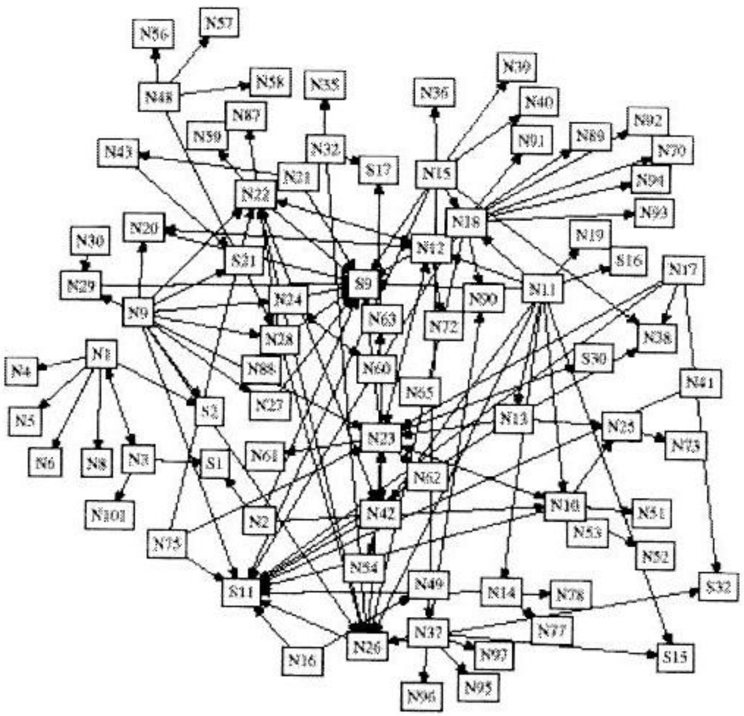
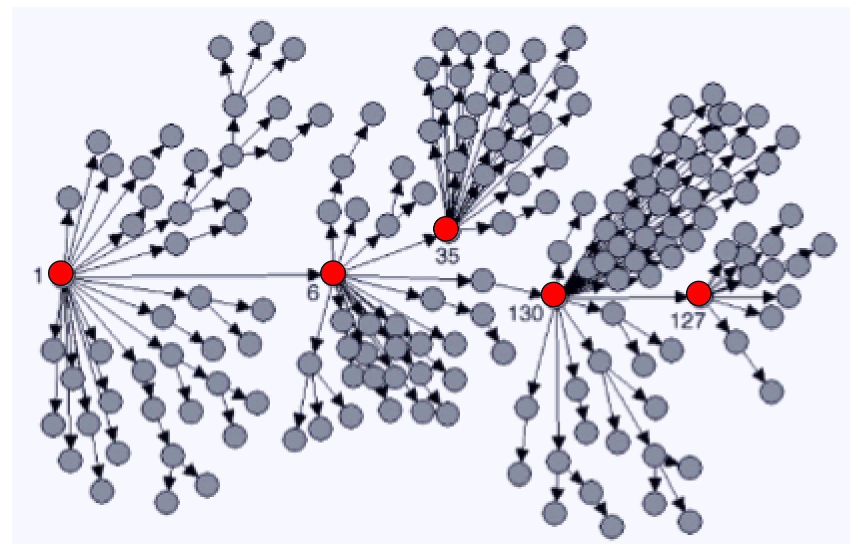
Lecture 13 – Partner Networks & Superspreaders





Disease Ecology

For EEMB40: Ecology of Disease class at UC Santa Barbara.

WEDNESDAY, FEBRUARY 8, 2012

Viral chatter

Virus hunter Nathan Wolfe is outwitting the next pandemic by staying two steps ahead: discovering deadly new viruses where they first emerge -- passing from animals to humans among poor subsistence hunters in Africa -- before they claim millions of lives.

Check out Nathan Wolfe's talk at the 2009 TED conference last year. TED (Technology, Entertainment, Design) invite some of the world's most fascinating thinkers and doers, and challenge them to give the talk of their lives. The best talks and performances are available on their website. You should all check out this talk, it is very interesting, very well presented and hugely relevant to this class.

LINKS

- Lecture 12 - AIDS
- Lecture 11 - Herd immunity
- List of glossary terms covered before midterm.
- Lecture 10 - Disease models
- Lecture 9 - Bubonic Plague
- Sample midterm
- Lecture 8 - Ecology of Lyme disease
- Lecture 7 - Lyme disease
- Lecture 6 - Antibiotic resistance
- Lecture 5 - Antibiotics
- Lecture 4 - Tuberculosis
- Lecture 3 - Epidemiology
- Lecture 2 - Cholera
- Lecture 1 - Introduction
- Syllabus
- Glossary
- The Evolution of Virulence - Paul Ewald

CONTRIBUTORS

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- Erin Mordecai

Safe Sex?

Why Not Just

SAVE SEX

Until Sex Is Safer?

It will still be there. Will you?

A reminder that some choices really are black and white from Do It Now Foundation • Box 27568 • Tempe, AZ 85285 • 480.736.0599 • www.doitnow.org

Donegan, E., Stuart, M., Niland, J. C., Sacks, H. S., Azen, S. P., Dietrich, S. L., Faucett, C., Fletcher, M. A., Kleinman, S. H., Operskalski, E. A., et al. (1990). **"Infection with human immunodeficiency virus type 1 (HIV-1) among recipients of antibody-positive blood donations".** Ann. Intern. Med. 113 (10): 733–739.

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Exposure Route	Probability of Infection
Childbirth	25 % (1 in 4)

Vertical transmission

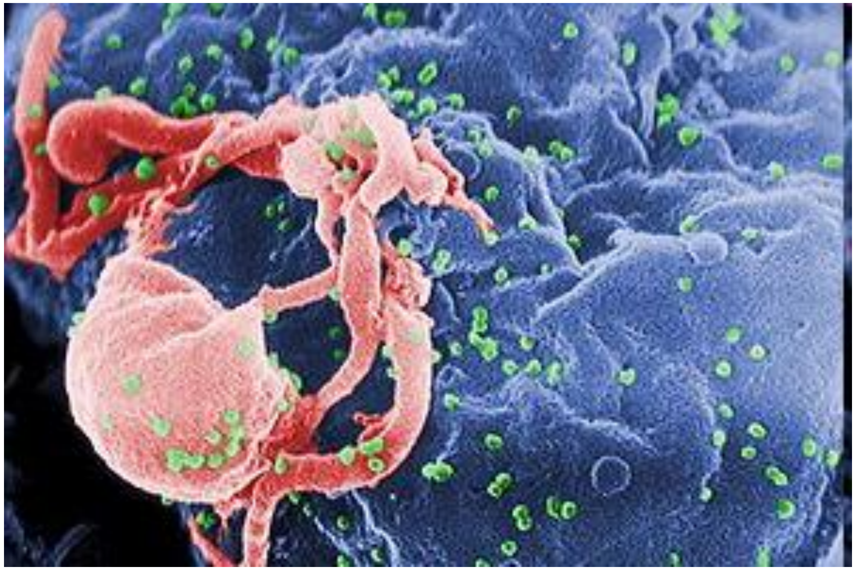
Transmission of an infection, such as HIV, from mother to child during the perinatal period, the period immediately before and after birth.

Exposure Route	Probability of Infection
Blood Transfusion	90 % (9 in 10)
Childbirth	25 % (1 in 4)
Needle-sharing injection drug use	1 % (1 in 100)
Receptive anal intercourse	1 %
Needle stick	0.5 %
Receptive penile-vaginal intercourse	0.1 % (1 in 1000)
Insertive anal intercourse	0.1 %
Insertive penile-vaginal intercourse	0.1 %
Receptive oral intercourse	0.01 % (1 in 10,000)
Insertive oral intercourse	0.01 %

Differences between HIV/AIDS and Cholera, TB, Bubonic Plague and Lyme Disease

1. AIDS is caused by a virus
   -High mutation rate (‘mutant swarm’ or ‘viral swarm’)

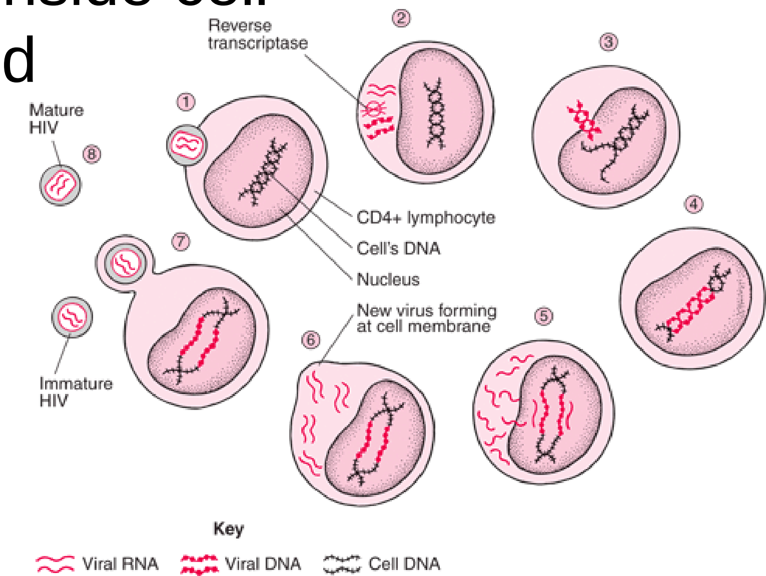
Viral swarm (aka mutant swarm)
A group of viruses of the same species but with slightly different genetic sequences



Differences between HIV/AIDS and Cholera, TB, Bubonic Plague and Lyme Disease

1. AIDS is caused by a virus
   -High mutation rate ('mutant swarm' or 'viral swarm')
   -Hard to target

- Attach to host cell
- Releases genes into host cell
- Viral components replicate inside cell
- Viral components assembled
- Viral particles released



Host Targeted Antiviral Therapy

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Home
Editorial Board
Table of Contents
Guidelines
Submission
Contact Us
About Us

Original Article

FGI-104: A Broad-Spectrum Small Molecule Inhibitor of Viral Infection

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Abstract: The treatment of viral diseases remains an intractable problem facing the medical community. Conventional antivirals focus upon selective targeting of virus-encoded targets. However, the plasticity of viral nucleic acid mutation, coupled with the large number of progeny that can emerge from a single infected cells, often conspire to render conventional antivirals ineffective as resistant variants emerge. Compounding this, new viral pathogens are increasingly recognized and it is highly improbable that conventional approaches could address emerging pathogens in a timely manner. Our laboratories have adopted an orthogonal approach to combat viral disease: Target the host to deny the pathogen the ability to cause disease. The advantages of this novel approach are many-fold, including the potential to identify host pathways that are applicable to a broad-spectrum of pathogens. The acquisition of drug resistance might also be minimized since selective pressure is not directly placed upon the viral pathogen. Herein, we utilized this strategy of host-oriented therapeutics to screen small molecules for their abilities to block infection by multiple, unrelated virus types and identified FGI-104. FGI-104 demonstrates broad-spectrum inhibition of multiple blood-borne pathogens (HCV, HBV, HIV) as well as emerging biothreats (Ebola, VEE, Cowpox, PRRSV infection). We also demonstrate that FGI-104 displays an ability to prevent lethality from Ebola in vivo. Altogether, these findings reinforce the concept of

January 2009

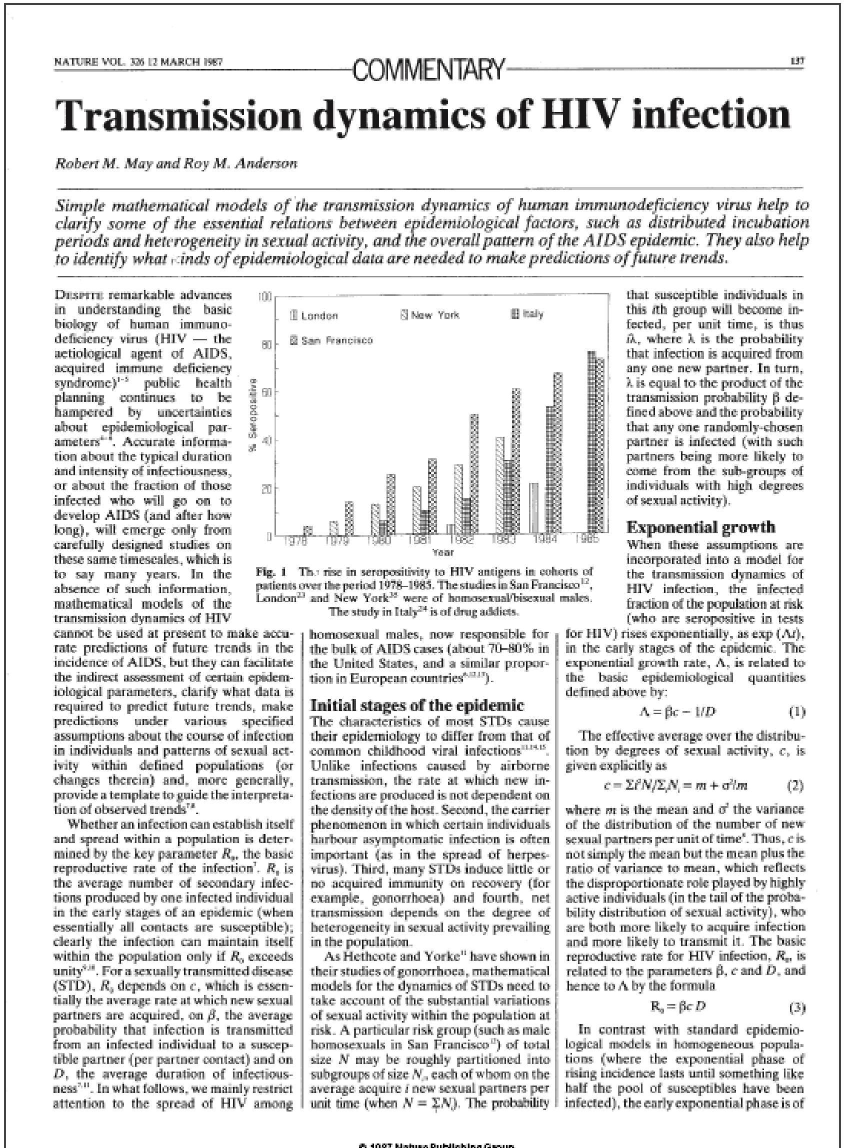
Differences between HIV/AIDS and Cholera, TB, Bubonic Plague and Lyme Disease

1. AIDS is caused by a virus
    - High mutation rate (‘mutant swarm’ or ‘viral swarm’)
    - Hard to target

2. HIV does not directly kill

3. AIDS is currently incurable

4. AIDS is a sexually transmitted disease



NATURE VOL. 326 12 MARCH 1987 — COMMENTARY — 137

Transmission dynamics of HIV infection

Robert M. May and Roy M. Anderson

Simple mathematical models of the transmission dynamics of human immunodeficiency virus help to clarify some of the essential relations between epidemiological factors, such as distributed incubation periods and heterogeneity in sexual activity, and the overall pattern of the AIDS epidemic. They also help to identify what kinds of epidemiological data are needed to make predictions of future trends.

DESPITE remarkable advances in understanding the basic biology of human immunodeficiency virus (HIV — the aetiological agent of AIDS, acquired immune deficiency syndrome)[1-5] public health planning continues to be hampered by uncertainties about epidemiological parameters[6-8]. Accurate information about the typical duration and intensity of infectiousness, or about the fraction of those infected who will go on to develop AIDS (and after how long), will emerge only from carefully designed studies on these same timescales, which is to say many years. In the absence of such information, mathematical models of the transmission dynamics of HIV cannot be used at present to make accurate predictions of future trends in the incidence of AIDS, but they can facilitate the indirect assessment of certain epidemiological parameters, clarify what data is required to predict future trends, make predictions under various specified assumptions about the course of infection in individuals and patterns of sexual activity within defined populations (or changes therein) and, more generally, provide a template to guide the interpretation of observed trends[7,8].

Fig. 1 The rise in seropositivity to HIV antigens in cohorts of patients over the period 1978–1985. The studies in San Francisco[12], London[23] and New York[35] were of homosexual/bisexual males. The study in Italy[24] is of drug addicts.

Whether an infection can establish itself and spread within a population is determined by the key parameter R_0, the basic reproductive rate of the infection[7]. R_0 is the average number of secondary infections produced by one infected individual in the early stages of an epidemic (when essentially all contacts are susceptible); clearly the infection can maintain itself within the population only if R_0 exceeds unity[9,10]. For a sexually transmitted disease (STD), R_0 depends on c, which is essentially the average rate at which new sexual partners are acquired, on β, the average probability that infection is transmitted from an infected individual to a susceptible partner (per partner contact) and on D, the average duration of infectiousness[7,11]. In what follows, we mainly restrict attention to the spread of HIV among homosexual males, now responsible for the bulk of AIDS cases (about 70–80% in the United States, and a similar proportion in European countries[6,12,13]).

Initial stages of the epidemic

The characteristics of most STDs cause their epidemiology to differ from that of common childhood viral infections[11,14,15]. Unlike infections caused by airborne transmission, the rate at which new infections are produced is not dependent on the density of the host. Second, the carrier phenomenon in which certain individuals harbour asymptomatic infection is often important (as in the spread of herpesvirus). Third, many STDs induce little or no acquired immunity on recovery (for example, gonorrhoea) and fourth, net transmission depends on the degree of heterogeneity in sexual activity prevailing in the population.

As Hethcote and Yorke[11] have shown in their studies of gonorrhoea, mathematical models for the dynamics of STDs need to take account of the substantial variations of sexual activity within the population at risk. A particular risk group (such as male homosexuals in San Francisco[12]) of total size N may be roughly partitioned into subgroups of size N_i, each of whom on the average acquire i new sexual partners per unit time (when $N = \sum_i N_i$). The probability that susceptible individuals in this ith group will become infected, per unit time, is thus $i\lambda$, where λ is the probability that infection is acquired from any one new partner. In turn, λ is equal to the product of the transmission probability β defined above and the probability that any one randomly-chosen partner is infected (with such partners being more likely to come from the sub-groups of individuals with high degrees of sexual activity).

Exponential growth

When these assumptions are incorporated into a model for the transmission dynamics of HIV infection, the infected fraction of the population at risk (who are seropositive in tests for HIV) rises exponentially, as $\exp(\Lambda t)$, in the early stages of the epidemic. The exponential growth rate, Λ, is related to the basic epidemiological quantities defined above by:

$$\Lambda = \beta c - 1/D \qquad (1)$$

The effective average over the distribution by degrees of sexual activity, c, is given explicitly as

$$c = \Sigma i^2 N_i / \Sigma_i N_i = m + \sigma^2/m \qquad (2)$$

where m is the mean and σ^2 the variance of the distribution of the number of new sexual partners per unit of time[6]. Thus, c is not simply the mean but the mean plus the ratio of variance to mean, which reflects the disproportionate role played by highly active individuals (in the tail of the probability distribution of sexual activity), who are both more likely to acquire infection and more likely to transmit it. The basic reproductive rate for HIV infection, R_0, is related to the parameters β, c and D, and hence to Λ by the formula

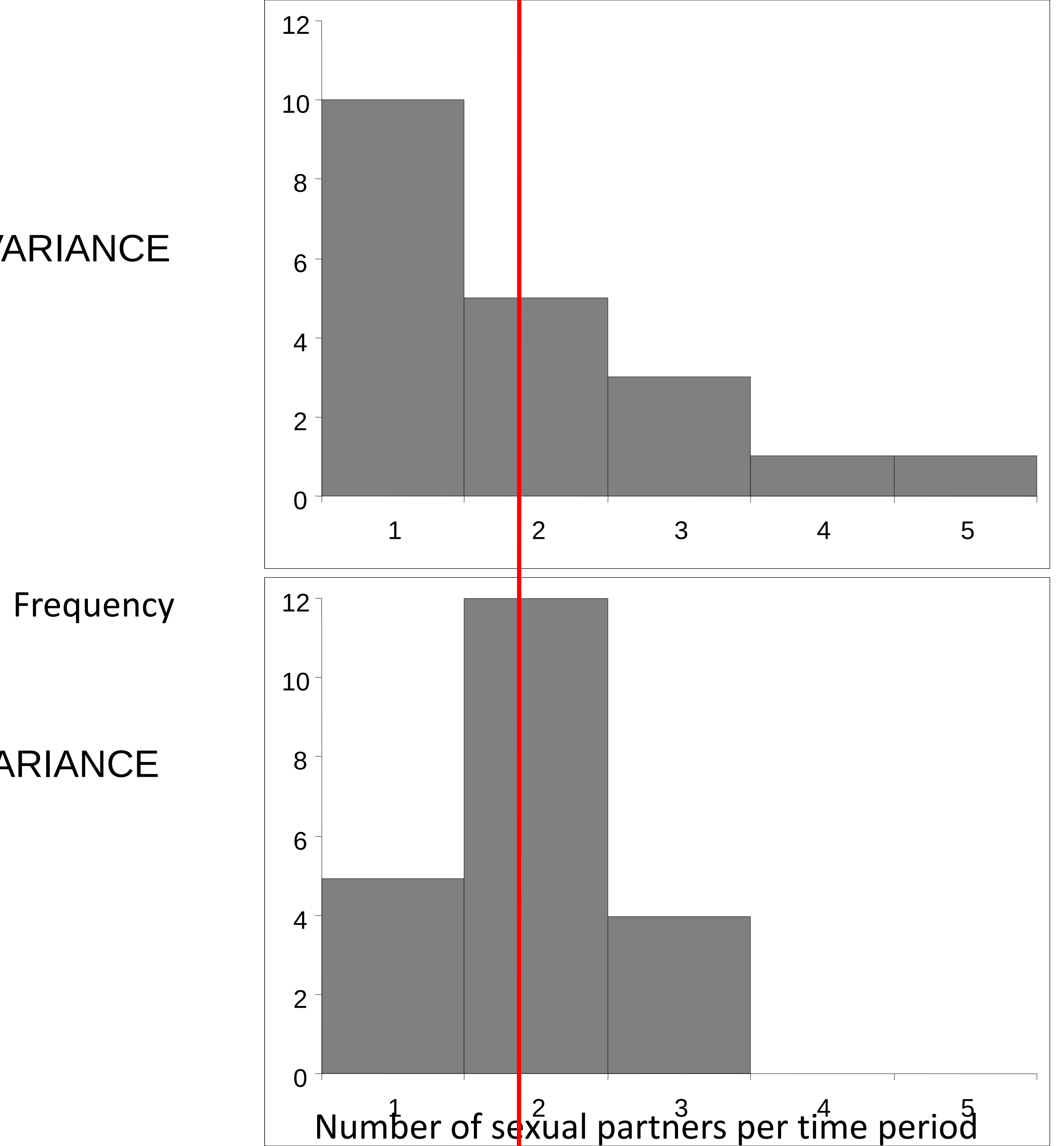
$$R_0 = \beta c D \qquad (3)$$

In contrast with standard epidemiological models in homogeneous populations (where the exponential phase of rising incidence lasts until something like half the pool of susceptibles have been infected), the early exponential phase is of

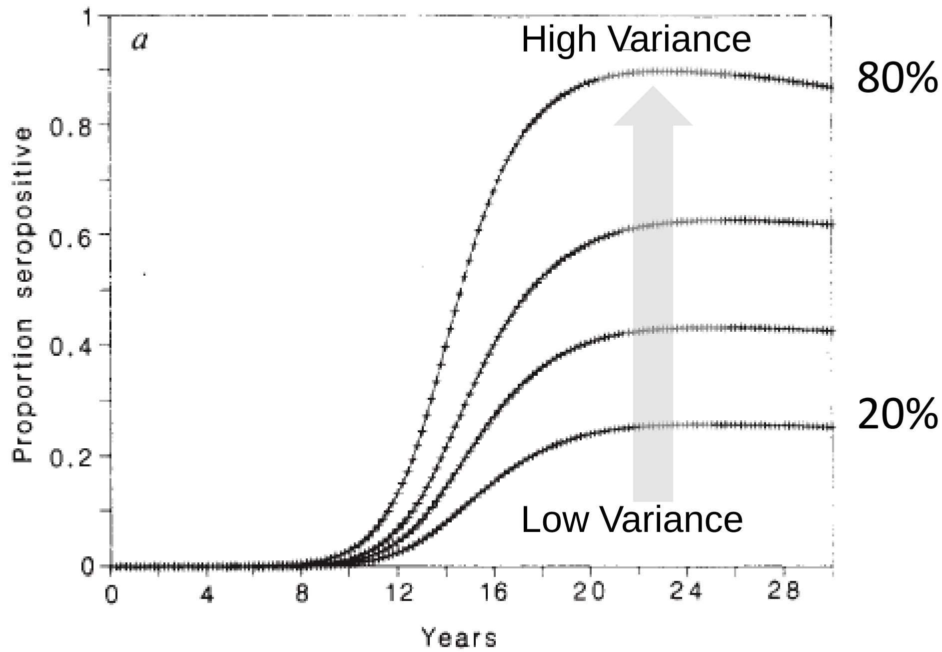
Reference: Robert M. May & Roy M. Anderson, Transmission dynamics of HIV infection. Nature, 1987, 326: 137 - 142

HIGH VARIANCE

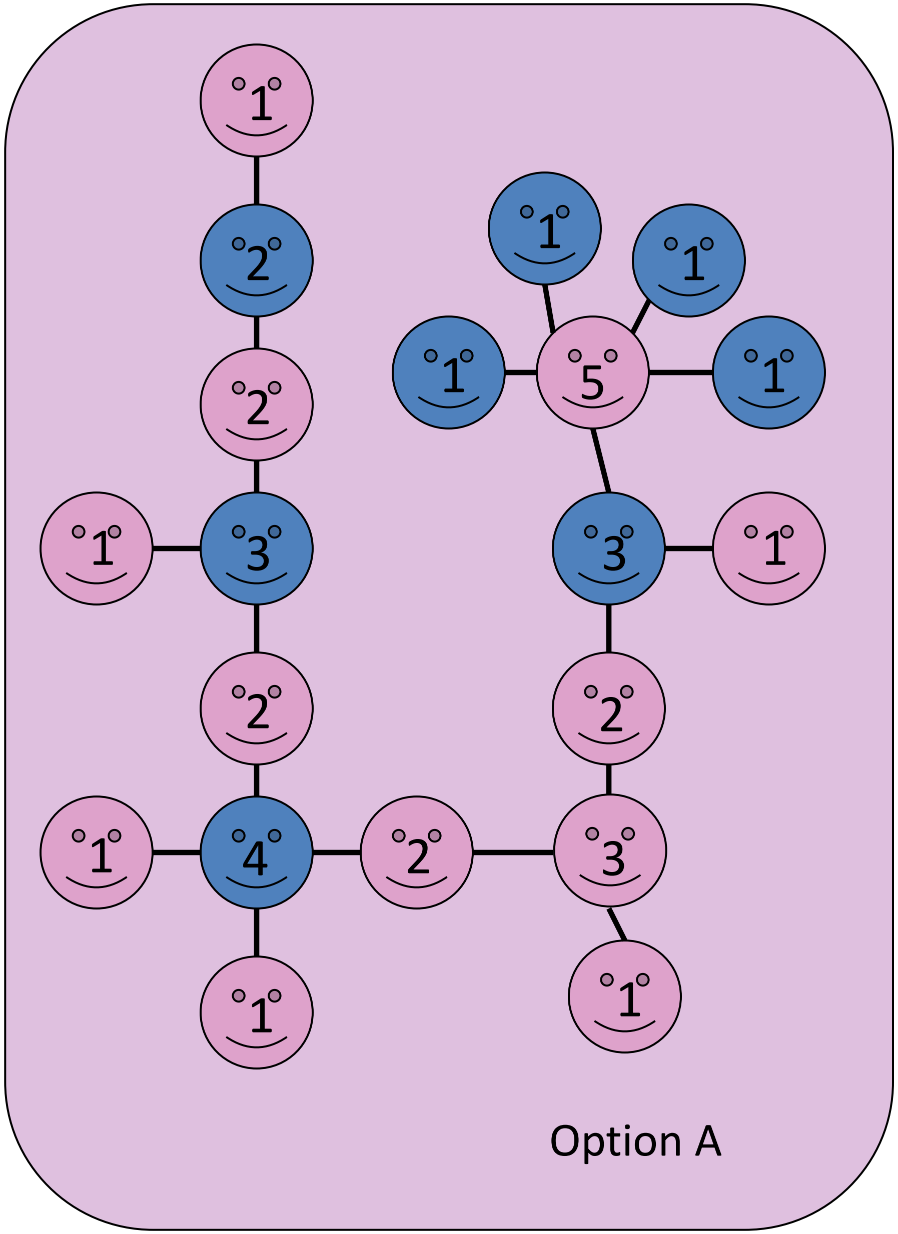
LOW VARIANCE

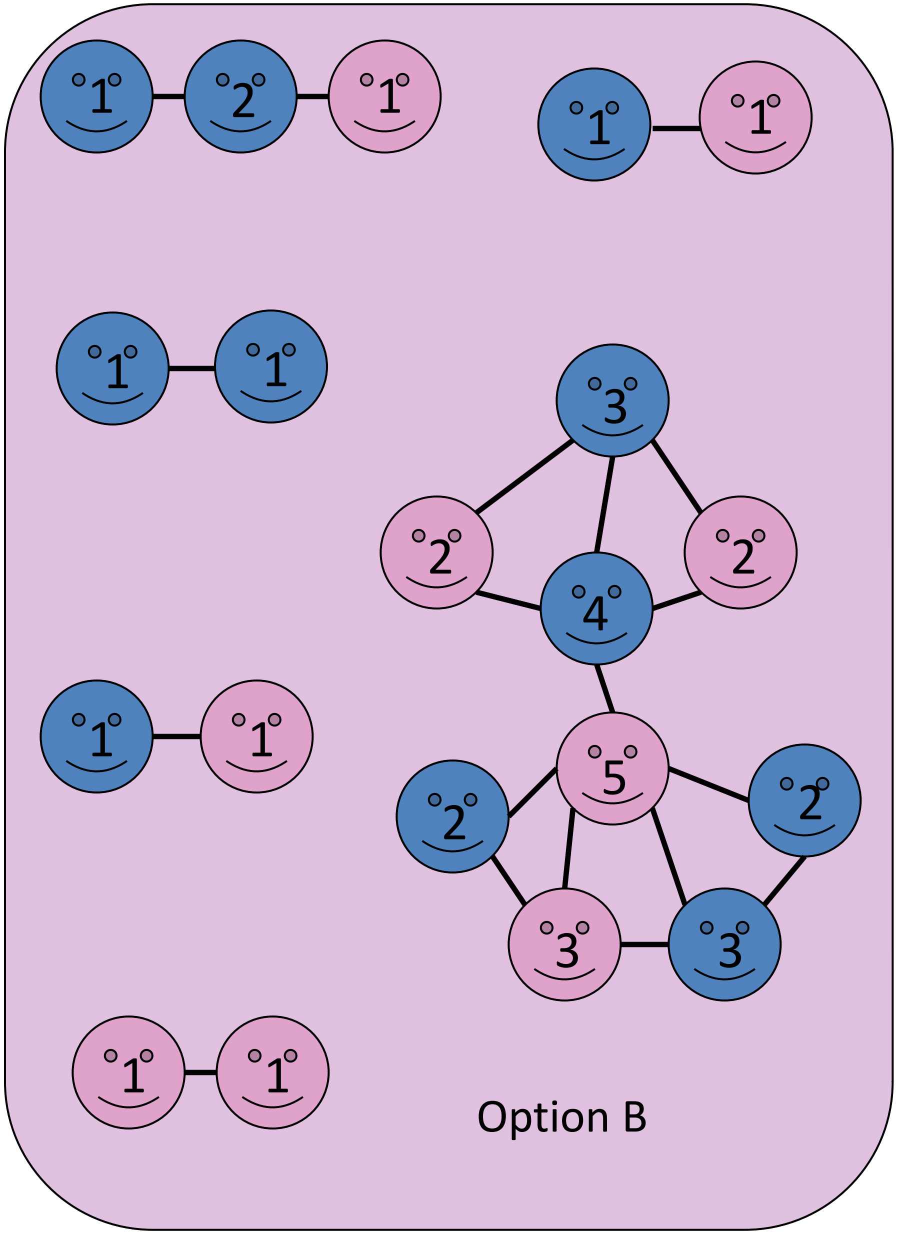


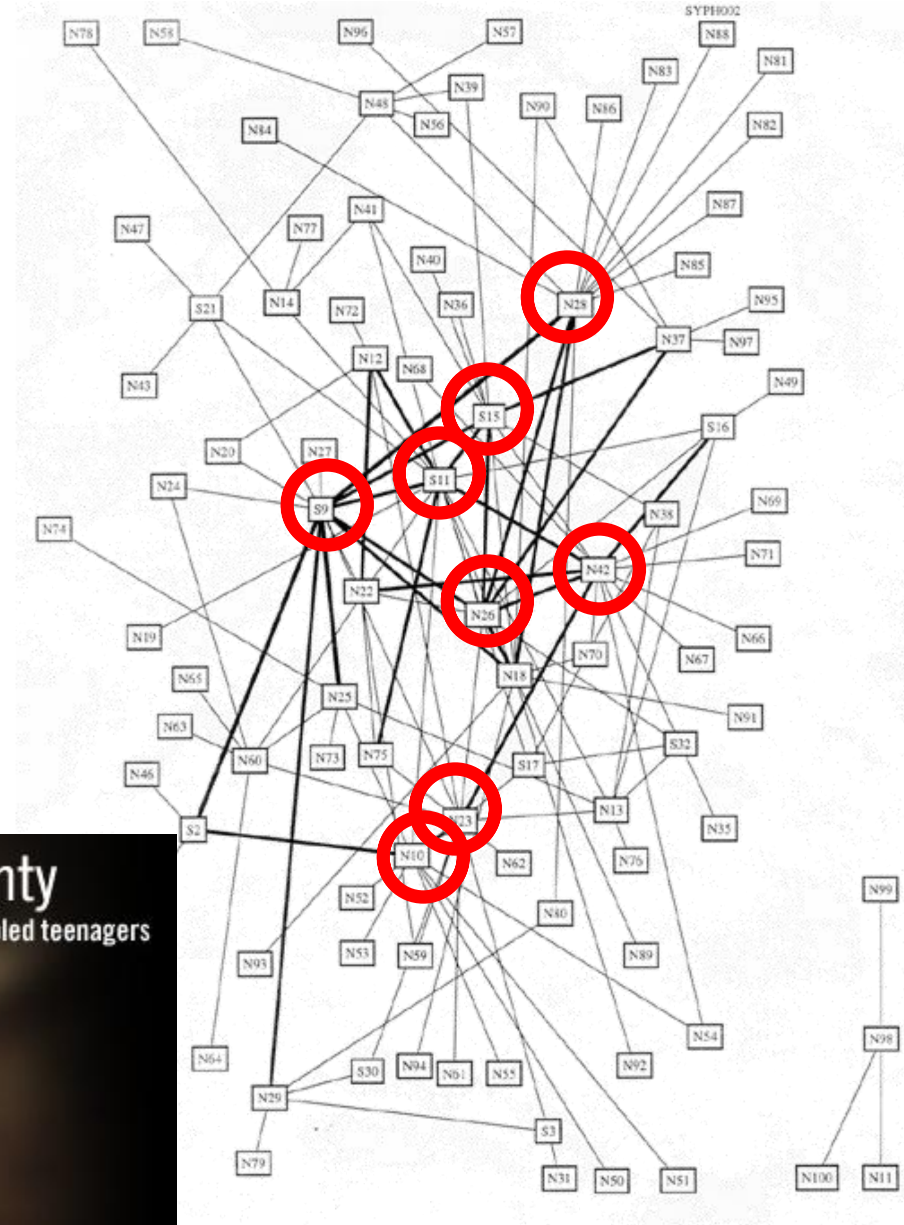
Effect of variance in the number of sexual partners on AIDS prevalence



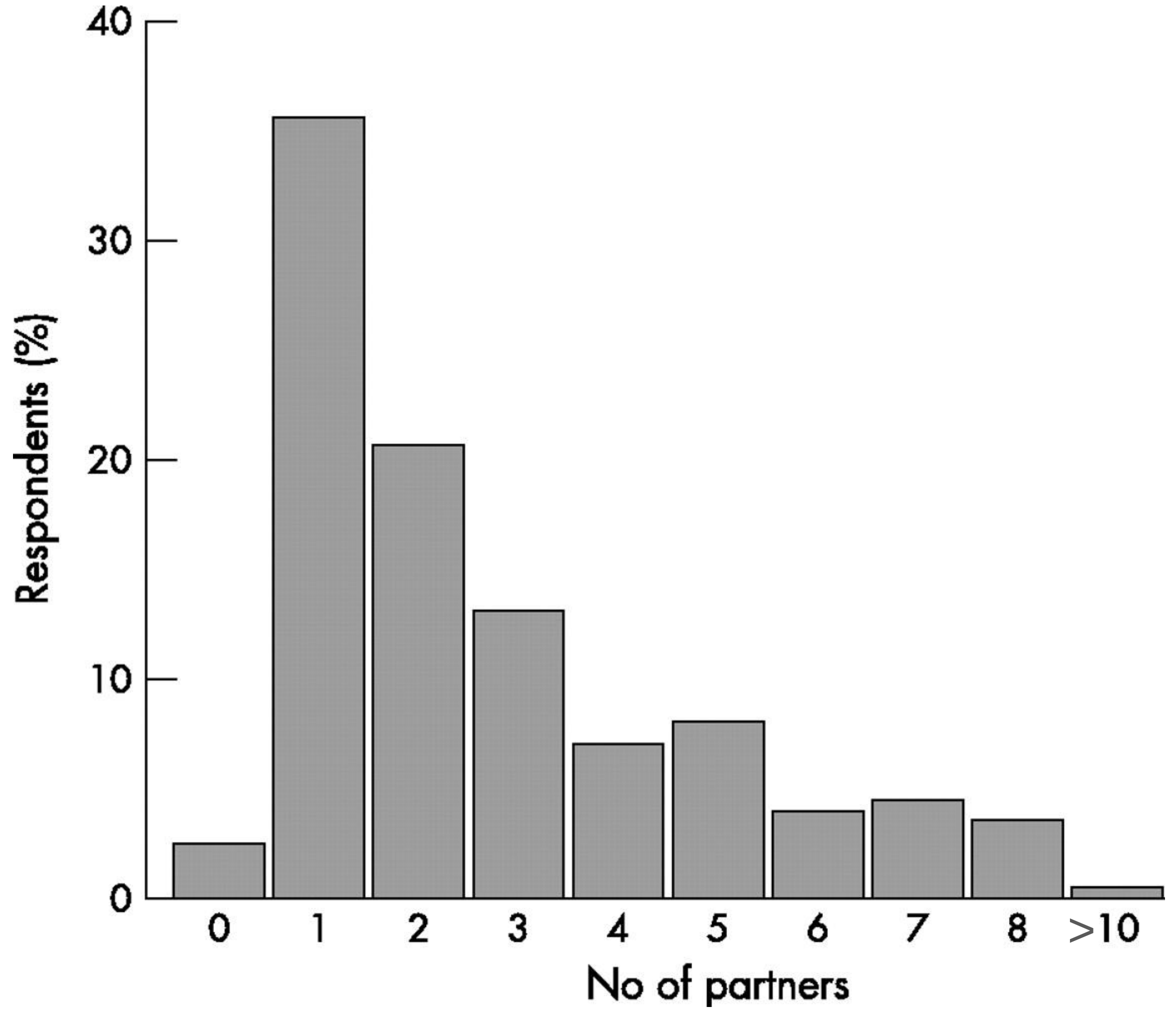
Modelling results from May & Anderson (1987)


Option A


Option B




The Lost Children of Rockdale County
a syphilis outbreak in an affluent community uncovers the hidden lives of troubled teenagers


40
30
20
10
0
Respondents (%)
0
1
2
3
4
5
6
7
8
>10
No of partners

NIH definition of ‘Multiple sexual partners’

1975	10-20 partners per year
1976	50 or more partners per year
1978	100 or more partners per year
1980	500 or more partners per year

R_o - the average number of new infections from 1 infected individual in a population of fully susceptible hosts.

R_o = contacts per unit time

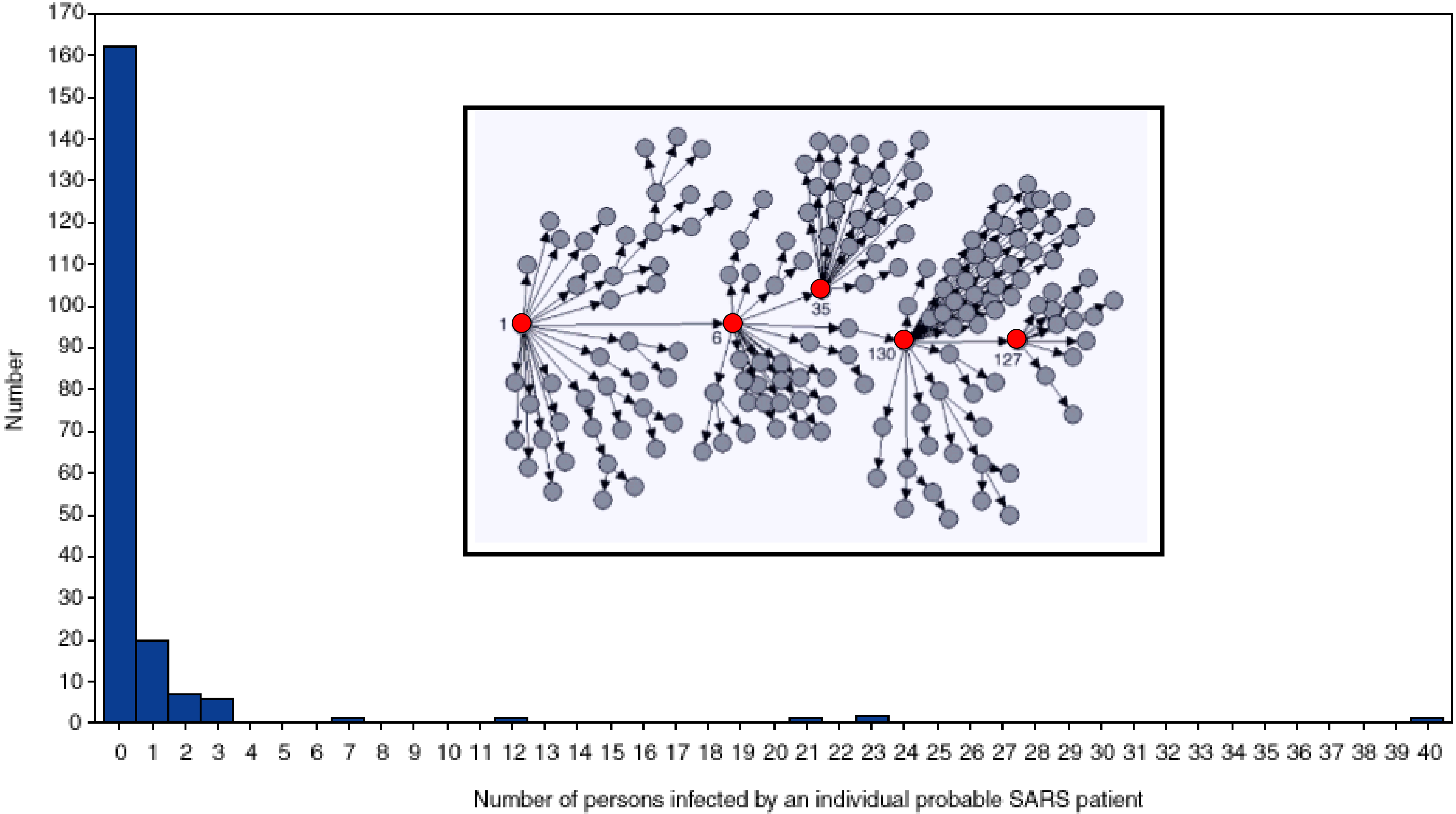
x

transmission probability

x

duration of infectiousness

SARS – Severe Acute Respiratory Syndrome – a newly identified viral disease.



Data from CDC MMWR 5/9/03

$$R_o = \text{contacts per unit time} \times \text{transmission probability} \times \text{duration of infectiousness}$$