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ON THE FINAL SIZE OF EPIDEMICS WITHIN HERDS

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ABSTRACT. We are concerned with an epidemic in a closed population under the assumption that the per capita number of contacts remains constant, when population size diminishes due to the fatal consequences of the disease. We focus on the final size as a function of the basic reproduction ratio R_0 (which now is independent of population size!) and the survival probability f. Mathematically, the model is described by a nonlinear Volterra integral equation of convolution type, just as the general Kermack-McKendrick model.

1. Introduction. As a rule, infectious agents either spread via a contamination of the environment or during a "direct" contact of two individuals. In any case, one has to model the contact process first and superimpose transmission of the agent afterwards. In this paper we scrutinize one of the assumptions underlying classical deterministic theory and then introduce a variant which seems particularly appropriate for animals living in "herds," such that the density within the "herd" remains constant when population size decreases, for instance due to fatal consequences of the disease. (Here "herd" includes prides of lions, packs of wolves, family groups of foxes, breeding colonies of birds, as well as real herds of ungulates. And farm animals are included too.) We concentrate on the basic reproduction ratio R_0 and on the final size of an epidemic within a completely susceptible closed population. The present work can be viewed as a generalization of a result of Lefevre and Picard [9] (see also [12 and 7]).

2. Model formulation and analysis. We assume that individuals have on average c contacts per unit of time and that, given a contact between a susceptible and an infective that was infected τ units of time ago, transmission occurs with probability $a(\tau)$. By $A(\tau)$ we denote

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the product $a(\tau)B(\tau)$, where $B(\tau)$ is the probability to be still alive at disease age τ. Let $S(t)$ denote the number of susceptibles at time t and $N(t)$ the total number of individuals (note that our variables are numbers, not densities!). Of all contacts that an infected makes, a fraction S/N will be with susceptibles.

The assumptions formulated above lead to the consistency relation

$$\dot{S}(t) = c\frac{S(t)}{N(t)}\int_0^\infty A(\tau)\dot{S}(t-\tau)\,d\tau. \tag{2.1}$$

To allow interpreting (2.1) as an equation for S, we still have to add an assumption that determines c.

If, when population size changes, the density changes accordingly, the principle of mass action suggests to take $c = \beta N(t)$. We then arrive at the celebrated [6] model and find for the basic reproduction ratio, i.e., the expected number of secondary cases produced by a typical infected individual during its entire infectious period,

$$R_0 = \beta\int_0^\infty A(\tau)\,d\tau N_0 \tag{2.2}$$

while the fraction $s(\infty) = S(\infty)/N_0$ that escapes from ever getting the disease is found as the solution of

$$\ln s(\infty) = R_0[s(\infty) - 1] \tag{2.3}$$

(see [**10, 11**] for a derivation and discussion in the spirit of this paper). Here, however, we shall assume that the density stays constant when numbers change. Our original motivation to consider such a situation came from a study of the spread of Phocid distemper virus among seals (see [8], in preparation, and the references given there for further information; also see [5] and [2]). Observations suggest that the distance between individuals that rest and sun bathe on sand banks are independent of the colony size. We can imagine that this applies more generally for animals living in groups, while space is not a limiting factor. If c is constant we find straightaway that the basic reproduction ratio is given by

$$R_0 = c\int_0^\infty A(\tau)\,d\tau \tag{2.4}$$

which is independent of population size. The latter is exactly what Heide-Jørgensen and Härkönen [4] found when analyzing data about Phocid distemper virus outbreaks in local seal colonies of different sizes. When we want to calculate $s(\infty)$, we need to be more specific about changes in N due to deaths. The meaning of $B(\tau)$ implies that

$$N(t) = S(t) - \int_0^\infty B(\tau)\dot{S}(t-\tau)\,d\tau \tag{2.5}$$

(note that $\dot{S}$ is negative!).

For any pair of nonnegative functions A and B, the equations (2.1) and (2.5) determine implicitly the fraction $s(\infty)$ that escapes the disease and its complement $1-s(\infty)$ that falls victim to it. We did not manage to give a simple characterization for the general case. However, if one is willing to assume that

$$\dot{B}(\tau) = -qA(\tau) = -qa(\tau)B(\tau) \tag{2.6}$$

for some nonnegative constant q, a simple characterization becomes possible. Before giving that characterization we discuss the biological interpretation of the relation (2.6). In fact, this relation states that the hazard rate of death is proportional to the rate of production (or, more precisely, dissemination) of the infectious agent by the host. Hence, it may not be an overly unreasonable condition.

A specific example of a submodel for infectivity and death is the following. Assume that an infected individual can be in n different states. So we have at the individual level a continuous time Markov chain. Let θ denote the initial probability vector (so θ_i is the probability that a newly infected individual has state i). Let H denote the state transition matrix conditional on survival, and let μ_i denote the probability per unit of time of dying, given that the state is i. Then the probability vector $x(t)$ satisfies

$$dx/dt = Hx - (\operatorname{diag}\mu)x, \qquad x(0) = \theta$$

where, as usual, $\operatorname{diag}\mu$ denotes the diagonal matrix with μ_i at position i. Let h_i denote the probability of transmission, given a contact between a susceptible and an infective in state i. Then

$$A(\tau) = \sum_{i=1}^{n} h_i x_i(\tau)$$

while

$$\dot{B}(\tau) = -\sum_{i=1}^{n} \mu_i x_i(\tau), \qquad B(0) = 1.$$

So the condition (2.6) amounts to the condition that the vectors h and μ are proportional: $\mu = qh$.

When (2.6) holds, it follows that

$$\begin{aligned}\frac{dN}{dt}(t) &= \dot{S}(t) - \int_0^\infty B(\tau)\ddot{S}(t-\tau)\,d\tau \\ &= \dot{S}(t) + [B(\tau)\dot{S}(t-\tau)]_0^\infty \\ &\quad - \int_0^\infty \dot{B}(\tau)\dot{S}(t-\tau)\,d\tau \\ &= q\int_0^\infty A(\tau)\dot{S}(t-\tau)\,d\tau.\end{aligned}$$

So if we divide (2.1) by $S(t)$ and integrate over $(-\infty, t]$, we find that

$$\ln\frac{S(t)}{N_0} = \frac{c}{q}\ln\frac{N(t)}{N_0}.$$

Here we assumed that in the distant past everybody was susceptible, i.e., we assumed that $S(-\infty) = N(-\infty) = N_0$. If we define

$$f = B(\infty), \tag{2.7}$$

then integration of (2.6) over $[0, \infty)$ yields

$$f - 1 = -q\int_0^\infty A(\tau)\,d\tau$$

which we rewrite as

$$\frac{c}{q} = \frac{R_0}{1-f}. \tag{2.8}$$

Thus, we obtain

$$\frac{S(t)}{N_0} = \left(\frac{N(t)}{N_0}\right)^{R_0/(1-f)} \tag{2.9}$$

and in the limit of $t \to \infty$,

$$s(\infty) = n(\infty)^{R_0/(1-f)}, \tag{2.10}$$

where

$$n(\infty) = \frac{N(\infty)}{N_0}.$$

A second equation is obtained by letting $t \to \infty$ in (2.5) while noting that

$$\int_0^\infty B(\tau)\dot{S}(t-\tau)\,d\tau = \int_{-\infty}^t B(t-\tau)\dot{S}(\tau)\,d\tau \overset{t\to\infty}{\longrightarrow} f(S(\infty) - N_0).$$

So this second equation reads

$$n(\infty) - s(\infty) = f(1 - s(\infty)). \tag{2.12}$$

Note that this is consistent with the interpretation of f as the probability to survive the infection, as the lefthand side is the fraction of the population that was infected and survived, while the second factor at the righthand side equals the fraction that was infected.

Together the equations (2.10) and (2.12) give a complete characterization of the final size parameters $s(\infty)$ and $n(\infty)$ in terms of R_0 and f. Conversely, one can estimate f and R_0 from data about $s(\infty)$ and $n(\infty)$ by using the formulae

$$f = \frac{n(\infty) - s(\infty)}{1 - s(\infty)} \tag{2.13}$$

$$R_0 = (1-f)\frac{\ln s(\infty)}{\ln n(\infty)} = \frac{1 - n(\infty)}{1 - s(\infty)}\frac{\ln s(\infty)}{\ln n(\infty)}. \tag{2.14}$$

3. What difference does it make? When there are no deaths, we are back to Kermack and McKendrick. And, indeed, one can recover (2.3) from (2.10) and (2.12) by letting $f \uparrow 1$.

Death has two effects, a direct one and an indirect one. The direct one is simply that a fraction $1 - f$ of $1 - s(\infty)$ dies. The indirect one is

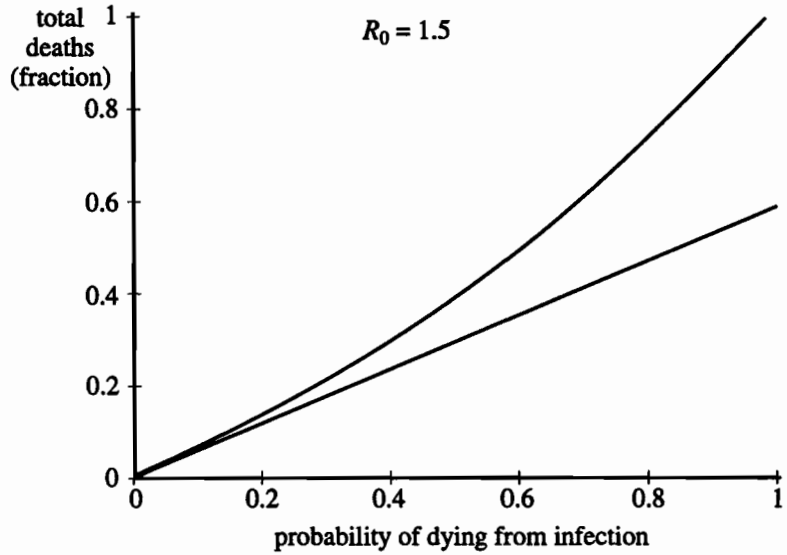

FIGURE 1. The straight line takes account only of the direct effect, as it simply multiplies the final size for $f = 1$ by the probability $1 - f$ to die. The curved line gives the fraction of the population that dies from the disease, according to (2.10) and (2.11) and so takes account of both effects. We see that the indirect effect is quite important for low values of R_0 and low values of f.

that $s(\infty)$ itself decreases since, while immunes hinder contacts between infectives and susceptibles, dead individuals don't do so. The indirect effect makes the difference between the present model and the Kermack-McKendrick model. When R_0 is big, $s(\infty)$ is very small ($\sim e^{-R_0}$) and so the indirect effect is negligible. If, on the other hand, R_0 is only little above the threshold value one, the indirect effect can be substantial, as the figure illustrates.

In the case of seals affected by Phocid distemper virus, the survival probability f may very well depend on the general physiological condition which, in turn, is determined by environmental conditions like food availability and pollution. Such aspects are discussed in [8] (in preparation).

4. The initial value problem. So far, our mathematical manip-

ulations have been quite formal. Limiting Volterra integral equations like (2.1) and (2.5) describe the dynamics on the whole line $(-\infty, +\infty)$, and they naturally appear when discussing omega-limit sets for dynamical systems defined in terms of Volterra integral equations on $[0, \infty)$, see, e.g., [1] and the references given therein. Yet we fear that some readers will find that our presentation lacks rigor, and for them we add this section.

The initial value problem is described by the equations

$$\dot{S}(t) = c\frac{S(t)}{N(t)}\left\{\int_0^t A(\tau)\dot{S}(t-\tau)\,d\tau + h(t)\right\} \tag{4.1}$$

$$N(t) = S(t) - \int_0^t B(\tau)\dot{S}(t-\tau)\,d\tau + g(t) \tag{4.2}$$

where

$$h(t) = -\int_0^\infty \frac{A(t+\tau)}{B(\tau)}\phi(\tau)\,d\tau \tag{4.3}$$

$$g(t) = \int_0^\infty \frac{B(t+\tau)}{B(\tau)}\phi(\tau)\,d\tau \tag{4.4}$$

for some nonnegative $\phi \in L_1(\mathbf{R}_+)$. The function ϕ describes the population state at time $t = 0$ in the sense that $\int_{\tau_1}^{\tau_2} \phi(\sigma)\,d\sigma$ equals the number of individuals at that time who were infected more than τ_1 and less than τ_2 time units ago. The conditional probability that an individual of disease age τ is still alive t units of time later is $B(t+\tau)/B(\tau)$ and then its probability to transmit the agent to a susceptible, given a contact, is $a(t+\tau)$, whence the expressions for h and g. In addition to ϕ we have to provide an initial condition for S:

$$S(0) = S_0. \tag{4.5}$$

Note that $N(0) = S_0 + \int_0^\infty \phi(\tau)\,d\tau$. Now assume that (2.6), which we here repeat as

$$\dot{B}(\tau) = -qA(\tau), \tag{4.6}$$

holds. As before, we find that

$$\dot{S}(t) = \frac{c}{q}\frac{S(t)}{N(t)}\dot{N}(t) \tag{4.7}$$

and by integration that

$$\frac{S(t)}{S_0} = \left(\frac{N(t)}{N(0)}\right)^{c/q}. \tag{4.8}$$

Using integration by parts once more, we can rewrite (4.2) as

$$N(t) = B(t)S_0 + q\int_0^t A(\tau)S(t-\tau)\,d\tau + g(t) \tag{4.9}$$

which, upon substitution of (4.8) becomes

$$\begin{aligned} N(t) &= B(t)S_0 + g(t) \\ &\quad + qS_0N(0)^{-c/q}\int_0^t A(\tau)(N(t-\tau))^{c/q}\,d\tau. \end{aligned} \tag{4.10}$$

This is a nonlinear renewal equation, i.e., a Volterra integral equation of convolution type, to which standard results of existence and uniqueness of solutions apply, e.g., [3]. Once N is "known," S follows from (4.8).

The next step is to prove that N is a decreasing function of t. In order to do so, we rewrite, using (4.6), (4.10) as

$$N(t) = S_0 + g(t) + qS_0\int_0^t A(\tau)\left\{\left(\frac{N(t-\tau)}{N(0)}\right)^{c/q} - 1\right\}d\tau.$$

Since g is differentiable (see (4.4) and recall that B is differentiable), so is N. By differentiation we obtain

$$\dot{N}(t) = \dot{g}(t) + cS_0\int_0^t A(\tau)\left(\frac{N(t-\tau)}{N(0)}\right)^{(c/q)-1}\frac{\dot{N}(t-\tau)}{N(0)}\,d\tau,$$

from which it follows at once that $\dot{N} \leq 0$. Rather directly (4.10) implies that $N \geq 0$. Hence, $\lim_{t\to\infty} N(t)$ exists. Taking the limit $t \to \infty$ in (4.10), we obtain, using (2.4), (2.7) and (2.8),

$$N(\infty) = fS_0 + g(\infty) + (1-f)S_0\left(\frac{N(\infty)}{N(0)}\right)^{R_0/(1-f)}.$$

Since (4.8) implies that

$$\frac{S(\infty)}{S_0} = \left(\frac{N(\infty)}{N(0)}\right)^{R_0/(1-f)}, \tag{4.11}$$

we can rewrite the identity as

$$N(\infty) - S(\infty) = f(S_0 - S(\infty)) + g(\infty). \tag{4.12}$$

Together, (4.11) and (4.12) are the rigorous version of (2.11) and (2.12), to which they tend for $g(\infty) \downarrow 0$.

5. Discussion. When animals live in herds, the number of contacts per unit of time per individual could very well be quite independent of herd size. If herd size diminishes due to a fatal infectious disease, the force of infection does not go down as quickly as it does in the standard Kermack-McKendrick model, which assumes that the density, and hence the per capita number of contacts per unit of time, is proportional to the population size. We have derived an equation for the final size of an epidemic in a closed population, as a function of the survival probability f and the basic reproduction ratio R_0 and compared the result with the Kermack-McKendrick case. The difference is substantial for R_0 values slightly above the threshold value 1 combined with small values of f, but rather small otherwise. The derivation is based on the assumption that the hazard rate of death is proportional to the rate at which the infectious agent is disseminated by the host. This assumption is warranted when replication of the infective agent is disseminated by the host. This assumption is warranted when replication of the infective agent in organs from which it is excreted to the outside world is responsible for the morbidity. For some agents, excretion and disease may relate to replication in different organs and then the assumption is less defendable. So it remains a relevant open problem to give a simple characterization of the final size in general, without making the special assumption.

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