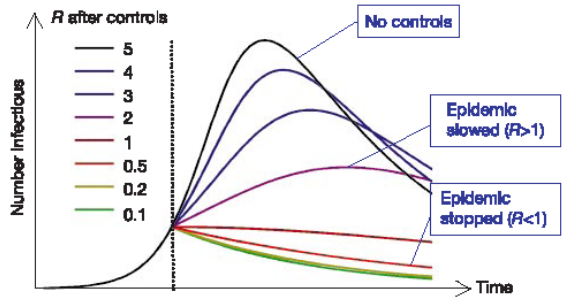
Planning for smallpox outbreaks



Controls either reduce susceptible numbers (such as vaccination) or limit transmission (for example, through movement controls). Both have the effect of reducing R and slowing the spread of an epidemic; reducing R below 1 means that the chains of transmission cannot be sustained and the epidemic dies out.
Nature 2003 Oct 16;425(6959):681

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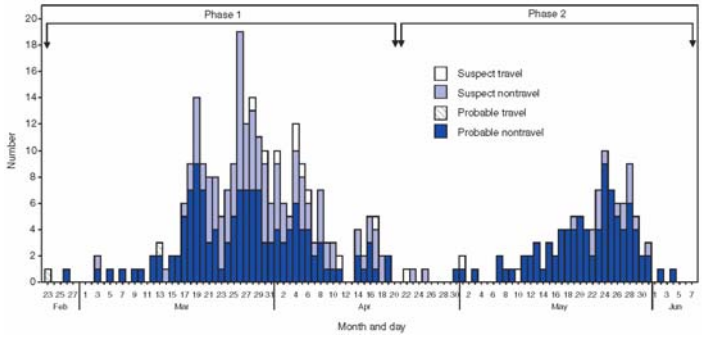
Notes:

Number of reported cases of severe acute respiratory syndrome, by classification and date of illness onset — Ontario, 2003



February 23–June 7, 2003 (N = 361)
CDC, MMWR 2003;52:547

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Control reproductive number: Vaccination example

$$R_c(t) = R_0[1 - hf]$$

Fraction of those vaccinated that have complete protection (vaccine efficacy)

Fraction of population that has been vaccinated (vaccine coverage)

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Control reproductive number: Vaccination example (cont'd)

Goal: $R_c(t) < 1$

Fraction to vaccinate: $f > \dfrac{1 - (1/R_0)}{h}$

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Notes:

Herd Immunity Thresholds for Selected Vaccine-Preventable Diseases

http://www.bt.cdc.gov/agent/smallpox/training/overview/pdf/eradicationhistory.pdf

Disease	R_0	Herd Immunity	Immunization Levels	
			1999 19-35 Months	1997-1998 Pre-School
Diphtheria	**6-7**	85%*	83%*	97%
Measles	**12-18**	83-94%	92%	96%
Mumps	**4-7**	75-86%	92%	97%
Pertussis	**12-17**	92-94%	83%*	97%
Polio	**5-7**	80-86%	90%	97%
Rubella	**6-7**	83-85%	92%	97%
Smallpox	**5-7**	80-85%	__	__

*4 doses
† Modified from Epid Rev 1993;15: 265-302, Am J Prev Med 2001; 20 (4S): 88-153, MMWR 2000; 49 (SS-9); 27-38

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Per-capita infection rate among susceptible hosts

$$I(t) = \frac{Number\ of\ new\ infections}{Person\text{-}time\ at\ risk}$$

Components

$$I(t) = c\ p\ P(t)$$

- c: Contact rate with a potentially infectious source
- p: Probability of transmission given contact with infectious source
- $P(t)$: Probability that source is infectious

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Per capita infection rate: HIV

$$I(t) = c\ p\ P(t)$$

- c: Contact rate with a potentially infectious source
  - Unprotected sex
  - Homogeneous mixing
  - Heterogeneous mixing(sexual sorting, risk factor sorting, agesorting, serosorting)
- p: Probability of transmission given contact with infectious source
  - Infectiousness (anti-viral therapy)
  - Susceptibility (ulcerative STDs)
  - Interrupt transmission (condoms)
- $P(t)$: Probability that source is infectious
  - Reduce Prevalence (Counseling, Testing, and Referral)

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Notes:

Estimated per-act risk for acquisition of HIV, by exposure route to an infected source

Exposure route	Risk per 10,000 exposures
Blood transfusion (BT)	9,000
Needle-sharing injection-drug use (IDU)	67
Receptive anal intercourse (RAI)	50
Percutaneous needle stick (PNS)	30
Receptive penile-vaginal intercourse (RPVI)	10
Insertive anal intercourse (IAI)	6.5
Insertive penile-vaginal intercourse (IPVI)	5
Receptive oral intercourse on penis (ROI)	1
Insertive oral intercourse with penis (IOI)	0.5

CDC MMWR 2005;54(No. RR-2)

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Generation or serial time (T)

- Generation or serial time is the average time between the onset of symptoms in a given infectious individual and the onset of symptoms in individuals that person has infected
- Communicable diseases with shorter generation times require more rapid detection and implementation of control measures (for example, influenza vs smallpox)

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Transmission dynamics and control points

Effective reproductive number

$$R(t) = c\ p\ d\ x(t)$$

Conditional infection rate

$$I(t) = c\ p\ P(t)$$

Control points	Prevention and control strategies
Contact rate (c)	1. Reduce contact rate
Prob. source infectious (P)	2. Reduce proportion infectious sources
Transmission prob. (p)	3. Reduce infectiousness 4. Reduce susceptibility 5. Interrupt transmission
Duration infectiousness (d)	(see #3)
Fraction susceptible (x)	6. Increase herd immunity

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Notes:

Control measures (strategies + interventions)

1. Reduce contact rate
   - Behavior change (host and/or source)
   - Case finding for intervention (e.g., isolation)
   - Contact tracing for intervention (e.g., quarantine)
   - Isolation of cases
   - Quarantine of exposed (individual, community, geographic boundary [Cordon sanitaire])
   - "Reverse" isolation (isolation of non-exposed)
   - Reduce number of infectious sources
   - Social distancing (school closures, restrict mass gatherings, etc.)

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Control measures [cont'd] (strategies + interventions)

5. Reduce proportion of infectious sources
   - Case finding for intervention (e.g., isolation, treatment)
   - Identify and control infectious sources
   - Environmental measures
3. Reduce infectiousness
   - Treatment
   - Vaccination
4. Reduce susceptibility
   - Vaccination
   - Immune globulin
   - Treatment (e.g., ulcerative STD)

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Control measures [cont'd] (strategies + interventions)

2. Interrupt transmission
   - Infectious control practices
   - Barrier methods (e.g., masks, condoms)
   - Insect repellent (e.g., reduce feeding time)
6. Increase herd immunity
   - Vaccination, consider the following
     - Naturally acquired immunity
     - Fraction vaccinated
     - Vaccine efficacy

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Notes:

Translating control strategies into smallpox control program

Control strategies

1. Reduce contact rate
2. Reduce infectiousness
3. Reduce susceptibility
4. Interrupt transmission
5. Reduce proportion of infectious sources
6. Increase herd immunity

CDC Prevention and control program

- Smallpox pre-event strategies
  - Vaccination program
  - Enhanced surveillance & detection
- Smallpox post-event strategies
  - Epidemiologic investigation
  - Surveillance and case reporting
  - Contact identification, tracing, vaccination, and surveillance
  - Isolation and Quarantine
  - Infection control
  - Personal protective equipment

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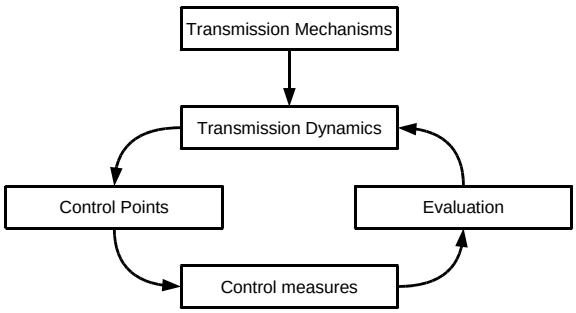

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