COMPENDIUM ON CYSTIC ECHINOCOCCOSIS

IN AFRICA AND IN MIDDLE EASTERN COUNTRIES WITH SPECIAL REFERENCE TO MOROCCO

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3. QUANTIFYING THE TRANSMISSION DYNAMICS OF THE FAMILY TAENIIDAE WITH PARTICULAR REFERENCE TO *ECHINOCOCCUS* SPP.: AN UPDATE

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ABSTRACT: The major factors contributing to the regulation and stability of populations of the family Taeniidae are described. Their description provides an important contribution to an understanding, and thus planning, of control programs. Of great significance to the regulation and stability of each system are the following: (1) biotic potential of the parasite in the definitive host, (2) acquired immunity as a density-dependent constraint by the intermediate host, and (3) climate as a density-independent constraint in the free-living egg phase.

Stability is an essential part of the description of stabilizing and destabilizing forces. Methods of determining endemic, hyperendemic, and extinction steady states empirically and mathematically are described, and examples of field investigations including field trials that can be applied to determine the force needed to drive endemic and hyperendemic systems to extinction status are given. A brief description is also given of successful transfer of eggs from dogs leading to clinical cystic echinococcosis (CE) in humans of any age.

I. INTRODUCTION

During the past decade considerable advances have been made in breaking the "epidemiological code" of the family Taeniidae with the aid of mathematical modelling. This family contains such zoonotic parasites as *Echinococcus granulosus*, *E. multilocularis*, *Taenia solium*, and *T. saginata*. From a human health point of view, some of these are difficult to study. Where data cannot be obtained for them, the sheep metacestodes, *T. hydatigena* and *T. ovis*, have been used with caution as models to describe the transmission dynamics and evaluate the stability of each system.

At any one time the parasite population consists of 3 sub-populations: adults in the definitive host, larvae in the intermediate host, and eggs in the environment. The first step in quantifying the transmission dynamics is to determine the contributions made by each host population to its stability. The second step must be to evaluate the role of intrinsic, extrinsic, and socioeconomic factors in modifying this stability. The third step involves quantifying the equilibrium steady state of the whole system in each socioecological situation. From this, a further step can be taken to determine effective and cost-effective control options, predict their outcome, and test feasibility by field trial.

This update, from Chapter 5 in the previous compendium (Gemmell, 1993), quantifies the contributions made by the parasite, host, and environment to the stability of taeniid systems and thereby contributes to a basic understanding of the methods that may now be applied in planning and implementing control of these cestode zoonoses, particularly *E. granulosus* (see Chapter 19).

II. BIOLOGICAL CONTRIBUTIONS BY THE PARASITE TO THE TRANSMISSION DYNAMICS

As with other taeniids of dogs and sheep (*T. hydatigena* and *T. ovis*), *E. granulosus* has an overdispersed distribution that fits a series of negative binomials in both hosts, with only a small number of animals harboring large numbers of worms or larvae (Fig. 3.1). There is neither a "crowding" effect nor parasite-induced host mortality, and this distribution does not contribute to the regulation of either adult or larval sub-populations. The pre-patent period is similar for all 3 species, patency being reached in dogs between 6 and 12 wk. The larvae of *E. granulosus* grow slowly in sheep, with only about 50% reaching fertility by 6.65 yr (Fig. 3.1). In contrast, there is little delay with *T. hydatigena* and *T. ovis*, and their larvae become infective to dogs within about 3 mo. Similarly, with *E. multilocularis* the time required to reach patency in definitive hosts is about 28 days, and the time taken to reach fertility in rodents may be only 60 days (Gemmell and Lawson, 1986; Gemmell et al., 1986a, 1986b, 1986c, 1987a, 1987b; Rausch, 1986; Roberts et al., 1986a, 1986b, 1987; Roberts and Gemmell, 1994; Gemmell and Roberts, 1995, 1996).

A. Significance of the Biotic Potential

The parasite's major contribution to the transmission dynamics is its biotic potential (Table 3.1). This can be defined as "the potential number of viable cysts that can be established in an intermediate host by an individual definitive host per day."

Estimates suggest that *E. granulosus* has about 1/100 and 1/30 the biotic potential of *T. hydatigena* and *T. ovis*, respectively. The generally reported mean worm burden for *E. granulosus* in its dog-sheep life cycle is about 200–400. However, with such highly susceptible animals as Turkana dogs in Kenya and dingoes in Australia, very high worm burdens may be present in the majority of animals. Similarly, there are also large variations in worm burdens of *E. multilocularis*. For example, that in arctic foxes (*Alopes lagopus*) in Alaska is 2 orders of magnitude greater than that in the red fox (*Vulpes vulpes*) in Dakota. It follows that the biotic potential and hence the transmission dynamics may vary widely in different ecological situations and climatic zones (Nelson and Rausch, 1963; Rausch and Richards, 1971; Fay 1979; Macpherson et al., 1985; Gemmell and Lawson, 1986; Gemmell et al., 1986a, 1987a).

III. IMMUNOLOGICAL CONTRIBUTIONS BY THE HOST TO THE TRANSMISSION DYNAMICS

In epidemiological terms, acquired immunity is a negative feedback system operating

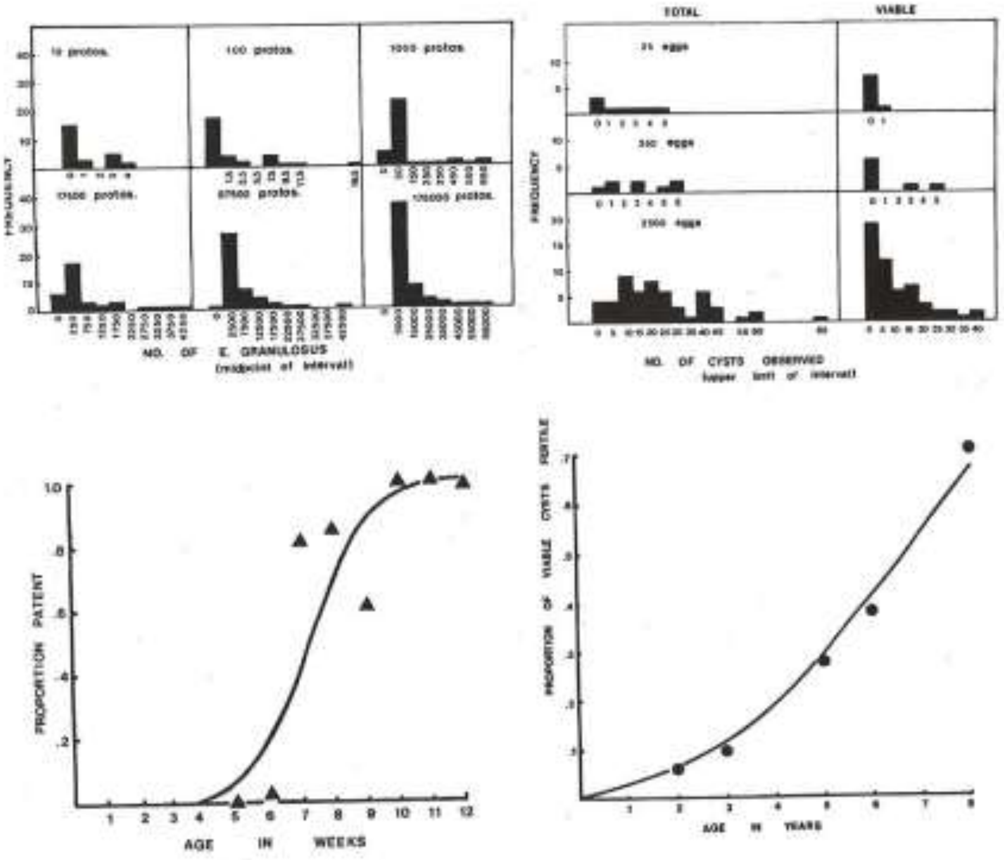


Fig. 3.1 Biological parameters of *E. granulosus* in dogs and sheep (Gemmell and Lawson, 1986; Gemmell et al., 1986a; Gemmell, 1993). Top left: Frequency distribution of *E. granulosus* in dogs given specified numbers of protoscoleces. Top right: Frequency distribution of *E. granulosus* in sheep given specified numbers of eggs. Bottom left: Relationship between patency and age (wk) of *E. granulosus* in dogs. Bottom right: Relationship between patency and age (yr) of *E. granulosus* in sheep.

as a density-dependent constraint to limit population abundance. Considerable knowledge has now been gained concerning the protective immune response to adult and larval tapeworm infections (Rickard and Williams, 1982; Rickard, 1983; Harrison and Parkhouse, 1985; Heath, 1986; Leid et al., 1987; Gemmell and Lawson, 1989; Lightowlers, 1989, 1990; Gemmell, 1990; Lightowlers et al., 1993; Lightowlers and Gottstein, 1995).

With the exception of the family Taeniidae, cyclophyllidean systems (class Eucestoda) usually have arthropods as intermediate hosts. With Hymenolepidae, immune regulation usually occurs through the definitive host. For example, with *Hymenolepis diminuta* and *H. microstoma*, resistance to superinfection or reinfection may be manifest by loss of worms, stunting, or failure to produce eggs. With Taeniidae, however, it is the intermediate host that is the density-dependent regulator of the parasite population. Thus, with any strong infection pressure, density-dependent constraints on unbounded growth of the population must first occur through that host (Gemmell and Lawson, 1986, 1989; Gemmell et al., 1986a; Roberts et al.,

TABLE 3.1 Estimates of the biological parameters of *Echinococcus granulosus*, *Taenia hydatigena*, and *T. ovis* contributing to the basic reproduction ratio (estimates from Gemmell et al., 1986a, 1987a).

Parameter	*E. granulosus*	*T. hydatigena*	*T. ovis*
Proportion of larvae transforming to tapeworms	0.047	0.74	?
Mean number of eggs/proglottid	587	38,000	87,000
Number of proglottids shed per worm/day	0.071	1	1
Mean number of worms/infected host	202	1	11
Number of eggs shed from average infected dog/day	8,470	38,000	87,000
Proportion of eggs transforming into viable cysts	0.0033	0.071	0.0074
Potential number of viable cysts/infected dog/day (biotic potential)	28	2,698	644

1986a, 1986b, 1987; Gemmell, 1990; Roberts and Gemmell, 1994; Gemmell and Roberts, 1995, 1996).

A. Definitive Hosts

Dogs by their lingual-anal grooming habits have abundant access to tapeworm eggs but appear only to acquire immunity to *E. granulosus* from the ingestion of protoscoleces. Each dog remains susceptible to infection for varying numbers of challenges, with about 50% of the population showing reduced susceptibility by the sixth infection (Fig. 3.2). An extrapolation suggests that 99% may do so by the twelfth infection (Gemmell and Lawson, 1986; Gemmell et al., 1986a; Gemmell, 1990).

Although immunity acquired by dogs must act as a density-dependent constraint, population regulation through this phase can intuitively be regarded as unimportant. This is because, with any strong infection pressure, constraints on unbounded growth must first occur through the intermediate host. Thus, acquired immunity by dogs to *E. granulosus* can be ignored in the epidemiological equation (Gemmell and Lawson, 1986; Roberts et al., 1986a, 1986b; Gemmell, 1990; Ming et al., 1992a).

B. Intermediate Hosts

Immunity to superinfection by *E. granulosus*, *T. hydatigena*, and *T. ovis* can be acquired or induced in sheep (Sweatman et al., 1963; Gemmell, 1966; Gemmell and Johnstone, 1981a; Gemmell and Lawson, 1986, 1989; Heath, 1986; Lawson and Gemmell, 1989; Gemmell, 1990). Insufficient studies have been made to quantify the role played by acquired immunity in the transmission dynamics of *E. multilocularis* in rodents. Some protection against superinfection in mice and cotton rats has been demonstrated (Rau and Tanner, 1973). Immunity was also induced in red-backed voles (*Clethrionomys rutilis*) by an injection of eggs (Rausch and Gemmell, unpublished). In addition, there is good reason to suppose that immunity also acts as the density-dependent constraint, preventing superinfection in these short-lived hosts, but its duration in the absence of ingestion of further eggs is unknown.

Based on studies with *T. hydatigena* and *T. ovis*, the characteristics of acquired immunity by sheep appear to be as follows:

(1) acquired within 7 to 14 days by the ingestion of as few as 10 eggs;

(2) life-long in the presence of eggs;

(3) lost between 6 and 12 mo in the absence of eggs;

(4) not dependent on the presence of larvae from a previous infection.

Without doubt, this is the density-dependent constraint that regulates the parasite population, but only under a high infection pressure (Fig. 3.2).

Passive immunity may also play a role as a density-dependent constraint in some systems. For instance, it operates with *T. ovis* but not with *T. hydatigena*. With the former, under a high infection pressure, there is no "window of susceptibility," as maternally derived intestinal antibodies provide protection until immunity is acquired (Fig. 3.2). In the latter case, under a similar high infection pressure, there is a "window of susceptibility" and infection can occur before immunity is acquired (Gemmell et al., 1990).

Little is yet known of the role played by passively transferred immunity with either *E. granulosus* or *E. multilocularis* under a high infection pressure, as the only experiments conducted so far have used donors that were infected but not necessarily immune (Heath, 1986).

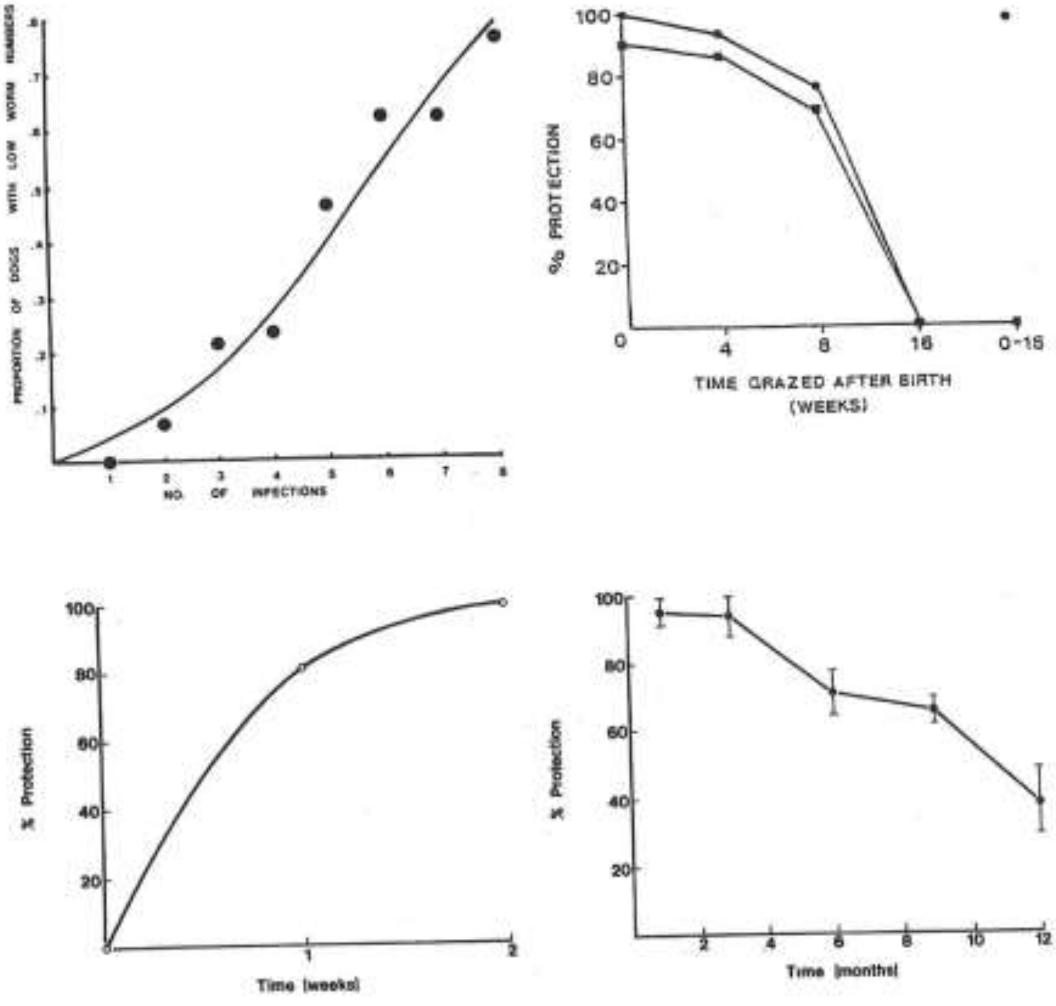


Fig. 3.2 Density-dependent constraints imposed by the host on adult and larval taeniids (Gemmell et al., 1986a, 1987a, 1990; Gemmell, 1990). Top left: Changes in the susceptibility of dogs to *E. granulosus* following reinfection. Top right: Changes in the protection given to lambs against *T. hydatigena* (■) and *T. ovis* (●) from passively transferred immunity when grazed for specified periods after birth or from birth for 1–16 wk on pasture contaminated with homologous eggs. Bottom left: Time interval (wk) between immunization and acquisition of immunity by lambs to *T. hydatigena*. Bottom right: Time interval (mo) between immunization and loss of immunity by lambs to *T. hydatigena*.

IV. ENVIRONMENTAL CONTRIBUTIONS TO THE TRANSMISSION DYNAMICS

A. Maturation-Aging Process of the Egg and Density-Independent Constraints

Eggs on expulsion from the proglottid are subject to aging by environmental effects (Fig. 3.3). Only the mature oncospheres may develop into larvae. Those that are senescent may immunize the intermediate host but will not develop into the larval form (Gemmell, 1977). Weather and climate are density-independent constraints and contribute to the basic reproduction ratio, but they do not regulate the parasite population (Gemmell and Johnstone, 1977; Gemmell, 1978a). Desiccation is lethal (Laws, 1968) and the end points of temperature are of the

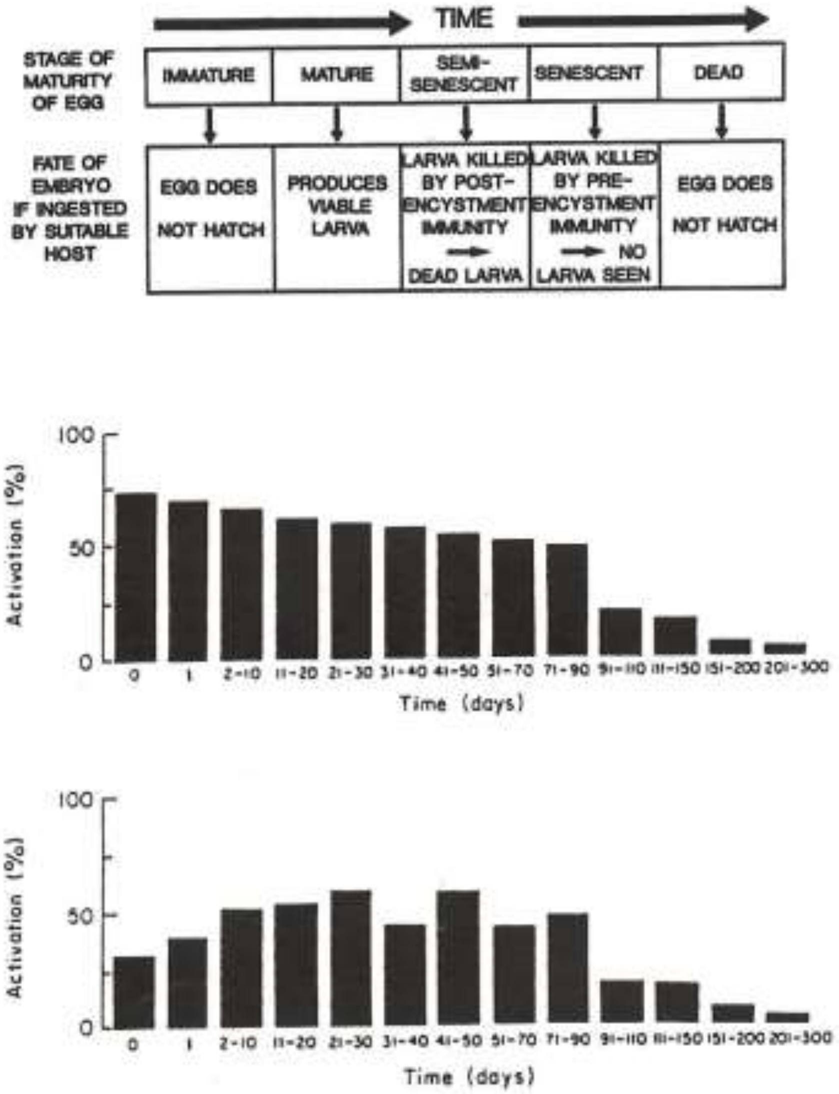


Fig. 3.3 Maturation-aging process of eggs of *Taenia hydatigena* (Gemmell, 1977, 1990; Gemmell and Johnstone, 1977; Lawson and Gemmell, 1983). Top: Diagrammatic representation of the stages in the aging process of taeniid eggs. Bottom: Variation in the hatching/activation of eggs after deposition by the dog and stored at 7°C (upper: mainly mature; lower: mainly immature at time of deposition).

order of +40°C to –70°C. Between these 2 extremes, temperature regulates the maturation-aging process (Fig. 3.4). For example, longevity of eggs of *T. ovis* was reduced from 150–300 to 2–10 days by raising the temperature from 7°C to 38°C. Similarly, eggs of *E. granulosus* survived for more than 200 days at 7°C, but only 50 days at 21°C (Fig. 3.4). In contrast, eggs of *T. hydatigena* and *E. granulosus* survive for only a few hours in the hot, dry climate of Turkana, Kenya (Wachira et al., 1991). It was concluded that eggs of *E. multilocularis* may survive up to 3 and 8 mo in the summer and winter in Europe, respectively (Frank, 1989). It is the duration of these seasonal effects on egg survival that *inter alia* modifies the transmission dynamics and

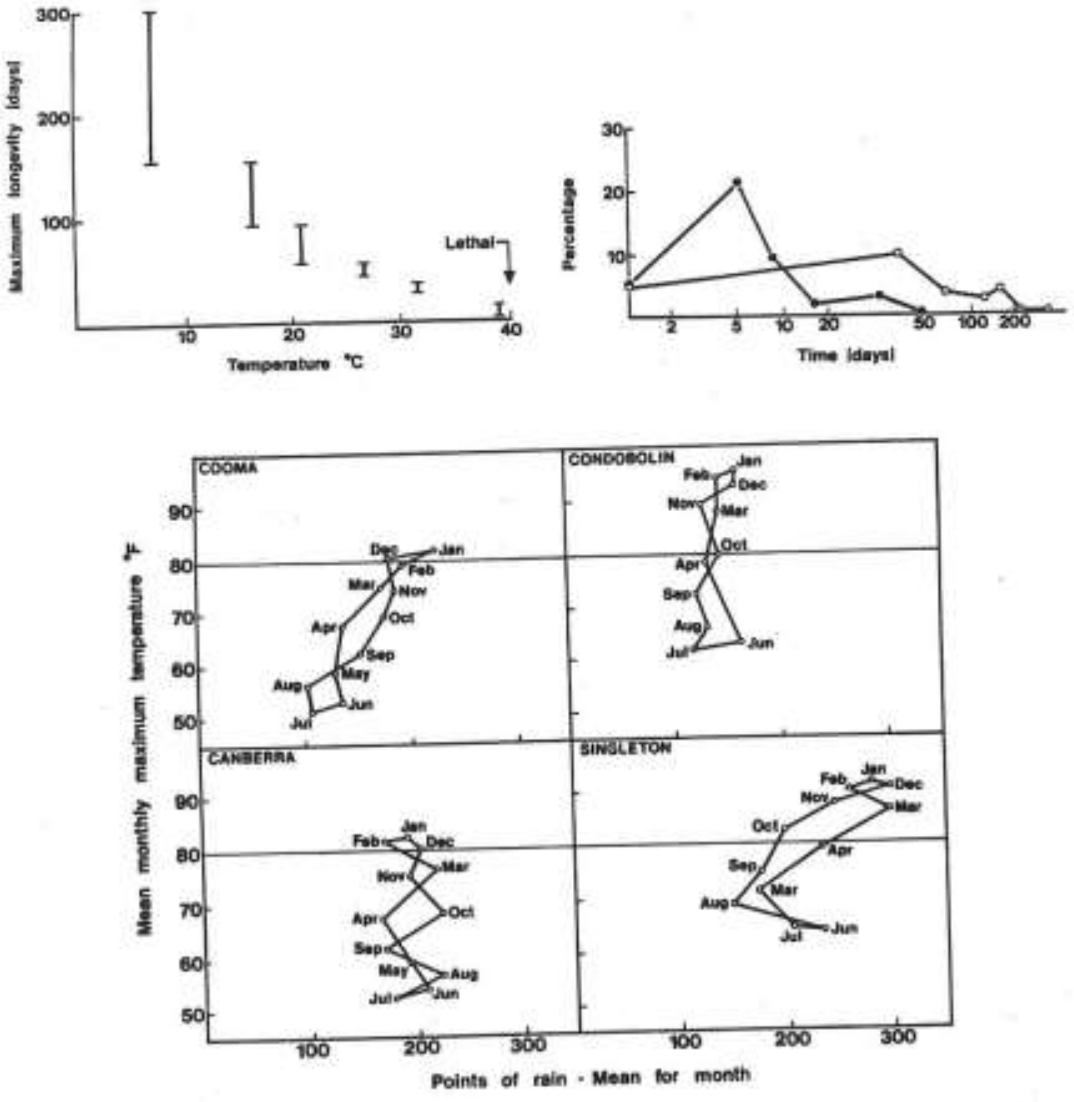


Fig. 3.4 Density-independent constraints modifying the survival of eggs (Gemmell, 1977, 1978a, 1990; Lawson and Gemmell, 1983; Gemmell and Lawson, 1986). Top left: Effect of temperature on the longevity of eggs of *T. ovis*. Top right: Longevity of *E. granulosus* stored at 21°C (●) and 7°C (○). Bottom: Bioclimatographs of some endemic regions of Australia, illustrating the number of months below 27°C with adequate moisture in which transmission of eggs of *E. granulosus* with its low biotic potential can occur without any density-independent constraints. It should be noted that *T. hydatigena* with its very high biotic potential is not affected by these low-level constraints.

in some cases geographical prevalence (Gemmell, 1977, 1990; Lawson and Gemmell, 1983; Gemmell and Lawson, 1986).

B. Egg Dispersal into the Environment and Agents Involved

Recent research on egg survival and dispersal using eggs of *T. hydatigena* and *T. ovis* shows that, although most eggs remain within about 80 m of the site of deposition, some disperse rapidly in all directions (Figs. 3.5 and 3.6). Observations suggest that a few may travel in all directions up to 10 km from the site of deposition and involve livestock over an area of 30,000 km (Gemmell and Johnstone, 1977, 1981b; Lawson and Gemmell

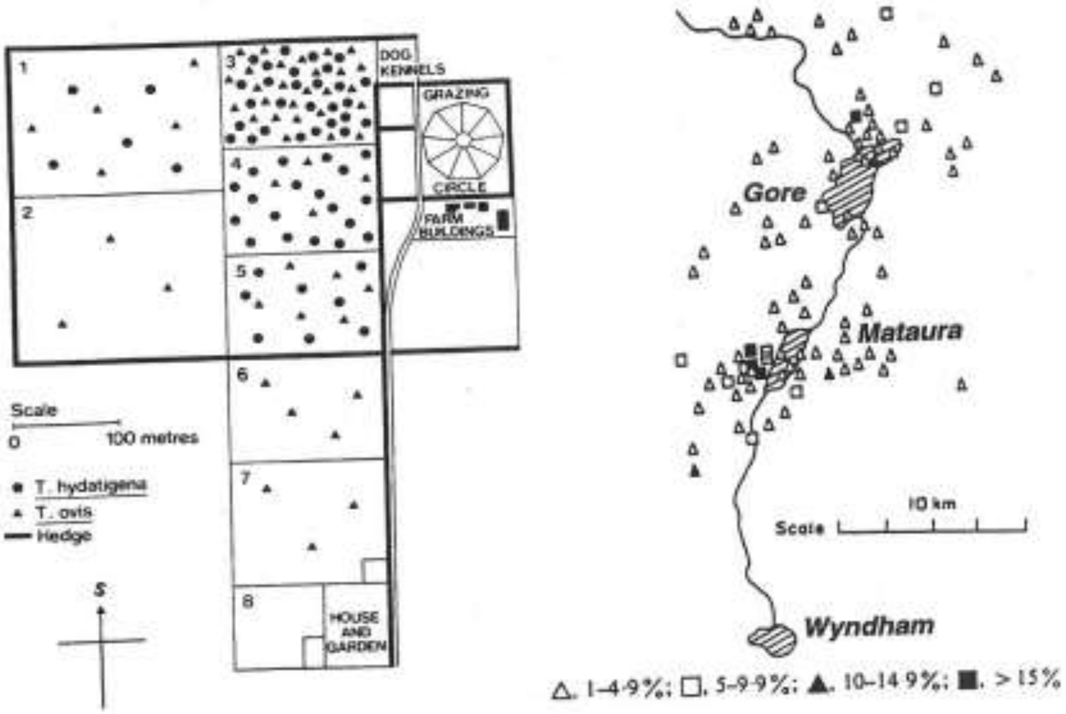


Fig. 3.5 Dispersal of taeniid eggs from the site of deposition in New Zealand (Lawson and Gemmell, 1983, 1985, 1989; Gemmell, 1990, 1993). Left: Dispersal of eggs of 2 species to a neighboring farm: (1) *T. hydatigena* from an experimental grazing circle in which infected dogs were kenneled and (2) *T. ovis* from kennels where infected dogs were kept (measurement made by grazing sentinel lambs and counting the larvae in them). Right: Dispersal of *T. ovis* eggs from infected dogs living on urban farms with 10% or more lambs infected.

1983, 1985, 1990; Gemmell and Lawson, 1986; Gemmell, 1990).

Suggested agents of egg dispersal have included birds, wind, rainfall, arthropods, and earthworms, as well as animal feet. Experimental evidence is now available that blowflies (particularly Calliphoridae) are important transport hosts for the eggs of *T. hydatigena* and *T. ovis*, and presumably *E. granulosus* and *E. multilocularis* (Lawson and Gemmell, 1983, 1985, 1990; Gemmell and Lawson, 1986, 1989). In addition, birds have also been reported as potential transport hosts for the eggs of *T. saginata* (Crewe, 1967; Crewe and Crewe, 1969; Collins and Pope, 1990).

More recently, transfer of *T. hydatigena* eggs upwind over a long distance has been reported (Torgerson et al., 1992, 1995). In this study on St. Kilda (an uninhabited archipelago in northwest Scotland), some 60 km from the nearest dog, the age-intensity prevalence of this parasite in sheep in years was calculated as 1 yr (3%), 2 yr (30%), 3 yr (31%), and >4 yr (53%). The number of cysts correlated with an increase in age, and thus an endemic steady state. Sheep acquired 0.17 cysts per year. Since an estimated 7.1% of eggs are capable of transforming into viable cysts (Gemmell et al., 1987a; Gemmell, 1990), each sheep was ingesting approximately 2.4 eggs per year. It was therefore estimated that this flock of between 600 and 1,600 animals grazing at 60 km from an infected dog(s) was ingesting between 1,440 and 3,840 eggs per year (Torgerson et al., 1992, 1995). The method of long-distance dispersal of eggs of this magnitude is not obvious but may be the result of birds acting as transport hosts or bird/insect interactions. Further work is needed to clarify the mechanisms involved.

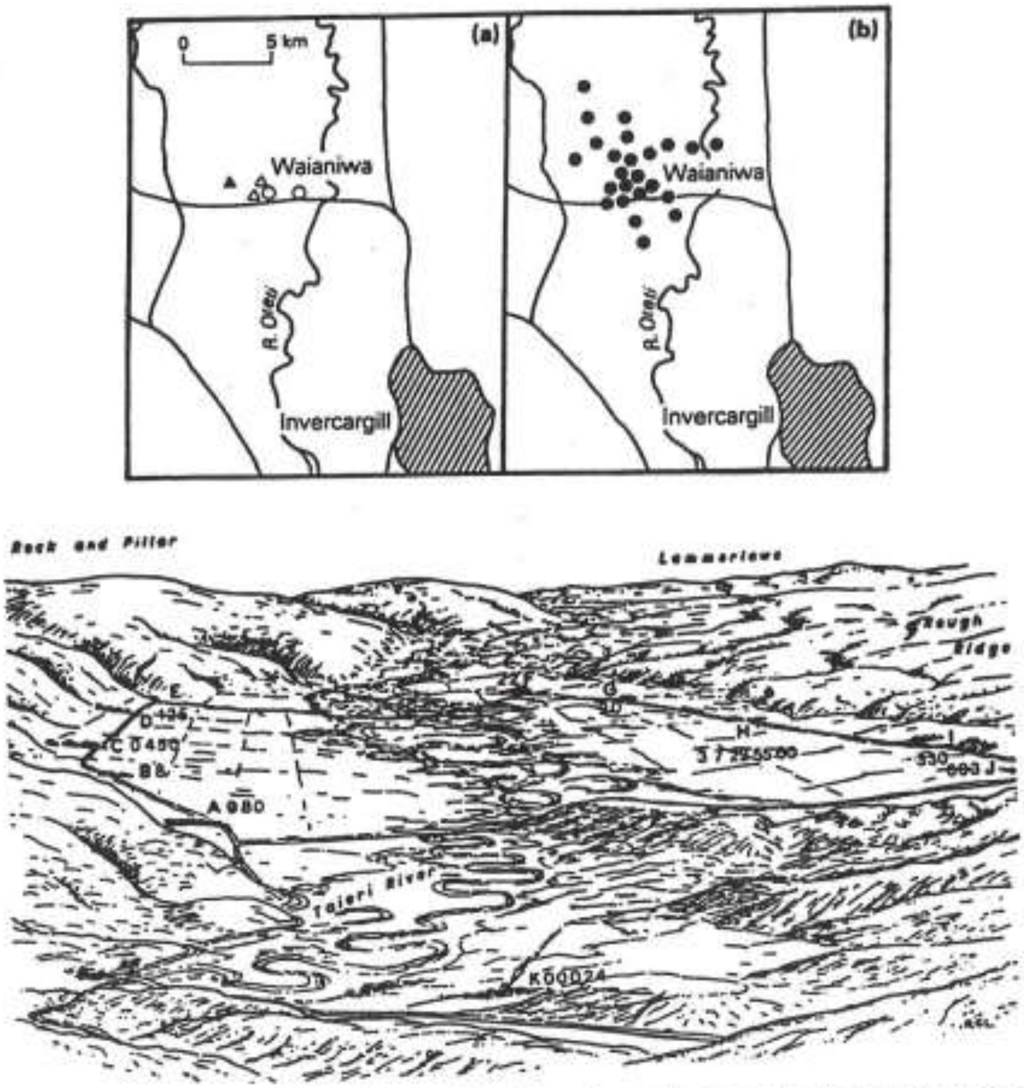
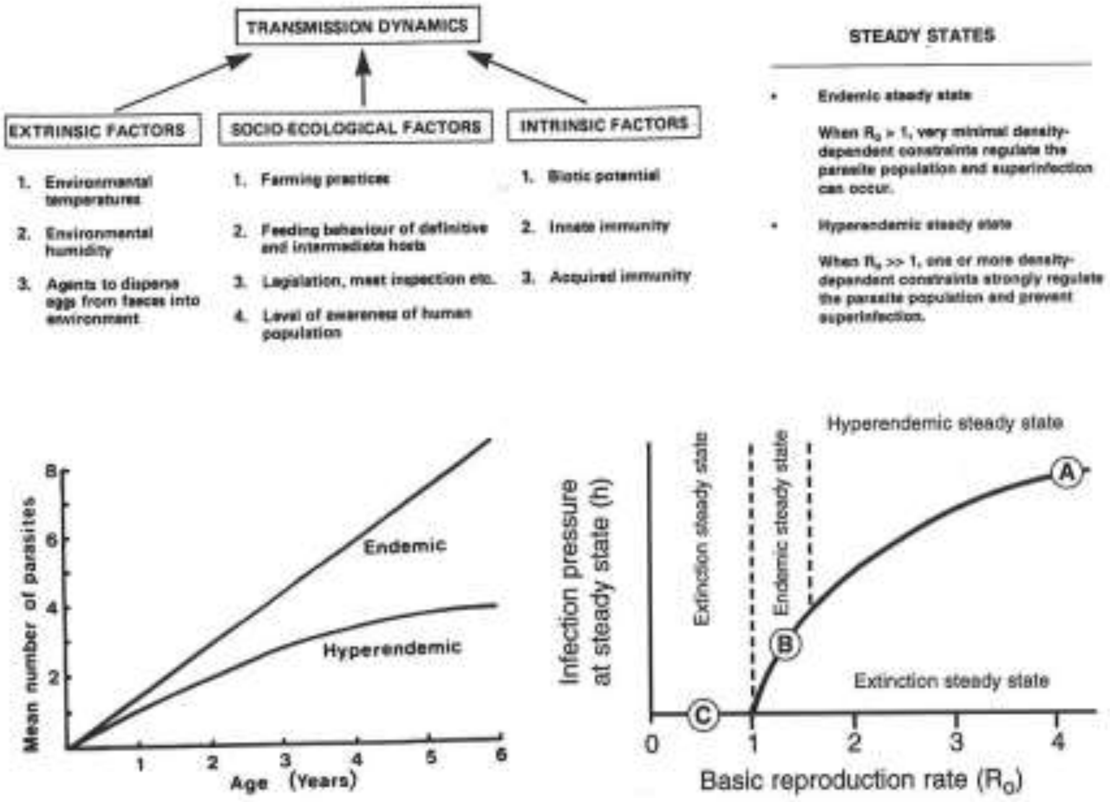


Fig. 3.6 Dispersal of eggs of *T. hydatigena* and *T. ovis* from farms in the same and consecutive years in New Zealand (Lawson and Gemmell, 1983, 1985, 1989, 1990; Gemmell and Lawson, 1986; Gemmell, 1990, 1993). Top: Dispersal of eggs of *T. ovis* from infected dogs in the first year (a, 1979) to other farms with infection in lambs in the following year (b, 1980), illustrating that eggs will disperse from one farm and survive on the other from one season to the next. (▲) 15%, (△) 10–14.9%, (○) 5–9.9%, (●) 1–4.9%. Bottom: Dispersal of eggs of *T. hydatigena* from a farm (H) with an infected dog. The letters A–K represent homesteads of all farms in the valley. The numbers 1–60 refer to the prevalence of *T. hydatigena* in sentinel lambs at the time each draft of animals was autopsied. The distance between farms H and B is approximately 10 km. In this dispersal pattern the parasite was hyperendemic on farm H and endemic elsewhere, illustrating the overall spread in a rural farm situation.

C. Biological and Environmental Interactions Modifying the Numerical Distribution of the Larval Population

In the natural environment the numerical distribution and degree of overdispersion of the larval sub-population in the animal intermediate host population is *inter alia* a product of the (1) spatial distribution of the eggs, (2) age of the eggs at the time of ingestion, (3) density-independent constraints, (4) proximity of grazing to the egg deposits, (5) age of the host when first exposed to eggs, (6) heterogeneity of the flock, and (7) density-dependent constraints.



STEADY STATES

- **Endemic steady state**

  When $R_0 > 1$, very minimal density-dependent constraints regulate the parasite population and superinfection can occur.

- **Hyperendemic steady state**

  When $R_0 >> 1$, one or more density-dependent constraints strongly regulate the parasite population and prevent superinfection.

Fig. 3.7 Quantifying the transmission dynamics of Taeniidae (Roberts et al., 1986a, 1986b; Gemmell et al., 1987b; Gemmell, 1990, 1993; Roberts and Gemmell, 1994; Gemmell and Roberts, 1995). Top left: Factors contributing to the transmission dynamics. Top right: Significance of the density-dependent constraints, namely acquired immunity in determining the equilibrium steady state. Bottom left: Empirical method of determining the equilibrium steady state from age-intensity prevalence. Bottom right: Bifurcation diagram showing the existence of steady states for different values of R_0 with *h* representing the infection pressure.

V. QUANTIFYING STABILITY AND EQUILIBRIUM STEADY STATES

A. Stability and Density-Dependent and Independent Constraints

Stability is an essential part of the description of host/parasite systems. The overall stability is a product of complex interactions between stabilizing and destabilizing forces, such as numerical distribution, biotic potential, and immunity. It describes the ability of biological systems in equilibrium to withstand perturbation, such as might be encountered in a control program, and, after that has ceased, to return to the previous equilibrium or reach a new one. In general, a parasite system is asymptotically stable if the parasite population returns to that state following a temporary perturbation away from it. It is structurally stable if its dynamics are qualitatively unchanged by perturbations in its parameters (Roberts et al., 1986a, 1986b, 1987; Roberts and Gemmell, 1994).

As already implied, parasite populations are subject to 2 types of constraint. A density-independent constraint, such as the action of weather on free-living stages, does not regulate the parasite population, while a density-dependent constraint, on the other hand, which is a constraint whose severity increases as the parasite density increases, does regulate the parasite population. An example of a density-dependent constraint would be the acquisition of immunity to infection by the host.

B. The Basic Reproduction Ratio and Equilibrium Steady States

The concept of the basic reproduction ratio (R_0) is central to an understanding of the transmission dynamics, stability in the environment, and control and eradication of parasites (Anderson and May, 1978). The ratio of the number of adult parasites in the "next generation" to the number of adults in "this generation" defines the basic reproduction ratio of the parasite population, and is usually denoted by R_0. In the past it has often been called the basic reproductive rate (Anderson, 1982), but the former term is now preferred as being more scientifically and grammatically correct (Diekmann et al., 1990; Heesterbeeck and Roberts, 1995). Some factors that contribute to R_0 are summarized in Figure 3.7.

If a parasite population is neither increasing nor decreasing with time, then it is in a steady state and its effective reproduction ratio (R) is 1. To distinguish epidemiological steady states for cestodes, a parasite population is said to be in an endemic steady state if the population size is constant ($R=1$) and the effects of the density-dependent constraints are insignificant ($R_0 > 1$, $R_0 \bumpeq 1$); and in the hyperendemic steady state when $R_0 >> 1$ and these constraints are effective. The extinction steady state is identified as that time when no parasite is present. The possible steady states as a function of R_0 are illustrated in Figure 3.7.

If $R_0 < 1$, the only possible steady state of the parasite population is the extinction steady state. Furthermore, if R_0 is reduced and maintained below unity, then the population becomes extinct with time. The extinction steady state is a possible realization of the dynamics of the parasite population regardless of the value of R_0. However, if a parasite population is near extinction but $R_0 > 1$, then the population will increase in size. Thus, if $R_0 > 1$, the extinction steady state is unstable.

1. Empirical method of determining the equilibrium steady state

Provided the infection pressure has remained constant throughout the lifetime of the host animals such as sheep, the equilibrium steady state can be defined by determining the intensity of infection in relation to age (Fig. 3.7). A linearly increasing age-intensity curve indicates endemicity, but if the curve is depressed below the straight line, then hyperendemicity.

2. Mathematical method of determining the basic reproduction ratio (R_0)

A mathematical method for quantifying the basic reproduction ratio has been developed by Roberts et al. (1986a, 1986b, 1987) using an integrodifferential equation of the form

$$h' = -\mu h + \lambda f' \bigstar (Sh)$$

where

h = infection pressure

μ = rate of loss of parasites from the system

λ = rate of transmission of parasites through the system in the absence of density-dependent constraints, $R_0 = \lambda/\mu$

f = probability density function for delays

S = proportion of intermediate hosts that are susceptible to infection

★ denotes convolution representing delays in the system

A nonlinear form is used for parasites with high biotic potentials, such as the ovine cysticercoses (*T. hydatigena* and *T. ovis*), and a linear form (with $S = 1$) is used for *E. granulosus*. If the parasite is in a steady state, R_0 can be estimated as follows:

$$R_0 = 1 + \frac{\text{(mean duration of immunity in the host population)}}{\text{(mean time to immunity in that population)}}$$

If the infection pressure is so high that acquired immunity lasts for life, then this formula is equivalent to:

$$R_0 = \frac{\text{(mean life expectancy of the host)}}{\text{(mean age at which immunity is acquired)}}$$

C. Application of the Concept of the Basic Reproduction Ratio to Eradication and Control

A steady state of a parasite population is said to be globally asymptotically stable if the population will tend to that state over time, regardless of the initial abundance. A steady state is said to be locally asymptotically stable if a population will return to that state over time if it was originally in that state but has been perturbated by a small amount. The threshold theorem states that if

$R_0 < 1$, the extinction steady state is globally asymptotically stable, and if $R_0 > 1$, it is unstable (Kermack and McKendrick, 1991).

If $R_0 > 1$, the hyperendemic steady state may be globally asymptotically stable or even unstable, depending on the long-term non-steady behavior. A cestode population is said to have extinction, endemic, or hyperendemic status depending on whether $R_0 < 1$, $R_0 > 1$ and $R_0 \doteq 1$, or $R_0 >> 1$, respectively. Clearly, the objective of any parasite eradication campaign must be to reduce the parasite population to extinction status and maintain this until no parasite remains. It is emphasized that if conditions are then relaxed and once again $R_0 > 1$, then the extinction steady state becomes unstable, and if the parasite is reintroduced it will reestablish. On the other hand, the objective of a control program is to reduce some measure of parasite abundance to an acceptable level and to maintain it at that level. A control program, therefore, is not time limited (Roberts et al., 1986a, 1986b, 1987; Gemmell, 1990; Roberts and Gemmell, 1994; Gemmell and Roberts, 1995, 1996). For further discussion on the value and limitations of modelling the transmission dynamics and in planning interventions, see Tolley and Ming (1993).

VI. FIELD INVESTIGATIONS ON TRANSMISSION

The relationship between the infection pressure (h) and the basic reproduction ratio (R_0) is illustrated in Figure 3.7. Where the transmission dynamics of *E. granulosus* have been quantified prior to control (namely, in New Zealand, China, and Uruguay), they have been found to be endemic (Gemmell et al., 1986a; Roberts et al., 1986a, 1986b; Gemmell, 1990; Ming et al., 1992b; Cabrera et al., 1995). Where those of *T. hydatigena* and/or *T. ovis* have been examined (namely, New Zealand and Uruguay), they have been determined to be hyperendemic (Roberts et al., 1986a, 1986b, 1987; Gemmell et al., 1987a; Cabrera et al., 1995).

A. Field Trials

Field investigations quantifying the behavior of endemic *E. granulosus* and hyperendemic *E. multilocularis* when perturbated have been described (Gemmell, 1978b, 1987, 1990; Gemmell and Lawson, 1986; Gemmell et al., 1986b, 1986c; Lawson and Gemmell 1989; Rausch et al., 1990).

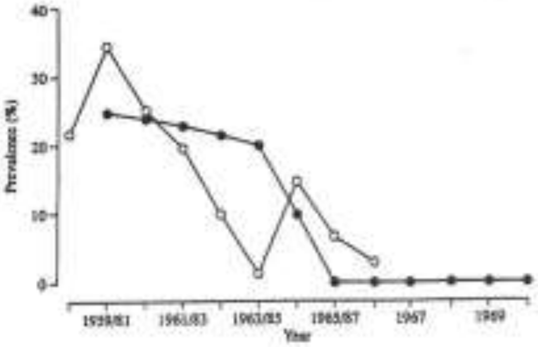


Fig. 3.8 Destabilizing the echinococcoses in the endemic and hyperendemic steady states (Gemmell, 1978b, 1993; Rausch et al., 1990). Force required (arecoline testing of dogs every 4 mo) to drive *E. granulosus* (●) from endemic ($R_0 = 1.3$) to extinction status ($R_0 = 0.4$) and then to extinction in the Styx field-trial. The force used with *E. multilocularis* (○) (dosing with praziquantel every 4 wk) was sufficient to drive this system from hyperendemic ($R_0 >> 1$) to extinction status ($R_0 < 1$) (A to C in Fig. 3.7). Interruption of this force resulted in a rapid return to hyperendemic status (C to A).

1. Endemic and hyperendemic echinococcosis

In the first trial, *E. granulosus* with its low biotic potential was destabilized by a dog-testing program with arecoline given every 3 mo in an endemic area of New Zealand (Gemmell, 1978b, 1987, 1990; Gemmell et al., 1986b; Lawson and Gemmell, 1989). In the second, dosing of Eskimo dogs with praziquantel every 4 wk was used to destabilize hyperendemic *E. multilocularis* with its high biotic potential in a village on St. Lawrence Island, Alaska (Rausch et al., 1990). Progress was measured by changes in the prevalence of hydatid cysts in sheep and rodents, respectively (Fig. 3.8). These results showed that the weak force used against *E. granulosus* was sufficient to drive it from endemic ($R_0 = 1.3$ to $R_0 = 0.4$) to extinction status (B to C in Fig. 3.7). With *E. multilocularis*, the strong force used drove it from hyperendemic to extinction status, but, when discontinued, it rapidly reverted to its original status (A to C then C to A in Fig. 3.7). The difference between these 2 situations is that in the endemic state there is a need only for a short-term and relatively weak intervention, whereas in the hyperendemic state, the need is for a strong, permanent intervention.

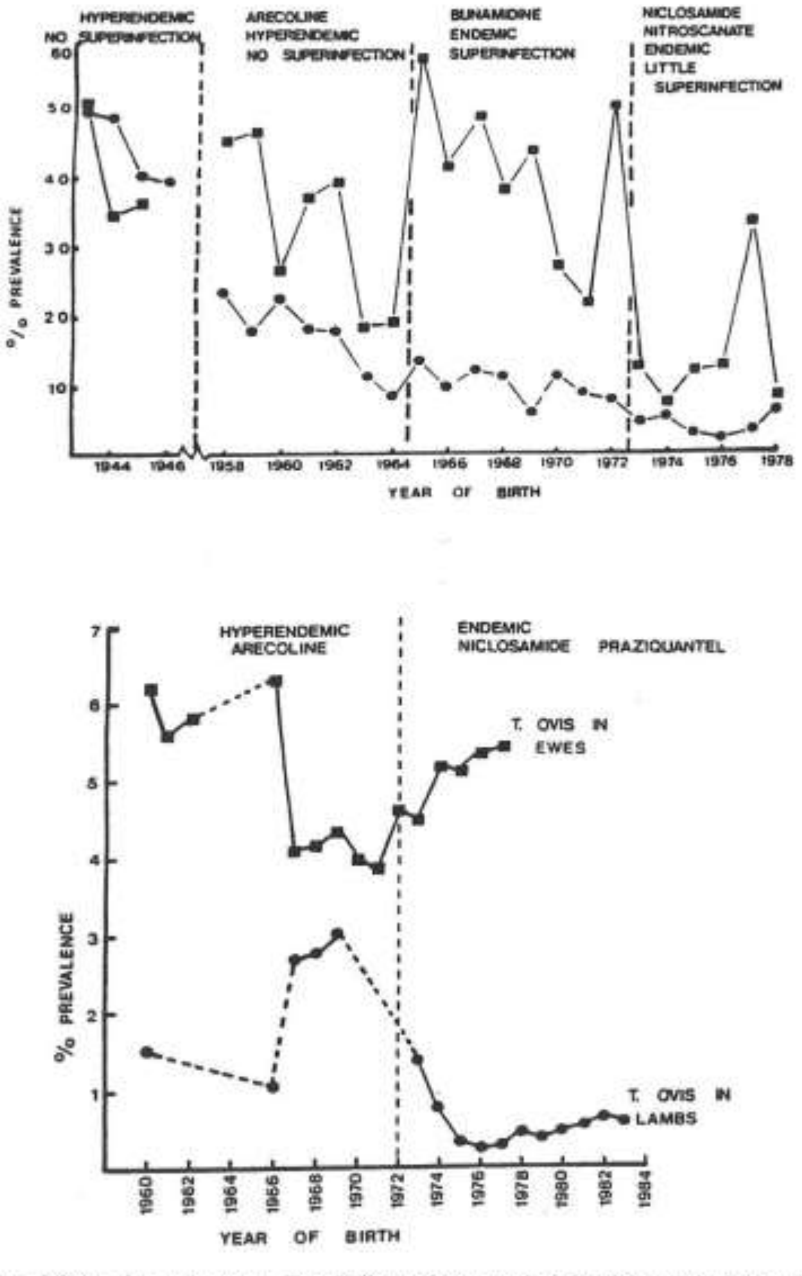


Fig. 3.9 Destabilizing the cysticercoses. Top: Different forces used to destabilize *T. hydatigena* in the hyperendemic state (R_0 = 4.3; Gemmell et al., 1986b; Lawson and Gemmell, 1989; Gemmell, 1990; 1993). Application of a dog-testing program with arecoline every 3 mo had no effect on prevalence in lambs (●) and sheep (■) of the same age-cohort and these remained similar from 1946 to 1964. Introduction of a dog-dosing program each month with bunamidine in 1964 caused an increase in the larval population in aged sheep through superinfection following the loss of immunity when driven from hyperendemic to endemic status (A to B in Fig. 3.7). Bottom: Different forces used to destabilize *T. ovis*. Following the decline in *T. hydatigena* above, *T. ovis* changed from suppressed hyperendemic to hyperendemic. Subsequent introduction of dog-dosing with niclosamide and then praziquantel every 6 wk drove this system from hyperendemic to endemic status also with an increase in superinfection following the loss of immunity (see A to B in Fig. 3.7).

2. Hyperendemic cysticercosis

A study was also made on destabilizing hyperendemic *T. hydatigena* in sheep in New Zealand ($R_0 = 4.3$). When dogs were subjected to arecoline testing every 3 mo, the effect on the parasite in sheep was negligible (1943–1946 and 1958–1963) as manifested by a similar prevalence in young and old animals of the same birth cohort (Fig. 3.9). Paradoxically, by increasing the force in 1964 with bunamidine hydrochloride treatments every 4 wk, *T. hydatigena* was driven from hyperendemic to endemic status (A to B in Fig. 3.7). This resulted in an increase in the larval population in old sheep from superinfection following the loss of immunity. A similar increase in *T. ovis* occurred in old sheep in New Zealand when dogs were dosed with niclosamide and later praziquantel every 6 wk (Fig. 3.9 and A to B in Fig. 3.7). In neither case was extinction status achieved (Gemmell, 1978b, 1987, 1990; Gemmell and Lawson, 1986; Gemmell et al., 1986c; Lawson and Gemmell, 1989).

B. Trials Required to Define Minimum Dog-Treatment Schedule Needed to Drive Endemic *E. granulosus* to Extinction Status

The normally accepted treatment schedule with praziquantel is every 1.5 mo (6 wk) for *E. granulosus*. This has been based on the concept that dogs become infected immediately after being treated. From the above studies it was shown that larval populations of large tapeworms actually increase in number from such a schedule, which cannot be regarded as cost effective. Where the 3 sheep metacestodes occur together, a treatment schedule should be used that drives *E. granulosus* toward extinction status (B to C in Fig. 3.7) without modifying the transmission dynamics of *T. hydatigena* or *T. ovis*. Field studies in Uruguay have shown that a few dogs became infected with *E. granulosus* between 2 and 4 mo after treatment (prevalence at 2, 4, 8, and 12 mo was 0, 6.8, 18.6, and 27.9%, respectively; Cabrera et al., 1996). In contrast, dogs became infected with *T. hydatigena* and *T. ovis* within 2 and 4 mo, respectively.

Field trials undertaken before control may show that a treatment schedule, say every 3 to 4 mo, may be quite sufficient to drive *E. granulosus* from endemic to extinction status and retain both *T. hydatigena* and *T. ovis* as asymptotically and structurally stable parasites in hyperendemic status. Such a result would substantially modify the costs and benefits of controlling *E. granulosus*.

VII. QUANTIFYING THE TRANSMISSION DYNAMICS OF CE IN HUMANS

A. Methods of Transmission

Until quite recently it was assumed that CE was a rural health problem caught in childhood (Dew, 1928) either by direct transfer of eggs from dog to mouth (disease of dirty hands), or from dogs contaminating the water supply with eggs or defecating on vegetables. While not disputing these and other possibilities (such as coprophagia or geophagia), experiments suggest that echinococcosis is likely to occur from eating eggs deposited by flies on foodstuffs or other media contacted by flies (Lawson and Gemmell 1983, 1985, 1989, 1990).

1. Evidence for potential transmission by flies

Blowflies (*Calliphora maculata*) were first allowed to feed on dog feces containing proglottids of *T. pisiformis* or *T. hydatigena* and then allowed contact with grass or cooked meats, respectively, that were then fed to rabbits or pigs (Lawson and Gemmell, 1990). The results demonstrated that taeniid eggs remain viable after passage through the gut of flies, and that these flies transmit them indirectly to animals by their normal activities of vomiting and defecating. If it is assumed that the grass and cooked meat used in these experiments represent the normal vegetable and meat diets of humans, then these results imply that, where there is an abundance of blowflies together with opportunities to contact dog feces and human foodstuffs, flies would provide a practical transport host for the eggs.

B. Age-Susceptibility of Humans to CE

That humans of more or less any age may become infected is implied by the intensive studies made during the control programs in New Zealand and Tasmania on changes in the age prevalence of CE in humans (Anonymous, 1961–1989, 1964–1988; Beard, 1969, 1978, 1979, 1987). Both programs were regarded as being in the

TABLE 3.2 Age distribution of new hospital cases of CE in New Zealand, 1958–1962 and 1963–1967 (adapted from Anonymous, 1961–1989; Beard, 1987).

Age groups	Number of cases 1958–1962	 1963–1967	Total	% reduction
0–4	19	3	22	84.2
5–14	98	35	133	64.3
15–24	82	46	128	43.9
25–44	112	64	176	42.9
45–64	98	48	146	51.0
> 65	44	25	69	43.2
Total	453	221	674	51.2

Chi-squared test shows that age distribution is not significantly different in the two 5-yr periods.

TABLE 3.3 Age distribution of new surgical cases of CE in Tasmania, 1958–1962 and 1963–1967 (adapted from Anonymous, 1964–1988; Beard, 1978, 1979, 1987).

Age groups	Number of cases 1958–1962	 1963–1967	Total	% reduction
0–4	3	0	3	100.0
5–14	11	4	15	63.6
15–24	9	7	16	22.2
25–44	15	7	22	53.3
45–64	16	8	24	50.0
> 65	5	2	7	60.0
Total	59	28	87	52.5

Chi-squared test shows that age distribution is not significantly different in the two 5-yr periods.

endemic steady state ($R_0 > 1$) prior to control. The former was initiated in 1959 and the latter in 1965. Data for New Zealand were collected only from public hospitals, but those in Tasmania included all hospitals conducting surgery using the criteria that a cyst verified at operation or at necropsy be confirmed as a cause of symptoms or death and not as incidental findings. Only new cases were collected for surgical incidence (Tables 3.2 and 3.3).

In Tasmania, incidences were collected annually; the most important were those for the first two 5-yr periods, 1966–1970 and 1971–1975 (Table 3.3), during which time the incidence halved. Age-specific rates were calculated from the estimated populations in each age group at the midpoint of each period. Of the 87 new patients, 77 (89%) were autochthonous. The incidence in the second period declined to about half without a significant change in the age distribution. This was also the case in New Zealand (Table 3.2). This means that adults are susceptible to clinical disease and commonly have a short latency of CE. The discovery of adult susceptibility with a short latency is still compatible with long latency in individuals. These data show that childhood infections (as proposed by Dew, 1928) can no longer be regarded as the rule. This casts no doubt on the existence of exceptions to longer-term latency before clinical symptoms occur, and there is no inconsistency with the fact that silent infections can still be discovered at autopsy. Indeed, silent infections may substantially exceed clinical cases.

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