

Modeling of Fish Disease Dynamics: A New Approach to an Old Problem

Hamdi Ögüt*

Karadeniz Technical University, Faculty of Marine Sciences, Department of Fisheries, 61530 Çamburnu, Trabzon, Turkey

* Corresponding Author: Tel.: +90. 462. 752 28 05; Fax: +90. 462. 752 21 58;
E-mail: hamdiogut@yahoo.com

Accepted 03 October 2001

Abstract

In the past, the focus of fish disease research was on various aspects of fish pathogens (biochemical, serological, virulence etc.) rather than the disease itself. Therefore, vast amounts of data are available on the responses of these pathogens to environmental and host related factors. Modeling of these accumulated data could be employed to understand the relative importance of the factors influencing the spread of disease. In particular, the data obtained from intensive aquaculture systems could be robust in applying modeling due to fewer assumptions involved. Each animal in a pond situation is exposed to the same conditions. Therefore, the chance of coming into contact with an infectious agent or animal is the same for each individual sharing the same pond. Thus, nonlinear relationships between various factors effecting disease outcome can be evaluated more efficiently, and realistic predictions can be obtained.

In this paper, it was intended to review knowledge on basic modeling concepts of fish disease dynamics. Accomplishing this goal would provide insight into the relative importance of parameters playing a major role in disease outbreaks.

Key Words: fish diseases, epizootiology, disease dynamics, dynamic modeling, epidemiology.

Introduction

The foundations of mathematical modeling of human and mammalian disease epidemics were first established by Kermarck and McKendrick (1927, 1932, 1933). Later, the extensive reviews of Anderson and May (1978), May and Anderson (1979), and Anderson (1982) contributed to the subject of disease dynamics opening new discussions for concepts, critical threshold, basic reproductive ratio, transmission coefficient, etc.

The importance of mathematical models in disease epidemics has been discussed extensively by many researchers (Bradley, 1982; Anderson and May, 1991 and Heesterbeek and Roberts, 1995). Heesterbeek and Roberts (1995) summarized their usefulness and weaknesses. They reported four important and "justified" aspects of mathematical models in disease epidemics.

First of all, mathematical models are useful in providing insight into the relative importance of factors influencing spread, and also improving our understanding of the relationship between mechanisms that operate on the level of the individual and the resulting effects on population. Second, these models should be formulated with precision, which is accomplished by considering an underlying hypothesis. This type of precise approach may reveal other underlying factors, if any, which may have been overlooked or not considered due to complexity of the system e.g. the critical threshold concept. Third, clarification is essential in determining the

parameters, which are critical in their influence on dynamic behaviour. This approach may lead to the discovery of key parameters whose numerical (range of) values may still be unknown. Finally, these models are widely used in "thought experiments". Sometimes actual experiments are impossible to carry out because of practical, economical or ethical reasons. For example, what would happen if the total cases of HIV cases were double, instead of what it is today? Experimentally, it is impossible to study due to ethical reasons, but possible with modeling techniques using retrospective data.

There are numerous studies carried out on different aspects of microparasitic fish pathogens (viruses, bacteria and protozoans), which are characterized by small size, short generation times, and extremely high rates of direct reproduction within the host. They usually induce immunity to reinfection in those hosts that survive initial infection (Mimms, 1977). Moreover, horizontal (fish to fish) and/or vertical transmission (parent to progeny) have been demonstrated for many fish diseases. However, quantitative mechanism and the efficiency of disease transmission have long been neglected in fish diseases.

In recent years, only a few studies emerged in this area of fish diseases. The disease dynamics of infectious pancreatic virus using rainbow trout were determined by Bebak (1996). However, the study was limited in terms of data collected due to the study design. Special attention needs to be given to the design of the experiments in order to measure targeted

parameters under the conditions provided, since a complex system in population level is targeted to study.

The study of the population dynamics of *Ichthyophthirius multifiliis* in black mollies, an aquarium variety of *Poecilia latipinna* (Lesueur), can be considered another significant study in terms of determining density dependency (McCallum, 1982, 1985). In another study, Ögüt (2001) evaluated modeling of *Aeromonas salmonicida* and infectious haematopoietic necrosis virus (IHNV) epizootics. Density dependence of spread in the both pathogens was also examined extensively.

In short, considering the vast amount of data available about various aspects of fish pathogens, potentials of disease dynamics and epidemiological models should be explored. Since these types of studies focus on diseases rather than pathogen, the information is invaluable in terms of understanding and controlling disease. In the following sections, general information about disease dynamics, components of population under an epidemic, and parameters governing an epidemic will be presented.

Modeling of Disease Dynamics

Components of epidemiological models in fish diseases

As mentioned above, there are three subsets of a population with reference to disease status. These

were described by Watman (1974) as; the susceptible class (S), the infective class (I), and the removed class (R). The susceptible class (S), are those individuals who are not infective, but who are capable of contracting the disease and becoming infective. The infective class (I), are those individuals who are infected with pathogen and capable of transmitting the disease to others. The removed class (R), are those individuals who have had the disease and died, or had the disease and recovered, and/or become permanently immune, and/or been isolated from the susceptible until recovery and permanent immunity occur.

In a population, the spread of an infectious disease follows the SIR (Susceptible->Infected->Removed) dynamics model and the analysis of this process has been carried out extensively in humans and animals (Anderson and May, 1978; Giesecko, 1994; Cairns, 1995) (Figure 1).

Deterministic models

It is assumed that in directly transmitted diseases, the dynamics proceed according to the mass action theory, namely that the net rate of hosts becoming infected is the product of density of S animals times the density of I animals. Thus, the number of successful contacts made between S and I (infectious) individuals determines the magnitude of the disease outcome.

A second assumption is that there is a certain

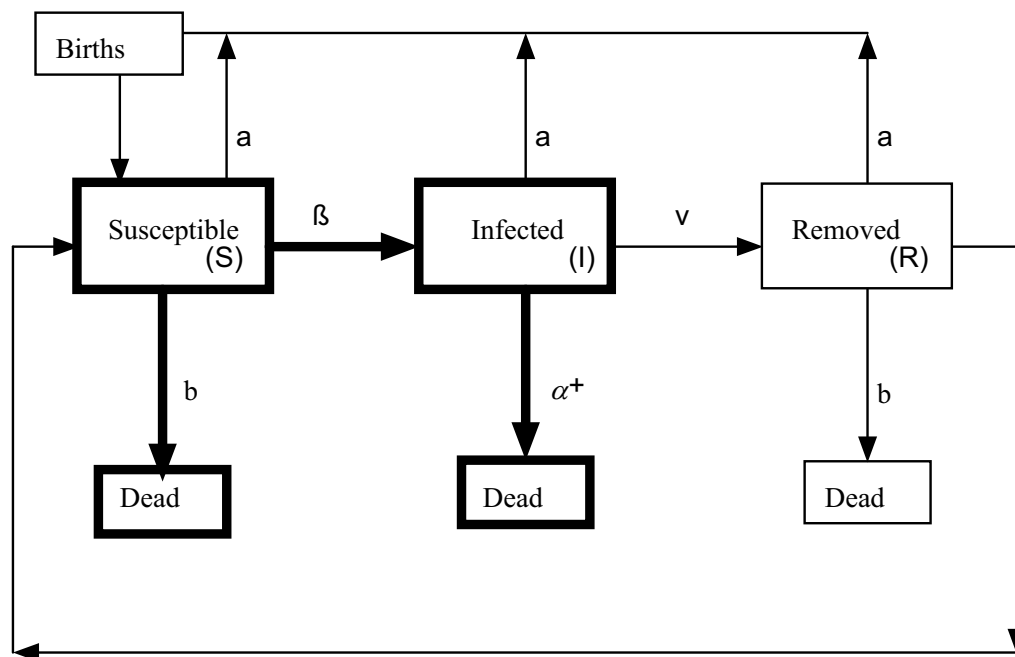


Figure 1. Disease dynamics of a population during the course of an epidemic. b = natural mortality, β = Transmission coefficient, α = disease related mortality, v = recovery rate, a = birth rate (Modified from Anderson and May, 1979).

proportion of the population (N), which are S and the remaining I. Per unit time, a proportion of I animals make βI potentially infective contacts. Therefore, the number of new cases arising per unit time;

$$\beta SI \quad (1)$$

were β is the transmission coefficient.

The following equations describe the deterministic models, which involve constant values for parameters. The number of individuals in classes S, I, and R are denoted by S_t , I_t and R_t , respectively at time t. At time t, the following set of equations are obtained

$$\frac{dS}{dt} = S_0 + (-bS_t - \beta S_t I_t + \nu R_t) \quad (2)$$

$$\frac{dI}{dt} = \beta S_t I_t - (\alpha + b + \nu) I_t \quad (3)$$

$$\frac{dR}{dt} = \nu I_t - b R_t \quad (4)$$

were β , α , ν and b are the transmission coefficient, disease related mortality rate of infected animals, removal rate, and the natural mortality rate. Using these equations the epidemic can be

demonstrated schematically as shown in Figure 2.

In order to construct the models above, there are three assumptions; a) Every individual in the population has the same chance of coming into contact with an infectious individual or agent; b) Animals recover from infections as a rate (ν) after which they are immune to further infection for some period of time; c) N is closed. That is, the time scale of the epidemic process of transmission and recovery is much shorter than the time scale on which the population size is changed due to natural births and deaths.

Transmission coefficient (β)

Transmission of a pathogen between hosts might occur directly or indirectly in fish diseases. Transmission type might be either horizontal (fish to fish, by feces, injuries or ingestion of bacteria) such as enteric redmouth disease, caused by *Yersinia ruckeri* (Bullock and Snieszko, 1975), vibriosis (Anderson and Conroy, 1970), or both vertical and horizontal such as bacterial kidney disease (Evelyn et al., 1986) and the infectious pancreatic necrosis virus which is also transmitted via eggs or sperm to progeny (Mulcahy and Pascho, 1984). The life cycle of macroparasites often involves one or more intermediate hosts before a major disease epidemic resulting in mortalities such as *Myxobolus cerebralis*, the causative agent of "whirling disease". Its life cycle

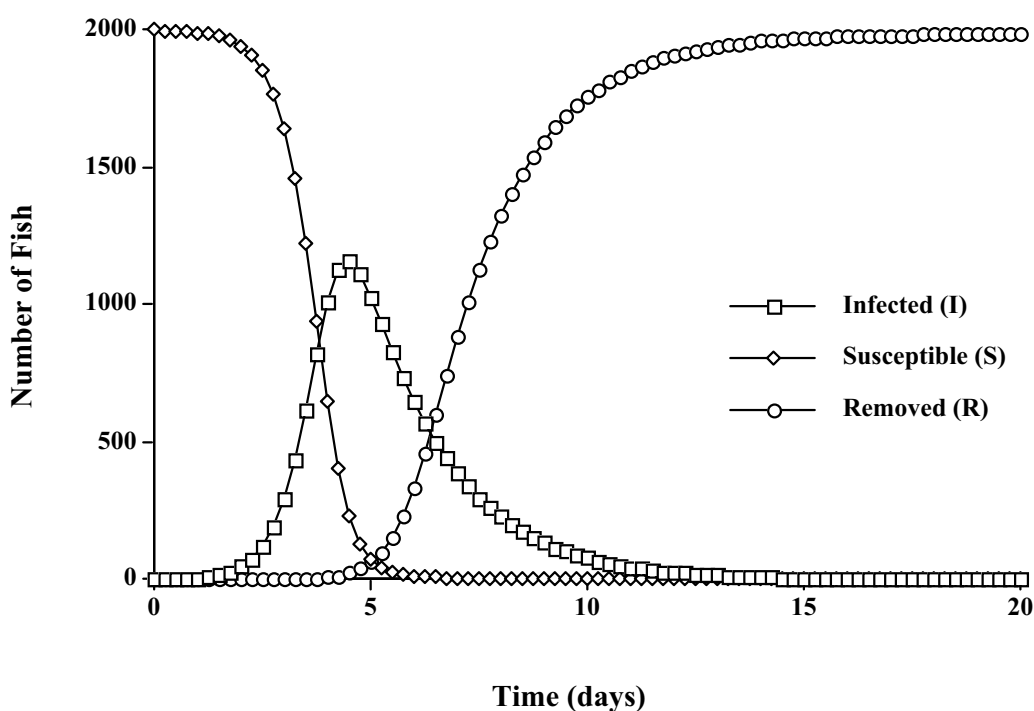


Figure 2. Development of an epidemic during a short (epidemic) time period. Initial values of corresponding parameters are: population (N) = 2,000 individuals, susceptible (S) = 2000 individuals, infected (I) = 1 individuals day⁻¹, disease related mortality rate (α) = 0.5 infecteds day⁻¹, natural mortality rate (b) = 0.001, transmission coefficient (β) = 0.0015 (individuals*day)⁻¹.

involves tubificid worms, *Tubifex tubifex*, in the development of the infective stage (Wolf and Markiw, 1985).

As described in Anderson (1982), β is determined by two factors; i) the frequency of contacts made which is directly related to the density of susceptible animals, and ii) the likelihood that a contact results in pathogen transmission. In fish culture conditions, all of the fish are exposed to the same environmental conditions. Since it is a closed environment, making an assumption on contact rate, that every fish has the same chance of coming into a contact with an infectious fish and/or an infectious agent in the water column is more than an assumption. It is actually a reality. However, the estimation of β is somewhat confusing to most. Therefore, the calculation of β is demonstrated in Table 1 below

Critical threshold density (N_T)

There is a threshold density below which disease cannot persist. Kermarck and McKendrick (1927) first reported the concept of threshold density. The critical threshold density is determined by the following relationship:

$$N_T = \frac{(\alpha + b + \nu)}{\beta} \quad (5)$$

For a disease outbreak to occur there should be a certain number of susceptible individuals in the population, higher than N_T (i. e., $S > N_T$) (Dietz, 1974; Anderson and May, 1986; Nåsel, 1995). N_T values for directly transmitted microparasites, such as viral and bacterial pathogens, which are of high pathogenicity and/or induce rapid recovery and lasting immunity, are quite high. For directly transmitted macroparasites, N_T is low due to the production of large numbers of macroparasites from individual hosts, and the fact that parasites often have long infective stages, which clearly indicates dependence of net rate of infected hosts on a certain critical density. The number of I (infected) will not increase

unless $N > N_T$ (Anderson and May, 1986).

Density dependence in host-parasitoid systems has been studied extensively by various researchers (May et. al., 1981). With the exception of sexually transmitted diseases (Yorke et al., 1978), the requirement of a certain number of individuals for a disease epidemic is true for virtually all diseases (Anderson and May, 1978).

Basic reproductive rate (R_0)

The basic reproductive rate (R_0), is the most crucial component of the disease dynamics modeling process. R_0 is the mean number of animals directly infected by an infectious case during the animals' entire infectious period after entering a totally susceptible population (McDonald, 1957; Anderson, 1982; Anderson and May, 1986; Giesecko, 1994). R_0 is determined by factors, which are specific to the disease agent (its virulence), the host (the level of susceptibility, which determines levels of latent period-the time required for an epidemic to occur), and environmental factors such as host density and behavior (Anderson, 1982).

The measurement of R_0 is essential in the determination of the spread of the disease, since it is the measure of the disease invasion in the population (Heesterbeek and Roberts, 1995). It determines whether an invasion will emerge after introducing the infected individual (s) into a totally susceptible population.

R_0 could take one of three possible values as shown below:

$R_0 < 1$ Disease will disappear over time.

$R_0 = 1$ Disease will be endemic, and persistent with no large scale epidemic occurring.

$R_0 > 1$ There will be an epidemic with elevated levels of disease related mortality in the population.

Because of the difficulty obtaining the transmission coefficient, which is acted upon by numerous factors, obtaining the "actual" value for R_0

Table 1. Calculation of the transmission coefficient (β), disease related mortality rate (α) and natural mortality using various classes of the population during the infection process.

Time (days)	S(*)	I(**)	R(***)	Incidence	β	Disease related Mortality	Natural Mortality	α	γ
0	S_0	I_0	0	0	0	0	0	0	0
1	S_1	$I_1=(I_0+X_1)-R_1$	M_1+N_1	$X_1=I_1-I_0$	$X_1/(S_0+I_0)$	M_1	N_1	M_1/I_0	$N_1/(S_0+I_0)$
2	S_2	$I_2=(I_1+X_2)-R_2$	M_2+N_2	$X_2=I_2-I_1$	$X_2/(S_1+I_1)$	M_2	N_2	M_2/I_1	$N_1/(S_1+I_1)$
3	S_3	$I_3=(I_2+X_3)-R_3$	M_3+N_3	$X_3=I_3-I_2$	$X_3/(S_2+I_2)$	M_3	N_3	M_3/I_2	$N_1/(S_1+I_1)$
4	S_4	$I_4=(I_3+X_4)-R_4$	M_4+N_4	$X_4=I_4-I_3$	$X_4/(S_3+I_3)$	M_4	N_4	M_4/I_3	$N_1/(S_1+I_1)$
5	S_5	$I_5=(I_4+X_4)-R_5$	M_5+N_5	$X_5=I_5-I_4$	$X_5/(S_4+I_4)$	M_5	N_5	M_4/I_4	$N_1/(S_1+I_1)$

(*) = S. number of susceptible. (**) = I. number of infected. (***) = R. number of dead. (Ögüt 2001)

is difficult in the nature. In modeling studies, only the factors that have proven to affect the outcome of a disease outbreak should be included to get the best estimate of the disease process, but this is also a difficult task. This is so, because under different environmental and physiological factors, different transmission coefficient values may be obtained.

R_0 can be estimated using the formula below:

$$R_0 = \frac{S}{N_T} \quad (6)$$

Therefore, substituting equation 6 for N_T in equation 5 yields:

$$R_0 = \frac{\beta N}{(\alpha + b + \nu)} \quad (7)$$

Discussion and Conclusions

When comparing to other types of wildlife modeling applications that are becoming popular in recent years, the modeling of fish disease dynamics offers potential benefits. The two fundamental assumptions are homogeneous mixing, and having a closed population that make models robust in terms of

predictive capabilities. Therefore, it is usually easier to pinpoint what direction the health status of the fish is going under conditions provided. In the wildlife situations, variables related to the system are difficult to determine and measure due to spatiality. When considering linear and non-linear synergic and antagonistic effects, systems are more complex to understand. However, in pond and cage culture situations, environment is homogenous for each individual sharing the same environment.

Disease epidemic is the result of the complex combination of environmental, host and pathogen related factors. Therefore, environmental (temperature, oxygen, pollutions), host (species, age, density, immunity), or pathogen related factors (virulence, strain) could be manipulated to control diseases. It is a fact that the system is very complex, however, not all parameters have the same amount of effect on the outcome of the disease (Figure 3). Some parameters playing a role in disease dynamics could be "key" factors. Adjusting just those key factors could make significant improvement in the system in terms of decreasing losses or prevalence.

Modeling disease dynamics totally focuses on disease by estimating R_0 and N_T values and observes changes on these parameters. Any significant decrease in these values indicates effectiveness of a control

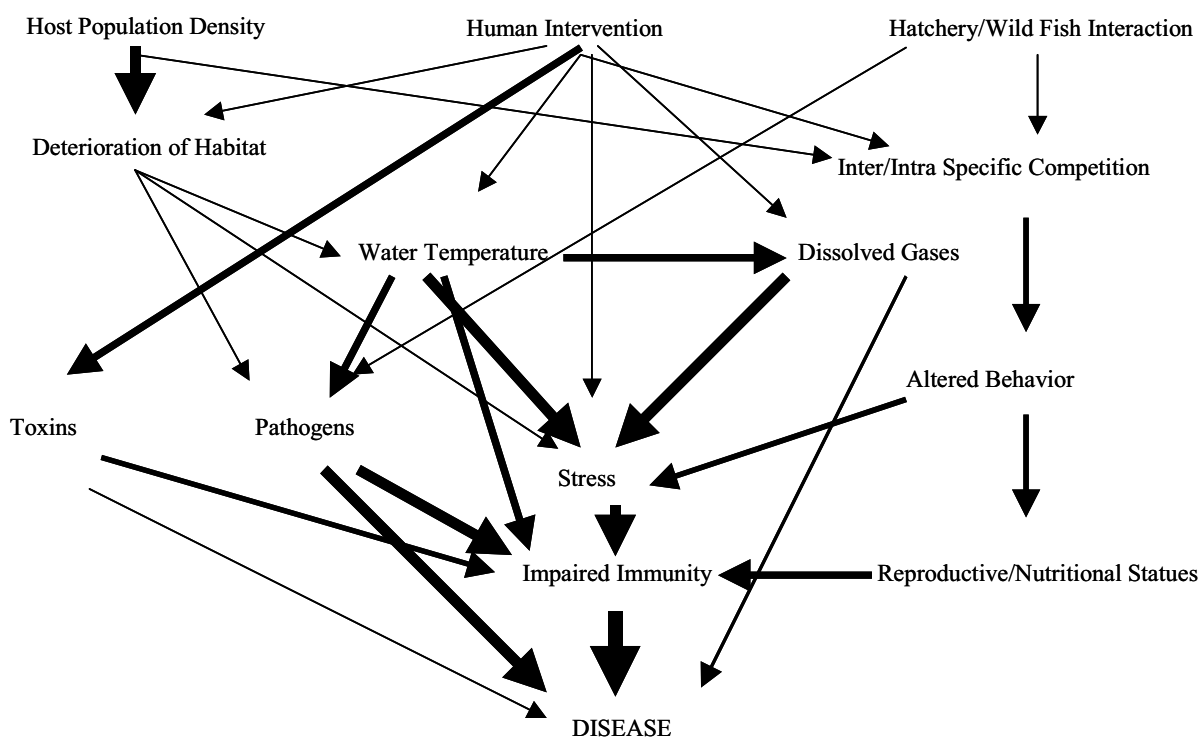


Figure 3. Interactions of different parameters in disease outbreaks of wild fish populations modified from Wobeser (1994). (Various levels of effects of different factors on disease outcome are represented with varying levels of bold lines).

measure, which could be a drug treatment or vaccination. Here, controlling the disease means pulling R_0 below unity. Therefore, there may not be any need to vaccinate the whole population but just enough proportion to draw R_0 below unity. This will decrease cost and effort of controlling the disease.

Every disease would have its own R_0 value. However, as mentioned above, the combination of parameter values for β , α and ν would also be different depending on pathogenic agent, host, and environment. For example, in the experiments carried out by Ögüt (2001), it took five days to observe the first disease related mortality after challenging with *Aeromonas salmonicida*, whereas some other diseases such as bacterial kidney disease (BKD) caused by *Renibacterium salmoninarum*, take about 30-35 days first mortality (Wood, 1974).

Moreover, some diseases can have chronic, acute, or per-acute stages.

Though not studied, we can comfortably assume that the R_0 values for different forms of the same disease is different due to host, pathogen, or environmental factors which all are summarized under the coefficient β . Take the example in Figure 1, different β values would produce a different scenario of the prevalence on a time scale (Figure 4). There are two points to consider from this demonstration. The first point is that were β values are small, infection is widespread on a time scale similar to chronic infections. Secondly, the day to peak prevalence is

delayed in epizootics with smaller β values. Note that smaller β means smaller R_0 . In attempts to control any disease, smaller β values would help in providing more time for a therapeutic to work. For example, antibiotic treatments need about 12 days to work efficiently. Therefore, any time in terms of days decreases losses significantly.

Density as a key factor

In fish, the disease epizootics density can have effects on furunculosis epizootic in two ways (Ögüt, 2001). First, as fish density increase, the probability of any susceptible individual making successful contact with an infectious individual or infectious agent in the same population increases (Anderson and May, 1978; Mollison, 1995, de Jong et al., 1995). A single infectious individual can shed >100 colony forming units (c.f.u.) of *A. salmonicida* /mL per day and infect 3 additional fish per day, within 3 days, 9 fish would be infected and shed about 1,000 cfu *A. salmonicida*/mL (Ögüt, 2001). If fewer fish were present, fewer would become infected and fewer bacteria would be released into the water. Secondly, various researchers have reported decreased resistance of stressed fish to furunculosis (Snieszko, 1973; Pickering and Duston, 1983). Thus, the stress generated from high loading densities may contribute substantially to an increase in the severity of disease. However, researchers largely ignore the contribution

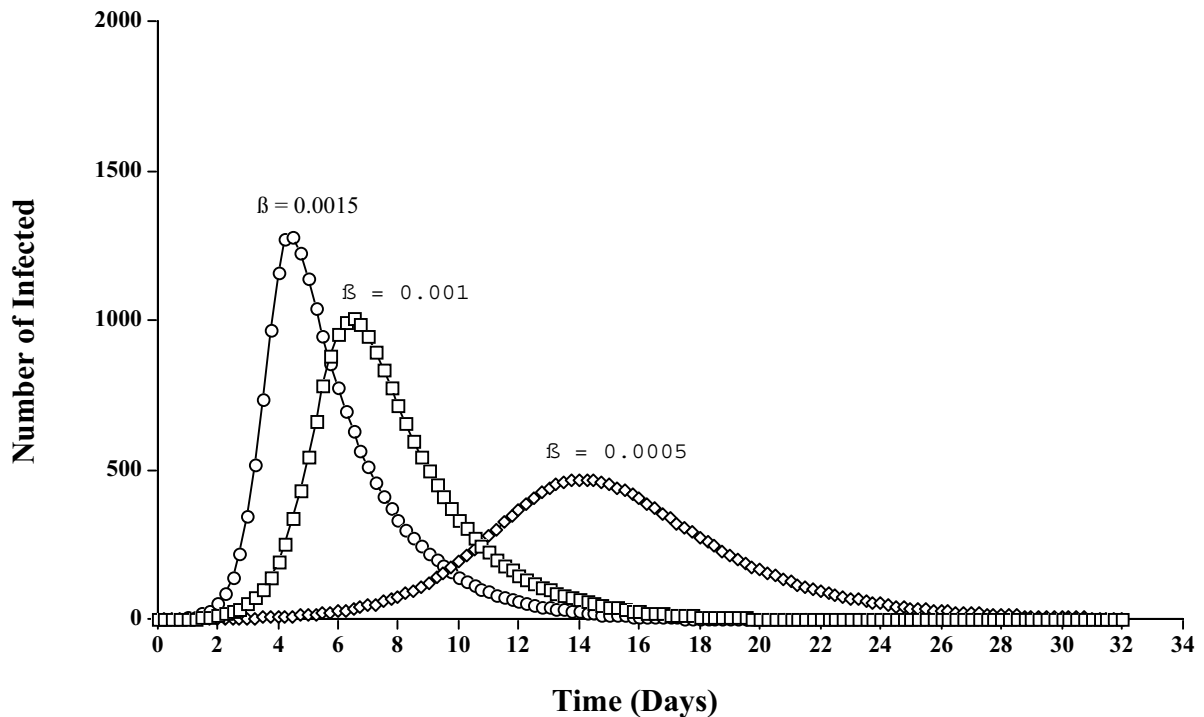


Figure 4. Changes in number of infected animals with varying transmission coefficient values (0.0005, 0.001 and 0.0015 (individuals*day)⁻¹). Equations 2, 3 and 4 were used to generate the chart.

of high loading densities to the disease, which is mostly due to the designing complexity of the experiments. That is why the information on the effects of loading densities to the disease outbreaks is mostly observational.

In brief, the large amounts of data have been accumulated on various pathogens of fish. For example, a tremendous amount of information on *A. salmonicida* is available in the literature. However, as Smith (1997) stated, "the list of things that we do not know about furunculosis is long, embarrassing and includes many issues of fundamental, practical, and theoretical importance". The main reason for this gap is that the disease itself has not been in focus but pathogen. Modeling is one approach studying disease itself. It is becoming more popular in other animal diseases, due to fewer assumptions involved; it offers more benefit for fish diseases.

References

- Anderson, R.M. 1982. The population dynamics of infectious diseases: Theory and applications. Chapman and Hall, London.
- Anderson, J.I.W. and Conroy, D.A. 1970. Vibrio disease in marine fishes. S. F. Snieszko (Ed.), A symposium on Diseases of Fishes and Shellfishes, Special Publications No. 5, American Fisheries Society, Washington, D.C., 266-272.
- Anderson, R.M. and May, R.M. 1978. Population biology of infectious diseases Part I, Nature, 280: 361-367.
- Anderson, R.M. and May, R.M. 1986. The invasion, persistence and spread of infectious diseases within animal and plant communities. Philosophical Transactions. Royal Society of London, B 314: 533-570.
- Anderson, R.M. and May, R.M. 1991. Infectious Diseases of Humans, Dynamics and Control. Oxford University Press, Oxford.
- Bebak, J. 1996. Infectious diseases of salmonids: Risk factors and disease dynamics. PhD dissertation, University of Pennsylvania.
- Bradley, D. J. 1982. Epidemiological Models -theory and reality. Population Dynamics of Infectious Diseases. Roy M. Anderson (Ed.), Chapman and Hall, London, 320-334.
- Bullock, G.L. and Snieszko, S.F. 1975. Hagerman redmouth, a disease of salmonids caused by a member of the Enterobacteriaceae. Fish Diseases Leaflet, 42: 1-5.
- Cairns, A. 1995. Primary components of epidemiological models. D. Mollison (Ed.), Epidemic models: Their Structure and Relation to Data, Newton Inst. Public, 350-371.
- de Jong, M.C.M., Diekmann, O. and Heesterbeek, H. 1995. How does transmission of infection depends on population size. D. Mollison (Ed.), Epidemic models: Their Structure and Relation to Data, Newton Inst. Public, 84-94.
- Dietz, K. 1974. Transmission and control of arbovirus diseases. Proceedings of society for industrial and applied mathematics, Philadelphia, 104-121.
- Evelyn, T.P.T., Prosperi-Porta, L. and Ketcheson, J.E. 1986. Experimental intra-ovum infection of salmonid eggs with *Renibacterium salmoninarum* and vertical transmission of the pathogen with such eggs despite their treatment with erythromycin. Diseases of Aquatic Organisms, 1: 197-202.
- Giesecko, J. 1994. Mathematical Models for Epidemics. Modern Infectious Disease Epidemiology. Edward Arnold, London, 109-123.
- Heesterbeek, J.A.P. and Roberts, M.G. 1995. Mathematical models for microparasites of wildlife. B.T. Grenfell, A.P. Dobson (Eds.), Ecology of infectious diseases in natural populations, Cambridge University Press, Cambridge, 91-122.
- Kermack, W.O. and McKendrick, A.G. 1927. Contribution to the mathematical theory of epidemics, part I, Proceedings of the Royal Society of London Series A. 115:700-721. [Reprinted (1991) as Bulletins of Mathematical Biology, 53: 33-55.]
- Kermack, W.O. and McKendrick, A.G. 1932. Contribution to the mathematical theory of epidemics, II- The problem of endemicity, Proceedings of the Royal Society of London Series A. 138:55-83. [Reprinted (1991) as Bulletins of Mathematical Biology, 53: 57-87.]
- Kermack, W.O. and McKendrick, A.G. 1933. Contribution to the mathematical theory of epidemics, III- Further studies of the problem of endemicity. Proceedings of the Royal Society of London Series A. 141:94-122. [Reprinted (1991) as Bulletins of Mathematical Biology, 53: 89-118.]
- May, R.M. and Anderson, R.M. 1979. Population biology of infectious diseases: Part II, Nature, 280: 455-461.
- May, R.M., Hassell, M.P., Anderson, R.M. and Tonkyn, D.W. 1981. Density dependence in host parasitoid models. Journal of Animal Ecology, 50: 855-865.
- McCallum, H.I. 1982. Infection dynamics of *Ichthyophthirius multifiliis*. Parasitology, 85: 475-488.
- McCallum, H.I. 1985. Population effects of host death: experimental studies of the interaction of *Ichthyophthirius multifiliis* and its fish host. Parasitology, 90: 529-547.
- McDonald, G. 1957. The Epidemiology and Control of Malaria. Oxford University Press, Oxford.
- Mimms, C.A. 1977. The Pathogenesis of Infectious Diseases, Academic Press, London.
- Mollison, D. 1995. The structure of epidemiological models. D. Mollison (Ed.), Epidemic models: Their Structure and Relation to Data, Newton Inst. Public, 17-33.
- Mulcahy, D., and Pascho, R.J. 1984. Adsorption to fish sperm of vertically transmitted fish viruses. Science, 255: 333-335.
- Näsel, I. 1995. The threshold concept in deterministic and stochastic models. D. Mollison (Ed.), Epidemic models: Their Structure and Relation to Data, Newton Inst. Public, 71-83.
- Ögüt, H. 2001. Biological and Mathematical Modeling of Dynamics of Furunculosis in Chinook Salmon (*Oncorhynchus tshawytscha*) and Infectious Hematopoietic Necrosis (IHN) in Rainbow Trout (*Oncorhynchus mykiss*). Ph.D Thesis, Corvallis: Oregon State University.
- Pickering, A.D., Duston, J. 1983. Administration of cortisol to brown trout, *Salmo trutta* L., and its effects on the susceptibility to saprolegnia infection and furunculosis. Journal of Fish Biology, 23: 163-175.
- Scott, M.E. and Anderson, R.M. 1984. The population dynamics of *Gyrodactylus bullatarudis* (Monogenea)

- within laboratory populations of the fish host *Poecilia reticulata*. *Parasitology*, 89: 159-194.
- Smith, P. 1997. The epizootiology of furunculosis: The present state of our ignorance. *Furunculosis Research*. E. Bermoth, A. E. Ellis, P. J. Midtlyng, G. Olivier and P. Smith (Eds.), *Multidisciplinary Fish Disease Research*, Academic Press, London, 25-54.
- Snieszko, S.F. 1973. Furunculosis of salmonidae. *EIFAC/T17 (suppl. 2)*, 157-162.
- Waltman, P. 1974. *Lecture Notes in Biomathematics, Deterministic Threshold Models in the Theory of Epidemics*. Springer-Verlag, New York.
- Wobeser, G.A. 1994. *Investigation and Management of Disease in Wild Animals*, Plenum, New York.
- Wolf, K. and Markiw, M.E. 1985. *Salmonid Whirling Disease*. US Fish and Wildlife Service, Fish Disease Leaflet 69.
- Wood, J.W. 1974. *Diseases of Pacific Salmon: Their Prevention and Treatment*. Washington Department of Fisheries, 27 pp.
- Yorke, J.A. Hethcote, H.W. and Nold, A. 1978. Dynamic and control of the transmission of gonorrhoea. *Sexually Transmitted Diseases*, 5: 51-56.