Infectious Disease Epidemiology: Basic Principles for Mathematical Modeling

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Goal

- To review concepts necessary for the study and control of infectious diseases
- Become familiar with some commonly used epidemiology terms
- Discuss how these concepts relate to mathematical modeling

Outline

- Part I- Basics of Infectious Disease Epidemiology
  - Epidemiological Triangle
  - Infection Transmission
  - Basic Epi Terms
- Part II- Sources of Epidemiological Data

Goals of Infectious Disease Epidemiology

1. Identify and describe a causative agent
2. Understand the relationship between the host, the agent and the environment
3. Interrupt disease transmission to prevent spread

Goals of Infectious Disease Modeling

1. Better understanding of how disease is spread

2. Predict future course of epidemics
   - medical costs
   - impact of outbreaks

3. How to control the spread of epidemics
   - Education?
   - Immunization?
   - Isolation?

DJ Daley & J Gani, Epidemic modelling: An introduction, 1999. p.13

Epidemiological Triangle

HOST

Age, gender, genetics
Behaviour (smoking, sex, work)
Exposures (animal)
Immune suppression, vaccination

Pathogenicity
Infectivity
Immunogenicity
Environmental stability
Infective dose

AGENT

Social
crowding
"networks"
public health

ENVIRONMENT

Physical
urban/rural
climate

Biological Classification

- Bacteria eg.TB, Gonorrhea, syphilis
- Viruses eg. HIV, Influenza, Measles
- Fungi eg. Cryptococcus
- Protozoan eg.Malaria, Giardia
- Prions eg.“Mad cow” disease

Site of Infection

Central Nervous System
-eg. Meningitis

Respiratory
-eg.cold/flu

Cardiovascular

Diarrheal Diseases

Hepatitis

Skin Infection/ Soft Tissue

STDs/Genitourinary

Bone/Joints

Modes of Transmission

- Contact -Direct – Skin/Sexual
  -Indirect- eg. Infected blood

- Airbourne: eg. TB, chickenpox

- Vectors (eg. mosquitos) eg. malaria
- Foodborne/Waterborne: eg.cholera

- Vertical- Transplacental
  - Perinatal
  - Post-partum (eg. breastfeeding)

Classification by Reservoir in Nature

- Human
  - eg. Gonorrhea, HIV, smallpox

- Environmental
  - Plants, Soil, Water
  - Cholera, Legionella – Water
  - Tetanus, Botulism - Soil

- Animals
  - Zoonoses (animal to human)
  - eg. Bats - Rabies
  - eg. Rodents – Hantavirus, Yersinia pestis

Transmission:

Nelson et al. Infectious Disease Epidemiology p.151

Latent Infection - SLIR (SEIR) Model

Example: TB

Susceptible

↓

Latent (Exposed)

↓

Infectious

↓

Recovered

Incubation Period

- Incubation period: time from exposure to development of disease
  - Expressed as a range
  - Time can be variable – depending on infection
  - Represents time needed for agent to reach a critical level to create clinical signs and symptoms
  - Can be infectious while being in the incubation period
    - Difficulty in control of spread,
      - eg. Measles, Hepatitis A, Chickenpox, etc.

Figure 2–2 Incubation periods of common bacterial diseases (*top panel*) and viral diseases (*bottom panel*). *Source:* Reprinted with permission from *Viral Infections of Humans*, 4th Edition, A.S. Evans and R.A. Kaslow, eds., p. 20, Copyright © 1997, Plenum Publishing Corporation.

HOURS
DAYS
MONTHS AND YEARS
4 8 12 16 20 1 4 8 12 16 20 24 28
FOOD POISONING
B. CEREUS
STAPHYLOCOCCUS
CL. PERFRINGENS
V. PARAHAEMOLYTICUS
BOTULINISM
SALMONELLOSIS
E. COLI DIARRHEA
PONTIAC FEVER
STREP SORE THROAT
TULAREMIA
PNEU. PNEUMONIA
OTHER BACT. PNEU.
SHIGELLOSIS
CHOLERA
ANTHRAX
GONORRHEA
PLAGUE
MENINGOCOCCAL INF.
CHLAMYDIA URETHRITIS
LEGIONNAIRES' DIS.
CHANCROID
ROCKY MT. SPOTTED FEVER
LEPTOSPIROSIS
TETANUS
DIPHTHERIA
PERTUSSIS
Q. FEVER
M. PNEU. PNEUMONIA
TYPHOID FEVER
SYPHILIS
LEPROSY
Range
Most Common
Incubation Period
Bacterial Diseases
70 days
7 mos–5 years
3–5 years

Outcomes of Exposure

http://www.nwcphp.org/docs/infectious/attachments/transcript.pdf

Infectivity

The proportion of exposed persons who become infected

$$\frac{\textit{Persons who become infected}}{\textit{Exposed persons in the population}}$$

–Related to dose of agent transmitted - i.e. number of infectious particles transmitted

Examples: Tuberculosis: Low Infectivity

Measles/Smallpox: High Infectivity

* This is related to beta (B) of models, eg.

$$\frac{dS}{dt} = -\frac{\beta SI}{N}$$

http://www.nwcphp.org/docs/infectious/attachments/transcript.pdf

Outcomes of Exposure

Pathogenicity

Proportion of infected people who develop clinical disease

$$\frac{\textit{Number infected and exhibiting disease}}{\textit{Total number infected}}$$

Examples:

Tuberculosis: Low Pathogenicity

Smallpox/Common cold: High Pathogenicity

ttp://www.nwcphp.org/docs/infectious/attachments/transcript.pdf

Outcomes of Exposure

Virulence

Proportion of persons with clinical disease who become severely ill or die

$$\frac{\textit{Number with severe disease}}{\textit{Total number with disease}} \quad \textit{or} \quad \frac{\textit{Fatal cases}}{\textit{Total cases}}$$

High virulence

- Ebola
- Smallpox
- Pandemic Flu

Low virulence

- Rhinovirus

http://www.nwcphp.org/docs/infectious/attachments/transcript.pdf

Outcomes of Exposure

Disease	Infectivity	Pathogenicity	Virulence
chickenpox	high	high	very low
common cold	intermediate	intermediate	very low
leprosy	very low	very low	high
measles	high	high	low
smallpox	high	high	high
tuberculosis	low	low	high

http://www.nwcphp.org/docs/infectious/attachments/transcript.pdf

Environment

- Interacts with agent and host
- Allows exposure to occur

- Physical: Geology, Climate, Habitat
- Biological: Human Populations, Flora, Fauna
  - Sources of Food, Influence on Habitat, Vectors
- Socioeconomic: Occupations, Crowding, Urbanization
- Disasters: Earthquakes, Floods, Wars

Animal-Human Co-Habitation

- Outbreaks of the H5N1 virus (Bird Flu) seen, especially in Asia
  - 330 cases since Nov 2003
  - >50% of cases are fatal
  - direct contact with infected poultry, or surfaces contaminated by their feces
- rural areas: households keep poultry flocks, which often roam freely, enter homes or share outdoor areas where children play

http://www.cdc.gov/flu/avian/gen-info/facts.htm

Conflict and HIV

- Sexual abuse/rape of female civilians
- Large proportion of military infected
  - 2-5X higher than general population
  - 2000, HIV prevalence rates among some South African military units of between 60% and 90%
  - Uganda, 27% of military personnel have tested HIV positive.

- Food insecurity – sex for food or money
- Forced migration
- Loss of Infrastructure

Host

- Factors Affecting the Risk of Contracting a Disease
- May be Biological, Behavioural or Sociodemographic
- Examples
  - Age (young/old)
  - Immunity
  - Genetic Susceptibility
  - Socioeconomic Status
  - Nutritional status

Example: Immunity / Vaccination

Direct Immunity

- by Infection
  - Protected by being infected again (variable length of time)
  - eg. Measles, Mumps, Rubella, Chickenpox, etc.

    (vs. infections that do not generate long-lasting immunity, eg. Chlamydia)
- By Vaccination
  - Variable Protection – may need multiple doses or boosters

SIR and Immunization

Susceptibles

↓

Infected

↓

Immune

Vaccinations

- 1798 Smallpox
- 1882 Rabies
- 1890's (Cholera)
- 1890's Typhoid
- 1920's BCG
- 1920's Diphtheria
- 1920's-90's Pertussis
- 1930's Yellow Fever
- 1940's Influenza
- 1950's/60's Polio
- 1960's Measles
  Mumps, Rubella
- 1970's Meningococcus
- 1980's Hemophilus B
- 1970's Varicella
- 1980's Hepatitis B
- 1920's-90's Pneumococcus
- 1980's Hepatitis A
- 1990's Rotavirus
- 1990's Lyme
- 2002 Papillomavirus

Impact of Immunization

TABLE 312-1 Baseline 20th Century Annual Morbidity and 1998 Provisional Morbidity from Nine Diseases with Vaccines Recommended before 1990 for Universal Use in Children—United States

Disease	Baseline 20th Century Annual Morbidity	1998 Provisional Morbidity	% Decrease
Smallpox	48,164*	0	100%
Diphtheria	175,885†	1	100%‡
Pertussis	147,271§	6279	95.7%
Tetanus	1314‖	34	97.4%
Poliomyelitis (paralytic)	16,316¶	0**	100%
Measles	503,282††	89	100%‡
Mumps	152,209‡‡	606	99.6%
Rubella	47,745§§	345	99.3%
Congenital rubella syndrome	823‖‖	5	99.4%
Haemophilus influenzae type B	20,000¶¶	54***	99.7%

Nelson et al. Infectious Disease Epidemiology p.151

Epidemiology of Immunity / Vaccination

- Indirect: Herd Immunity
  - The number of people immune in the population decreases the risk of infection to the susceptible by diminishing the probability of exposure.
  - Related to the proportion of individuals with complete immunity in order to prevent transmission/epidemics

  (e.g. measles & other vaccine-preventable infections)

Herd Immunity

Susceptible

Immune

Infected

Disease transmission

http://www.nwcphp.org/docs/infectious/attachments/transcript.pdf

Basic reproductive rate (or ratio)

R_0

The number of secondary cases generated from a single infective case introduced into a susceptible population

Basic reproductive rate (R_0)

- If $R_0 > 1$, then disease will increasingly spread (epidemic)
- If $R_0 = 1$ then disease will become stable (endemic)
- If $R_0 < 1$ then disease will die out

Level of Immunization to achieve $R_0<1$

If p=prevalence of persons immunized

$$p > 1 - 1/ R_0$$

<u>Eradication of Measles (WHO):</u>

- $R_0 = 15$ (western countries)
- to prevent a measles epidemic (herd immunity)

$$p > 1-1/15=0.94=94\%$$

Epidemiological Triangle

Public Health/Prevention Interventions
at individual, community or global level

- Improved water supply
- Sanitation
- Hygiene
- Vaccination
- Vector control
- Treatment of infectious cases

- Sexual behaviour change
- Regulatory measures, e.g quarantine, food standards
- Other, e.g. Antimicrobial prophylaxis, Screening of blood supply

Model

Other Epi Terms

- Incidence vs. Prevalence
- Incidence:
  - Number of New Cases in a given time period
- Prevalence:
  - Number of cases existing at a given time

Incidence Rate

Rates measure disease levels in population.

Incidence Rate

$$\frac{\textit{\# of new cases of disease}}{\textit{\# at risk for the disease}}$$

http://www.nwcphp.org/docs/infectious/attachments/transcript.pdf

Prevalence

Prevalence

$$\frac{\text{\# of existing cases of disease present at a specified time}}{\text{\# at risk for disease at that specified time}}$$

http://www.nwcphp.org/docs/infectious/attachments/transcript.pdf

HIV-Epidemic in Numbers

People newly infected with HIV in 2002	Total	5.0 million
	Adults	4.2 million
	Women	2.0 million
	Children < 15 years	800,000
Number of people living with HIV/AIDS in 2002	Total	42.0 million
	Adults	38.6 million
	Women	19.2 million
	Children < 15 years	3.2 million
AIDS deaths in 2002	Total	3.1 million
	Adults	2.5 million
	Women	1.2 million
	Children < 15 years	610,000
AIDS deaths since the beginning of the epidemic until the end of 2001	Total	21.8 million
	Adults	17.5 million
	Women	9.0 million
	Children < 15 years	4.3 million
AIDS orphans since the beginning of the epidemic until the end of 2001		14.0 million

Estimates of the worlwide HIV epidemic, end of year 2002.
Source: UNAIDS (Joint United Nations Programme on HIV/AIDS)

© AIDS Information Switzerland

Incidence

Prevalence

Part II: Sources of Epidemiological Data

We have the model-

$$\frac{dS_N}{dt} = (1-p)(1-q)A - \beta_s S_N(I_N + I_D) - \mu S_N$$

$$\frac{dI_N}{dt} = q(1-p)A + \beta_s S_N(I_N + I_D) - (\mu + d)I_N$$

– now where's the data?

"And, it was so typically brilliant of you to have invited an epidemiologist"

Types of Data

- Surveillance Data
- Research Studies
  - Laboratory
  - Medical
  - Epidemiological: Observational Studies

Surveillance Data

"Public Health Surveillance is the:

- ongoing,
- systematic collection,
- analysis,
- interpretation and
- dissemination of health data to help guide public health decision making and action"

<u>Surveillance is Data for Action</u>

Functions of Surveillance

1. Estimate the magnitude of a health problem
2. Determine the distribution of illness
3. Detect an epidemic or outbreak
4. Evaluate control measures (eg. vaccines)
5. Monitor changes in infectious agent (eg. drug resistant strains)
6. Facilitate planning and setting priorities
7. Respond to emerging health threats

Notifiable Diseases

- Mandatory reporting of these infections by Physicians and/or Laboratories
- Choice of Diseases are based on factors such as:
  - Incidence
  - Severity
  - Transmissibility
  - Preventability

Some Notifiable Diseases in Alberta

Blood Borne Pathogens

- HIV/AIDS
- Hepatitis B
- Hepatitis C

STIs

- Chlamydia
- Chancroid
- Gonorrhea
- Lymphogranuloma Venereum
- Syphilis

Communicable Diseases

- Congenital CMV
- Congenital Rubella
- Diphtheria
- Leprosy
- Malaria
- Measles
- Mumps
- Pertussis
- Poliomyelitis
- Rubella
- Tuberculosis

Reporting Process

Figure 11

	1998	1999	2000	2001	2002	2003	2004	2005	2006
Number of Cases	5,253	5,420	6,032	6,488	7,358	7,901	8,347	8,839	10,452
Rate per 100,000	184.1	185.4	203.2	214.6	238.4	252.1	262.6	274.3	316.9

Source: Communicable Disease Reporting System - Sexually Transmitted Infections Database as of April 30, 2007
Provided by: Disease Control & Prevention and Public Health Surveillance & Environmental Health Branches, Alberta Health & Wellness - May 4, 2007

Syphilis Outbreak - Alberta

Figure 19

	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006
Case	4	1	9	6	2	16	23	17	37	75	146	218
Rate	0.1	0	0.3	0.2	0.1	0.5	0.8	0.5	1.4	2.3	4.5	6.6

Note: Includes primary, secondary and early latent stages of syphilis. Early congenital cases are excluded.

Source: Communicable Disease Reporting System - Sexually Transmitted Disease Database (April 30/07).
Provided by: Disease Control & Prevention and Public Health Surveillance and Environmental Health Branches, AHW.

Figure 20

	94	95	96	97	98	99	00	01	02	03	04	05	06
Canada	0.7	0.5	0.4	0.4	0.5	0.6	0.6	0.9	1.5	2.9	3.5	3	5.1
Alberta	0.3	0.1	0	0.3	0.2	0.1	0.5	0.8	0.6	1.2	2.3	4.5	6.6

Note: Includes primary, secondary and early latent stages. National rates for 2005 and 2006 are preliminary.

Source: Surveillance and Epidemiology Section, Centre for Infectious Disease Prevention and Control, Public Health Agency of Canada 2006; http://www.phac-aspc.gc.ca/std-mts/stdcases casmts/index.html)(April 30/07)

Provided by: Public Health Surveillance and Environmental Health Branch, AHW.

Figure 32

Rates of Infectious Syphilis by Region, Alberta 2006 and 2000-2006 Combined

2006 Data | **2000 -2006 Combined**

Note: Includes primary, secondary and early latent stages of syphilis.

Source: Communicable Disease Reporting System - Sexually Transmitted Disease (STD) Database as of April 30, 2007.
Provided by: Disease Control & Prevention and Public Health Surveillance and Environmental Health Branches, AHW.

Research- As a Source of Data

- Animal Studies
- In-vitro Studies

} Laboratory Studies

- Cross-Sectional Studies
- Case-Control Studies
- Cohort Studies
- Randomized Clinical Trials

Cross-Sectional Study

- Also called “prevalence survey”
- Taking a “snapshot” of a population in terms of infection status and exposure risks
- Can give you hints as to causation

Case-Control Studies

- Compare exposures of people with disease (case) and people without a disease (control)
- Can identify exposures associated with an outcome

Cohort Study

- Compare disease status of people with and without exposure
- Follow cohort prospectively, therefore can calculate Incidence

Randomized Clinical Trial

-population is randomized to two treatments – new and current (or placebo)

-follow subjects forward in time and determine outcomes

-used to Test Hypotheses

Male Circumcision and HIV

- Postulated that circumcision will prevent infection (and transmission) of HIV
  - biological reasons
  - positive trends seen in cross-sectional, case-control and cohort studies
- Randomized HIV negative men to circumcision or no circumcision
- Followed up over time and measured HIV incidence

Why Use Modelling?

- conduct conceptual experiments that would be difficult/impossible
  - easier to manipulate than a whole system
  - predict impact of changes on a system

    eg. using simulations
- determine plausibility of epidemiological explanations
- improve understanding of unexpected relationships
- (relatively) low cost

Acknowledgements

- Dr Stan Houston – for his slides!
- References:
  - Giesecke. Modern Infectious Disease Epidemiology.
  - Nelson. Infectious Disease Epidemiology.
  - Gordis. Epidemiology.