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INTERNATIONAL CENTRE FOR THEORETICAL PHYSICS
34100 TRIESTE (ITALY) - P.O.B. 586 - MIRAMARE - STRADA COSTIERA 11 - TELEPHONES: 224281/2/3/4/5/6
CABLE: CENTRATOM - TELEX 460392 - I

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AUTUMN COURSE ON MATHEMATICAL ECOLOGY

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POPULATION BIOLOGY OF INFECTIOUS DISEASES I

Robert M. MAY

Department of Biology
Princeton University
Princeton, NJ 08544
U.S.A.

TRIESTE LECTURES

Robert May

These are literally lecture *notes* --- not complete or beautifully written, but designed to help the lectures to be intelligible.

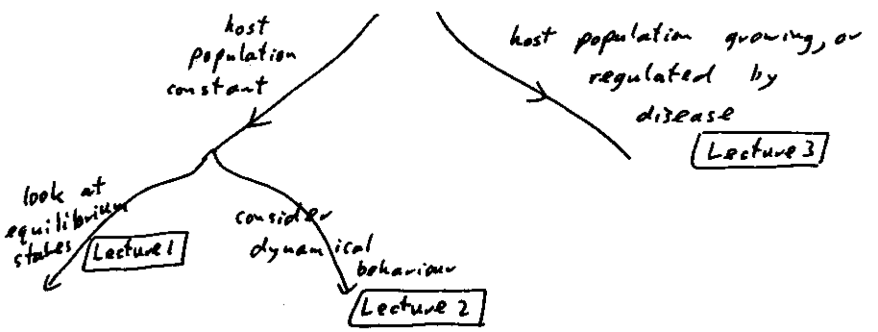
① Distinction -- necessarily rough -- between

MICROPARASITES ⟷ "compartment models" → $\boxed{\text{May}}$

and → $\boxed{\text{Anderson}}$

MACROPARASITES ⟷ distribution of parasites among hosts

② Kinds of studies (both for micro-p's and for macro-p's)



MICROPARASITES : most viruses
most bacteria
many protozoans

Divide host population into discrete classes :

(over)

$X(a,t)$ = number susceptible, of age $\underline{a}$, at time t

$Y(a,t)$ = infectious, age $\underline{a}$, time $\underline{t}$

$Z(a,t)$ = recovered and immune, age $\underline{a}$, time $\underline{t}$.

The basic partial differential equations for this system, as discussed by Dietz, Bailey, and others, are :

change with respect to time — change with respect to age — "force of infection" (below) — age specific death rate

$$\frac{\partial X}{\partial t} + \frac{\partial X}{\partial a} = \cancel{B} - \left[\lambda(t) + \mu(a)\right] X(0,t) \qquad (1)$$

~~natural death rate~~

disease induced deaths — recovery rate (constant)

$$\frac{\partial Y}{\partial t} + \frac{\partial Y}{\partial a} = \lambda X - \left[\alpha(a) + \mu(a) + \nu\right] Y(a,t) \qquad (2)$$

$$\frac{\partial Z}{\partial t} + \frac{\partial Z}{\partial a} = \nu Y - \mu(a) Z(a,t) \qquad (3)$$

with initial and boundary conditions
→ $t=0$: specify $X(a,0)$, $Y(a,0)$, $Z(a,0)$
→ $a=0$: $X(0,t) = B\left\{\begin{matrix}\text{BIRTH}\\ \text{RATE}\end{matrix}\right\}$; $Y(0,t)=Z(0,t)=0$

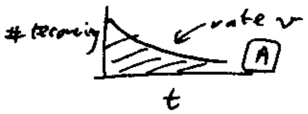
COMMENTS

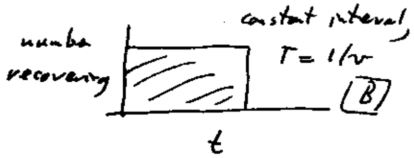
(i) A latent class (infected but not yet infectious) can be added.

(ii) Maternal antibodies may protect for first 3-9 months, so infants are born into a new, protected class, and lose immunity in first year [**exercise** : include this !]

(iii) Immunity may be lost, not lifelong as here [**exercise** : include loss of immunity !]

(iv) We have a constant recovery <u>rate</u> --- but recovery may be after some defined interval -- or some more general statistical recovery : this leads to integro-differential equations (and to similar conclusions).





We use $\boxed{A}$

(v) The "force of infection" is the per capita rate of acquiring infection --- the probability to acquire infection in unit time. Sometimes λ is deduced from data [see below]; sometimes λ is related to the number of infectious individuals, by

$$\lambda(t) = \beta \int Y(a,t)\, da \qquad \text{--- (4)}$$

(*) The assumption that all local details -- school, family, etc --- can be averaged out, to treat new infections as arising at a rate proportional to X and Y, is called the assumption of <u>HOMOGENEOUS MIXING</u>.

EQUILIBRIUM

Everything steady -- assume NO time dependence

$X(a,t) \rightarrow X(a)$, etc.

We also here assume

(a) Births and deaths <u>exactly</u> balance [usually they do not, particularly in developing countries, and this leads to complications]

(b) $\alpha = 0$: infection does not cause significant number of deaths (also can be wrong)

$$\frac{dX}{da} = -(\lambda + \mu(a))X(a) \qquad (5)$$

$$\frac{dY}{da} = \lambda X - (v + \mu(a))Y(a) \qquad (6)$$

$$\frac{dZ}{da} = vY - \mu(a)Z(a) \qquad (7)$$

$$\frac{dN}{da} = -\mu(a)N(a) \quad ; \quad N(a) = X(a) + Y(a) + Z(a) \qquad (8)$$

These equations may readily be solved, with the boundary condition $X(0) = N(0)$, $Y(0) = Z(0) = 0$ --- all are born susceptible

$$X(a) = N(0)\, e^{-\lambda a} \phi(a), \qquad (9)$$

where, for convenience, I define

$$\phi(a) = \exp\left\{-\int_0^a \mu(s)\, ds\right\} \qquad (10)$$

<u>Exercise</u>: find expressions for $Y(a)$ and $Z(a)$. The total number of age a is

$$N(a) = N(0)\, \phi(a) \qquad (11)$$

The fraction of people of age who are susceptible is

$$x(a) \equiv \frac{X(a)}{N(a)} = e^{-\lambda a} \qquad (12)$$

"AGE AT FIRST INFECTION"

Can be deduced from data on case records, or from serological studies

$$A \equiv \frac{\int_0^\infty a \lambda x(a)\,da}{\int_0^\infty \underbrace{\lambda x(a)}\,da} = \int_0^\infty x(a)\,da \qquad (13)$$

fraction of age a who get sick at that age

Prove this, using (12) and a partial integration

Thus, using (12),

$$\boxed{A = 1/\lambda} \quad \text{-- (14)}$$

This relates the "observable" A with the more abstract "λ" --- PROVIDED we treat λ as independent of age: this is usually done in mathematical work, but usually is not true!

BASIC REPRODUCTIVE RATE

R_0 -- number of secondary cases produced, on average, when ~~Ag~~ everyone is susceptible

Clearly R_0 combine biology (or "etiology") of infection with social and behavioural factors influencing contact rates.

Assuming homogeneous mixing, effective reproductive rate, R, when X of N are susceptible is

$$R = R_0 X/N \qquad (15)$$

But at equilibrium $R = 1$: so R_0 is related to the equilibrium fraction susceptible by

$$\boxed{R_0 = (N/X)_{equil}} \qquad (16)$$

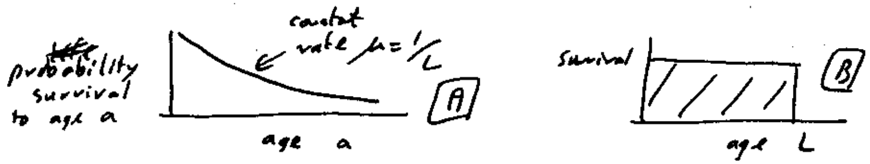
From before,

$$N = \text{total number} = \int_0^\infty N(a)\,da \qquad (17)$$

$$X = \text{" susceptible} = \int_0^\infty X(a)\,da \qquad (18)$$

First -- CASE A -- assume human mortality is at constant rate -- μ = constant (usual epidemiological ~~as~~ assumption, though clearly inaccurate)

Second -- CASE B -- assume all live exactly to ~~age~~ L



$\boxed{A}$ $\phi(a) = e^{-\mu a}$; $\boxed{B}$ $\phi(a) = 1$; $a < L$ --(19)
$= 0$; $a > L$

Exercise: show, using (11) in (17) and (9) in (18), that for CASE ~~A~~

$$R_0 = 1 + \frac{\lambda}{\mu} = 1 + \frac{L}{A} \qquad (20)$$

and for CASE B (over)

$$R_0 = \frac{\lambda L}{1-e^{-\lambda L}} \simeq \frac{L}{A} \quad (\text{for } L \gg A) \qquad (21)$$

VACCINATION : New Equilibrium

Vaccination has two main effects ---

Direct -- some are removed to the immune class and so there are fewer infections.

Indirect -- Fewer infected people implies a weaker "force of infection" --- so there is also indirect protection. We do not have to immunise everyone to eradicate the infection.

Let us calculate the new equilibrium value of the force of infection, λ', when a fraction p of each cohort are immunised at age b. At the new equilibrium,

$$\left.\begin{aligned} X'(a) &= N(0)\, e^{-\lambda' a} \phi(a) \quad ; \quad a \le b \\ X'(a) &= (1-p) N(0)\, e^{-\lambda' a} \phi(a) \quad ; \quad a > b \end{aligned}\right\} \quad (22)$$

[Proof -- exercise!]. $N(a)$ still obeys (11)

Using (16), (17), (18), we get [exercise]

(constant $\mu = 1/L$)

CASE A: $$R_0 = \frac{1+\lambda' L}{1 - p \exp[-(\lambda'+\mu) b]} \qquad (23)$$

CASE B: (step μ) $$R_0 = \frac{\lambda' L}{1 - p e^{-\lambda' b} - (1-p) e^{-\lambda' L}} \qquad (24)$$

Given A -- age at first infection before vaccination programme --- find R_0 from (20) or (21). Now (23) or (24) give new (smaller) λ' (and now $A' = 1/\lambda'$ --- $A' > A$).

Eradication is the limit $\lambda' \to 0$:

Exercise -- Show the critical fraction that must be immunised at age b to eradicate infection is given by

$$p_c = \left(\frac{L}{A+L}\right) e^{b/L} \text{ for CASE A} ; \quad p_c = \frac{L - A(1-e^{-L/A})}{L-b} \text{ for CASE B}$$

N.B. if $b \neq 0$, these p_c are $\not< 1$ $\Rightarrow$ eradication NOT POSSIBLE

DOES VACCINATION REDUCE DISEASE?

Suppose the infection is much worse for older people --- e.g.: rubella (german measles) is a problem mainly for pregnant women.

Direct effects --- fewer people get rubella

Indirect effects --- those who do get it, get it at an older age

CAN BE that # case of rubella in pregnant ♀♀ actually increases.

Define

$$W(a_1, a_2) = \frac{\text{number of people acquiring infection between ages } a_1 \,\&\, a_2 \text{ at equil after vacc}}{\text{Corresponding number at equil before vacc}}$$

That is $$W(a_1, a_2) = \frac{\int_{a_1}^{a_2} \lambda' X'(a)\, da}{\int_{a_1}^{a_2} \lambda X(a)\, da}$$

← Exercise

CASE A, $b=0$

$$W = \frac{\lambda' [\exp\{-(\lambda'+\mu) a_1\} - \exp\{-(\lambda'+\mu) a_2\}]}{\lambda [\exp\{-(\lambda+\mu) a_1\} - \exp\{-(\lambda+\mu) a_2\}]}$$

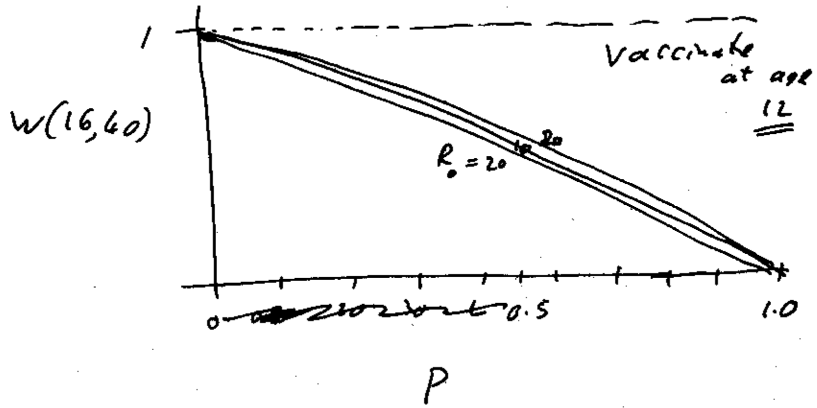
Exercise →

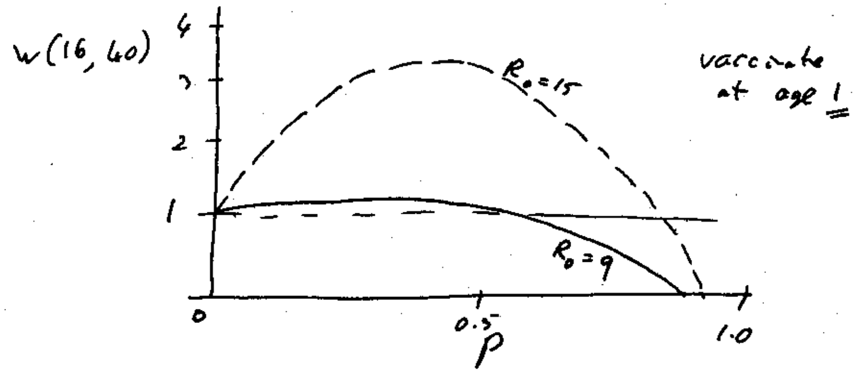
CASE B, $b=0$

$$W = (1-p) \frac{[e^{-\lambda' a_1} - e^{-\lambda' a_2}]}{[e^{-\lambda a_1} - e^{-\lambda a_2}]}$$

Consequently, the value of $w(a_1, a_2)$ depends on the fraction vaccinated, but also on R_0 (or, equivalently, on age at infection before vaccination programme).

For instance, consider the ratio w for people between the ages of 16 – 40 yrs:





Clearly, the number getting sick at older ages can increase if coverage, p, is not $\to 1$ and R_0 is large.