POPULATION DYNAMICS OF THE RAT TAPEWORM, *HYMENOLEPIS DIMINUTA*.

by

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Quantitative estimation of some of the population parameters involved in the life-cycle of *Hymenolepis diminuta* was carried out under specified experimental conditions, using the laboratory rat and the flour beetle, *Tribolium confusum*, as final and intermediate host respectively. Parameters for which estimates were obtained include the survival of infective-stages and larval parasites, the transmission of parasites between hosts, and the rates of intermediate host mortality and fecundity.

The influence of infective-stage density and distribution on the dynamics of infection of the intermediate host was investigated, together with the effects of factors such as host age, sex and population density, and the influence of the duration of exposure to infection. The dynamics of definitive host infection and the effects of density-dependent constraints on adult worm population growth are also discussed. Experiments were carried out in order to determine the effects of parasitism on the survival and fecundity of *T.confusum*. These effects were found to result in a considerable depression of the host equilibrium population size under given laboratory conditions.

The relevance of the experimental results to host-parasite interactions in the field is discussed, and the major factors controlling the growth of *H.diminuta* populations under natural conditions are considered. Lastly, the form of the experimentally investigated parameters is used to examine the behaviour of a model for host-cestode population interactions. Consideration is given to the use of this model in the description of cestode infections of public health and economic significance.

CONTENTS.

LIST OF TABLES

LIST OF FIGURES

INTRODUCTION

In recent years, considerable advances have been made in the understanding of the processes which control the dynamical behaviour of animal populations in real communities. These advances are to some extent a result of the recent trend towards the combination of experimental and theoretical methods with fieldwork, to form an integrated approach to ecological study. The majority of this work has been carried out in reference to terrestrial arthropod systems (see Hassell, 1978), both because of their economic importance, and their ease of manipulation in the laboratory. Relatively little is known to date, however, about the population biology of parasitic organisms, in spite of their obvious economic and public health significance. It is mainly because of the complexity of many parasitic life-cycles, and the intimacy of the relationship between individual parasites and their hosts (which makes sampling difficult and often necessarily destructive), that few ecologists in the past have turned their attention towards parasitological problems. In consequence, the understanding of the ecology of parasitic organisms lags behind that of their free-living counterparts, particularly with respect to the availability of quantitative data suitable for use in conjunction with theoretical techniques.

The basis of this thesis is the presentation of quantitative information concerning the factors which regulate the dynamics of a specific host-parasite interaction within a controlled experimental framework in the laboratory. The rat tapeworm, *Hymenolepis diminuta* (Rudolphi, 1819), with hosts *Tribolium*

confusum, Duval, and *Rattus rattus* (Linnaeus, 1758), was used as a laboratory model. Many aspects of the biology of this parasite are well known, in particular factors concerning the adult worm and its relationship with the final host. For this reason, the experimental work described in the present thesis was concerned mainly with the dynamics of intermediate host infection and the population biology of the larval parasite. In conjunction with the experimental programme, simple mathematical models were used in order to gain conceptual insight into the processes affecting the dynamics of the host-parasite interaction, and to aid in experimental design by the clarification of the parameter components in need of investigation . The models described are based on a theoretical framework developed by Anderson and May (1978) and May and Anderson (1978), consisting of coupled differential equations for each of the parasite and host populations involved in the interaction. Details of this model framework, in the context of a review of literature concerning experimental and theoretical studies of parasite population dynamics and epidemiology, are given in Section 1.

Results of the experimental programme are presented in Section 2. Following brief descriptions of the biology of the parasite (2.1) and the experimental methods used (2.2), results pertaining to the dynamics of intermediate host infection and the population biology of the larval parasite / intermediate host association are given in Sections 2.3 and 2.4 respectively. The remaining Section (2.5) gives a review of available

information concerning the population dynamics of the adult parasite, together with the results of a small amount of supplementary experimental work carried out in the present study. The experimental data from which the figures in Section 2 were drawn are given collectively in Appendix 1, each table being numbered to correspond with the figure to which it refers. The forms of the individual population parameters described in Section 2 are then used in Section 3 to create a model for the entire life-cycle of the parasite, in order to gain qualitative insights into the dynamical behaviour of a host-parasite interaction with the type of life-cycle exemplified by *H.diminuta*.

Although not of direct applicability to parasitic infections of man, the use of a laboratory model such as the rat tapeworm is of significance in the attempted acquisition of knowledge concerning the processes which govern the dynamics of host-parasite population interactions. In this context, a discussion of the extent to which the model developed for *H.diminuta* is of use in the description of the dynamics of cestodes of economic and public health significance is given in Section 4.

SECTION 1

PARASITE POPULATION DYNAMICS AND EPIDEMIOLOGY.

Epidemiology, the study of disease as a mass phenomenon, is one of the oldest medical sciences. The mathematical approach to the study of the causes and conditions of epidemics may be traced back to John Graunt's Bills of Mortality (1662). It was not until the work of Ross (1911), however, that the use of theoretical techniques began to be accepted as a valid approach to the subject. In comparison with the epidemiology of microparasites (i.e. viruses, bacteria and protozoa), the quantitative study of the transmission of helminths is a more recent development, pioneered primarily by the work of Macdonald (1965). There remains, to date, an artificial dichotomy between the two branches of disease dynamics, largely maintained by the distinctive disciplines in which they are classified (i.e. medical microparasite epidemiology and ecological helminth population biology). The present review relates primarily to advances made in the population biology of macroparasites, in the context of the study of disease transmission in general.

It has been pointed out by many authors, that although concerted research effort in many different disciplines is required for attempted control of infectious disease, exact discussion can only proceed on the basis of adequately formulated mathematical models (see, for example, Bailey, 1957; Muench,1959; Bartlett, 1960). These may range in form from 'tactical' models which aim to mirror completely the dynamics of specific systems and thus to be of practical use, to 'strategic' models formulated to capture the essential features of a generalized population

interaction in order to give qualitative insight into its behaviour (Holling 1966; Levins, 1966). It is the latter end of this spectrum which is of interest in the present context. Model formulation proceeds by first defining various components, which are then integrated to form a simple preliminary model. Discrepancies in the comparison of model behaviour with observed data are then used to determine the appropriate refinements, which may involve the addition or alteration of certain individual components, or the functional manner in which they are connected (see Royama, 1971; Pielou, 1969). It should be noted that good agreement between observed and predicted results does not necessarily imply that the model gives a correct explanation of the generative mechanisms of the phenomenon. It is thus of importance to ensure that the information obtained by model formulation is used only within the boundaries of the philosophy of disproof (see Popper, 1959; Medawar, 1969). The applicability of the results of general models to an understanding of real ecological systems remains a subject of some controversy. As discussed, for example, by May (1973), Royama (1971) and Bartlett (1960), an appreciation of the behaviour of an hypothetical, idealised system is regarded by many as an essential preliminary in the interpretation of complex, biological reality.

One of the first contributions to theoretical epidemiology was made by Ross (1911) in relation to the transmission of malaria.

By considering a constant human community divided into susceptible, infected and removed (i.e. recovered) classes, Ross concluded that the prevalence of malaria tends towards an equilibrium level determined by the relationship between the rates of infection and recovery. In addition, he derived an expression for the 'critical density' of mosquitoes in a given community below which the disease is unable to persist. This work provided a basis for the development of models for disease transmission in general, which was continued by McKendrick (1912), Lotka (1923) and Kermack and McKendrick (1927). Later refinement of this classical epidemic theory was then related to the introduction of stochastic components (see Bailey, 1957; Bartlett, 1960) and seasonality (e.g. Dietz, 1976; London and Yorke, 1973; Yorke *et al*, 1979). Little further development of these ideas occurred until Macdonald (1957) rederived the threshold mosquito density concept for malaria, and clarified the ideas of Ross (1911) for a biological audience.

The basic unit of study in the compartmental models (i.e. those in which the host population is divided into classes such as susceptible, infected and immune) discussed above is the infected host. The details of these models will not be given here, since they are not directly applicable to the study of host-helminth interactions, (although they have recently been modified to describe the dynamics of schistosomiasis in snail populations (Goffman and Warren, 1970; Lewis, 1975)).

In diseases caused by macroparasites, the number of parasites harboured per host (which cannot readily be determined for microparasitic infections) is of considerable dynamical significance, and so the individual parasite is normally taken as the basic unit of study.

Concurrently with the development of compartmental models, a second type of theoretical framework was developed to describe the population dynamics of direct life-cycle helminth parasites (Kostitzin, 1935). This deterministic framework was based on the assumption that the host population H, could be divided into an infinite number of categories, each representing the number of hosts, H_i, harbouring a specified parasite burden i. The total number of hosts is then given by the summation of each of these categories

$$H = \sum_{i=o}^{\infty} H_i \qquad (1.1)$$

and the number of parasites, P, is given by the summation of each host category multiplied by its respective parasite burden

$$P = \sum_{i=o}^{\infty} i.H_i. \qquad (1.2)$$

Given sufficient information concerning the nature of the parasite life-cycle, the rate of change in the size of each of the host categories through time may then be expressed by an infinite series of differential equations. Kostitzin pointed out, however,

that the system is highly non-linear and therefore difficult to handle analytically.

No further development took place in the area of host-helminth population interactions (except for work relating specifically to schistosomiasis, to be discussed below) until 1971, when Crofton (1971a and b) proposed a quantitative approach to host-parasite population dynamics based on the three following general features : (a) the infection process produces an over-dispersed distribution within the host population; (b) all hosts harbouring a certain 'lethal level' of parasites are subject to parasite-induced host mortality and (c) the parasite species has a higher reproductive potential than the host species. Crofton incorporated these features into a computer simulation model, assuming in addition that the host population exhibits exponential growth in the absence of the parasite and that the parasites have distinct generations equal in length to those of the host. The model was thus formulated in difference equations, although no details of these were given in published work. From a numerical analysis of model behaviour, Crofton concluded that the parasite regulates host population growth to a stable equilibrium level, as a result of parasite-induced host mortality.

Although this model is of significance as the first comprehensive description of parasitism as a population phenomenon, especially with respect to the incorporation of the observed over-dispersion in the statistical distribution of

parasite numbers per host, and its description by the negative binomial probability model, it contains two biologically unrealistic assumptions. The first of these concerns the relationship between the rate of transmission and host population density. Crofton assumed that this was one of direct proportionality, but failed to realize that the transmission factor (i.e. the probability that a given parasite infective-stage succeeds in infecting a host) must be constrained to saturate to unity. The second relates to the lethal level concept. By examination of experimental results from several host-parasite interactions, it has since been found that there exists a range of functional relationships between the rate of parasite-induced host mortality and parasite burden, varying from direct proportionality to more complex, non-linear patterns (Anderson, 1978a). The lethal level represents one possible extreme of this spectrum, which is, however, almost never observed under natural conditions. In addition to these two features, a further objection to the validity of Crofton's model stems from the observation that all conclusions were drawn on the basis of numerical simulation using only a very restricted range of parameter values.

The two basic model defects have recently been corrected by May (1977a). An analysis of the behaviour of the modified framework for a range of parameter values revealed that the patterns of dynamical behaviour generated are considerably more varied than Crofton had assumed. In essence, parasite-induced host mortality is only able to regulate host population

growth in a stable manner for intermediate levels of over-dispersion of parasite numbers per host (as measured inversely by the parameter k), and transmission-stage production per parasite, λ. If λ is too large, and/or k too small, an equilibrium host population level is not achieved .

A further general theory of the epidemiology of parasitic infections was put forward by Bradley (1972), who suggested that parasite population growth may be regulated by either density-independent control of transmission success (type I) or by density-dependent constraints on parasite build up within individual hosts (by 'complete' (type II) or 'concomitant' immunity (type III)). It was suggested that the differences between type I and types II and III might be useful in an examination of the differences between endemic and epidemic infections. Bradley again pointed out the natural tendency towards over-dispersion in parasite numbers per host in the vast majority of parasitic infections, and also the liklihood of a functional relationship between parasite load and the probability of morbidity and mortality. Although not based on formal analysis, this work was most useful in its emphasis of the stabilizing properties of parasite aggregation.

The most comprehensive model framework for host-helminth interactions to date is that proposed by Anderson and May (1978) and May and Anderson (1978). Their 'basic model' consists of coupled differential equations representing the dynamics of host

(H) and parasite (P) populations. It applies to direct life-cycle parasites which do not have a reproductive phase contributing directly to the size of the parasite population within the host. The host population is assumed to undergo exponential increase in the absence of the parasite, determined by the relative instantaneous rates of natality (a) and mortality (b) per host. The parasite is assumed to have a constant per capita instantaneous rate of transmission-stage production, λ. But, in contrast to Crofton's model, the proportion of transmission-stages successfully gaining entry to a new host saturates to unity. The dynamics of the infective-stage population may be incorporated by use of the term $H/(H_o+H)$. H_o determines the efficiency of transmission and is equal to $\hat{\mu}/\beta$, where $\hat{\mu}$ and β are the per capita instantaneous rates of infective-stage mortality and transmission respectively. The parasites are assumed to exhibit a constant instantaneous rate of mortality while inside the host, μ representing losses due to parasite senescence as well as to the effects of host immunological responses.

The model is hybrid in nature. The components defined above are deterministic, but the framework also includes stochastic terms which enable the probability distribution of parasite numbers per host to be taken into account. The instantaneous rate of parasite-induced host mortality per parasite per unit time, α, may thus be related to the number of parasites per host, and in the basic model is assumed to be directly

proportional to parasite burden. The net rate of loss of hosts in a population of size H may therefore be represented by

$$\alpha H \sum_{i=o}^{\infty} i.p(i) \qquad (1.3)$$

where p(i) is the probability that a host harbours i parasites. Similarly, the net rate of loss of parasites as a result of natural host mortalities is given by

$$b H \sum_{i=o}^{\infty} i.p(i). \qquad (1.4)$$

Net parasite losses from parasite-induced host deaths, however, where the per capita host loss rate is taken to be αi, take the form

$$\alpha H \sum_{i=o}^{\infty} i^2.p(i). \qquad (1.5)$$

The sums represented in expressions (1.4) and (1.5) are, by definition, the average, E(i), and mean-square, $E(i^2)$, numbers of parasites per host respectively. Although the mean parasite burden may be represented by P/H irrespective of the parasite distribution, the precise value of $E(i^2)$ is critically dependent on the form of the probability distribution of parasite numbers per host (see Anderson and May, 1978, Appendix 1). Although p(i) is in reality determined as a result of the functional form of the dynamical processes making up the interaction, considerable simplification may be achieved by making a phenomenological assumption concerning the form of the distribution based on

empirical evidence, and incorporating this into model structure, (see Section 3 of the present thesis).

The biological components described above may be drawn together to give the following differential equations

$$dH/dt = (a - b)H - \alpha P \qquad (1.6)$$

$$dP/dt = \lambda PH/(H_o + H) - (\mu + b)P - \alpha HE(i^2). \qquad (1.7)$$

An analysis of the behaviour of equations (1.6) and (1.7) led Anderson and May to conclude that parasites may in certain circumstances play an important role in regulating or controlling the growth of the host population. The model is neutrally stable and is thus biologically unrealistic in the absence of further modification. Incorporation of other features based on empirical evidence has shown that over-dispersion of parasite numbers per host, non-linear functional relationships between parasite burden and host death rate, and density-dependent constraints on parasite population growth within individual hosts are of particular significance in stabilizing the dynamical behaviour of the host-parasite interaction and so enhancing the regulatory role of the parasite. Similarly, features such as parasite-induced reduction in host reproductive potential, direct parasite reproduction within a host, and time delays in parasite reproduction and transmission are shown to have a destabilizing influence. Host-parasite associations under natural conditions which exhibit

destabilizing features are thus also likely to display compensatory stabilizing elements.

The basic model framework outlined above has recently been modified to describe a wide variety of host-parasite interactions, and has proved useful in highlighting significant aspects of their population biology. It has been applied, for example, to the dynamics of specific direct life-cycle helminths such as hookworm (Anderson, 1980a) and indirectly transmitted diseases such as schistosomiasis (Anderson 1980c). A preliminary investigation of the use of the model in the description of host-cestode interactions is given in Sections 3 and 4 of the present thesis.

Recent developments have also been made in the extension of classical compartmental epidemic models to replace the standard assumption of a constant host population by one in which the total number of hosts is assumed to be a variable determined by both the dynamics of the disease, and the natural birth and death rates of the host (Anderson, 1979c). This type of framework has been used most successfully in the interpretation of the results of classical epidemiological studies carried out by Greenwood *et al* (1925; 1936) and later extended by Fenner (1948; 1949) using the mouse pathogens ectromelia (virus) and *Pasteurella muris* (bacterium).

A comparison of the behaviour of the modified compartmental

model with that of the 'helminth' framework described above has done much to unify the two previously distinct areas of research (see Anderson, 1979c; Anderson and May, 1979a; May and Anderson 1979). In this context, the derivation and clarification of the concept of the basic reproductive rate of the parasite (R) originally described by Macdonald (1957) has facilitated the clarification of the similarities and distinctions in the dynamics of the two types of disease agent (Anderson, 1980c). The dimensionless parameter, R, describes the potential number of secondary cases arising from a single primary case in a large population of susceptible hosts (for microparasites) or alternatively, the potential number of infective stages produced by an adult parasite during its reproductive lifespan which develop successfully to reproductive maturity (for macroparasites). A discussion of the relationship between R and Fisher's net reproductive rate and reproductive value, is given by Anderson (1980b). The form of the basic reproductive rate may be used in the evaluation of the efficacy of potential disease control programmes (Anderson, 1980a;c) and also to examine parasite reproductive strategies in order to gain an understanding of the evolution of parasite-host relationships (Anderson, 1980b).

In addition to their use in examination of the dynamics of parasite transmission, both types of model structure facilitate an understanding of the effects of parasitism on host population

dynamics (Anderson, 1978a; 1979a; 1980d). The conclusion that the maximum degree of host population depression may be achieved by direct life-cycle parasites of moderate to low pathogenicity has important implications for the use of pathogens as biological control agents (Anderson, 1979b) and in the interpretation of naturally occurring insect population cycles (Anderson and May, 1980).

The majority of epidemiological investigations relating to the transmission of helminth parasites have been carried out in reference to schistosomiasis. There exists a substantial literature of mathematical models of this disease (see Cohen, 1977; Fine and Lehman, 1977), which may be roughly divided into two broad categories; those concerning transmission throughout the entire life-cycle, and others describing the trends in age-specific prevalences and intensities of infections in either humans or snails, by the use of catalytic or immigration-death models.

The use of catalytic curves (i.e. those originally derived in relation to enzyme kinetics) in epidemiology was first described by Muench (1959). It is assumed that a cohort of hosts is entirely susceptible to infection at birth and is thereafter exposed to a constant 'force of infection', ε, measured in effective contacts per unit time. If x and y represent the uninfected and infected fractions of the cohort at time t (so that $x + y = 1$), then the temporal changes in

these fractions may be represented by the differential equations

$$dx/dt = - \varepsilon x \qquad (1.8)$$

$$dy/dt = - dx/dt. \qquad (1.9)$$

Given that $y = 0$ when $t = 0$, the solution of these equations takes the form

$$y = 1 - \exp(-\varepsilon t). \qquad (1.10)$$

Assuming that all infections are detectable, and that the 'force of infection' has remained constant over the lifespan of the oldest host age-class, then equation (1.10) may be used in the interpretation of age-prevalence data taken from a cross-sectional survey of a community at a single point in time. Application of catalytic models to the prevalence of schistosomiasis in man has revolved around modification of the simple curve described by equation (1.10) to include an irreversible (Hairston, 1965) or reversible (Lewis, 1975; Rosenfield *et al*, 1977) loss of infection, stochastic description of the distribution of parasites between hosts (Tallis and Leyton, 1969) and human mortality and immigration (Cohen, 1973). These models have proved valuable in permitting quantitative estimates of rate parameters to be made. Curve-fitting is, however, of little use in distinguishing the effects of factors such as parasite-induced host mortality, age-dependent variation in water contact, immunity, and age-

dependent detectability of infection in the generation of the observed trend towards a declining parasite prevalence in older age-classes.

Age-prevalence snail infection data has also been described by immigration-death models incorporating loss of infection (Sturrock and Webbe, 1971), differential mortality of infected snails (Cohen, 1973; Sturrock, *et al*, 1975) and snail latency (Nasell, 1976; Anderson and May, 1979b). Although possessing a considerably higher degree of experimental tractability, field surveys of snail populations provide less reliable age-prevalence data than those relating to human infection, as a result of the difficulties associated with age-determination. The relationship between snail age and size is complicated by many factors including the availability of environmental resources (e.g. Chernin and Michelson, 1957) and the presence of parasitic infection (e.g. Sturrock, 1966). Catalytic models are thus of use in the interpretation of observed patterns of snail infection, but of limited value in the quantitative estimation of rate parameters for comparison of transmission between areas. In the future, however, they should prove useful in the development of techniques for the estimation of parasite basic reproductive rates (see Anderson 1980a).

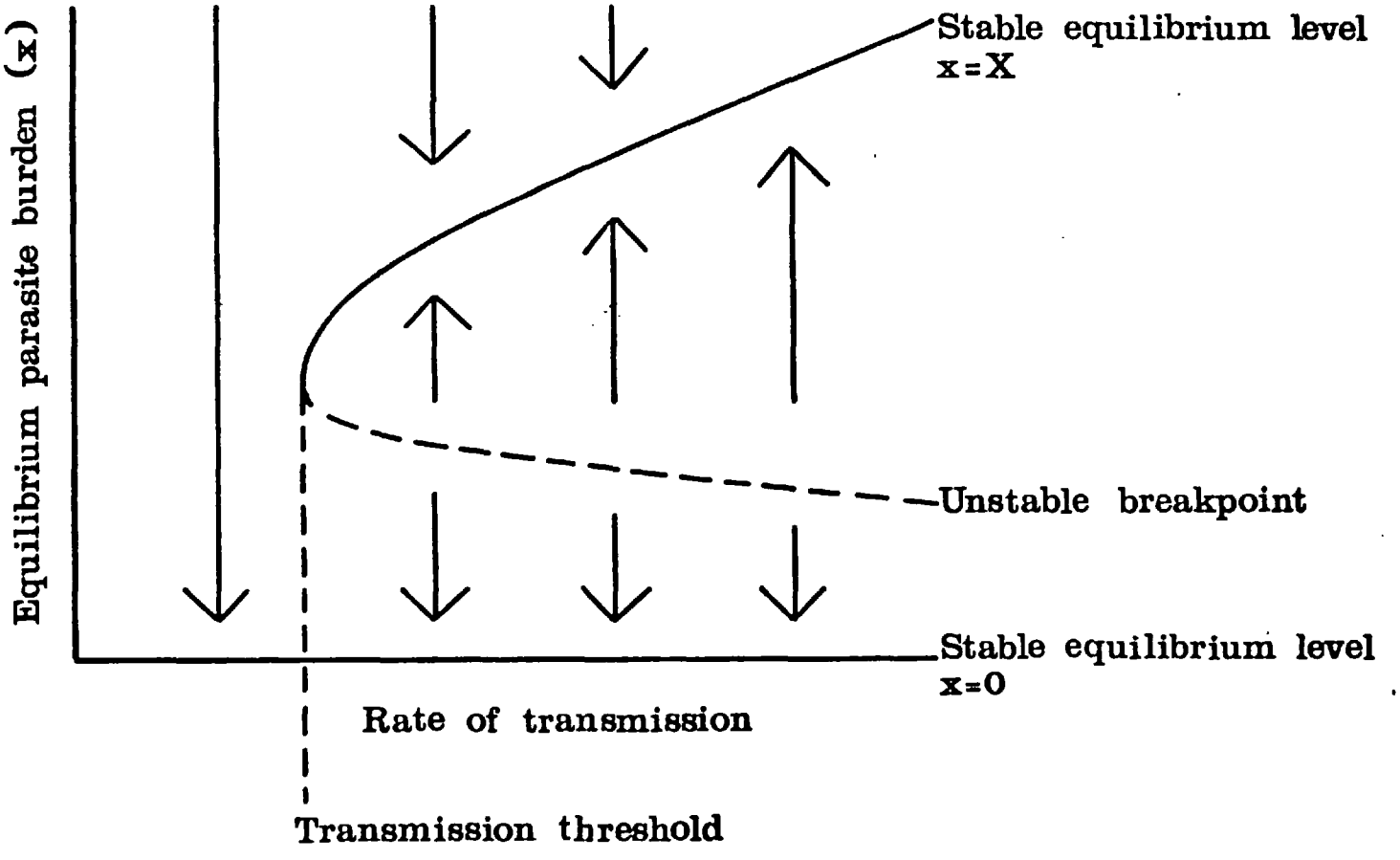
One of the first discussions of the overall transmission dynamics of schistosomiasis was put forward by Macdonald (1965) and subsequently elaborated by Nasell and Hirsch (1973).

Two variables were considered in this model; the mean worm load per human host (x) and the fraction of the snail population which is infected and shedding cercariae (y). Temporal changes in x are given by a differential equation describing the balance between the force of infection (i.e. the product of the probability of human infection by a cercaria , the snail population size, the fraction of those which are shedding cercariae, and the rate of shedding per infected snail) and the mortality rate of mature schistosomes. Similarly, the rate of change of y is described by the force of snail infection (i.e. the product of the probability of snail infection by a miracidium, the mean number of paired female worms per host, their rate of egg laying and the size of the host population) and the rate of snail death.

Given three simplifying assumptions : (a) a constant host population size, (b) no differential mortality between infected and uninfected snails, and (c) a random distribution of parasite numbers per host, Macdonald concluded that there is a threshold parameter level below which the transmission factors are too low to maintain endemic schistosomiasis. In addition, for parameter values above the transmission threshold, he described the existence of two stable worm load equilibria (x=o and x=X) separated by a positive unstable equilibrium level which he called the 'breakpoint' (see Figure 1.1). Whether the disease returns to its original equilibrium level, X, or becomes extinct after perturbation, will depend on whether or not the perturbation

Figure 1.1 An illustration of the breakpoint concept.

The graph illustrates the predicted relationship between the equilibrium mean intensity of infection (x) and the rate of disease transmission (see Macdonald, 1965). The dashed line indicates the unstable breakpoint, and the arrows denote the dynamical trajectories of the system following a perturbation from the two stable equilibrium states, x=X and x=0. The infection cannot be maintained below the transmission threshold.


Equilibrium parasite burden (x)
Stable equilibrium level
x=X
Unstable breakpoint
Stable equilibrium level
x=0
Rate of transmission
Transmission threshold

succeeded in lowering the mean worm burden per host below the breakpoint. The description of this phenomenon had obvious implications with respect to disease control.

Several modifications to Macdonald's model have recently been made. Incorporation of over-dispersion in the distribution of parasite numbers per host has shown that the epidemiological conclusions derived by Macdonald are not robust to variations from the Poisson distribution (May, 1977b; Bradley and May, 1978). If male and female worms each follow a separate aggregated probability distribution, then the breakpoint theorem remains intact. If, however, male and female worms are aggregated together, the breakpoint mean worm burden tends to zero as the degree of aggregation becomes more severe. Unfortunately, little information is available concerning worm distribution per host from epidemiological field studies, or even from experimental investigations. The quantitative determination of breakpoint and transmission threshold levels (and their potential application to control measures in the field) thus awaits the acquisition of accurate quantitative data.

Further work based on the model framework of Anderson and May (1978) and May and Anderson (1978) has confirmed the existence of an unstable breakpoint for direct life-cycle dioecious helminths in a dynamic host population (Anderson, 1980a). Interestingly, the breakpoint phenomenon has as yet not been described as a result of any phenomenon other than the probability of worm pairing

in sexually dimorphous species. Using epidemiological data of hookworm infection in India and Taiwan, Anderson has suggested that in real communities, the breakpoint worm burden is likely to be so low (approximately 0.3 worms per host) that it would be of little value in disease control. Instead of reducing the mean worm burden in an effort to cross the breakpoint level, control programmes should perhaps be aimed at reducing transmission to below the threshold level (i.e. lowering the basic reproductive rate of the parasite to a value below unity). It should be emphasized that this is the only existing estimation of the precise value of the breakpoint based on epidemiological data. No comparable analysis of schistosome infections has as yet been carried out.

Improvements in model structure since the pioneering work of Macdonald give a good illustration of the limited use of theoretical techniques in the absence of relevant field and experimental data. Just as attempts at disease control are hampered in the absence of insight into the important aspects of parasite transmission and those parameters likely to be most sensitive to control perturbation, conclusions drawn from theoretical analysis must of necessity remain speculative unless suitable data is available.

To date, few practical studies have been carried out with the aim of supplying data in a form convenient for theoretical analysis. One exception, however, relates to recent laboratory investigations of an ectoparasitic fish digenean, *Transversotrema*

patialense. Although of no direct relevance to the economic problems of parasitic disease, this work has served to clarify several aspects of parasite population dynamics in general, which can then be put to use in an understanding of the dynamics of other host-parasite interactions (see Anderson, Whitfield *et al*, 1975; 1977; 1978a; 1978b; Mills *et al*, 1979). As a consequence of the paucity of specifically planned information, the potential benefits of joint theoretical and practical investigations are hindered at present by the necessity for parameter estimation from data resulting from studies originally designed for other purposes (e.g. Greenwood *et al*, 1925; 1936; Webster, 1946; Fenner, 1948; 1949; Stiven, 1964; 1967; 1968).

Although statistical methods of parameter estimation from conventional epidemiological information is a necessary development at the present time, close collaboration between field and theoretical epidemiology remains the first priority. If successful, this would optimize opportunities for efficient disease control, and might reduce the sometimes warranted criticism of theoretical methods as being intellectually respectable but capable of being safely ignored for all practical purposes (Greenwood, 1932).

SECTION 2

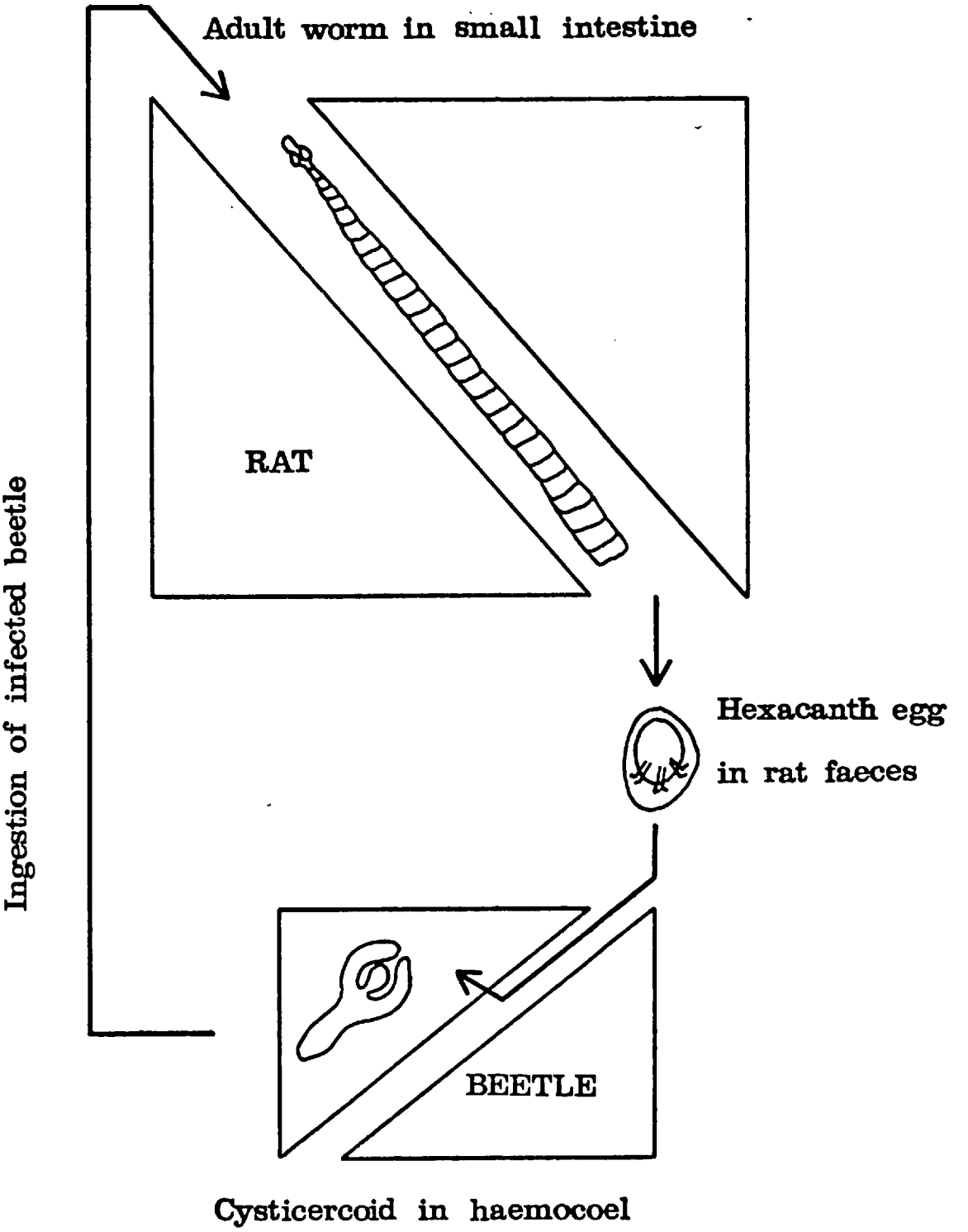
POPULATION DYNAMICS OF *H.DIMINUTA*.

2.1 THE BIOLOGY OF THE PARASITE.

The life-cycle of *Hymenolepis diminuta*, a cyclophyllidean cestode of widespread distribution,is diagrammatically portrayed in Figure 2.1.1. The adult worm develops in the intestine of the definitive host, and eggs are released with the host faeces. On ingestion by a suitable insect, the hexacanth embryo hatches in the midgut, penetrates the midgut wall, and develops to the cysticercoid stage in the haemocoel. The cycle is completed via a predator-prey link between the definitive and intermediate host.

In evolutionary terms, it is probable that the life-cycle developed in small rodents and their associated fleas, although successful cysticercoid development has now been demonstrated in more than 30 other insect species (Smyth, 1962). Rats are the most common definitive hosts; prevalence levels of between 3 and 50% having been recorded from various regions of the world (e.g. Ash, 1962; Calhoun, 1962; Habermann *et al*, 1954; Kitikoon *et al*, 1975; de Leon, 1964; Wiroreno, 1975). Infection of man has been noted in several areas including New Guinea (McMillan *et al*, 1971), Alabama (Ratliff and Donaldson, 1965), Iran (Ghadirian and Arfaa, 1972), Thailand (Chitchang *et al*, 1978) and Malaysia (Sinniah, 1978). In most cases, infection is thought to occur as a result of accidental ingestion of insects as contaminants of food items. The exception, however, is in certain regions of Malaysia, where live beetles are eaten as a folk medical practice in the treatment of a variety of ailments (Chu *et al*, 1977).

Figure 2.1.1 *Diagrammatic representation of the life-cycle of* Hymenolepis diminuta.


Adult worm in small intestine
RAT
Hexacanth egg
in rat faeces
Ingestion of infected beetle
BEETLE
Cysticercoid in haemocoel

Over the past 50 years, *H.diminuta* has become an important laboratory model for research in cestode physiology and biochemistry, as well as the mechanism of immune responses to helminth infections. The usual hosts for laboratory maintenance are the flour beetle, *Tribolium confusum* and the laboratory rat. In the present study, unless otherwise stated, the terms intermediate and definitive host will be used in reference to these two species.

H.diminuta has a high growth rate in the definitive host, with an initial mitotic index of 8.5 hours (Bolla and Roberts, 1971). Full length (of 200 - 600 mm) is achieved in 10 - 14 days post infection (Roberts, 1961),although growth is density-dependent (Section 2.5(vi)) and may also vary in response to the species of host (Read and Voge, 1954). Worms migrate anteriorly during their development (Crompton and Whitfield, 1968; Braten and Hopkins, 1969), possibly in response to changes in nutrient requirement (Mettrick, 1972). Age-dependent, developmental migration, however, must be distinguished from circadian movements (Tanaka and MacInnis, 1975) which were first described by Read and Kilejan (1969) and later shown to occur in response to host feeding (Hopkins, 1970; Bailey 1971). Recent research has been concerned with the so far unsuccessful delineation of the causal factors involved (Mead, 1976; Dunkley and Mettrick, 1977). The only conclusion which may be drawn to date is that migration is believed to be related to the optimization of opportunities for absorbing organic molecules produced by host digestion (Whitfield, 1979).

The mechanism of adult cestode nutrition, together with other aspects of physiology and biochemistry, has been extensively reviewed (e.g. Read and Simmons, 1963; Smyth, 1969). The surface of *H.diminuta* is a complex syncytium, which may produce its own digestive enzymes (Arme and Read, 1970) as well as bearing mechanisms for adsorption of those produced by the host (Read, 1973). In addition, there is evidence to suggest that the surface of the worm is able to inactivate substances such as trypsin (Pappas and Read, 1972) and lipase (Ruff and Read, 1973), which may be important in the prevention of autodigestion. There has been much controversy over the possible effect of host dietary variation on the growth and physiology of gut parasites such as *H.diminuta* (e.g. Hopkins and Young, 1967; Mettrick, 1968). Conclusions reached by Read (1959) and Dunkley and Mettrick (1969) indicate that most species are capable of using only certain monosaccharides, and that the availability of glucose in the intestinal lumen may be a limiting factor in the growth of *H.diminuta*.

Following infection of the definitive host, there is a time delay of 17 days before patency is achieved (Section 2.5(ii)). Viable eggs may be produced as a result of cross or self-fertilization, and eggs are released throughout the life of the worm (Section 2.5(iv)). The number of eggs produced, however, is highly density-dependent (Section 2.5(vi)). On release from the final host, the eggs are immediately infective, but hatching occurs only on ingestion by a susceptible intermediate host within the egg survival period (Section 2.3(i)). Descriptions of the structure of the embryonic envelopes of *H.diminuta* have been

given by Ogren (1961), Lethbridge(1971b) and Rybicka (1972). On hatching, the various coats are disrupted by the action of the host mouthparts and proteolytic enzymes, combined with the repeated cyclical movements of the 6 embryonic hooks (Voge and Berntzen, 1961; Berntzen and Voge, 1965; Ogren, 1972).

Survival of the hatched hexacanth has been shown to be age-dependent, with a maximum value of 11 hours (Anderson and Lethbridge, 1975). If successful completion of the life-cycle is to occur, penetration of the midgut wall of the intermediate host must take place within this period. Penetration is thought to be due to hexacanth movement together with the associated liberation of a secretion from the penetration gland which occurs within 2.5 hours of hatching (Lethbridge and Gijsbers, 1974). Experimental evidence suggests that the thickness of the midgut wall is a critical factor in determining the liklihood of successful transmission. A large proportion of those hexacanths which hatch in the midgut fail to penetrate, and die trapped within the tissues (Lethbridge, 1971a; Voge and Graiwer, 1964).

Once successful penetration has occurred, development to the cysticercoid stage takes place in the haemocoel, infectivity being achieved after a developmental time delay ranging from 5 days at 37°C to 65 days at 15°C (Voge and Turner, 1956). Development may be prevented by exposure to 39°C during the critical period, which corresponds to days 3 - 5 of normal development at 30°C

(Voge, 1959a; 1961). A detailed description of the 5 developmental stages into which the process of cysticercoid maturation may be divided has been given by Voge and Heyneman (1957). The site of development has been shown to depend on parasite burden. At low densities, most cysticercoids are found in the meso-metathorax, whereas at densities greater than 18 per beetle, most are found in the abdomen (Macdonald and Wilson, 1964). Survival and developmental time may also be density-dependent (Section 2.5(iv)).

Mature cysticercoids take up glucose, aminoisobutyric acid and sodium acetate via kinetically distinct transport loci (Arme *et al*, 1973). Some of the energy derived is presumably used for growth of the tail, which continues throughout the life of the cysticercoid (Prescott and Voge, 1959) and for the considerable cysticercoid motility which has been noted by Voge (1975). Once infectivity has been achieved, no further development takes place until the infected insect is ingested by a suitable definitive host. Several physiological factors are then necessary for excystment. Pepsin, combined with low pH, has a priming effect on the cysticercoid, after which bile salts cause surface alteration in addition to scolex movement. The action of trypsin on the cyst wall at elevated temperature then initiates excystment (Read, 1955; Rothman, 1959).

The newly-excysted worm attaches to the intestinal wall by means of the four acetabula present on the scolex, and begins

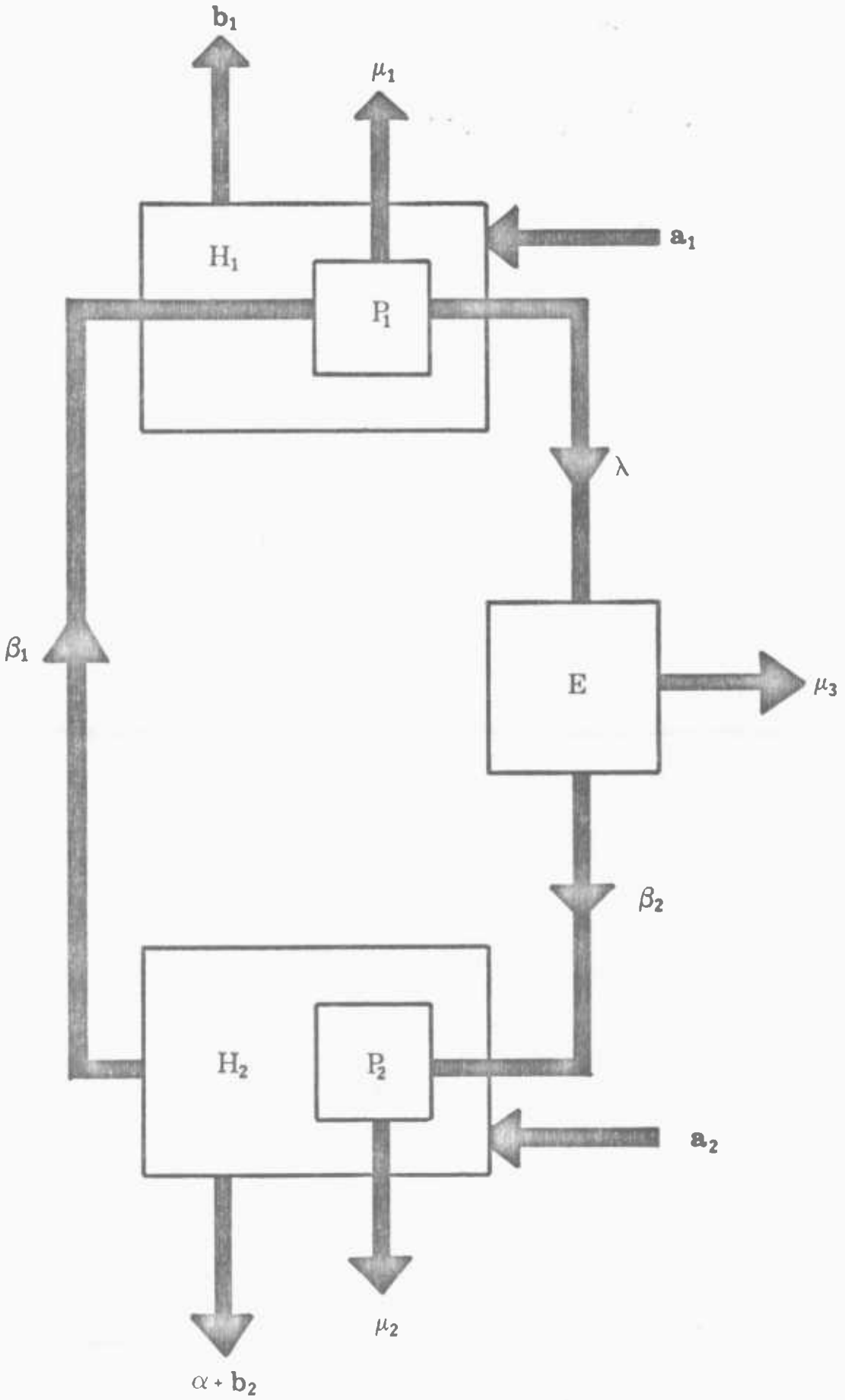
the generation of a new strobila. *H.diminuta* may survive for long periods in the definitive host, although survival is severely density-dependent (Section 2.5(vi)). In contrast with the cysticercoid in the intermediate host (Section 2.4(v)), the adult worm appears to have no marked pathogenic effect (Section 2.5(vii)).

With respect to the population dynamics of a host-parasite interaction, the life-cycle may be most clearly represented by means of a flow chart. The flow-chart for *H.diminuta*, together with definitions of the principal symbols used in this study, are given in Figure 2.1.2.

Figure 2.1.2 Representation of the life-cycle of H.diminuta *as a flow chart.*

Symbol	Definition
H_1	Density of final host population at time t
P_1	Density of adult worm population at time t
E	Density of parasite egg population at time t
H_2	Density of intermediate host population at time t
P_2	Density of cysticercoid population at time t
b_1	Instantaneous rate of final host mortality/ rat/unit time.
a_1	Instantaneous rate of final host fecundity/ rat/unit time
μ_1	Instantaneous rate of adult worm mortality/ worm/unit time
λ	Instantaneous rate of parasite egg production/ worm/unit time
β_2	Instantaneous rate of transmission to intermediate host/egg/unit time/beetle/unit area
μ_3	Instantaneous rate of parasite egg mortality/ egg/unit time
a_2	Instantaneous rate of intermediate host fecundity/host/unit time
b_2	Instantaneous rate of intermediate host mortality/host/unit time
α	Instantaneous rate of parasite-induced intermediate host mortality/parasite/unit time
μ_2	Instantaneous rate of cysticercoid mortality/ cysticercoid/unit time
β_1	Instantaneous rate of transmission to final host/ cysticercoid/unit time/rat/unit area

N.B. Other symbols used are defined in the text where appropriate.


b_1
μ_1
H_1
P_1
a_1
λ
β_1
E
μ_3
β_2
H_2
P_2
a_2
μ_2
$\alpha + b_2$

2.2 MATERIALS AND METHODS.

2.2(i) Host and parasite strains.

The strain of *H.diminuta* used in this study was kindly supplied by Dr. P. J. Whitfield, King's College, London. The parasite was maintained in Sprague-Dawley rats bred in the Department of Biochemistry, Imperial College, from a CFY strain obtained from Anglia Laboratory Animals. *T.confusum* was used as intermediate host, and was obtained from the Pest Infestation Control Laboratory, Slough.

2.2(ii) Maintenance of the definitive host.

Rats were maintained in an air-conditioned animal house at a temperature of 20 ± 2°C. They were given Oxoid Pellets (Herbert Styles Ltd.) and water, *ad libitum*.

2.2(iii) Maintenance of the intermediate host.

T.confusum was maintained in a flour-yeast medium consisting of 95% household flour and 5% dried brewer's yeast (by weight) passed through a 150μ sieve. All glassware and food, with the exception of yeast, was heat treated by exposure to 70°C in a

dry oven for a minimum of 6 hours to eliminate possible infestations of mites, psocids etc., and then allowed to cool before use.

Stock cultures were maintained in 2.5 litre glass jars containing approximately 300 gm flour-yeast medium. These were sealed with filter paper fixed to the rim using Sealastrip (Expandite Ltd.). At weekly intervals, approximately 500 beetles were taken from the oldest of the 7 cultures (which was then destroyed), placed in a new culture jar and left for 7 days for oviposition to occur. The adults were then removed and destroyed. By this method, a supply of beetles of approximately uniform age was available at any time.

Adult beetles could be most easily removed from stock cultures by allowing them to ascend filter paper strips placed in the culture jar. For experimental purposes, adults, pupae and larvae could be removed from a culture jar by the use of a 1mm sieve, and eggs by a 250μ sieve. All stages were handled using a fine paintbrush, the methods of aspirator use recommended by Hoy (1965) being found unnecessary. Both stock and experimental cultures were maintained in a constant temperature room at $30 \pm 1^{\circ}C$ and 70% relative humidity. At intervals during the period in which the stocks were maintained, samples of beetles were screened for viral, bacterial and fungal pathogens at the Unit for Invertebrate Virology, Oxford.

2.2(iv) Infection of the definitive host.

Cysticercoids were obtained by careful dissection of infected beetles in distilled water, and transferred within 30 minutes to a disposable 1 ml syringe bearing a curved needle with a bore diameter of 1mm. Rats were infected while under light carbon dioxide anaesthetization, by insertion of the needle into the pharynx to elicit a lapping reaction. The number of worms established was determined by counting the number of scolices present in the intestine of dissected rats at 4 weeks post infection. At a dose level of 10 cysticercoids per rat, this method resulted in recovery of 9.29 ± 0.37 adult worms. Unless otherwise stated, the rats used were 6-week old males weighing 180 ± 10 gm. Each rat was given a standard dose of 10, 16-18 day old cysticercoids.

2.2(v) Infection of the intermediate host.

As standard practice, infection of *T.confusum* with *H.diminuta* was carried out using glass arenas 13cm^2 in basal area. These were sealed using plastic covers fitted with a 2.5 x 2.5cm filter paper insert. For stock infections, starved beetles were allowed to feed on worm proglottids (obtained from fresh faeces) for 24 hours. For experimental infections, it was necessary to obtain a suspension of *H.diminuta* eggs of known density. Faeces from 12 rats with tapeworm infections of known

age and intensity (10 worms at 8 weeks post infection, unless otherwise stated), were collected over a 4 day period, and the tapeworm eggs recovered using a modification of the sucrose gradient method described by Lethbridge (1971c). Sucrose gradients were created in 4, 30ml centrifuge tubes, using 6ml of each of the following sucrose concentrations: 347gm/l, 406gm/l and 693gm/l. The faecal sample was covered in water, allowed to soak for 30 minutes and then macerated in a pestle and mortar. The homogenate was passed first through a 150μ sieve and then through a 53μ sieve. The sediment remaining in the latter was distributed between the 4 sucrose gradients which were then centrifuged at 170g for 5 minutes. Eggs were removed by pipette from the interface between the 347gm/l and the 406gm/l sucrose solutions. The eggs were washed by resuspension and centrifugation in distilled water. The density of the resultant egg suspension was estimated using an Improved Neubauer haemocytometer. Repeated estimation of the density of a single egg suspension (mean density 3000 eggs/ml) gave results of which the 95% confidence limits were 200 eggs/ml.

To expose a population of *T.confusum* to an estimated number of *H.diminuta* eggs, a specified volume of egg suspension was pipetted onto filter paper lining the base of the infection arena. Since it was found that eggs extracted by this method did not retain their infectivity in suspension at 4°C for longer than 48 hours (in contrast with the results of Hundley and Berntzen, 1969), infection was always carried out immediately after egg extraction. After exposure, the filter paper bearing the eggs was removed from the arena, and approximately 30gm flour-yeast medium introduced. After 2 weeks, the parasite

burdens of the beetles were determined by dissection of each specimen under low-power magnification. Repeated exposure of 10 beetle populations (each of 30 beetles) to 0.5ml samples from a stock egg suspension (estimated density 3000 eggs/ml) gave values for the mean parasite burden of the exposed beetle population of which the 95% confidence limits were 0.8 cysticercoids per beetle. Although time-consuming, the method of parasite burden determination described above resulted in greater accuracy than the radiographic detection technique described by Zeakes *et al* (1971) and less damage to the cysticercoids than the homogenization technique described by Ridley and MacInnis (1968). A 'standard infection' is defined as one in which 30 beetles (14 - 21 days post eclosion) were exposed to a specified density of *H.diminuta* eggs for 3 hours, having previously been starved for 6 days.

2.2(vi) Faecal egg counts.

Faecal egg counts were made using a modification of the McMaster technique. A faecal sample of 1gm fresh weight was ground up to form a homogenate with 29ml saturated salt solution. The homogenate was then passed through a 150μ sieve to eliminate large faecal particles. The remaining suspension was mixed thoroughly, and 4 samples were transferred to McMaster counting chambers using a wide-bore pasteur pipette. After 2 minutes to allow for egg flotation, counts of the number of eggs per chamber

were made. This process was then repeated using a second 1gm faecal sample, so that each egg count was computed as the mean of 8 replicates. Since the volume of the counting chamber was 0.15ml, the number of eggs per gm faeces could be calculated, where

no. eggs/gm faeces = no. eggs/McMaster chamber x 200 (2.2.1)

2.3 INFECTION OF THE INTERMEDIATE HOST.

Infection of *T.confusum* by *H.diminuta* occurs as a result of ingestion of infective parasite eggs by susceptible beetles. Section 2.3 describes an experimental investigation of some of the factors influencing transmission, for example egg survival, duration of exposure to infection, density and spatial distribution of parasite eggs, and host population density. Factors influencing the susceptibility of beetles to infection, such as host age and sex, and the possibility of an acquired host resistance to infection are also discussed.

2.3(i) Egg survival.

Under natural conditions.

As well as variation in the initial infectivity of eggs on release from the parent worm (see Section 2.5), the rate of transmission of *H.diminuta* from the definitive to the intermediate host is affected by both the survival of eggs in the external environment, and the survival of the hexacanth embryos once released from the eggshell. Using motility as an index, the maximum survival time of free hexacanths has been estimated as 11 hours (Anderson and Lethbridge, 1975). Since hatching does not normally occur until the egg has been ingested by a suitable intermediate host, and since penetration to the haemocoel of

Tenebrio molitor takes place within 90 minutes of an egg meal (Lethbridge, 1971a), hexacanth survival as determined by depletion of food reserves is unlikely to be a limiting factor in parasite transmission.

On the other hand, transmission is dependent on the survival of the egg in the external environment until encounter with a suitable intermediate host is made. Egg survival and the way in which this is affected by environmental conditions is thus likely to play an important part in determining the rate of intermediate host infection. Cestode eggs are non-motile and non-feeding, and tend to have fairly long expected lifespans under natural conditions. Factors affecting the infectivity of Taeniid eggs have been reviewed by Lawson and Gemmell (in preparation), but few estimates of the survival of *H.diminuta* eggs are available.

There are two principal methods by which egg survival may be assessed. The first is to measure the proportion of eggs which hatch successfully when hatching is initiated *in vitro*. Using this method, survival of *H.diminuta* eggs in rat faecal pellets has been estimated as approximately 40 weeks at 10°C, 20 weeks at 20°C and 2 weeks at 28°C (Coleman, 1978). The second method is to measure the infectivity of the eggs to the intermediate host. Since infectivity, rather than survival, is of importance with respect to parasite population dynamics, the latter method was used throughout the present study, and the term survival will hereafter be used in reference to the time-dependent

maintenance of egg infectivity.

Standard infections were carried out using eggs extracted from faecal pellets which had been stored at 10°C for varying periods of time. All faecal samples had been obtained from the same group of 12 infected rats over periods of 4 days. It may be assumed that the initial infectivity of the eggs released by the worms did not change over the 24 day period of faecal collection (see Section 2.5). The parasite burdens of host populations each exposed to 1500 *H.diminuta* eggs are depicted in Figure 2.3.1(a). Since all beetle populations were of the same age at the time of infection, the results give an indirect indication of the survival of the eggs within the faecal pellet. A good fit to the data is obtained by use of the following age-dependent survival model (Anderson and Whitfield, 1975)

$$dN_t/dt = - \mu(t)\ N_t \qquad (2.3.1)$$

where N_t is the number of eggs surviving to time t (as indicated indirectly by the resultant parasite burden per host), and $\mu(t)$ is the age-dependent instantaneous rate of egg mortality per egg per unit time. This model may be fitted to the experimental data by assuming that $\mu(t)$ is constant over small intervals of time, so that

$$\mu(t+0.5) = \ln N_{t-1} - \ln N_t \qquad (2.3.2)$$

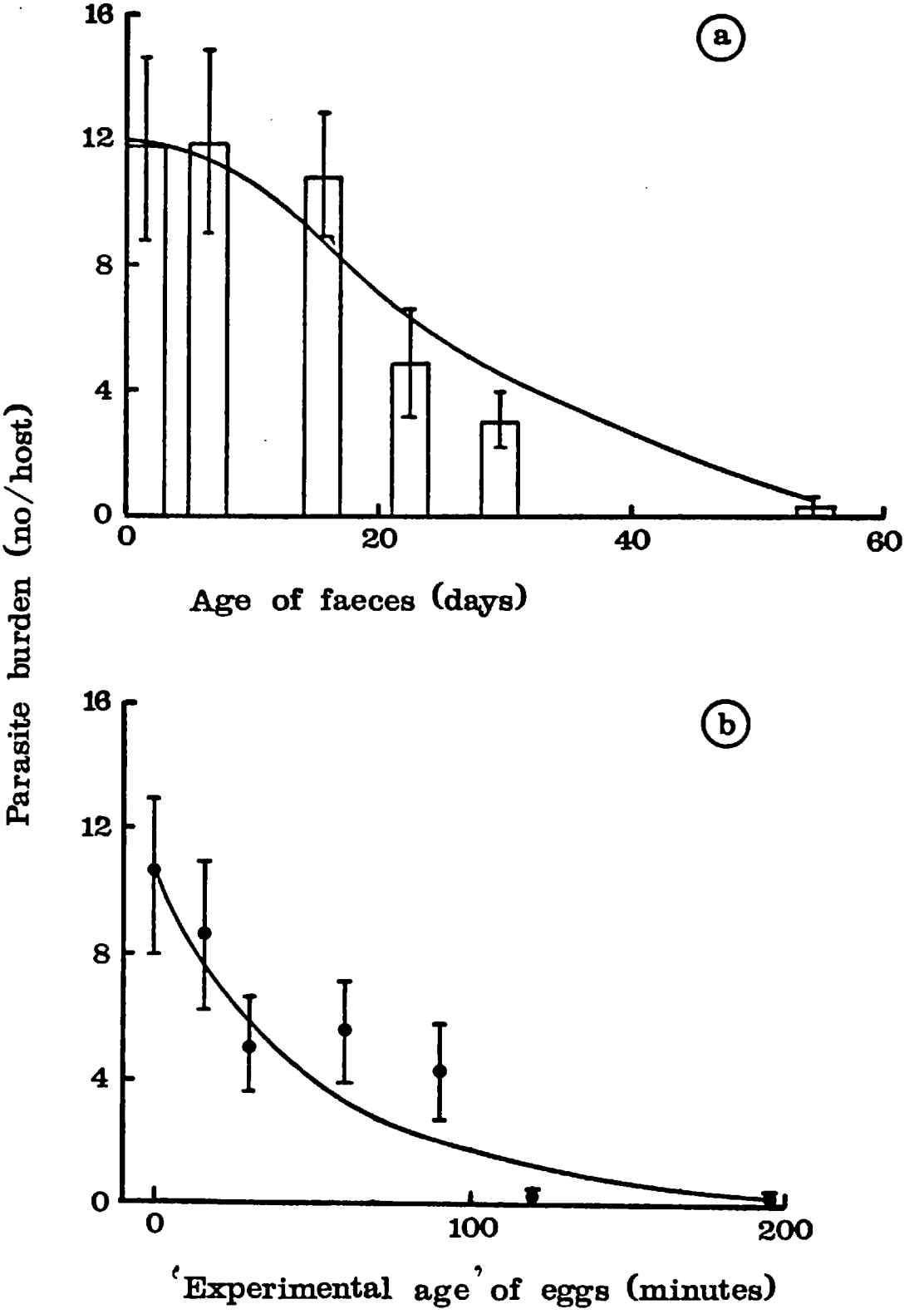
where N_{t-1} and N_t are the number of eggs surviving at the beginning

Figure 2.3.1 *Survival characteristics of* H.diminuta *eggs as measured by their infectivity to the intermediate host.*

The solid circles and histogram bars represent observed means, and the vertical bars give the 95% confidence limits of the means. The solid lines represent the predictions of the age-dependent survival model defined in equation (2.3.4).

(a) Survival of eggs maintained in rat faecal pellets at 10°C (m=0.02, n=0.002).

(b) Survival of eggs under 'experimental conditions' (see text) (m=0.02, n=0.03).


a
16
12
8
4
0
0
20
40
60
Age of faeces (days)
b
16
12
8
4
0
0
100
200
'Experimental age' of eggs (minutes)
Parasite burden (no/host)

and end of a time interval small in comparison with the total experimental time period. The relationship between t and $\mu(t)$ calculated in this manner may be described empirically by the equation

$$\mu(t) = m \exp.(nt) \qquad (2.3.3)$$

and estimates of the constants m and n may then be obtained by linear regression of $\ln \mu(t)$ on t. The model may then be fitted to the data by substitution of the estimated values of m and n in the solution of equation (2.3.1), given by

$$N_t = N_o \exp\left(m \left(1 - \exp(nt) \right) / n \right). \qquad (2.3.4)$$

Although the age-dependent characteristics of a survival process are of some importance to host-parasite population dynamics, they are often omitted in population models which aim to capture only the essential features of an interaction. To obtain an order of magnitude estimate of the expected lifespan of *H.diminuta* eggs, it is assumed as an approximation that they exhibit a constant instantaneous rate of mortality per egg per unit time (μ_3). Then

$$1/\mu_3 = \sum_{t=o}^{\infty} p(t).t \; / \sum_{t=o}^{\infty} p(t) \qquad (2.3.5)$$

where p(t) is the probability of survival of an egg to an age of t time units, and $1/\mu_3$ is the expected lifespan. Using the data

given in Table 2.3.1(a), $1/\mu_3$ may be estimated as approximately 12 days. The instantaneous per capita mortality rate of eggs maintained in faecal pellets at 10°C is thus approximately 0.09/egg/day. This value will be used in Section 3 as an approximate estimate of the survival of *H.diminuta* eggs under natural conditions, although it is realized that the magnitude of this parameter will be subject to considerable variation as a result of fluctuation in factors such as temperature, humidity and microbial contamination (Gemmell, 1977). The estimate obtained in the present study is substantially different from the results given by Coleman (1978), illustrating that parasite survival and infectivity are not equivalent, and should be carefully distinguished.

Under experimental conditions.

Since desiccation (compounded by high temperature) is an important factor in relation to egg survival, the experimental conditions under which *T.confusum* was exposed to infection by *H.diminuta* (Section 2.2(v)) were obviously non-optimal for parasite survival. To test the duration of infectivity of eggs under experimental conditions, 7 standard infection arenas were set up, each containing an estimated density of 1500 parasite eggs. Beetle populations were introduced into each arena after periods varying from 0 to 195 minutes following the introduction of the egg suspension. The exposure period was maintained constant at 24 hours from the introduction of the beetles. The resultant

parasite burdens of the exposed host populations are shown in Figure 2.3.1(b).

Egg infectivity, under the specified conditions, declines almost to zero in the space of 3 hours. Survival is age-dependent (as seen by the fit of the model defined in equation (2.3.4)), but less markedly so than under natural conditions. This pattern is characteristic of populations in which the natural period of survival (as defined by senescence) is curtailed by stress-induced mortality. Using equation (2.3.5), approximate estimates of the instantaneous mortality rate (μ_3) and expected lifespan ($1/\mu_3$) of the eggs under experimental conditions are obtained as 0.03/egg/minute and 33 minutes respectively.

2.3(ii) Exposure duration.

In any infection process, the duration of the period during which hosts are exposed to infective parasites will obviously affect the resultant parasite burden of the host population. This relationship has been discussed with respect to snail infection by miracidia (Anderson 1978b) and infection of the fish, *Brachydanio rerio* by cercariae of the ectoparasitic digenean, *Transversotrema patialense* (Anderson, Whitfield *et al*, 1978a). In both cases, when the infective-stage density at the start of infection experiments is held constant, the mean number

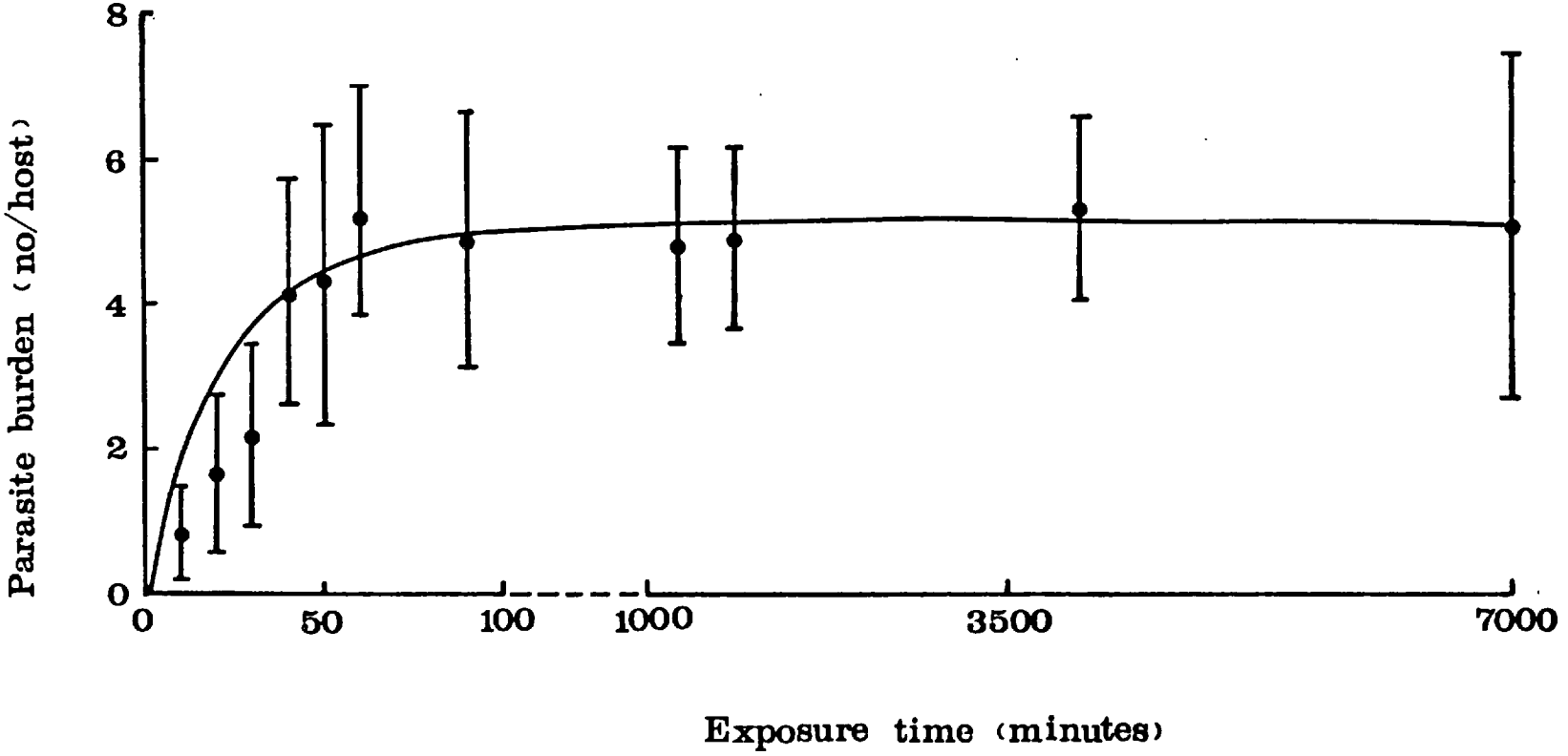
of successful infections per host rises to a plateau as the time of exposure to infection lengthens. The height of the plateau is determined by the initial number of infective-stages present and the magnitude of the rate of infection. In the *T.patialense* system, the relationship is complicated by the fact that the fish host also acts as a predator of the cercarial infective-stages.

No detailed reports have been given, to date, concerning the effect of variation in exposure time on infection of *T.confusum* by *H.diminuta*. Although Dunkley and Mettrick (1971) state that the number of cysticercoids established is influenced by exposure time, their results show only that exposure of beetles to a second batch of parasite eggs immediately after infection results in a significant increase in the resultant parasite burden. In order to investigate this relationship more closely, 11 infection arenas were set up, each containing an estimated density of 500 parasite eggs. Populations of 30 beetles, which had been starved for 6 days, were introduced into each arena, and left for exposure periods varying from 10 to 7,000 minutes. The results show that the mean parasite burden of the exposed host population rises with increasing exposure time, reaching a plateau after approximately 60 minutes (see Figure 2.3.2).

Two factors affect the form of this relationship. First, as infection proceeds, the pool of infective-stages which may be encountered by the exposed host population declines, effectively decreasing the net rate of infection through time. Second, the

Figure 2.3.2 *The relationship between the duration of exposure and the resultant parasite burden of the exposed host population.*

The solid circles represent observed mean values, and the vertical bars give the 95% confidence limits of the means. The solid line indicates the predictions of the model defined in equation (2.3.9); $H=30/13cm^2$, $E_o=500/13cm^2$, $\mu_3=0.03$/egg/minute and $\beta_2=0.0004$/egg/minute/host/$13cm^2$.


Parasite burden (no/host)
8
6
4
2
0
0
50
100
1000
3500
7000
Exposure time (minutes)

expected lifespan of 33 minutes estimated in Section 2.3(i) indicates that death of infective-stages begins to occur within the experimental exposure period, causing additional depletion of the pool of viable eggs. If it is assumed that the instantaneous rate of infection per egg per unit time per host per unit area, β_2, is constant and proportional to the density of living, infective eggs, E, and the number of hosts per unit area, H_2 (as conventionally assumed in epidemiological models, see Section 1), then the temporal change in the parasite burden of the exposed host population is described by the differential equation

$$dP_2/dt = \beta_2 E H_2. \qquad (2.3.6)$$

Similarly, assuming that the instantaneous rate of egg mortality per egg per unit time, μ_3, is constant and independent of egg age or density, then the change in the number of infective eggs remaining in the infection arena through time is given by

$$dE/dt = - \mu_3 E - \beta_2 E H_2. \qquad (2.3.7)$$

Given that the number of eggs present in the arena at the start of an infection experiment (when t=0) is E_o, equations (2.3.6) and (2.3.7) have the solutions

$$E = E_o \exp (- (\mu_3 + \beta_2 H_2) t) \qquad (2.3.8)$$

and

$$P_2 = \frac{\beta_2 H_2 E_o}{(\mu_3 + \beta_2 H_2)} \left[1 - \exp (- (\mu_3 + \beta_2 H_2) t) \right] \quad (2.3.9)$$

Inherent in this model are three simplifications. First, the rate of egg mortality is assumed to be constant. As shown in Section 2.3(i), egg survival is, in fact, age-dependent, but may be approximated by a constant value of 0.03/egg/minute. Second, the infection rate, β_2, is not, in reality, directly proportional to the density of viable eggs, as a result of complications imposed on infection dynamics by the feeding behaviour of the host (see Section 2.3(v)). The assumption of direct proportionality is, however, thought to be justifiable at this experimental egg density. Lastly, the model is based on the assumption that all hosts are equally susceptible to infection, and that the infection events are independent of each other (i.e. random). Although this represents a further approximation (see Section 2.3(vi)), heterogeneity in infection does not affect the mean parasite burden per host, only the statistical distribution around the mean. Interestingly, the tendency for increased over-dispersion of parasite numbers per host as exposure duration becomes greater (as indicated by the size of the confidence limits shown in Figure 2.3.2), is a direct consequence of heterogeneity in infection within the experimental arena. A constant degree of heterogeneity in the *T.patialense / B.rerio* association, for example, has been shown to result in increased variance/mean ratios as infective-stage density rises (Anderson, Whitfield *et al*, 1978a).

Given these limitations, the experimental design described in this section provides an approximate method of estimating the value of the transmission parameter, β_2. Transmission parameters are always difficult to measure under both laboratory and field conditions, and very few detailed estimates are as yet available for host-parasite systems. From equation (2.3.9), it is clear that, as $t \to \infty$, $P_2 \to (\beta_2 H_2 E / (\mu_3+\beta_2 H_2))$, and thus the value of β_2 may be obtained from the mean parasite burden at the plateau in Figure 2.3.2. Substituting the values μ_3=0.03/egg/minute, H_2=30/13cm², and E_o=500/13cm², the estimated value of β_2 is 0.0004/egg/minute/host/13cm², (or 7.5×10^{-8}/egg/day/host/hectare). The predictions of the model described by equation (2.3.9) are shown in Figure 2.3.2.

It should be noted that the transmission parameter estimated in this section has a precise biological interpretation. The parameter β_2 may be considered as the product of two subsiduary parameters, $\bar{\rho}$ and $\hat{\beta}$, where $1/\hat{\beta}$ represents the average duration of the interval between egg-beetle contacts, and $\bar{\rho}$ is the average probability that such a contact results in successful infection. Unfortunately, no successful method of measuring the value of $\bar{\rho}$ was found in the present study (see Section 2.3(v)).

2.3(iii) Host density.

In models of infection processes, the rate of infection is generally assumed to be directly proportional to the number of

host organisms present. It has been pointed out, however, that an increase in host density beyond a certain level will not result in increased parasite acquisition per unit of time if there are only a finite number of infective-stages available (Macdonald, 1961; Anderson and May, 1978). The nature of the relationship between host density and the mean number of infections per host has been clarified with respect to the infection of snails by miracidia (Anderson, 1978b), but no detailed experimental results for this system are as yet available.

In order to highlight the effects of host density on infection dynamics in the present study, experimental conditions were chosen such that egg density was likely to prove a limiting factor. Standard infection arenas were set up, each containing an estimated density of 50 *H.diminuta* eggs. Beetles which had been starved for 6 days were immediately introduced into each of the 5 arenas in population sizes varying between 5 and 75. They were removed after an exposure period of 24 hours, and dissected 2 weeks later. The results are shown in Figure 2.3.3.

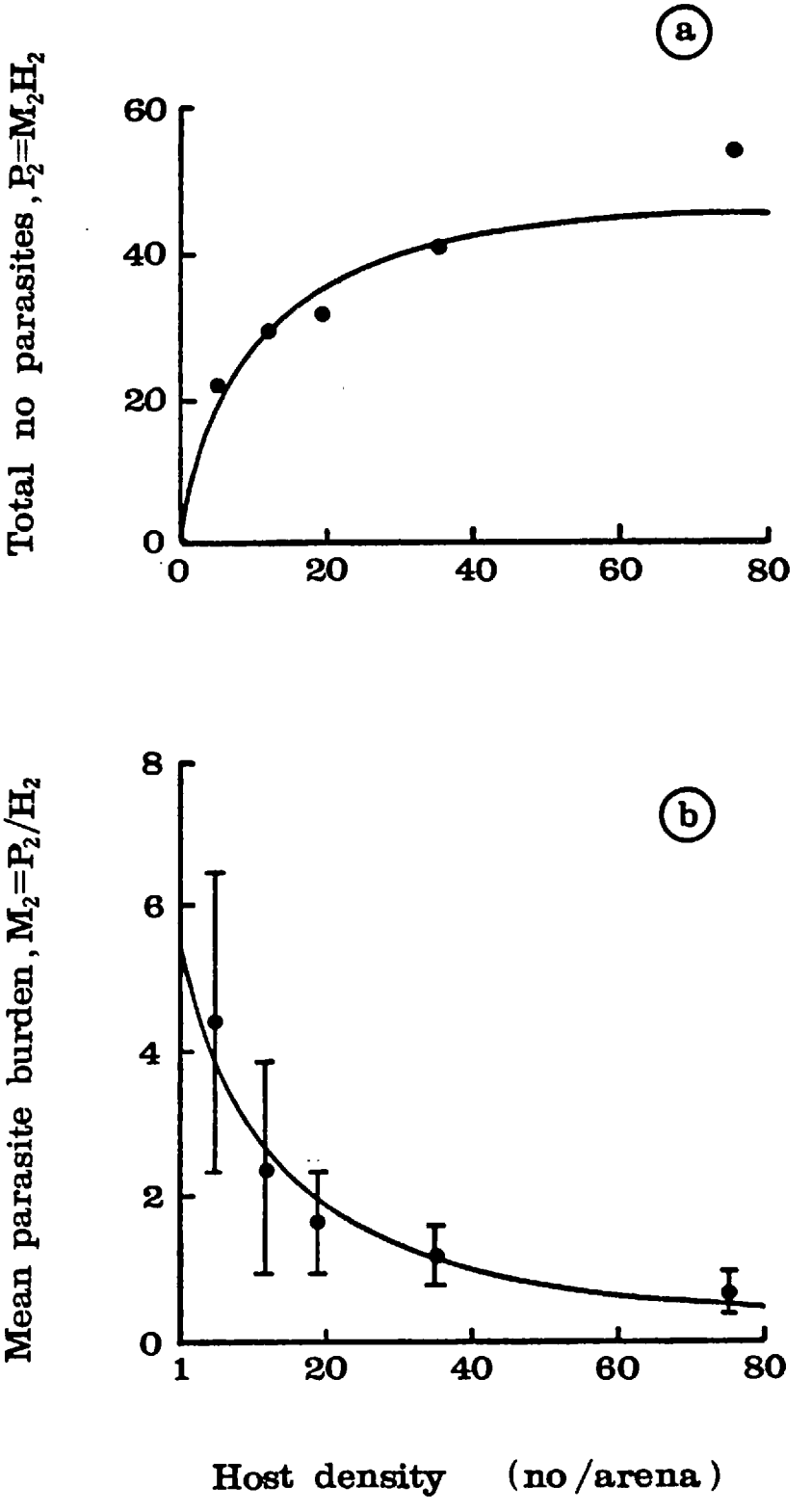
Under the specified experimental conditions, increased host density results in an increase to a plateau in the total number of infections, and a simultaneous exponential decline in the mean number of infections per host. The dynamics of infection has been discussed in Section 2.3(ii) and may be described by the model defined in equation (2.3.9). The predictions of this model are shown in Figure 2.3.3. The exceptionally good fit to the

Figure 2.3.3 *The relationship between host density and the resultant parasite burden of the exposed host population.*

(a) The total number of parasites in the host population, $P_2=H_2M_2$.

(b) The mean parasite burden per host, $M_2=P_2/H_2$.

The solid circles represent observed values and the vertical bars give the 95% confidence limits of the means. The solid lines indicate the predictions of the model defined in equation (2.3.9). Parameter values: $E_o=50/13cm^2$, t=24 hours, $\mu_3=0.03$/egg/minute, $\beta_2=0.004$/egg/minute/host/$13cm^2$.


a
Total no parasites, $P_2=M_2H_2$
60
40
20
0
0
20
40
60
80
b
Mean parasite burden, $M_2=P_2/H_2$
8
6
4
2
0
1
20
40
60
80
Host density (no/arena)

data indicates that processes such as interference between searching hosts are not detracting from the appropriateness of the model in the description of infection within the experimental arena. It is important to note that an increase in host density is exactly equivalent to an extension of the period of exposure to infection (see equation (2.3.9)). The process of fitting the model to the experimental data yields an independent estimate of the value of the transmission parameter β_2, of 0.004/egg/minute/host/13cm^2, which should be compared with the estimate obtained in Section 2.3(ii). The tenfold difference between the two estimates may be related to one or more of a number of possible errors, the most likely of which are differences in egg viability or beetle behaviour between the two series of experiments. The precise explanation of the discrepancy is unknown.

The data obtained from this experimental work highlight one of the most important sources of experimental error in this study. The total number of infections arising from the exposure of a host population of 75 is greater than the estimated number of infective eggs introduced into the arena. This is indicative of the margin of error inherent in the egg density estimation procedure used (see Section 2.2(v)).

2.3(iv) Density-dependence in cysticercoid establishment and growth.

There are two principal mechanisms which could possibly generate density-dependence in larval parasite population growth within a single intermediate host. First, reactions mounted by the host in response to parasitic invasion might serve either to prevent cysticercoid establishment, or to reduce the survival potential of established larvae (see Section 2.5(iv)). However, although encapsulation reactions in insects are well documented (Nappi, 1975; Lackie, 1980), Heyneman and Voge (1971) have reported that no such reaction is mounted by *T.confusum* against cysticercoids of *H.diminuta*. They conclude that there is no effective host resistance to the establishment of the parasite. Two mechanisms have been proposed which might explain this phenomenon. In 1970, Ubelaker *et al* reported the presence of a possible defence mechanism on the part of the cysticercoid against beetle haemocytes, in the form of secretory microvilli. Alternatively, it has been suggested that inherent similarity between the larval surface and the host tissues might prevent recognition of the parasite by the host's haemocytes (Lackie, 1976).

In order to test experimentally for the existence of density-dependence in parasite establishment, beetle populations were repeatedly exposed to *H.diminuta* infection as follows. A group of 180 beetles of uniform age was starved for 6 days, and then divided into 6 populations of 30 beetles each. On the 7th

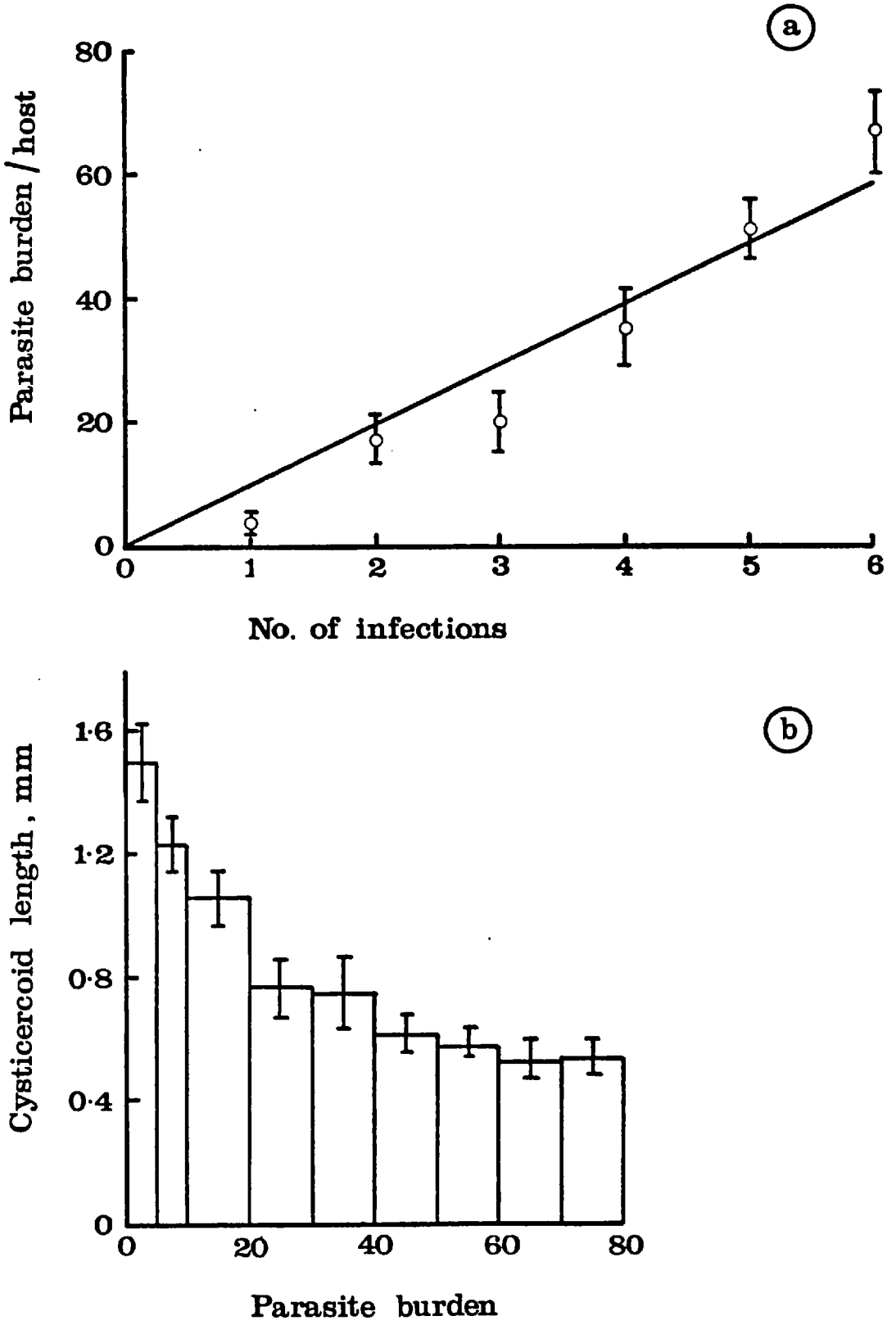
day, each population was exposed to an estimated density of 1500 *H.diminuta* eggs for 3 hours and then fed. This infection process was repeated at weekly intervals, omitting 1 beetle population on each successive week. Throughout the experiment, all 6 populations were exposed to the same regime of feeding and starvation. After 6 weeks, groups of beetles were available which had been exposed to infection 1 to 6 times respectively. After a further 2 weeks to allow development of the cysticercoids arising from the most recent infection, the beetles were dissected, and their parasite burdens determined. The results are depicted in Figure 2.3.4(a).

There is an indication of non-linearity in the relationship between the number of exposures to infection and the resultant mean parasite burden of the exposed host population, which could possibly be due to facilitated hexacanth penetration at high parasite burdens, as a result of increasing damage to the midgut wall. However, the mean parasite burden of the population exposed to a single infection is exceptionally low, and it seems likely that an appearance of non-linearity is created by the inclusion of this aberrant point. Furthermore, the best-fit model to the data is of linear form (see Figure 2.3.4(a)) and it will hereafter be assumed that there is direct proportionality between the number of exposures to infection and the resultant mean parasite burden per host. This indicates that, at least over the experimental exposure range, there are no density-dependent constraints on parasite establishment within individual beetles.

Figure 2.3.4 Density-dependence in cysticercoid establishment and growth.

(a) The relationship between the "number of infections" (see text) and the resultant parasite burden of the exposed host population. The points represent observed means, and the vertical bars give the 95% confidence limits of the means. The solid line indicates the predictions of the best-fit linear model, $M_2=9.9x$, where M_2=mean parasite burden per host and x=no. infections. N.B. Correlation coefficients (r^2): linear model = 0.97; exponential model = 0.89.

(b) The relationship between parasite burden and cysticercoid length. The histogram bars are observed mean values, and the vertical bars represent the 95% confidence limits of the means.


a
Parasite burden / host
80
60
40
20
0
0
1
2
3
4
5
6
No. of infections
b
Cysticercoid length, mm
1·6
1·2
0·8
0·4
0
0
20
40
60
80
Parasite burden

The process of repeated infection described above forms the basis of further experimental work described in Section 2.4. From the results shown in Figure 2.3.4(a), a factor of proportionality of 9.9 (i.e. the gradient of the linear model) may be used in replacement of the observed 'number of infections' by an estimate of the resultant mean parasite burden per host, in the analysis of further results pertaining to the use of this experimental infection method. It is of interest to note that these results give an estimate of the ratio of successful parasite establishment to egg exposure density of 20% for a 3 hour exposure period.

A second mechanism possibly involved in the generation of density-dependence in parasite population growth is intraspecific competition for a limiting resource. Although it has been established that cysticercoids take up host glucose (Voge, 1959b; Arme *et al*, 1973), the possibility that food or space might constitute limiting resources has never been conclusively tested. Reports on the manifestation of density-dependent growth in larval *Hymenolepis* spp. vary considerably. Soltice *et al*(1971) found no correlation between infection intensity and cysticercoid volume in *H.diminuta*, whereas several authors have reported a decrease in capsular membrane thickness and tail length in cysticercoids from hosts with heavy infections (Voge and Heyneman, 1957; Dunkley and Mettrick, 1971). No cases of decreased cysticercoid viability have been described (Section 2.5(iv)), in contrast to the situation in *H.nana*, in which a decrease in infectivity and an increase in developmental time have been noted

at high parasite burdens (Schiller, 1959; Voge and Heyneman, 1957; Heyneman, 1958).

In order to gain a quantitative assessment of the relationship between parasite burden and cysticercoid size, groups of 10 parasites from hosts with differing levels of infection were measured (length from anterior to posterior including tail). The results are shown in Figure 2.3.4(b). The size of established cysticercoids clearly declines as parasite burden increases, indicating that competition for nutrient resources, or, more probably, for space, is operative once the parasites are established within the coelom. Although no experiments were carried out to investigate the generative mechanism, the results would comply with the hypothesis that there exists a 'growth capacity' for the insect haemocoel (c.f. Meakins and Walkey, 1973).

2.3(v) Egg density.

In cases where the transmission of parasites from host to host is achieved by means of a free-living infective-stage, the rate of encounter is influenced by both the densities of the organisms concerned and their respective spatial distributions (Crofton, 1971a; 1971b; Anderson, 1978a). Recent studies have explored the impact of infective-stage density on the dynamics of parasite transmission in associations where infection takes

place by means of parasite attachment to the surface of the host (Anderson, Whitfield *et al*, 1978a), or direct penetration of the host epithelial layers (Anderson, 1978b). In both cases, transmission was found to be directly proportional to the number of infective-stages to which the hosts were exposed.

Infection of *T.confusum* by *H.diminuta* might be expected to have different transmission properties, since it occurs as a result of parasite ingestion. It is hence directly comparable to a predator-prey association in which the number of prey items eaten can be assessed by its relationship to the number of parasites which develop. Several observations on the effect of *H.diminuta* egg density on the infection of the intermediate host have been made (Soltice *et al*, 1971; Dunkley and Mettrick, 1971; Coleman, 1978). Their qualitative nature however, is concordant with the earlier observation that quantitative egg feedings are not normally employed (Kelly *et al*, 1967).

In the present study, the influence of infective-stage density was assessed by setting up 10 arenas containing estimated egg densities varying from 60 to 6000. Populations of 30 beetles (which had been starved for 6 days) were immediately introduced into each arena and left for an exposure period of 24 hours. The relationship between egg density and the resultant mean parasite burden per host is clearly non-linear (see Figure 2.3.5(a)), rising to a plateau of between 15 and 20 larvae per beetle. The two principal mechanisms which might generate such a pattern are as follows.

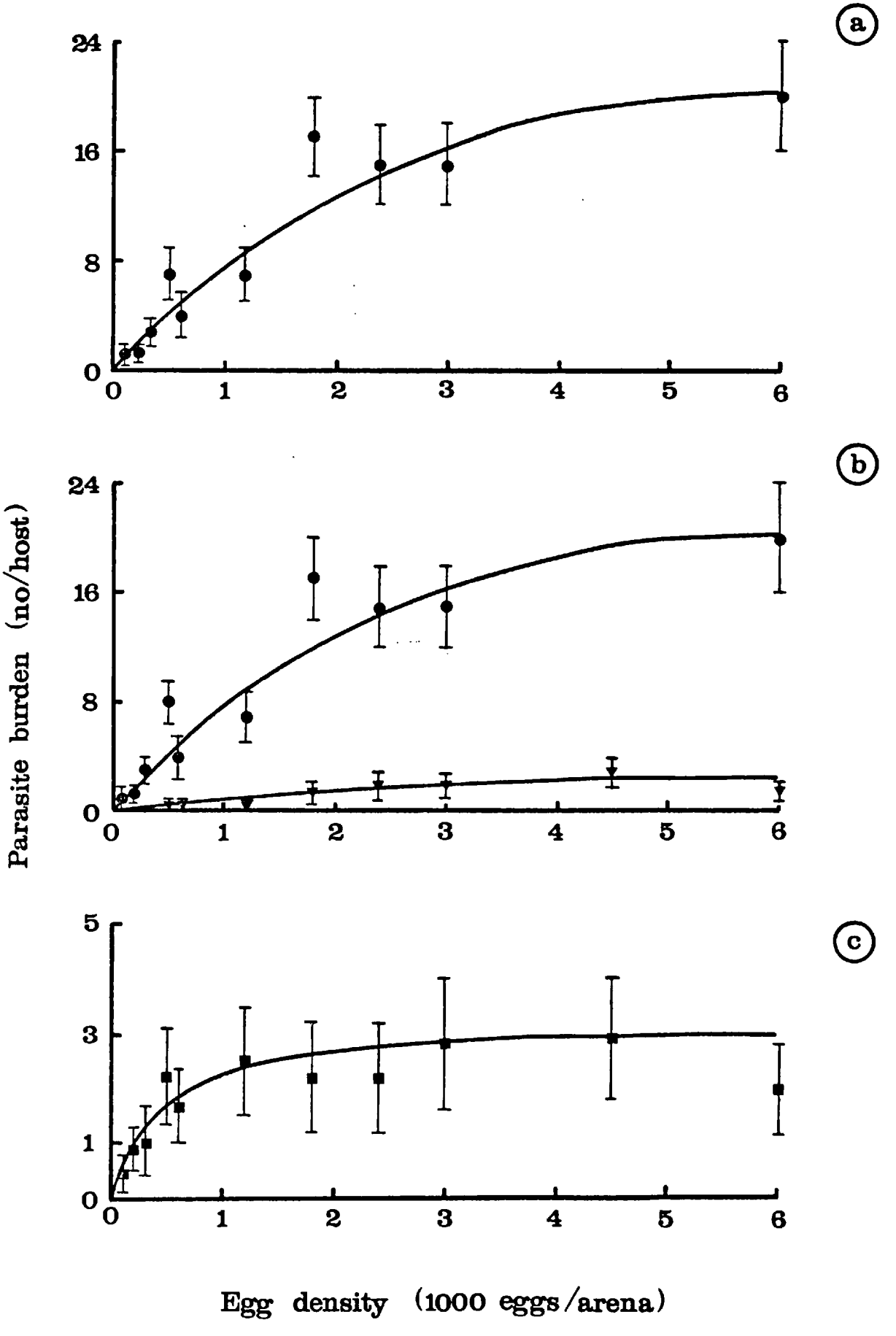
Figure 2.3.5 *The relationship between infective-stage exposure density and the resultant parasite burden of the exposed host population.*

The points are observed means and the vertical bars represent the 95% confidence limits of the means. The solid lines indicate the predictions of the functional response model as defined in equation (2.3.13).

(a) Beetles starved for 6 days; exposure period 24 hours (υ=0.016/beetle/hour, t_h=0.63 hours).

(b) Upper curve as in (a). Lower curve: beetles satiated; exposure period 24 hours (υ=0.001/beetle/hour, t_h=1.05 hours).

(c) Beetles starved for 6 days; exposure period 0.25 hours (υ=0.0005/beetle/minute, t_h=0.15 minute).


a
b
c
24
16
8
0
5
3
1
0 1 2 3 4 5 6
Parasite burden (no/host)
Egg density (1000 eggs/arena)

Density-dependent constraints.

The possible occurrence of density-dependent constraints on parasite population growth within individual hosts has been discussed in Section 2.3(iv). The number of parasites established per host was found to rise linearly with increasing number of exposures to infection, up to parasite burdens of 60/beetle. Density-dependent constraints are thus not considered to be involved in the generation of the plateau observed in Figure 2.3.5(a).

Host feeding behaviour.

When placed in experimental arenas with no alternative food, starved beetles actively search for and consume *H.diminuta* eggs. The dynamics of infection is thus likely to be controlled, to a large extent, by the feeding behaviour of the host. In order to assess the validity of this hypothesis, the experiment described above was repeated using satiated beetles (i.e. beetles removed from stock cultures immediately prior to infection). The relationship between egg density and parasite burden for starved and satiated hosts is compared in Figure 2.3.5(b). Using satiated beetles, the same non-linear pattern is observed, but the infection plateau is reduced to approximately 2 larvae per host. This pattern is undoubtedly associated with the differing predatory activities of starved and satiated beetles, and gives a clear illustration of the importance of the predator-prey interaction in

the dynamics of infection.

A well documented feature of predator-prey associations is the so-called functional response, which describes the change in predation rate occurring in response to variation in prey density (Holling, 1959b; Murdoch and Oaten, 1975). Three types of functional response have been distinguished, which vary in form, but possess the common feature of rising to a plateau as prey density becomes large. The characteristic differences between them are shown diagrammatically in Figure 2.3.6. As a broad generalization, handling time (i.e. the average time taken by an individual predator to discover, handle and consume an item of prey) is considered to be the generative mechanism creating the upper asymptote of the functional response in the literature concerning arthropod predation (Hassell *et al*, 1976). In the corresponding literature on vertebrate predation, causality is normally ascribed to satiation effects (Ivlev, 1961). Both concepts are obviously closely interrelated.

The dynamics of infection of *T.confusum* by *H.diminuta* may be considered within the framework of a predator-prey association by the incorporation of the concept of a finite handling time. Two differential equations may be formulated to mimic the dynamics of predation within the experimental design used in the present study. These equations describe the rate of change with respect to time (t), of E (the number of eggs remaining in the arena) and P_2 (the number of eggs ingested). Since the experimental

Figure 2.3.6 *Diagrammatic representation of the characteristic differences between the 3 types of functional response described by Holling (1959b).*

Type I

Rare; restricted to simple filter-feeders which take a constant proportion of the filtered material up to the limit of their filtering capacity.

Type II

Attack rate per predator per unit time constant.

Type III

Attack rate per predator per unit time an increasing function of prey density (i.e. the predator "learns" to search for certain prey items once they reach a threshold abundance).

TYPE I
TYPE II
TYPE III
No. killed/unit time
% killed/unit time
Prey density

design excludes the addition of eggs after the start of an exposure period, the initial egg density (E_o) is related to E and P for all values of t, where

$$E_o = E + P_2. \qquad (2.3.10)$$

It is assumed that the instantaneous rate of egg attack per egg per unit time per beetle per unit area (υ) is constant and unaffected by changes in prey density, corresponding to the type II response described by Holling (1959b). Assuming that the rate of ingestion is directly proportional to the densities of eggs and hosts (H_2) within the arena, the equations take the form

$$dP_2/dt = \upsilon\ E\ H_2 \qquad (2.3.11)$$

$$dE/dt = -\ dP_2/dt \qquad (2.3.12)$$

If the experimental exposure period is of length T time units and the handling and comsumption of an egg takes, on average, t_h time units, then the solution of equations (2.3.11)and (2.3.12) is obtained by integrating over the time interval 0 to $(T-t_hP_2)$ and is of the form

$$P_2 = E_o\ (1 - \exp\ (-\upsilon H_2(T-t_hP_2)) \qquad (2.3.13)$$

where (t_hP_2) is the amount of time taken up in consuming P_2 eggs. Equation (2.3.13) is well documented in the ecological literature

and was originally described by Rogers (1972), although here it is derived in a different manner. It predicts that the number of eggs ingested per beetle (P_2/H_2) will rise to an asymptote (value T/t_h) as the egg exposure density (E_o) increases.

The model may be fitted to experimental data by use of a non-linear least squares method (Conway *et al*, 1970) and comparisons of observed and predicted values are shown in Figure 2.3.5. The goodness of fit of the model to the observed data provides further support for the hypothesis that the form of the relationship is determined by the predatory behaviour of the host. It is important to note, however, that the estimates of υ and t_h obtained by fitting the model to the data do not accurately reflect the true rates of egg ingestion and egg handling time within the experimental arena, since many ingested eggs fail to complete their larval development. A large number of eggs fail to hatch in the intestine, and, of those which do, many fail to penetrate the midgut wall (see Section 2.1). Attempts to quantify the actual number of eggs ingested per beetle in the present study were unsuccessful, and the value of the proportion of ingested eggs which develop to cysticercoids remains unknown. A second factor which tends to decrease the net rate of parasite acquisition per host is egg mortality during the experimental exposure period. However, although they are determinants of its numerical size, neither unsuccessful development of ingested eggs, nor egg mortality, is responsible for the generation of the functional response plateau.

In order to minimize egg mortality, the experimental design described at the beginning of this section was repeated using an exposure period of 15 minutes. The results are shown in Figure 2.3.5(c), and, by fitting the model defined by equation (2.2.13) to this data, estimates of υ and t_h approximating to the predation of a population consisting only of infective eggs are obtained. The functional response model may be rederived to include the effects of egg mortality during the exposure period, to give

$$dE/dt = - \upsilon H_2 E - \mu_3 E \qquad (2.3.14)$$

and

$$dP_2/dt = \upsilon H_2 E \qquad (2.3.15)$$

where μ_3 is the instaneous rate of egg mortality under experimental conditions. The solution of these equations over the integration interval 0 to $(T-t_h P_2)$ is of the form

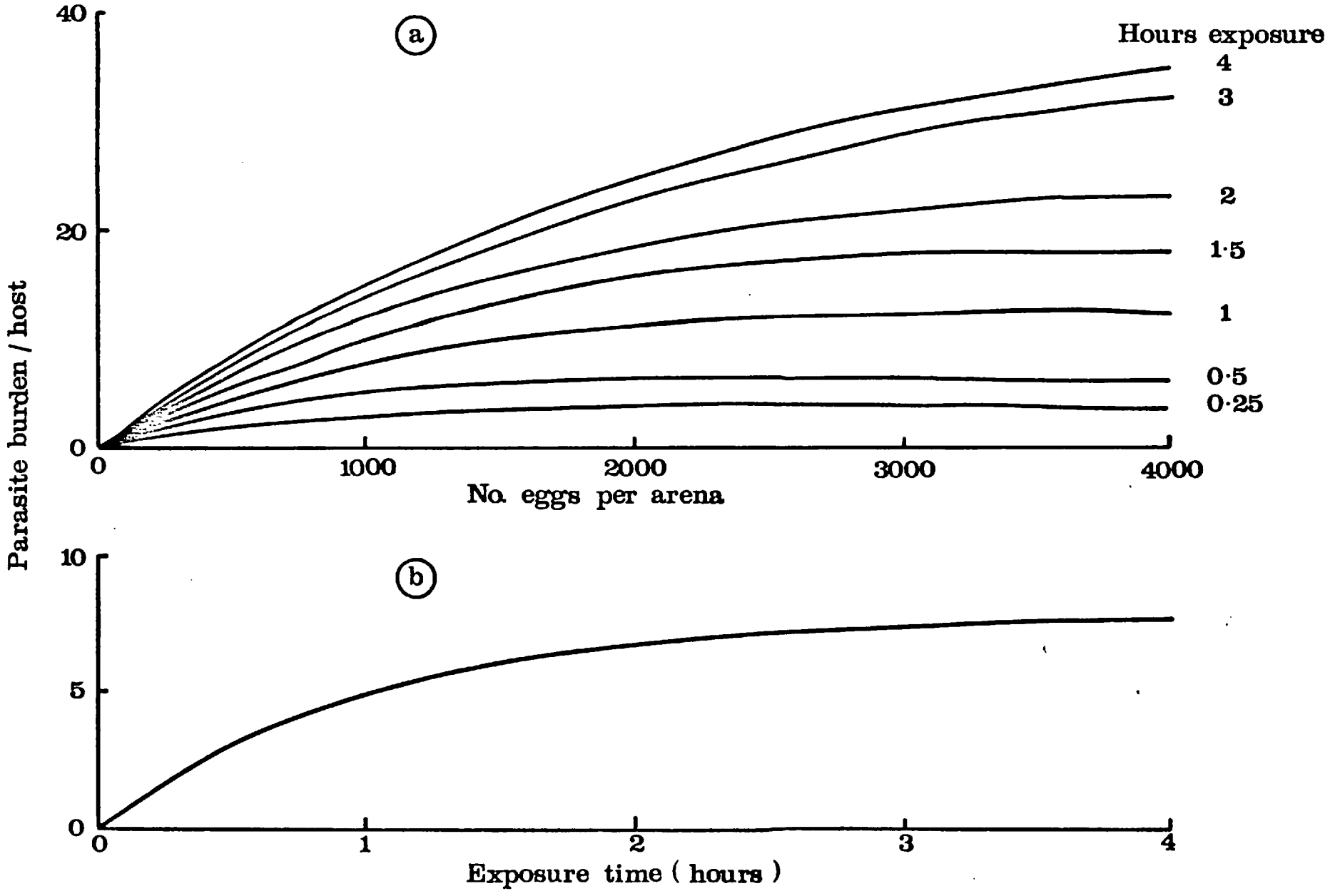
$$P_2 = \frac{\upsilon H_2 E_o}{(\upsilon H_2 + \mu_3)} \left[1 - \exp\left(-(\upsilon H_2+\mu_3)(T-t_h P_2)\right) \right] \qquad (2.3.16)$$

Using the estimates of υ and t_h obtained for a 15 minute exposure period, and the estimated value of μ_3 obtained in Section 2.3(i) (μ_3=0.03/egg/minute), equation (2.3.16) may be used to simulate the relationship between mean parasite burden per host and initial egg density per arena for varying experimental exposure times. The results are shown in Figure 2.3.7(a). The plateau of the functional response becomes numerically greater as the exposure time is increased, reaching an upper limit when the exposure time

Figure 2.3.7 *Simulated relationships between egg density, exposure duration and resultant mean parasite burden per host, as predicted by the model defined in equation (2.3.16).*

(a) Simulated relationship between egg density and resultant mean parasite burden per host, for varying periods of exposure. Parameter estimates : μ_3=0.03/egg/minute, H_2= 30/arena, υ=0.0005 eggs/host/minute, t_h=0.15 minutes.

(b) Simulated relationship between exposure duration and resultant mean parasite burden per host. Parameter estimates as in (a) except E_o=500/arena.


a
Hours exposure
4
3
2
1·5
1
0·5
0·25
40
20
0
0
1000
2000
3000
4000
No. eggs per arena
Parasite burden / host
b
10
5
0
0
1
2
3
4
Exposure time (hours)

is equal to the maximum survival period of the eggs.

Similarly, equation (2.3.16) may be used to simulate the relationship between exposure time and parasite burden for a constant egg exposure density. Figure 2.3.7(b) shows the predicted results of exposure of 30 beetles to densities of 500 parasite eggs, for comparison with experimental results portrayed in Figure 2.3.2. In both Figures 2.3.7(a) and (b), the predicted plateau values are substantially greater than the equivalent experimental results, indicating inaccuracy in the estimated values of υ and t_h. This inaccuracy is a result of egg mortality occurring during the first 15 minutes of exposure, which (since μ_3=0.03/egg/minute) is likely to be as high as 46%. This source of error cannot be eliminated within the present experimental design, since an exposure period of only 2 minutes would be necessary in order to achieve 95% egg survival. If this were possible, equation (2.3.12) could be used in conjunction with experimental data to gain an independent estimate of the rate of egg mortality, μ_3.

2.3(vi) Egg distribution.

The dynamics of all infection processes are influenced by the relative spatial distributions of infective-agents and hosts. Crofton (1971a; b), for example, suggested spatial clumping of infective-stages as a contributary factor in the generation of over-dispersion in parasite numbers per host, a pattern which is

commonly observed in natural associations (see Section 1).

The impact of egg spatial distribution on the rate of acquisition of *H.diminuta* by *T.confusum* was tested by varying the distribution of tapeworm eggs within the experimental infection arenas. Boxes of basal dimensions 10 x 20 cm. were lined with filter paper on which were delineated 10 quadrats each measuring 4 x 5 cm. Using 8 such boxes, 2 replicates each of 4 different spatial patterns were created by pipetting known volumes of egg suspension into each quadrat. These patterns ranged from uniform (under-dispersed) with a variance to mean ratio of eggs per quadrat approaching zero, to extreme spatial aggregation (over-dispersion) with a variance to mean ratio of eggs per quadrat of 2700. The 2 intermediate distributions had variance to mean ratios of 300 and 540. It should be noted that the values given are calculated using the number of eggs within each quadrat. Thus, although the number of eggs per quadrat may have an even distribution, the eggs are in fact distributed in 10 patches throughout the arena as a whole. Although approximate, this method does give an indication of the effect of spatial distribution, within the limitations imposed by the practical manipulation of *H.diminuta* eggs.

The total egg density per arena was maintained at a constant initial level of 3000,irrespective of the egg spatial distribution. Populations of 30 beetles, which had been starved for 6 days, were placed into each arena immediately after the introduction of the

egg suspension, for an exposure period of 3 hours. Dissection after 2 weeks enabled the parasite burdens of the host populations to be assessed. There were no significant differences between the 2 replicates for any of the distributions, and so the results were combined to give a single data set for each of the 4 egg patterns. The frequency distributions of parasite numbers per host are shown in Figure 2.3.8.

The numerical values of the parasite burdens per beetle are lower than might be expected for an infection with the characteristics described above. This may be explained by the greater basal area of the infection arenas used in this experiment (200 cm^2) compared with those used in standard infections (13 cm^2). Assuming that the rate of infection is inversely related to the area of the infection arena, the results are equivalent to those arising from a standard infection using an egg density of approximately 200.

From Figure 2.3.8, it is clearly evident that the frequency distribution of parasite numbers per host is dependent on the spatial distribution of the infective-stages to which the hosts were exposed. Even when subjected to an approximately uniform pattern of eggs, the resultant distribution of cysticercoids per beetle is over-dispersed (Figure 2.3.8(d)). As the spatial distribution becomes more aggregated, the resultant frequency distribution of parasite numbers per host shows a correspondingly higher degree of over-dispersion (through Figures 2.3.8(c) and (b)

Figure 2.3.8 *The relationship between the frequency distribution of parasite numbers per host and the spatial pattern of the infective-stages to which the host population was exposed.*

The histogram bars represent observed frequencies and the solid lines indicate the predictions of the negative binomial probability distribution (Bliss and Fisher, 1953) as fitted to the data by means of the program TOPFIT (Reyna Robles, 1969).

	Variance to mean ratio of egg numbers per quadrat.	Over-dispersion of parasite numbers per host (as indicated by the parameter k of the negative binomial probability distribution).
(a)	2700	1.04 (χ^2_{17}=11.92)
(b)	540	1.02 (χ^2_{13}=24.58)
(c)	300	1.81 (χ^2_{13}=11.42)
(d)	0	2.88 (χ^2_{11}=13.06)

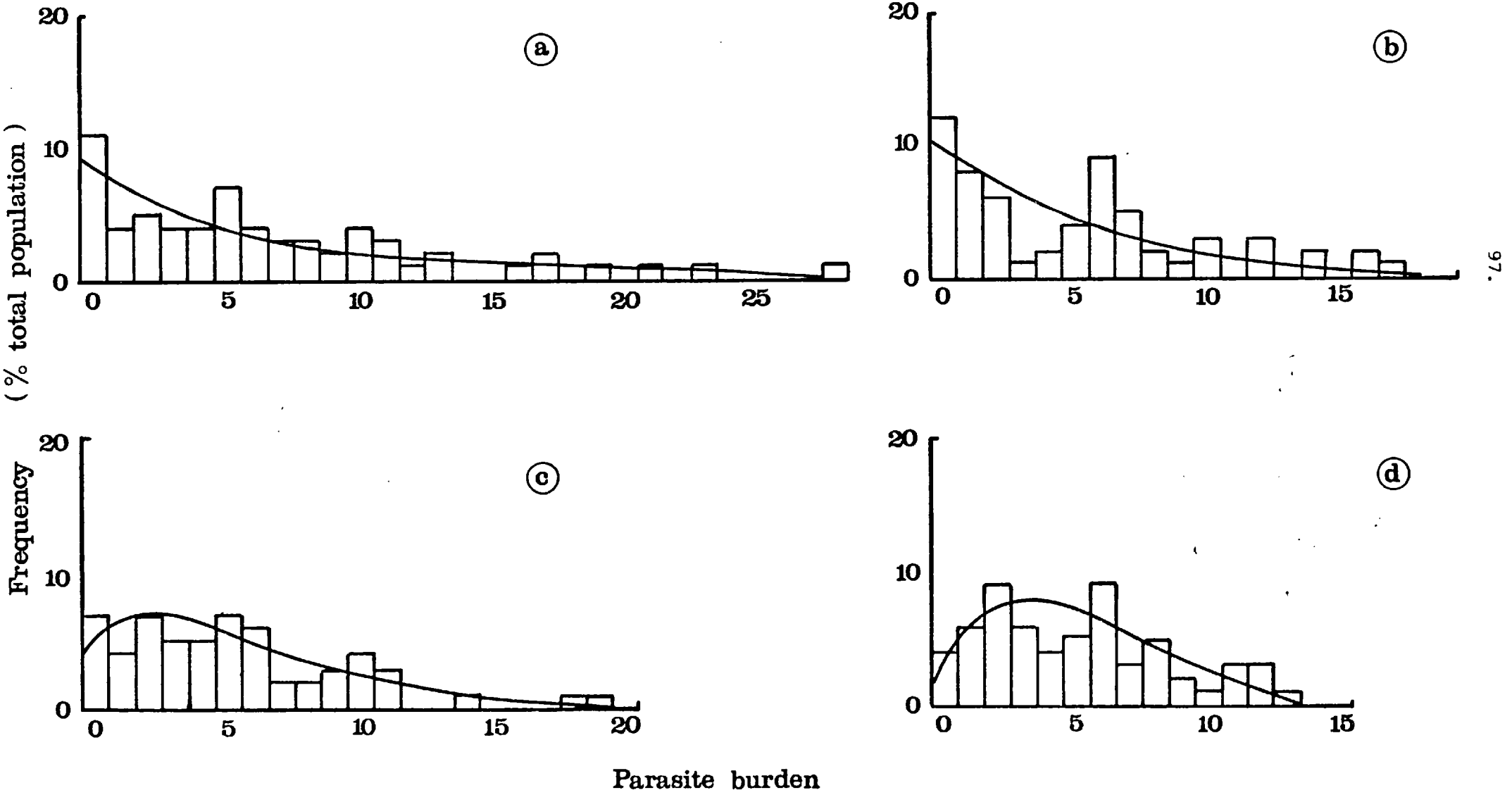
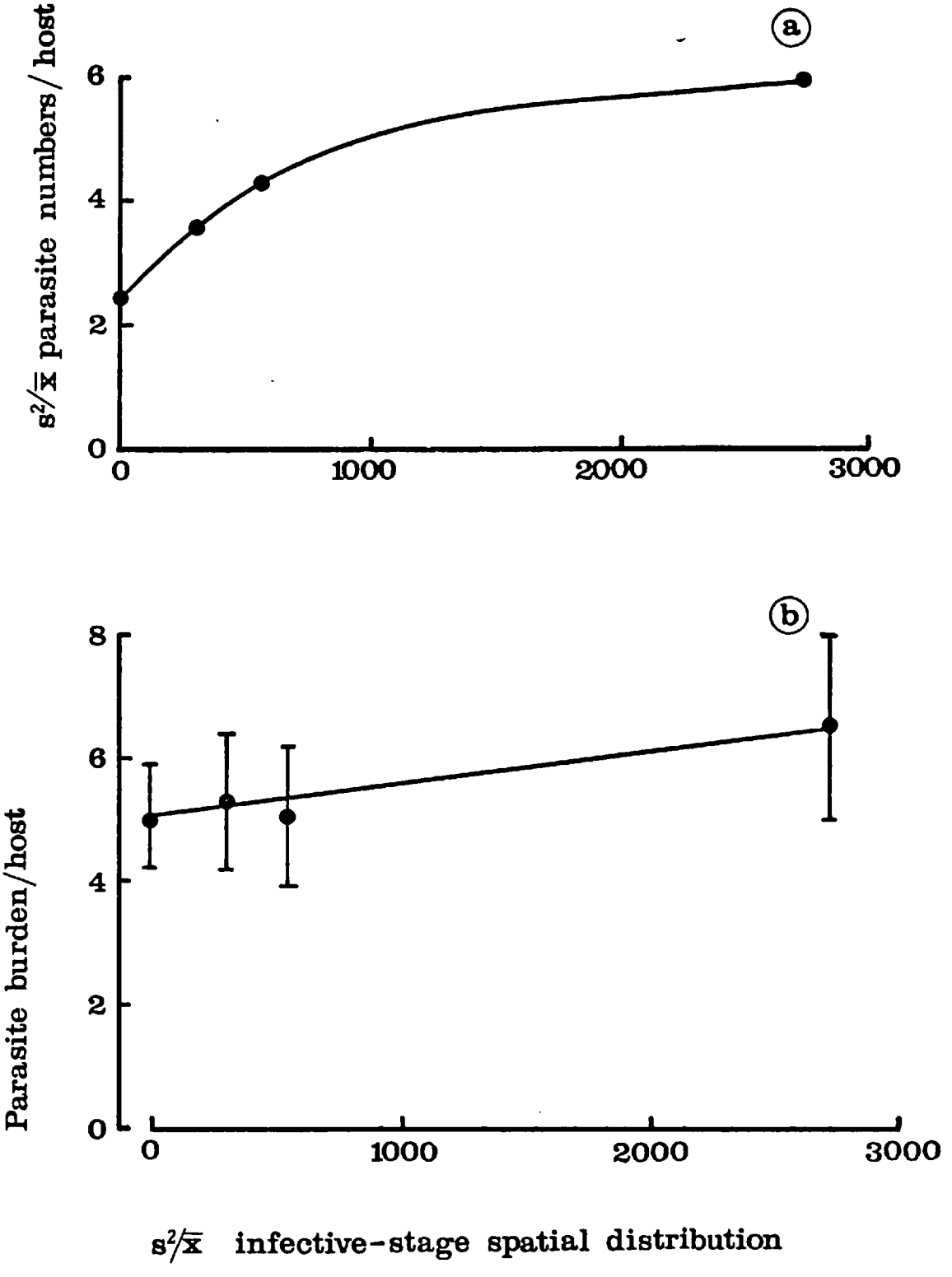

(% total population)
Frequency
a
b
c
d
20
10
0
0
5
10
15
20
25
Parasite burden

Figure 2.3.9 *The relationship between the spatial distribution of eggs in the infection arena and the resultant mean parasite burden and variance to mean ratio of parasite numbers per host.*

(a) The relationship between the variance to mean ratio $(s^2/\bar{x})$ of the frequency distribution of the number of parasites per host and the variance to mean ratio $(s^2/\bar{x})$ of the spatial distribution of eggs in the infection arena. The points represent observed values. The curve is fitted by eye.

(b) The relationship between the mean parasite burden of the host population and the variance to mean ratio $(s^2/\bar{x})$ of the spatial distribution of eggs in the infection arena. The points are observed values and the vertical bars represent the 95% confidence limits of the means. The solid line indicates the predictions of the best-fit linear model.


a
$s^2/\bar{x}$ parasite numbers / host
0
2
4
6
0
1000
2000
3000
b
Parasite burden/host
0
2
4
6
8
0
1000
2000
3000
$s^2/\bar{x}$ infective-stage spatial distribution

to Figure 2.3.8(a)). Using the variance to mean ratio of parasites per host as a direct measure of contagion, it is interesting to note that the degree of over-dispersion tends to an upper asymptote as the distribution of eggs becomes highly aggregated (Figure 2.3.9(a)).

A further point of interest to emerge from these results is that the average rate of parasite acquisition (as measured by the mean cysticercoid burden per beetle) is constant and independent of the infective-stage spatial distribution. This is shown in Figure 2.3.9(b), in which the slope of the regression line of the mean parasite burden on the variance to mean ratio of the egg distribution is not significantly different from zero (d.f.=2,P(t=1.0)>0.4).

2.3(vii) Host age and sex.

It has been established that both *H.nana* and *H.microstoma* may successfully complete their development in *T.confusum* larvae (Schiller,1959; Tan and Jones, 1969). Only very few *H.diminuta* hexacanths develop in larval *Tenebrio molitor,* however, although development proceeds normally if hexacanths are injected into the haemocoel (Voge and Graiwer, 1964). Similarly, despite numerous attempts to infect *T.confusum* larvae, no *H.diminuta* cysticercoids were found in larval beetles in the present study. It is thus concluded that *T.confusum* larvae are not efficient

hosts of *H.diminuta*, perhaps due to characteristics of gut wall thickness or intestinal emptying time. The influence of host age and sex will thus be considered with respect to adult beetles only.

It has been shown that the intensity of infection of *T.confusum* with *H.diminuta* increases with host age up to 16 days post eclosion (Dunkley and Mettrick, 1971) and decreases, in female beetles only, at 47 - 51 weeks post eclosion (Kelly *et al*, 1967). Host sex has been reported to have no effect on infection intensity (Mankau *et al*, 1971), although further data presented by Mankau (1977) indicated that both prevalence and intensity was significantly greater in female than in male hosts. The differences between these reports cannot be explained by host age, since all beetles were infected at 6 weeks of age.

In the present study, groups of *T.confusum* were sexed at the pupal stage using the method described by Head (1968). At 2 weeks post eclosion, 2 groups each of 30 males and 30 females were starved for 6 days and exposed to estimated densities of 250 *H.diminuta* eggs for 3 hours. The results given in Table 2.3.10 indicate that there is no significant difference in the parasite burdens of male and female *T.confusum* (d.f.=54, $P(t=0.3)>0.8$) of similar age. This does not preclude the possibility that sexual differences in susceptibility develop in older beetles, and the results of Kelly *et al* (1967) must be borne in mind until further experimental work has been carried out.

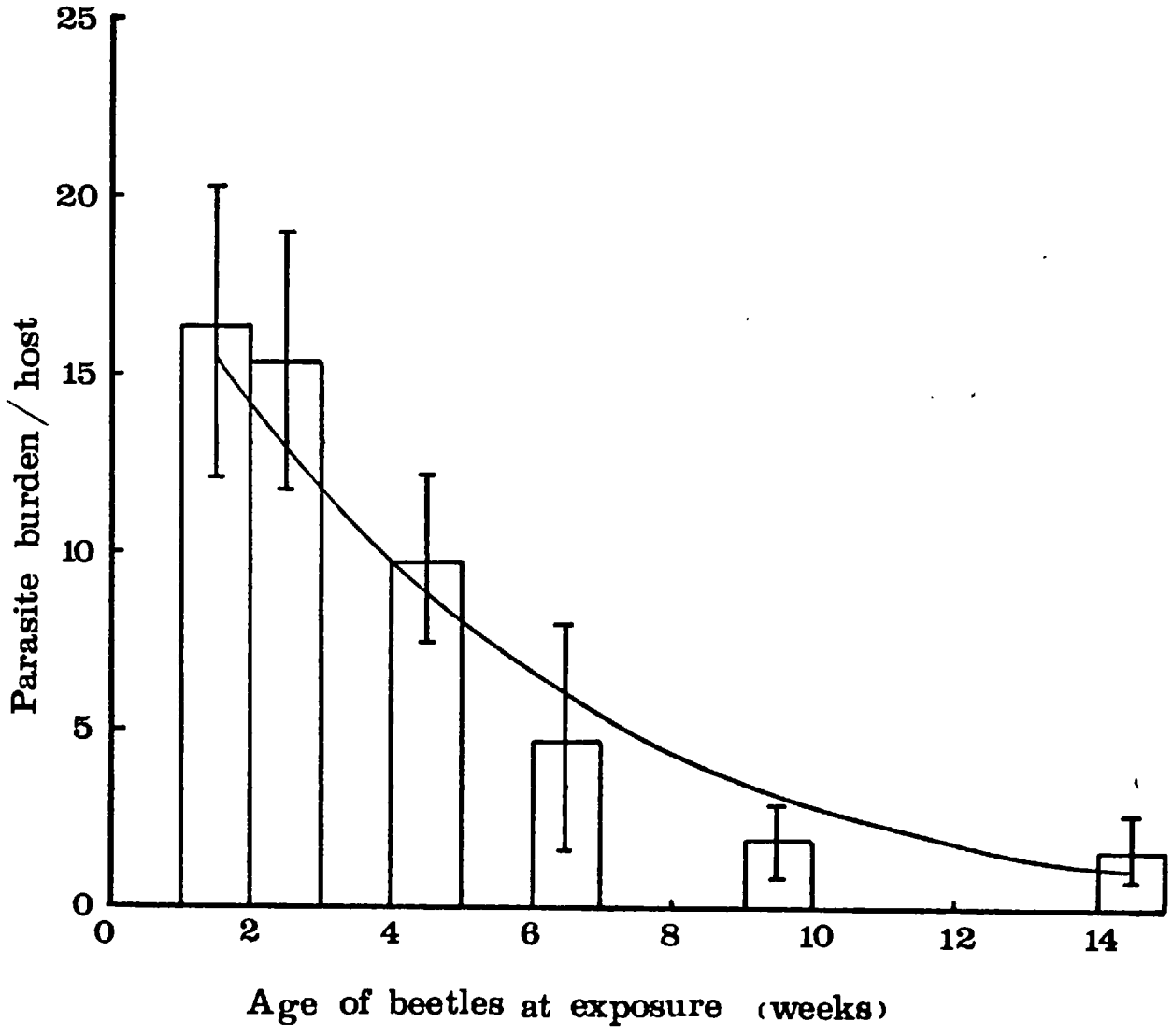
In order to assess the effect of beetle age on susceptibility to infection, groups of 30 beetles of differing ages, which had been starved for 6 days, were exposed to estimated densities of 3000 *H.diminuta* eggs for 3 hours. The results shown in Figure 2.3.10 reveal a decrease in infection intensity with increasing host age which may be empirically described by an exponential model. This pattern could be due to an increase in natural resistance to infection in older beetles (perhaps associated with thickening of the midgut wall), or to a decrease in food intake with age associated with decreasing energy requirements.

2.3(viii) Alternative food sources.

The experimental work described in this section constitutes a preliminary consideration of some factors which might influence the dynamics of infection of *T.confusum* by *H.diminuta* under natural conditions. The first series of experiments carried out was designed to investigate the attractiveness of *T.confusum* eggs as an alternative food source, since egg cannibalism is of major significance as a density-dependent constraint on beetle population growth (Park *et al*, 1965; see Section 2.4(ii)). Infection arenas were set up containing densities of *T.confusum* eggs varying between 0 and 300, and estimated densities of 1000 *H.diminuta* eggs. Populations of 30 starved beetles were then introduced for an exposure period of 3 hours. The resultant

Figure 2.3.10 *The relationship between host age at the time of exposure, and the resultant parasite burden of the host population.*

The histogram bars are observed mean values and the vertical bars represent the 95% confidence limits of the means. The solid line indicates the predictions of the best-fit exponential model.


25
20
15
10
5
0
Parasite burden / host
0
2
4
6
8
10
12
14
Age of beetles at exposure (weeks)

parasite burdens of the host populations are depicted in Figure 2.3.11(a). The gradient of the regression line shown on the graph is not significantly different from zero (d.f.=5,P(t=0.13)>0.9) and it may be assumed that the presence of *T.confusum* eggs has no effect on the dynamics of infection. *H.diminuta* eggs thus presumably provide such a strong food stimulus to the host that they are eaten in preference to *T.confusum* eggs, which would superficially appear to be of much higher nutritional value.

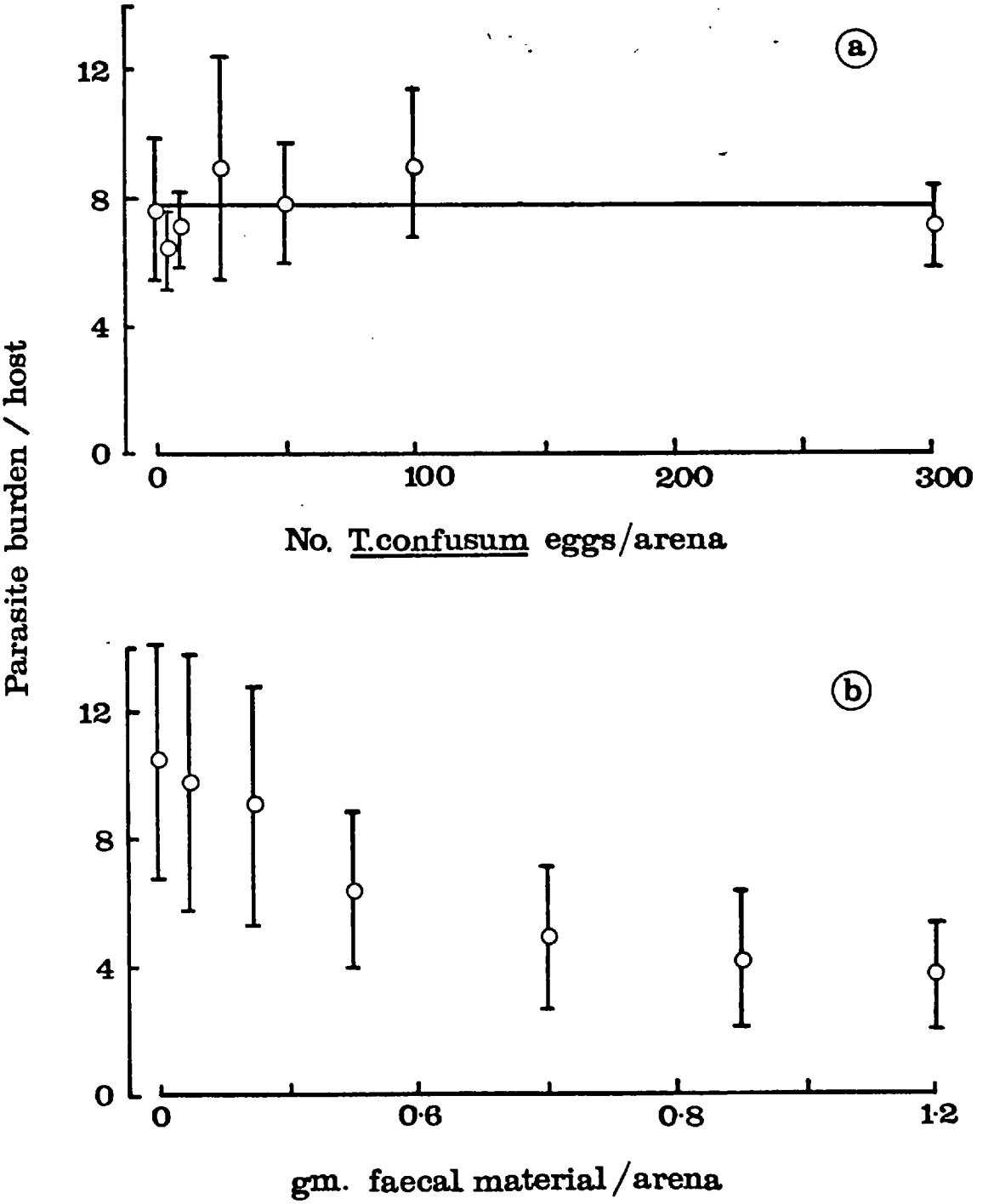
The second series of experiments was designed to gain some insight into the manner in which infection occurs when *H.diminuta* eggs are dispersed within the host faecal pellet. Infection arenas were set up containing varying weights of fresh faecal material from uninfected rats, together with estimated densities of 1500 *H.diminuta* eggs. The distribution of faecal material and egg suspension did not overlap. Populations of 30 beetles (which had been starved for 6 days) were then introduced into each arena for an exposure period of 3 hours. From the results shown in Figure 2.3.11(b), it can be seen that there is an inverse relationship between the rate of infection and the amount of faecal material present in the infection arena. This indicates that active predation of rat faecal material occurs in preference to predation of *H.diminuta* eggs present in suspension. This gives a qualitative indication that infection under natural conditions is likely to occur as a result of the ingestion of contaminated faecal

Figure 2.3.11 The influence of alternative food sources on infection.

(a) The relationship between the numbers of *T.confusum* eggs in the infection arena and the resultant mean parasite burden of the host population. The solid line indicates the predictions of the best-fit linear model to the data.

(b) The relationship between the weight of fresh faecal material in the infection arena and the resultant mean parasite burden of the host population.

The points are observed means, and the vertical bars represent the 95% confidence limits of the means.


a
12
8
4
0
0
100
200
300
No. T.confusum eggs/arena
b
12
8
4
0
0
0·6
0·8
1·2
gm. faecal material/arena
Parasite burden / host

material rather than the consumption of infective eggs as prey items *per se*. No information is available concerning the predation of *H.diminuta* proglottids present in the host faeces, which may rank separately in the list of preferred prey items. However, it should be noted that the manner in which infection occurs (i.e. whether eggs are consumed actively, or ingested passively as a contaminant of other items of prey) does not affect the conclusions drawn in Section 2.3(v) concerning the dynamical properties of the predator-prey interaction.

2.3(ix) Discussion.

Infection of the intermediate host is critically dependent on the probability of contact between infective eggs and susceptible hosts, and thus on the survival of the eggs in the free-living habitat. This in turn is dependent on the prevailing environmental conditions. In this context, it should be noted that any single estimate of egg survival will be subject to extremely wide variation, and may be representative of transmission only within a very narrow range of conditions.

As shown in the present section, the characteristics of parasite acquisition are influenced by the densities of beetles and eggs, as well as their respective spatial distributions. The results displayed in Figure 2.3.5 reveal a regulatory

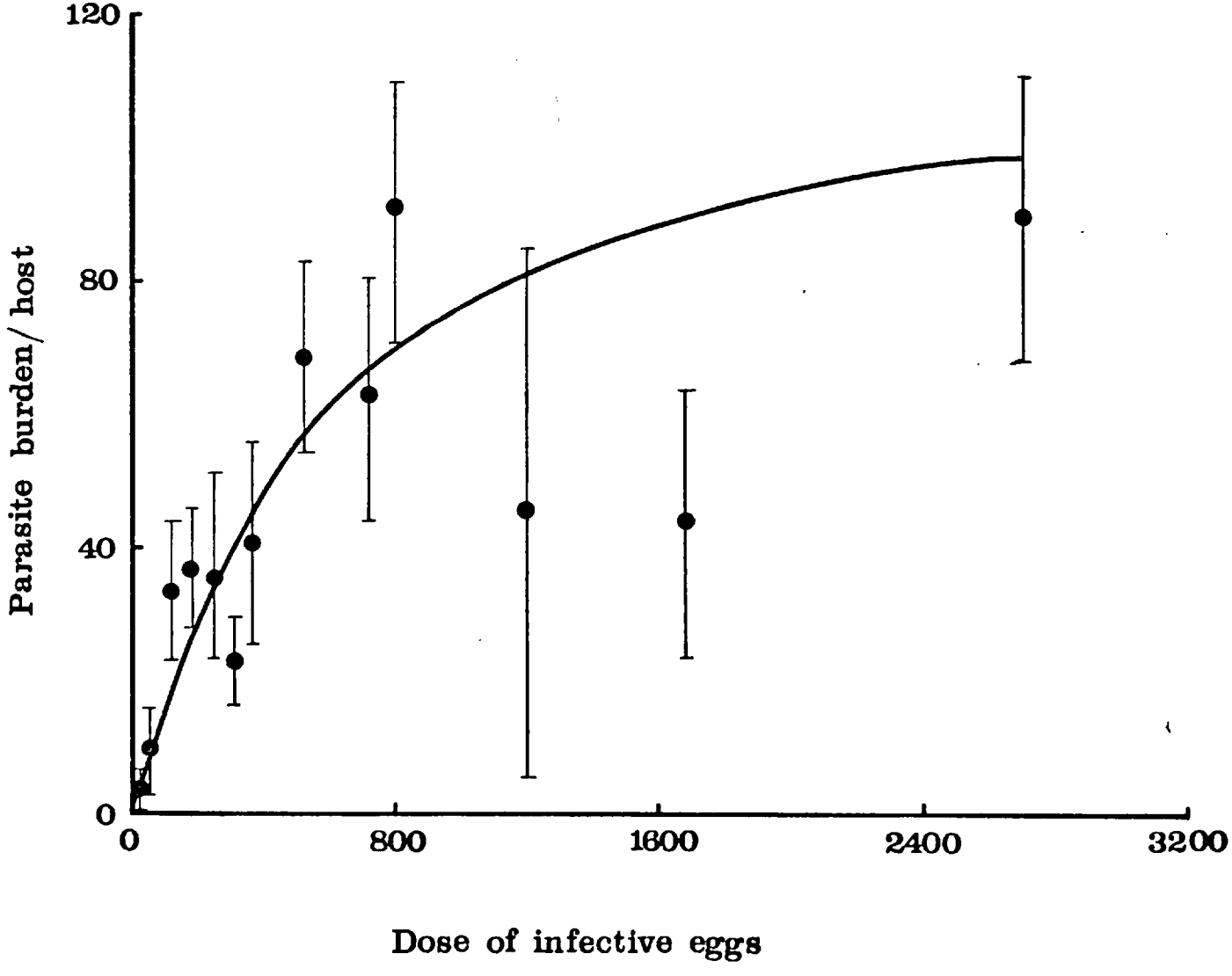
constraint on the flow of *H.diminuta* through its life-cycle. Even when the parasite egg density is very high within a specific habitat, the rate of acquisition of parasites by the intermediate host will reach an asymptote as a result of host feeding behaviour.

Observations in the present study have shown that beetles actively search for *H.diminuta* eggs in the absence of any other food source. The results shown in Figure 2.3.11(b), however, indicate that when the eggs are distributed within a faecal pellet, they are more likely to be ingested accidentally. It is probable that tapeworm eggs are only very rarely consumed actively under natural conditions, and where alternative and more desirable food sources are available, undoubtedly the maximum rate of parasite intake will be low. It must be emphasized, however, that whether ingestion is deliberate or accidental, the functional response still provides a potential density-dependent constraint on the population growth of the parasite.

Transmission across adjacent links in community trophic webs occurs in many host-parasite associations. Interestingly, results closely resembling those displayed in Figure 2.3.5 were given by Lackie (1972) for the relationship between the egg density of the acanthocephalan, *Moniliformis dubius* and the resultant mean parasite burden of the intermediate host, *Periplaneta americana* (see Figure 2.3.12). The observed plateau was not

Figure 2.3.12 *The relationship between the mean parasite burden of* Periplaneta americana *females and the density of infective* Moniliformis dubius *eggs to which they were exposed. Data from Lackie (1972).*

The points are observed means and the vertical bars represent the 95% confidence limits of the means. The solid line indicates the predictions of the functional response model as defined in equation (2.3.13). Parameter values : T=1 day, H=1/arena, υ=0.19 eggs/host/day, t_h=0.008 days.


120
80
40
0
Parasite burden/ host
0
800
1600
2400
3200
Dose of infective eggs

attributed to host predatory behaviour, but to a factor or factors occurring before or during penetration of the midgut wall. Unfortunately, the density of the batch of eggs given was corrected for hatching percentage to give a 'dose' of infective eggs, and the original egg densities were not given. This is of importance, since infective and uninfective eggs alike contribute to the handling time or satiation factors responsible for generation of the plateau of the functional response. The observed variability in the results led Lackie to suggest that the plateau shown in Figure 2.3.12 might be spurious, especially since individual cockroaches were found with up to 400 parasites. The possibility that this might be due to heterogeneity in cockroach predatory behaviour, infective-stage distribution and viability, as well as to individual differences in host susceptibility, was not considered.

Although the functional response model, as defined by equation (2.3.16) serves to focus attention on the mechanism behind the observed relationship between egg density and parasite burden, it does not provide an accurate description of the process for two reasons. First, it is based on the assumption of random encounter between beetles and eggs. This represents an oversimplification both because the eggs are distributed in a clumped manner in the centre of the infection arena, and because the beetles exhibit a definite attraction towards the eggs as prey items. Second, the calculated estimates of υ and t_h do not accurately reflect the true rates of egg capture and handling

time, since only a proportion of ingested eggs are recovered as fully developed cysticercoids.

Infective eggs which are ingested but which fail to develop form part of the massive proportion of eggs which are removed from the pool of potentially transmissible infective-agents by ingestion by unsuitable hosts, or destruction in other ways. In common with observations in the present study, Rau (1979) found that larval intermediate host insects in natural populations were very rarely infected and bore very few cysticercoids. He suggested that *Tenebrio* larvae may be responsible for the destruction of large numbers of *H.diminuta* eggs that would otherwise be available to adult beetles. Although ingestion by unsusceptible hosts may be an important factor in some host-parasite associations (Anderson, 1980b), it seems likely that *H.diminuta* eggs lost as a result of larval beetle predation under natural conditions would be insignificant in comparison with the massive egg losses arising from other causes.

The results shown in Figure 2.3.8 indicate that spatial distribution is an important factor in the dynamics of transmission. The spatial pattern of infective-stages has a distinct influence on the resultant distribution of parasite numbers per host, but it is of importance to note that the mean parasite burden is unaffected. The results shown in Figure 2.3.8(d) indicate that a degree of over-dispersion in parasite numbers per host is generated

even when the spatial distribution of eggs is approximately uniform. The generative mechanisms of this pattern are probably associated with heterogeneity in beetle behaviour and susceptibility to infection. Spatial heterogeneity in infective-stage distribution accentuates the resultant over-dispersion in parasite numbers per host. This is likely to represent one of the major causal factors of the high levels of contagion which have been reported for *H.diminuta* in natural intermediate host populations (Rau, 1979), since rat faeces are not distributed randomly in the environment of the intermediate host, nor are eggs distributed at random within the faecal pellet itself.

Cysticercoids of *H.diminuta* act to reduce host survival and fecundity in a manner related to the parasite burden per host (see Section 2.4). Predator functional responses of the type displayed in Figure 2.3.5 will thus tend to reduce the impact of the parasite on the growth of the host population by restricting the rate of build up of parasites within individual hosts under conditions of high egg density. In addition, the net effect of the parasite on its intermediate host population will also be critically dependent on the statistical distribution of parasite numbers per host. In the first place, over-dispersion is a strong stabilizing influence on host parasite population associations (Anderson and May, 1978). More importantly, however, the more aggregated the distribution, the less the resultant impact of the parasite on the growth of the host population, since the majority of the parasites are harboured by a small proportion of the hosts (Anderson, 1979a). In general terms, therefore, the degree of

depression of intermediate host population growth by *H.diminuta* infections in natural habitats will tend to be reduced both by the functional response of the host to parasite egg density, and also by the over-dispersed nature of the infective-stage spatial distribution.

2.4 DYNAMICS OF THE INTERMEDIATE HOST.

The biology and single species population dynamics of the flour beetles *Tribolium confusum* and *T.castaneum* are well documented and the present section gives an outline of the most salient features. The results of simple experimental studies are given to determine the basic rates of mortality and fecundity of the beetle strain used. The majority of this section is concerned with the experimental determination of the relationships between parasite burden and parasite-induced reductions in host fecundity and survival. Lastly, the manner in which parasite-induced effects on individual hosts may influence the equilibrium population level of *T.confusum* is considered.

2.4(i) The biology of T.confusum.

The genus *Tribolium* (MacLeay, 1825) is thought to have originated during the cretaceous period (Hinton, 1948). The *confusum* species-group evolved in Africa, where its 'natural' habitat is still tree bark (Good, 1936). Although its feeding preferences are unknown, predatory, scavenging and fungal feeding habits have all been suggested (Linsley, 1944). At the present time, *T.confusum* is commonly associated with stored cereal products throughout the world, and flour supplemented with brewer's yeast has become the standard medium for maintenance of cultures in the laboratory (Sokoloff *et al* 1966).

The biology of *T.confusum* has been reviewed by Sokoloff (1974), from which much of the following data is taken. Like all Coleoptera, *T.confusum* undergoes complete metamorphosis. Eggs measuring approximately 0.6 x 0.4 mm are laid by females in tunnels in the flour. These hatch in about 6 days at 29°C to produce larvae weighing 0.02 mg. The larvae moult between 6 and 12 times depending on environmental conditions, until, in the resting stage just prior to pupation, their weight has increased to approximately 1.9 mg. The larval period, which constitutes approximately 62% of the complete developmental time, is about 22 days at 29°C. Final stage larvae migrate to the surface of the medium and pupate. The duration of the pupal stage is about 7 days at 29°C, after which an adult weighing 2.1 mg. emerges. The length of the developmental period, which totals 35 days at 29°C, is obviously dependent on environmental factors, particularly temperature and humidity. The optimum conditions for rapid development are 32.5°C and 70% relative humidity, when the developmental period is reduced to 25 days. The limits for successful development are 37.5°C and 17.5°C, except at low or high humidity, when it is restricted to a narrower temperature range.

Adult *Tribolium* beetles are among the most long-lived stored-product insects (Good, 1936). The mean expected lifespan of *T.confusum* has been estimated as 315 ± 7 days (Park *et al*, 1964). Among adult populations, the sex ratio is normally unity, and females begin to lay viable eggs within 1 week of emergence at

27°C (Gray, 1946). Females kept at this temperature in the presence of males may lay 6.3± 0.2 eggs per day (Chapman and Baird, 1934) and, at 26°C, the oviposition period may last 235 days (Good, 1936), although the fecundity may be reduced considerably towards the end of this period.

2.4(ii) Single-species population dynamics.

In an analogy of Darwin's argument that the reproductive potential of all animal species is far in excess of that required to maintain a steady population level, Sokoloff (1974) has estimated that it would take only a little more than 2 years for a single pair of *T.castaneum* to produce more progeny than the number of electrons estimated for the visible universe (10^{79}). It is evident that such exponential growth is not sustained in real communities. In addition to density-independent factors such as climatic variation, population growth is effectively controlled by density-dependent effects on survival, fecundity and dispersal.

Dispersal.

The importance of spatial migration with respect to population regulation has been emphasized by Taylor and Taylor (1977) and by Hamilton and May (1977). Although of obvious significance in the maintenance of stable population levels in natural habitats, large-scale dispersal can do little to explain the equilibrium levels noted by Park (1948) in closed

Tribolium communities under experimental conditions. The aspect of spatial patterning noted by Naylor (1959) however, whereby the distribution of adult *T.confusum* in the medium is shown to be dependent on population density, could quite possibly have indirect influences on beetle survival or fecundity.

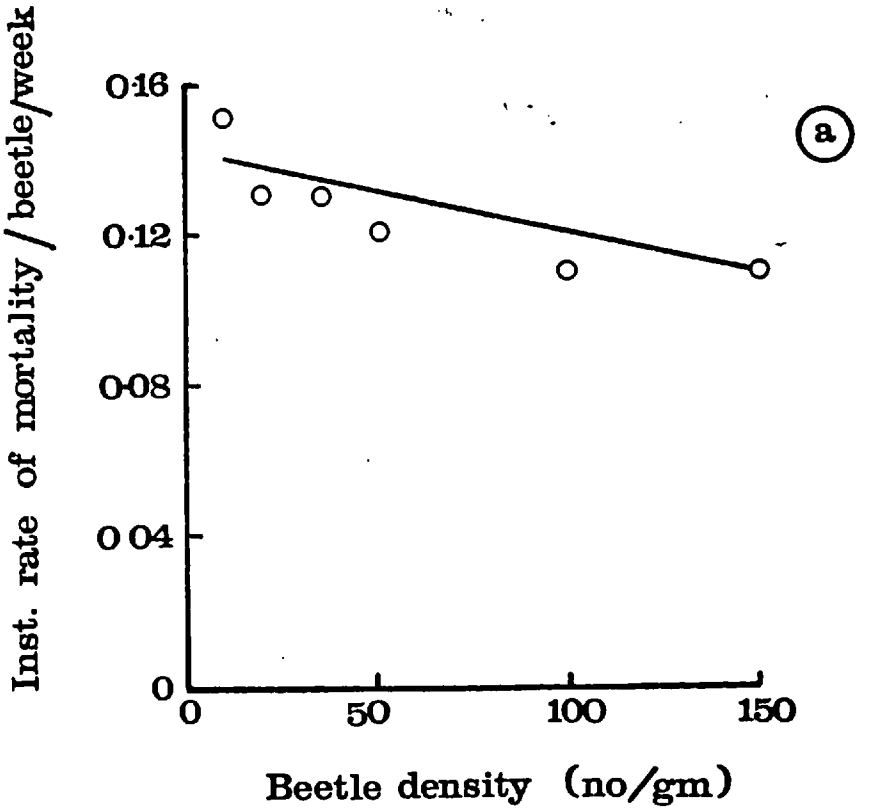
Survival.

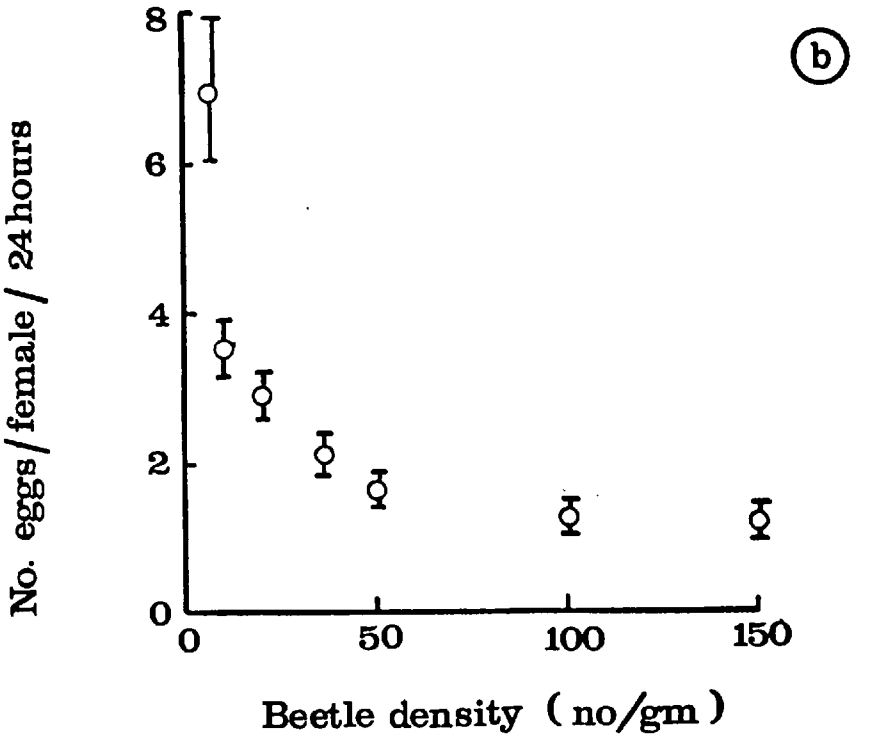
Although Brereton (1962) failed to show any change in the survival of *T.confusum* larvae, pupae or adults during population growth to equilibrium, little quantitative data relating adult survival to population density is available. In order to test the nature of this relationship, *T.confusum* populations consisting of adults 1 - 7 days post eclosion were created in 1 gm. flour-yeast medium in glass specimen tubes. Population sizes from 10 - 150 beetles/gm. were set up (3 replicates of each of 7 densities). Survival was monitored and any larvae and dead adults were removed. The food medium was renewed at 2 weekly intervals. There were no significant differences between the 3 replicates at any of the 7 densities, and so the results were combined to give 1 data set for each population level. The instantaneous rate of beetle mortality, b_2, was estimated using equation (2.3.5) and the results are shown in Figure 2.4.1(a). The trend towards a lower instantaneous mortality rate at high population density cannot be readily explained, and is not significant at the 1% level (d.f.=4, $P(t=4.0)>0.01$). No density-dependent effects causing increased mortality at high population density are revealed over the

Figure 2.4.1 *Density-dependent constraints on the population growth of* T.confusum.

a) The relationship between beetle density and the instantaneous rate of beetle mortality (b_2). The points represent observed values and the line represents the best-fit linear model.

b) The relationship between beetle density and the number of eggs recovered per female per 24 hours. The points represent observed means and the vertical bars represent the 95% confidence limits of the means.


Inst. rate of mortality / beetle/week
0·16
0·12
0·08
0 04
0
0
50
100
150
Beetle density (no/gm)
a


No. eggs/female / 24 hours
8
6
4
2
0
0
50
100
150
Beetle density (no/gm)
b

experimental range, although, of course, such effects would be more likely to occur under conditions in which food was a limiting resource. The results shown in Figure 2.4.1(a) may be averaged to give an estimate of the instantaneous rate of beetle mortality (b_2) of 0.02/beetle/day (when food is non-limiting). It should be noted that this estimate is considerably higher than that obtained by Park *et al* (1964), possibly due to differences in environmental conditions or beetle strain.

One of the most important effects of population density is its influence on the rate of cannibalism. The phenomenon of population control by egg cannibalism was first noted by Chapman (1928). Its significance was clarified by Park *et al* (1965), who demonstrated that both adults and larvae may cannibalize eggs, larvae, pupae and young adults. Although the per capita rate of cannibalism per beetle is reduced by an increase in adult density (Rich, 1956), the total number of individuals eaten is increased (Park *et al*, 1965) so that, at equilibrium, over 99% of all progeny are eaten during the period between oviposition and adult maturation (Mertz and Cawthorn, 1973). Mertz and Davies (1968) have suggested that it is the cannibalistic behaviour of the larvae which generates cycles in the numbers of immature beetles present in populations founded with adults (see, for example, Park, 1948), while the adult component remains relatively constant.

An experimental investigation of the rate of egg cannibalism in the absence of other food was carried out by exposing groups of

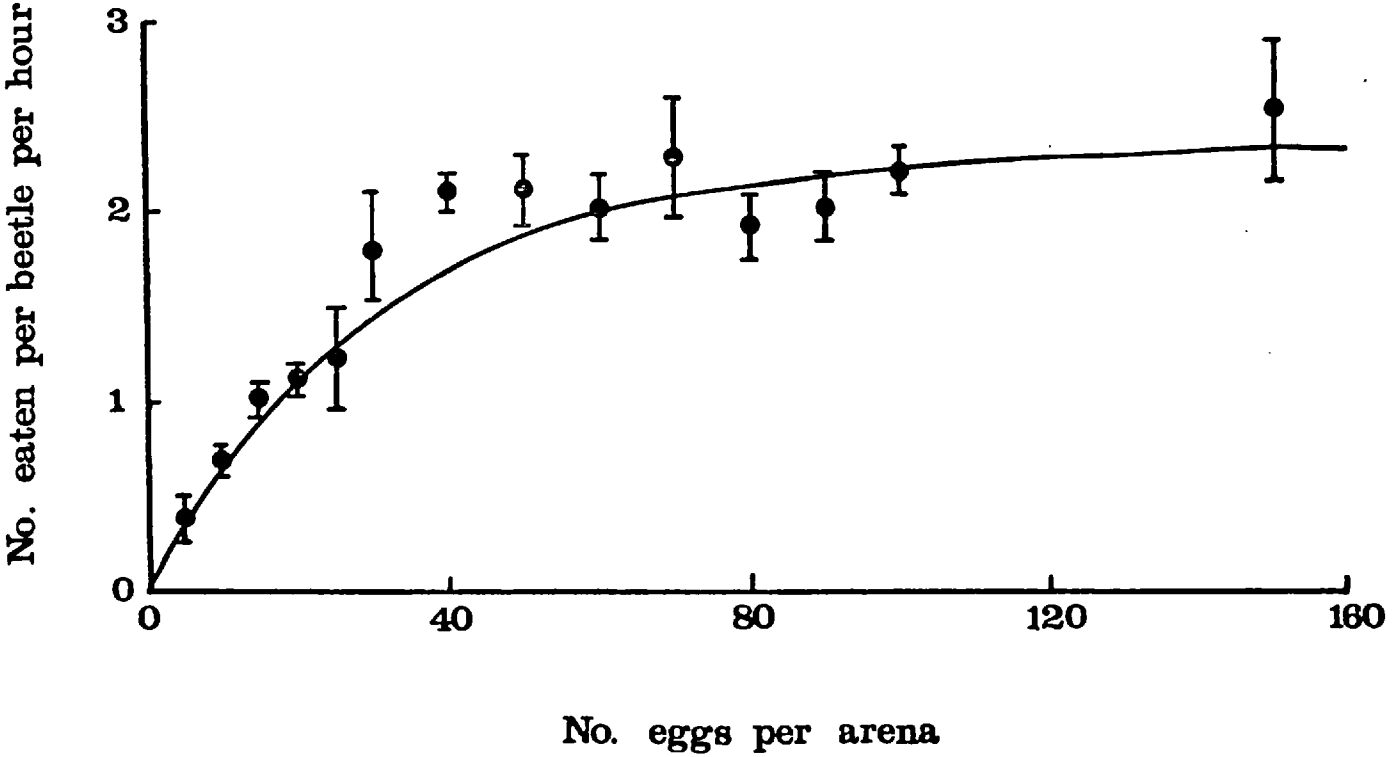
10 beetles of uniform age (which had been starved for 6 days) to known numbers of *T.confusum* eggs in arenas 4 cm. in diameter. Each point was replicated 5 times. After an exposure period of 1 hour, the beetles were carefully removed. Microscopic examination enabled the number of undamaged eggs remaining in the arena to be determined. The results reveal a type II functional response between the rate of predation and egg density, which may be described by the model defined in equation (2.3.13), (see Figure 2.4.2). Although type II responses do not provide density-dependent prey regulation *per se* (see Murdoch and Oaten, 1975), the results indicate the potential role of cannibalism in population control when all adult members are considered. By similar experimental methods, predation on *Lasioderma serricorne* by *T.castaneum* has been shown to provide effective regulation of the density of the former species (LeCato, 1977).

Fecundity.

Park (1938) noted that crowding in *T.confusum* is not detrimental to larval and pupal development, but is of importance as the factor controlling the rate and degree of 'environmental conditioning'. Conditioning is due to the accumulation of faecal matter and moulted skins, together with the nutritional depletion of the medium, and is thought to contribute significantly to the regulation of *Tribolium* populations by causing a reduction in reproductive rate (Park, 1936). A decrease in real fecundity rate (in contrast to an increase in the rate of egg cannibalism) with increasing population density has been demonstrated by Birch *et al* (1951) and by Rich (1956).

Figure 2.4.2 *The relationship between the density of* T.confusum *eggs and the rate of egg predation by* T.confusum *adults.*

The points are the means of 5 observed values and the vertical bars represent the 95% confidence limits of the means. The solid curve indicates the predictions of the functional response model defined in equation (2.3.13); υ=0.09 eggs/beetle/hour, t_h=0.33 hours.


No. eaten per beetle per hour
0
1
2
3
0
40
80
120
160
No. eggs per arena

To illustrate the combined effects of fecundity reduction and cannibalism, populations of beetles (1 - 7 days post eclosion, sexed at the pupal stage) with sex ratios of 1:1 were set up in 1 gm. flour-yeast medium in glass specimen tubes. Densities of between 2 and 150 beetles per gm. were used (3 replicates of each of 7 densities). At intervals of 24, 48 and 72 hours, the contents of the tubes were passed through a 250μ sieve, the number of eggs present determined, and the beetles replaced in 1 gm. fresh medium. The results shown in Figure 2.4.1(b) indicate a clear decrease in the number of eggs present in populations at high density. Age-dependent fecundity was not considered, neither did the experimental design allow any assessment of the relative importance of fecundity and cannibalism to be made. This does not detract however, from the conclusion that there is a severe density-dependent constraint on the number of eggs which survive to hatching in populations of *T.confusum* when food is non-limiting.

2.4(iii) The influence of infection on host fecundity.

Changes in host reproductive potential as a result of parasitic infection are well documented (Lanciani, 1975; Frye and Olson, 1974; Milner, 1972; Etges and Gresso, 1965). In all cases where quantitative data are available, the degree of reduction in fecundity has been shown to be dependent on the burden of parasites harboured (Anderson, 1978a; May and

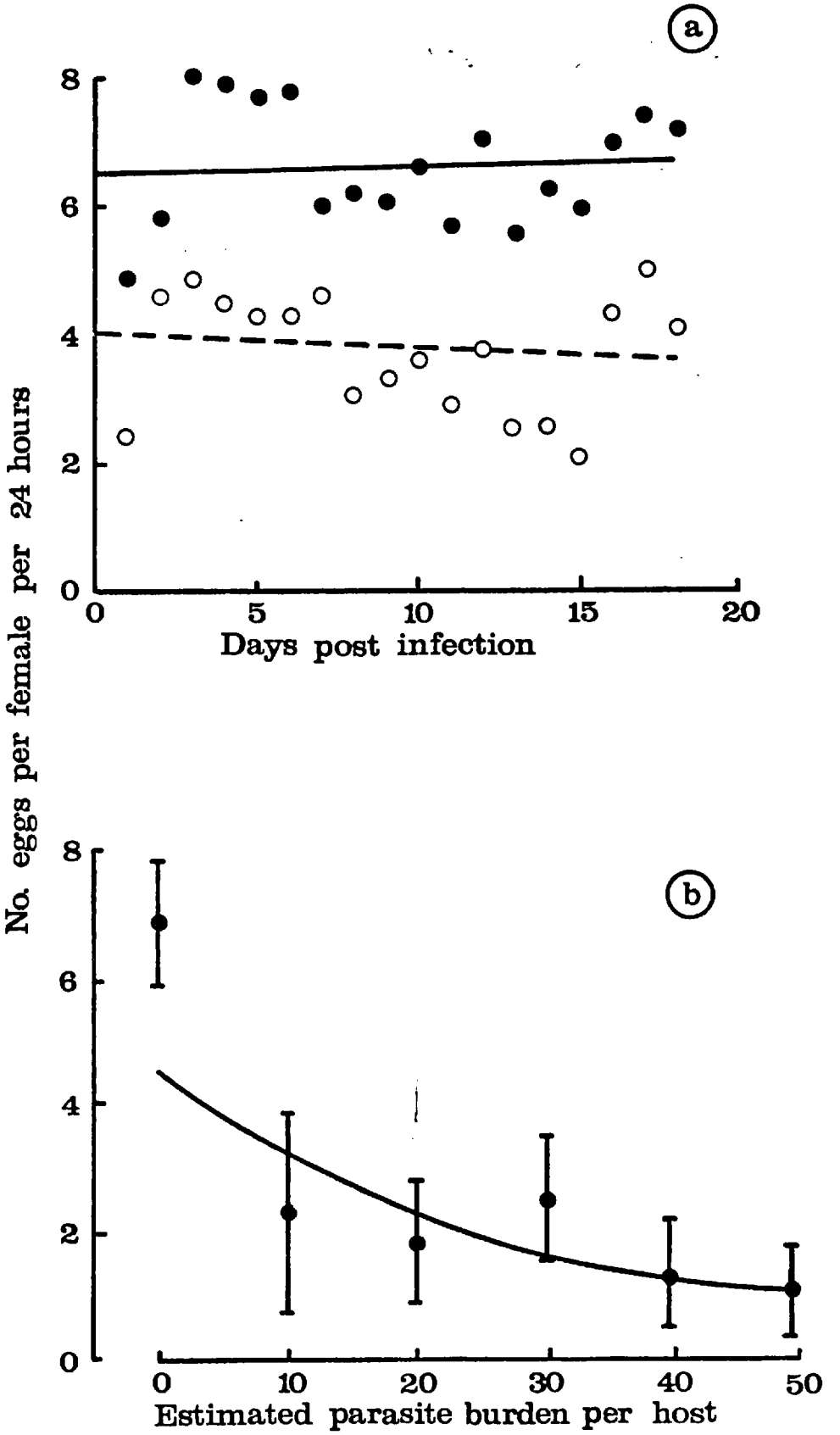
Anderson, 1978). None of these detailed studies relate to the influence of parasitism on *Tribolium*, although both *Nosema whitei* (Milner, 1972) and *H.diminuta* (Coleman, 1978) have been reported to reduce the fecundity of *T.castaneum*. The results from these two studies are subject to error, since fecundity was estimated indirectly by counting the number of larvae present in a population over a period of time. Because of the effects of cannibalism (see Section 2.4(ii)),this is not a reliable indication of the number of eggs produced. In addition, neither report gives any information relating the reduction in fecundity to the burden of parasites harboured per host.

In the present study, preliminary experiments were carried out to investigate the influence of infection on the fecundity of *T.confusum* as follows. Beetles were sexed at the pupal stage to give groups of 60 male and 60 female beetles. At 21 days post eclosion, both groups were starved. After 6 days, 30 males and 30 females were fed, while the other 2 groups were exposed to estimated densities of 1000 *H.diminuta* eggs for 3 hours prior to feeding. After a period of 24 hours, 10 infected pairs and 10 uninfected pairs were each placed in 1 gm. flour-yeast medium in glass specimen tubes. Fecundity was monitored daily for 18 days by the passage of the tube contents through a 250μ sieve in order to extract the eggs. This was accompanied by renewal of the food medium. The results shown in Figure 2.4.3(a) reveal a significantly lower level of fecundity in infected than in uninfected beetles.

Figure 2.4.3 *The influence of infection on host fecundity*

(a) A comparison of egg production in infected and uninfected beetles. The solid circles represent the mean egg output of 10 uninfected beetle pairs, and the open circles represent the mean egg output of 10 infected beetle pairs. The solid and dashed lines represent the best-fit linear models for uninfected and infected beetles respectively.

(b) The relationship between parasite burden and host fecundity. The points are observed values and the vertical bars represent the 95% confidence limits of the means. The solid line indicates the predictions of the best-fit exponential model as defined in equation (2.4.1); a=4.5 eggs/female/24 hours, b=0.03.


a
8
6
4
2
0
0
5
10
15
20
Days post infection
No. eggs per female per 24 hours
b
8
6
4
2
0
0
10
20
30
40
50
Estimated parasite burden per host

Given these preliminary results, the following experiments were carried out in order to assess the relationship between fecundity and the burden of parasites harboured per host. The repeated infection process described in Section 2.3(iv) was carried out using groups of male and female beetles which had been sexed at the pupal stage, to give single sex populations with 0 to 5 infections respectively. The uninfected group was used as a control. Two weeks after the last exposure, beetles with the same level of infection were paired (10 pairs at each of the 6 infection levels) and each pair was placed separately in a specimen tube with 1 gm. flour-yeast medium. At 3, 24 hour intervals, the medium in each tube was passed through a 250μ sieve to determine the number of eggs laid. It is assumed that the rate of cannibalism is negligible over the experimental range of egg densities (Rich, 1956).

The relationship between the mean number of eggs laid per female beetle per 24 hours and the estimated parasite burden per host is shown in Figure 2.4.3(b). Host fecundity decreases markedly as the mean parasite burden per host is increased. The form of the relationship may be empirically described by an exponential model,

$$y = a.\exp(-bM) \qquad (2.4.1)$$

where y is the number of eggs laid, and M is the mean parasite burden per host. The fecundity in uninfected beetles is then

given by a, and b is a constant relating to the severity of the decrease due to infection. The results show that, in reality, the detrimental effect is more severe at low levels of parasitism than this model would suggest.

The important point to emerge from these experiments is that the relationship between parasite burden and depression in host fecundity is non-linear, indicating that fecundity is not directly proportional to the number of hexacanths entering the haemocoel. Although the generative mechanisms were not investigated experimentally, it may be postulated that host fecundity is related to the biomass of parasites harboured, since an inverse relationship between parasite burden and cysticercoid size has been demonstrated (see Section 2.3(iv)). Alternatively, the observed pattern could be due to some other aspect of host physiology affected by parasitism (e.g. hormonal regulation).

In some relationships, there may be a parasite-induced reduction in the survival potential of the offspring from infected parents, which, together with the possible decrease in fecundity, contributes to the parasite-induced reduction in the reproductive potential of the host population. This effect has been demonstrated for mice infected with *Trichinella spiralis*(Weatherly, 1971). In the *H.diminuta* - *T.confusum* association, egg viability was measured by placing eggs from infected and uninfected females (5 replicates of 10 eggs each)

in flour-yeast medium and leaving them to hatch. The percentage hatch was assessed at the late larval stage. The results given in Table 2.4.3(c) indicate that there is no significant difference in the percentage hatch from infected and uninfected beetles ($d.f.=8, P(t=0.5)>0.5$).

2.4(iv) The influence of infection on host survival.

Parasite-induced host mortality is a common phenomenon (e.g. Lanciani, 1975; Frye and Olson, 1974; Cheatum, 1951; Samarawickrema and Laurence, 1978) and examination of the results of several experimental studies has revealed a range of possible functional relationships between parasite burden and host mortality. Linear relationships, as well as more complex, non-linear patterns have been described (Anderson, 1978a; Anderson and May, 1978). Larval *T.castaneum* infected with the microsporidian *Nosema whitei* have been shown to develop more slowly and die more quickly than their uninfected counterparts, the rate of development and mortality being proportional to the dose of spores to which the beetles were exposed (Milner, 1972). A similar retardation of the growth and development of larval and pupal stages of *T.confusum* infected with both *H.diminuta* and *H.microstoma* has been reported (Tan and Jones, 1969). Adult beetle survival characteristics, however, are less well documented and experiments were carried out in the present study to investigate the relationship between the number of *H.diminuta* cysticercoids harboured by an adult beetle, and the

probability of beetle survival per unit time.

One of the most important factors influencing the nature of a host-parasite relationship is host stress, in particular that caused by inadequate food supply (e.g. Chandler, 1953; Noble 1961; Gordon, 1963; Cheatum, 1951). It seems likely that parasite infections which are apparently non-pathogenic in healthy hosts may precipitate disease and mortality when the host is subjected to malnutrition, although surprisingly little evidence is available to support this assumption (see Anderson, 1979a). The influence of dietary stress on the larval *T.castaeum* / *N.whitei* association has been examined by George (1971), who found that differential mortality between infected and uninfected larvae was increased in hosts given inadequate diets, although dietary deficiency did not alter susceptibility to infection.

The first experiment carried out in the present study included an assessment of the effect of dietary stress. Groups of 50 beetles (1 - 7 days post eclosion) were starved for 6 days, after which 3 groups were exposed to 0.7 gm. fresh *H.diminuta* proglottid, and the remaining 3 groups were given 0.7 gm. boiled proglottid. After a 24 hour exposure period, 2 of the infected populations (together with their uninfected controls) were given 20 gm. and 0.5 gm. flour-yeast medium respectively, while the third infected population and control were starved. Survival was monitored daily, and dead beetles were removed to prevent scavenging behaviour. The results shown in Figure 2.4.4 indicate that

Figure 2.4.4 *The influence of parasitism on beetle survival under varying dietary conditions.*

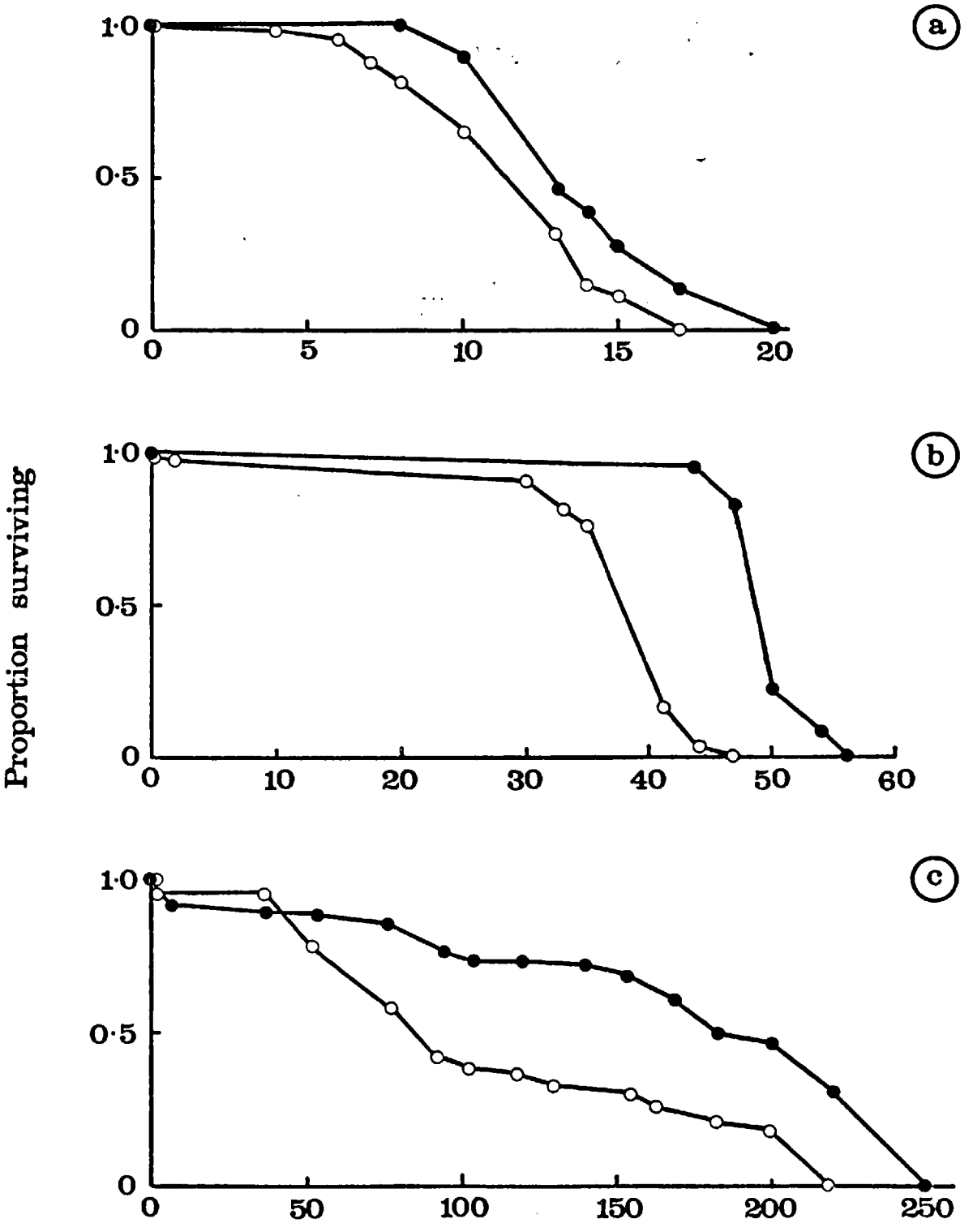
(a) Host populations starved

(b) 0.5 gm. flour-yeast medium/50 hosts

(c) 20 gm. flour-yeast medium/50 hosts

Solid circles; uninfected beetles.

Open circles; infected beetles.


a
1·0
0·5
0
0
5
10
15
20
b
1·0
0·5
0
0
10
20
30
40
50
60
c
1·0
0·5
0
0
50
100
150
200
250
Proportion surviving
Days post infection

H.diminuta infection has a severe effect on the survival of *T.confusum* which is apparent even when food is non-limiting. Nutritional stress does not appear to intensify the effect.

Having demonstrated the existence of parasite-induced host mortality, further work was necessary in order to examine the nature of the relationship between host mortality and parasite burden. Since the effect was not dependent on host diet, all further experiments were carried out using starved beetles to increase the rate of host mortality and thus to decrease the necessary experimental time period. The determination of the precise influence of parasitism on host survival proved difficult, since the parasite burden may only be determined by destructive sampling of living hosts. It was thus necessary to design the experiments so that the results could be used in conjunction with indirect methods of determination.

In the second experimental series, the repeated infection process (see Section 2.3(iv)) was used to produce groups of 50 beetles with 0 to 5 infections respectively. After the last infection, all groups were fed for 12 hours and then starved. Dead beetles were removed daily, and the proportion surviving in each group was monitored. From the results shown in Figure 2.4.5, it can be seen that the most heavily infected populations tend to survive less well than those with lower mean parasite burdens. This is shown both by the maximum survival times of each population, and by the shape of the survival curves.

Figure 2.4.5 *The survival of host populations harbouring different levels of infection.*

The points represent observed values and the solid lines indicate the predictions of the age-dependent survival model defined in equation (2.3.4):

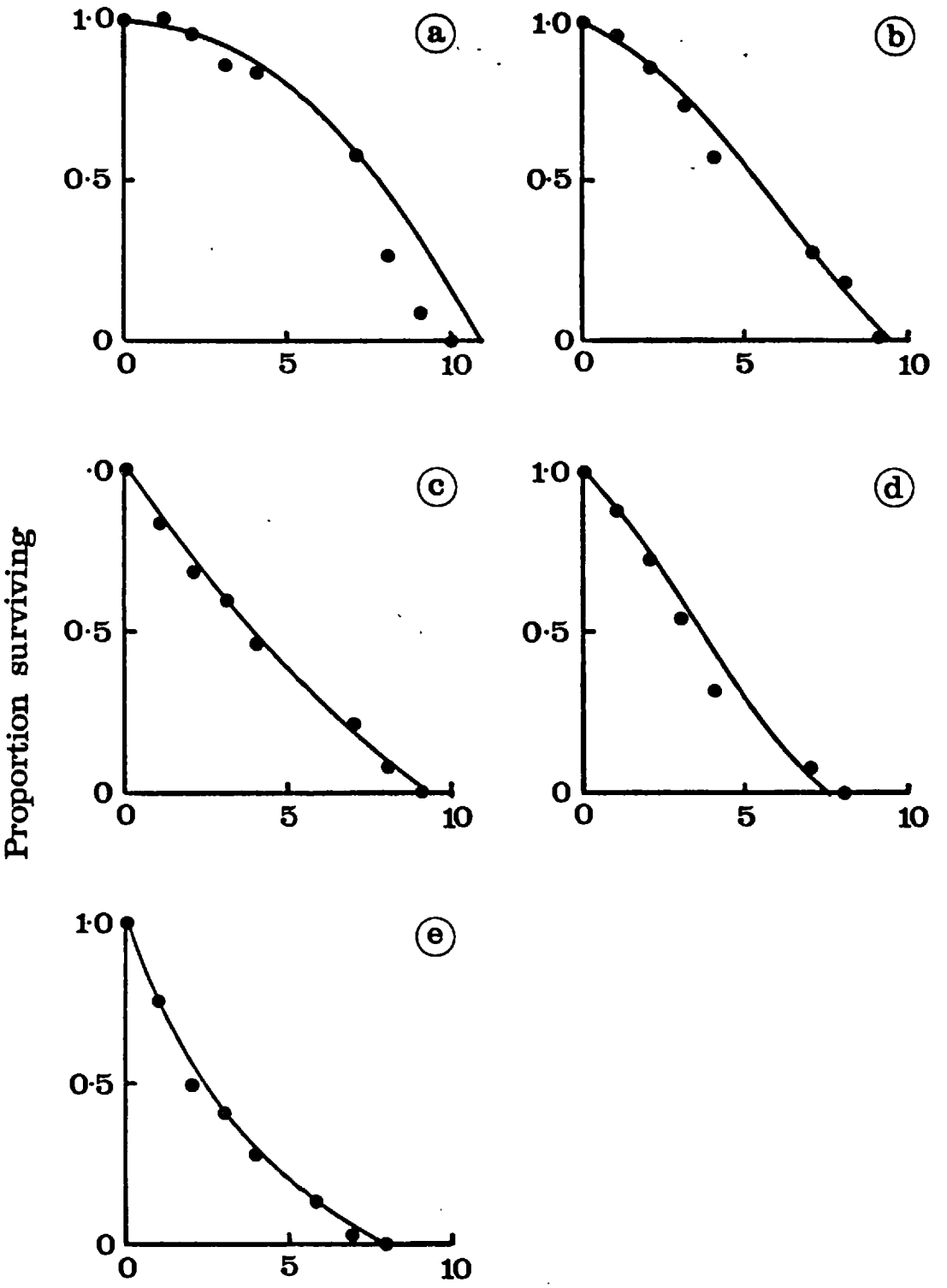
(a) Uninfected beetles (Parameter values for equation (2.3.4): m=0.01, n=0.45).

(b) 1 infection, estimated mean burden per host 9.9 (m=0.05, n=0.31).

(c) 3 infections, estimated mean burden per host 29.6 (m=0.12, n=0.18).

(d) 4 infections, estimated mean burden per host 39.4 (m=0.08, n=0.41).

(e) 5 infections, estimated mean burden per host 49.3 (m=0.21, n=0.16).


1·0
0·5
0
0
5
10
a
b
c
d
e
Proportion surviving
Days post starvation

Survival in all populations is age-dependent (as shown by the fit of the model defined in equation (2.3.4) to the experimental data) but the age-dependence is less marked in the heavily infected populations, indicating that the rate of stress-induced mortality is large in comparison to the rate of 'natural' mortality occurring under the given conditions.

Assuming that $\bar{b}_2$, the observed per capita instantaneous host death rate per unit time is constant through time (t), the temporal change in the number of beetles alive at time t, H_2, may be described by the differential equation

$$dH_2/dt = - \bar{b}_2 H_2. \qquad (2.4.2)$$

Given the initial condition that the number of beetles alive at the beginning of the experiment is $H_2(0)$, equation (2.4.2) has the solution

$$H_2 = H_2(0) \exp(-\bar{b}_2 t). \qquad (2.4.3)$$

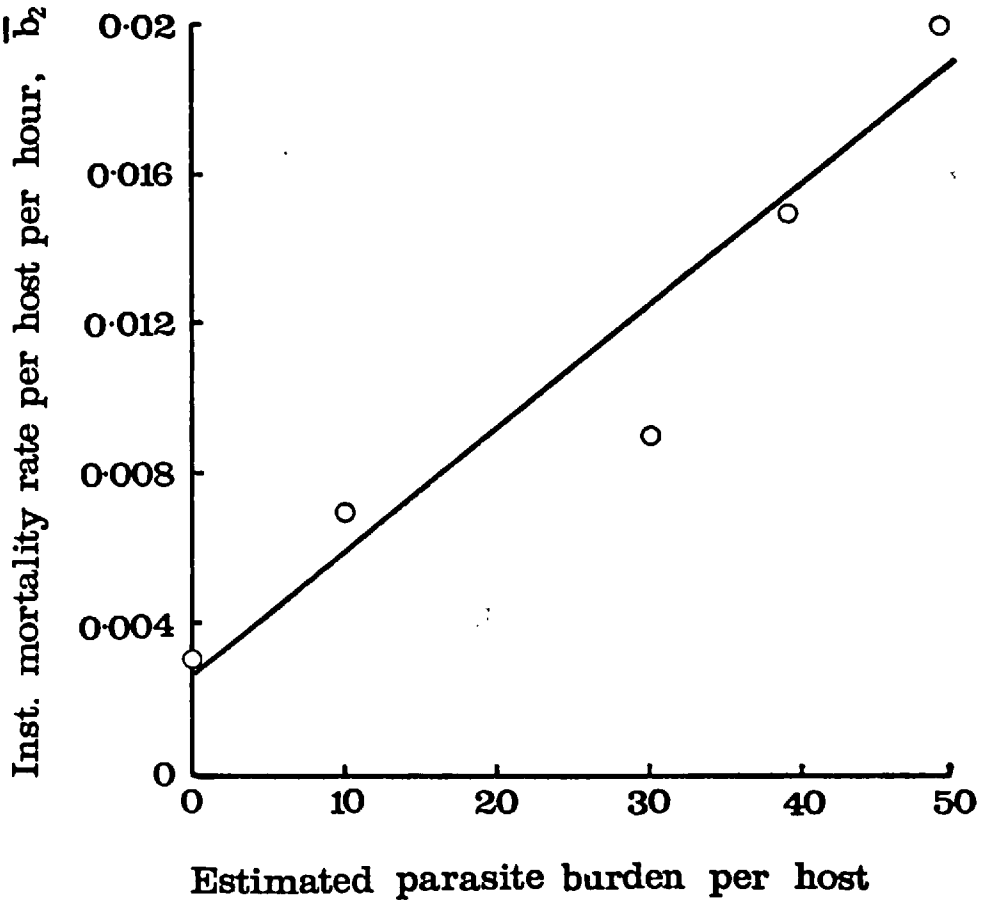
The host mortality rate, $\bar{b}_2$, may be estimated from the experimental data by rearranging equation (2.4.3) to give

$$\bar{b}_2 = (\ln H_2(0) - \ln H_2) / t. \qquad (2.4.4)$$

The relationship between $\bar{b}_2$ and the estimated parasite burden of the host population is given in Figure 2.4.6. From this rather

Figure 2.4.6 The relationship between host mortality and parasite burden.

The relationship between the instantaneous rate of host mortality, $\bar{b}_2$, and the mean parasite burden per host, M_2, as estimated using the model defined in equation (2.4.4) from the data given in Table 2.4.5. The solid line represents the predictions of the best-fit linear model ($\bar{b}_2 = 0.0026+0.0003M_2$).


Inst. mortality rate per host per hour, $\bar{b}_2$
0·02
0·016
0·012
0·008
0·004
0
0
10
20
30
40
50
Estimated parasite burden per host

crude estimation procedure, there is an indication of linearity in the relationship between observed host mortality and parasite burden, which serves as a hypothesis for further investigation.

A third, more detailed series of experiments was then carried out as follows. Six replicated groups of 50 or 60 beetles were exposed to a known level of infection, after which they were fed and left for 2 weeks to allow cysticercoid development to take place. All 6 replicates were then starved. The beetles in one population were dissected immediately, and their parasite burdens determined. The survival of the other 5 populations was monitored daily. They were sacrificed and dissected sequentially, after mortality of approximately 1/6 the population had occurred. Dissection of the final population thus took place when only 1/6 the beetles remained alive. Both the parasite burdens of the dissected beetles and the time of dissection (measured as hours post starvation) were monitored. This experimental process was then repeated 4 times at different initial levels of infection, to yield a detailed set of data from which a second estimate of the relationship between host mortality and parasite burden could be derived. Throughout the experiment, all populations were exposed to the same regime of feeding and starvation.

The experimental design was such that the change in the frequency distribution of parasite numbers per host through time, was available for 5 different initial infection levels, (a) to

(e). This data is depicted in Figure 2.4.7. The program TOPFIT (Reyna Robles, 1971) was used to ascertain which of the 3 following probability distributions provided the best empirical model for each set of frequency data; Poisson, negative binomial and Neyman Type A. At each of the 5 infection levels, the frequency distribution of parasite numbers per host clearly becomes less over-dispersed as time proceeds and the population declines in size as a result of mortality. This gives substantial evidence in support of the hypothesis that individual hosts with high parasite burdens tend to die more rapidly than those harbouring fewer parasites, and thus that there is a direct relationship between host mortality and parasite burden.

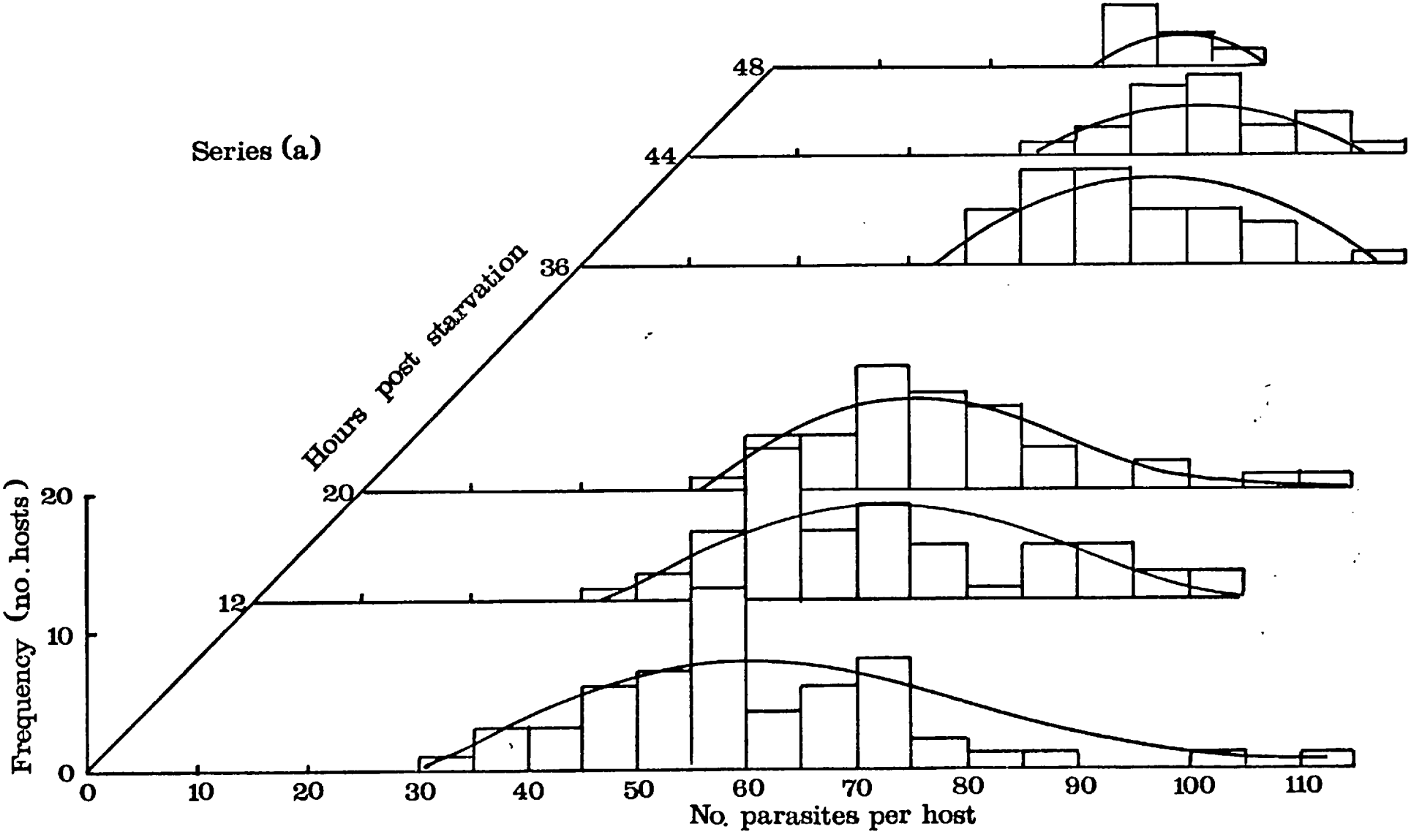
The total set of data obtained from these experiments may be conveniently summarized by representing each frequency distribution by 2 parameters, the mean and variance. The change in the mean parasite burden of the host populations through time, for initial infection levels (a) to (e), is presented in Figure 2.4.8 (drawn from data given in Table 2.4.7). The decrease in the mean parasite burden through time, together with the relationship between the initial infection level and the duration of population survival, again reinforce the hypothesis that the parasite burden of the host has a distinct influence on its probability of survival.

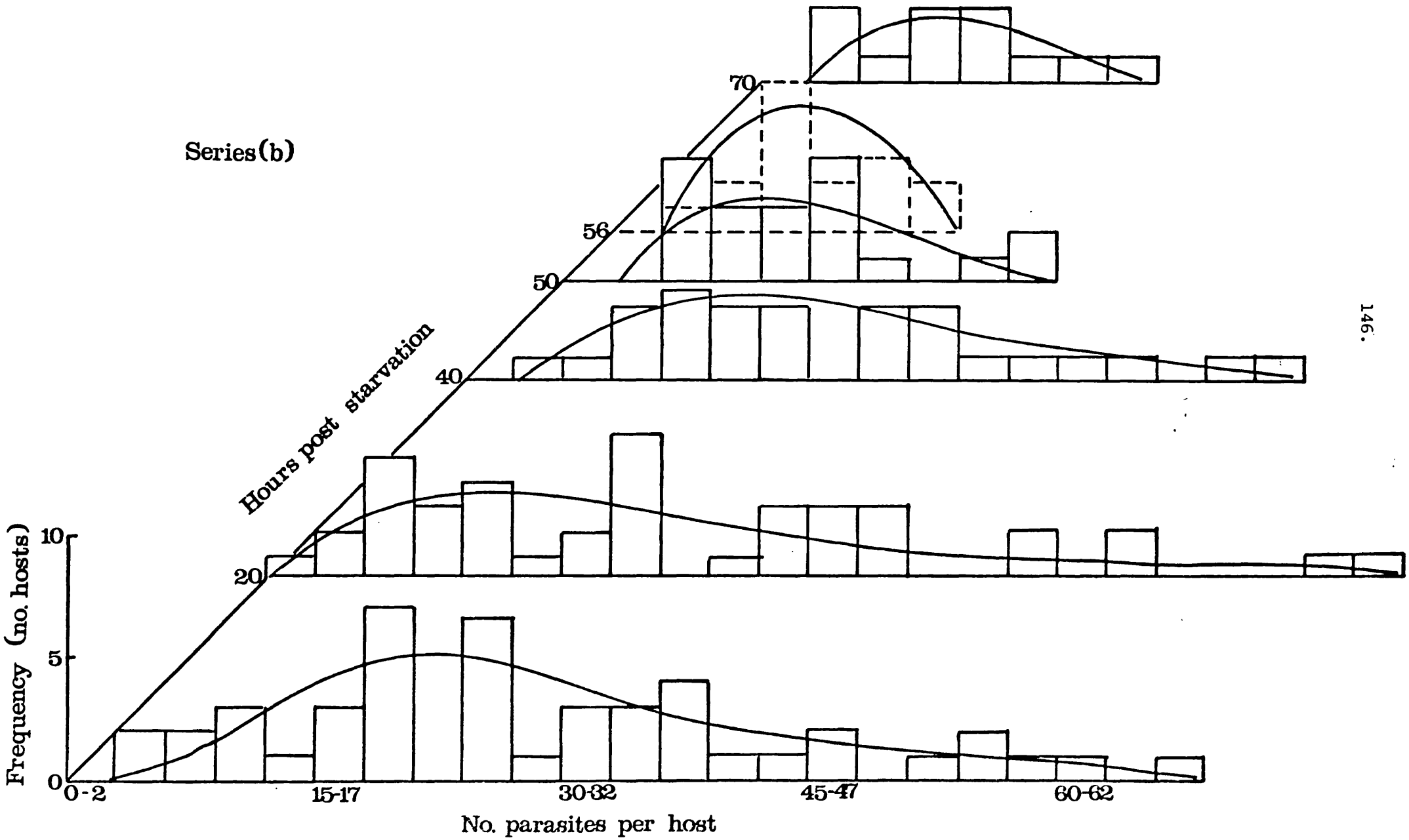
In addition to these qualitative observations, the data obtained is amenable to a more detailed investigation of the causes

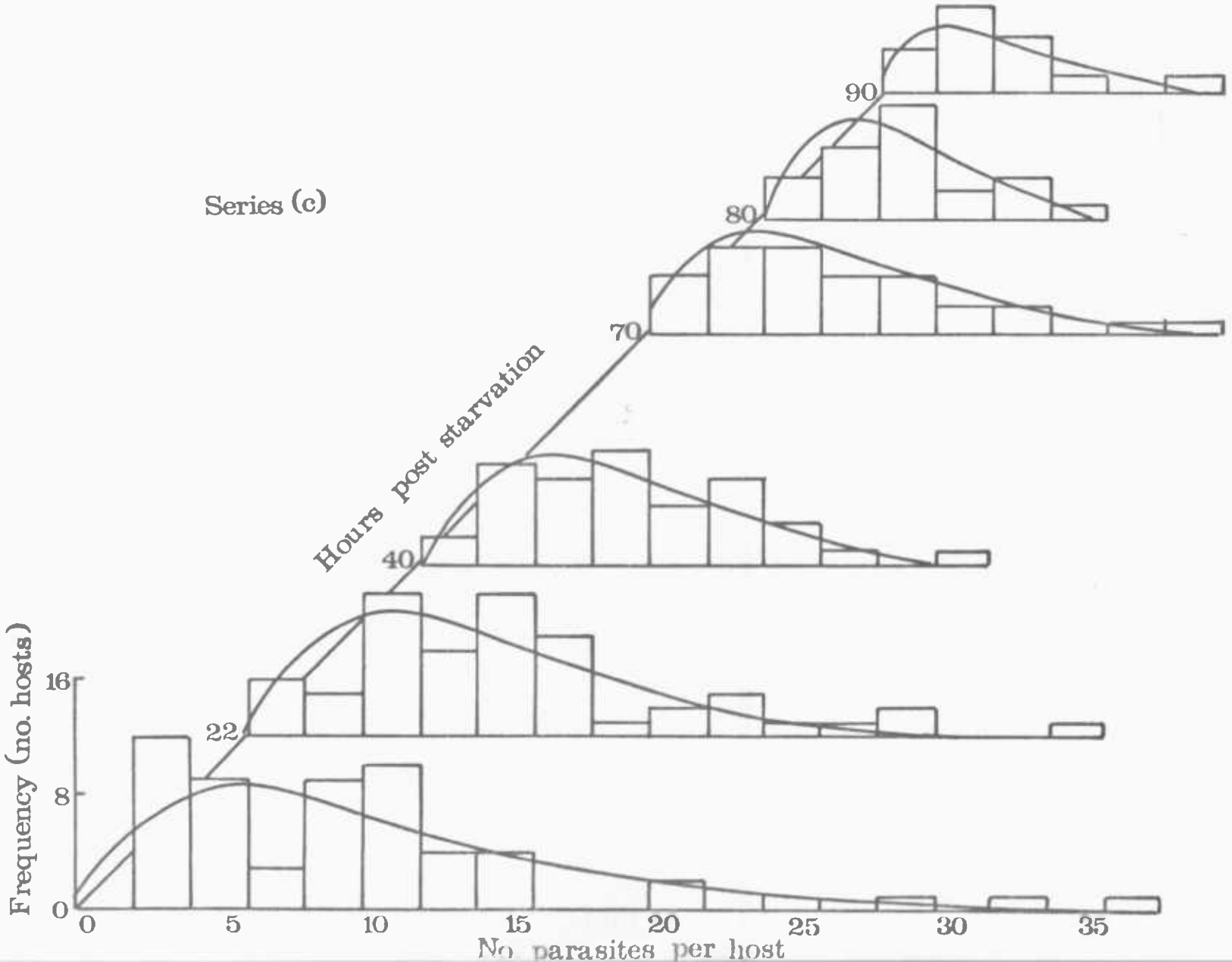
Figure 2.4.7 *The change in the frequency distribution of parasite numbers per host through time.*

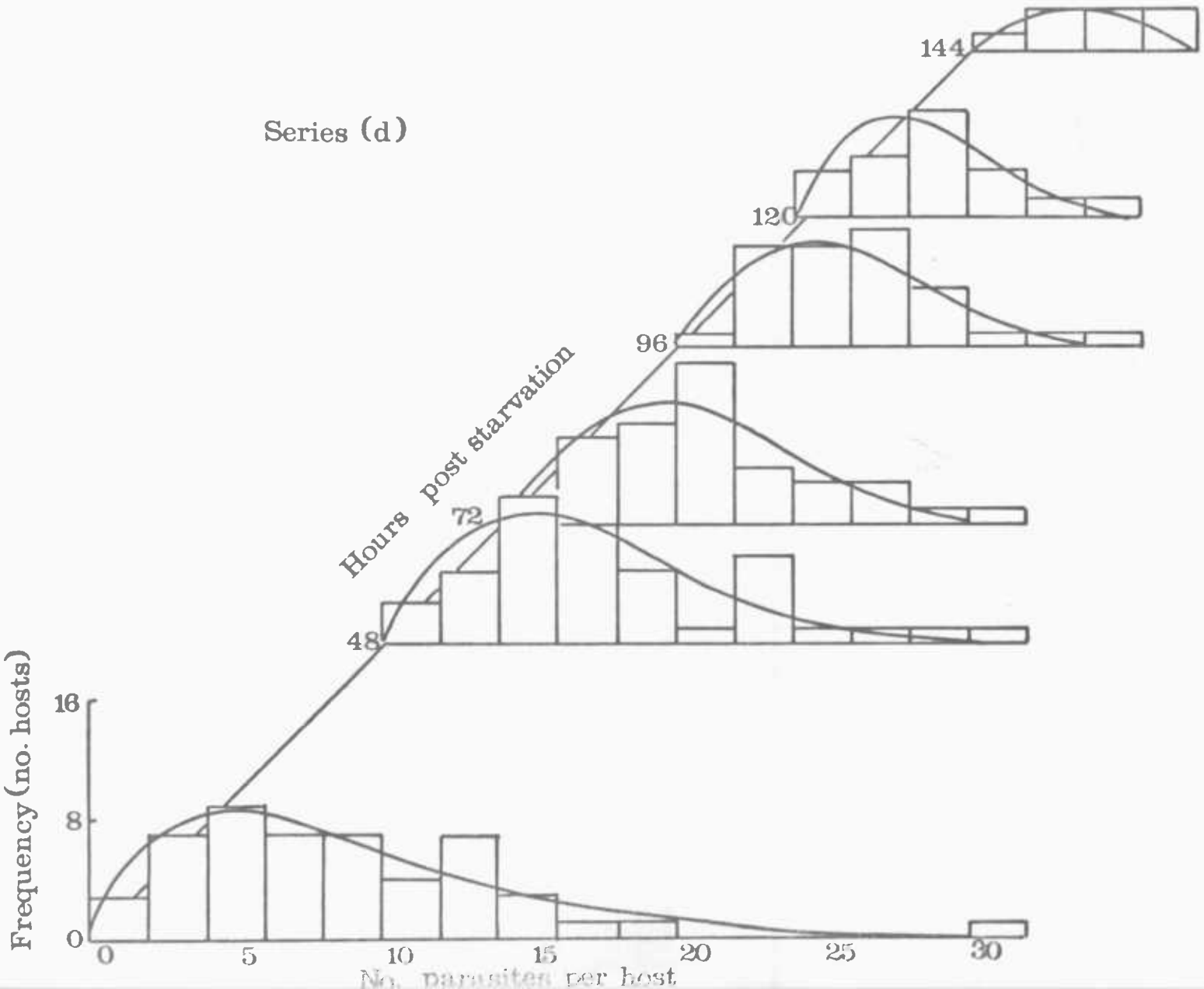
The histogram bars represent observed frequencies, and the solid lines indicate the predictions of the negative binomial (N.B.) or Poisson (P) probability distribution models (see below).

	Hours post starvation	Distribution	k	χ^2	d.f.
Series (a)	0	N.B.	22.68	52.11	39
	12	N.B.	23.43	36.59	34
	20	N.B.	29.07	22.19	27
	36	P.		12.61	18
	44	P.		56.60	12
	48	P.		7.09	6
Series (b)	0	N.B.	3.50	87.93	34
	20	N.B.	2.10	63.44	28
	40	N.B.	4.09	22.13	16
	50	N.B.	6.45	39.16	13
	56	P.		23.99	8
	70	N.B.	5.21	8.17	6
Series (c)	0	N.B.	2.21	86.28	19
	22	N.B.	2.19	62.76	17
	40	N.B.	3.29	42.58	12
	70	N.B.	1.70	25.91	11
	80	N.B.	3.40	21.68	6
	90	N.B.	1.86	14.89	4
Series (d)	0	N.B.	2.23	57.53	15
	48	N.B.	2.63	53.75	14
	72	N.B.	5.23	38.42	11
	96	N.B.	5.67	28.53	8
	120	N.B.	3.07	24.98	6
	144	P.		3.65	3
Series (e)	0	N.B.	0.24	3.04	9
	72	N.B.	0.44	10.39	9
	120	N.B.	0.60	7.53	6
	144	N.B.	0.41	1.78	3
	173	N.B.	0.48	0.03	2
	216	N.B.	0.98	1.79	1


Series (a)
Hours post starvation
48
44
36
20
12
Frequency (no. hosts)
0
10
20
0
10
20
30
40
50
60
70
80
90
100
110
No. parasites per host


Series (b)
70
56
50
40
20
Hours post starvation
10
5
0
Frequency (no. hosts)
0-2
15-17
30-32
45-47
60-62
No. parasites per host


Series (c)
Hours post starvation
22
40
70
80
90
Frequency (no. hosts)
0
8
16
0
5
10
15
20
25
30
35
No. parasites per host


Series (d)
144
120
96
72
48
Hours post starvation
16
8
0
Frequency (no. hosts)
0
5
10
15
20
25
30
No. parasites per host

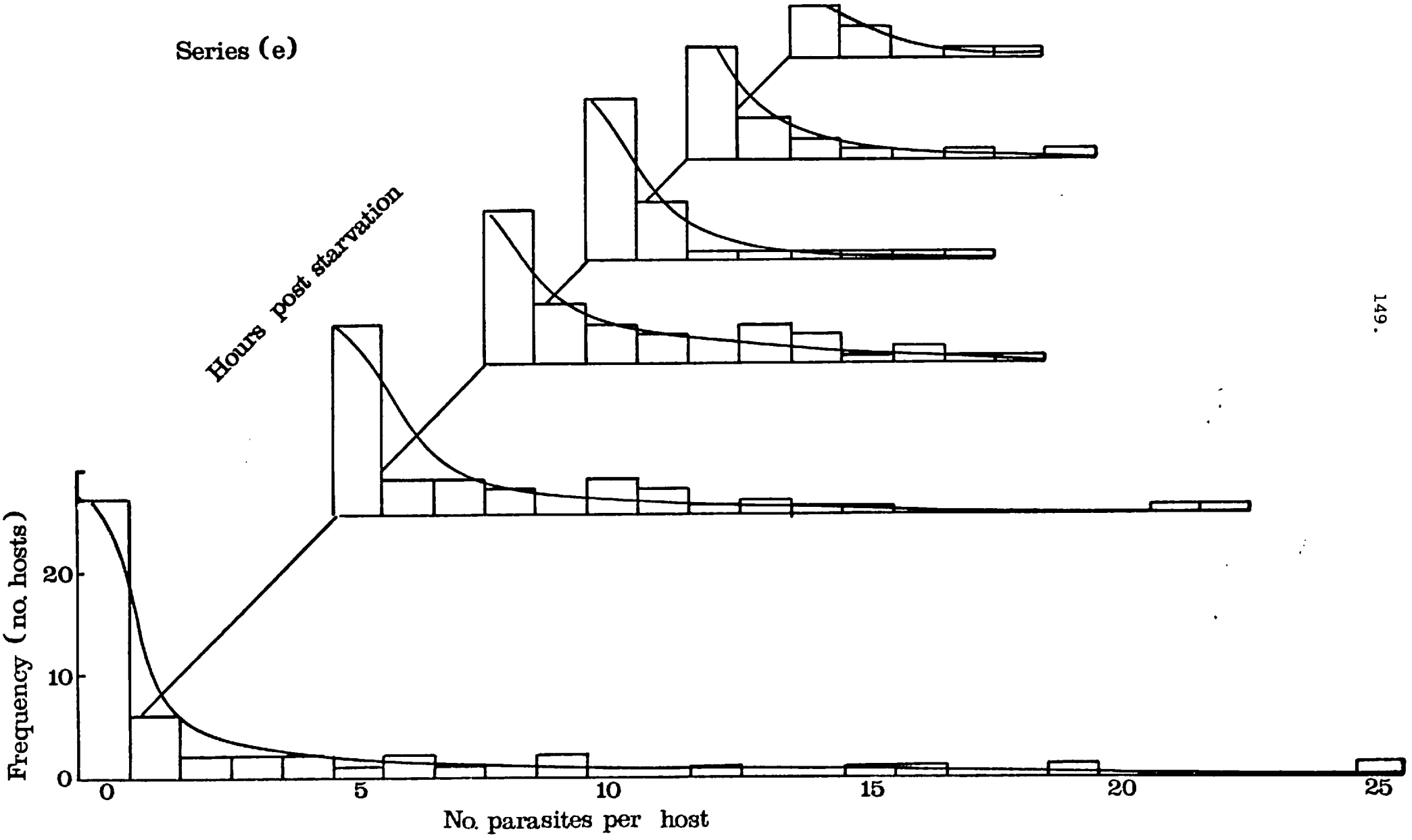

Series (e)
Hours post starvation
Frequency (no. hosts)
0
10
20
0
5
10
15
20
25
No. parasites per host

Figure 2.4.8 *The change in the mean parasite burden of infected beetle populations through time.*

The points represent observed values for initial infection levels (a) to (e) and the solid lines indicate the predictions of the best-fit linear models, $M_2 = dx+c$ where M_2 = mean parasite burden per host and x = hours post starvation.

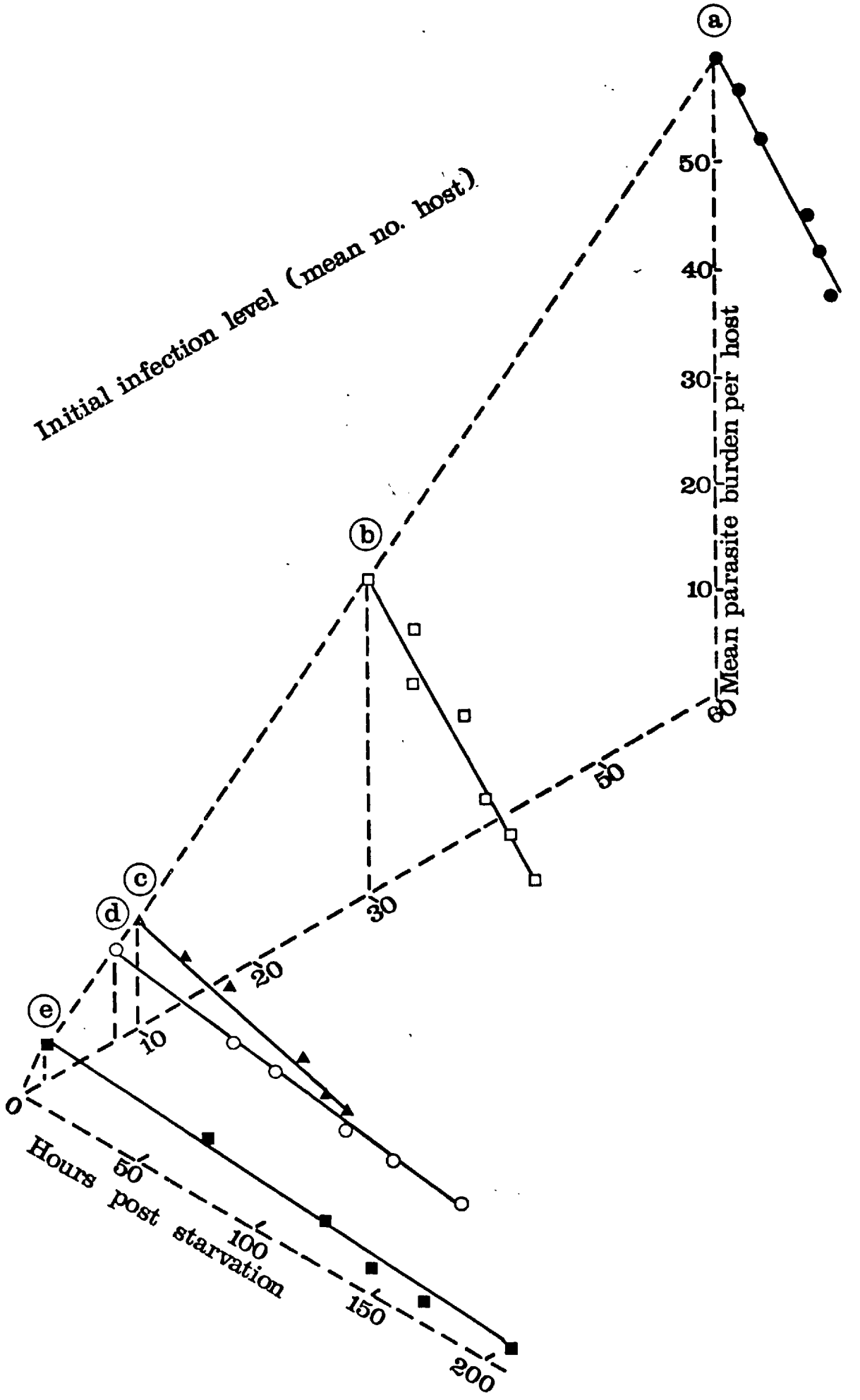
(a) d = -0.34, c = 61.6 parasites/host

(b) d = -0.26, c = 28.9 parasites/host

(c) d = -0.07, c = 9.8 parasites/host

(d) d = -0.03, c = 8.4 parasites/host

(e) d = -0.01, c = 3.3 parasites/host


Initial infection level (mean no. host)
a
b
c
d
e
50
40
30
20
10
0
Mean parasite burden per host
50
30
20
10
0
50
100
150
200
Hours post starvation

of mortality occurring in the population. The overall observed host mortality rate, $\bar{b}_2$, is a composite parameter with two distinct components. First there is an instantaneous rate of natural mortality per host per unit time, b_2, which would occur in the absence of parasitism, and second, the additional mortality which is induced by the presence of the parasites. Indirect methods are necessary in order to examine the relationship between parasite burden and host mortality, and to separate these effects from the natural mortalities occurring in the population. The precise functional form of the relationship may be most easily derived by comparing the experimental data with the predictions of a model incorporating an assumption of linearity between the parasite burden per host, i, and the instantaneous rate of parasite-induced host mortality per parasite per unit of time, α. If this assumption is valid, the values of α calculated from the experimental data should be constant (allowing for experimental variation) and independent of the initial mean parasite burden of the host population.

Given this assumption, the rate of change of the number of hosts harbouring i parasites at time t, $H_2(i)$ may be described by the differential equation

$$dH_2(i)/dt = - (\alpha i + b_2)\ H_2(i) \qquad (2.4.5)$$

where b_2 is the per capita instantaneous rate of natural host

mortality in the absence of parasitism (assumed to be age-independent over the experimental time period) and α is the instantaneous rate of parasite-induced host mortality per parasite per unit time. Given the initial condition that the number of hosts harbouring i parasites when t=0 is $H_2(i,0)$, equation (2.4.5) has the solution

$$H_2(i) = H_2(i,0) \exp (-(\alpha i+b_2) t). \qquad (2.4.6)$$

Since the death rate of individual hosts depends on the number of parasites they harbour, the overall observed host mortality in the population will be critically dependent on both the mean parasite burden and also the statistical distribution of parasites within the host population. The latter is almost always over-dispersed (Anderson, 1978a) and has been found to be extremely contagious for both laboratory (see Section 2.3(vi)) and field (Rau, 1979) populations of *H.diminuta* in the intermediate host. A good empirical description of the pattern of parasites per host is given by the negative binomial probability model (Bliss and Fisher, 1953; see Figures 2.3.8 and 2.5.9). The probability generating function (p.g.f.) of this model is defined as

$$\Pi(z) = (Q-Rz)^{-k} \qquad (2.4.7)$$

where k is an inverse measure of the degree of over-dispersion or aggregation, R is the probability of a successful infection, and Q=1+R (see Pielou, 1969). An expression for the total number of hosts surviving at time t, H_2, may then be derived by summing

equation (2.4.6) over all values of i, to give

$$H_2 = \sum_{i=o}^{\infty} H_2(i) = H_2(0).(Q - Re^{-\alpha t})^{-k}.e^{-b_2 t} \qquad (2.4.8)$$

where $H_2(0)$ is the initial size of the host population. Similarly, an expression for the total number of parasites present at time t, P_2, is given by the product of the number of hosts harbouring i parasites at time t, $H_2(i)$ and the parasite burden, i, summed over all values of i

$$P_2 = \sum_{i=o}^{\infty} i.H_2(i) = H_2(0).(Q - Re^{-\alpha t})^{-(k+1)}. Rk\, e^{-t(\alpha+b_2)}. \qquad (2.4.9)$$

An expression for the mean number of parasites per host at time t, M_2 (where $M_2=P_2/H_2$), may then be derived by combining equations (2.4.8) and (2.4.9) to give

$$M_2 = (kR\, e^{-\alpha t}) / (Q - R\, e^{-\alpha t}). \qquad (2.4.10)$$

The rearrangement of equation (2.4.10) leads to the following expression which may be used to obtain estimates of α from the experimental data

$$\alpha = -\frac{1}{t} \ln (QM_2/R(M_2+k)). \qquad (2.4.11)$$

Five estimates of α were calculated for each of the 5 time intervals between dissections, and these were combined to give average values for each initial infection level (a) to (e),

as shown in Figure 2.4.9(a). There is no significant difference between the values (d.f.=3, $P(t=1.09)>0.3$), thus supporting the hypothesis that the relationship between the rate of parasite-induced host mortality per parasite per unit time and the parasite burden per host is of linear form. The method by which the estimates of α were obtained encompasses certain simplifying assumptions, the major one being the assumed constancy of the degree of over-dispersion in the frequency distribution of parasite numbers per host through small intervals of time. This is necessarily an approximation, as indicated by the experimental data shown in Figure 2.4.7. Despite this discrepancy, the method provides a useful guide to the nature of the relationship between α and i.

To gain an estimate of the overall rate of observed host mortality ($\bar{b}_2$/unit time/host), the expression for H_2 given in equation (2.4.8) may be substituted into equation (2.4.4) to give

$$\bar{b}_2 = b_2 + \frac{k}{t} \ln (Q - Re^{-\alpha t}). \qquad (2.4.12)$$

From this expression, it is apparent that the rate of mortality observed in a host population is a function of the statistical distribution of parasite numbers per host. The relationship between the instantaneous rate of observed host mortality, $\bar{b}_2$, and the negative binomial parameter, k, for a constant mean parasite burden is shown in Figure 2.4.10(a). The rate of observed host mortality reaches a maximum as k increases in magnitude;

Figure 2.4.9 The estimated rate of parasite-induced host mortality.

(a) The relationship between the instantaneous rate of parasite-induced host mortality per parasite per unit time, (α), and the mean parasite burden per host. The solid line indicates the predictions of the best-fit linear model, the points represent observed means, and the vertical bars represent the 95% confidence limits of the means.

(b) The relationship between the instantaneous rate of host mortality per host per unit time ($\bar{b}_2$) and the mean parasite burden per host. The solid line indicates the best-fit linear model, and the points represent observed values.

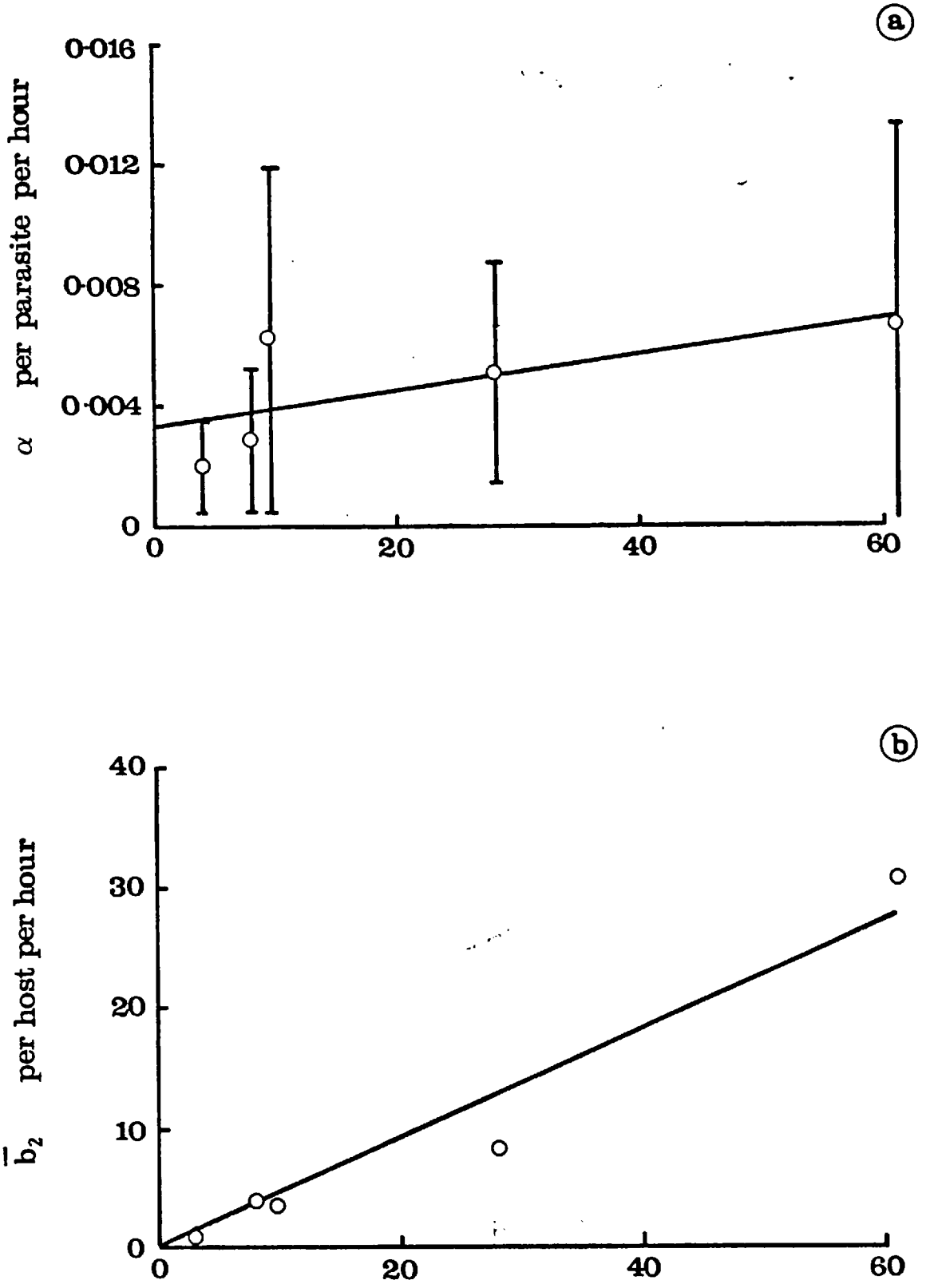
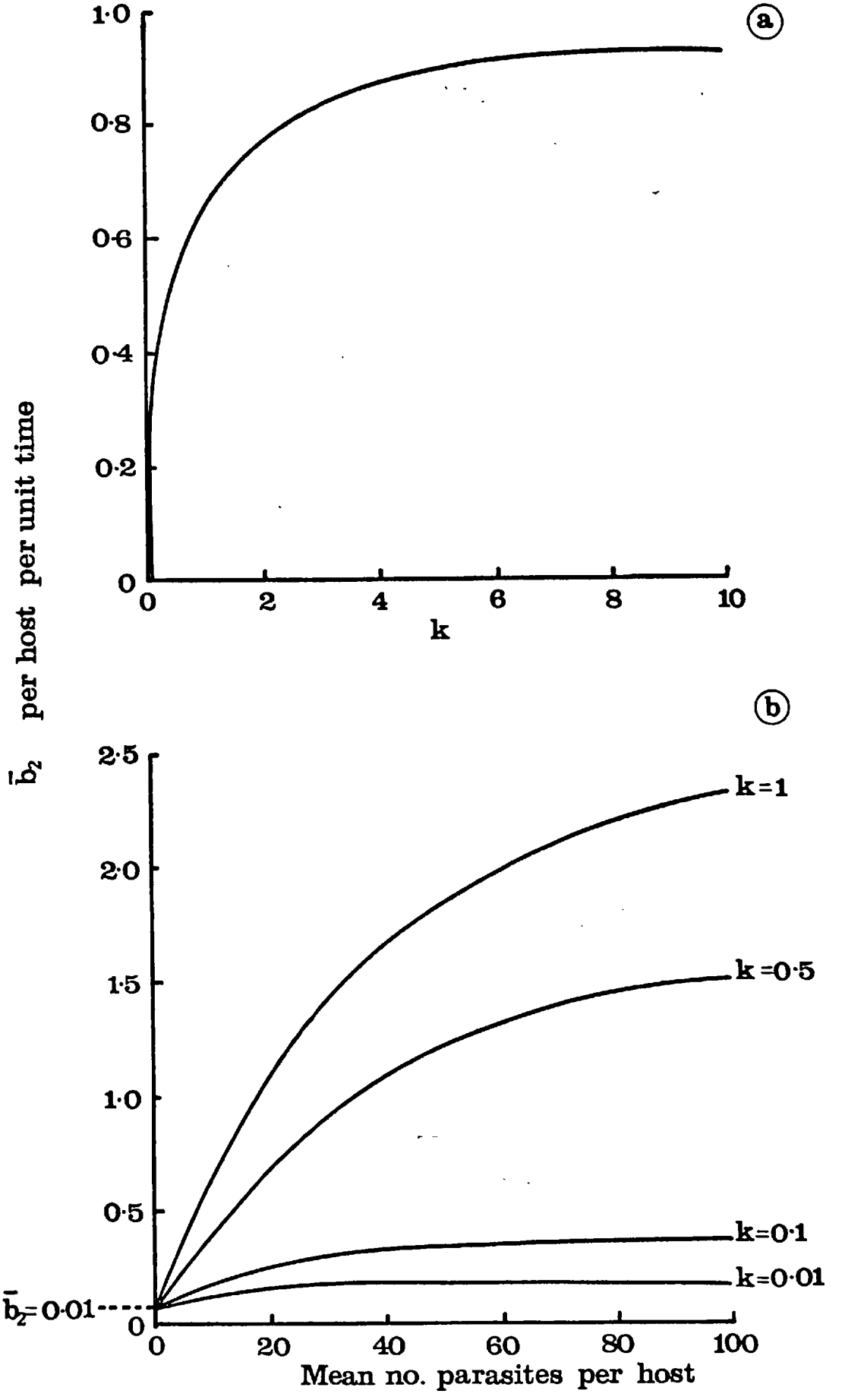

a
0·016
0·012
0·008
0·004
0
α per parasite per hour
0
20
40
60
b
40
30
20
10
0
b_2 per host per hour
0
20
40
60
Initial mean parasite burden no. per host

Figure 2.4.10 Predictions of the beetle survival model as defined in equation (2.4.12).

(a) The relationship between the instantaneous rate of observed host mortality per host per unit time ($\bar{b}_2$) and the degree of over-dispersion in the distribution of parasite numbers per host, as indicated by the negative binomial parameter, k (b_2=0.01/host/unit time, α=0.1/parasite/unit time, M_2=10 parasites/host, t=1 time unit).

(b) The relationship between the instantaneous rate of observed host mortality per host per unit time ($\bar{b}_2$) and the mean parasite burden of the host population, M_2. (b_2=0.01/host/unit time, α=0.1/parasite/unit time, t=1 time unit).


(a)
1·0
0·8
0·6
0·4
0·2
0
0
2
4
6
8
10
k
$\bar{b}_2$ per host per unit time
(b)
2·5
2·0
1·5
1·0
0·5
0
k=1
k=0·5
k=0·1
k=0·01
$\bar{b}_2$=0·01
0
20
40
60
80
100
Mean no. parasites per host

when k is greater than 8, the distribution of parasites within the host population is effectively random. When the value of k is decreased, the observed rate of host mortality is also decreased, since the prevalence of infection is lower and thus the effect of parasite-induced host mortality on the population is less severe.

A second point of some importance is apparent from the structure of equation (2.4.12). If the parasites are over-dispersed within the host population, then a linear relationship between the rate of parasite-induced host mortality per parasite per unit time (α) and the parasite burden per host (i) will not generate a linear relationship between *observed* host mortality and *mean* parasite burden. This is illustrated in Figure 2.4.10(b), where observed host mortality is plotted against the mean parasite burden of the host population, for 4 different values of k. In all cases, when the population is parasite free, the rate of mortality observed in the population is equal to b_2 (the rate of natural mortality per host per unit time). It is important to note, however, that the model predictions illustrated in Figure 2.4.10 are based on the assumption that the degree of over-dispersion of parasite numbers per host is constant through time.

Equation (2.4.12) may be used to obtain estimates of $\bar{b}_2$ from the data given in Table 2.4.7. The relationship between $\bar{b}_2$ and the mean parasite burden per host is shown in Figure 2.4.9(b). In contrast to the theoretical relationship derived above, it is of approximately linear form. This discrepancy between observed

results and theoretical predictions most probably arises because the experimental infection range represents only the lower part of the theoretical range shown in Figure 2.4.10(b).

Figures 2.4.6 and 2.4.9(b) represent the relationships between host mortality and parasite burden as obtained from two separate series of experiments. The magnitude of the estimates obtained, however, are not comparable; the rate of host mortality being much higher in Figure 2.4.9(b) than in Figure 2.4.6. The major difference in experimental design which may explain this discrepancy is that the host populations were starved 12 hours after infection in the earlier series of experiments, whereas in the later experimental design, starvation did not commence until 2 weeks post infection. Thus the beetles had already harboured the parasites for 2 weeks, and had a correspondingly higher death rate when stress induced by starvation commenced. In addition, beetle survival in both the experiments discussed above was lower than beetle survival in the preliminary experiments relating survival to dietary stress (Figure 2.4.4). This is probably because, in these preliminary experiments, the beetles had not been subjected to the 6 week period of alternate feeding and starvation associated with the repeated infection process used in both later series of experiments.

In summary, the reported results reveal a direct proportionality between the rate of parasite-induced host mortality per parasite per unit time and the number of parasites harboured

per host. It must be emphasized, however, that this may not result in a linear relationship between overall host mortality and parasite burden if the parasites have an aggregated distribution within the host population. Although nothing is known of the generative mechanisms behind these patterns, the results are consistent with the hypothesis that host survival is related to the number of parasites which penetrate and cause damage to the midgut wall.

2.4(v) The influence of infection on host population growth.

The influence of parasitic infection on the dynamics of host population growth has been reviewed by Anderson (1979a and b; 1980d), and although little direct evidence is available, several studies have been carried out which indicate indirectly the adverse influence of disease on the population growth of stored-product insects (Milner 1972; George, 1971; Ashford,1967). In a survey of pathogens occurring naturally in *T.castaneum* taken from British food stores, 53% of collected samples were found to be infected (Burges and Weiser, 1973). In spite of this, the authors concluded that disease is unlikely to curb beetle infestation before the level of economic importance is reached.

One of the few experimental investigations of the effect of parasitism on insect population growth was carried out by

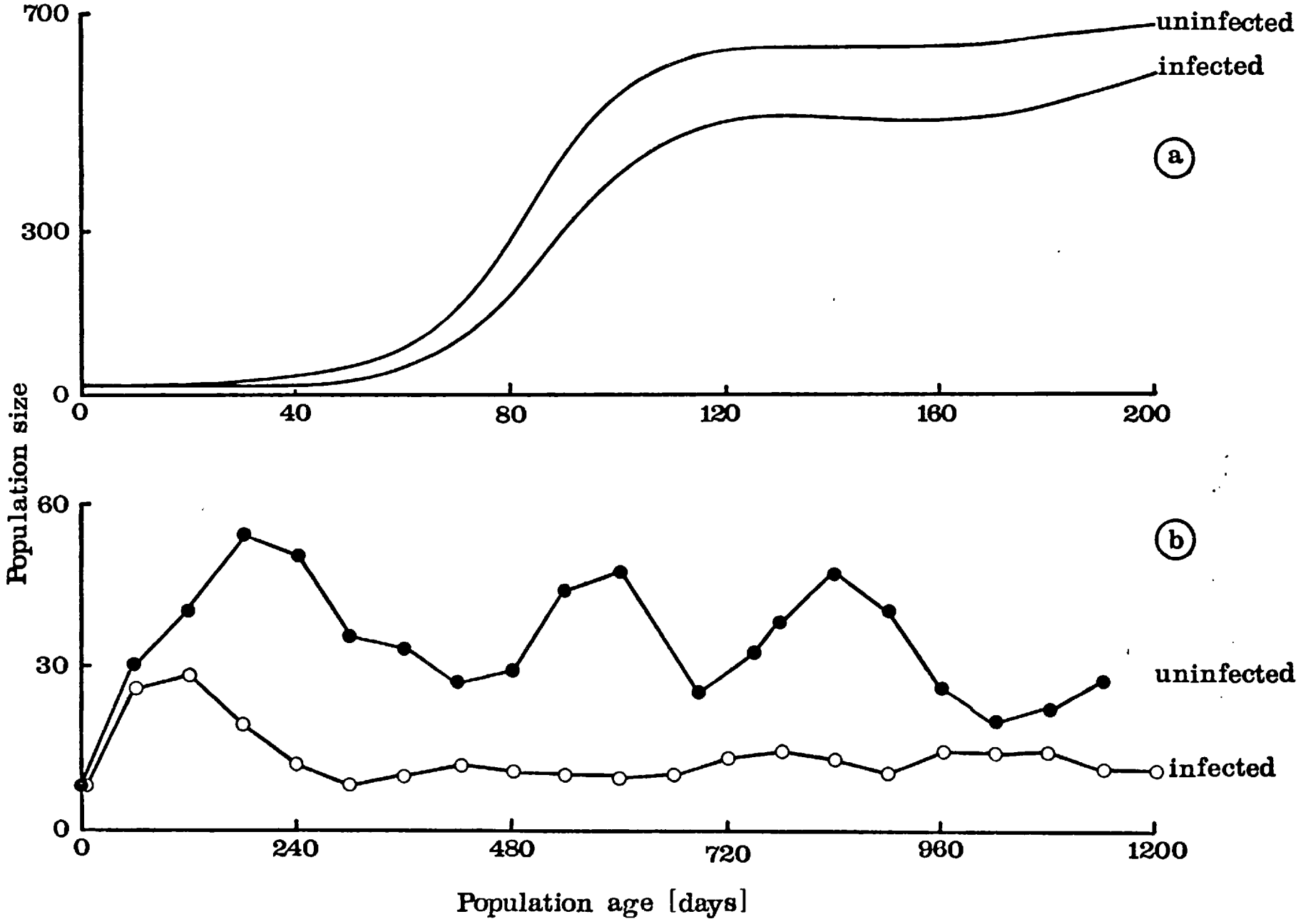
Dowell and Jones (1966). Populations of *T.confusum* were established using uninfected larvae, and larvae which had been exposed to infection by *H.microstoma*. The results shown in Figure 2.4.11(a) give a direct indication of the potential of the parasite to reduce the natural intrinsic growth rate of the host population. The study was unfortunately not continued, and so the total time taken for the population to recover from the initial effects of parasitism remains unknown. A further illustration of the regulatory potential of an insect pathogen is found in the work carried out by Park (1948), in which free-running populations of *T.castaneum* were monitored at 30 day intervals for over 3 years. The equilibrium population size attained by uninfected populations was found to be over 50% greater than that in populations infected with the sporozoan *Adelina tribolii* (see Figure 2.4.11(b)). Park concluded that *A.tribolii* influences *T.castaneum* populations through the agency of increased mortality directed especially to the immature stages, although it was noted that a reduction in host fecundity might also be important.

Having demonstrated *H.diminuta*-induced effects on the survival and fecundity of *T.confusum*, long term experiments were carried out in the present study in order to determine their combined effect on the natural intrinsic growth rate of the beetle population. Since the parasite has an indirect life-cycle, it was unfortunately impossible to maintain free-running infected populations without experimental intervention, but the following experimental design was employed in order to minimize the amount of interference

Figure 2.4.11 *Laboratory examples of the depression of insect population growth by parasitic infection.*

(a) Establishment of *T.confusum* populations from uninfected beetles, and from beetles infected with *H.microstoma*. Data from Dowell and Jones (1966).

(b) Free-running populations of *T.castaneum*: uninfected, and infected with sporozoan,*Adelina tribolii*. Data from Park (1948).


700
300
0
0
40
80
120
160
200
uninfected
infected
a
Population size
60
30
0
0
240
480
720
960
1200
b
uninfected
infected
Population age [days]

necessary. A population of 400 beetles of uniform age was starved for 6 days and then divided in 20 groups of 20 beetles each. Half these groups were each exposed to an estimated density of 3000 *H.diminuta* eggs for 3 hours in a standard infection arena. Each population (10 replicates uninfected and 10 replicates infected) was then placed in a specimen tube containing 1 gm. food medium, sealed with gauze secured by an elastic band.

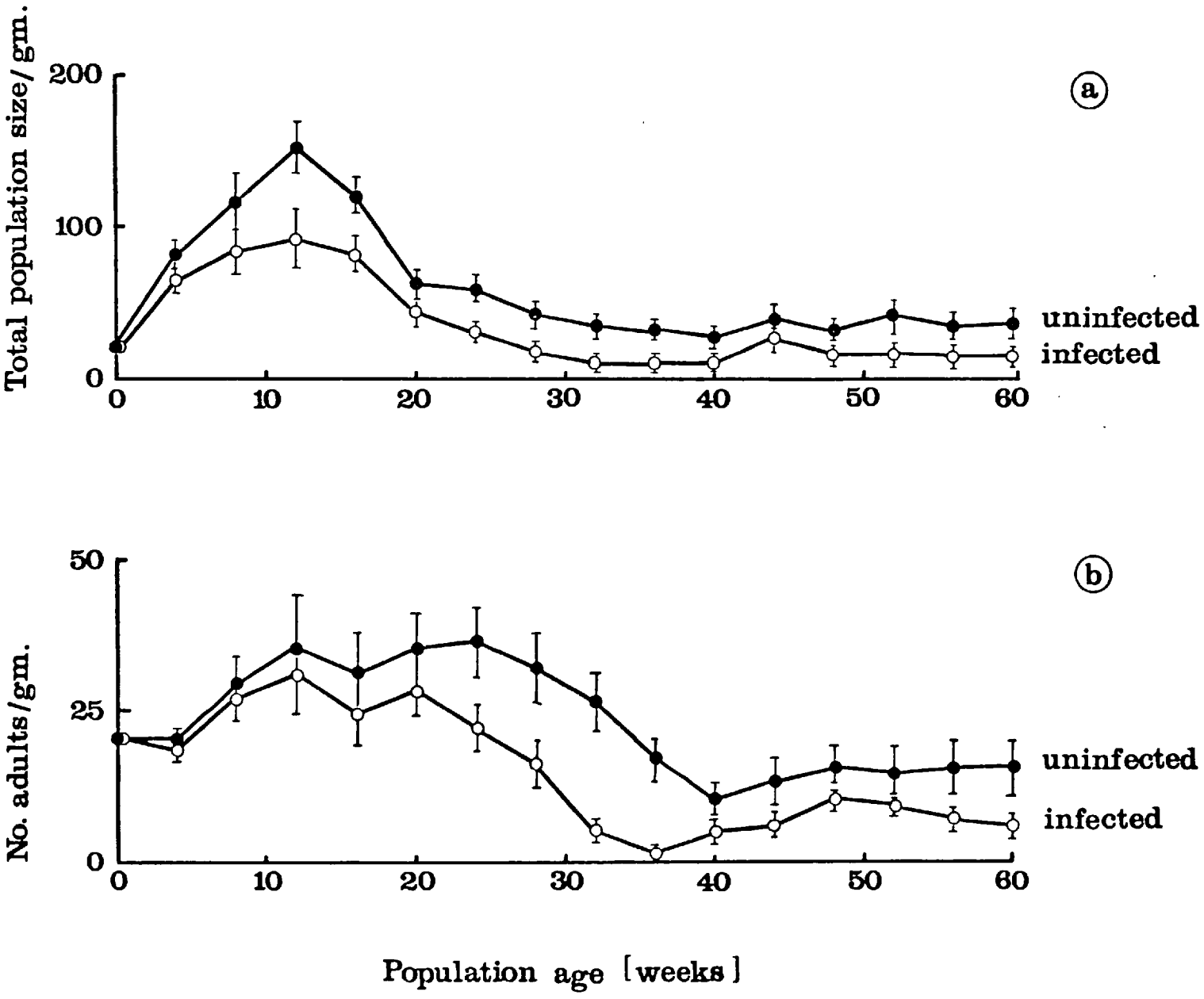
On every 28th day, a census of each population was made as follows. The contents of the tube were passed through a 250μ sieve, dead forms were removed and chaff was eliminated by gentle blowing. The living adult beetles present were counted and placed in a labelled 4 cm. diameter glass jar. The numbers of pupae and larvae present were determined, and these, together with the eggs retained by the sieve (which were not counted) were returned to a fresh, labelled specimen tube containing 1 gm. food medium. After 6 days, the groups of adults from the 10 infected cultures were each exposed to 3000 *H.diminuta* eggs for 3 hours in standard infection arenas. Following this, all 20 groups of adult beetles were returned to their respective cultures. This procedure was repeated at 4-weekly intervals for a total of 60 weeks. Experimental error unfortunately led to the loss of 2 uninfected populations on the 12th week, leaving thereafter 8 uninfected and 10 infected replicate populations. Their temporal development is portrayed in Figure 2.4.12.

Figure 2.4.12 *The influence of infection with* H.diminuta *on the population growth of* T.confusum.

The points represent observed values (mean of 8-10 replicates) and the vertical bars indicate the 95% confidence limits of the means.

(a) Total population size (no. adults, larvae and pupae per gm. food medium).

(b) No. adult beetles per gm. food medium.


Total population size/gm.
200
100
0
0
10
20
30
40
50
60
a
uninfected
infected
No. adults/gm.
50
25
0
0
10
20
30
40
50
60
b
uninfected
infected
Population age [weeks]

From these results, it is evident that under laboratory conditions, the effects of parasitism on the survival and fecundity of individual hosts may result in a 50% depression of equilibrium population size. The observed pattern of population growth, with an initial 'overshoot' before the equilibrium level is reached, is characteristic of *Tribolium* populations founded with adult beetles. It is thought to be a consequence of intraspecific predation in a population of particular age-structure (Lloyd, 1968). The first wave of pupae probably satiates the original adult population, thus leading to a slightly delayed adult overshoot before cannibalism and other density-dependent constraints succeed in regulating the population.

In order to compare the observed depression in host equilibrium population level, with that predicted on the basis of the parasite-induced effects demonstrated to occur in individual hosts, a model for the growth of beetle populations may be constructed as follows. For simplicity, it is assumed that the age-structure of the population is stable, and that growth is logistic (see Pielou, 1969). The temporal change in the size of the uninfected beetle population (H_2) may then be described by the Verhulst-Pearl logistic equation,

$$dH_2/dt = (a_2 - b_2 - \gamma H_2)\ H_2 \qquad (2.4.13)$$

where a_2 and b_2 are the per capita rates of adult fecundity and

mortality per beetle per unit time (assumed constant) and γ is a constant relating to the severity of the density-dependent constraints on population increase. From this, the carrying capacity of the habitat, K (set by a combination of arena size and food input) is defined by

$$K = (a_2-b_2) \; / \; \gamma. \qquad (2.4.14)$$

In the present experiments, the value of K may be estimated from the uninfected beetle population size at equilibrium. The mean of 9 values from 28 - 60 weeks gives an estimate of K as 34.4 beetles/gm. Taking approximate estimates of beetle mortality and beetle fecundity at this density (see Section 2.4(ii), Figure 2.4.1) of 0.13/beetle/week and 7 eggs/beetle/week respectively, γ may be roughly estimated (using equation (2.4.14)) as 0.20.

Assuming for simplicity that the rate of infection of beetles is directly proportional to the number of eggs present in the arena E, and to the number of hosts H_2 (see Section 2.3(ii)), the rate of change in the number of eggs present can be expressed by the differential equation

$$dE/dt = \lambda - \mu_3 E - \beta_2 H_2 E \qquad (2.4.15)$$

where λ is the constant rate of input of parasite eggs into the population (i.e. 3000 eggs/4 weeks), μ_3 is the instantaneous

rate of egg mortality, and β_2 is the instantaneous rate of beetle infection. Estimates of μ_3 and β_2 under experimental conditions of 0.03/egg/minute (see Section 2.3(i)) and 0.004/egg/minute/host/13cm² (see Section 2.3(iii)) respectively, have been obtained in earlier sections.

Given that the rate of parasite-induced host mortality is directly proportional to the number of parasites harboured per host (see Section 2.4(iv)) and that the relationship between beetle fecundity and parasite burden may be approximated by an exponential function (see Section 2.4(iii)), the rates of change of the number of hosts (H_2) and cysticercoids (P_2) present in an infected population can be expressed by the equations

$$dH_2/dt = a_2H_2 \exp(-\omega H_2 \sum_{i=o}^{\infty} i.p(i)) - (b_2+\gamma H_2)H_2 - \alpha H_2 \sum_{i=o}^{\infty} i.p(i) \qquad (2.4.16)$$

$$dP_2/dt = \beta_2 EH_2 - (b_2+\gamma H_2)H_2 \sum_{i=o}^{\infty} i.p(i) - \alpha H_2 \sum_{i=o}^{\infty} i^2.p(i) \qquad (2.4.17)$$

where p(i) represents the probability that a host harbours i parasites, and α and ω are the instantaneous rate of parasite-induced host mortality and proportional reduction in fecundity respectively. Estimates of α and ω of 0.005/parasite/hour (Section 2.4(iv)) and 0.03/parasite (Section 2.4(iii)) have previously been obtained. Both provide only approximate estimates, since α was measured in starved beetles and ω is a parameter of an

exponential model which provides only a rough description of the data.

Since the tapeworm eggs under experimental conditions have an extremely short lifespan (approximately 0.5 hours, see Section 2.3(i)) when compared with the cysticercoids and beetles (approximately 8 weeks, see Section 2.4(ii)), the above set of differential equations can be decoupled by assuming that the infective-stages are adjusted almost instantaneously to their equilibrium level ($dE/dt=0$) for any given value of H_2 and P_2 (see Anderson and May, 1979a). Assuming also that the distribution of parasites within the host population may be empirically described by the negative binomial distribution, such that

$$\sum_{i=o}^{\infty} i.p(i) = P_2/H_2 \qquad (2.4.18)$$

$$\sum_{i=o}^{\infty} i^2.p(i) = P_2^2(k+1)/H_2^2k + P_2/H_2 \qquad (2.4.19)$$

(see Anderson and May, 1978), the model may be simplified to give

$$dH_2/dt = a_2H_2e^{-\omega P_2} - (b_2+\gamma H_2)H_2 - \alpha P_2 \qquad (2.4.20)$$

$$dP_2/dt = \beta_2H_2\lambda/(\mu_3+\beta_2H_2) - (b_2+\gamma H_2+\alpha)P_2 - \alpha P_2^2(k+1)/kH_2 \qquad (2.4.21)$$

where k is the parameter of the negative binomial distribution describing the pattern of cysticercoids within the beetle population. An approximate value for k in populations of beetles exposed to a

single patch of parasite eggs is 1.04 (see Section 2.3(vi)).

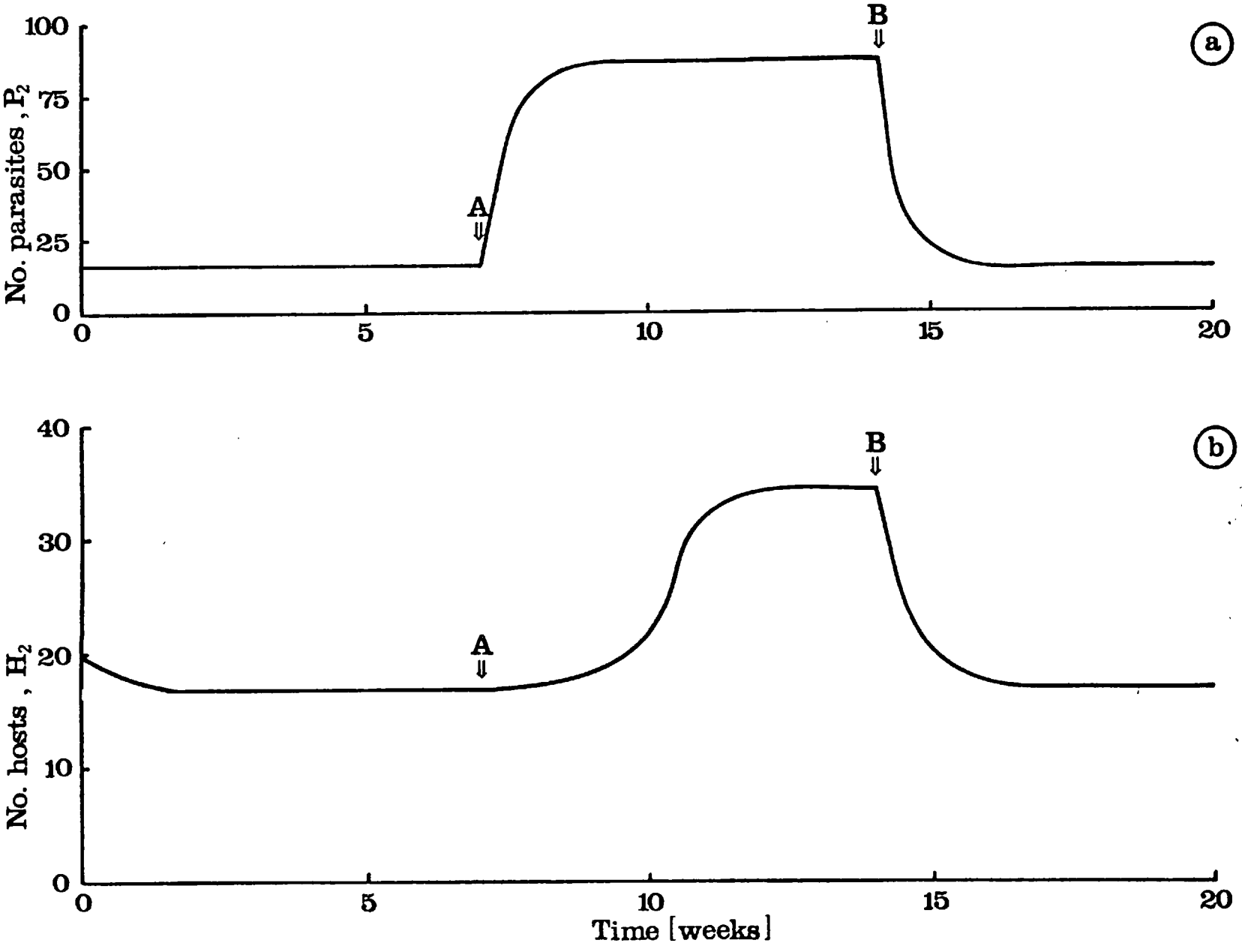
Since the values of the parameters were estimated at equilibrium, the model defined in equations (2.4.20) and (2.4.21) does not mimic accurately the population growth of infected hosts, but it may be analysed numerically to give an estimate of the equilibrium size expected for populations subjected to known rates of parasite egg input. A summary of the parameter estimates used in the model is given in Table 2.4.13 and the results of a simulation using these values are depicted in the corresponding figure.

Figure 2.4.13(b) illustrates the size of the infected host population. From its initial level of 20 beetles/gm., the population soon equilibrates to a level of 17 beetles/gm. This is quite similar to the observed equilibrium of 14 beetles per gm. in the experimentally infected populations shown in Figure 2.4.12(a). At point A, the parasite-induced effects on host survival and fecundity are removed, whereupon it can be seen that the population grows in approximately 4 weeks to the carrying capacity of 34.4 beetles/gm (as defined in equation (2.4.14)). On reintroduction of the parasite-induced effects at point B, the host population is depressed again to its original level.

Figure 4.13(a) illustrates the corresponding changes in the parasite population. The effect of removal of the parasite-

Figure 2.4.13 Simulated effects of parasitism on the population growth of T.confusum.

The graphs illustrate the equilibrium population size of beetles (Figure 2.4.13(b)) and cysticercoids (Figure 2.4.13(a)), as predicted by the model defined in equations (2.4.20) and (2.4.21). The significance of points A and B is detailed in the text. Parameter values are listed in Table 2.4.13.


100
75
50
25
0
No. parasites , P_2
A
B
a
0
5
10
15
20
40
30
20
10
0
No. hosts , H_2
A
B
b
0
5
10
15
20
Time [weeks]

induced effects on host fecundity and survival at point A provides a very clear illustration of the density-dependent constraints they impose on the parasite population. In the absence of these constraints, the parasite population grows within 1 week to an equilibrium level set by the immigration-death process, where

$$P_2 = \frac{\beta_2\lambda(a_2-b_2)}{a_2(\gamma\mu_3+\beta_2(a_2-b_2))} \quad . \qquad (2.4.22)$$

The original equilibrium is restored as soon as the density-dependent constraints are reinstated at point B. The response times of the host and parasite populations to changes at points A and B gives an indication of their relative time-scales, and an inverse measure of their reproductive potentials. The rates of immigration and death controlling the dynamics of the parasite population operate on a faster time-scale than the corresponding birth and death rates of the host. This feature is common to the majority of host-parasite associations.

The model as defined in equations (2.4.20) and (2.4.21) provides only a very simplified explanation of the experimental results shown in Figure 2.4.12. It contains several unrealistic assumptions, the most important of which are listed below

1) The effects of the functional response of the beetles to egg density on the dynamics of transmission are not considered.

2) The relationship between parasite-induced reduction in host fecundity and parasite burden is assumed to be exponential,

whereas experimental results have indicated the relationship to be of a more complex non-linear form.

3) The population is assumed to consist of continuous, overlapping generations. In a population founded with adults, however, the generations are initially of discrete form, and would perhaps be more accurately described by a model couched in difference equations.

4) The model does not include the time delays which occur as a result of beetle development to the adult stage.

5) Beetle fecundity and survival are assumed constant and independent of beetle age.

Inclusion of these concepts would not alter the qualitative behaviour of the model, which is believed to provide a good illustration of the principal mechanisms behind the observed association of host and parasite populations. More importantly, the model gives a parameter-free prediction of the parasite-induced depression of host equilibrium level (except for the value of γ, which measures the density-dependent constraints on population growth under given conditions). The similarity between observed and predicted results indicates both that the estimated values of the individual host and parasite population parameters are reasonably accurate, and that these parameters have been connected together to form a model which provides a relatively successful description of the dynamics of the host-parasite interaction. This approach will be continued in Section 3.

2.4(vi) Discussion.

The experimental results presented in this section illustrate that *H.diminuta* exerts a considerable adverse effect on the innate capacity for increase of the intermediate host. The overall consequences of parasitism on the dynamics of a *T.confusum* population will obviously depend on both the mean parasite burden, and also the statistical distribution of parasite numbers per host. Under laboratory conditions, where the mean parasite burden is high, and the degree of over-dispersion relatively low, the effects of parasitism on the survival and fecundity of individual hosts result in a significant degree of depression of the equilibrium host population level (see Section 2.4(v)). Under natural conditions, however, the degree of over-dispersion in the frequency distribution of parasite numbers per host is likely to be extremely high (Rau, 1979). This, together with the relatively low incidence of parasitism which might be expected, will tend to reduce the regulatory impact of the parasite on the growth of its host population, since the majority of parasites will be harboured by a small proportion of the hosts.

In addition, it might be expected that a large proportion of insects die in the natural habitat (as a result of predation, adverse environmental conditions etc.) before parasite-induced effects on survival and fecundity come into operation. For these reasons, it is not suggested that parasitism by *H.diminuta* plays any significant part in the regulation of *T.confusum* populations

under natural conditions, although the experimental results reported here indicate that it has the potential to do so.

In addition to the constraints imposed by the functional response to egg density, discussed in Section 2.3(v), the results displayed in Figures 2.4.3 and 2.4.9 reveal a further density-dependent constraint on the population growth of the parasite. The tendency for host density to be reduced at high levels of parasitism,as a result of parasite-induced effects on host survival and fecundity,will provide a strong regulatory force on the flow of *H.diminuta* through its life-cycle. This is illustrated by the results given in Figure 2.4.13. The relative effectiveness of the various density-dependent processes will be discussed in a later section.

2.5 INFECTION OF THE DEFINITIVE HOST.

In common with virtually all other cestode transmission links, infection of the definitive host by *H.diminuta* is achieved by means of a predator-prey association. The rate of infection is thus dependent on both the level of infection in the prey species, and the rate of predation on the infected prey by the predatory definitive host. The present section contains a discussion of factors pertaining to the rate of infection, such as the rate of beetle predation by rats, and the relationships between cysticercoid age, density per beetle, and resultant infectivity to the final host. Lastly, consideration is given to age-dependent and density-dependent effects in adult worm population dynamics.

2.5(i) Predation on the intermediate host.

Much of the recent literature on predator-prey dynamics is concerned with terrestrial arthropod systems (e.g. Rogers, 1972; Hassell *et al* 1976; Hassell, 1978), both because of their economic importance and their ease of manipulation in the laboratory. Work on mammalian predators is rather more limited (e.g. Holling, 1959a; Anderson, Whitfield *et al*, 1978b; Peterman and Gatto, 1978; Ivlev, 1961), primarily due to the complexity of the responses involved in predatory behaviour.

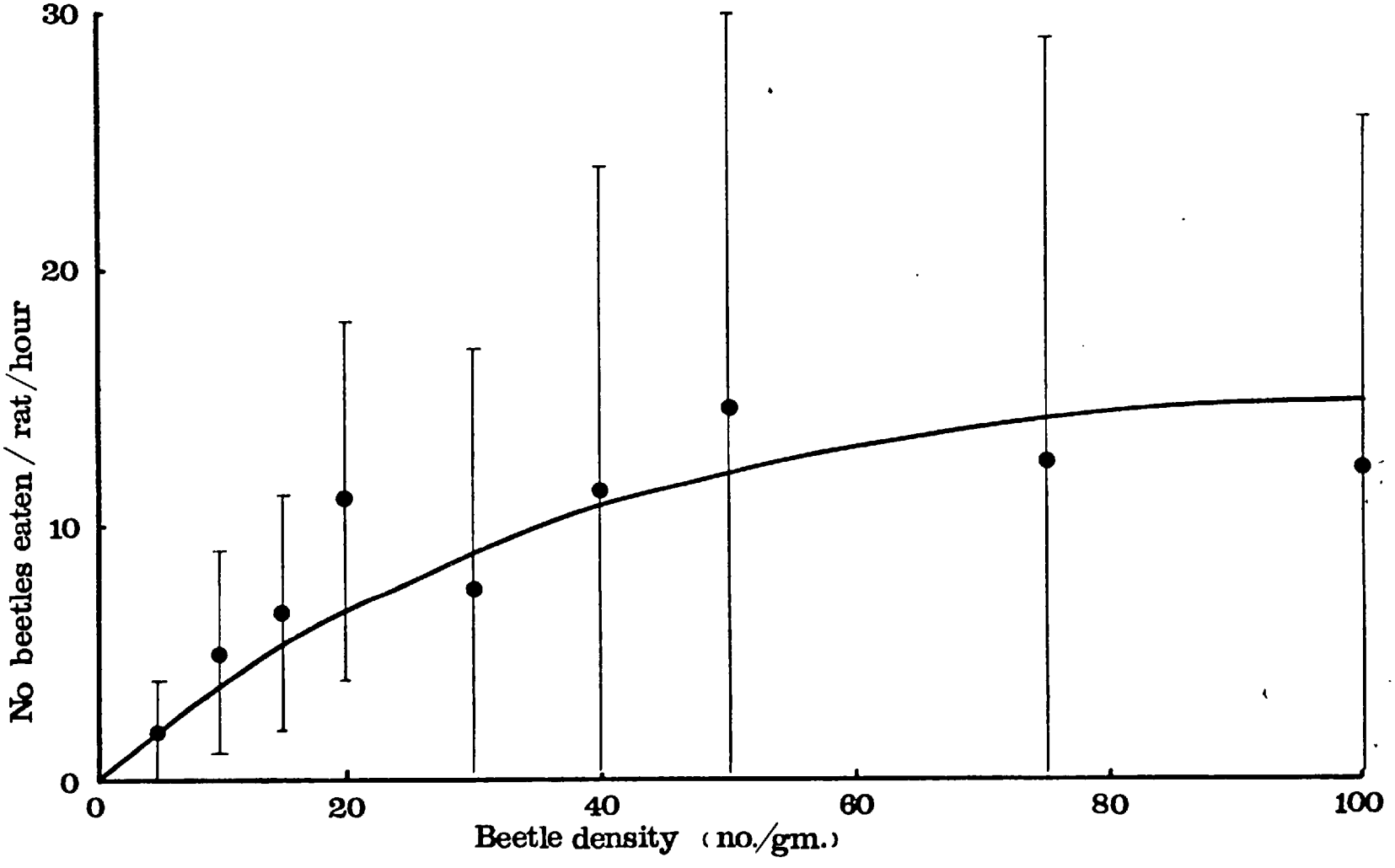
In order to investigate the relationship between beetle

density and the rate of predation by rats under controlled laboratory conditions, the following method was used. Six male rats, of approximate age 6 weeks and weight 285 ± 10 gm. were acclimatized over a period of weeks to live *T.confusum* as a source of food. During the experimental period, which lasted 9 days, each rat was placed in a separate cage of basal area 1500 cm^2 at 9 a.m. each morning without access to food. At 2 p.m., a glass petri dish 7 cm. in diameter, containing 1 gm. flour and a known number of uninfected beetles of uniform age was introduced into each cage. After an exposure period of 1 hour, the number of beetles remaining in each cage was determined, and the rats were returned to their maintenance cages until the following day.

The results given in Figure 2.5.1 may be adequately described by the type II functional response model as defined in equation (2.3.13). It would seem likely that the response is generated by limitations on the period available for predation by the time taken up in capturing each prey item (handling time effects), although satiation concepts could equally well be involved. The type II response shown in Figure 2.5.1 provides no density-dependent regulation of the prey population, but it should be noted that the effects of numerical responses (i.e. the relationship between prey density and predator numbers) would also have to be taken into account under natural conditions. In addition, response type is not dependent on the phylogenetic status of the predator, but is a function of the conditions under

Figure 2.5.1 *The functional response between beetle density and the rate of beetle predation by laboratory rats.*

The points represent the mean values of 5 replicates and the vertical bars indicate the 95% confidence limits of the means. The solid line gives the predictions of the functional response model as defined in equation (2.3.13). Parameter values: υ = 0.6 beetles/rat/hour, t_h = 0.05/hour. Rats were maintained singly in cages 1500 cm^2 in area without any alternative food source.


30
20
10
0
No beetles eaten / rat /hour
0
20
40
60
80
100
Beetle density (no./gm.)

which the predation is taking place (Murdoch and Oaten, 1975).

Although no conclusions can be drawn concerning the possible density-dependent regulation of *T.confusum* populations by rat predation, the results shown in Figure 2.5.1 do indicate another potential density-dependent constraint on the flow of *H.diminuta* through its life-cycle, directly comparable to the functional response in the transmission link between tapeworm egg and intermediate host (see Section 2.3(v)). In this case, however, the relationship between the functional response and the rate of infection is dependent on the number of cysticercoids present in the predated beetles, which is in turn determined by the mean level of intermediate host parasitism, and the statistical distribution of parasite numbers per host. In addition, some effect of parasitism by *H.diminuta* on *T.confusum* might render the beetle more susceptible to capture by mammalian predators (see Anderson, 1979a). No observations have been made, however, relating parasitism to alteration of beetle characteristics such as colour, size, movement etc., and in the absence of any experimental evidence to the contrary, it will be assumed that the rate of predation is independent of parasite incidence in the prey.

The importance of the functional response as a density-dependent constraint on parasite population growth under natural conditions is difficult to assess. Beetles are not likely to form an important natural source of food (Calhoun, 1962) although the dietary requirement of rats for grain (Davis, 1951) may increase the probability of accidental ingestion of stored product

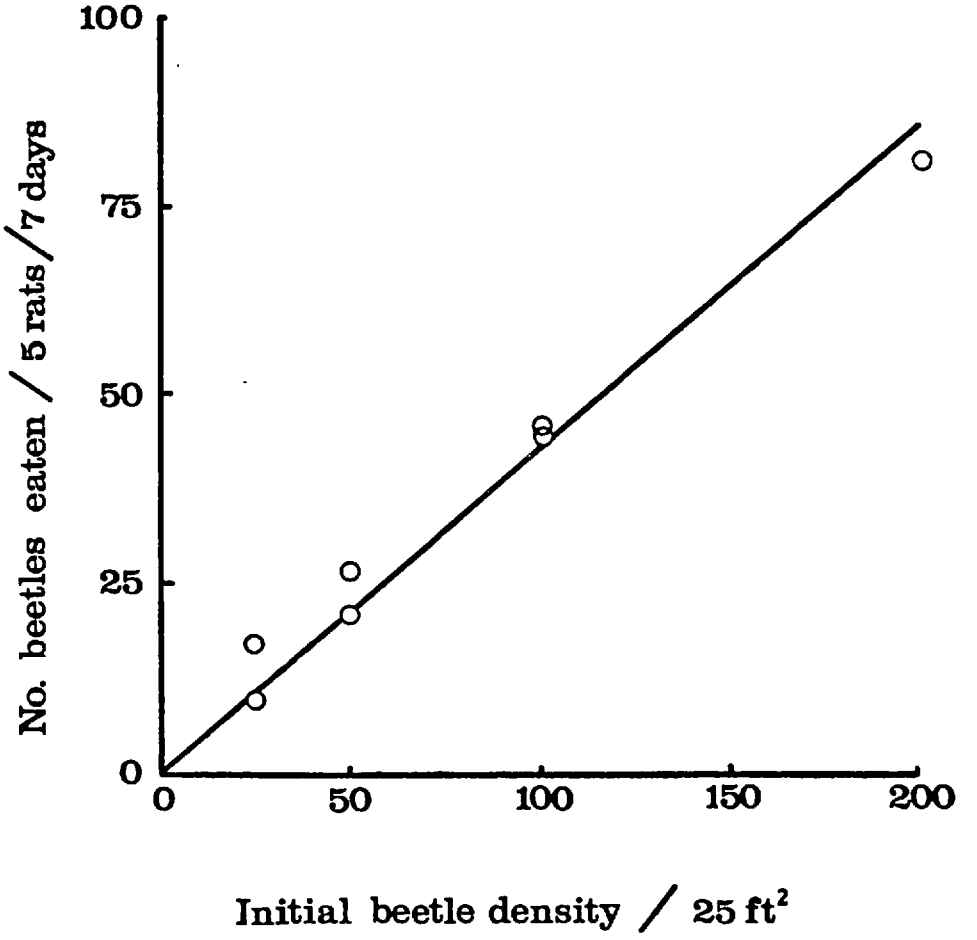
insects such as *T.confusum*. However, the densities of infected beetles encountered by potential definitive hosts are unlikely to be high enough to consistently cause the generative mechanisms of the functional response to come into operation. It is thus thought reasonable to assume that the rate of beetle predation by rats under most conditions is directly proportional to beetle density, corresponding to the lower part of the range shown in Figure 2.5.1.

Given this assumption, an approximate estimate of the rate of transmission per cysticercoid per unit time per rat per unit area, β_1, may be derived from the results of experiments carried out by Coleman (1978), in which known numbers of infected beetles were released into a 5 x 5 ft. cage containing 5 uninfected rats and an *ad libitum* source of proprietary food. The level of infection of the beetles was estimated by dissection of a sample of 30 beetles derived from the same population as those used experimentally. The rats were removed from the cage after 7 days and the number of beetles remaining determined. The number of tapeworms which developed per rat was determined by dissection after a period of 3 weeks.

The results are reproduced in Table 2.5.2. By plotting the estimated number of beetles eaten against the initial density of beetles introduced into the cage (see Figure 2.5.2), it can be seen that the rate of predation over the experimental range is directly proportional to beetle density. Interestingly,

Figure 2.5.2 *The relationship between beetle density and the rate of beetle predation by laboratory rats. Data from Coleman (1978).*

The points represent observed values and the solid line gives the predictions of the best-fit linear model. Rats were maintained in groups of 5 in cages 25ft^2 in area with an *ad libitum* supply of proprietary rat food.


100
75
50
25
0
No. beetles eaten / 5 rats / 7 days
0
50
100
150
200
Initial beetle density / 25 ft²

the density range per unit area used by Coleman corresponds to the lower end of the range shown in Figure 2.5.1 (up to 13 beetles/1500 cm^2), where the relationship between predation and prey density may also be approximated by a linear model. The differences in the estimated rates of predation per rat between the two sets of experiments may presumably be accounted for by differences in experimental conditions, especially the availability of alternative food supplies.

Assuming that the rate of infection is proportional to beetle density (H_2), rat density (H_1) and the level of beetle infection, and that there is no death of established adult worms over the duration of the experiment, the change in the number of adult parasites (P_1) in the rat population through time may be described by the differential equation

$$dP_1/dt = \beta_1 H_1 H_2 \sum_{i=o}^{\infty} i.p(i) \qquad (2.5.1)$$

where p(i) represents the probability that a beetle harbours i cysticercoids. Similarly, the rate of change in the cysticercoid population (P_2) is given by

$$dP_2/dt = - dP_1/dt \qquad (2.5.2)$$

The solution of these two simultaneous equations gives

$$P_1 = P_2(0)\ (1-e^{-\beta_1 H_1 t}) \qquad (2.5.3)$$

Where $P_2(0)$ represents the number of cysticercoids present in the beetle population initially introduced into the arena. The values of β_1 estimated using equation (2.5.3) from the results of Coleman's experiments are given in Table 2.5.2. The average is 0.14/parasite/week/rat/25 ft² or (4.3×10^{-6}/parasite/day/host/hectare).

The level of experimental error inherent in this estimation is indicated by a comparison of the number of worms recovered with the estimated number of cysticercoids consumed (i.e. the product of the number of beetles eaten and their estimated mean cysticercoid burdens). In two of the experiments (see Table 2.5.2) the number of established worms exceeds the estimated number of cysticercoids consumed. Although of limited accuracy, the value of β_1 given above is of significance as one of the few existing estimates of the transmission rate of an ingested helminth to the final host under laboratory conditions without experimental intervention.

2.5(ii) Prepatent periods.

Two developmental time delays are involved in the life-cycle of *H.diminuta*; the prepatent periods of the cysticercoid in the intermediate host (T_2) and the adult worm in the final host (T_1). Time delays are of considerable significance in the overall

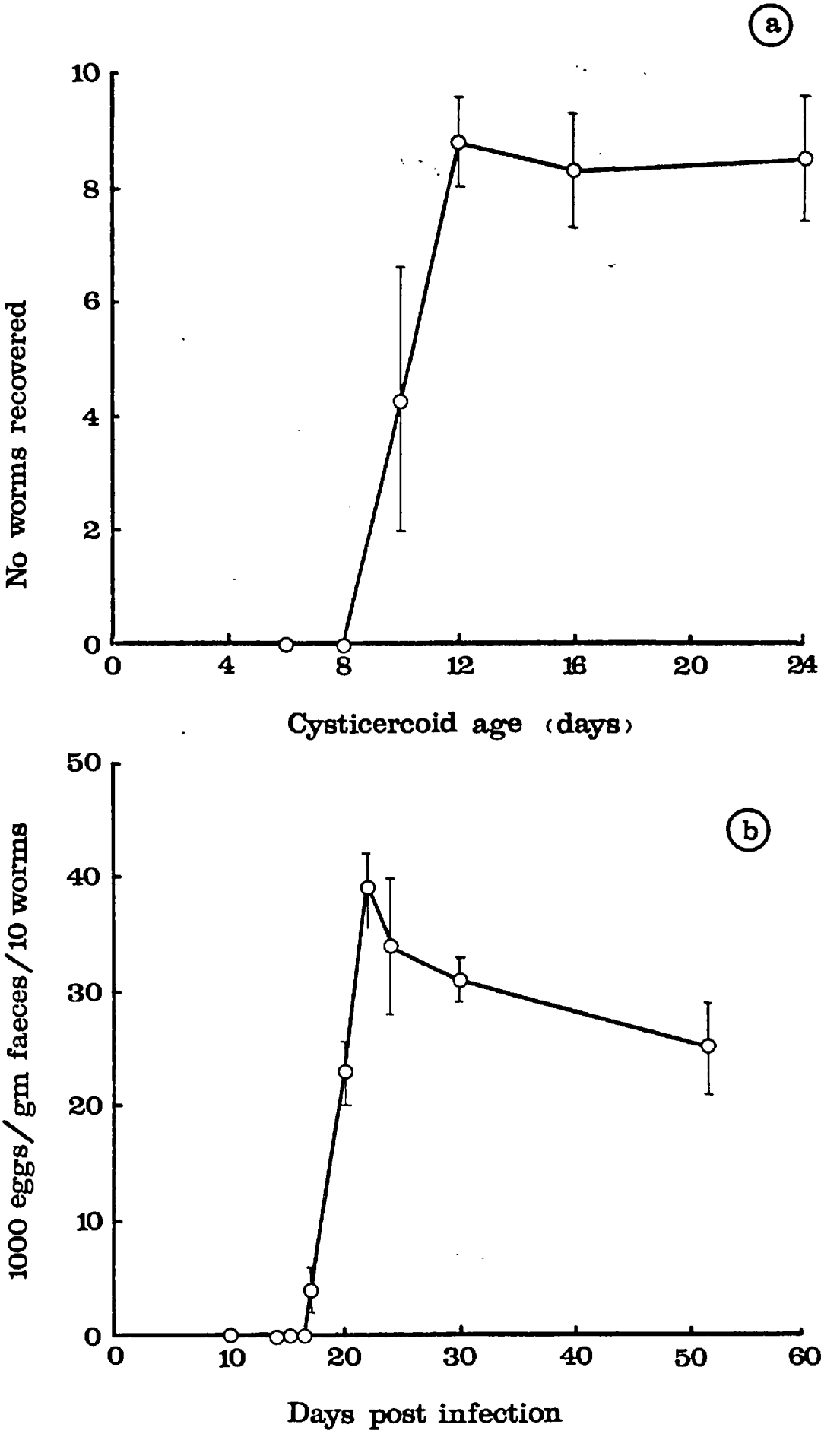
dynamics of a host-parasite interaction, since parasite losses due to natural mortality, or as a result of natural or parasite-induced host mortality during the prepatent period, cause a decrease in transmission success. It was thus of interest to determine the lengths of the two time delays under the specific experimental conditions used in the present study.

The course of development of *H.diminuta* cysticercoids in the intermediate host has been extensively studied (Voge and Heyneman, 1957; Caley, 1974; Voge 1975) and in particular, the effect of temperature on the rate of development is well known (Voge and Turner, 1956; Voge 1959a; 1959b; 1961). In order to determine the value of T_2 in the present study, beetles were infected with *H.diminuta*, and groups of 10 cysticercoids from hosts with parasite burdens of 5 to 8 inclusive were used to infect replicate groups of 4 rats after periods varying from 6 to 24 days. The results are shown in Figure 2.5.3(a), from which it can be seen that there is little variability in developmental time; percentage recovery rising from 0% at 8 days to its maximum value of 88% at 12 days. This does not preclude the possibility that variation in cysticercoid development increases at higher parasite burdens, a hypothesis consistent with the retarded development observed in some *H.nana* cysticercoids at burdens higher than 50 per beetle (Heyneman, 1958). In the present study, the average value of T_2 under the specified experimental conditions will be taken as 10 days, slightly greater than the minimum value of 8 days at 30°C given

Figure 2.5.3 Developmental time delays in H.diminuta.

(a) The relationship between cysticercoid age (i.e. days post beetle infection) and the number of worms recovered from rats given 10 cysticercoids. The points are the means of 4 observed values, and the vertical bars represent the 95% confidence limits of the means.

(b) The relationship between adult worm age (i.e. days post rat infection) and egg production. The points are the means of 8 observed values, and the vertical bars represent the 95% confidence limits of the means.


a
No worms recovered
0
2
4
6
8
10
0
4
8
12
16
20
24
Cysticercoid age (days)
b
1000 eggs/gm faeces/10 worms
0
10
20
30
40
50
0
10
20
30
40
50
60
Days post infection

by Voge and Turner (1956).

The length of the prepatent period of *H.diminuta* in the rat (i.e. the delay between ingestion of a cysticercoid and first production of infective eggs) is well established as 18 - 20 days irrespective of worm size or burden (Read and Rothman, 1957; Roberts, 1961; Beck, 1952). In order to check that the strain of *H.diminuta* used in the present study conforms to this developmental pattern, egg counts were taken from random faecal samples from a group of 28 rats each infected with 10 cysticercoids. The results given in Figure 2.5.3(b) confirm that egg output begins at 17 days post infection and reaches its maximum value at 20 to 22 days post infection. The estimated value of T_1, will therefore be taken as 17 days.

2.5(iii) Cysticercoid age and density.

Cysticercoids elicit no known encapsulation reactions (Ubelaker, *et al*, 1970; Heyneman and Voge, 1971; Lackie, 1976) and are often assumed to 'remain alive and infective throughout the life of the intermediate host' (Schiller, 1959), which may be as long as 19 months (Voge and Heyneman, 1957). However, thickening of the internal membrane has been shown to continue throughout the life of the cysticercoid (Schiller, 1959), and since membrane thickness has been correlated with excystment success (Schiller, 1959; Caley, 1974; Goodchild and Harrison, 1961), it was

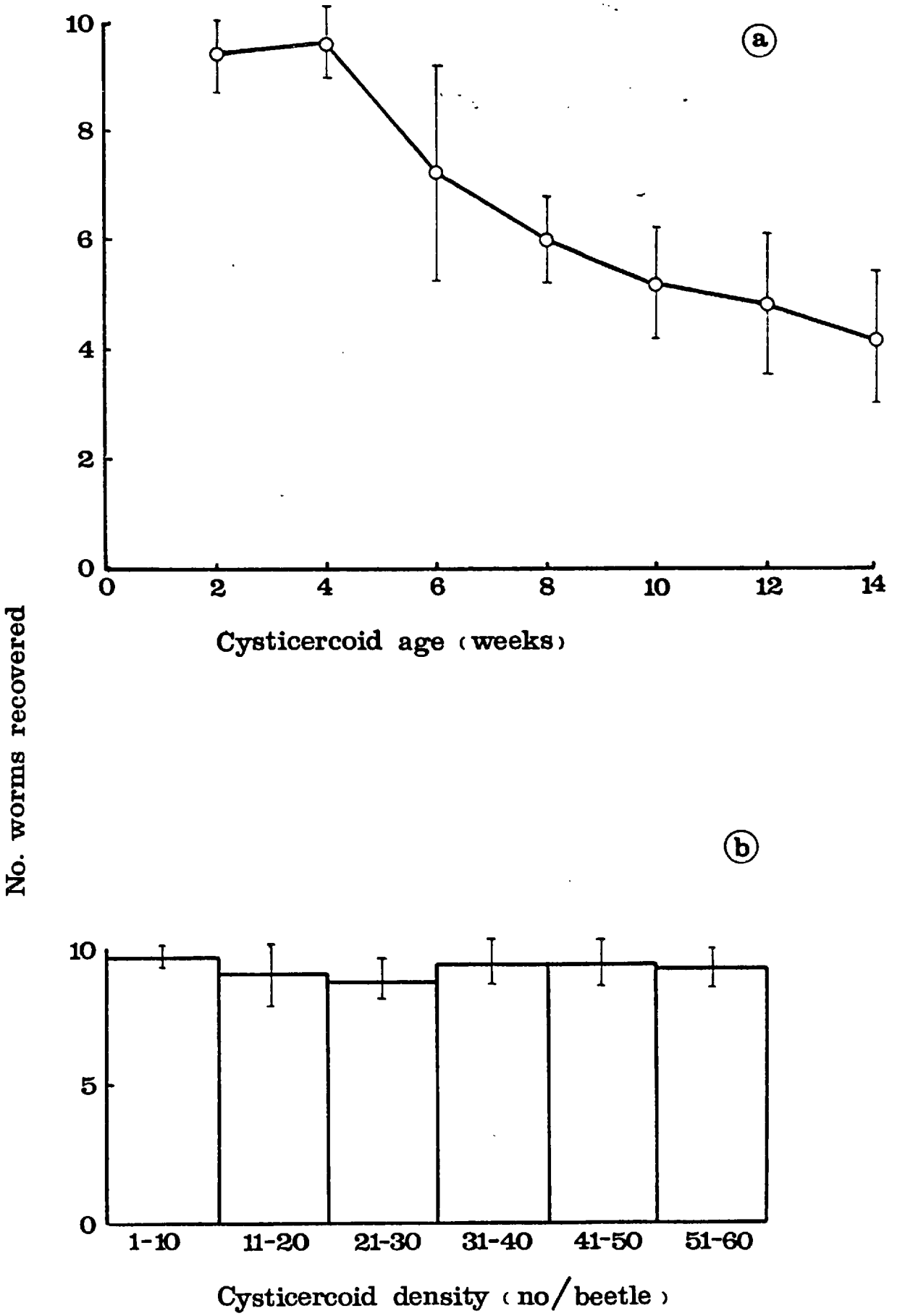
considered necessary to carry out an experimental investigation of the infectivity of a population of cysticercoids through time.

Beetles of uniform age were infected with *H.diminuta*, and groups of 10 cysticercoids from beetles with parasite burdens of 5 - 8 inclusive were used to infect replicate groups of five, 6-week old rats at 2-week intervals until no further beetles remained alive. Worm burdens were determined 4 weeks after infection. The results shown in Figure 2.5.4(a) indicate that the parasites suffer a definite loss of infectivity through time, beginning at approximately 4 to 5 weeks post infection. In order to incorporate this effect into a model of host-parasite dynamics (see Section 3) with maximum simplicity, it is assumed that cysticercoids have a constant, instantaneous per capita mortality rate in living intermediate hosts, μ_2. Given this assumption, the expected lifespan of cysticercoids (i.e. the time at which 50% remain infective) may be estimated by eye as approximately 14 weeks (see Figure 2.5.4(a)). An order of magnitude estimate of μ_2 may then be obtained (the reciprocal of the expected lifespan) of 0.01/cysticercoid/day. This mortality is independent of the loss which occurs as a result of natural and parasite-induced host mortality. No experimental investigation of the generative mechanism behind the loss of infectivity was carried out. The results, however, are consistent with the hypothesis that, in some old cysticercoids, the ensheathing membranes are so thick

Figure 2.5.4 Cysticercoid age and density and resultant infectivity to the final host.

(a) The relationship between cysticercoid age and infectivity to the final host. The points represent the means of 5 replicate observations, and the vertical bars represent the 95% confidence limits of the means.

(b) The relationship between cysticercoid density in the intermediate host and infectivity to the final host. The histogram bars are the means of 4 observed values, and the vertical bars represent the 95% confidence limits of the means.


a
10
8
6
4
2
0
0
2
4
6
8
10
12
14
Cysticercoid age (weeks)
No. worms recovered
b
10
5
0
1-10
11-20
21-30
31-40
41-50
51-60
Cysticercoid density (no/beetle)

that excystment does not occur within the time spent in the intestine of a suitable mammalian host.

Density-dependence in parasite growth, whereby cysticercoids from hosts harbouring high parasite burdens tend to be smaller than those from lightly infected hosts, has been discussed in Section 2.3(iv). Both Dunkley and Mettrick (1971) and Voge and Heyneman (1957) made the qualitative observation that viability is independent of cysticercoid density. In addition, Chandler *et al* (1950) found that the size of the adult worm was not affected by the size of the cysticercoid from which it originated. However, since it has been suggested that the capsular membranes of cysticercoids developing in heavily infected beetles might fail to acquire a thickness sufficient to afford adequate protection for the larva during gastric digestion in the definitive host (Schiller, 1959), further experimentation was considered necessary.

Populations of beetles of uniform age were exposed to a variety of densities of *H.diminuta* eggs (distributed with extreme over-dispersion within the infection arena) in order to obtain a wide range in the resultant levels of infection per host. After 2 weeks, the beetles were dissected, and cysticercoids from hosts with similar levels of infection were pooled together and used to infect groups of 4 rats, each rat receiving 10 cysticercoids. The number of worms established per rat was determined by dissection after a period of 4 weeks.

The results shown in Figure 2.5.4(b) indicate that densities of up to 60 cysticercoids per beetle do not impair the viability of the cysticercoids at 2 weeks of age. The possibility that age-dependent loss of infectivity might be accelerated at high parasite burdens seems likely but was not investigated in the present study.

2.5(iv) Age-dependent worm fecundity and survival.

In the absence of host reactions leading to worm expulsion (see Section 2.5(vi)), it is often assumed that singly established *H.diminuta* may survive the entire lifespan of the definitive host. Read (1967) maintained adult worms in laboratory rats for 14 years by 13 successive surgical transplantations of the scolex and first 2 cm of the strobila. This illustrates only the potential lifespan of the isolated scolex, since it is probable that detachment of the strobila has a rejuvinating effect. Little experimental data is available in relation to worm longevity under more natural conditions.

In the present study, age-dependent survival was investigated at an infection level of 10 worms per rat, a burden low enough to exclude the effects of density-dependence (see Section 2.5(v)). Groups of 10 2-week old cysticercoids from beetles with parasite burdens of 5 - 8 inclusive were used to infect 20, 6-week old male

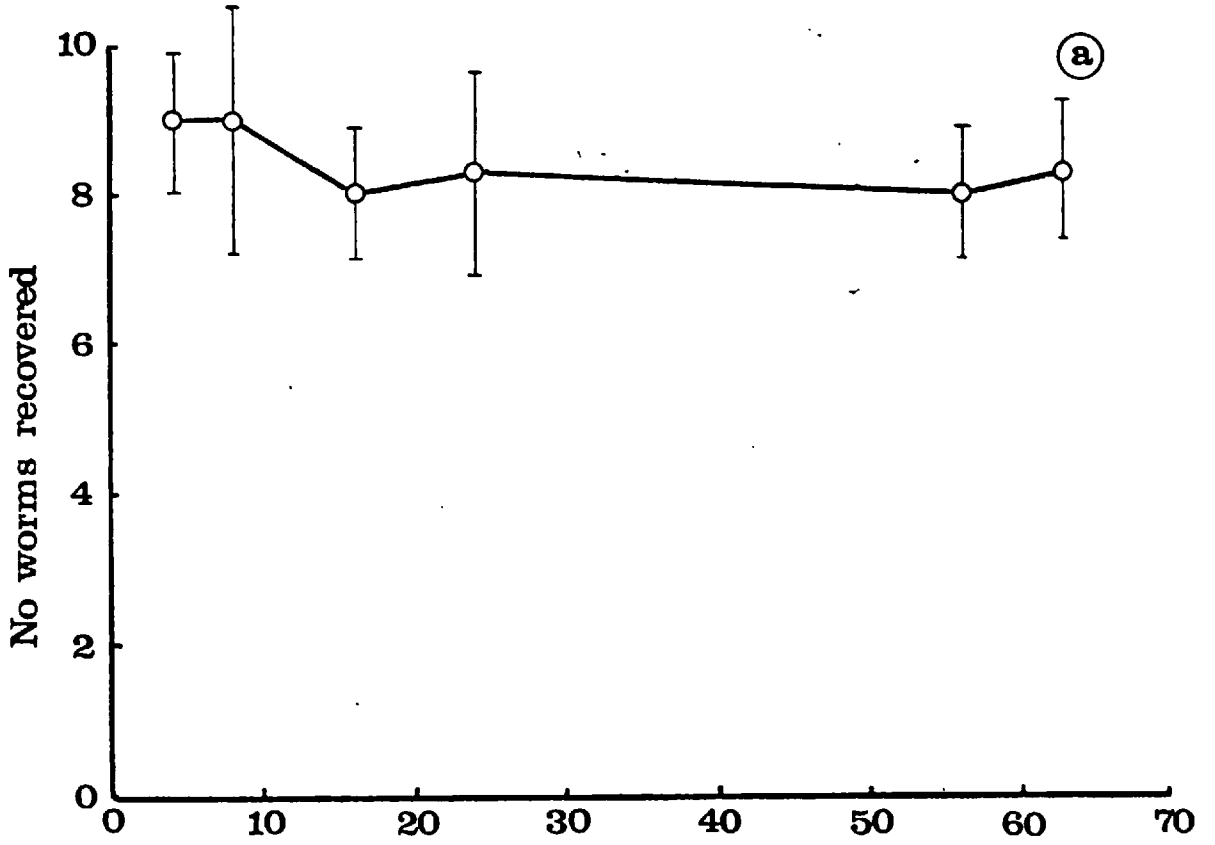
rats. Groups of 3 rats were then sacrificed and dissected at varying intervals post infection. The results shown in Figure 2.5.5(a) indicate that there is no age-dependent worm loss at this infection level up to 63 weeks post infection. However, even though the potential lifespan of singly established worms may be longer than that of the laboratory rat, it would seem extremely unlikely that entire specimens of *H.diminuta* escape the effects of senescence. In the present study, it is assumed that adult, singly established worms have a constant, although very low instantaneous per capita rate of mortality, μ_1. An arbitrary value of μ_1 of 0.001/worm/day (giving an expected lifespan of roughly 3 years) is used as an approximate estimate.

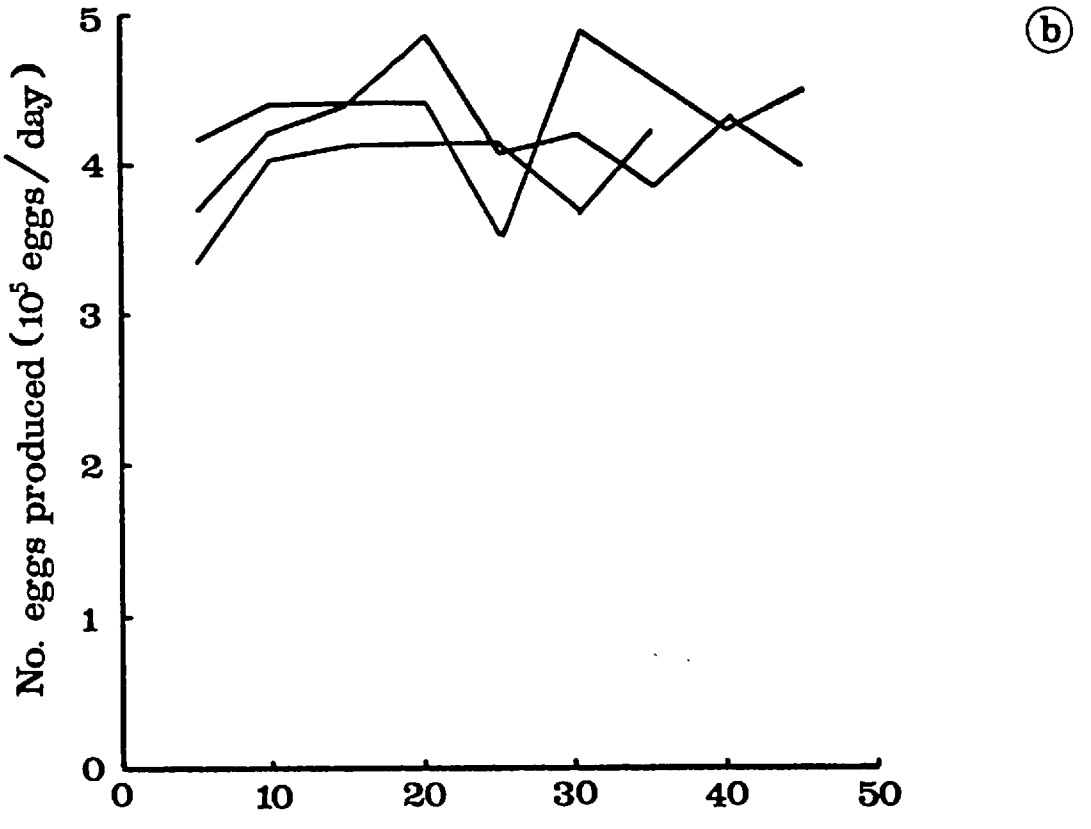
Age-dependent fecundity in *H.diminuta* has been measured by Coleman (1978). The results reproduced in Figure 2.5.5(b) indicate that the number of eggs produced per day by single worm infections is independent of worm age up to 50 weeks post infection. Further work by Coleman (1978) has shown in addition that egg production per worm does not show any age-dependent decrease in the first 20 weeks of infection in burdens of up to 20 worms per rat. Although fecundity may be age-dependent at high levels of infection, it will be assumed for simplicity in the present study that the instantaneous per capita rate of egg production (λ/worm/day) is constant and independent of worm age for any given worm burden. The relationship between the estimated value of λ and worm density is discussed in Section 2.5(v).

Figure 2.5.5 Age-dependent worm fecundity and survival.

(a) The relationship between adult worm recovery and worm age, at an infection level of 10 worms per rat. The points are the means of 3 replicate observations and the vertical bars represent the 95% confidence limits of the means.

(b) The relationship between egg production from single worm infections and worm age. Each point is the mean of 3 daily counts. Data from Coleman (1978).


a
No worms recovered
0
2
4
6
8
10
0
10
20
30
40
50
60
70


b
No. eggs produced (10^5 eggs / day)
0
1
2
3
4
5
0
10
20
30
40
50
Weeks post infection

2.5(v) Density-dependent worm fecundity and survival.

Density-dependent size

Density-dependent constraints on the size of adult worms in a cestode infection are well known (e.g. Woodland, 1924; Chandler, 1939; Reid, 1942) and are normally termed the 'crowding effect' (see Figure 2.5.6). Lumen-dwelling tapeworms were formerly considered non-immunogenic (Chandler, 1939; Culbertson, 1941; Heyneman, 1962), and early demonstrations of the crowding effect were attributed other causes. Competition for carbohydrate was at first not thought to be involved (Reid, 1942; Read, 1951). Later, however, it was found that tapeworms are severely limited in their capacity to metabolize sugars (Read, 1959) and this led to a reinterpretation of results in terms of intraspecific competition for utilizable carbohydrate (Read and Phifer, 1959; Holmes, 1959; Roberts, 1961). Similarities in the developmental characteristics of worms from crowded infections and those from hosts given suboptimal carbohydrate diets later provided support for this view (Roberts, 1966). Recent work concerning the nature of host immunological responses to gut helminths (see Section 2.5(vi)) has indicated that host response to infection may also be involved. No satisfactory agreement has yet been reached concerning the relative contributions of these factors.

Figure 2.5.6 The relationship between parasite burden and parasite size.

(a) Dry weight *H.diminuta* in the rat (Bailey, 1972).

(b) Fresh weight *H.microstoma* in the mouse (Moss, 1971).

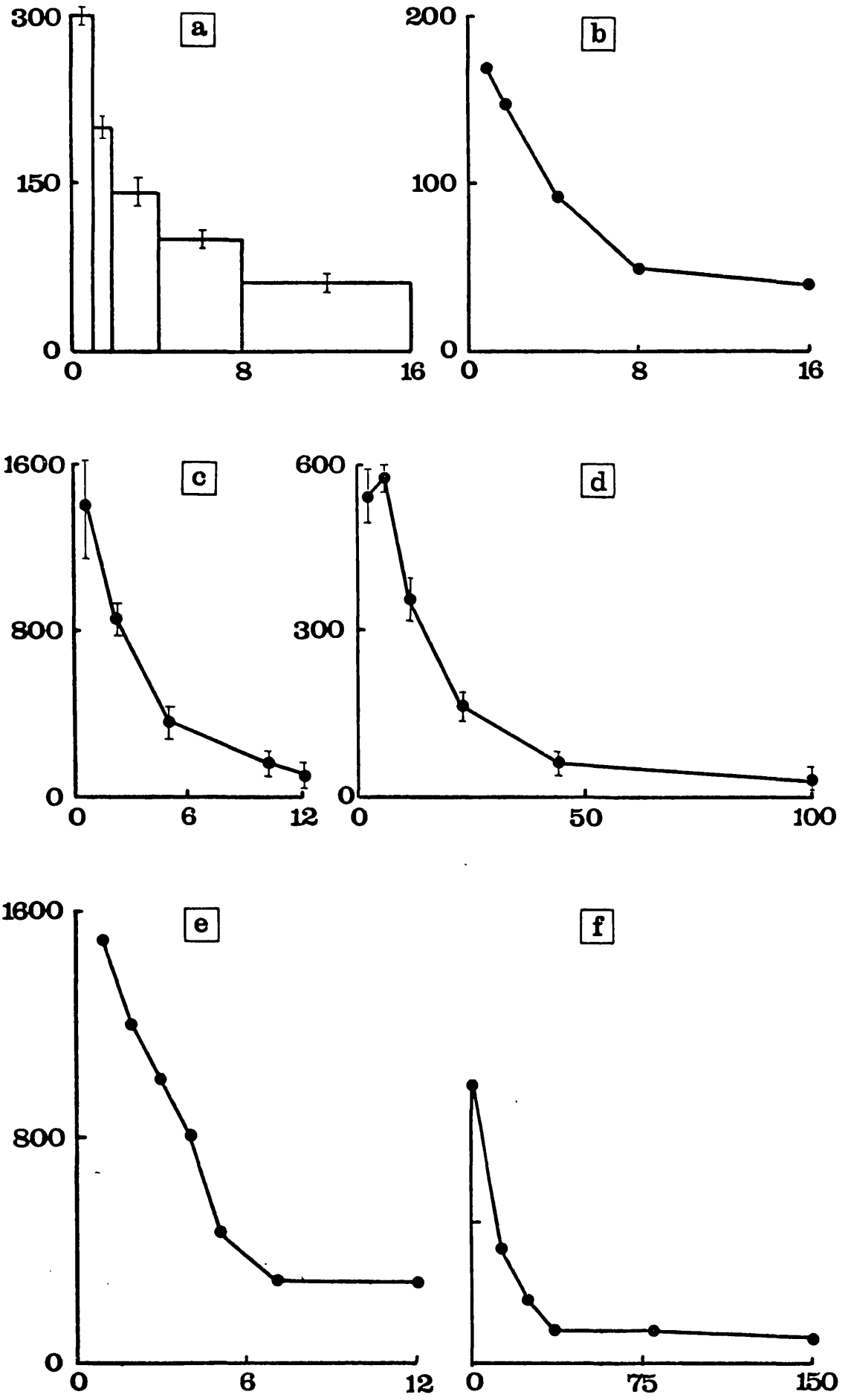
(c) Fresh weight *H.diminuta* in the rat (Hesselberg and Andreassen, 1975).

(d) Fresh weight *H.diminuta* in the rat (Roberts, 1961).

(e) Fresh weight *D.dendriticum* in the golden hamster (Halvorsen and Andersen, 1974).

(f) Fresh weight *H.nana* in the mouse (Ghazal and Avery, 1974).

Vertical bars represent the 95% confidence limits of the mean (where available).


a
b
c
d
e
f
300
150
0
200
100
1600
800
600
300
0
6
12
50
100
75
150
8
16
Worm weight (mg)
Worm burden (no/host)

Density-dependent survival

Establishment of ingested *H.diminuta* cysticercoids (Hesselberg and Andreassen 1975; see Figure 2.5.7(a)) and survival of established worms (Chappell and Pike, 1976; 1977) are both density-dependent. Using equation (2.4.4) in conjunction with survival data given by Chappell and Pike (1976; 1977), it can be seen that the relationship between the instantaneous per capita rate of adult worm mortality, μ_1, and worm burden, is of approximately linear form (Figure 2.5.7(b)). Taking the gradient of the best-fit linear model, together with the estimate of μ_1 in single worm burdens discussed in Section 2.5(iv), density-dependent worm mortality $\mu(i)$ may be expressed as

$$\mu(i) = \mu_1 + \delta i \qquad (2.5.4)$$

where μ_1=0.001/worm/day and δ (a coefficient relating to the severity of density-dependence) = 0.0004.

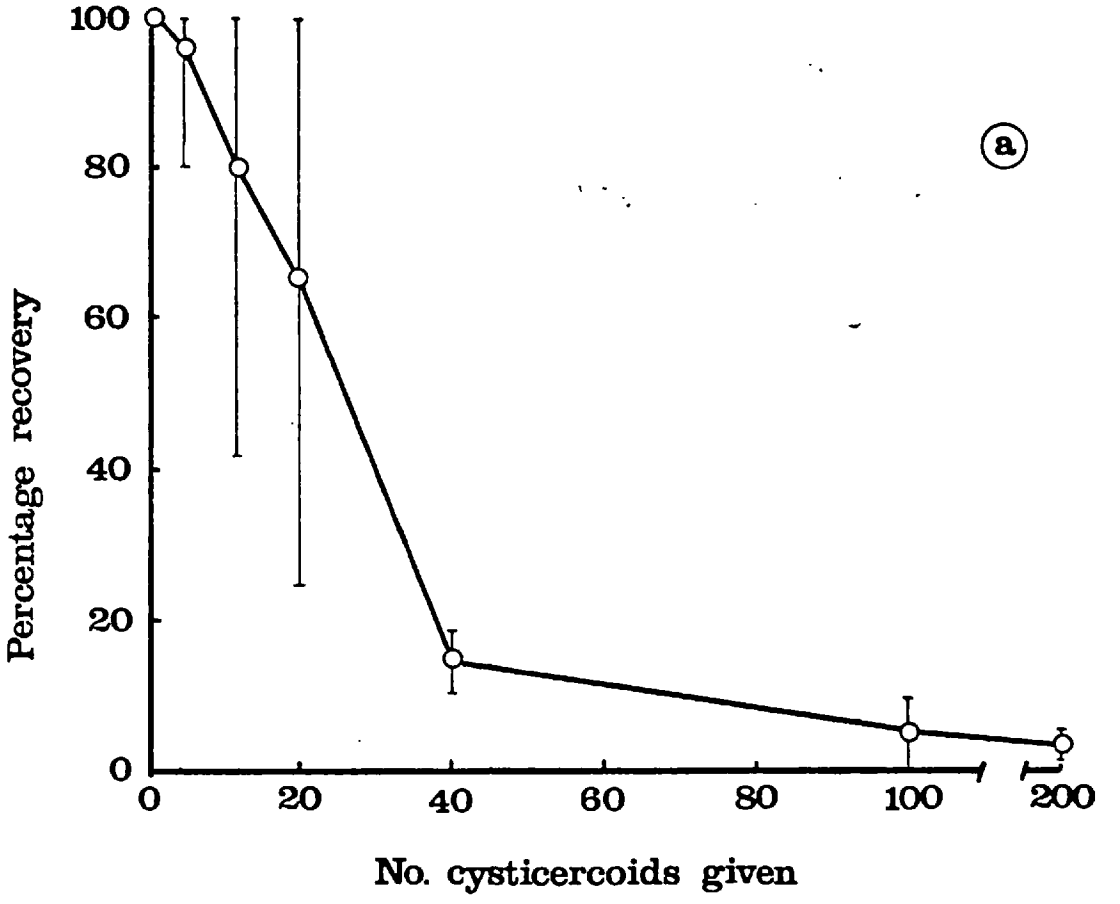
Density-dependent fecundity

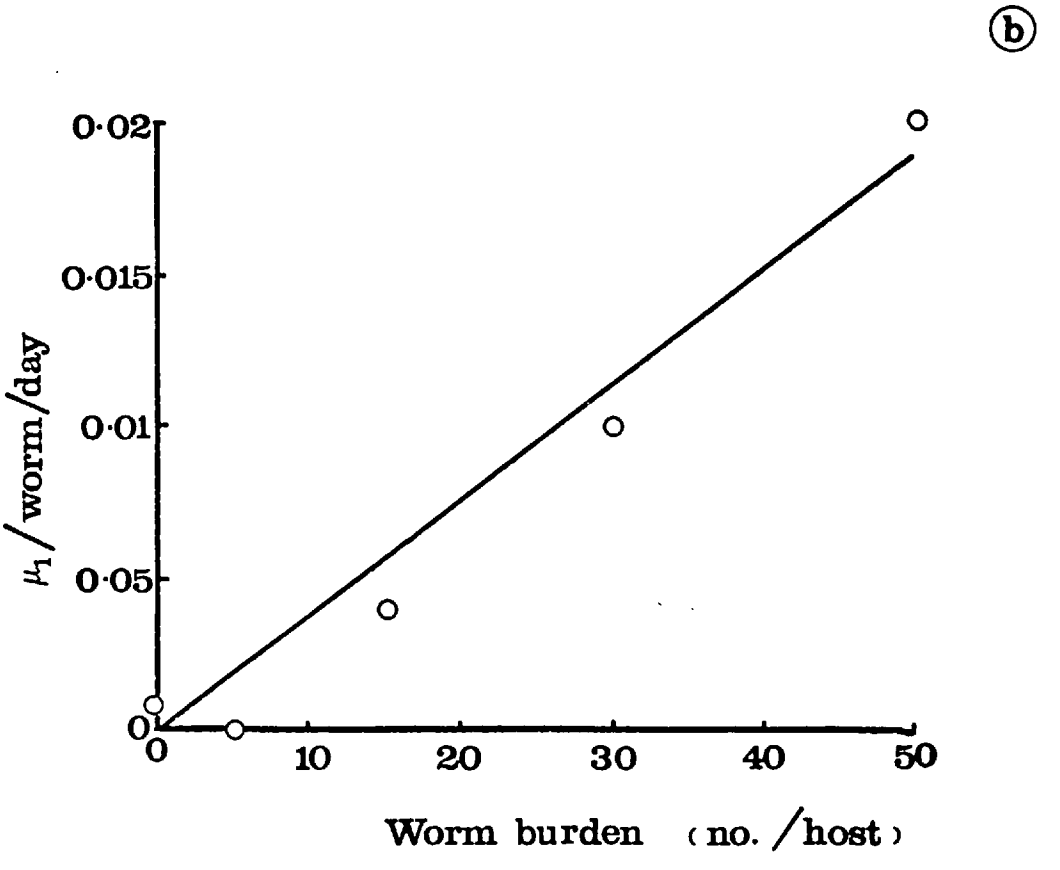
The mating behaviour of parasites in the final host is of considerable significance to the relationship between fecundity and parasite burden. If the parasites are dioecious, the net rate of egg production will depend on the probability of a female worm being mated, and hence on the mean worm burden, and the statistical

Figure 2.5.7 *Density-dependence in adult worm establishment and survival.*

(a) The relationship between the number of *H.diminuta* cysticercoids ingested, and the percentage which successfully become established in the rat. Vertical bars represent the range of observed values. Data from Hesselberg and Andreassen (1975).

(b) The relationship between the burden of *H.diminuta* adults per rat, and the instantaneous rate of parasite mortality per worm per day (μ_1) estimated using equation (2.4.4) from data given by Chappell and Pike (1976; 1977). The solid line represents the predictions of the best-fit linear model.


(a)
Percentage recovery
100
80
60
40
20
0
0
20
40
60
80
100
200
No. cysticercoids given


(b)
0·02
0·015
0·01
0·05
0
μ_1/worm/day
0
10
20
30
40
50
Worm burden (no./host)

distribution of worm numbers per host. Mating success will also be dependent on whether the parasites are polygamous or monogamous. These relationships have been discussed by Anderson (1980a).

Tapeworms are hermaphroditic and thus fecundity is potentially independent of parasite burden, as long as self-fertilization and cross-fertilization result in equal numbers of viable eggs. Methods of sperm transfer in Tetraphyllidea have been discussed by Williams and McVicar (1968), who observed both cross and self-insemination. *H.microstoma* has been maintained by self-fertilization for 14 generations without any change in the viability of the eggs or cysticercoids (Jones *et al*, 1971), whereas the corresponding decrease in viability is so great in *H.nana* that no strain could be maintained by self-fertilization beyond the fifth generation (Rogers and Ulmer, 1962). Interstrobilar sexual activity has been noted between two specimens of *H.diminuta in vitro* (Wilson and Schiller, 1969) and self-insemination has been confirmed in single worm infections by radioactive labelling techniques (Nollen, 1975). In multiple worm infections, labelled worms were found to inseminate themselves and to cross-inseminate with 92% of the unlabelled worms present.

In the present study, the following method was used to test the viability of eggs resulting from single worm infections. A group of 8 rats was infected with cysticercoids from the same beetle population; 4 were given single cysticercoids and the other

4 were each given 10 cysticercoids. The worm burdens of the rats were checked by dissection after termination of the experiment. After 4 weeks, populations of 30 starved beetles were exposed to 3000 eggs derived from faecal samples from each of the 2 groups of rats. The beetles infected with eggs from single adult worm infections were later found to harbour a mean cysticercoid burden of 6.35±2.34 compared with 5.81±1.81 resulting from eggs derived from multiple worm infections. There is thus no significant difference (d.f=58, $P(t=1.33)>0.1$) in the viability of eggs resulting from single or multiple worm infections after a single generation. Although continued self-fertilization is likely to be detrimental (see Maynard Smith, 1978) and is unlikely to occur under natural conditions, it is assumed in the present study that fecundity in *H.diminuta* is not dependent on worm mating.

Fecundity in cestode infections, is, however, severely density-dependent. The number of proglottids per worm (Roberts, 1961), the number of proglottids shed per day per worm (Bailey, 1972) and the number of eggs per proglottid (Jones and Tan, 1971) are all affected by population density. The combined effects of all these variables are taken into account by measuring the number of eggs released per worm per day. Experimental results of this form are shown in Figure 2.5.8. Although fecundity is not age-dependent at low parasite burdens (see Section 2.5(iv)), age-dependence may be invoked at high levels of parasitism. This would have the effect of increasing the severity of the

Figure 2.5.8 *The relationship between parasite burden and the number of eggs produced per parasite per day.*

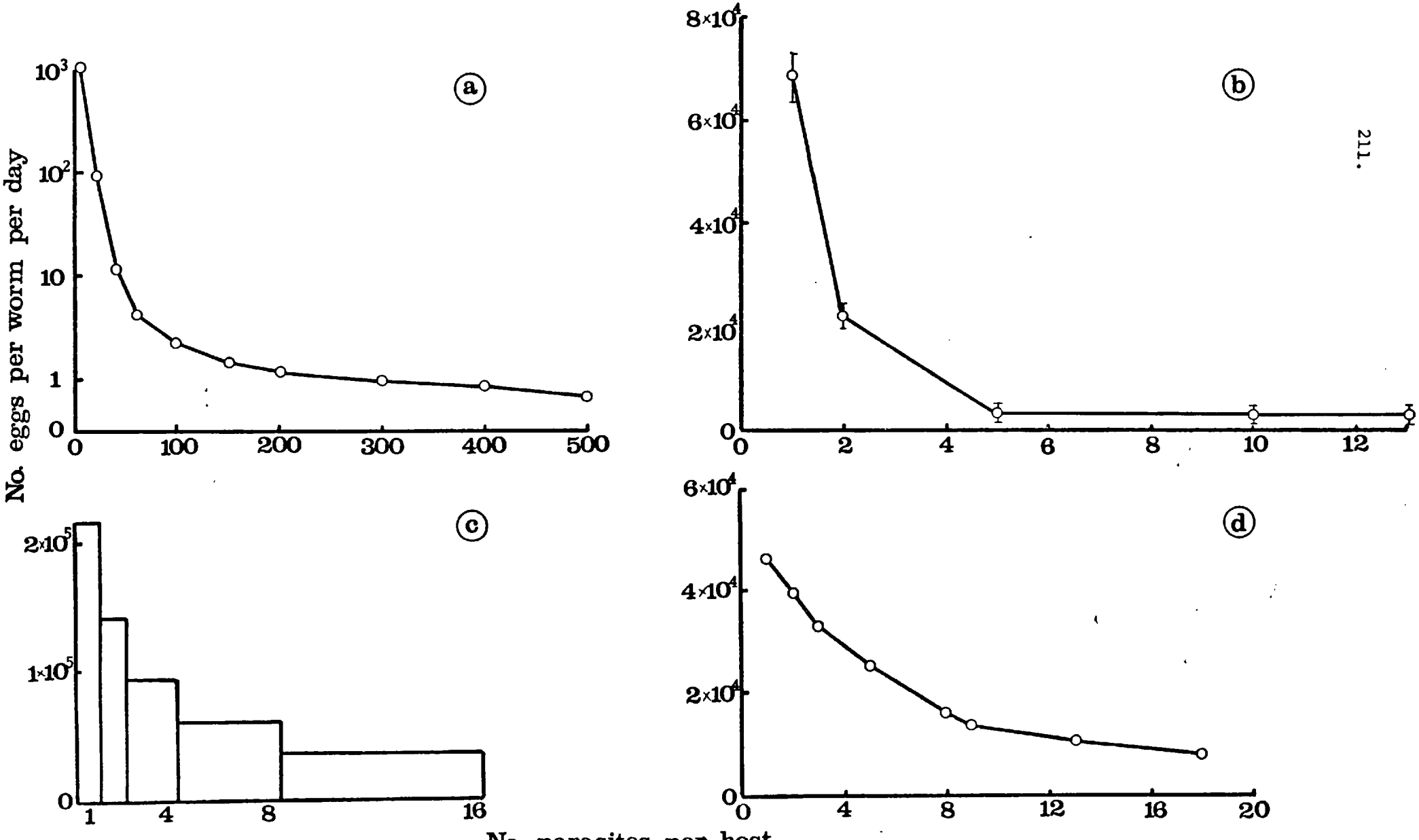
(a) *H.nana* in mice (Ghazal and Avery, 1974).

(b) *H.diminuta* in rats (Hesselberg and Andreassen, 1975).

(c) *H.diminuta* in rats (Bailey, 1972).

(d) *H.microstoma* in mice (Jones and Tan, 1971).

Vertical bars represent the 95% confidence limits of the mean (where available).


No. eggs per worm per day
(a)
10^3
10^2
10
1
0
0
100
200
300
400
500
(b)
8×10^4
6×10^4
4×10^4
2×10^4
0
0
2
4
6
8
10
12
(c)
2×10^5
1×10^5
0
1
4
8
16
(d)
6×10^4
4×10^4
2×10^4
0
0
4
8
12
16
20
No. parasites per host

density-dependent constraints on parasite population growth. In the present study, an approximate estimate of λ (the instantaneous rate of egg production per parasite per unit time) will be taken as 70000 eggs/worm/day for single worm burdens.

2.5(vi) Host response to infection.

Since it appears to be non-pathogenic in healthy laboratory rats (Bailey, 1972) and also in man (Muller, 1975), *H.diminuta* has classically been regarded as an example of an organism which is well-adapted to the parasitic mode of life. Insler and Roberts (1976) could demonstrate no adverse effects on host nutrient utilization or consumption, and suggested that *H.diminuta* should be considered endocommensal rather than endoparasitic. On the other hand, the amount of glucose present in the intestine of rats harbouring 10 *H.diminuta* following a 1 gm. glucose meal has been shown to average 59% less than that in the intestines of uninfected controls (Dunkley and Mettrick, 1977). It would seem unrealistic to suggest that worms which exhibit this degree of nutritional predation could be without adverse effects on hosts under stress. Preliminary work has shown, in fact, that both rats and mice infected with *H.diminuta* have lower rates of weight increase than uninfected controls (Goodchild and Moore, 1963). In addition, *H.microstoma* has been shown to produce a 58% increase in host metabolic rate in the mouse (Mayer and Pappas, 1976) and may cause fatal pathological changes in the hamster (Litchford,

1963), probably in response to excretory or secretory parasite products.

It was originally believed that host immunological responses to cestode infection were mounted only against *H.nana*, since this is the only species to have a tissue phase in the final host (Larsh, 1943; Heyneman, 1954). Later, premunition (the term used to describe protection conferred on a host by an existing parasite load,against reinfection with the same parasite) was demonstrated in mice harbouring *H.microstoma* (Tan and Jones, 1967; 1968). The response was characterized as a production of IgG, IgA and IgE, although no relationship between antibody production and worm rejection could be demonstrated (Moss, 1971).

Research on the immunogenicity of *H.diminuta* was at first concentrated on its relationship with the laboratory mouse, in which spontaneous destrobilation of most worms occurs 9 - 12 days post infection. The response was found to be thymus dependent (Bland, 1976) and suppressed by cortisone (Hopkins *et al*, 1972). It was later correlated with darkened areas found on the worm tegument thought to be sites of worm pathology induced by host immunity (Befus and Threadgold, 1975). The response was found to be characterized by antibody production (Hopkins and Zajac, 1976) and IgA was later identified bound to antigens on the worm tegument (Befus, 1977). The immune response is dose-dependent, and in a study on *H.citelli* infections in mice, Hopkins and Stallard (1974) suggested that worm surface area constitutes the

immune threshold above which the rejection response is initiated. In *H.diminuta*, the functional antigens are thought to be related to the scolex region, so that the time of rejection is related to the number of worms present, rather than to their combined surface area (Andreassen *et al*, 1978).

Although it is known that the immune responses evoked in the rat by other tapeworms have the ability to cross-react with *H.diminuta* (e.g. Heyneman, 1962), *H.diminuta* was thought to be non-immunogenic in this host (Roberts and Mong, 1968) until an antibody response was reported by Harris and Turton in 1973. Later work has shown that worm loss in crowded infections can be prevented by cortisone treatment and that challenge infection after 16 weeks results in only a very low level of worm recovery (Andreassen *et al*, 1974).

The nature of the relationship between *H.diminuta* and the laboratory rat is as yet unclear. Neither the effect of the parasite on the host, nor the effect of host immune responses on the parasite are fully understood. Both are of importance with respect to the population dynamics of the interaction. In the absence of further information, it will be assumed in the present study that *H.diminuta* exerts no detrimental effect on the innate capacity for increase in the definitive host. For the purposes of the present study, the instantaneous mortality rate of the definitive host, b_1, is estimated as 0.001/host/day, based on an average lifespan of approximately 3 years.

2.5(vii) Discussion.

Very little data is available concerning the prevalence and intensity of *H.diminuta* infection in naturally occurring host populations, although prevalence levels of 28, 42 and 50% have been recorded from wild rats in Puerto Rico (de Leon, 1964), Bethesda (Calhoun, 1962) and Hawaii (Ash, 1962) respectively. The most extensive study of this kind to date has been carried out on samples of beetles and rats obtained from a riding stable in Quebec (Rau, 1979). An extremely high level of over-dispersion in parasite numbers per host is seen in both *Tenebrio molitor* and *T.obscurus*, the two species considered to be the principal intermediate hosts in this particular location (see Figure 2.5.9). Together with factors such as heterogeneity in rat predatory behaviour and susceptibility to infection, clumping in the larval parasite distribution tends to create over-dispersion in the distribution of adult parasites in the final host population. This is supported by the results of a dissection of 9 rats in which the mean number of worms harboured was found to be 35, with a variance of 6716.6. Almost one half the total worm population of 315 was found in a single rat.

Some distribution data from a second study of *H.diminuta* under natural conditions are shown in Figure 2.5.10. This study relates to infection of *Apodemus sylvaticus* in Tollymore, County Down (Montgomery, personal communication). Again, there is a considerable degree of over-dispersion and the intensity of

Figure 2.5.9 *The frequency distribution of* H.diminuta *cysticercoids in a natural beetle population. Data from Rau (1979).*

The histogram bars are observed frequencies and the solid lines represent the predictions of the negative binomial probability distribution.

(a) *Tenebrio obscurus*

Mean level of infection = 72.7 cysticercoids/beetle

No. beetles in sample = 102

k = 0.39

(b) *Tenebrio molitor*

Mean level of infection = 4.9 cysticercoids/beetle

No. beetles in sample = 102

k = 0.20

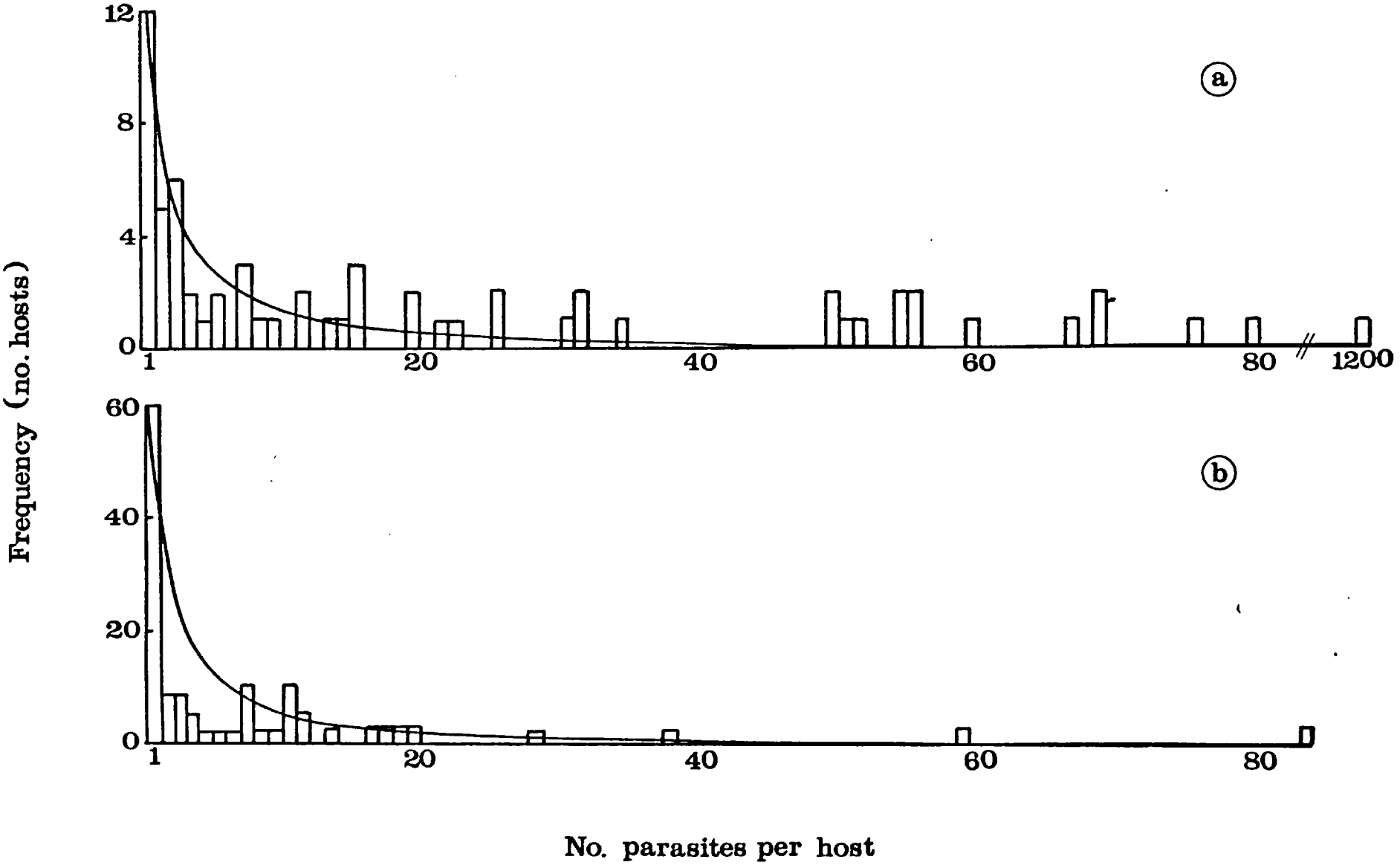

12
8
4
0
1
20
40
60
80
1200
a
60
40
20
0
1
20
40
60
80
b
Frequency (no. hosts)
No. parasites per host

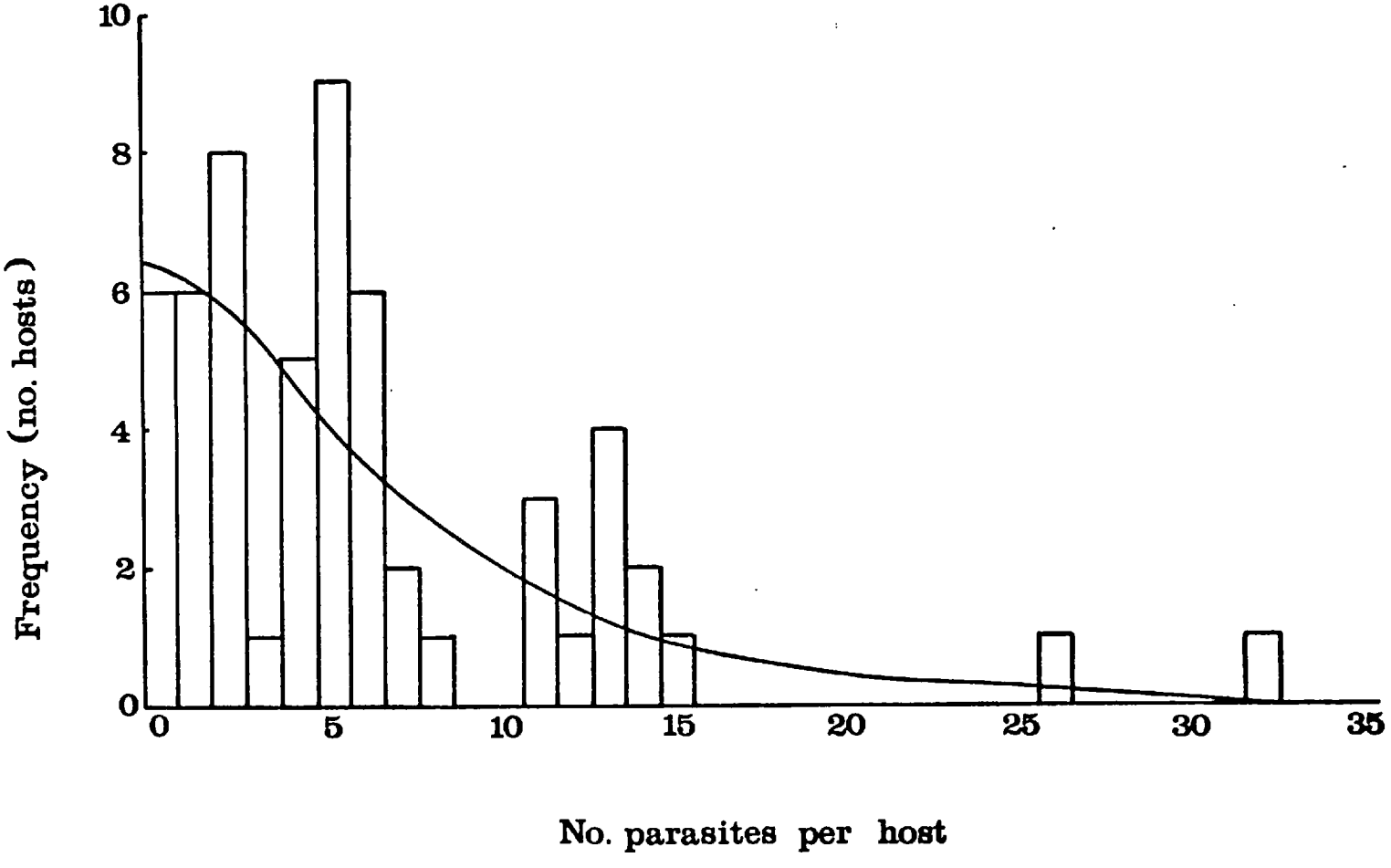
Figure 2.5.10. The frequency distribution of H.diminuta *in a natural population of* Apodemus sylvaticus. *Data from Montgomery (personal communication).*

The histogram bars represent observed frequencies and the solid line indicates the predictions of the negative binomial probability distribution.

Mean level of infection : 6.07 worms/host.

No. beetles in sample : 57.

$k=1.27$ ($\chi^2=28.48$, d.f.=15).


Frequency (no. hosts)
10
8
6
4
2
0
0
5
10
15
20
25
30
35
No. parasites per host

infection (average 6.07 worms per host) is extremely high considering that *H.diminuta* does not normally survive in laboratory mice for more than 12 days post infection. The insect species acting as intermediate host for the parasite in this area are unfortunately unknown.

In any host-parasite association, survival and reproduction of the adult parasites in the definitive host will play an important part in the determination of the prevalence and intensity of infection observed in the population. As shown in the present section, there are severe density-dependent constraints on both adult survival and fecundity in *H.diminuta* and it seems likely that these constitute important regulatory factors in parasite population growth under natural conditions. The phenomenon commonly referred to as failure of establishment is more correctly an early rejection of established parasites, since crowding has no effect on establishment or growth during the first 3 days of infection (Goodchild and Harrison, 1961). The importance of this feature with respect to the host-parasite population dynamics is that the parasites fail to reach sexual maturity, and thus do not contribute to the reproductive success of the parasite, and hence its perpetuation. The impact of density-dependent establishment will be dependent on the number of cysticercoids ingested at any one time, and hence on the frequency distribution of cysticercoids in the intermediate host. The high degree of over-dispersion already noted in both natural and laboratory populations of *H.diminuta* cysticercoids indicates that

this phenomenon may provide an important regulatory constraint on parasite population growth.

A second density-dependent constraint in adult worm dynamics is created by the existing relationship between worm burden and worm fecundity. The degree of reduction in fecundity in multiple worm burdens is so great that egg output per host is a constant (Hager, 1941) or decreasing (Hesselberg and Andreassen, 1975) function of worm burden. In analysing results from *H.nana, H.microstoma* and *H.diminuta* infections, Ghazal and Avery (1974) have suggested that the degree of reproductive inhibition resulting from competition between individual worms is proportional to parasite weight. Although an inverse relationship between egg oncosphere diameter and worm burden has been found (Bailey, 1972), no differences in egg viability have been noted. Similarly, preliminary results from the present study indicate no significant difference in the viability of eggs from 8 week old and 52 week old worms (d.f.=116,P(t=0.3)>0.7).

Survival of established worms provides a third density-dependent constraint on parasite population growth. In natural populations, individual rats are likely to be subject to continual reinfection, although the characteristics of this process are not well known. An experimental investigation of the differences between simultaneous and trickle infection on subsequent parasite survival and fecundity would be of considerable interest.

Laboratory experiments indicate that density-dependent reductions in parasite establishment, survival and fecundity are extremely effective regulators of parasite population growth within individual hosts. The extent to which these factors are operative in natural infections will depend on the statistical distribution of worm numbers per host in the final host population, which is in turn a consequence of the dynamics of the entire host-parasite interaction.

SECTION 3

THEORETICAL CONSIDERATIONS OF THE POPULATION DYNAMICS OF *H.DIMINUTA*.

This section describes some preliminary results concerning the population biology of *H.diminuta* obtained by means of the construction and analysis of simple mathematical models, based on the framework proposed by Anderson and May (1978) and May and Anderson (1978). The aim of this work is to gain general qualitative insight into the population behaviour of the type of host-parasite interaction exemplified by *H.diminuta* (see Section 1). Although the intention is not to draw conclusions based on precise quantitative results, the approximate laboratory parameter estimates described in Section 2 are used for numerical analysis of model behaviour where appropriate. The estimated values of the principal population parameters are summarized in Table 3.1.1.

Section 3.1 describes a basic model constructed to capture the most important features of the flow of the parasite through its life-cycle within fixed, unchanging final and intermediate host populations. Sections 3.2 and 3.3 then describe the respective changes in model behaviour which occur as a result of incorporation of the predator functional response to parasite density, and intermediate host population dynamics.

Table 3.1.1 *Laboratory estimates of the parameters included in the basic model.*

Parameter	Symbol	Estimated Value	Reference Section
Instantaneous rate of adult worm mortality (Single worm burdens)	μ_1	0.001/worm/day	2.5(iv)
Constant relating to severity of density-dependence in adult worm mortality	δ	0.0004	2.5(v)
Adult worm prepatent period	T_1	17 days	2.5(ii)
Larval worm prepatent period	T_2	10 days	2.5(ii)
Instantaneous rate of egg production by adult worms	λ	70×10^3/worm/day	2.5(v)
Instantaneous rate of egg mortality under 'natural' conditions	μ_3	0.09/egg/day	2.3(i)
Instantaneous rate of larval worm mortality in intermediate host	μ_2	0.01/parasite/day	2.5(iii)
Instantaneous rate of final host mortality	b_1	0.001/host/day	2.5(vi)
Instantaneous rate of intermediate host mortality	b_2	0.02/host/day	2.4(ii)
Instantaneous rate of final host infection	β_1	4.3×10^{-6}/cysticercoid/day/host/hectare	2.5(i)
Instantaneous rate of intermediate host infection	β_2	7.5×10^{-8}/egg/day/host/hectare	2.3(ii)
Parameter of the negative binomial distribution representing the distribution of adult worms in the final host	k_1	1.3	2.5(vii)

3.1 BASIC MODEL

The basic model is developed to describe the dynamics of the larval (P_2) and adult (P_1) parasite populations. It is assumed that both the final and intermediate host populations possess stable age-distributions and are of constant sizes H_1 and H_2 respectively. The components of the model (as based on results described in Section 2) are as follows

Infection of the intermediate host

Infection of the intermediate host occurs as a result of ingestion of free-living infective-stages, and so is governed by the dynamics of a predator-prey interaction (see Section 2.3(v)). In most natural situations, however, the density of tapeworm eggs relative to the density of the intermediate host population is unlikely to be consistently high. It is therefore assumed that parasite transmission may be approximated by a linear model, corresponding to the lower range of egg densities in a non-linear functional response between rate of predation and prey density such as that shown in Figure 2.3.5. In the basic model, intermediate hosts are therefore assumed to acquire parasites at a rate proportional to the density of hosts, H_2, and the density of infective parasite eggs, E. The net rate of parasite acquisition is thus $\beta_2 H_2 E$, where β_2 is a coefficient representing the instantaneous rate of transmission per egg per unit time per unit host density (see Section 2.3(ii)).

Of those parasites acquired by an individual host, only a proportion survive to reach infectivity, as a result of parasite and host mortalities during the developmental period. In host-parasite interactions where the achievement of infectivity takes place as a continuous process beginning immediately after host entry, developmental time delays may be modelled most accurately by the use of coupled differential equations for immature and mature parasites, where the per capita rate of leaving one class and joining the next is a constant per unit of time. However, in cases where infectivity is achieved by all parasites surviving the time delay with little variation, after a well-defined prepatent period (e.g. cestodes), the time delay may be incorporated more simply as follows. Taking the average prepatent period in the intermediate host as T_2 time units, the proportion of established cysticercoids which survive to reach infectivity, D_2, may be expressed as

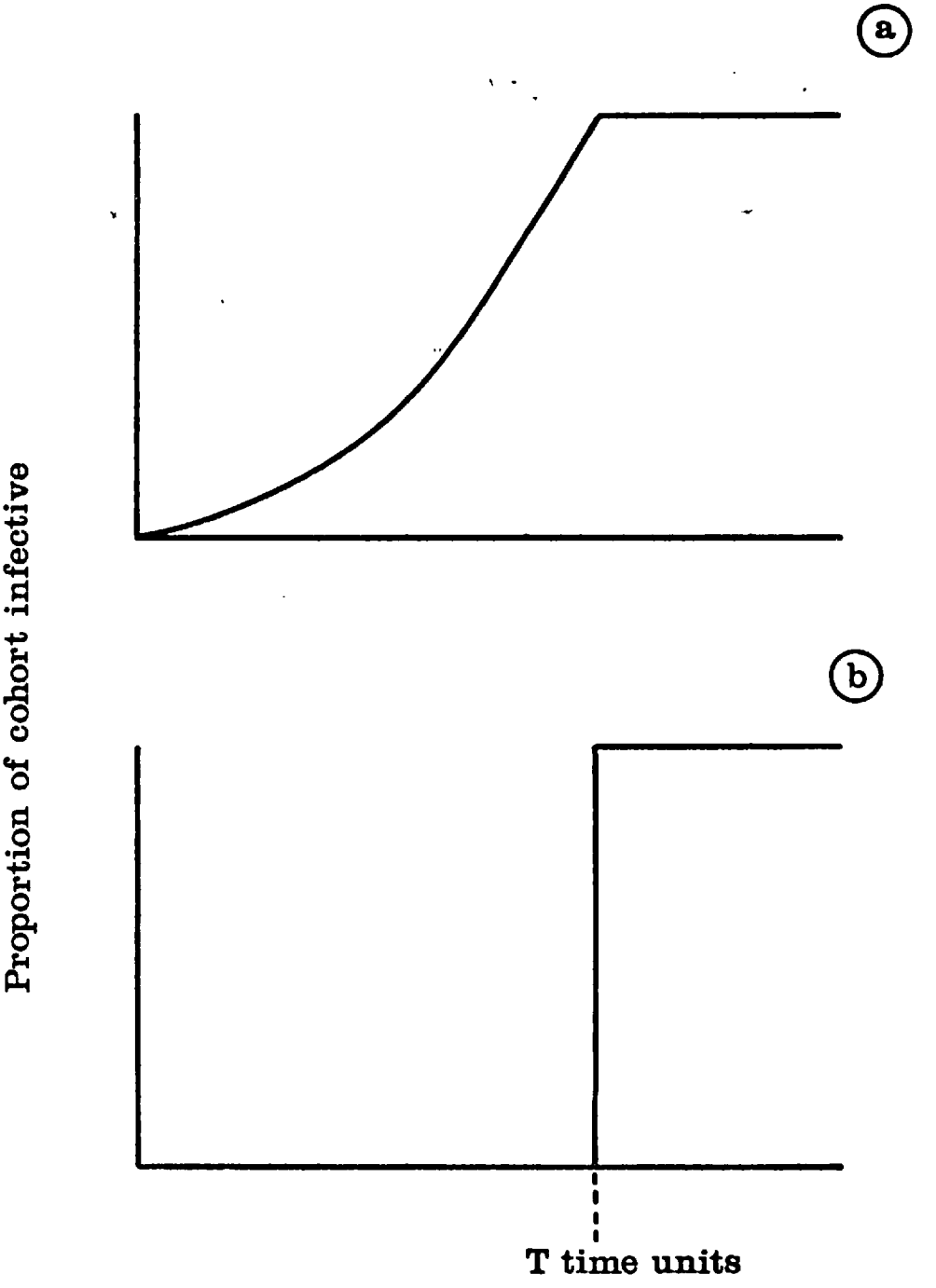
$$D_2 = \exp\ (-T_2(\mu_2+b_2)) \qquad (3.1.1)$$

where μ_2 and b_2 represent losses of larval parasites during the prepatent period as a result of parasite and host mortalities as defined in the next section. The net rate of gain to the population of infective larval parasites is thus $\beta_2 H_2 D_2 E(t-T_2)$. The difference between the two methods of time delay incorporation is diagrammatically portrayed in Figure 3.1.1.

Figure 3.1.1 Methods of modelling developmental time delays.

(a) Parasites leave the uninfective proportion of the cohort and become infective at a constant per capita rate, beginning immediately after host entry.

(b) All parasites achieve infectivity simultaneously after a prepatent time delay of T time units.


a
b
Proportion of cohort infective
T time units
Time after gaining entry to host

Natural larval parasite mortality

H.diminuta cysticercoids in adult *T.confusum* suffer a definite loss of infectivity with time, (see Section 2.5(iii)). In the basic model, larval parasites are assumed to have a constant per capita instantaneous mortality rate, μ_2, independent of either their density or age. The net loss of parasites is thus $\mu_2 P_2$, and the expected lifespan of a larval parasite is $1/\mu_2$.

Loss of larval parasites due to intermediate host mortality

Intermediate hosts are assumed to die at a constant per capita rate b_2, such that the net rate of loss of parasites is $b_2 H_2 \sum_{i=o}^{\infty} i.p(i)$ where $p(i)$ represents the probability that an individual host contains i parasites. Although parasite-induced effects on host survival and fecundity have been demonstrated in the laboratory (see Sections 2.4(iii) and 2.4(iv)),it is assumed here that few intermediate hosts survive long enough under natural conditions for these effects to become operative.

Loss of larval parasites as a result of final host infection

Final host infection is achieved by means of a second predator-prey association, this time between final and

intermediate hosts (see Section 2.5(i)). In the basic model, it is assumed, for simplicity, that intermediate host density is unlikely to reach high enough levels to cause a reduction in ingestion rate to occur as a result of satiation or handling-time limitations, especially since *T.confusum* is unlikely to form a primary food source for the rat in natural habitats. Ingestion is thus assumed to be directly proportional to the density of final and intermediate hosts, H_1 and H_2 respectively, such that the net rate of loss to the larval parasite population is $\beta_1 H_1 H_2 \sum_{i=o}^{\infty} i.p(i)$, where β_1 represents the instantaneous rate of parasite transmission per parasite per unit time per unit final host density, and $p(i)$ is the probability that an individual host harbours i parasites.

The acquisition of adult parasites by the final host

As stated above, ingestion of intermediate hosts by prospective final hosts is assumed to be directly proportional to their densities, H_1 and H_2, such that the net rate of acquisition is $\beta_1 H_1 H_2 \sum_{i=o}^{\infty} i.p(i)$. Since $\sum_{i=o}^{\infty} i.p(i)=M_2$, the mean number of parasites per host, transmission is proportional to the total density of the larval parasite population, M_2H_2. Of those parasites acquired by an individual host, only a proportion, D_1 survive to reach sexual maturity, since some are lost due to parasite and host mortalities during the prepatent period. If the average length of the prepatent period in the final host is T_1 time units, then the proportion D_1 may be expressed as

$$D_1 = \exp\ (-T_1(\mu_1+b_1)) \qquad (3.1.2)$$

where μ_1 and b_1 are the instantaneous per capita rates of adult parasite and final host mortalities respectively. The net rate of gain of sexually mature adult parasites is thus $\beta_1 H_1 D_1 H_2 \sum_{i=o}^{\infty} i.p(i)\,(t-T_1)$.

Natural adult parasite mortality

The observations of Ghazal and Avery (1974) and Hesselberg and Andreassen (1975) indicate that both survival and fecundity are density-dependent in *Hymenolepis* spp. (see Section 2.5(v)). In the basic model, density-dependent constraints are limited for simplicity to parasite mortality. The per capita instantaneous rate of natural parasite mortality is assumed to be linearly related to parasite burden, i, such that

$$\mu(i) = \mu_1 + \delta i \qquad (3.1.3)$$

where $1/\mu_1$ represents the expected lifespan of mature parasites in the absence of density-dependence (i.e. in single worm burdens) and δ is a coefficient representing the severity of density-dependent constraints on worm survival. The net rate of parasite losses is therefore $H_1 \sum_{i=o}^{\infty} \mu(i).i.p(i)$.

Parasite losses due to definitive host mortality

Hosts are assumed to have a constant, instantaneous rate of mortality, b_1, such that the net loss of parasites is

$b_1 H_1 \sum_{i=0}^{\infty} i.p(i)$. Adult tapeworms are often considered to be without serious pathogenic effects on the definitive host (see Section 2.5(vi)) and in the basic model it will be assumed that there is no parasite-induced host mortality.

The production of infective eggs

H.diminuta is an hermaphroditic parasite, and is thought to be able to carry out both self and cross-fertilization (see Section 2.5(v)). Here it will be assumed that all worms in the definitive host are capable of producing eggs, whether present in single or multiple burdens. Assuming for simplicity that the instantaneous rate of egg production per worm per unit time, λ, is constant and independent of worm age or density, the net rate of egg production is equal to λP_1.

Natural mortality of infective eggs

The population of infective eggs is subject to considerable mortality while in the external environment (see Section 2.3(i)). Assuming that the instantaneous rate of mortality, μ_3/egg/ unit time, is constant, the net rate of loss is equal to $\mu_3 E$.

Loss of infective stages as a result of host infection

Infective eggs are removed from the population as a consequence of ingestion by potential intermediate hosts.

The net rate of loss is equal to $\beta_2 H_2 E$, as described earlier. Loss of eggs as a result of ingestion by animals unsuitable as intermediate hosts is assumed to be incorporated into the term describing the natural mortality of infective eggs.

The components detailed above give rise to the following differential equations describing the changes through time of the adult parasite (P_1), larval parasite (P_2) and tapeworm egg (E) populations.

$$dP_1/dt = \beta_1 H_1 D_1 H_2 \sum_{i=o}^{\infty} i.p(i)\,(t-T_1) - H_1 \sum_{i=o}^{\infty} \mu(i).i.p(i) - b_1 H_1 \sum_{i=o}^{\infty} i.p(i) \qquad (3.1.4)$$

$$dP_2/dt = \beta_2 D_2 H_2 E(t-T_2) - \mu_2 P_2 - b_2 H_2 \sum_{i=o}^{\infty} i.p(i) - \beta_1 H_1 H_2 \sum_{i=o}^{\infty} i.p(i) \qquad (3.1.5)$$

$$dE/dt = \lambda P_1 - \mu_3 E - \beta_2 H_2 E \qquad (3.1.6)$$

It is clear from the structure of equations (3.1.4) to (3.1.6) that the dynamical behaviour of the basic model is dependent on the nature of the statistical distribution of parasites within the host population. In reality, the form of this distribution is determined by the population processes involved in the parasite-host interaction. It is difficult however, to deduce this in all but the most simple stochastic models (see Bartlett, 1960; Bailey, 1964) and its introduction would be beyond the

scope of the present thesis.

Considerable simplification in relatively complex models such as that described above may be achieved by making a phenomenological assumption concerning the distribution based on patterns observed in real host-parasite interactions. In the vast majority of such associations, the parasites have a clumped or contagious distribution within the host population, which is usually well described by the negative binomial probability model (see Section 1). This distribution has been found to provide a good empirical description of the distribution of *H.diminuta* in the intermediate host in both laboratory and field populations (see Figures 2.5.9 and 2.3.8) and also of adult worms in mouse populations under natural conditions (see Figure 2.5.10).

The negative binomial may be defined by its mean M (where M=P/H) and the parameter k, which varies inversely with the degree of aggregation. The probability generating function of the negative binomial has been given earlier (see Section 2.3(vi)) and it should be noted that it corresponds to the Poisson distribution (variance equal to mean) in the limit when $k \to \infty$. By the use of the statistical moments of the negative binomial distribution, namely

$$\sum_{i=o}^{\infty} i.p(i) = E(i) = P/H \qquad (3.1.7)$$

and

$$\sum_{i=o}^{\infty} i^2 p(i) = E(i^2) = P^2(k+1)/H^2k + P/H \qquad (3.1.8)$$

equations (3.1.4) to (3.1.6) may be simplified to give

$$dP_1/dt = \beta_1 H_1 D_1 P_2(t-T_1) - P_1(b_1+\mu_1+\delta) - \delta P_1^2(k_1+1)/H_1 k_1 \qquad (3.1.9)$$

$$dP_2/dt = \beta_2 H_2 D_2 E(t-T_2) - P_2(\mu_2+b_2) - \beta_1 H_1 P_2 \qquad (3.1.10)$$

$$dE/dt = \lambda P_1 - \mu_3 E - \beta_2 H_2 E \qquad (3.1.11)$$

where k_1 is the parameter of the negative binomial distribution describing the adult worms in the final host.

In common with many other parasitic organisms (see May and Anderson, 1979a), the expected lifespans of mature and larval *H.diminuta* are greater than that of the infective egg (see Table 3.1.2). The dynamics of the infective egg population thus operate on a much faster time-scale than the dynamics of the other two parasite populations and so the egg population may be assumed to have the equilibrium value appropriate to the prevailing conditions among the larval and adult parasite populations. In addition, the developmental time delays T_1 and T_2 are short in relation to the lifespans of the hosts and parasites (see Table 3.1.2), which suggests that the prepatent periods are unlikely to be of great significance to the dynamics of the parasite populations viewed over a number of generations. By noting these time-scale effects, the model may be simplified

Table 3.1.2 *The relative time-scales of the populations involved in the life-cycle of* H.diminuta.

		Approximate value
Expected lifespan	Final host	Several years
	Adult parasite	Several years
	Intermediate host	Several weeks
	Larval parasite	Several weeks
	Parasite egg	Several days
Prepatent period	Adult parasite	17 days
	Larval parasite	10 days

and collapsed to two equations. Further simplification may be achieved by noting that the variables P_1 and P_2 may be replaced by M_1H_1 and M_2H_2respectively, where M_1 and M_2 are the mean adult and larval worm burdens per host. Rescaling with M_1 and M_2 gives

$$dM_1/dt = \beta_1 D_1 H_2 M_2 - M_1(b_1+\mu_1+\delta) - \delta M_1^2(k_1+1)/k_1 \qquad (3.1.12)$$

$$dM_2/dt = \frac{\lambda H_1 D_2 M_1 \beta_2}{\mu_3+\beta_2 H_2} - M_2(\mu_2+b_2+\beta_1 H_1) \qquad (3.1.13)$$

The dynamical behaviour of the coupled equations(3.1.12) and (3.1.13) may be examined by setting dM_1/dt and dM_2/dt equal to zero and constructing isoclines in the M_1 - M_2 plane (see Pielou, 1969; Maynard Smith, 1968). Using this method, two general patterns emerge, as illustrated in Figure 3.1.2. In the first (Figure 3.1.2(a)), the two isoclines intersect only at the origin, indicating that the parasite is unable to persist within the host populations. In the second (Figure 3.1.2(b)), the two isoclines intersect at the origin, and, in addition, at the point M*, which represents a positive parasite equilibrium level.

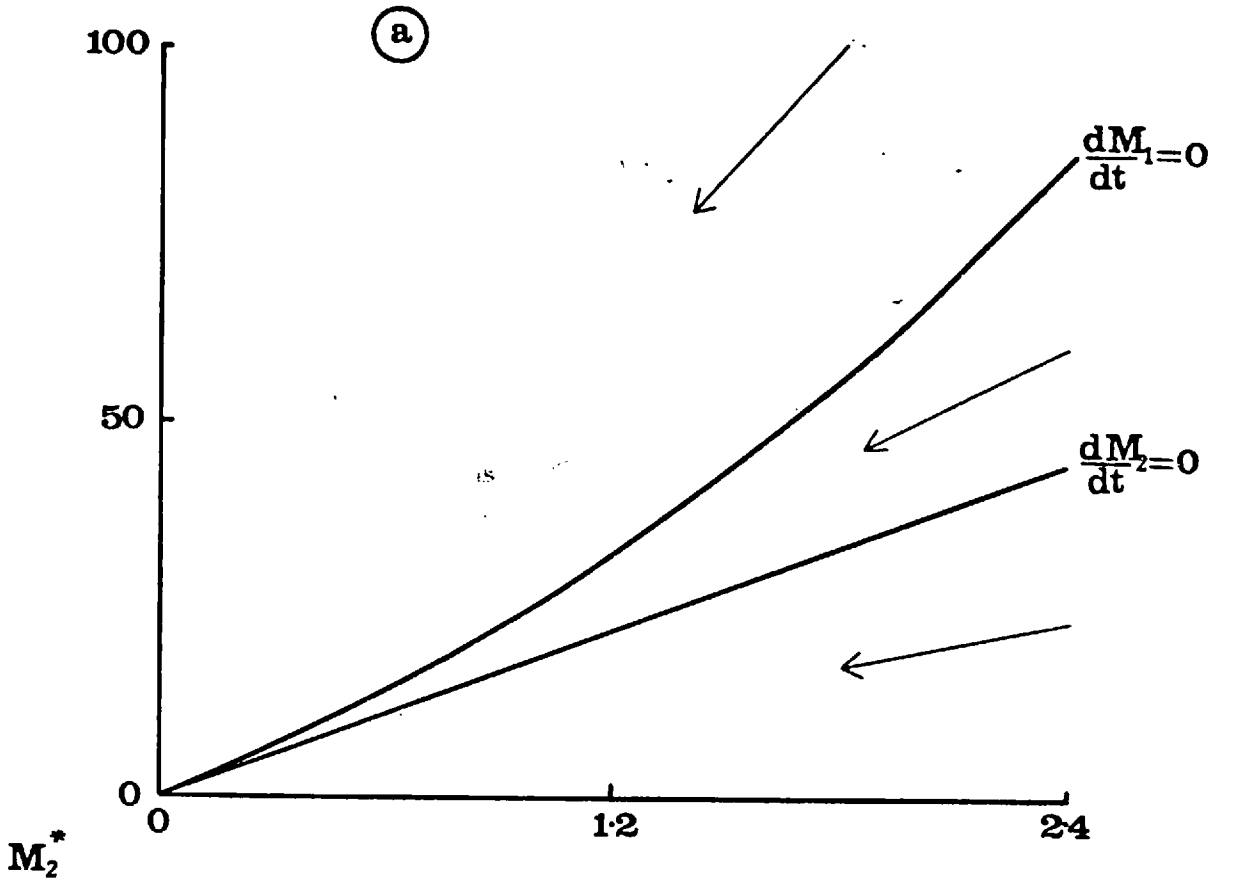
These two behaviour patterns represent cases when the parameters are above (Figure 3.1.2(b)) or below (Figure 3.1.2(a)) a transmission threshold. When the threshold is exceeded, all positive trajectories are attracted to the point M*; when it is not, they are attracted to the point M=0. Both M* and M=0 represent locally stable equilibrium levels (see Appendix 2.1).

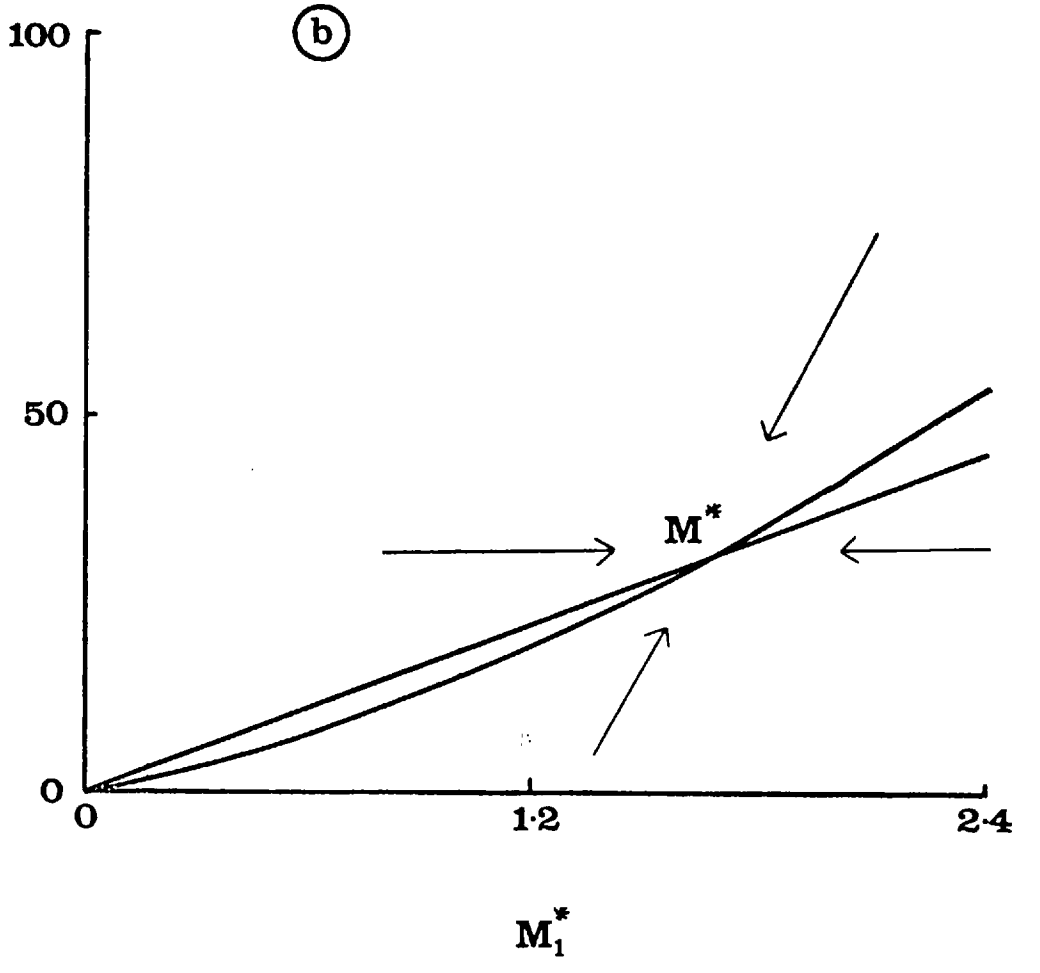
Figure 3.1.2 Phase-plane analysis of the behaviour of the basic model (equations (3.1.12) and (3.1.13)).

The arrows indicate how the dynamical trajectories of M_1 and M_2 behave in the various regions into which the M_1 - M_2 plane is dissected by the isoclines $dM_1/dt=0$ and $dM_2/dt=0$.

(a) Population parameters below the transmission threshold. The infection cannot persist, and all trajectories are attracted to the origin($M_1^*=M_2^*=0$). Parameter values as in Table 3.1.1. In addition $H_1=10$/hectare, $H_2=30$/hectare.

(b) Population parameters above the transmission threshold. All positive trajectories are attracted to the stable point M*. Parameter values as in (a) except $H_2=41$/hectare.


a
100
50
0
0
1·2
2·4
M_2^*
$\frac{dM_1}{dt}=0$
$\frac{dM_2}{dt}=0$


b
100
50
0
0
1·2
2·4
M^*
M_1^*

In contrast to models of dioecious helminths (e.g. hookworms and schistosomes), where multiple stable states occur as a direct consequence of a worm mating probability fuction (Macdonald, 1965; Anderson, 1980a), the present model does not exhibit more than one positive equilibrium point for any given combination of parameter values.

The precise value of the transmission threshold mentioned above has been examined in detail by Anderson (1980a), and may be characterized by the basic reproductive rate of the parasite, R. If a parasite is introduced into a large population of uninfected hosts (so that density-dependent effects created by existing parasites are negligible), R represents the number of eggs produced during the reproductive lifespan of that parasite, which successfully complete their own development to reproductive maturity. The transmission threshold may then be precisely defined by the point at which R is equal to unity. The numerical value of R must be greater than one in order for parasite persistence to be achieved.

From equations (3.1.12) and (3.1.13), the dynamical response times of the adult and larval parasites are approximately $1/(b_1+\mu_1+\delta)$ and $1/(\mu_2+b_2+\beta_1 H_1)$ respectively. Since $(\mu_2+b_2+\beta_1 H_1) >> (b_1+\mu_1+\delta)$, (see Table 3.1.1), it follows that M_2 has a much faster response time than M_1. As an approximation, it may thus be assumed that M_2 is almost instantaneously adjusted to the

equilibrium level M_2^* for all values of M_1. The basic model may then be reduced to a single equation for the variable M_1, giving

$$dM_1/dt = M_1 \left[\frac{\lambda\beta_1\beta_2 H_1 H_2 D_1 D_2}{(\mu_3+\beta_2 H_2)(\mu_2+b_2+\beta_1 H_1)} - (b_1+\mu_1+\delta) - \delta M_1 (k_1+1)/k_1 \right] \tag{3.1.14}$$

The precise manner in which the various population parameters determine the probable persistence of the parasite are apparent from the structure of equation (3.1.14). Essentially, for the transmission threshold to be exceeded, the basic reproductive rate, R, must be greater than unity, where

$$R = \frac{\lambda\beta_1\beta_2 H_1 H_2 D_1 D_2}{(\mu_3+\beta_2 H_2)(\mu_2+b_2+\beta_1 H_1)(b_1+\mu_1+\delta)} \tag{3.1.15}$$

The numerator of equation (3.1.15) consists of the product of the model parameters involved in parasite transmission, and the denominator consists of the product of the accumulated rates of mortality in the adult parasite, larval parasite and parasite egg populations. Reproductive success is thus determined by the relative rates of transmission and loss. Alternatively, the basic reproductive rate may be interpreted as the product of the reproductive contributions of the egg, the larval parasite and the adult parasite. Although the egg and larval parasite do not directly contribute to reproduction, they do so indirectly by placing the parasite in a situation suitable for reproduction to take place.

From equation (3.1.15), it is clear that, for a given combination of parameter values, there exist critical host density levels for parasite persistence. Since β_1 and β_2 are very small, the terms $\beta_1 H_1$ and $\beta_2 H_2$ are negligible in comparison with the terms (μ_2+b_2) and μ_3 (see Table 3.1.1). The critical density, defined as the product $H_1 H_2$, is thus given from equation (3.1.15) as

$$H_1 H_2 > \frac{\mu_3(\mu_2+b_2)(b_1+\mu_1+\delta)}{\lambda\beta_1\beta_2 D_1 D_2} \qquad (3.1.16)$$

Although experiments have not yet been carried out to examine this relationship for *H.diminuta* (or for any other host-parasite interaction), equation (3.1.16) may be used to estimate the threshold host densities required for maintenance of the infection. Given the parameter values listed in Table 3.1.1, the critical product of rat and beetle densities may be estimated as 400 hosts/hectare. A low rat density of, for example, 5 rats/hectare may thus be offset by a correspondingly higher density of 80 beetles/hectare or *vice versa*. Bearing in mind that the parameter estimates used are only approximate values obtained under specific laboratory conditions, the main point of interest resulting from the above procedure is the extremely low critical host density required for parasite transmission. This may be typical of many indirect life-cycle helminths which have the ability to persist endemically in low density populations. Furthermore, it has been argued that the ability of a low density

of one host species to be offset by a correspondingly higher density of the other host has provided a major selective advantage for the development of an indirect life-cycle during parasite evolution (Anderson, 1980b). In addition, the structure of equation (3.1.16) indicates that the high rate of egg production observed in many helminths is of importance in reducing the threshold host density required for parasite transmission.

Equations (3.1.14) and (3.1.15) may be combined to give

$$dM_1/dt = M_1 \left[(b_1+\mu_1+\delta)(R-1) - \delta M_1 (k_1+1)/k_1 \right] \qquad (3.1.17)$$

from which it can be seen that the value of R will play a large part in the determination of the intensity of infection in the final host population. Equation (3.1.17) is a modification of the logistic equation (see, for example, Pielou, 1969) consisting of a term describing the rate of reproduction, and a negative term describing the degree of density-dependence acting on the reproductive rate. In this case, the severity of this density-dependent constraint becomes greater as parasite contagion increases. The equilibrium infection intensity is given by

$$M_1^* = k_1 (b_1+\mu_1+\delta)(R-1)/\delta(k_1+1) \qquad (3.1.18)$$

and, from the zero term of the negative binomial probability distribution, the prevalence of infection at equilibrium, p*

(i.e. the proportion of hosts infected)is simply

$$p^* = \left[1 - \left[1 + \frac{M_1^*}{k_1} \right]^{-k_1} \right] \qquad (3.1.19)$$

Using estimated parameter values for *H.diminuta*, the relationship between R and the prevalence and intensity of final host infection is shown in Figure 3.1.3. Above the transmission threshold (R=1), intensity is directly proportional to the value of R, whereas prevalence rises to a plateau as R increases. The rate of approach to the asymptotic prevalence at 100% infection is dependent on the statistical distribution of parasite numbers per host, becoming slower as the degree of over-dispersion of parasite numbers per host becomes more severe (k_1 small).

Further general insight into the dynamical behaviour of the basic model may be gained by evaluating equation (3.1.14) at equilibrium. The influence of the values of k_1 and δ on the mean adult worm burden per host is shown in Figure 3.1.4. Figure 3.1.4(a) shows the relationship between the degree of over-dispersion in the frequency distribution of adult parasite numbers in the final host, and the mean worm burden of the final host population. Heterogeneity acts as a form of density-dependence. It is exerted through the constraints on parasite population growth within individual hosts, which tend to cause heavy parasite mortality when the parasite population per host

Figure 3.1.3 The influence of R on the prevalence and intensity of infection (basic model).

(a) The relationship between the basic reproductive rate of the parasite, R, and the mean intensity of final host infection at equilibrium, M_1^*, as predicted by the model defined in equations (3.1.18) and(3.1.19). The arrows denote the dynamical trajectories of the system following a perturbation from the two equilibrium states, M_1^* and zero.

(b) The relationship between the value of R and the percentage prevalence of infection at equilibrium, ρ^*.

The dashed vertical lines indicate the transmission threshold (R=1). Parameter values as listed in Table 3.1.1.

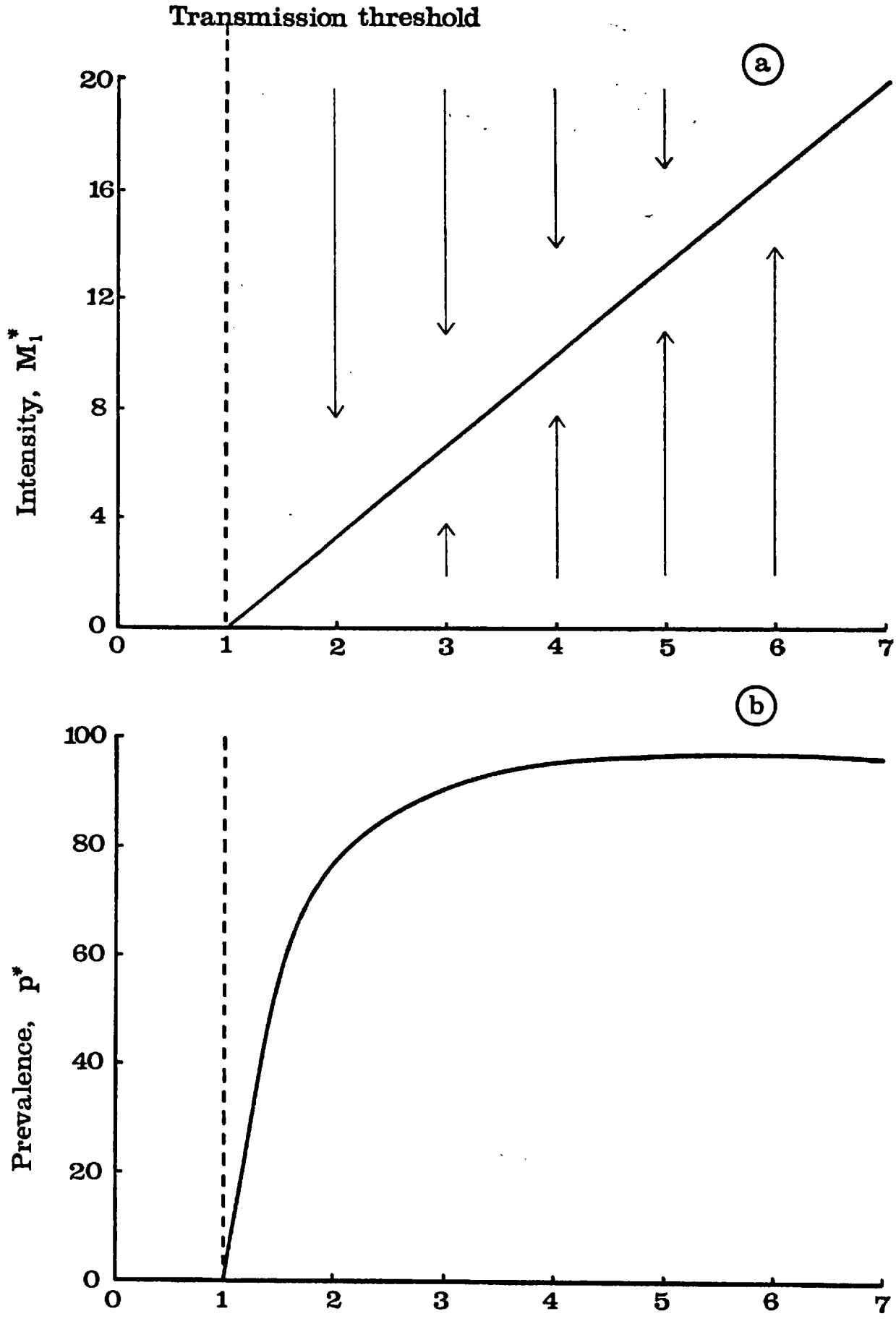
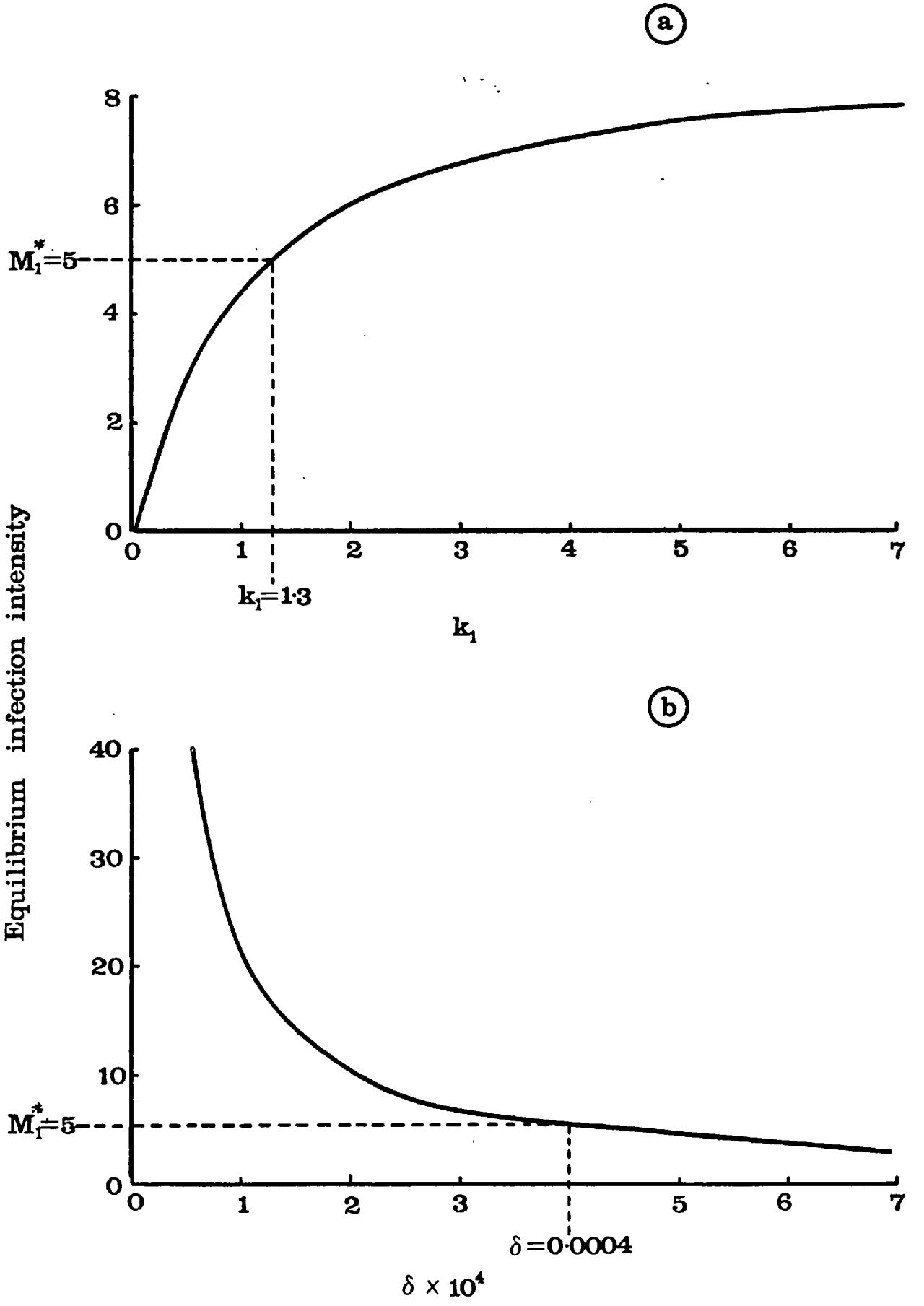

Transmission threshold
a
Intensity, M_1^*
20
16
12
8
4
0
0
1
2
3
4
5
6
7
b
Prevalence, p^*
100
80
60
40
20
0
0
1
2
3
4
5
6
7
Basic reproductive rate, R

Figure 3.1.4 *The influence of over-dispersion in parasite numbers per host and density-dependent parasite mortality on the predicted intensity of infection at equilibrium (basic model).*

The graphs indicate the influence of the values of the parameters k, (Figure 3.1.4(a)) and δ (Figure 3.1.4(b)) on the mean number of adult worms per host at equilibrium (M_1^*) as predicted by the model defined in equation (3.1.14). Parameter values as listed in Table 3.1.1. In addition, H_1=20/hectare, H_2=50/hectare.


a
8
6
$M_1^*=5$
4
2
0
0
1
2
3
4
5
6
7
$k_1=1{\cdot}3$
k_1
b
40
30
20
10
$M_1^*=5$
0
0
1
2
3
5
6
7
$\delta=0{\cdot}0004$
$\delta \times 10^4$
Equilibrium infection intensity

is high.

Figure 3.1.4(b) illustrates the effect of the degree of density-dependence on adult worm survival on the mean worm burden per host. It is apparent that density-dependence may exert stringent regulation on parasite population growth, and has the important consequence of stabilizing the dynamics of the host-parasite interaction (Anderson and May, 1978). It is of interest to note that the estimated values of the parameters listed in Table 3.1.1, when connected in the manner defined by the basic model, indicate that both over-dispersion of adult parasites within the final host population, and density-dependent constraints on adult worm survival, may have significant roles in the regulation of parasite population growth (see Figure 3.1.4).

3.2 NON-LINEAR PARASITE TRANSMISSION

As discussed in Section 2, functional responses between prey ingestion rate per predator and prey density exist in both the transmission links of the *H.diminuta* life-cycle. For reasons outlined earlier, it has been assumed in the basic model that there is direct proportionality between the rate of infection and the densities of both hosts and infective parasites. The effects on model behaviour of inclusion of non-linear parasite transmission is considered in the present section.

Since the densities of tapeworm eggs encountered by a beetle are likely to be much greater than the densities of beetles encountered by a rat, it is assumed as a first approximation that the functional response between beetles and tapeworm eggs is of greater significance to the population dynamics of *H.diminuta* than the functional response between rats and beetles. As a further simplification, it is assumed that the number of eggs removed from the total egg population as a result of beetle predation, is negligible in comparison with the number lost as a result of other causes of mortality (i.e. in equation (3.1.11), $\beta_2 H_2 E \to 0$).

As discussed earlier, the relationship between beetle infection and egg density may be described by the model defined in equation (2.3.9). For simplicity however, the functional

response may be incorporated into the basic model by use of the expression

$$x = \rho_2 H_2 E/(g_2+E) \qquad (3.2.1)$$

where x is the number of established parasites, and ρ_2 and g_2 are coefficients relating to the numerical value of the plateau and the rate of rise to the plateau respectively (see Holling, 1959b). Equation (3.2.1) gives a good empirical description of the functional response observed under experimental conditions, as shown in Figure 3.2.1(a). The difference between linear transmission as used in the basic model, and non-linear transmission as described by equation (3.2.1) is shown in Figure 3.2.1(b). The parameter estimates used in this figure (ρ_2=26 eggs/day/host/hectare, $g_2=2\times10^8$), which result in net transmission roughly comparable with that obtained using the estimated value of β_2 given in Table 3.1.1, will be used for numerical investigation of model behaviour in the remainder of this section.

Inclusion of equation (3.2.1) in the basic model gives rise to the following differential equations

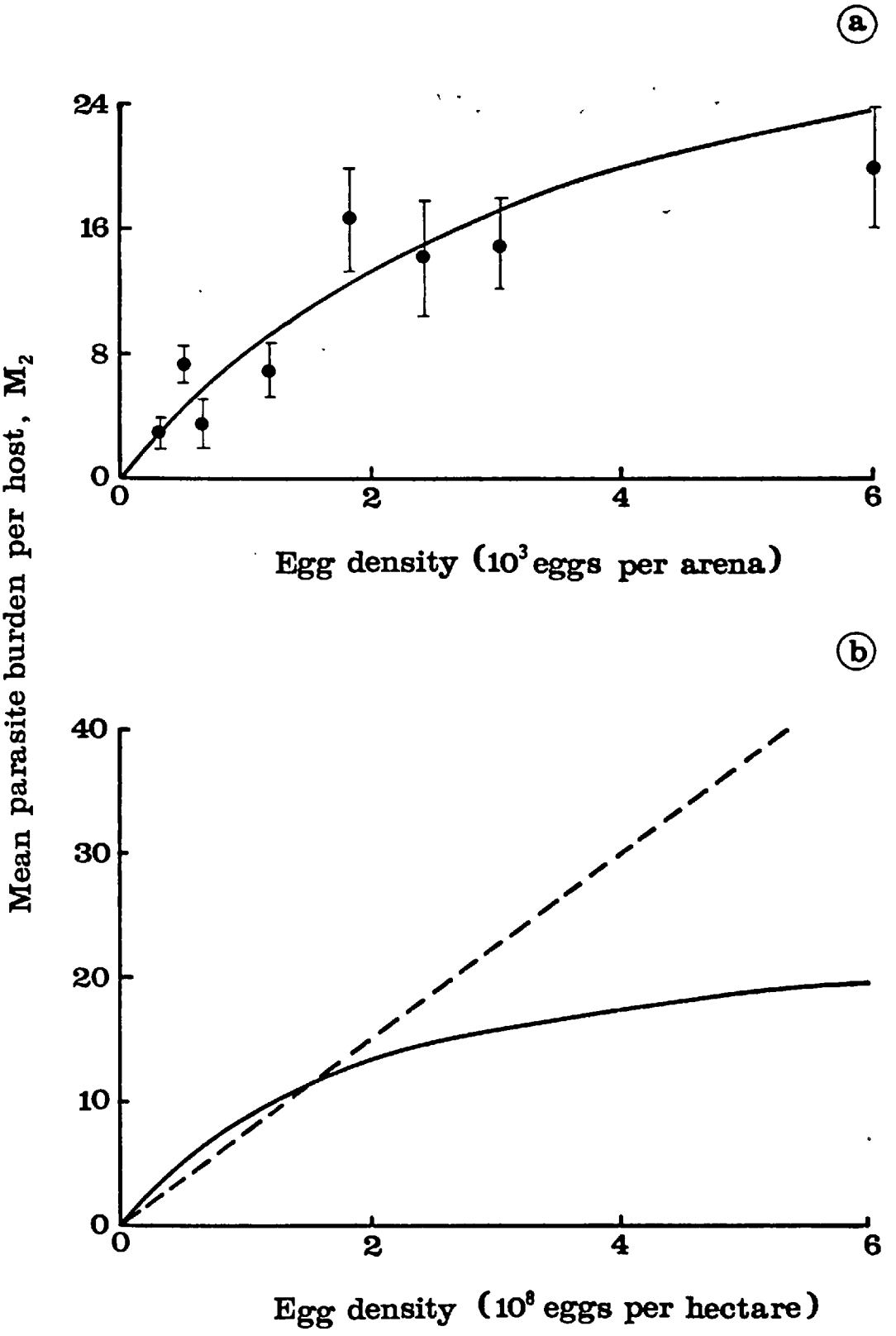
$$dP_1/dt = \beta_1 H_1 D_1 P_2(t-T_1) - P_1(b_1+\mu_1+\delta) - \delta P_1^2(k_1+1)/H_1 k_1 \qquad (3.2.2)$$

$$dP_2/dt = \rho_2 D_2 H_2 E(t-T_2)/(g_2+E) - P_2(\mu_2+b_2+\beta_1 H_1) \qquad (3.2.3)$$

Figure 3.2.1 *The use of the model defined in equation (3.2.1) in the description of non-linear parasite transmission.*

(a) The use of equation (3.2.1) in the description of the experimentally observed relationship between egg density and the resultant parasite burden of the exposed host population. Experimental data from Table 2.3.5(a); g_2=4000; P_2=40 eggs/24 hours/host/13cm^2.

(b) An illustration of the differences between linear and non-linear parasite transmission. Dashed line represents linear transmission, where $M_2 = \beta_2 E$ and β_2=7.5x10^{-8}/egg/day/host/hectare. Solid line represents non-linear transmission, where $M_2=\rho_2 E/(g_2+E)$; ρ_2=26 eggs/day/host/hectare, g_2=2x10^8.


a
24
16
8
0
0
2
4
6
Mean parasite burden per host, M_2
Egg density (10^3 eggs per arena)
b
40
30
20
10
0
0
2
4
6
Egg density (10^6 eggs per hectare)

$$dE/dt = \lambda P_1 - \mu_3 E \qquad (3.2.4)$$

By noting the time-scale effects outlined in Section 3.1 and by replacing P_1 and P_2 by the variables M_1 and M_2 respectively, considerable simplification may be achieved, giving

$$dM_1/dt = \beta_1 D_1 H_2 M_2 - M_1(b_1+\mu_1+\delta) - \delta M_1^2(k_1+1)/k_1 \qquad (3.2.5)$$

$$dM_2/dt = \rho_2 \lambda M_1 H_1 D_2/(\mu_3 g_2+\lambda M_1 H_1) - M_2(\mu_2+b_2+\beta_1 H_1) \qquad (3.2.6)$$

A phase-plane analysis of equations (3.2.5) and (3.2.6) is shown in Figure 3.2.2. The behaviour is qualitatively similar to that of the basic model, with a single positive equilibrium point generated if the parameter values fall above the critical transmission threshold. The value of this threshold may be examined by evaluating the model at equilibrium, to give

$$0 = M_1 \left[\frac{\lambda\beta_1\rho_2 H_1 H_2 D_1 D_2}{(\mu_3 g_2+\lambda M_1 H_1)(\mu_2+b_2+\beta_1 H_1)} - (b_1+\mu_1+\delta) - \delta M_1(k_1+1)/k_1 \right] \qquad (3.2.7)$$

Apart from $M_1^*=0$, equation (3.2.7) yields the 2 following non-zero solutions, $M_1^*(1)$ and $M_1^*(2)$,

$$M_1^*(1), M_1^*(2) = \frac{-(wz\mu_3 g_2+yz\lambda H_1) \pm \sqrt{(wz\mu_3 g_2+yz\lambda H_1)^2 - 4wz\lambda H_1(yz\mu_3 g_2 - x)}}{2wz\lambda H_1} \qquad (3.2.8)$$

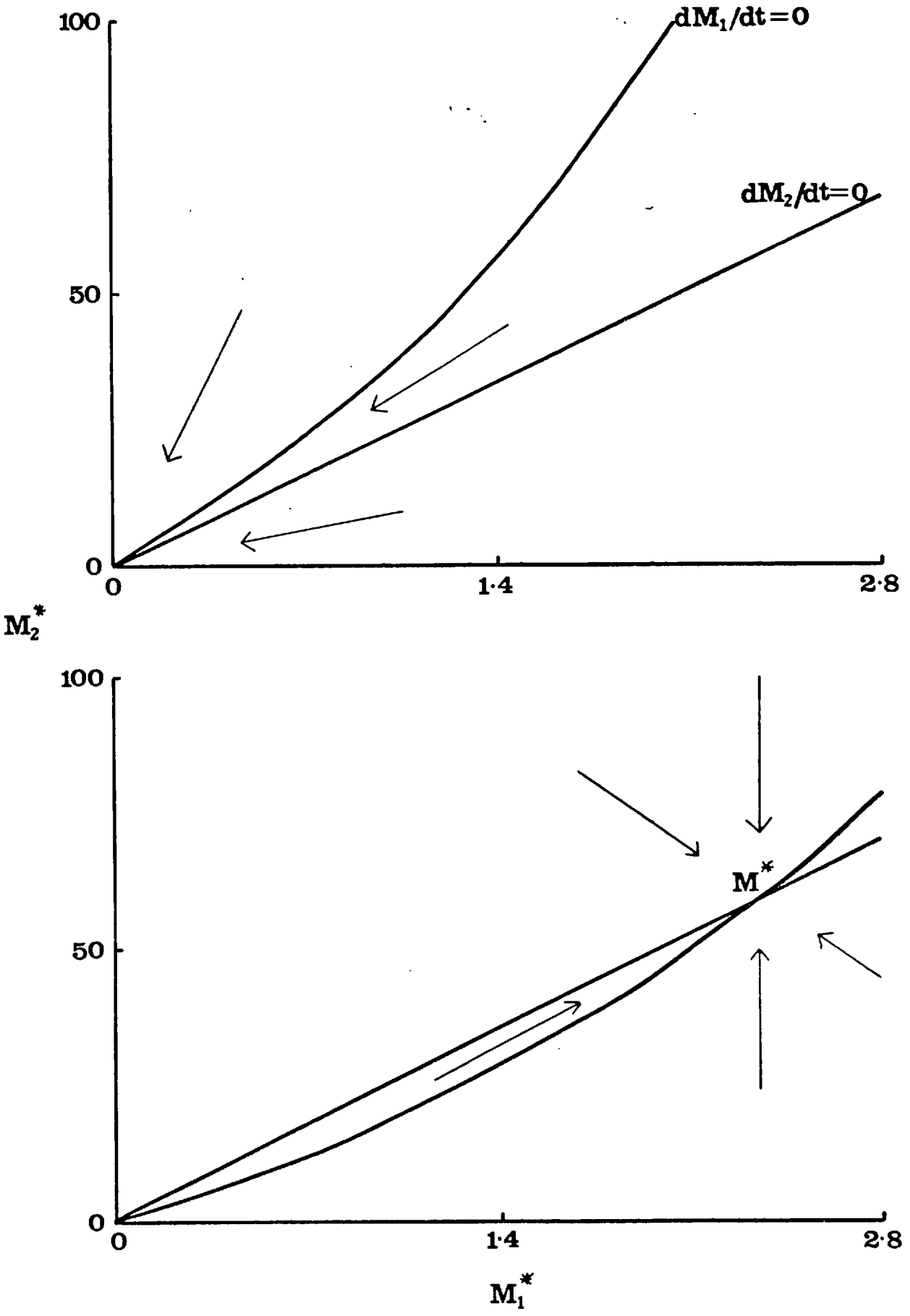
where $x = \lambda\beta_1\rho_2 H_1 H_2 D_1 D_2$, $y = (b_1+\mu_1+\delta)$, $w = \delta(k_1+1)/k_1$ and $z = (\mu_2+b_2+\beta_1 H_1)$. From equation (3.2.8), it can be seen that

Figure 3.2.2 Phase-plane analysis of the behaviour of equations (3.2.5) and (3.2.6).

The arrows indicate how the dynamical trajectories of M_1 and M_2 behave in the various regions into which the M_1-M_2 plane is dissected by the isoclines $dM_1/dt=0$ and $dM_2/dt=0$.

(a) Population parameters below the transmission threshold. The infection cannot persist, and all trajectories are attracted to the origin ($M_1^*=M_2^*=0$). Parameter values as in Table 3.1.1. In addition $\rho_2=26$ eggs/day/host/hectare, $g_2=2\times10^8$, $H_1=10$/hectare, $H_2=20$/hectare.

(b) Population parameters above the transmission threshold. All positive trajectories are attracted to the stable point M^*. Parameter values as in (a) except $H_2=39$/hectare.


100
50
0
0
1·4
2·8
M_2^*
$dM_1/dt=0$
$dM_2/dt=0$
100
50
0
0
1·4
2·8
M_1^*
M^*

the only non-negative, and thus realistic value of M_1^* is obtained when $x > yz\mu_3 g_2$. The critical transmission threshold is thus defined by the point when the basic reproductive rate of the parasite, R, is equal to unity, where

$$R = \frac{\lambda\beta_1\rho_2 H_1 H_2 D_1 D_2}{\mu_3 g_2 (b_1+\mu_1+\delta)(\mu_2+b_2+\beta_1 H_1)} \qquad (3.2.9)$$

If $R < 1$, the parasite is unable to persist, and $M_1^*=0$. The neighbourhood stability analysis of equations (3.2.5) and (3.2.6) is given in Appendix 2.2, from which it can be seen that the equilibrium points $M_1^*=0$ and $M_1^* > 0$ are stable to local perturbations when $R < 1$ and $R > 1$ respectively.

General insight into the effect of the functional response as a density-dependent constraint on parasite population growth may be obtained by comparing the behaviour of equations (3.2.5) and (3.2.6) with that of equations (3.1.12) and (3.1.13) when $R > 1$. In the absence of other density-dependent constraints (i.e. when $\delta=0$), the mean adult worm burden per host as predicted by the basic model grows exponentially at a rate r, where

$$r = \left[\frac{\lambda\beta_1\beta_2 D_1 D_2 H_1 H_2}{(\mu_3+\beta_2 H_2)(\mu_2+b_2+\beta_1 H_1)} - (b_1+\mu_1) \right] \qquad (3.2.10)$$

The influence of the functional response (equations (3.2.5) and

(3.2.6)) is to regulate parasite population growth to a stable equilibrium level, M_1^*, where

$$M_1^* = \frac{\beta_1 \rho_2 \lambda H_1 H_2 D_1 D_2 - (\mu_1+b_1)(\mu_2+b_2+\beta_1 H_1+\mu_3 g_2)}{\lambda H_1 (\mu_1+b_1)} . \qquad (3.2.11)$$

Whether or not the potential of the functional response to cause density-dependent regulation of parasite population growth is important under natural conditions will depend on the relative values of the population parameters (see General Discussion).

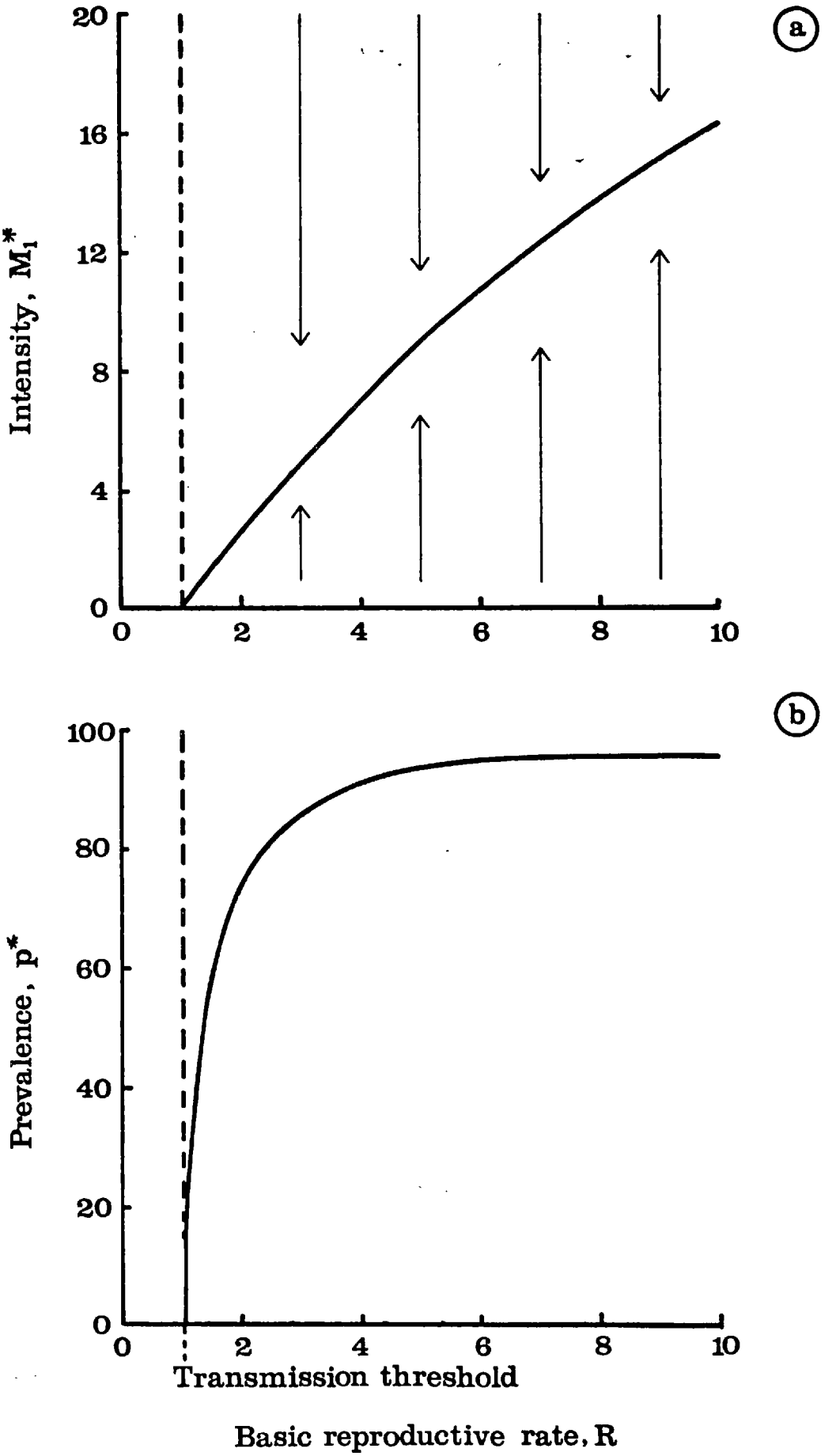
The relationship between R and the intensity and prevalence of infection in a population may be examined by combining equations (3.2.8) and (3.2.9), and using the resultant expression in conjunction with the zero probability term of the negative binomial distribution as defined in equation (3.1.19). The results are shown in Figure 3.2.3. By a comparison of Figures 3.2.3 and 3.1.2, it can be seen that the functional response creates non-linearity in the relationship between the value of R and the resultant intensity of infection in the final host, M_1^*, tending towards an asymptote as R becomes large. It is of interest to note, however, that, since the model predicts only one value of M_1^* for any given value of R, there is no 'breakpoint equilibrium' as described for dioecious helminths such as schistosomes and hookworms (Macdonald, 1965; Anderson, 1980a; see Section 1). The model behaviour shown in Figure

Figure 3.2.3 *The influence of R on the prevalence and intensity of infection as predicted by the model defined in equations (3.2.5) and (3.2.6).*

(a) The relationship between the basic reproductive rate of the parasite, R, and the mean intensity of final host infection at equilibrium, M_1^*. The arrows denote the dynamical trajectories of the system following a perturbation from the two equilibrium states, M_1^* and zero.

(b) The relationship between the value of R and the percentage prevalence of infection at equilibrium, ρ^*.

The dashed vertical lines indicate the transmission threshold (R=1). Parameter values as listed in Table 3.1.1. In addition, ρ_2=26 eggs/day/host/unit area, $g_2=2\times10^8$, H=10/hectare, H_2=27/hectare.


a
20
16
12
8
4
0
Intensity, M_1^*
0
2
4
6
8
10
b
100
80
60
40
20
0
Prevalence, p^*
0
2
4
6
8
10
Transmission threshold
Basic reproductive rate, R

3.2.3 points to the conclusion that control measures should be aimed at reducing parasite transmission to below the threshold (R=1), rather than reducing infection intensity *per se*, since, unless total eradication is achieved, intensity will tend to return to its original level on cessation of control operations.

3.3 HOST POPULATION DYNAMICS

One of the major simplifying assumptions of the basic model is that the host populations are assumed constant. Since the dynamics of the intermediate host operate on a much faster time-scale than the dynamics of the final host (see Table 3.1.1), the models in the present section are designed to describe the dynamics of beetle and parasite populations within a closed final host community of constant size.

In order to investigate any possible regulatory impact of the parasite on the intermediate host population, it is first assumed that the host population exhibits exponential growth in the absence of the parasite. In addition, density-dependent constraints on parasite population growth are limited to the effects of parasite-induced host mortality, rather than to adult parasite mortality as in the basic model. Transmission of parasites from host to host is again assumed to be directly proportional to both the number of hosts and the number of infective eggs or infected intermediate hosts, corresponding to the lower range of parasite density shown in Figure 3.2.1(b). Assuming that the instantaneous rate of parasite-induced host mortality, α/parasite/unit time, is constant and directly proportional to the parasite burden harboured per host, i, as suggested by the experimental

results presented in Section 2.4(iv), the basic model may be modified to give

$$dP_1/dt = \beta_1 H_1 D_1 H_2 \sum_{i=o}^{\infty} i.p(i)(t-T_1) - \mu_1 P_1 - b_1 H_1 \sum_{i=o}^{\infty} i.p(i) \qquad (3.3.1)$$

$$dH_2/dt = (a_2-b_2)H_2 - \alpha H_2 \sum_{i=o}^{\infty} i.p(i) - \beta_1 H_1 H_2 \qquad (3.3.2)$$

$$dP_2/dt = \beta_2 D_2 H_2 E(t-T_2) - \mu_2 P_2 - b_2 H_2 \sum_{i=o}^{\infty} i.p(i) - \beta_1 H_1 H_2 \sum_{i=o}^{\infty} i.p(i) - \alpha H_2 \sum_{i=o}^{\infty} i^2.p(i) \qquad (3.3.3)$$

$$dE/dt = \lambda P_1 - \mu_3 E - \beta_2 H_2 E \qquad (3.3.4)$$

where a_2 and b_2 are the instantaneous rates of intermediate host birth and mortality respectively. Hosts are also lost from the population as a result of parasite-induced host mortality and by final host predation.

It is assumed for simplicity that the larval parasites are randomly distributed within the intermediate host population (so that $E(i)=P/H$ and $E(i^2)=P^2/H^2+P/H$). Noting also that the expected lifespan of the parasite egg and the prepatent time delays, T_1 and T_2, are short in relation to the lifespans of the parasites and hosts (see Table 3.1.1), the model may be simplified to give

$$dM_1/dt = \beta_1 D_1 M_2 H_2 - (\mu_1+b_1)M_1 \qquad (3.3.5)$$

$$dH_2/dt = (a_2-b_2)H_2 - \alpha M_2 H_2 - \beta_1 H_1 H_2 \qquad (3.3.6)$$

$$dM_2/dt = \beta_2 D_2 \lambda M_1 H_1/(\mu_3+\beta_2 H_2) - (\mu_2+a_2+\alpha)M_2 \qquad (3.3.7)$$

where M_1 and M_2 represent the mean number of adult and larval worms per host respectively. The basic reproductive rate of the parasite, R, may be derived by evaluating the model at equilibrium. Specifically

$$R = \frac{\lambda\beta_1\beta_2 D_1 D_2 H_1 H_2}{(\mu_1+b_1)(\mu_3+\beta_2 H_2)(\mu_2+a_2+\alpha)} \qquad (3.3.8)$$

where H_2 is a variable whose dynamics is determined by equation (3.3.6).

An analysis of equations (3.3.5), (3.3.6) and (3.3.7) reveals that several patterns of dynamical behaviour are possible. If $R < 1$, the parasite is unable to persist, and the host population grows exponentially at a rate $(a_2-b_2-\beta_1 H_1)$, where (a_2-b_2) represents the natural intrinsic growth rate of the intermediate host, and $\beta_1 H_1$ represents the extent to which this growth rate is depressed as a result of predation by the rat population, H_1.

Provided $R > 1$, parasite persistence is possible, and one of two possible patterns of behaviour may occur. From equations (3.3.5) to (3.3.7), the intermediate host population size at

equilibrium is given by

$$H_2^* = \frac{\mu_3(\mu_1+b_1)(\mu_2+a_2+\alpha)}{\lambda\beta_1\beta_2 D_1 D_2 H_1 - \beta_2(\mu_1+b_1)(\mu_2+a_2+\alpha)} \qquad (3.3.9)$$

A positive host equilibrium level is thus only possible if

$$\lambda\beta_1 D_1 D_2 H_1 > (\mu_1+b_1)(\mu_2+a_2+\alpha) \qquad (3.3.10)$$

If equation (3.3.10) is satisfied, and $R > 1$, host population growth is regulated, and settles to the equilibrium level defined in equation (3.3.9). If $R>1$ but equation (3.3.10) is not satisfied, the parasite persists but is unable to regulate host population growth, which continues in an exponential manner at a rate proportionately lower than the disease-free rate mentioned earlier. The relationships between the various patterns of behaviour described above are illustrated in Figure 3.3.1.

This model is considerably more complex than those analysed previously, due to the additional non-linearities resulting from inclusion of host population dynamics. The neighbourhood stability analysis is non-trivial, and the equilibrium level H_2^* may or may not be stable depending on the parameter values (see Appendix 2.3). Further work is required in order to analyse the full dynamical properties of the model, in particular to determine whether stable limit-cycles are generated in

Figure 3.3.1 *An illustration of the boundaries between areas of parameter space which lead to parasite persistence and parasite eradication, as predicted by the model defined in equations (3.3.5), (3.3.6) and (3.3.7).*

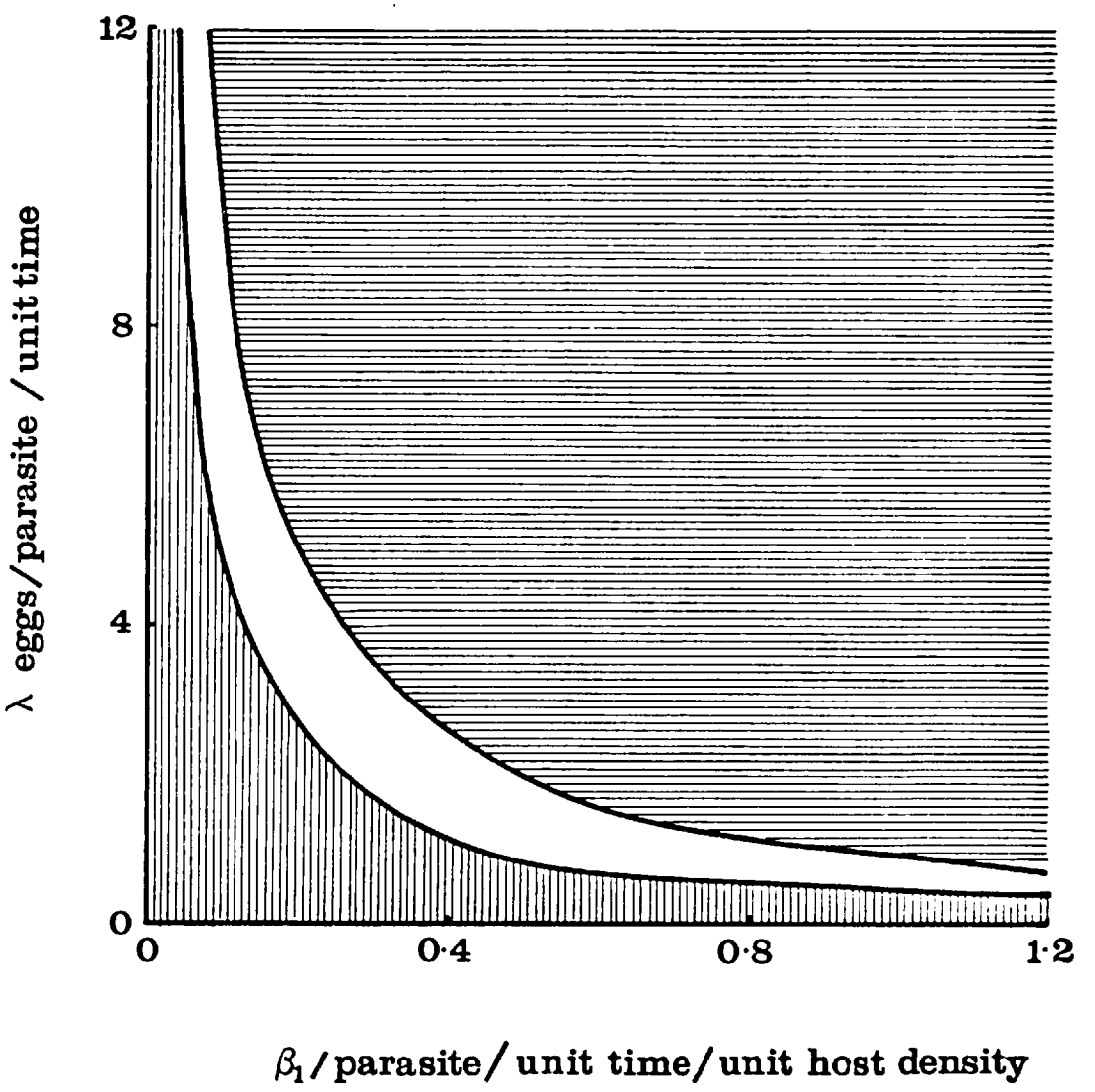
The graph illustrates the boundaries between areas of parameter space with changing values of λ (instantaneous rate of parasite egg production) and β_1 (instantaneous rate of transmission to the final host).

Horizontally hatched area: parasite persists and regulates host population growth to a stable equilibrium level, H_2^*.

Unshaded area: parasite persists, but fails to regulate host population growth.

Vertically hatched area: parasite unable to persist, host population grows exponentially.

Parameter values: $(\mu_1+b_1) = (\mu_2+a_2+\alpha) = D_1D_2H_1 = 1.0$, $(\mu_3+\beta_2H_2)/\beta_2H_2 = 0.5$.


12
8
4
0
0
0·4
0·8
1·2
λ eggs/parasite/unit time
β_1/parasite/unit time/unit host density

certain regions of parameter space.

The model as defined in equations (3.3.1) - (3.3.4) may be modified to include the two functional responses inherent in the transmission of eggs to the intermediate host, and cysticercoids to the final host. Both may be described by expressions of the form shown in equation (3.2.1), where the parameters ρ_2 and g_2 relate to the transmission of parasite eggs, and ρ_1 and g_1 to the transmission of cysticercoids. Having shown that the parasite is capable of regulating intermediate host population growth under certain conditions, density-dependent constraints on natural host mortality are hereafter included, in order to examine any possible depression of the host equilibrium population level which may occur as a result of parasitism by *H.diminuta*. In the absence of the parasite, the host population thus grows to an equilibrium level determined by environmental resources, the carrying capacity of the environment, K ($H^*=K$, $M^*=0$). Depression of host population abundance by the parasite may be estimated by measuring the difference between K and the host equilibrium level in the presence of the parasite ($H^*<K$, $M^*>0$). This degree of depression, d, may be defined as

$$d = 1 - H^*/K \qquad (3.3.11)$$

where d varies between 0 and 1 in direct proportion to the magnitude of the parasite's impact on the size of the host

population equilibrium (see Anderson, 1980d). Inclusion of these modifications gives rise to the expressions

$$dP_1/dt = \frac{\rho_1 H_1 D_1 H_2}{g_1+H_2} \sum_{i=o}^{\infty} i.p(i)(t-T_1) - \mu_1 P_1 - b_1 H_1 \sum_{i=o}^{\infty} i.p(i) \qquad (3.3.12)$$

$$dH_2/dt = a_2 H_2 - (b_2+\gamma H_2)H_2 - \alpha H_2 \sum_{i=o}^{\infty} i.p(i) - \rho_1 H_1 H_2/(g_1+H_2) \qquad (3.3.13)$$

$$dP_2/dt = \frac{\rho_2 D_2 H_2 E(t-T_2)}{g_2+E} - \alpha H_2 \sum_{i=o}^{\infty} i^2.p(i) - \mu_2 P_2 - (b_2+\gamma H_2)H_2 \sum_{i=o}^{\infty} i.p(i)$$

$$\frac{-\rho_1 H_1 H_2}{g_1+H_2} \sum_{i=o}^{\infty} i.p(i) \qquad (3.3.14)$$

$$dE/dt = \lambda P_1 - \mu_3 E - \rho_2 H_2 E/(g_2+E) \qquad (3.3.15)$$

where γ is a coefficient relating to the severity of the density-dependent constraints on intermediate host population growth. It is assumed for simplicity that the larval parasites are randomly distributed within the intermediate host population. By noting in addition that the time delays T_1 and T_2 are short in relation to the expected lifespans of larval and adult parasites, and replacing the variables P_1 and P_2 by the mean numbers of parasites per host, M_1 and M_2, the model may be simplified to give

$$dM_1/dt = \rho_1 D_1 M_2 H_2/(g_1+H_2) - (\mu_1+b_1)M_1 \qquad (3.3.16)$$

$$dH_2/dt = aH_2 - (b+\gamma H_2)H_2 - \alpha M_2 H_2 - \rho_1 H_1 H_2/(g_1+H_2) \qquad (3.3.17)$$

$$dM_2/dt = \rho_2 D_2 E/(g_2+E) - (\mu_2+a_2+\alpha)M_2 \qquad (3.3.18)$$

$$dE/dt = \lambda M_1 H_1 - \mu_3 E - \rho_2 H_2 E/(g_2+E) \qquad (3.3.19)$$

Unlike the model described in Section 3.2, loss of eggs and cysticercoids as a result of predation by beetles and rats is taken into account.

The system of equations described above is highly non-linear and its dynamical behaviour is therefore difficult to determine by analytical methods. The following discussion presents an illustration of model behaviour for a small range of parameter values. The results were obtained by numerical simulation and may not represent the full spectrum of possible behaviour. They do, however, illustrate some of the possible interactions between parasitism and predation on the dynamics of the intermediate host population.

In the absence of both parasites and rats, the beetle population exhibits logistic growth to an equilibrium level ($H_2^*=K$), where

$$K = (a_2-b_2)/\gamma \qquad (3.3.20)$$

(see Figure 3.3.2(a)). In the absence of the parasite, the

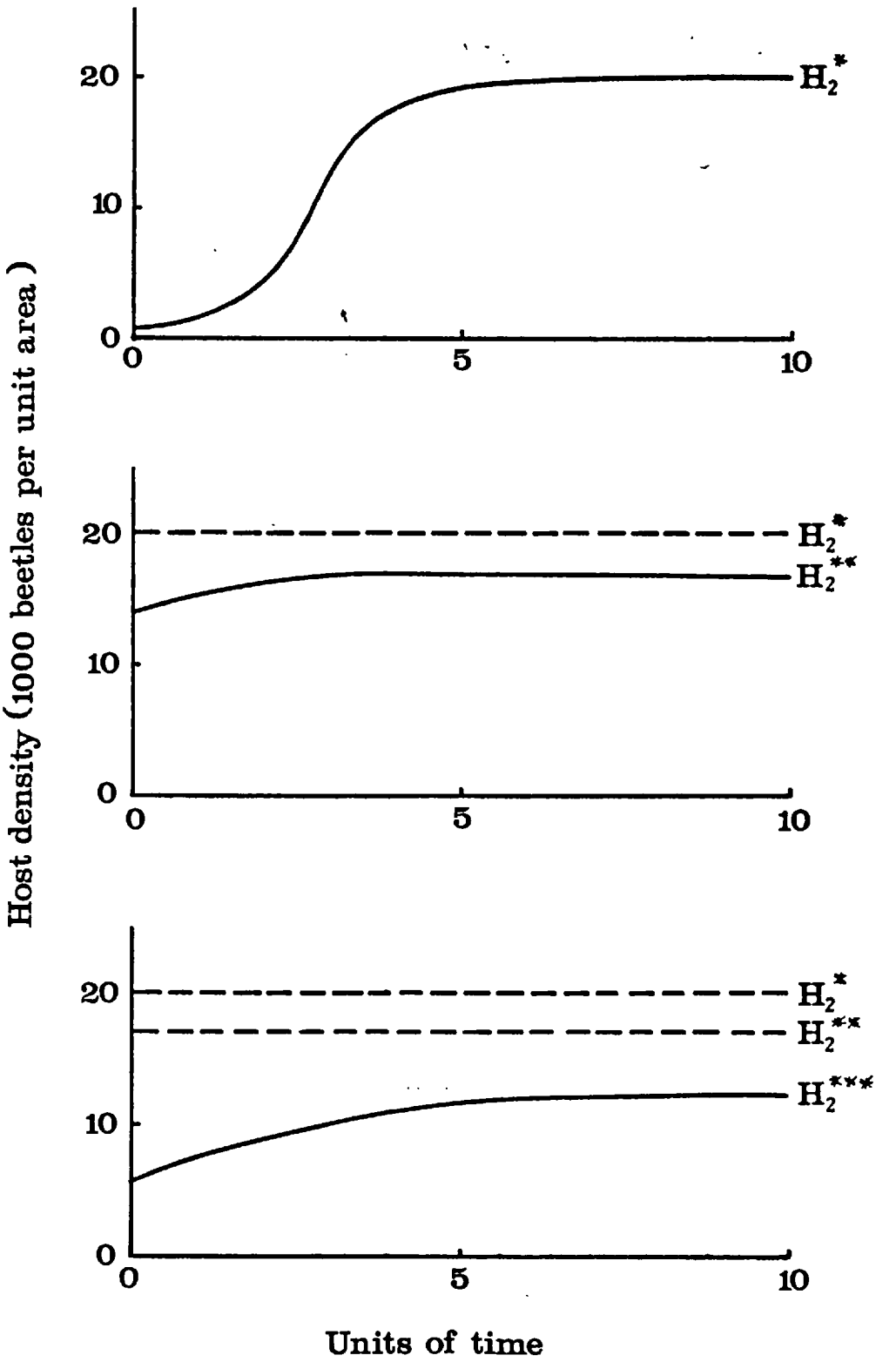
Figure 3.3.2 *A numerical analysis of intermediate host population growth as predicted by equations (3.3.16) to(3.3.19).*

(a) Final host and parasite populations absent. Intermediate host population growth limited by density-dependent constraints to the environmental carrying capacity.

(b) Final host present, parasite absent. Intermediate host population regulated by density-dependent constraints and by the effects of predation.

(c) Both final host and parasite populations present. Intermediate host population growth regulated by density-dependent constraints, predation and parasitism.

Parameter values : α=0.1/parasite/unit time, ρ_1=20 beetles/unit time/rat/unit area, ρ_2=8 eggs/unit time/beetle/unit area, $g_1=g_2=50$, μ_1=0.02/worm/unit time, Υ=0.0001, λ=50,000 eggs/worm/unit time, μ_3=0.03/egg/unit time, H_1=100 rats/unit area, a_2=2 eggs/beetle/unit time, b_2=0.01/beetle/unit time.


Host density (1000 beetles per unit area)
20
10
0
0
5
10
H_2^*
H_2^*
H_2^{**}
H_2^*
H_2^{**}
H_2^{***}
Units of time

effect of predation by the rat population is to depress the host equilibrium to a level H_2^{**}, where $H_2^{**} < K$ (see Figure 3.3.2(b)). Figure 3.3.3 shows the relationship between the predator-controlled equilibrium level, H_2^{**}, and the value of the parameter ρ_1, which represents the attack rate per predator per unit time. Two stable equilibria are generated ($H_2=H_2^{**}$ and $H_2=0$), separated by an unstable host equilibrium. As might be expected, the beetle population level declines as ρ_1 increases, until, at a certain threshold level, the predation pressure imposed by the rat population is so intense that the beetle population cannot compensate, and becomes extinct.

In the presence of *H.diminuta*, the beetle population equilibrium is depressed even further from the environmental carrying capacity ($H_2^{***} < H_2^{**}$, see Figure 3.3.2(c)). The magnitude of this depression is dependent on the value of α, the instantaneous rate of parasite-induced host mortality per parasite per unit time. Figures 3.3.4(a) and (b) illustrate the relationship between α and host equilibrium population density for 2 values of ρ_1. Again, 2 stable equilibria ($H_2=H_2^{***}$ and $H_2=0$) are separated by an unstable host population level. When α is zero, and the parasite has no detrimental effect on host survival, the beetle population grows to the predator controlled equilibrium level. As α increases, the equilibrium point is depressed until, when α reaches a critical value, the beetle population (and thus also

Figure 3.3.3 *An illustration of the influence of final host predation intensity on intermediate host population size at equilibrium, as predicted by equations (3.3.16) to (3.3.19).*

The graph illustrates the relationship between intermediate host population size at equilibrium, H_2^*, and the value of the parameter ρ_1. The arrows denote the dynamical trajectories of the system following perturbations from the two equilibrium states, H_2^{**} and zero, which each have their own domain of attraction. The dashed line indicates the unstable boundary between these domains.

Parameter values as in Figure 3.3.2.

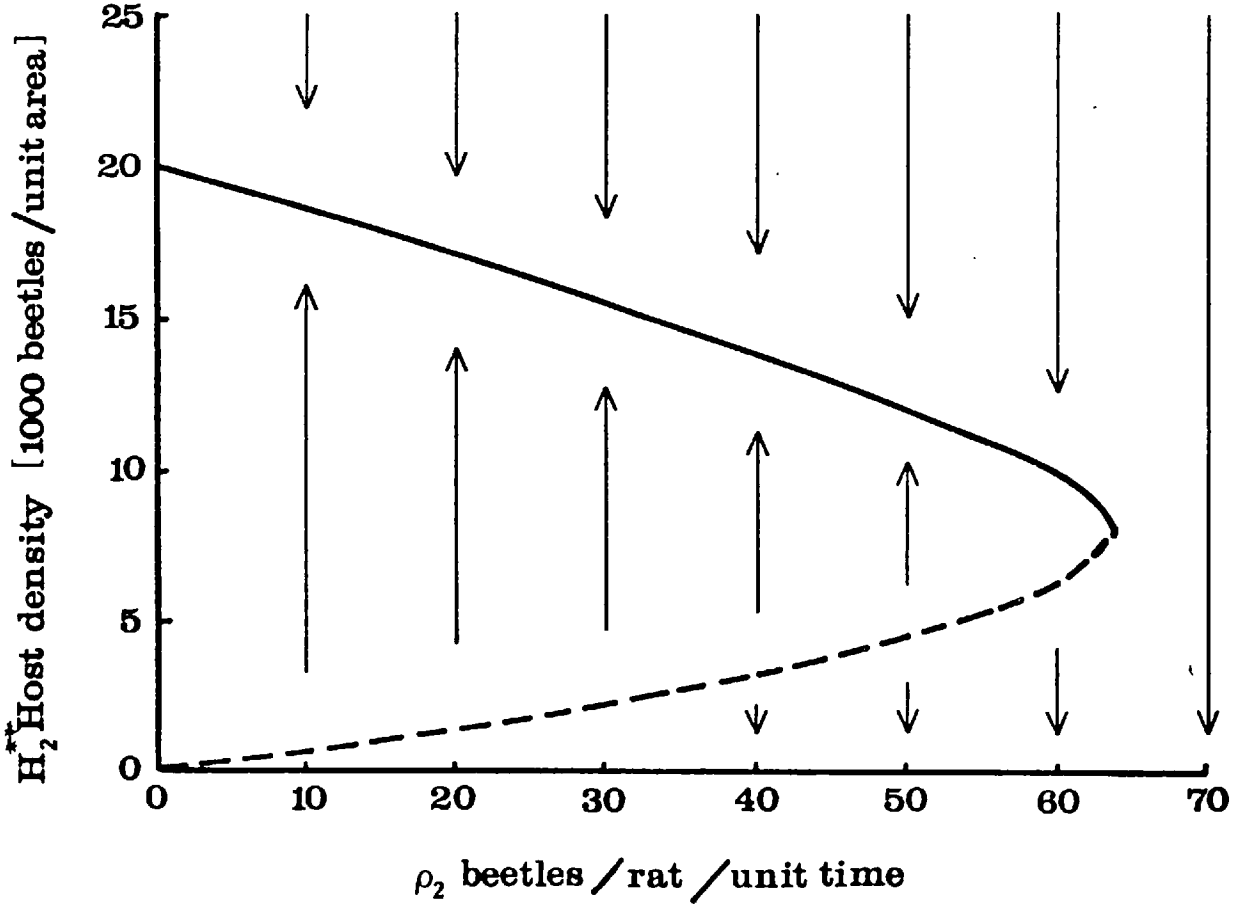
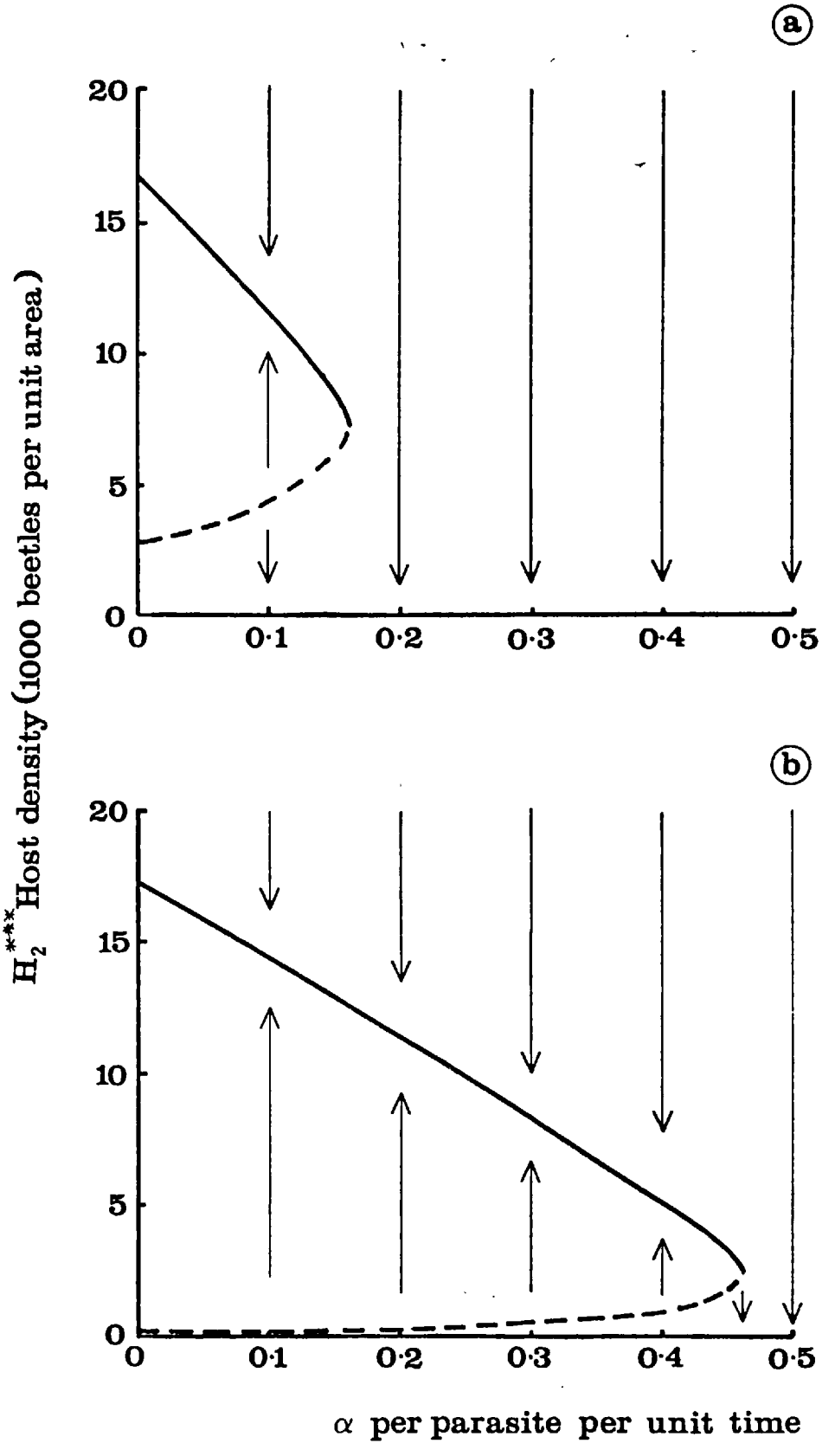

25
20
15
10
5
0
0
10
20
30
40
50
60
70
H_2^{**} Host density [1000 beetles / unit area]
ρ_2 beetles / rat / unit time

Figure 3.3.4 *An illustration of the influence of the severity of parasite-induced host mortality on intermediate host population size at equilibrium, as predicted by equations (3.3.16) to (3.3.19).*

The graphs illustrate the relationship between intermediate host population size at equilibrium, H_2^{**}, and the value of the parameter α, for two different values of ρ_1. The arrows denote the dynamical trajectories of the system following perturbations from the two equilibrium states, H_2^{***} and zero, which each have their own domain of attraction. The dashed lines indicate the unstable boundaries between these domains.

(a) Parameter values as in Figure 3.3.2

(b) Parameter values as in Figure 3.3.2 except ρ_1=5 beetles/unit time/host/unit area.


(a)
20
15
10
5
0
0
0·1
0·2
0·3
0·4
0·5
(b)
20
15
10
5
0
0
0·1
0·2
0·3
0·4
0·5
H_2^{***} Host density (1000 beetles per unit area)
α per parasite per unit time

the parasite population) becomes extinct. As might be expected, a higher level of parasite-induced host mortality can be tolerated by the host population when predation pressure is smaller than when it is large.

The illustrated relationship between the value of α and the resultant host equilibrium level contrasts with the pattern of the relationship predicted for direct life-cycle macroparasites (Anderson, 1980d), in which moderate pathogenicity causes the greatest host population depression, and high pathogenicity results in parasite extinction and host return to the uninfected equilibrium level, H_2^{**}. Since α is related to i (the parasite burden per host), the rapid death of a heavily infected host leads to a decrease in total parasite population size. As α increases in severity, the parasite suffers proportionally greater losses than the host, as a direct consequence of which the parasite population decreases and the host population exhibits increased growth. The different pattern presented in Figure 3.3.4 is not thought to represent a general difference between direct and indirect life-cycle parasites, since it stems from analysis using only a small range of parameter values, and does not preclude the generation of other patterns of behaviour in different regions of parameter space.

SECTION 4

THE EPIDEMIOLOGY OF CESTODES OF ECONOMIC AND PUBLIC HEALTH SIGNIFICANCE.

4.1 INTRODUCTION.

Cestode parasites are the causal agents of significant public health and economic problems in many areas of the world, infecting both man and his domestic stock. The 5 most important species and their associated diseases are listed in Table 4.1.1.

4.1(i) Cestode life-cycles

Most species, like *H.diminuta*, live as adult worms in the gut of a vertebrate host and release eggs into the external environment with the host faeces. The majority of cestode life-cycles are indirect, larval stages being passed as a developmental necessity in one or more intermediate hosts. For example, both *Taenia solium* and *T.saginata* are specific adult parasites of man. Eggs are deposited with human faeces, and hatch to release oncosphere larvae on ingestion by a suitable intermediate host (cattle for *T.saginata* and swine for *T.solium*). The oncospheres develop to infective cysticercus larvae in the voluntary muscles, so initiating the disease 'cysticercosis'. Man becomes infected by consuming undercooked beef or pork, either by mistake or as a result of deliberate culinary procedures. An additional complication exists, since cysticerci of *T.solium* may develop in human intermediate hosts, probably by ingestion of eggs as a contaminant from the environment (Webbe, 1967). Cysticercus cellulosae is thus a

Table 4.1.1 Tapeworms of public health significance in man and economic significance in animals.

Species.	Order.	Popular Name.	Final Host.	Intermediate Host.	Disease Name.	
					Adult.	Larva.
Diphyllobothrium latum	Pseudophyllidea	Broad fish tapeworm	Man	1st copepod spp.	Diphyllo-bothriasis	
Taenia saginata	Cyclophyllidea	Beef tapeworm	Man	Cattle	Taeniasis saginata	Cysticercus bovis
Taenia solium	Cyclophyllidea	Pork tapeworm	Man	Pig or man	Taeniasis solium	Cysticercus cellulosae
Hymenolepis nana	Cyclophyllidea	Dwarf tapeworm	Man	None or beetle spp.	Hymenolepiasis	
Echinococcus granulosus	Cyclophyllidea		Dog	Man, sheep, cow, goat, camel, buffalo etc.		Hydatid disease

disease of both man and pigs, whereas cysticercus bovis exists only in cattle.

The other 3 species listed in Table 4.1.1 differ in some respect from the life-cycle pattern just described. For example, although *Hymenolepis nana* may undergo larval development in an insect intermediate host, most transmission occurs as a result of a direct life-cycle link, eggs being immediately infective to the final host (Witenberg, 1964), which may be man or one of a variety of other mammalian species. *Echinococcus granulosus* has a two-host life-cycle, adults occurring in carnivorous mammals (commonly dogs), and larval hydatid cysts in other mammals such as cattle, goats, camels, buffalo and man (Smyth and Smyth, 1964). The interesting feature of the *E.granulosus* life-cycle with respect to the parasite-host population dynamics is the asexual reproduction which occurs in the intermediate host. Each hydatid cyst, derived from a single egg, may contain up to a million infective protoscolices (Smyth, 1977). The pseudophyllidean cestode, *Diphyllobothrium latum*, has a three-host life-cycle, eggs hatching in water to release a free-swimming coracidium larva (so adding a further time delay component to the population dynamics). Two further stages of larval development are then necessary (in copepod and fish intermediate host species) before infection of the human definitive host can occur.

Despite these differences, all cestode life-cycles are similar in that transmission is always achieved by predator-prey links

across trophic levels, either between two host species, or between a host and a free-living infective stage. In common with *H.diminuta* and many other parasitic organisms, the expected lifespans of mature and larval tapeworms of species listed in Table 4.1.1 are generally many orders of magnitude greater than that of the infective egg (Anderson and May 1979a; May and Anderson 1979; see Table 4.1.2). In addition, the developmental time delays T_1 and T_2 are generally short in relation to the lifespans of the hosts and parasites (see Table 4.1.2). An exception to both these generalities is *E.granulosus*, which has long prepatency and a relatively short lived adult worm.

4.1(ii) Prevalence of cestode infections in man.

An estimate of the world prevalence of cestode infections in man, as given by Peters (1978), is shown in Table 4.1.3, from which it may be calculated that approximately 3.4% of the total world population at this time was affected.

From Table 4.1.3, it can be seen that *T.saginata* is the most widespread and prevalent tapeworm in man. Moreover, it must be remembered that the estimates given are to a large extent based on the results of faecal sampling, a method notorious for consistent underestimation of true prevalence levels. Autopsy studies in Kenya, for example, have revealed a prevalence of more

Table 4.1.2 The estimated lifespans and prepatent periods of various tapeworms.

	Expected lifespan adult worm.	Expected lifespan larval worm.	Expected lifespan egg.	Prepatent period adult worm, T_1.	Prepatent period larval worm, T_2
T.saginata	many years	21-30 months	16 days	6 - 8 weeks	10 - 12 weeks
T.solium	10 - 15 years	several years	several weeks	5 - 12 weeks	60 - 75 days
H.nana	few months	-	11 days	30 days	90 hours
E.granulosus	6 months	several years	6 - 12 months	6 - 7 months	5 months
D.latum	25 years	procercoid several weeks / plerocercoid several years	1 - 2 days	3 - 5 weeks	procercoid 14-21 days / plerocercoid 4 weeks

Data from: Muller, 1975; Pawlowski and Schultz, 1972; Dogiel, 1962; Bonsdorff, 1977.

Table 4.1.3 *Estimates of the number of people infected with tapeworm parasites in different regions of the world in 1975.*

	Africa.	Asia (excl.USSR).	C and S America.	Oceania.	North America.	Europe (excl.USSR).	USSR.	World Total.
Taenia saginata	32	11	2	1	1	1	29	77
Hymenolepis nana	2	27	2		1	2	5	39
Diphyllobothrium latum		2				3	10	15
Others	1	2					1	4

Figures in millions. Data Source: Peters, 1978.

than 90% in areas where routine surveys indicated that only 10% of the population was infected (Joint FAO/UNEP/WHO Report, 1976). In addition, prevalence is extremely heterogeneous within large areas, the percentage infection in Kenya, for example, varying between 3 and 65% (Froyd, 1965).

By far the most serious tapeworm infection occurring in man, although by no means the most prevalent, is echinococcosis or hydatid disease. It has a worldwide distribution (Schantz and Schwabe, 1969) and although it has been eradicated in Iceland (Dungal, 1946) and successfully controlled in New Zealand (Burridge and Schwabe, 1977b), Cyprus (Polydorou, 1977) and Tasmania (McConnell and Green 1979), it still represents a major public health problem in many countries. For example echinococcosis accounts for 0.85% of hospital admissions in Libya (Dar and Taguri, 1978) and 0.5% in Iran (Anon., 1976). The cost of surgical treatment for the removal of cysts is extremely high and is an unnecessary burden on the economy of countries in which eradication is a feasible proposition by methods involving destruction of stray dogs and widespread use of chemotherapeutic agents.

Cases of tapeworm infection in man are relatively infrequent in areas with high standards of public hygiene. For example, 82 cases of *T.saginata* infection were reported in the United Kingdom in 1976, and 98 in 1977 (Crewe and Owen, 1978). Hydatid disease in Britain was formerly believed to be confined to sheep

farming areas of Wales, where up to 37% of sheep may carry the infection (Walters, 1977) and where there were 98 human deaths from hydatidosis during the period 1957-1965 (Sullivan, 1977). Within recent years, however, a dramatic increase in the incidence of hydatid disease has become apparent, the adult worm being found in 29% of foxhounds and the larval worm in 60% of associated horses throughout Britain in 1974 (Thompson and Smyth, 1974). Although human hydatid disease has not yet shown any increase in incidence, this obviously represents a potential health hazard in a country in which tapeworms are normally dismissed as a curiosity.

4.1(iii) The economic significance of cestode infections in animal stock.

The cestode species of greatest economic significance are *T.saginata*, *T.solium* and *E.granulosus*. World prevalence data are not readily available, since the infections are extremely heterogeneous, but approximate figures are given in Table 4.1.4, based to a large extent on abattoir data from local regions of each country. It is likely that prevalence is, in reality, substantially higher than indicated here, since current methods of meat inspection vary between countries, and, in addition, there are no means by which disease incidence in animals slaughtered privately may be taken into account (Chambers, 1978; Dada, 1978).

Table 4.1.4 *Percentage prevalence of hydatidosis and cysticercosis in domestic stock in different regions of the world.*

	Africa.	Asia.	C & S America.	Oceania.	N. America.	Europe.	USSR.
Hydatidosis	6	3.5 - 48	19 - 40	12 - 30	1 - 4	1 - 37	2 - 52
Cysticercosis	10 - 29	0.3 - 70	1 - 4	0.21	0.04 - 1	0.01 - 1	1 - 20

Data from: Gemmell, 1960; Basson *et al*, 1970; Pawlowski & Schultz, 1972; Rahman *et al*, 1975; Islam & Rashid, 1977; Walters, 1977; Crewe & Owen, 1978; Grindle, 1978; Dajani, 1978; Griffiths, 1979; Karim, 1979.

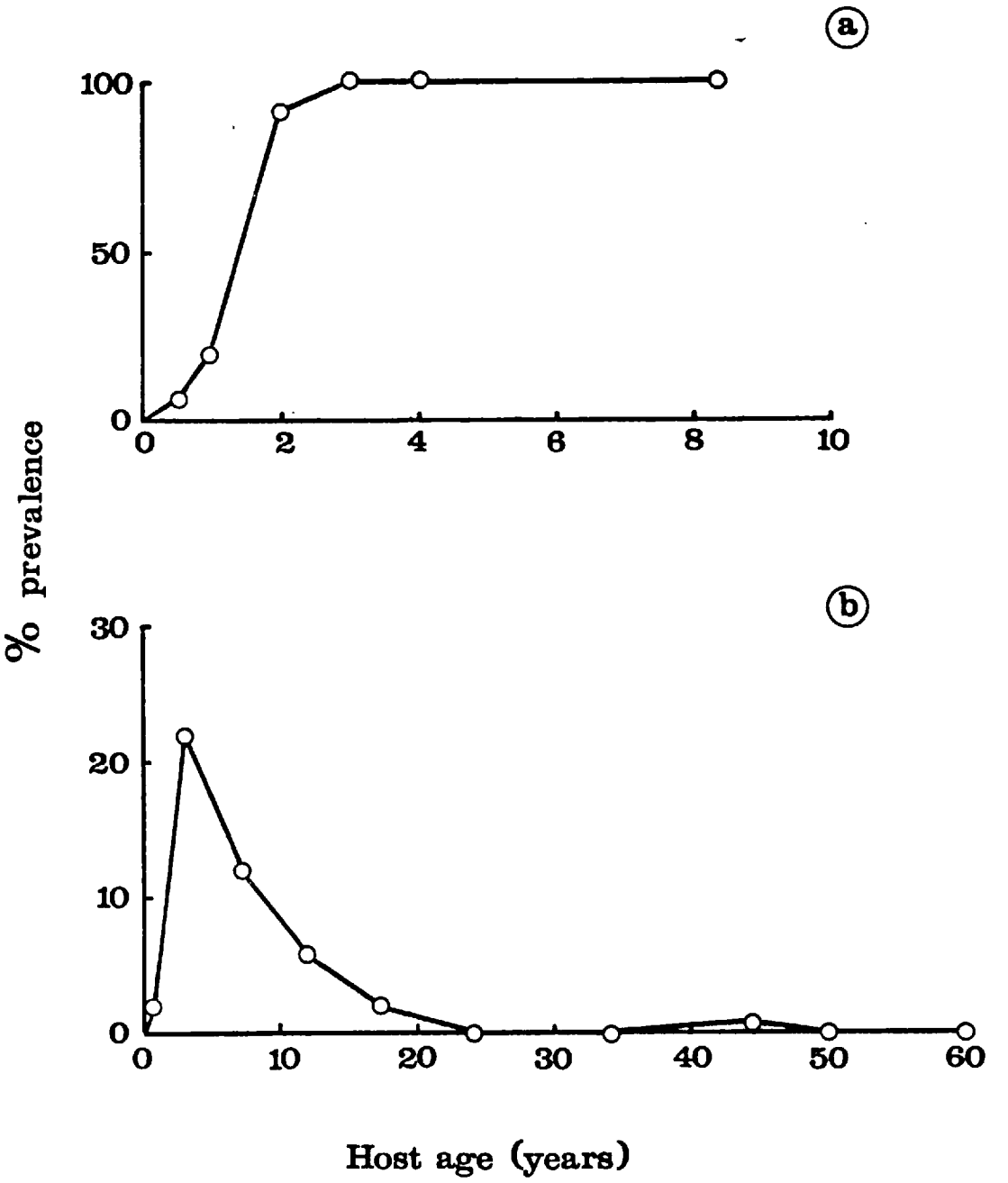
The economic loss sustained as a result of these infections is again difficult to assess realistically, but figures from the United Kingdom indicate that recent annual losses due to cysticercosis and hydatidosis amount to £0.5m and £0.1m respectively (Crewe and Owen, 1978; Walters, 1977). In Nigeria, 500 tonnes of meat valued at US $1.8m was condemned in 1978 (Alonge and Fasanmi, 1979), while losses in Botswana and Kenya were estimated to be £0.5m and £1.0m in 1977 (Grindle, 1978). In addition to the condemnation of heavily infected carcasses, further economic loss is sustained as a result of the treatment and subsequent depreciation of lightly infected meat, which is sold at approximately 60% its true value (Grindle, 1978).

Diphyllobothrium latum, the fish tapeworm, is of both economic and public health importance. As with many cestode species, the significance of *D.latum* infection as a human disease is compounded by the impact of the parasite on potential food source populations. This species is somewhat unusual among tapeworms in that prevalence of the larval stage in second intermediate host fish species such as *Perca fluviatilis* and *Esox lucius* may reach 100% in the older age-classes (see Figure 4.1.1(a)).

Figure 4.1.1 Age-prevalence of cestode infections.

(a) *Diphyllobothrium latum* in the fish, *Esox lucius* (from Dogiel, 1962).

(b) *Hymenolepis nana* in a human population in south-west Iran (from Sahba *et al*, 1967).


a
100
50
0
0
2
4
6
8
10
b
30
20
10
0
0
10
20
30
40
50
60
% prevalence
Host age (years)

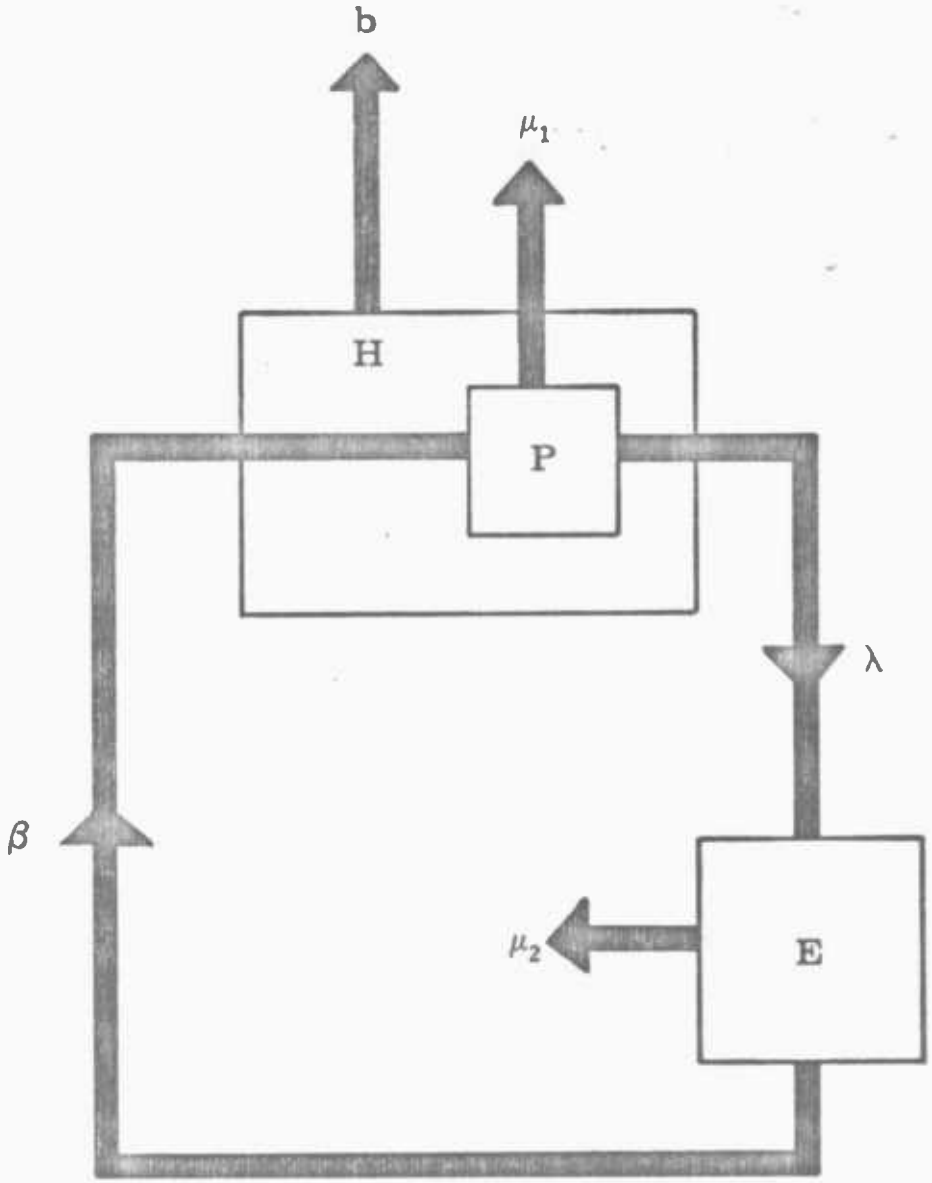
4.2 THE POPULATION DYNAMICS OF *H.NANA*

H.nana is among the most intensively studied tapeworms of man. Even for this species, however, epidemiological data and quantitative estimates of the various population parameters are extremely scarce. *H.nana* has a life-cycle very similar to that of *H.diminuta* except that man may act as both the final and intermediate host. This may be represented by the flow chart shown in Figure 4.2.1, and it is assumed that, in human epidemiology, this type of transmission is likely to be more frequent than that involving a beetle intermediate host, although the latter may also occur.

In the direct life-cycle, the parasite undergoes larval development in the intestinal wall of the host prior to emergence as an adult worm. This, however, may be effectively ignored with respect to the overall dynamics of the interaction, as long as the developmental time lag is increased to include both larval worm development and adult worm prepatency. The total time delay is nevertheless still very short in comparison with the expected lifespans of hosts and adult parasites (see Table 4.1.2). Recapitulating the assumptions given for the basic model (equations (3.1.2) and (3.1.3)), the dynamics of *H.nana* may be represented by the following equations for E (parasite eggs) and M (mean parasite burden per host)

Figure 4.2.1 *Representation of the life-cycle of* Hymenolepis nana *as a flow chart.*

Symbol	Definition
H	Density of host population at time t
P	Density of parasite population at time t
E	Density of parasite egg population at time t
b	Instantaneous rate of host mortality/ host/unit time
μ_1	Instantaneous rate of parasite mortality/ parasite/unit time
λ	Instantaneous rate of parasite egg production/ parasite/unit time
μ_2	Instantaneous rate of parasite egg mortality/ egg/unit time
β	Instantaneous rate of transmission/egg/unit time/host/unit area


b
μ_1
H
P
λ
β
μ_2
E

$$dM/dt = \beta DE - (b+\mu_1+\delta)M - \delta M^2(k+1)/k \qquad (4.2.1)$$

$$dE/dt = \lambda MH - (\mu_2+\beta H)E \qquad (4.2.2)$$

where the population parameters are as shown in Figure 4.2.1. As depicted in Figure 4.2.2, the dynamical behaviour of equations (4.2.1) and (4.2.2) is similar to that of the basic model, with two general patterns of behaviour. If the population parameters are below the transmission threshold (Figure 4.2.2(b)), the parasite is unable to persist in the host population ($M^*=E^*=0$). If above,(Figure 4.2.2(a)), there is, in addition to the stable point $M^*=0$, a second locally stable equilibrium level, M^*, to which all positive trajectories are attracted (see Appendix 2.4).

The precise value of the transmission threshold (i.e. the point at which the basic reproductive rate of the parasite, R, is equal to unity) may be easily derived from equations (4.2.1) and (4.2.2). Specifically,

$$R = \frac{\beta\lambda HD}{(\mu_2+\beta H)(b+\mu_1+\delta)} \qquad (4.2.3)$$

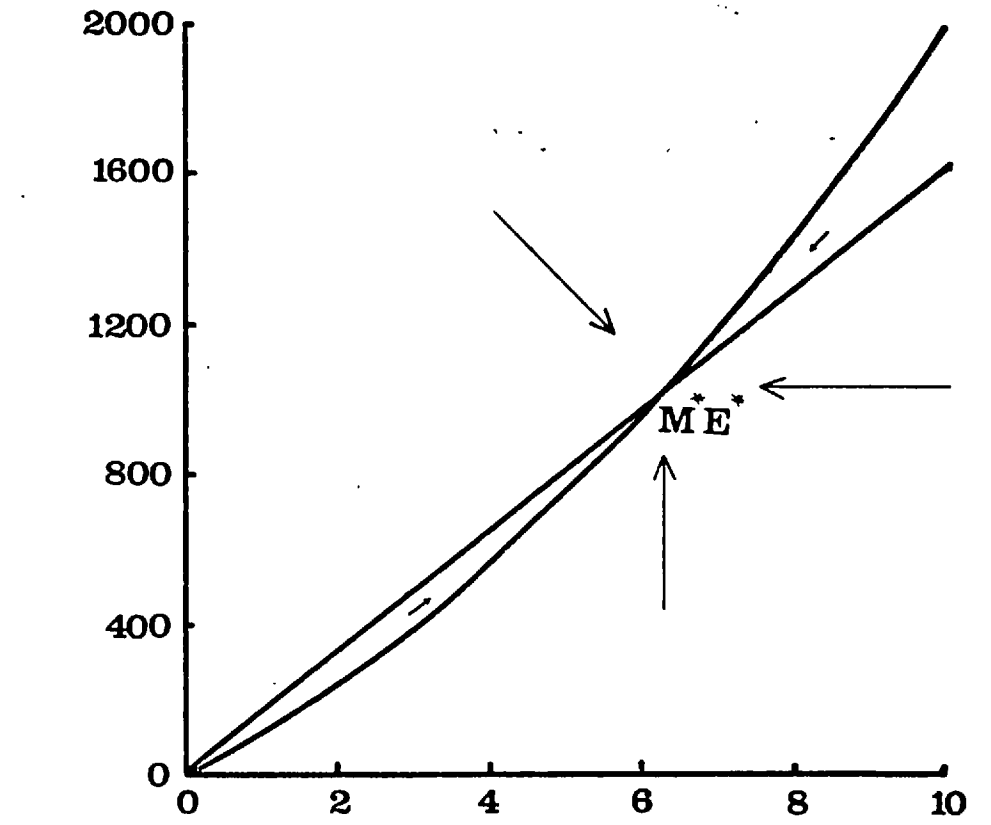
As before, R consists of the product of the transmission parameters divided by the compounded rates of mortality, and must exceed unity in order for parasite persistence to be achieved.

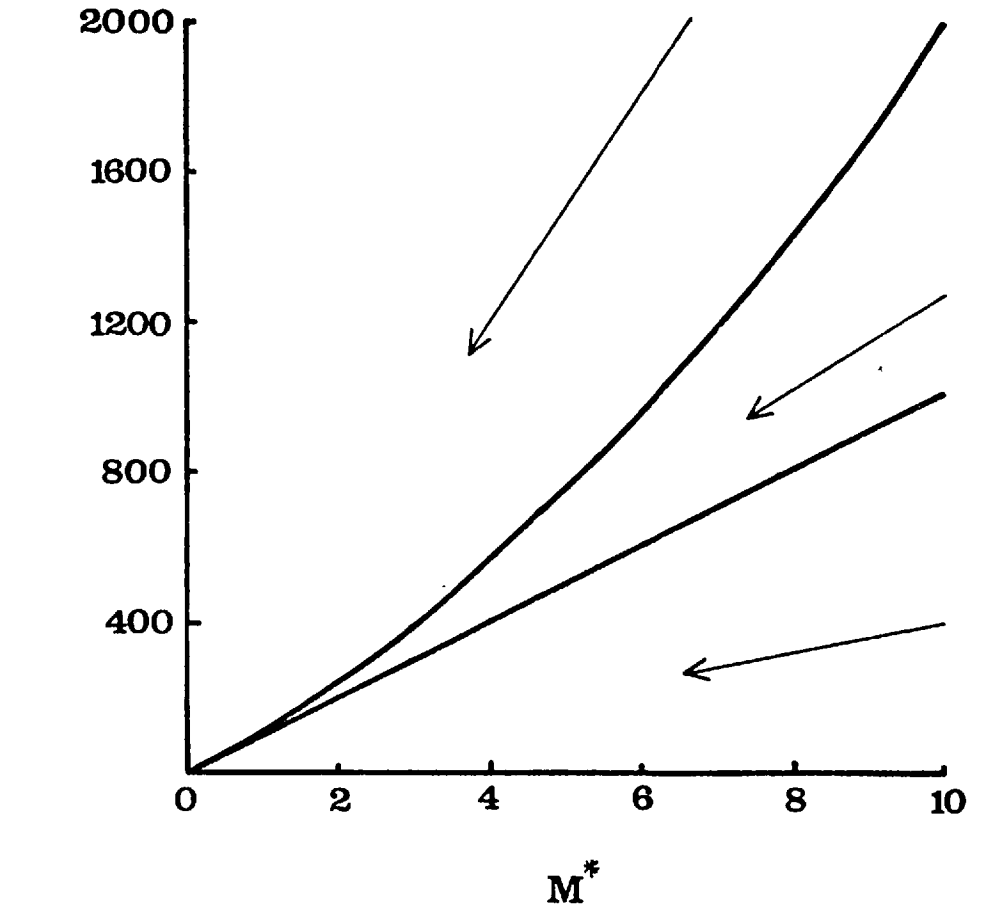
Figure 4.2.2 Phase-plane analysis of the behaviour of equations (4.2.1) and (4.2.2).

The arrows indicate how the dynamical trajectories of M_1 and M_2 behave in the various regions into which the M-E plane is dissected by the isoclines dE/dt=0 and dM/dt=0.

(a) Population parameters above the transmission threshold. All positive trajectories are attracted to the stable point M*E*. Parameter values: $(\mu_2+\beta H)=1$, $(b+\mu_1+\delta)=1$, $\delta(k+1)/k=0.1$, $\beta D=0.01$, $\lambda H=160$.

(b) Population parameters below the transmission threshold. The infection cannot persist, and all trajectories are attracted to the origin (M*=E*=0). Parameter values as in (a) except $\lambda H=100$.


2000
1600
1200
800
400
0
0
2
4
6
8
10
M*E*
E*


2000
1600
1200
800
400
0
2
4
6
8
10
M*

Evaluation of the parameters which constitute the basic reproductive rate is extremely difficult, since little quantitative information relating to human infection is available. Approximate estimates for some of the parameters are given in Table 4.2.1. The values of both the fecundity and mortality rates of the adult worm are taken from laboratory studies of *H.nana* in the mouse, and thus are unlikely to represent accurately the dynamics of the worm in a human host, although the estimate of mortality of 0.02/day/worm does accord favourably with the expected lifespan of a 'few months' given for *H.nana* in man by Muller (1975). In the absence of any quantitative information relating to the parameters δ(the severity of density-dependent constraints on worm population growth) and β(the rate of transmission), no evaluation of R can at present be attempted. This highlights the necessity for further epidemiological research in relation to cestode infections, especially since the absolute numerical value of R clearly plays a large part in determining the level of parasitism in the population. From equations (4.2.1), (4.2.2) and (4.2.3.), the equilibrium average burden of parasites is simply

$$M^* = k(R-1)(b+\mu_1+\delta)/\delta(k+1) \qquad (4.2.4)$$

This corresponds to the special case of the direct life-cycle helminth model proposed by Anderson in which the mating function (i.e. the probability of a worm being able to produce viable

Table 4.2.1 Estimates of the population parameters involved in the life-cycle of Hymenolepis nana.

Parameter	Symbol	Value	Data Source
Instantaneous mortality rate mature worms (single worm burdens)	μ_1	0.02/day/worm	Ghazal & Avery 1974
Expected life-span of adult parasite	$1/\mu_1$	50 days	
Constant relating to density-dependence in adult worm mortality	δ	?	
Prepatent period (time from ingestion of egg to maturation of adult worm)	T	20 days	Muller 1975
Instantaneous rate of egg production per worm	λ	3400 eggs/ worm/day	Ghazal & Avery 1974
Rate of egg mortality	μ_2	0.09/egg/day	Muller 1975
Rate of infection	β	?	
Instantaneous host mortality rate (man)	b	0.000055/day	Based on an expected lifespan of 50 years
Parameter of negative binomial distribution describing worm numbers per host	k	?	

eggs) is unity. A discussion of the properties of this model is given by Anderson (1980a). The solution of equation (4.2.4) yields the age-intensity curve

$$M(a) = K \left[\exp\left(-(R-1)(b+\mu_1+\delta)a\right) + \delta(k+1)/k(R-1)(\mu_1+b+\delta) \right]^{-1} \qquad (4.2.5)$$

where M(a) is the mean intensity of infection at age a, and K is the infection intensity defined by initial conditions. The age-prevalence curve (which is the form in which most human epidemiological data is available) can be obtained from the zero probability term of the negative binomial distribution with mean M(a) and parameter k, where the prevalence in age-class a, p(a) is

$$p(a) = 1 - \left[1 + M(a)/k \right]^{-k} \qquad (4.2.6)$$

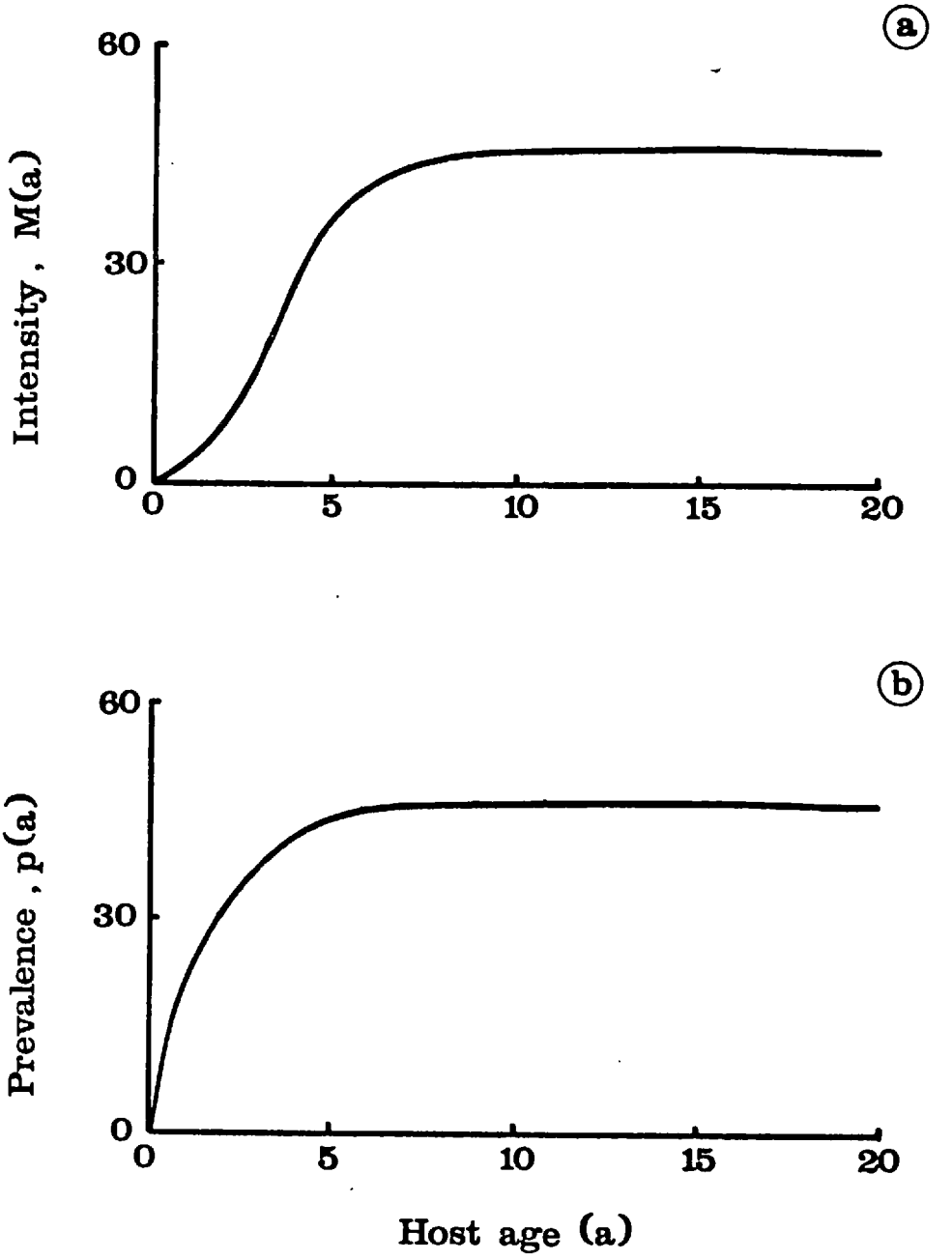
The general shape of the predicted age-intensity and age-prevalence curves are shown in Figure 4.2.3. Models of this form have been shown to provide reasonable qualitative descriptionsof observed trends in data relating to human hookworm infection (Anderson, 1980a), and therefore might be expected, also, to mirror the prevalence of tapeworm infections in man.

Figure 4.1.1(b) shows age-prevalence data for *H.nana*

Figure 4.2.3 *An illustration of the shape of the age-prevalence and age-intensity curves as predicted by the model defined in equations (4.2.5) and (4.2.6)*

(a) The relationship between the average intensity of infection, M(a), and the age of the host, a. Parameter values: R = 2, k = 0.1, δ = 0.002, $(b+\mu_1+\delta)$ = 1, K = M(1)=1.

(b) The prevalence of infection, p(a), in different age-classes of the population. Parameter values as in (a).


a
60
30
0
Intensity , M(a)
0
5
10
15
20
b
60
30
0
Prevalence , p(a)
0
5
10
15
20
Host age (a)

infections in Iran (Sahba *et al* 1967) obtained by stool examination of 100 inhabitants in each of 10 villages in the area around Dezful. In contrast to the predicted results in which prevalence increases to a plateau in the older age-classes, *H.nana* infection is highest in the 2 - 4 year age-group, declining thereafter to extremely low prevalence levels in adults. This data is supported by qualitative assertions from many other areas of the world in which *H.nana* is said to be primarily an infection of children (Witenberg, 1964). Clearly, the model described in equation (4.2.6) is inadequate to describe the observed prevalence of *H.nana*, although it does mirror the prevalence of certain other cestode infections, for example *D.latum* in the fish intermediate host (Figure 4.1.1(a)). Although the generative mechanisms of the pattern shown in Figure 4.1.1(b) are unknown, two potential explanations may be postulated.

1) Age-dependent variation in transmission.

Given the life-cycle of *H.nana*, it would seem reasonable to suggest that behavioural differences between children and adults may cause age-dependent variation in the rate of transmission of the disease to occur. Within the confines of the model, this may be described by making the transmission parameter, β, a decreasing function of age, such that

$$\beta = \beta' e^{-\gamma a} \qquad (4.2.7)$$

where β' is the rate of transmission in newborn children, and

γ is a coefficient of proportionality. Clearly, behavioural factors are likely to change in a manner much more complex than that described by this equation, which is used merely to gain qualitative insight into the influence of the transmission parameter on the dynamics of the infection.

2) Age-dependent development of immunity against infection.

A high prevalence of infection in children could equally be the result of age-dependent immunity (whereby the ability of the immune system to react against helminth infections such as *H.nana* increases as the host becomes older). In the present model, this may be described by making the worm mortality rate, μ_1, an increasing function of host age, a, such that

$$\mu_1 = \mu_1 + \omega a \qquad (4.2.8)$$

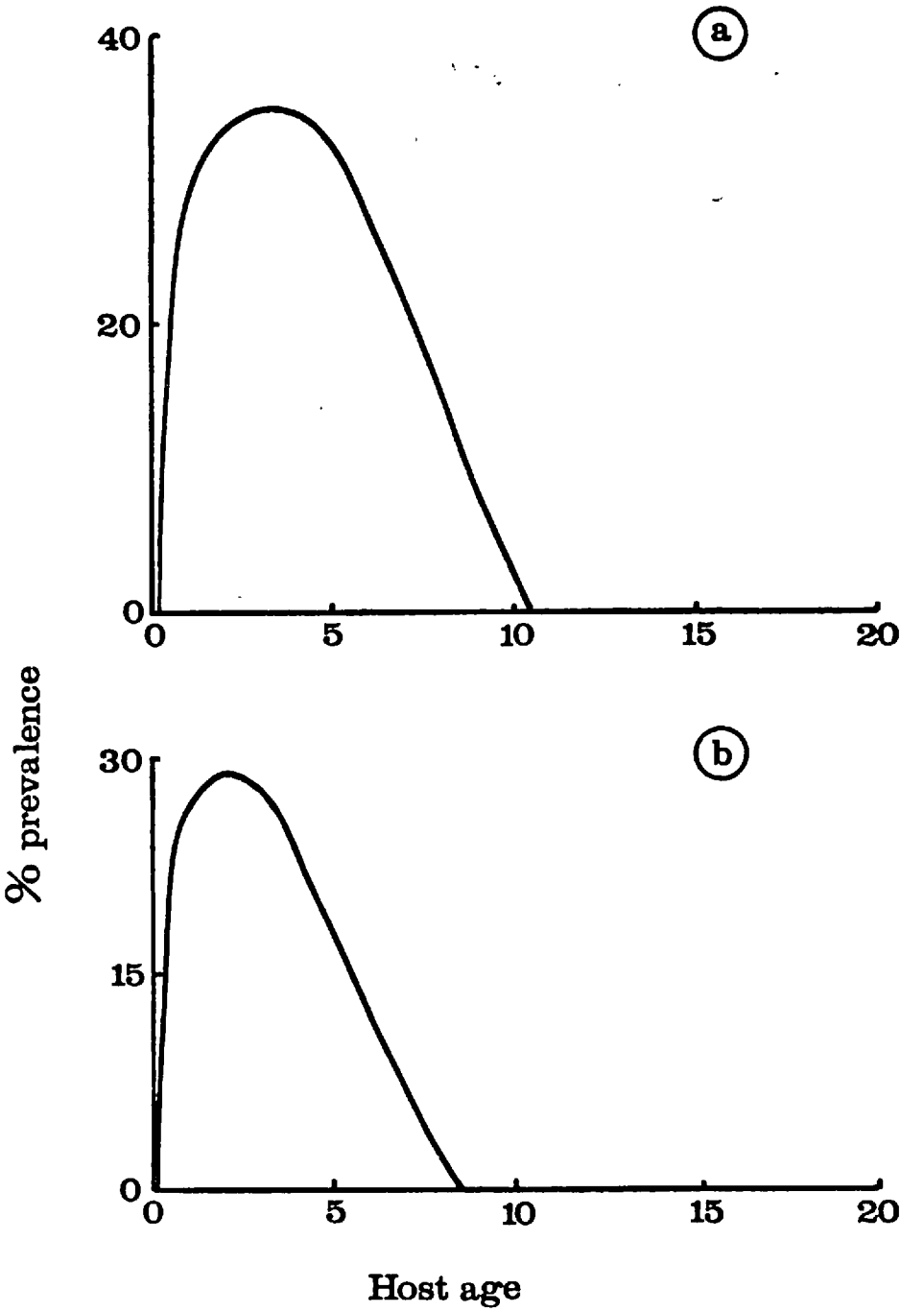
where μ_1 is the worm mortality rate in the absence of any immune reaction (i.e. in newborn children) and ω is a coefficient of proportionality.

The results of these two modifications to the basic model are shown in Figure 4.2.4. Both generate age-prevalence curves with qualitative similarity to the data shown in Figure 4.1.1(b). In the absence of experimental verification, the relative merits of these hypotheses, and others which have not been discussed here, cannot at present be analysed.

Figure 4.2.4 *Modifications of the age-prevalence model defined in equation (4.2.6) to include age-dependent transmission of infection and development of immunity.*

(a) Age-dependent transmission of infection, where $\beta = \beta' \exp(-\gamma a)$. Parameter values: $\beta' = 0.001$, $\gamma = 0.1$, $(b+\mu_1+\delta) = 1$, $H = 20$, $\lambda = 1000$, $D = 0.1$, $\mu_2 = 0.8$, $k = 0.1$, $\delta = 0.002$.

(b) Age-dependent immunity, where $\mu_1 = \mu_1 + \omega a$. Parameter values as in (a) except $\beta = 0.001$, $\omega = 0.2$, $(b+\delta) = 0.9$, $\mu_1 = 0.1$, $(\mu_2+\beta H) = 1$.


a
40
20
0
0
5
10
15
20
b
30
15
0
0
5
10
15
20
% prevalence
Host age

4.3 SEASONAL CHANGES

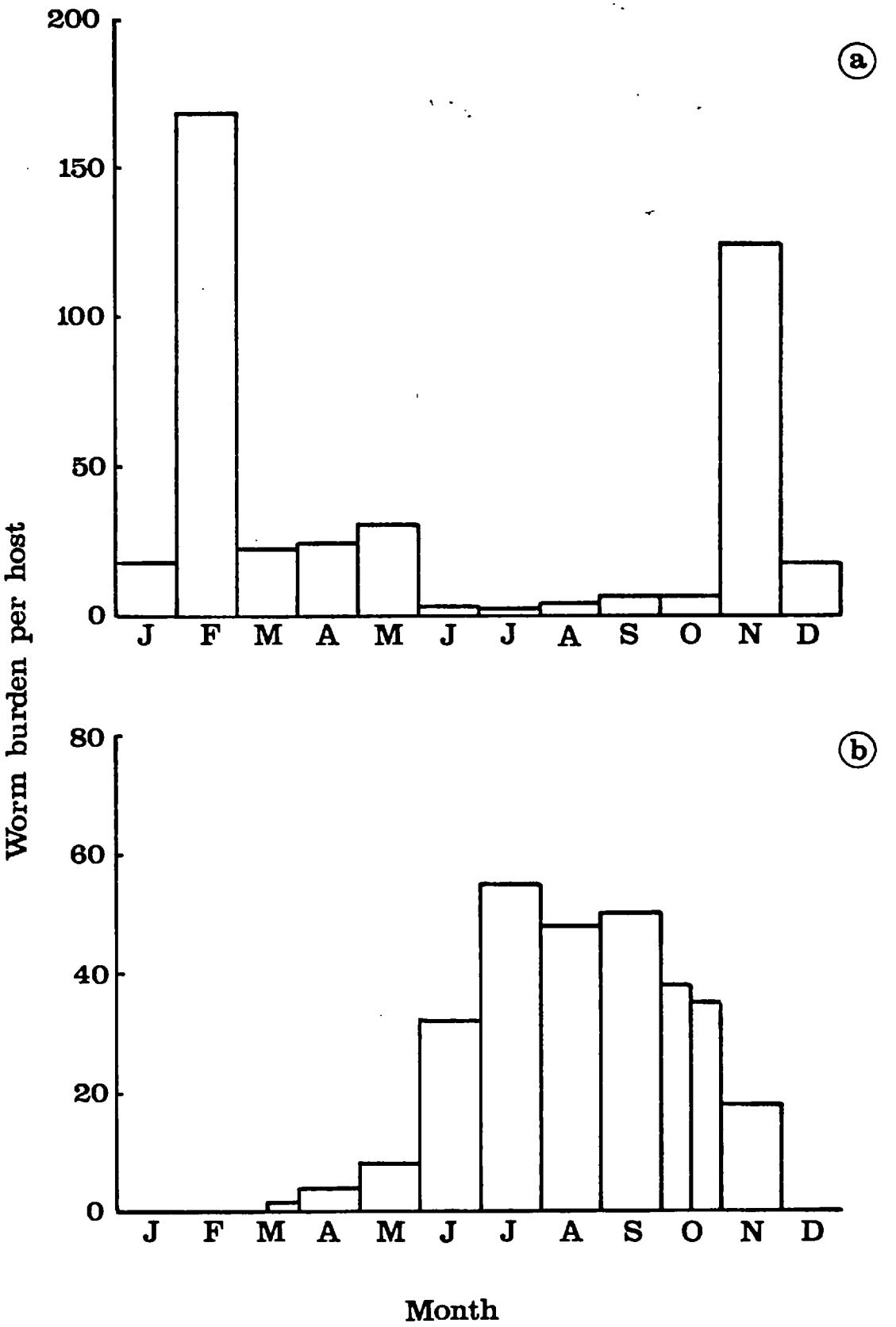
In addition to the possibility that the value of certain population parameters may vary with age, it is also likely that seasonal patterns will occur. The survival of cestode eggs, for example, is critically dependent on temperature, humidity and microbial contamination (see Section 2.3(i)). Larval development of tapeworms in poikilothermic intermediate hosts is also influenced by climate, both because the size of the host population may vary with the time of year, and also because developmental time may be inversely related to temperature (Section 2.5(iii)). Many other factors, such as seasonal changes in host behaviour (which may affect the value of the transmission parameter, β), and changes in host health (perhaps due to variation in diet or the presence of concurrent infections) which may alter the value of μ_1, the rate of parasite mortality, are also likely to be important.

Seasonal changes in the value of individual parameters may result in cyclical differences in the value of R, which may in turn be reflected in monthly variation in the prevalence of infection. An example is given in Figure 4.3.1, which shows mean monthly worm burdens of the sheep tapeworm, *Monezia expansa* in South Africa (Horak and Louw, 1977) and the United States (Stoll,1938). In both cases, low prevalence during the cooler months is attributed to retarded development of the cysticercoids in the oribatid mites

Figure 4.3.1 *Seasonal prevalence of* Monezia expansa *in sheep.*

(a) Data from South Africa (Horak and Louw, 1977).

(b) Data from U.S.A. (Stoll, 1938).


200
150
100
50
0
a
J F M A M J J A S O N D
80
60
40
20
0
b
J F M A M J J A S O N D
Worm burden per host
Month

which serve as the intermediate host.

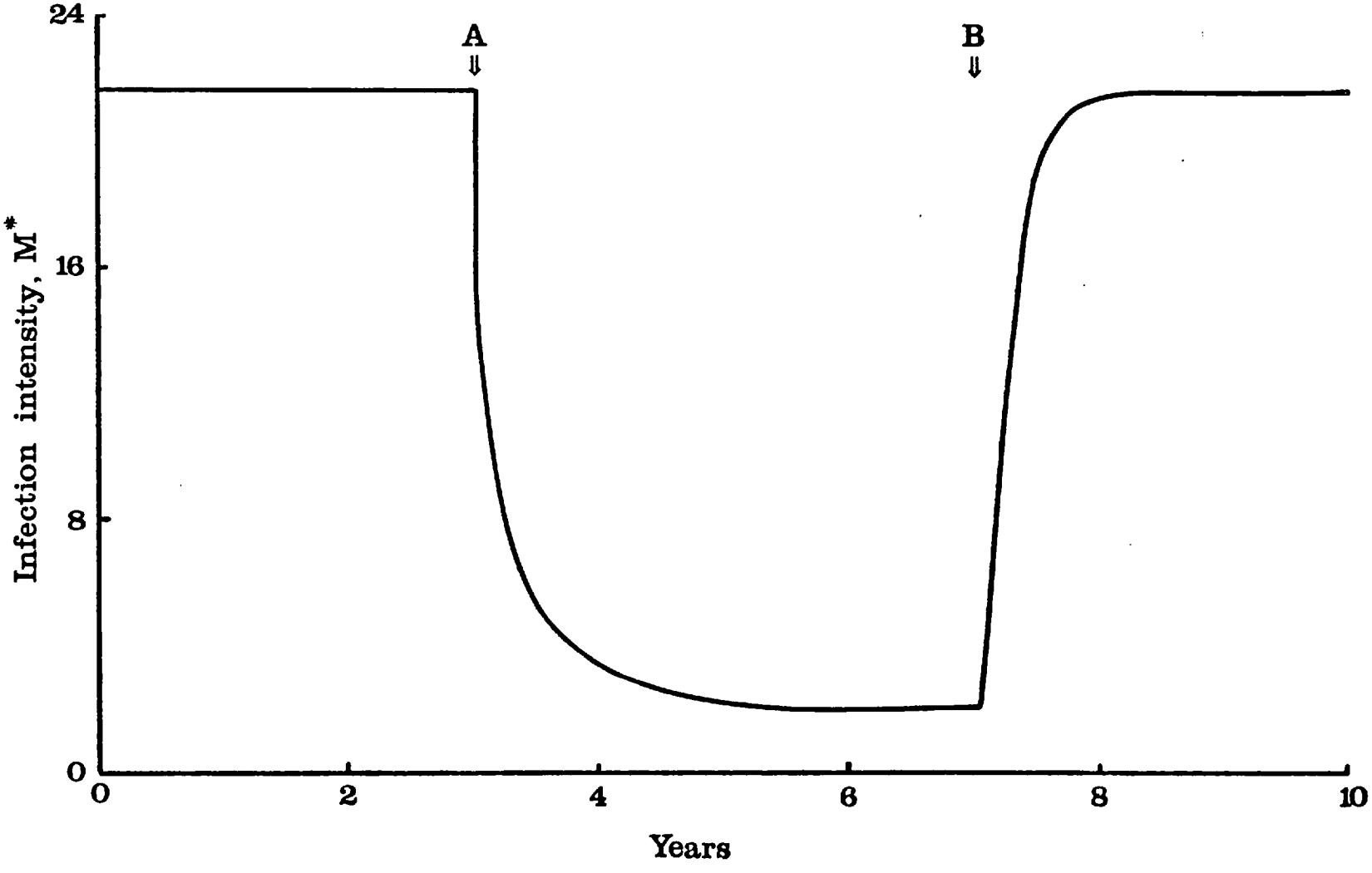
Seasonal parameter changes may be such that the value of the basic reproductive rate may fall below unity during certain periods of the year, indicating that parasite transmission may occur only at certain times. For parasite persistence in a defined region, however, the period during which R falls below unity must be less than the maximum lifespan of any one stage in the parasite life-cycle. There is unfortunately insufficient data available to allow examination of these possibilities. In cestode infections, however, where the lifespan of the adult worm varies between 6 months in *E.granulosus* to many years in *T.saginata* and *D.latum* (Table 4.1.2), seasonal changes in R are likely to be of little significance to the overall persistence of the parasite from year to year. The model development outlined in Sections 3 and 4 may thus be used to explore the dynamics of parasites on a yearly basis, as long as the parameter components are regarded as average yearly values.

4.4 CONTROL

In recent years, several advances have been made in research for drugs of use in the treatment of both adult and larval tapeworm infections (FAO/UNEP/WHO, 1976; Heath and Lawrence, 1978; Kern *et al*, 1979). Within the confines of the model described in the present section, chemotherapy acts to increase the parasite death rate in a density-independent manner, if applied randomly within the host population. As described earlier, this model generates a single stable equilibrium point for any combination of parameter values, and thus predicts that, while continued application of anthelminthics may be effective in reducing the mean worm burden per host, discontinuation of the treatment before total eradication has been achieved is likely to result in a return to the original intensity of infection. For example, Figure 4.4.1 shows a simulation (using the parameter values given in Table 4.2.1, together with estimates of β and δ based on data from other cestode infections) of the effect of a blanket chemotherapeutic treatment for *H.nana* resulting in a 2-fold increase in worm mortality rate. The results indicate a dramatic decrease in the mean worm burden per host from 22 to 4 in the first year of treatment, which is reversed on discontinuation of drug application, resumption of the initial level of parasitism occurring within a period of 6 months. In as far as the significance of this model formulation may be applied to

Figure 4.4.1 *An example of the predicted influence of a specified control programme on* Hymenolepis nana *infection, based on the model defined in equations (4.2.1) and (4.2.2).*

Parameter values as in Table 4.2.1. In addition, $\delta = 0.1$, $\beta = 3 \times 10^{-7}$/egg/year/host/hectare, H = 2000/hectare. Control measures are implemented at point A and discontinued at point B. During control, the expected lifespan of the adult parasite is decreased from 0.14 years to 0.07 years.


24
16
8
0
A
B
Infection intensity, M*
0
2
4
6
8
10
Years

parasite-host systems in the field, these results may indicate that chemotherapeutic treatment alone is not the best strategy for attempted long-term control of cestode infections.

The only tapeworm disease for which large-scale control has been attempted is echinococcosis. Control programmes have included the restriction of access of dogs to raw offal at abattoirs and farms, the reduction of the dog population in conjunction with mass dog-treatment, and extensive anti-echinococcus education campaigns (Gemmell, 1979). The results of such programmes in Cyprus, Tasmania, Iceland and New Zealand are shown in Figure 4.4.2. Interestingly, the echinococcus campaign had no effect on the prevalence of *T.ovis* in dogs in Tasmania (Gregory, 1977), although the control measures included annual dog purging. Similarly, an 8-fold increase in the national prevalence of *T.ovis* was noticed during the implementation of an *Echinococcus* programme in New Zealand (Burridge and Schwabe, 1977a). These effects are thought to reflect the change in source of food for dogs from raw viscera to sheep carcasses, although the effects of cross-immunity (Gemmell, 1967) and the increased emphasis on diagnosis of infections may be involved.

These observations, together with the fact that tapeworm infections survive in areas where the standards of education and public health are high, indicate that eradication may not always prove as easy as the foregoing results might suggest.

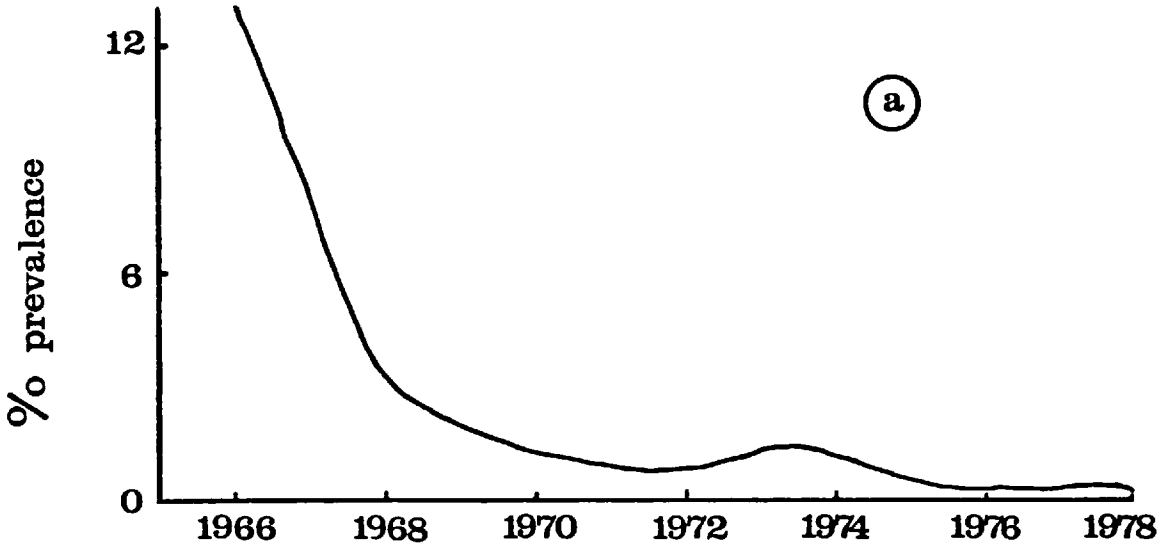
Figure 4.4.2 *The results of control programmes for* E.granulosus.

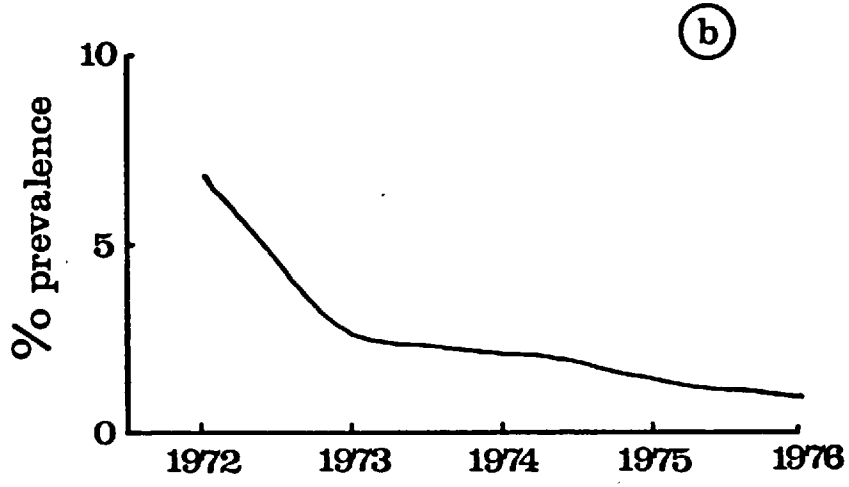
(a) % prevalence in dogs in Tasmania (McConnell and Green, 1979).

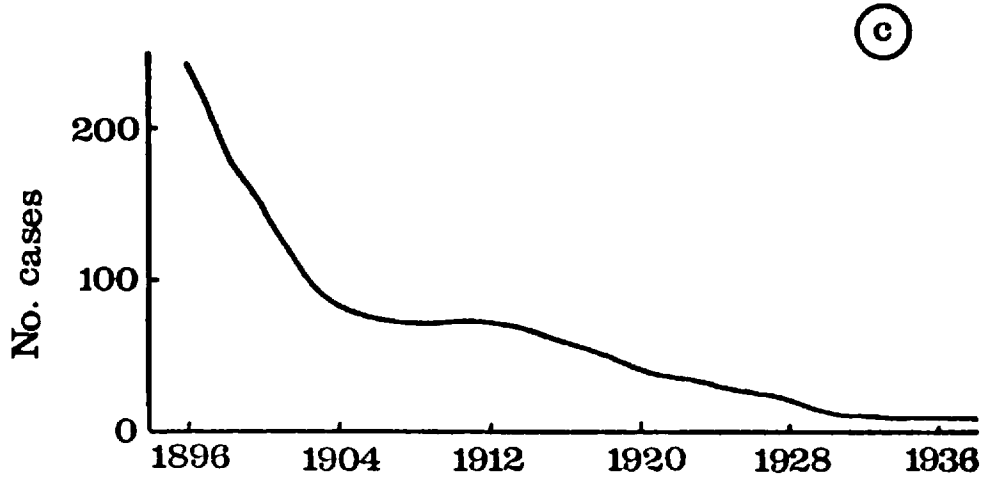
(b) % prevalence in dogs in Cyprus (Polydorou, 1977).

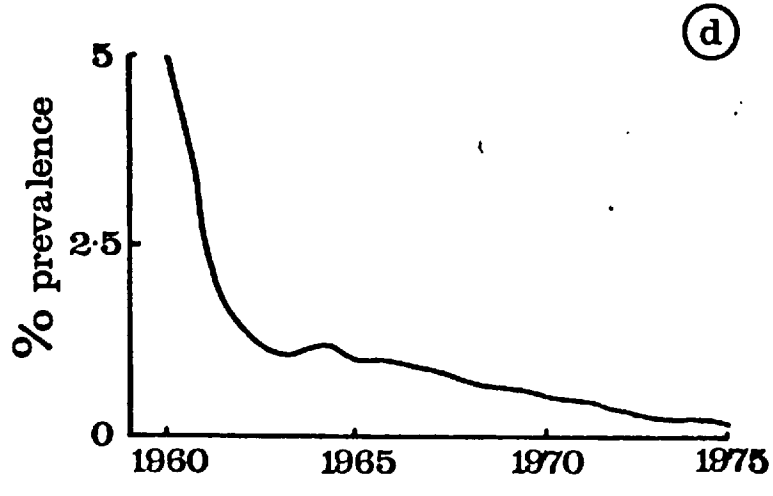
(c) No. reported human cases in Iceland (Dungal, 1946).

(d) % prevalence in dogs in New Zealand (Burridge and Schwabe, 1977b).


a
% prevalence
12
6
0
1966
1968
1970
1972
1974
1976
1978


b
% prevalence
10
5
0
1972
1973
1974
1975
1976


c
No. cases
200
100
0
1896
1904
1912
1920
1928
1936


d
% prevalence
5
2·5
0
1960
1965
1970
1975

It would be of interest to discover whether the success of *Echinococcus* control may be in any way explained by the behaviour of a model modified to include aspects of the *E.granulosus* life-cycle such as asexual reproduction in the intermediate host, the relatively short lifespan of the adult worm, and the long prepatent periods of both adult and larval parasites.

GENERAL DISCUSSION AND RECOMMENDATIONS

FOR FURTHER RESEARCH.

Although an immune response to cestode infection may be of importance in regulating parasite build up within single hosts, a truly immune category within the host population does not in general appear to exist (see Weinmann, 1966; Gemmell, 1976). Thus, in contrast to microparasitic infections (see Section 1), regulation of parasite population growth is not primarily determined by factors such as herd immunity and the rate of immigration of susceptible hosts, but rather by density-dependent constraints acting on parasite subpopulations within individual hosts. It should be noted that a single constraint of this type is capable of exerting efficient regulation of overall parasite population growth throughout the entire life-cycle (see Anderson, 1976). In the case of *H.diminuta*, potential regulatory processes may be listed as follows

1) Adult worm establishment and survival.

Severe density-dependent constraints on parasite build up within individual hosts are created by the early rejection of worms in heavy parasite burdens. Many parasites are expelled before they become patent, and in those that reach maturity, mortality is directly related to parasite burden, probably in a linear manner (see Section 2.5(vi)). These constraints may be mediated either by intraspecific parasite competition, or by a host response to infection. Both mechanisms have the same consequences with respect to the overall population biology of the interaction. The dynamics of simultaneous and trickle infections would be of some interest as a subject for continued

research, since laboratory infection procedures are, in general, somewhat different from those likely to occur under natural conditions.

2) Adult parasite fecundity.

Density-dependent reductions in parasite fecundity are also well documented and are probably non-linearly related to parasite burden (see Section 2.5(v)). This, together with constraints imposed on adult worm establishment and survival, would seem likely to provide the most effective regulation of parasite population flow in natural communities.

3) Functional response in parasite transmission.

As discussed in Sections 2.3(v) and 2.5(i), the dynamics of infections which occur as a result of ingestion are subject to density-dependent constraints as a result of the functional response of the predator to changes in prey density. Even when parasite egg or infected intermediate host densities are extremely high within a given habitat, the rate of parasite transmission will be subject to a finite maximum limit as a result of the feeding behaviour of the prospective hosts. As discussed earlier, however, functional responses are unlikely to provide very effective regulation of parasite population growth under natural conditions, since the densities of parasite infective-stages are unlikely to be consistently high in relation to predator density. For these reasons, it is suggested that the assumption of direct proportionality between the rate

of infection and infective-stage density provides a reasonable approximation of the transmission of ingested parasites, even though infection may be potentially regulated in a density-dependent manner at high infective-stage densities.

4) Parasite-induced reductions in host survival and fecundity.

These effects have been demonstrated to date in the intermediate host of *H.diminuta* only. Their potential effectiveness as a density-dependent constraint on parasite population growth is shown by the results of the simulation detailed in Section 2.4(v). They are not, however, thought to be important regulatory features in natural infections, as a result of the high rate of intermediate host mortality which is likely to result from factors such as environmental stress, predation and competition for finite resources. This conclusion, however, is speculative, and further research would seem justifiable in this area. First, it would be of interest to investigate the possibility of parasite-induced increase in susceptibility to predation. If the predator were a susceptible final host, an increase in transmission success would ensue. If not, preferential predation of infected insects would result in density-dependent regulation of parasite population growth. A second factor worthy of further investigation is the effect of final host stress on the ecology of the host-parasite interaction, especially since natural infections often occur in hosts subsisting in less than optimal dietary conditions. As well as parasite-induced effects on the host, survival and fecundity of the parasites themselves are likely to be dependent on available

nutrient resources (Anderson, 1979a). In addition, few infections in populations in natural habitats consist only of a single parasite species, and the influence of concomitant infection is of considerable interest (e.g. Holmes, 1961). Lastly, no studies have been made to date concerning possible parasite-induced susceptibility to predation or reduced competitive fitness in mammalian hosts such as rats harbouring intestinal helminths. Several density-dependent constraints which are not apparent in laboratory infections could therefore operate under natural conditions where factors such as stress, competition and predation are in operation.

5) Cysticercoid establishment and survival.

Although no density-dependent constraints on cysticercoid establishment have been demonstrated up to parasite burdens of 60/host (Section 2.3(iv)), there must be a potential limit to the number of parasites able to establish per host, imposed by the finite carrying capacity of the insect haemocoel. This must be true even though there is a decrease in cysticercoid size at high parasite burdens. Density-dependent constraints on cysticercoid establishment are not thought to play an important part in parasite regulation, however, since the effects of parasite-induced host mortality are likely to become operative before the finite carrying capacity is reached.

6) Cysticercoid mortality.

Although cysticercoid infectivity to the final host at 2 weeks

of age is not density-dependent up to burdens of 60 parasites per beetle (Section 2.5(iii)), it may be possible that the demonstrated age-dependent loss of infectivity is accelerated at high parasite burdens. Further experimental work to investigate the relationship between cysticercoid age, density and resultant infectivity would be of interest, since this may provide a further potential density-dependent constraint on parasite population growth.

Regulation of parasite population growth by the mechanisms listed above is facilitated by aggregation in the statistical distribution of parasite numbers per host. Although not a regulatory factor *per se*, heterogeneity enhances density-dependent control by creating high parasite burdens in individual hosts. In addition to the density-dependent constraints listed above, parasite population growth is also influenced by density-independent factors such as climatic variation. This is likely to have the most considerable effect on the survival of *H.diminuta* eggs in the external environment, and to a lesser extent on the survival of the intermediate host. No experimental work relating to the influence of environmental factors on parasite population dynamics was carried out in the present study, and thus the estimated parameter values obtained are representative of transmission only under specified laboratory conditions. However, the basic aim of the experimental programme was not to gain data which could be extrapolated to transmission in natural communities, but rather to obtain insight into the functional form of the processes affecting transmission and population behaviour.

In addition to providing parasite regulation, parasite-induced effects on host survival and reproduction have been shown experimentally to result in a substantial depression of host equilibrium population level under experimental conditions (see Section 2.4(v)). The behaviour of the model described in Section 3 supports these observations, and indicates that parasitism is potentially capable of regulating host population growth. The concept of the basic reproductive rate of the parasite, and the associated threshold host densities required for parasite transmission (Sections 3 and 4) would form a very good basis for the development of further experimental work. *H.diminuta* may be maintained in free-running populations of rats and beetles under laboratory conditions (Coleman, 1978) and this would provide a good method of testing the threshold host density hypothesis. In addition, a longitudinal study of the build up of parasites in a free-running population through time would provide a further method of estimating the transmission parameter, β. As with all experimental studies, care should be taken in extrapolating from results obtained using inbred laboratory strains to natural situations, since variations in susceptibility to infection must play an important part in parasite transmission and survival (Wakelin, 1978; Wassom *et al*,1973). The genetic control of susceptibility and resistance, and its relationship to the evolution of parasite-host interactions, is at present little understood, and is a subject worthy of further research effort, both in experimental and theoretical fields (see Gillespie, 1975; Clarke, 1976; Price, 1980).

The basic model framework developed by Anderson and May (1978) and May and Anderson (1978) may be adapted to mimic the dynamics of a wide range of helminth parasites. Sections 3 and 4 of the present thesis represent only a preliminary investigation of the use of this model in the description of host-tapeworm interactions. Further work relating to improvement of model structure is obviously necessary. For example, several density-dependent constraints on parasite population growth shown to occur in the laboratory have not been incorporated. Although their inclusion is a necessary and interesting development, it is unlikely to invalidate the conclusion that the observed equilibrium level of infection is likely to be stable to perturbation in regions where cestode infection is endemic. Further work should also include modifications of the structure of the basic model to mirror the life-cycles of tapeworms which multiply in the larval stage (e.g. *Echinococcus granulosus)* and those which make use of more than one intermediate host (e.g. *Diphyllobothruim latum*).

Theoretical techniques are of considerable value when used in conjunction with experimental methods, in the acquisition of conceptual insight into the influence of various physical and biological processes on the dynamics of the host-parasite interaction. The formulation of mathematical models is also of significance in the facilitation of experimental design by the clarification of the precise form of the parameter components worthy of quantitative investigation. In addition to their

analytical value, the manipulation of model frameworks is of use in a predictive capacity, since they may be used in conjunction with available data to predict the effects of various control measures, and thus to evaluate the potential benefits of programmes proposed within specified economic boundaries.

SUMMARY.

1) Survival of *H.diminuta* eggs (as measured by their infectivity to the intermediate host) was found to be age-dependent with a life expectation of 11 days when the eggs were retained within the faecal pellet at 10°C. The expected lifespan of eggs under experimental conditions (i.e. extracted from faecal material and placed on filter paper at 30°C) was estimated as 33 minutes.

2) The mean parasite burden of populations of *T.confusum* exposed to known densities of *H.diminuta* eggs was found to rise to a plateau with increasing exposure time. The experimental results provided a method of estimating the instantaneous rate of parasite transmission. A value of 0.0004/egg/minute/host/13cm^2 was obtained.

3) The mean parasite burden of populations of *T.confusum* exposed to known densities of *H.diminuta* eggs was found to decrease exponentially with increasing host density. A second estimate of the instantaneous rate of parasite transmission of 0.004/egg/minute/host/13cm^2 was obtained from the experimental results.

4) No density-dependent constraints on larval parasite establishment within individual intermediate hosts were found up to parasite burdens of 60/beetle. An inverse relationship between cysticercoid length and cysticercoid burden per host,

however, indicated that intraspecific competition is operative once the parasites become established within the coelom.

5) The mean parasite burden of populations of *T.confusum* exposed to known densities of *H.diminuta* eggs was found to rise to a plateau with increasing egg density. This is thought to result from limitations imposed on parasite acquisition by the feeding behaviour of the host (i.e. by the effects of satiation and/or the time taken to handle and consume each prey item within a finite experimental time period). The importance of the "functional response" to infective-stage density as a potential density-dependent constraint on parasite population growth is discussed.

6) Over-dispersion in parasite numbers per host was found to result even when populations of *T.confusum* were exposed to *H.diminuta* eggs arranged in an approximately uniform distribution throughout the infection arena. This is thought to result from heterogeneity in egg infectivity, beetle feeding behaviour or susceptibility to infection. Heterogeneity in egg spatial distribution was found to accentuate the resultant over-dispersion in parasite numbers per host but did not affect the average rate of parasite acquisition.

7) No differences in susceptibility to infection between 2-week old male and female beetles were found, although susceptibility decreased markedly with increasing beetle age up to 14 weeks post

eclosion. The relationship between age-related susceptibility and beetle sex was not considered.

8) Preliminary experimental results showed that, although *H.diminuta* eggs are actively predated by *T.confusum* in the absence of preferred food sources, they are likely to be consumed passively as a contaminant of rat faecal material when distributed within a faecal pellet.

9) Experimental results indicated that regulation of *T.confusum* population growth results from density-dependent constraints on fecundity (both "real" fecundity and egg cannibalism) rather than reduced adult survival at high population densities. The expected lifespan of adult *T.confusum* under the specified experimental conditions was estimated as approximately 8 weeks. Average fecundity (single pairs in non-limiting environmental conditions) was estimated as approximately 7 eggs/female/24 hours.

10) Beetle fecundity was found to decrease non-linearly with increasing parasite burden from approximately 7 eggs/female/24 hours to approximately 1 egg/female/24 hours in beetles with estimated parasite burdens of 50 parasites/host. No differences in viability between eggs from uninfected and infected beetles were demonstrated.

11) Direct proportionality between the instantaneous rate of

parasite-induced host mortality per parasite per unit time and parasite burden per host was demonstrated. This was manifested in a linear relationship between beetle survival and parasite burden. The possible significance of parasite-induced effects on host survival and fecundity as density-dependent constraints on parasite population growth is considered.

12) The results of long-term experiments under specified experimental conditions revealed a 50% depression of *T.confusum* equilibrium population level as a result of parasitism by *H.diminuta*.

13) The dynamics of transmission of *H.diminuta* from the intermediate to the final host was also shown to be dependent on host feeding behaviour. A functional response between the rate of predation of *T.confusum* by laboratory rats and prey density was demonstrated and an estimate of the instantaneous rate of parasite transmission of 0.14/parasite/week/rat/25 ft^2 was obtained from the results of experiments carried out by Coleman (1978).

14) The lengths of the prepatent periods of *H.diminuta* in the final and intermediate host (at 30°C) were confirmed as 17 and 10 days respectively.

15) No density-dependent decrease in the infectivity of *H.diminuta* cysticercoids to the final host were demonstrated up to parasite burdens of 60 cysticercoids/beetle. However,

a definite decrease in infectivity with increasing cysticercoid age was demonstrated, beginning at approximately 4 weeks post infection. No investigation of the possibility of increased age-dependent loss of infectivity at high cysticercoid densities was carried out.

16) Adult worm survival was shown to be independent of worm age at low parasite burdens up to 63 weeks post infection. Results present in the literature indicate that worm fecundity may also be considered age-independent.

17) The density-dependent nature of adult worm fecundity and survival, and the effects of *H.diminuta* on the definitive host are reviewed using published experimental results.

18) Using the experimentally determined population parameter forms described in the first part of the thesis, a model for the *H.diminuta* life-cycle is discussed (based on the model framework proposed by Anderson and May (1978) and May and Anderson (1978)). Within the confines of the model, the influence of factors such as density-dependent parasite population growth, over-dispersion of parasite numbers per host and non-linear parasite transmission on the dynamics of the host-parasite interaction are considered. The possibility of parasite-induced regulation and depression of intermediate host population growth is also discussed.

19) Consideration is given to the use of the model in the description of the population dynamics of cestodes of economic and public health significance.

20) The relative effectiveness of the various potential regulatory factors on parasite population growth under natural conditions are discussed. It is thought that density-dependent constraints an adult worm fecundity and survival are likely to be of greatest significance. Non-linear parasite transmission and parasite-induced reductions in intermediate host fecundity and survival are thought to be of little importance in parasite regulation in the majority of natural situations.

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Appendix 1

Tables 2.3.1 - 2.5.5.

Table 2.3.1 *Survival of* H.diminuta *eggs as measured by their infectivity to the intermediate host.*

(a) Survival of eggs maintained in rat faecal pellets at 10°C.

Age of faecal pellets.	Parasite burden of exposed host population.	
Days	Mean ± 95%C.L.	Variance.
0 - 3	11.73 ± 2.97	68.67
5 - 8	11.93 ± 2.81	61.55
14 - 17	10.87 ± 1.95	29.65
21 - 24	4.89 ± 1.66	21.52
28 - 31	3.11 ± 0.86	5.74
53 - 56	0.40 ± 0.27	0.57

(b) Survival of eggs under 'experimental conditions'.

Experimental age of eggs.	Parasite burden of exposed host population.	
Minutes	Mean ± 95%C.L.	Variance.
0	10.53 ± 2.49	48.38
15	8.55 ± 2.46	48.70
30	5.00 ± 1.48	17.13
60	5.50 ± 1.73	23.25
90	4.19 ± 1.50	18.03
120	0.20 ± 0.18	0.16
195	0.05 ± 0.09	0.05

Table 2.3.2 *The relationship between the duration of exposure of hosts to infective stages, and the resultant parasite burden of the exposed host population.*

Duration of exposure.	Parasite burden of exposed host population.	
Minutes.	Mean ± 95%C.L.	Variance.
10	0.83 ± 0.73	4.20
20	1.66 ± 1.15	10.29
30	2.17 ± 1.32	13.67
40	4.19 ± 1.54	18.52
50	4.37 ± 2.12	35.17
60	5.24 ± 1.88	27.49
90	4.87 ± 1.78	24.72
1200	4.79 ± 1.44	16.26
1600	4.88 ± 1.33	13.85
4000	5.25 ± 1.33	13.80
7000	5.12 ± 1.86	27.00

Table 2.3.3 The relationship between the density of hosts exposed to infection and the resultant parasite burden of the exposed host population.

Host density.	Parasite burden of host population.	
No./arena	Mean ± 95%C.L.	Variance.
5	4.40 ± 2.12	5.84
12	2.42 ± 1.49	6.91
19	1.68 ± 0.76	2.85
35	1.17 + 0.40	1.46
75	0.73 ± 0.23	1.08

Table 2.3.4 *Density-dependence in cysticercoid establishment and growth.*

(a) The relationship between the "no. of infections" (see text) and the parasite burden of the host population.

No. infections.	Parasite burden of host population.	
	Mean ± 95%C.L.	Variance.
1	3.66 ± 1.46	16.64
2	16.81 ± 3.53	97.56
3	20.26 ± 4.86	184.41
4	35.20 ± 6.49	328.43
5	51.45 ± 5.70	253.63
6	66.76 ± 5.95	276.75

(b) The relationship between parasite burden and cysticercoid length.

Parasite burden.	Cysticercoid length (mm).	
No./host.	Mean ± 95%C.L.	Variance.
1 - 5	1.50 ± 0.12	0.04
6 - 10	1.23 ± 0.09	0.02
11 - 20	1.06 ± 0.09	0.02
21 - 30	0.77 ± 0.09	0.02
31 - 40	0.75 ± 0.12	0.04
41 - 50	0.62 ± 0.06	0.01
51 - 60	0.58 ± 0.06	0.01
61 - 70	0.53 ± 0.06	0.01
71 - 80	0.54 ± 0.06	0.01

Table 2.3.5 *The relationship between infective-stage exposure density and the resultant parasite burden of the exposed host population.*

(a) Beetles starved for 6 days; exposure period 24 hours.

Egg density. (no./arena).	Parasite burden of host population. Mean ± 95%C.L.	Variance.
60	0.93 ± 0.67	3.49
180	1.19 ± 0.64	3.16
300	3.10 ± 0.99	7.62
500	7.70 ± 1.60	20.06
600	3.62 ± 1.36	14.47
1200	6.96 ± 1.84	26.32
1800	17.14 ± 3.28	83.77
2400	14.53 ± 3.01	70.92
3000	15.10 ± 3.20	79.82
6000	20.33 ± 3.66	104.39

(b) Beetles satiated; exposure period 24 hours.

Egg density. (no./arena).	Parasite burden of host population. Mean ± 95%C.L.	Variance.
60	0.00	
180	0.03 ± 0.06	0.03
300	0.20 ± 0.17	0.23
500	0.38 ± 0.44	1.48
600	0.39 ± 0.38	1.14
1200	0.43 ± 0.42	1.38
1800	1.41 ± 1.09	9.21
2400	1.75 ± 1.02	8.19
3000	1.53 ± 0.78	4.78
4500	2.67 ± 0.93	6.81
6000	1.33 ± 0.63	3.09

(c) Beetles starved for 6 days; exposure period 15 minutes.

Egg density. (no./arena)	Parasite burden of host population. Mean ± 95%C.L.	Variance.
60	0.40 ± 0.27	0.57
180	0.94 ± 0.47	1.61
300	1.07 ± 0.75	4.42
500	2.27 ± 0.89	6.20
600	1.66 ± 0.70	3.81
1200	2.53 ± 1.10	9.38
1800	2.16 ± 1.18	10.94
2400	2.20 ± 1.24	12.03
3000	2.84 ± 1.20	11.26
4500	2.93 ± 1.06	8.74
6000	2.00 ± 0.77	4.67

Table 2.3.8 *The relationship between the spatial distribution of the* H.diminuta *eggs in an infection arena, and the resultant frequency distribution of parasite numbers per host.*

No. parasites/host.	Variance/Mean of egg numbers per quadrat.			
	2700	540	300	0
0	11	12	7	4
1	4	8	4	6
2	5	6	7	9
3	4	1	5	6
4	4	2	5	4
5	7	4	7	5
6	4	9	6	9
7	3	5	2	3
8	3	2	2	5
9	2	1	3	2
10	4	3	4	1
11	3		3	3
12	1	3		3
13	2			1
14		2	1	
15				
16	1	2		
17	2	1		
18			1	
19	1		1	
21	1			
23	1			
28	1			

The table gives the number of hosts in each population harbouring a given number of parasites.

Table 2.3.9 *The relationship between the spatial distribution of the* H.diminuta *eggs in an infection arena, and the resultant parasite burden of the exposed host population.*

Parasite burden of host population.	Spatial distribution of *H.diminuta* eggs (as measured by the variance to mean ratio of egg numbers per quadrat, see text).			
	2700	540	300	0
Mean	6.50	5.05	5.26	5.05
Variance	38.03	21.65	18.23	12.24
$\frac{\text{Variance}}{\text{Mean}}$	5.85	4.29	3.47	2.42

Table 2.3.10 The influence of host age and sex on infection.

(a) Sex.

	Parasite burden of host population.	
	Mean ± 95%C.L.	Variance
Females.		
Replicate 1	2.25 ± 1.05	9.69
Replicate 2	1.94 ± 0.90	6.29
Total	2.09 ± 0.97	7.40
Males.		
Replicate 1	1.71 ± 0.76	4.49
Replicate 2	1.94 ± 0.95	7.11
Total	1.84 ± 0.87	5.94

(b) Age.

Age of host.	Parasite burden of host population.	
Weeks.	Mean ± 95%C.L.	Variance
1 - 2	16.22 ± 4.06	128.98
2 - 3	15.38 ± 3.29	84.73
4 - 5	9.80 ± 2.62	53.59
6 - 7	4.81 ± 2.40	44.78
9 - 10	1.96 ± 1.02	8.18
14 - 15	1.78 ± 0.93	6.73

Table 2.3.11 The influence of alternative food sources on infection.

(a) The influence of *T.confusum* eggs in the infection arena.

Density *T.confusum* eggs.	Parasite burden of host population.	
No./arena.	Mean ± 95%C.L.	Variance.
0	7.62 ± 1.92	28.90
5	6.53 ± 1.01	7.90
10	7.05 ± 1.00	7.75
25	8.85 ± 2.29	40.90
50	7.84 ± 1.47	16.98
100	9.00 ± 1.94	29.44
300	7.09 ± 1.26	12.43

(b) The influence of faecal material in the infection arena.

Wt. fresh faecal material.	Parasite burden of host population.	
gm./arena.	Mean ± 95%C.L.	Variance.
0	10.52 ± 3.36	88.09
0.05	9.80 ± 2.92	66.43
0.15	9.14 ± 3.29	84.57
0.30 (1 pellet)	6.36 ± 2.25	39.41
0.60	4.93 ± 2.14	35.70
0.90	4.20 ± 1.82	25.86
1.20 (4 pellets)	3.75 ± 1.39	14.99

Table 2.4.1 *Density-dependent constraints on the population growth of* T.confusum.

(a) The relationship between beetle density and beetle survival.

	Initial beetle density (no/gm)					
	10	20	35	50	100	150
weeks						
0	1.00	1.00	1.00	1.00	1.00	1.00
1	0.97	1.00	0.99	0.97	0.97	0.99
2	0.97	1.00	0.98	0.97	0.97	0.98
3	0.97	0.98	0.97	0.96	0.96	0.97
4	0.90	0.98	0.95	0.96	0.96	0.96
5	0.87	0.95	0.95	0.95	0.95	0.96
6	0.87	0.93	0.95	0.95	0.95	0.96
8	0.87	0.92	0.94	0.94	0.94	0.96
10	0.87	0.92	0.92	0.93	0.90	0.95
12	0.83	0.85	0.88	0.91	0.88	0.93
15	0.73	0.80	0.79	0.86	0.86	0.89
17	0.60	0.77	0.50	0.81	0.83	0.84
19	0.30	0.55	0.30	0.72	0.76	0.71
21	0.03	0.18	0.08	0.48	0.63	0.57
23	0.03	0.08	0.06	0.23	0.42	0.40
25	0.00	0.00	0.00	0.09	0.23	0.17
27				0.00	0.07	0.09
28					0.05	0.05
29					0.00	0.00
Expected lifespan (weeks)	6.73	7.45	7.67	8.31	9.04	8.89
Instantaneous mortality rate (b_2/beetle/week)	0.15	0.13	0.13	0.12	0.11	0.11

The table gives the proportion surviving through time, for 6 population densities.

(b) The relationship between beetle density and the number of eggs recovered from beetle populations.

	Initial beetle density (no/gm)						
	2	10	20	35	50	100	150
Time (hours)							
	9.00	2.20	2.90	1.72	1.48	1.64	1.66
24	9.00	3.60	3.10	2.22	1.52	1.48	1.46
	4.00	3.20	1.60	2.92	1.88	1.48	1.20
	8.00	3.40	3.90	2.40	1.80	1.34	1.14
48	6.00	3.80	3.60	1.88	1.88	1.56	1.14
	5.00	4.60	3.00	2.80	1.96	1.58	1.12
	8.00	3.20	2.80	1.78	1.40	0.84	0.86
72	6.00	3.00	3.00	1.78	1.36	1.02	0.94
	7.00	4.20	2.20	1.88	1.40	0.62	0.76
No. eggs recovered /pair/24 hours							
Mean	6.89	3.47	2.90	2.15	1.63	1.28	1.14
Variance	2.77	0.44	0.42	0.19	0.05	0.12	0.07

The table gives the no. eggs recovered/beetle pair for 7 population densities.

Table 2.4.2 *The relationship between the density of* T.confusum *eggs and the rate of egg predation by* T.confusum *adults.*

Egg density. (no./arena)	No. eggs eaten /beetle/hour. Mean 95%C.L.	Variance.
5	0.38 ± 0.10	0.014
10	0.66 ± 0.04	0.002
15	1.02 ± 0.10	0.014
20	1.08 ± 0.10	0.014
25	1.24 ± 0.26	0.090
30	1.82 ± 0.31	0.122
40	2.10 ± 0.12	0.020
50	2.06 ± 0.30	0.114
60	2.04 ± 0.18	0.042
70	2.28 ± 0.30	0.118
80	1.94 ± 0.17	0.038
90	1.98 ± 0.15	0.030
100	2.20 ± 0.12	0.052
150	2.52 ± 0.39	0.198

Table 2.4.3 The influence of infection on host fecundity.

(a) A comparison of egg production in infected and uninfected beetles.

Days post infection.	No. eggs produced/female/24 hours.			
	Uninfected beetles.		Infected beetles.	
	Mean	Variance	Mean	Variance
1.	4.90	11.49	2.38	3.73
2.	5.80	4.56	4.63	1.73
3	8.00	4.60	4.88	2.11
4	7.90	4.89	4.50	3.50
5	7.70	3.61	4.34	2.73
6	7.80	3.36	4.38	2.73
7	6.00	2.40	4.63	1.23
8	6.20	1.56	3.13	0.86
9	6.10	2.90	3.25	0.69
10	6.60	2.24	3.63	2.98
11	5.70	2.01	2.88	1.61
12	7.10	1.09	3.75	1.19
13	5.60	1.24	2.63	2.23
14	6.30	0.81	2.63	0.73
15	5.90	1.49	2.13	1.61
16	7.00	3.80	4.38	2.98
17	7.40	2.84	5.00	3.50
18	7.20	5.16	4.12	2.86

(b) The influence of parasite burden on host fecundity.

No. infections given.	Estimated mean parasite burden per host.	No. eggs produced /female/24 hours.	
		Mean	Variance
0	0	6.83	3.14
1	9.9	2.25	7.52
2	19.7	1.80	2.56
3	29.6	2.50	2.92
4	39.4	1.27	1.93
5	49.3	1.06	1.72

(c) The influence of infection on egg viability.

Replicate No.	No. larvae hatched from 10 eggs.	
	Uninfected beetles.	Infected beetles.
1	9	10
2	9	10
3	8	9
4	9	6
5	10	8
Mean	9.00	8.60
Variance	0.40	2.24

Table 2.4.4 *The influence of* H.diminuta *on host survival under varying dietary conditions.*

(a) Hosts starved.

Days post infection.	Proportion surviving.	
	Infected	Uninfected
0	1.00	1.00
4	0.98	1.00
6	0.96	1.00
7	0.88	1.00
8	0.81	1.00
10	0.65	0.89
13	0.31	0.46
14	0.15	0.39
15	0.12	0.28
17	0.00	0.12
20	0.00	0.00

(b) 0.5gm food medium / 50 hosts.

Days post infection.	Proportion surviving.	
	Infected	Uninfected
0	1.00	1.00
2	0.98	0.96
27	0.98	0.96
30	0.91	0.96
33	0.85	0.96
35	0.77	0.96
41	0.17	0.96
42	0.11	0.96
44	0.02	0.96
47	0.00	0.82
50	0.00	0.22
54	0.00	0.08
56	0.00	0.00

(c) 20gm flour-yeast medium / 50 hosts.

Days post infection.	Proportion surviving.	
	Infected	Uninfected
0	1.00	1.00
1	0.96	1.00
6	0.96	0.92
37	0.96	0.90
52	0.78	0.88
77	0.58	0.86
93	0.42	0.78
102	0.38	0.74
119	0.36	0.74
140	0.32	0.72
154	0.30	0.68
161	0.26	0.68
169	0.24	0.60
183	0.20	0.50
200	0.18	0.46
220	0.00	0.30
245	0.00	0.00

Table 2.4.5 *The survival of host populations harbouring different levels of infection.*

Days post starvation.	No. infections given	0	1	3	4	5
	Estimated mean burden	0	9.9	29.6	39.4	49.3
0		1.00	1.00	1.00	1.00	1.00
1		1.00	0.95	0.84	0.88	0.76
2		0.95	0.84	0.69	0.73	0.50
3		0.86	0.73	0.59	0.55	0.41
4		0.84	0.57	0.47	0.33	0.29
7		0.58	0.29	0.22	0.08	0.03
8		0.26	0.19	0.09	0.00	0.00
9		0.09	0.00	0.00		
10		0.00				

Table 2.4.6 *The relationship between the instantaneous rate of host mortality, $\bar{b}_2$, and the mean parasite burden per host.*

No. infections.	Estimated mean parasite burden/host.	$\bar{b}_2$ (per host per hour).
0	0	0.003
1	9.9	0.007
3	29.6	0.009
4	39.4	0.015
5	49.3	0.021

The values of $\bar{b}_2$ were calculated using the model defined in equation (2.4.4) from the data given in Table 2.4.5.

Table 2.4.7 *The change in the frequency distribution of parasites per host through time.*

(a) Initial infection level (a)

No. parasites per host.	Hours post starvation. 0	12	20	36	44	48
30		1				
32	1					
35			1		1	
36				1		1
37		1				
38	1		1	1		
39			2	2	1	2
40	2	1	1		1	1
41		1		1		1
42				2		2
43	1	3	1	1	1	
44			2	2	2	1
45	2	1	1	1	2	1
46	1	1	2	2	2	
47		2		2	1	
48	5	2	1	1		
49		4	4		1	1
50		2	2	2	2	1
51	1		1	1		
52	2	2	1			
53			2		2	
54	1		1	1		
55	3	3	2	2		1
56	1	2	2	2	2	
57	4	1	1	2		
58		3	1			
59	5					
60	3	1	2		1	
62	1	1		1		
63	1		1			
64				1		
65	2	3	2	1	1	
66	1					
68	2					
69	1	1				
70	2					
71		2		1		
72	3	2				
73	3					
74			1			
75	2		1			

78		2				
79	1	1				
80	1	1				
82			1			
83	1					
84		1				
85		1				
86		1				
89	1					
90		1	1			
101	1					
112	1					
Proportion surviving	0.95	0.82	0.63	0.50	0.33	0.20
Mean no. parasites/host	61.35	58.35	53.61	49.67	48.30	43.50
Variance	217.70	199.74	140.03	74.36	50.81	27.25

(b) Initial infection level (b).

No. parasites per host.	Hours post starvation. 0	19	41	49	56	70
0		1				
3	1					1
4	1				1	
5		2	1			2
6		2		1	1	1
7	1	1	1	2		
8	1	2		1	1	
9		1	1	1	2	1
10	1	1		1	2	1
11	2	1	2	1	2	1
12		2	1	1		1
13			1		1	2
14	1	2	2	2	1	
15	1		1	1		
16	1		1	4	1	1
17	1	1	1		2	
18	3	1	1		1	1
19	1	1	1	1	1	
20	3		1			
21	2	2				1
22	3	1				
23		3				
24	2		1			
25	4		1	1		
26			1			
27	1		1	1		
28		1	2			

29				1		
30	2	1				
32	1	2	1			
33	1	1	1			
34		2				
35	2					
36	2					
37	1	1				
38	1	2	1			
39			1			
40	1					
43	1					
45	1	2				
46			1			
47	1					
48			1			
51	1	2				
55	1					
56	1					
57	1					
62	1					
65		1				
67	1					
68		1				
Proportion surviving	1.00	0.80	0.54	0.38	0.32	0.25
Mean no. parasites/host	27.92	24.38	22.04	14.56	12.00	10.92
Variance	228.47	273.33	130.26	42.24	18.75	26.84

(c) Initial infection level (c).

No. parasites per host.	Hours post starvation.					
	0	22	40	70	80	90
0		1	1			1
1		3	1	4	3	2
2	7	1	4	4	3	2
3	5	2	3	2	2	4
4	7	3	1	5	2	3
5	2	7	5	1	6	1
6	1	4	2	3	1	1
7	2	2	6	1	1	
8	4	6	2	4	2	
9	5	4	2		1	
10	7	3	5	1		
11	3	4	1	1	1	1
12	2		3	1		
13	2	1		1		

14	1	2	1			
15	3					
16		1				
17		2		1		
18		1	1	1		
20	1	1				
21	1					
22		2				
24	1					
28	1		1			
33	1					
37	1					
Proportion surviving	1.00	0.83	0.65	0.50	0.37	0.25
Mean no. parasites/host	9.46	8.54	7.49	6.03	4.64	3.47
Variance	55.30	28.45	25.94	20.37	7.14	6.38

(d) Initial infection level (d).

No. parasites per host.	Hours post starvation. 0	48	72	96	120	144
0	1	1			1	
1	2	2	1	1	3	1
2	4	3	1	4	2	1
3	3	2	5	3	3	2
4	5	6	4	3	3	2
5	4	4	3	4	5	1
6	4	6	6	3	2	2
7	3	2	5	5	2	1
8	3	4	2	4		
9	4	1	2		1	
10	4	1	3	1		
11					1	
12	5	3	1			
13	2	3	2	1		
14	1		1	1		
15	2	1				
16		1	1			
17	1					
18	1					
19		1				
20		1				
32	1					
Proportion surviving	1.00	0.84	0.74	0.60	0.46	0.20
Mean no. parasites/host	8.02	7.24	6.81	5.73	4.30	4.10
Variance	31.14	22.85	12.37	9.33	6.82	3.29

(e) Initial infection level (e)

No. parasites per host.	Hours post starvation. 0	72	120	144	173	216
0	27	19	15	16	11	5
1	6	4	6	6	4	3
2	2	4	4	1	2	
3	2	3	3	1	1	1
4	2		1	1		1
5	1	4	2	1	1	
6	2	3		1		
7	1	1	3	1	1	
8		2	1			
9	2	1				
10		1	1			
12	1					
15	1					
16	1	1				
17		1				
19	1					
25	1					
Proportion surviving	1.00	0.88	0.72	0.58	0.40	0.20
Mean no. parasites/host	3.06	3.05	2.11	1.41	1.15	1.00
Variance	30.30	17.04	7.38	5.21	3.43	1.80

The tables give the number of hosts in each population harbouring a given number of parasites.

Table 2.4.9 a) The relationship between the rate of parasite-induced host mortality per parasite per hour (as calculated using equation (2.4.11) and the mean parasite burden per host.

The table gives the values of Q, R and k calculated for the time interval between each dissection, where Q = variance/mean, R = Q - 1, k = mean/R. Δt = time interval between dissections (hours).

Series (a)

Δt	M_2	Q	R	k	α
12	58.35	3.55	2.55	24.06	0.0012
8	53.61	3.42	2.42	24.11	0.0032
16	49.67	2.61	1.61	33.30	0.0019
8	48.30	1.50	0.50	99.34	0.0023
4	43.50	1.05	0.05	966.00	0.025

Series (b)

Δt	M_2	Q	R	k	α
19	24.38	8.18	7.18	3.89	0.0009
22	22.04	11.21	10.21	2.39	0.0004
8	14.56	5.91	4.91	4.49	0.0100
7	12.00	2.90	1.90	7.66	0.0100
14	10.92	1.56	0.56	21.43	0.0040

Series (c)

Δt	M_2	Q	R	k	α
22	8.54	5.85	4.85	1.95	0.0008
18	7.49	3.33	2.33	3.63	0.0021
30	6.03	3.46	2.46	3.05	0.0023
10	4.64	3.38	2.28	2.65	0.0058
10	3.47	1.54	0.54	8.60	0.0200

Series (d)

Δt	M_2	Q	R	k	α
48	7.24	3.88	2.88	2.79	0.0006
24	6.81	3.16	2.16	3.35	0.0008
24	5.73	1.82	0.82	8.30	0.0041
24	4.30	1.63	0.63	9.09	0.0077
24	4.10	1.59	0.59	7.29	0.0013

Series (e)

Δt	M_2	Q	R	k	α
72	3.05	9.90	8.90	0.34	0.0000
48	2.11	5.59	4.59	0.66	0.0016
24	1.41	3.50	2.50	0.84	0.0055
29	1.15	3.70	2.70	0.52	0.0020
43	1.00	2.98	1.98	0.58	0.0011

Summary

Initial mean parasite burden/host	α/parasite/hour ± 95% confidence limits
61.35	0.0067 ± 0.0067
27.92	0.0051 ± 0.0037
9.46	0.0062 ± 0.0062
8.02	0.0029 ± 0.0024
3.06	0.0020 ± 0.0016

b) The relationship between the rate of observed host mortality, $\bar{b}_2$, per host per hour (as calculated using equation (2.4.12)), and the mean parasite burden per host.

Initial mean parasite burden (no/host)	$\bar{b}_2$/host/hour
61.35	30.4
27.92	8.15
9.46	3.44
8.02	3.76
3.06	0.77

Table 2.4.12 *The long-term effects of parasitism by* H.diminuta *on the population growth of* T.confusum.

(a) Uninfected populations.

Population age. (weeks)	Population size (no./gm.)			
	Larvae	Pupae	Adults	Total
0	0	0	20	20
4	61.0 ± 7.9	0	19.7 ± 0.3	80.7 ± 8.0
8	86.1 ±13.8	1.7 ±1.8	28.8 ± 4.6	116.6 ±17.7
12	116.9 ±14.5	1.4 ±1.3	34.6 ± 8.9	152.9 ±16.0
16	88.6 ±11.5	0	31.4 ± 7.6	120.0 ±12.0
20	19.1 ± 6.6	6.1 ±3.8	35.3 ± 6.2	60.6 ± 7.5
24	17.1 ± 6.1	2.8 ±1.6	35.8 ± 5.9	55.6 ± 6.4
28	6.6 ± 3.6	2.5 ±2.6	32.0 ± 5.6	41.1 ± 6.2
32	27.5 ±39.3	0.8 ±1.4	26.4 ± 5.0	34.8 ± 5.1
36	15.4 ± 3.1	0.6 ±0.9	16.6 ± 3.4	32.6 ± 2.1
40	10.3 ± 6.3	4.8 ±2.6	10.0 ± 2.0	25.0 ± 5.8
44	20.3 ±10.9	1.0 ±0.6	13.3 ± 3.9	34.5 ±10.9
48	12.3 ± 5.1	2.3 ±1.6	15.3 ± 4.6	29.8 ± 4.8
52	24.6 ± 9.8	1.6 ±1.1	14.1 ± 4.5	40.4 ±10.6
56	19.8 ± 8.6	1.3 ±1.2	14.9 ± 4.9	35.9 ± 7.0
60	18.6 ± 7.5	1.6 ±1.2	15.4 ± 4.1	35.8 ± 7.3

(b) Infected populations.

Population age. (weeks)	Population size (no./gm.)			
	Larvae	Pupae	Adults	Total
0	0	0	20	20
4	46.2 ± 6.5	0	19.1 ± 0.9	65.3 ± 6.4
8	57.9 ± 13.3	0.7 ± 0.5	26.9 ± 3.4	85.3 ± 14.0
12	61.5 ± 17.7	0.4 ± 0.5	30.7 ± 6.5	92.6 ± 19.5
16	56.3 ± 12.0	1.1 ± 1.3	24.0 ± 5.4	81.4 ± 12.3
20	12.7 ± 4.5	1.7 ± 1.6	28.2 ± 3.6	42.6 ± 4.0
24	5.9 ± 2.6	2.3 ± 1.1	22.3 ± 3.9	30.5 ± 4.7
28	1.1 ± 0.8	0.7 ± 0.5	16.0 ± 3.6	17.7 ± 3.5
32	3.1 ± 1.5	0.4 ± 0.3	5.1 ± 1.5	8.6 ± 2.1
36	5.9 ± 2.9	0.6 ± 0.5	1.0 ± 0.6	7.5 ± 2.6
40	2.0 ± 1.6	1.7 ± 1.0	4.6 ± 2.1	8.3 ± 3.1
44	18.4 ± 8.8	1.1 ± 0.8	6.0 ± 1.8	25.5 ± 9.8
48	2.6 ± 2.2	2.4 ± 1.9	9.9 ± 2.8	15.3 ± 4.6
52	6.8 ± 2.3	0.4 ± 0.7	8.7 ± 2.3	15.9 ± 4.4
56	6.9 ± 2.4	0.9 ± 1.3	6.7 ± 1.7	14.5 ± 3.9
60	5.9 ± 4.3	1.3 ± 1.4	6.0 ± 1.7	13.2 ± 4.7

Figures are the mean value of 8 - 10 replicates ± 95% confidence limits.

Table 2.4.13 Approximate estimates of the population parameters involved in the model of host population growth defined in equations (2.4.20) and (2.4.21).

Parameter	Definition	Estimated value	Reference Section
a_2	Instantaneous rate beetle fecundity	7 eggs/beetle/week	2.4(ii)
b_2	Instantaneous rate beetle mortality	0.13/beetle/week	2.4(ii)
γ	Severity of density-dependence on beetle population growth	0.2	2.4(v)
β_2	Instantaneous rate beetle infection	0.004/egg/minute/host/13cm^2	2.3(iii)
λ	Constant rate of egg immigration	3000 eggs/4 weeks	(2.4(v)
μ_3	Instantaneous rate egg mortality under experimental conditions	0.03/egg/minute	2.3(i)
ω	Parasite-induced reduction in beetle fecundity	0.03/parasite	2.4(iii)
α	Instantaneous rate parasite-induced host mortality	0.005/parasite/hour	2.4(iv)
k	Parameter of negative binomial distribution describing the frequency distribution of parasite numbers per host	1.04	2.3(vi)

Table 2.5.1 *The relationship between the rate of predation by laboratory rats on* T.confusum, *and beetle density.*

Beetle density. (no. /1500cm²)	No. beetles eaten/rat/hour. Mean	Variance
5	2.00	5.00
10	4.70	18.20
15	6.67	32.60
20	11.00	76.70
30	7.70	115.60
40	11.50	201.60
50	14.70	318.10
75	13.17	407.50
100	11.50	274.58

Table 2.5.2 *The results of experiments in which groups of 5 rats were exposed to populations of* T.confusum *infected with* H.diminuta *for periods of 7 days. (Data from Coleman, 1978).*

No. beetles introduced into arena.	Mean no. cysticercoids per beetle.	Estimated no. cysticercoids introduced into arena $P_2(0)$.	No. beetles remaining after 7 days.	Estimated no. beetles eaten.	No. worms recovered from 5 rats P_1	Estimated no. cysticercoids eaten.	Estimated value β_1 (per cysticercoid per week per rat per 25ft^2)
25	5.6	140	16	9	27	50	0.043
25	5.6	140	8	17	86	95	0.191
50	0.8	40	29	21	32	17	0.322
50	3.2	160	23	27	60	86	0.094
100	2.1	210	44	56	35	118	0.036
100	3.2	320	46	54	191	173	0.182
200	2.3	460	119	81	160	186	0.085

Table 2.5.3 Developmental time delays in H.diminuta.

(a) In the intermediate host.
Replicates of 4 rats each infected with 10 cysticercoids.

Cysticercoid age.	No. worms recovered. Mean ± 95%C.L.	Variance
6	0	0
8	0	0
10	4.25 ± 2.34	5.69
12	8.75 ± 0.81	0.69
16	8.25 ± 1.07	1.19
24	8.50 ± 1.10	1.25

(b) In the definitive host.
Replicates of 8 faecal egg counts.

Days post infection.	1000 eggs/gm. faeces/10 worms. Mean ± 95%C.L.	Variance
10	0	0
14	0	0
15	0	0
16	0	0
17	3.93 ± 1.96	8.04
20	23.23 ± 3.00	19.01
22	38.53 ± 11.10	255.60
24	34.13 ± 5.80	69.91
30	30.68 ± 1.70	6.18
52	25.28 ± 4.36	39.61

Table 2.5.4 Cysticercoid age and density.

(a) The relationship between cysticercoid age and infectivity to the final host.

Replicates of 5 rats each infected with 10 cysticercoids.

Cysticercoid age. weeks	No. worms recovered. Mean ± 95%C.L.	Variance
2	9.40 ± 0.70	0.64
4	9.60 ± 0.70	0.64
6	7.20 ± 2.03	5.36
8	6.00 ± 0.78	0.80
10	5.20 ± 1.02	1.36
12	4.80 ± 1.29	2.16
14	4.20 ± 1.16	1.76

(b) The relationship between cysticercoid density in the intermediate host and infectivity to the final host.

Replicates of 4 rats each infected with 10 cysticercoids.

No. cysticercoids per beetle	No. worms recovered. Mean ± 95%C.L.	Variance
1 - 10	9.75 ± 0.42	0.19
11 - 20	9.00 ± 1.20	1.50
21 - 30	8.75 ± 0.81	0.69
31 - 40	9.50 ± 0.85	0.75
41 - 50	9.50 ± 0.85	0.75
51 - 60	9.25 ± 0.81	0.69

Table 2.5.5 *The relationship between adult worm recovery and worm age, at an infection level of 10 worms per rat.*

Weeks post infection.	No. worms recovered.	
	Mean ± 95%C.L.	Variance
4	9.00 ± 0.92	0.67
8	9.00 ± 1.60	2.00
16	8.00 ± 0.92	0.67
24	8.33 ± 1.41	1.56
56	8.00 ± 0.92	0.67
63	8.33 ± 1.07	0.89

Appendix 2

Stability properties of the models described in Sections 3 and 4

Appendix 2.1 The neighbourhood stability properties of the basic model (equations (3.1.12) and (3.1.13)).

This appendix outlines the analysis of the stability properties of the basic model; similar analysis pertains to those in Appendices 2.2 - 2.4.

The model under consideration has the mathematical form

$$dM_1/dt = H_2\beta_1 D_1 M_2 - M_1(b_1+\mu_1+\delta) - \delta M_1^2(k_1+1)/k_1 \qquad (A.1.1)$$

$$dM_2/dt = \lambda D_2 H_1 \beta_2 M_1/(\mu_3+\beta_2 H_2) - M_2(\mu_2+b_2+\beta_1 H_1) \qquad (A.1.2)$$

from which there are two possible equilibrium solutions; either

$$M_1^* = 0 \qquad (A.1.3)$$

or

$$M_1^* = \left[\frac{\lambda\beta_1\beta_2 H_1 H_2 D_1 D_2}{(\mu_3+\beta_2 H_2)(\mu_2+b_2+\beta_1 H_1)} - (b_1+\mu_1+\delta)\right]\frac{k_1}{\delta(k_1+1)} \qquad (A.1.4)$$

A linearized stability analysis of these equilibrium points may be carried out along standard lines (see, e.g., May, 1973). The temporal behaviour of M_1 and M_2 then goes as exp (Λ), where the stability-determining damping rates (or eigen values) Λ are given from equations (A.1.1) and (A.1.2.) by the quadratic equation

$$\Lambda^2 + A\Lambda + B = 0 \qquad \text{(A.1.5)}$$

Here

$$A \equiv (b_1+\mu_1+\delta) + 2\delta M_1(k_1+1)/k_1 + (\mu_2+b_2+\beta_1 H_1) \qquad \text{(A.1.6)}$$

and

$$B \equiv (\mu_2+b_2+\beta_1 H_1)(b_1+\mu_1+\delta+2\delta M_1(k_1+1)/k_1) - H_1 H_2 D_1 D_2 \beta_1 \beta_2 \lambda/(\mu_3+\beta_2 H_2) \qquad \text{(A.1.7)}$$

The requirement for neighbourhood stability is that the real part of both eigen values Λ be negative; the necessary and sufficient condition for this to be so is given by the Routh-Hurwitz criterion A>0 and B>0. From equation (A.1.6) it can be seen that A is always positive. The equilibrium points defined by equations (A.1.3) and (A.1.4) will thus be locally stable if B>0, that is if

$$(\mu_2+b_2+\beta_1 H_1)(b_1+\mu_1+\delta+2\delta M_1(k_1+1)/k_1) > H_1 H_2 D_1 D_2 \beta_1 \beta_2 \lambda/(\mu_3+\beta_2 H_2) \qquad \text{(A.1.8)}$$

By substitution from equation (A.1.4), it can be seen that the non-zero equilibrium solution of M_1^* will be locally stable if R > 1, where

$$R = \frac{\lambda H_1 H_2 \beta_1 \beta_2 D_1 D_2}{(\mu_3+\beta_2 H_2)(\mu_2+b_2+\beta_1 H_1)(b_1+\mu_1+\delta)} \qquad \text{(A.1.9)}$$

Similarly (by substitution from equation (A.1.3)), it follows that the equilibrium solution $M_1^* = 0$ will be locally stable provided R < 1.

Appendix 2.2 The neighbourhood stability properties of equations (3.2.5) and (3.2.6).

The local stability analysis of the coupled equations

$$dM_1/dt = \beta_1 D_1 H_2 M_2 - M_1(b_1+\mu_1+\delta) - \delta M_1^2(k_1+1)/k_1 \qquad (A.2.1)$$

$$dM_2/dt = \rho_2 \lambda M_1 H_1 D_2/(\mu_3 g_2+\lambda M_1 H_1) - M_2(\mu_2+b_2+\beta_1 H_1) \qquad (A.2.2)$$

may be carried out as outlined in Appendix 2.1. In this case

$$A \equiv K + 2CM_1 + G \qquad (A.2.3)$$

and

$$B \equiv KG + 2CGM_1 - JDE/(E+FM_1)^2 \qquad (A.2.4)$$

where $C = \delta(k_1+1)/k_1$, $D = \rho_2 \lambda H_1 D_2$, $E = \mu_3 g_2$, $F = \lambda H_1$, $G = (\mu_2+b_2+\beta_1 H_1)$, $J = \beta_1 D_1 H_2$ and $K = (b_1+\mu_1+\delta)$.

Since A is always positive, the equilibrium points generated by equations (A.2.1) and (A.2.2) will be locally stable provided

$$KG + 2CGM_1 > JDE/(E+FM_1)^2 \qquad (A.2.5)$$

Three equilibrium solutions are possible from equations (A.2.1) and (A.2.2); either

$$M_1^* = 0 \qquad (A.2.6)$$

or

$$M_1^*(1), M_1^*(2) = \frac{-(CGE+KGF) \pm \sqrt{(CGE+KGF)^2 - 4CGF(KGE-JD)}}{2CGF} \quad (A.2.7)$$

By substitution into equation (A.2.5), it can be seen that the equilibrium point defined by equation (A.2.6) will be locally stable provided $R < 1$, where

$$R = JD/EKG \quad (A.2.8)$$

Similarly, the stability conditions are satisfied by the positive value of M_1^* generated by equation (A.2.7) when $R > 1$.

Appendix 2.3 The neighbourhood stability properties of equations (3.3.5), (3.3.6) and (3.3.7).

The local stability of the coupled equations

$$dM_1/dt = \beta_1 D_1 M_2 H_2 - (\mu_1+b_1)M_1 \qquad (A.3.1)$$

$$dH_2/dt = (a_2-b_2)H_2 - \alpha M_2 H_2 - \beta_1 H_1 H_2 \qquad (A.3.2)$$

$$dM_2/dt = \beta_2 D_2 \lambda M_1 H_1/(\mu_3+\beta_2 H_2) - (\mu_2+a_2+\alpha)M_2 \qquad (A.3.3)$$

may be carried out along standard lines (see, e.g., May, 1973). The temporal behaviour of M_1 and M_2 then goes as exp (Λ) where the stability-determining damping rates, Λ, are given from equations (A.3.1), (A.3.2) and (A.3.3) by the expression

$$\Lambda^3 + X\Lambda^2 + Y\Lambda + Z = 0 \qquad (A.3.4)$$

Here

$$X \equiv J + DM_2 + B - C \qquad (A.3.5)$$

$$Y \equiv GEM_1DH_2/(F+GH_2)^2 - AH_2E/(F+GH_2) + DJM_2 - CJ + BJ + BDM_2 - BC \qquad (A.3.6)$$

and

$$Z \equiv GEM_1DH_2B/(F+GH_2)^2 + AEH_2(C-DM_2)/(F+GH_2) + AM_2DH_2E/(F+GH_2) + DBJM_2 - BCJ \qquad (A.3.7)$$

where $A = \beta_1 D_1$, $B = (\mu_1+b_1)$, $c = (a_2-b_2-\beta_1 H_1)$, $D = \alpha$,

$E = \beta_2 D_2 \lambda H_1$, $F = \mu_3$, $G = \beta_2$, $J = (\mu_2+a_2+\alpha)$.

The requirement for neighbourhood stability is that the real part of the eigen values Λ be negative; the necessary condition for this to be so is given by the Routh-Hurwitz criterion, $X > 0$; $Z > 0$; $XY > Z$.

By substitution of the equilibrium properties $M_2 = C/D$ and $BJ(F+GH_2) = AH_2E$, it can be shown that X and Z are always positive, and $XY > Z$ only if $GJ^2 > AE$.

The equilibrium point generated by equations (A.3.1), (A.3.2) and (A.3.3) is thus locally stable provided

$$(\mu_2+a_2+\alpha)^2 > \beta_1 D_1 D_2 \lambda H_1 \qquad \text{(A.3.8)}$$

Appendix 2.4 The neighbourhood stability properties of equations (4.2.1) and (4.2.2).

The local stability analysis of the coupled equations

$$dM/dt = \beta DE - (b+\mu_1+\delta)M - \delta M^2(k+1)/k \qquad (A.4.1)$$

$$dE/dt = \lambda MH - (\mu_2+\beta H)E \qquad (A.4.2)$$

may be carried out as outlined in Appendix 2.1. In this case

$$A \equiv (b+\mu_1+\delta) + 2\delta M(k+1)/k + (\mu_2+\beta H) \qquad (A.4.3)$$

$$B \equiv (\mu_2+\beta H)((b+\mu_1+\delta) + 2\delta M(k+1)/k) - \beta D\lambda H \qquad (A.4.4)$$

Since A is always positive, the equilibrium point generated by equations (A.4.1) and (A.4.2) will be locally stable provided

$$(\mu_2+\beta H)((b+\mu_1+\delta) + 2\delta M(k+1)/k) > \beta D\lambda H \qquad (A.4.5)$$

Two equilibrium solutions are possible from equations (A.4.1) and (A.4.2); either

$$M^* = 0 \qquad (A.4.6)$$

or

$$M^* = \frac{\beta D\lambda H - (b+\mu_1+\delta)(\mu_2+\beta H)}{(\mu_2+\beta H)(\delta(k+1)/k)} \qquad (A.4.7)$$

By substitution into equation (A.4.5), it can be seen that the equilibrium points defined by equations (A.4.6) and (A.4.7) will be locally stable provided $R < 1$ and $R > 1$ respectively, where

$$R = \frac{\beta\lambda DH}{(\mu_2+\beta H)(b+\mu_1+\delta)} \qquad \text{(A.4.8)}$$

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CONCOMITANT PREDATION AND INFECTION PROCESSES: AN EXPERIMENTAL STUDY

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SUMMARY

(1) The functional response of the fish predator *Brachydanio rerio* Hamilton-Buchanan to changes in the density of two prey species, *Daphnia magna* L. and the cercarial stage of the ectoparasitic digenean *Transversotrema patialense* (Soparkar), is shown to be of the type II form where the instantaneous predation rate is unaffected by changes in prey density.

(2) A model is developed to describe this functional response, based on the concept of predator satiation. The number of prey items required to create satiation is shown to be dependent on the experimental procedures used to elicit the functional response.

(3) The fish predator, *Brachydanio rerio*, acts in the dual role of predator/host for the cercarial stage of *Transversotrema patialense*. The concomitant predation and infection processes created by this ecological association are shown to be characterised by constant instantaneous predation and infection rates which appear to be unaffected by changes in prey/parasite density.

(4) The infection process is unaffected by density dependent constraints over a wide range of exposure densities and the number of parasites attached per host is shown to be directly proportional to cercarial numbers.

(5) Stochastic elements are shown to be important determinants in the dynamics of the infection process and overdispersion in the frequency distribution of the number of parasites attached per host is thought to be generated by heterogeneity between fish and heterogeneity in time created by changes in infective stage density.

(6) The relevance of concomitant predation and infection processes to the dynamics of digenean life cycles is discussed.

INTRODUCTION

The possible influences of predation on parasite population dynamics are twofold. First, many helminth parasite life cycles traverse one or more adjacent links in predator food chains; the completion of the life cycle being dependent on the predatory association between either host species or host and larval parasite. These predator–prey relationships are obviously important determinants in the evolution of host-parasite associations.

There is, however, a second means by which predation can influence the dynamics of a parasite population. In many cycles, transmission stages pass into the free living environ-

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ment in order to facilitate infection of new members of the host population or a new host species. These free living populations, (existing either as resistant eggs or mobile larvae), suffer predation losses imposed by a variety of animal predators. The cercarial stages of digenean parasites, for example, are often preyed upon by small aquatic predators, since the larvae are soft bodied and rich in nutrient reserves (Anderson & Whitfield 1975).

An intriguing ecological association arises in the life cycle of the ectoparasite digenean *Transversotrema patialense* (Soparkar). The cercarial stage of this parasite, an active aquatic larva, attaches to the surface of various species of freshwater fish (the parasite being loosely host specific in the adult form), where it grows to the adult form in the recesses under the fish scales. Many of its host species find the larvae an attractive prey item and hence act as both host and predator. The parasites ingested by the fish are unable to survive in the intestine of the host, since *T. patialense* is specifically adpated to an ectoparasitic existence on the surface of the fish. The size of a cercarial population within a habitat is therefore partly determined by the complex interplay of infection and predation processes operating concurrently.

A previous publication (Anderson, Whitfield & Mills 1977) examined, in general terms, the factors responsible for controlling the size of the cercarial and adult populations of *T. patialense*. This present paper explores the nature of the functional response of the fish predator/host (*Brachydanio rerio*, Hamilton-Buchanan), to changes in cercarial density and examines the influence of this response on the dynamics of infection of the host.

The paper is divided into three sections. First we examine predation in isolation from infection by exposing fish to various densities of a substitute prey species, the crustacean *Daphnia magna* L. A model, based on the concept of host satiation (Ivlev 1951), is formulated to describe the nature of the functional response of *Brachydanio rerio* within an experimental framework. The model's structure is discussed in relation to other models of the functional response component of predator-prey interactions (Rogers 1972; Murdoch & Oaten 1975; Hassell, Lawton & Beddington 1976, 1977).

In the second part of the paper we explore the dynamics of concomitant predation and infection when the predator/host is exposed to the larvae of *Transversotrema patialense*, the prey/parasite. We extend the model developed in the first section to encompass a description of the dynamics of infection in order to explore the relationship between infective stage density and infection rate.

Finally, we detail the influence of infective stage density on the probability distribution of the number of parasites per host and discuss the relevance of our experimental results and model predictions to the dynamics of digenean life cycles.

MATERIALS AND METHODS

Fish and parasite maintenance

Infections of *Transversotrema patialense* in their intermediate, snail host *Melanoides tuberculata* (Müller) and on their final host *Brachydanio rerio*, were maintained in the laboratory using the technique and conditions described in a previous publication (Anderson & Whitfield 1975).

Predation experiments: prey species Daphnia magna

Specimens of *Brachydanio rerio* (length class 20–30 mm), were used to assess the effect of prey density on predation rate. Two series of experiments were carried out. First, single predators which had been starved for 24 h prior to experimentation, were used to assess

the predation rate at varying prey densities, over a 5 min experimental time period. The arenas used consisted of glass crystallizing dishes, diameter 14·5 cm, containing 400 ml of water at 24–25 °C, in constant light. Direct counting of the initial and final prey densities allowed the number of prey eaten during 5 min to be estimated. Replicated trials, at least two at each density, were carried out over the range 5–220 *Daphnia magna* per 400 ml (size class 1·5–2·0 mm).

The second series of experiments were identical to the first, except that the experimental predators had been fed an excess of proprietary fish food 1 h before experimentation.

All the fish used in these experiments had prior experience of *D. magna* as a food source.

Predation and infection experiments: prey/parasite species Transversotrema patialense

Specimens of *Brachydanio rerio* in the length class 25–35 mm were used to examine the influence of cercarial density on the predation of these larvae and their infection of the fish host. Crystallizing dishes of diameter 19 cm containing 1 litre of tapwater were used as experimental arenas. Throughout the experiment, and for 1 h preceding it, they were kept at 24–25 °C in diffuse light of 150 lux intensity. Cercariae of *Transversotrema patialense* were collected at the same time on each day from a batch of snails infected 6 months previously. Cercariae of age 0–2 h were used in the experiments. Two hours prior to the experiment, five uninfected fish were placed in an arena containing an excess of food, an hour later they were removed and placed in a similar arena with no food. After a further hour, the fish were transferred to the arena containing the cercariae for the experimental time period of 5 min. The fish were then removed, a 40% formaldehyde solution was added and the remaining cercariae counted against a dark background. Between 18 and 72 h following the experiments the fish were anaesthetized, using MS 222 (Sandoz) solution at 1:8300 w/v in tapwater, and the number of attached adult parasites assessed. The number of cercariae predated were estimated by subracting the number remaining in the arena plus the number which successfully attached from the original cercarial density. Counting errors were estimated to be less than 2% over the density range, used, (5–400 cercariae per 1000 ml). Time course experiments were run on identical lines to the above but at a constant initial density of 200 cercariae per litre and over a range of exposure periods from 2·5 to 15 min.

RESULTS

The functional response of Brachydanio rerio *to changes in prey density*

To facilitate a better understanding of the predatory activities of *B. rerio*, in isolation from infection by *Trasversotrema patialense*, experiments were carried out to investigate the functional response of the fish to changes in the density of the prey species *Daphnia magna*.

The results of two series of experiments, in which the fish were subjected to differing feeding regimes prior to exposure to *D. magna* are shown in Fig. 1. In the first series of experiments (Fig. 1(a)) the predators were satiated 1 h before introduction into the experimental arenas by exposure to an excess of dried fish food. In contrast, the fish used in the second series of experiments were starved for 24 h before experimentation (Fig. 1(b)).

Within the framework of the terminology of Holling (1965), both functional responses are of the type II form, where the instantaneous predation (attack) rate does not alter significantly with changes in prey density. However, the upper asymptotes of the func-

tional response is clearly determined by the prior feeding experience of the predator (Fig. 1(a) and (b)). This asymptote, as discussed by, among others, Holling (1965), Murdoch & Oaten (1975) and Hassell *et al.* (1976), is generated by an amalgam of effects including the amount of time required to pursue, capture and consume a prey item (handling time) and the maximal ration a predator can consume due to its physiological and psychological states (satiation). Prior feeding experiences, before experimentation, will obviously alter satiation states and the amount of time (within the experimental time period) spent in hunting activities. As a broad generalization, within the literature on arthropod predation, handling time is usually envisaged as the generative mechanism creating the upper asymptote in a functional response (see Hassell *et al.* 1976). In the corresponding literature on vertebrate predation, causality is usually ascribed to satiation effects (Ivlev 1951).

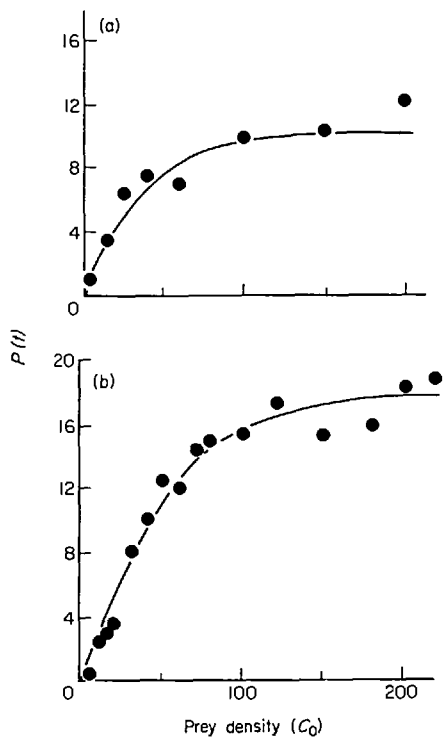

FIG. 1. The functional response of *Brachydanio rerio* to changes in density of the prey species *Daphnia magna*. $P(t)$ represents the number of prey eaten per fish per unit of time (5 min), and C_o the prey density at the start of the experiment. Solid circles—observed points; solid line—predicted functional response (eqn (7)). Graph (a): fish satiated 1 h prior to experimentation; $K = 11{\cdot}34$, $a = 0{\cdot}026$. Graph (b): fish starved for 24 h before experimentation; $K = 18{\cdot}12$, $a = 0{\cdot}023$.

Functional response model

In order to provide a framework for the consideration of concomitant predation and infection processes, we proceed in this section to construct a model, based on our experimental design, to describe the functional response of *Brachydanio rerio* in which we consider both handling time and satiation concepts.

The concept of handling time

Two differential equations can be formulated to mimic the dynamics of predation within our experimental design. These equations describe the rate of change, with respect to time, of $C(t)$, the number of prey left at time t, and $P(t)$, the number of prey consumed by time t. Since the experimental design excludes the addition of prey after time $t=0$, the initial prey density, C_o, is related to $C(t)$ and $P(t)$ for all values of t where

$$C_0 = C(t) + P(t).$$

We assume that the instantaneous predation rate α, (/prey/predator/unit of time) is constant and unaffected by changes in prey density. The net rate of predation is thus assumed to be directly proportional to prey density ($C(t)$) and predator numbers (F). The differential equations have the form

$$\frac{dP(t)}{dt} = \alpha C(t)F \tag{1}$$

$$\frac{dC(t)}{dt} = -\alpha C(t)F. \tag{2}$$

If the experimental time period is of length T time units and the handling and consumption of a prey item takes on average t_h time units then the solution of eqn (1) and (2) is obtained by integrating over the time interval zero to $(T - t_h P(t))$ and is of the form

$$P(t) = C_0[1 - \exp(-\alpha F(T - t_h P(t))]. \tag{3}$$

The integration limits $[0 \rightarrow (T - t_h P(t))]$ define the amount of time available to a predator, within the total experimental time period (T), for hunting prey. This period of time is obviously determined by the number of prey items captured ($t_h P(t)$). Equation (3) is the well known 'Random predator' equation, originally described by Rogers (1972), although here it is derived in a different manner. It is worth noting that the linear regression procedure outlined by Rogers (1972) for estimating the attack (instantaneous predation) rate, α, and the handling time coefficient, t_h, are subject to error. Non-linear least squares methods provide more accurate estimates of both parameters (i.e. Conway, Wilcox & Glass 1970).

Direct observation of predatory activity can, for certain biological systems, yield good estimates of the handling time parameter. In the case of fish predators feeding on small prey items, however, t_h tends to be extremely small (prey items being captured and consumed extremely rapidly) and hence difficult to measure. For this reason and others associated with our understanding of the biology of predation by *B. rerio*, we proceed in this paper to formulate a different model where the functional response component is based on the concept of predator satiation.

Maximal ration concept

We base our model construction on the assumption that a fish predator can only consume a finite amount of food (K units) within a unit of experimental time due to the effects of satiation. The concept of satiation relates both to the physiological and the psychological states of the predator. More precisely, the amount of food ingested in a unit of time will be a function of, among other factors, the capacity of the predator gut and the rate of digestion which determines the amount of food leaving the gut lumen per unit of time. These physiological determinants will generate behavioural changes in the preda-

tor's hunting activities and hence the rate of ingestion of prey items. This concept of satiation although rather simplistic, enables a rough biological interpretation to be placed on the maximal ration parameter K. For example, in the case of a starved predator feeding in a habitat or experimental arena with superabundant prey, the parameter K will be approximately equivalent to the number of prey items required to fill the predator's gut. This interpretation of predator satiation is analogous to Ivlev's 'maximal ration' (Ivlev 1951).

Within the framework of our experiments we envisage K as the number of prey items of a given size and type required to satiate a predator of known size during a unit of time. The value of K will obviously depend on a variety of factors within any given experimental design. For example, the upper asymptote (K) in the functional response of *B. rerio* to changes in *Daphnia magna* density (Fig. 1), will vary according to the feeding regimes to which a fish is exposed before experimentation.

We assume in our model that the predation rate α varies, during an experimental period, in relation to the number of prey items consumed. More exactly we assume that as the number of items consumed ($P(t)$) approaches K, α tends to zero. We represent this assumption as

$$\alpha = a(1 - P(t)/K) \tag{4}$$

where a is the instantaneous predation rate at the start of the experiment.

The model represented by eqn (1) and (2) can be modified to incorporate the assumption depected in eqn (4), where

$$\frac{dP(t)}{dt} = aF(1 - P(t)/K)\, C(t) \tag{5}$$

and

$$\frac{dC(t)}{dt} = -\frac{dP(t)}{dt}. \tag{6}$$

This new model has the solution

$$P(t) = C_0\left[1 - \exp\left(\frac{aF}{K}(C_0 - K)t\right)\right] \Big/ \left[1 - \frac{C_0}{k}\exp\left(\frac{aF}{k}(C_0 - K)t\right)\right]. \tag{7}$$

The predictions of this equation closely approximate the observed functional responses of *Brachydanio rerio* shown in Fig. 1. The parameters a and K were estimated by a non-linear least squares technique (Conway, Wilcox & Glass 1970).

The model contains the assumption that the parameter a is constant and unaffected by changes in prey density. Using eqn (7) it is possible to obtain estimates of a for various prey densities (C_0) in order to check the validity of this assumption. The values of a are shown in Fig. 2 and it can be seen that they remain approximately constant over a wide range of prey densities.

Two other points concerning the structure of eqns (5) and (6) are important. First, it is worth noting that the parameter K, representing maximal ration assumption, is related to the handling time concept of Holling (1959). The constant K can be envisaged as being approximately equal to T/t_h in the terminology of eqn (3).

The second point concerns an important limitation in the use of the model's predictions in interpreting experimental results. The model represented by eqns (4) and (5) is

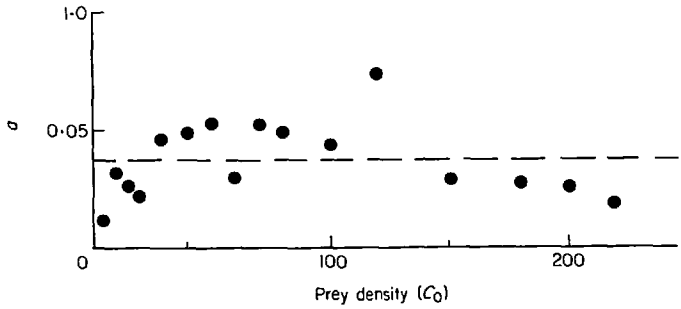

FIG. 2. The relationship between a, the instantaneous predation rate at the start of the experiment, and C_0, the initial prey density. Solid circles: observed rates; dashed line: best fit linear regression model ($a = xC_0 + y$, where $x = -0{\cdot}94 \times 10^{-4}$, and $y = 0{\cdot}0348$).

specifically designed to mimic the dynamics of predation within an experimental period of short duration. Over longer time periods, other biological mechanisms influence the shape of a functional response. Specifically, the rate of digestion and assimilation of consumed prey will influence the total number of prey items consumed (Nakamura 1977). To encompass predatory activities over longer time periods eqn (4) should contain an additional positive term which mimics the rate at which a predator becomes 'hungry' again due to food digestion, food assimilation and energy consumption (Rashevsky 1959; Nakamura 1972a, b, 1977). In reality the instantaneous predation rate is determined by two components acting in opposition. The effects of satiation tend to decrease α, while the rate of digestion of food and energy utilisation acts to increase this rate.

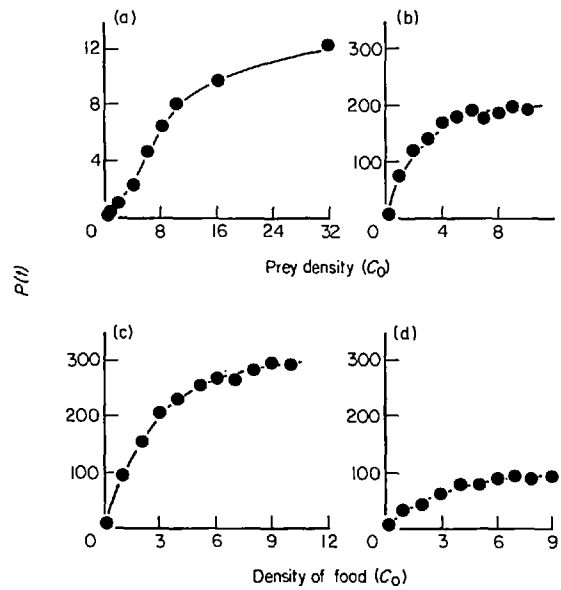

FIG. 3. Functional responses of four fish species to changes in prey density. Graph (a): *Lepomis macrachirus* (L.) feeding on mosquito larvae (data from Murdoch & Oaten 1975). Graph (b): *Rutilus rutilus* (L.) feeding on chironomid larvae (data from Ivlev 1951). Graph (c): *Cyprinus cyprinus* (L.) feeding on dried fish food (data from Ivlev 1951). Graph (d): *Alburnus alburnus* (L.) feeding on *Daphnia magna* (L.) (data from Ivlev 1951). Solid circles: observed points, solid lines: functional response curve (fitted by eye). $P(t)$ and C_0 as defined in Fig. 1.

The form of the functional response of *B. rerio* to *Daphnia magna* is approximately type II in nature, the instantaneous rate of predation appearing to be unaffected by changes in prey density. Other studies of the predatory activities of fish species have demonstrated similar patterns. Four such responses are shown in Fig. 3, where all but one (graph (a)) is of the type II form. A crucial determinant of the form of such predator responses to changes in prey density appears to be the state of 'familiarity' of the predator with the prey species. As noted by Murdoch & Oaten (1975) fish learn to recognize prey species as potential food sources. Fish which have had prior experience of eating a particular prey species usually exhibit type II functional responses since they immediately initiate hunting activity once placed in an experimental chamber containing the previously encountered prey. In contrast, fish which have no previous experience of a particular prey species may show type III responses, since initially at low prey densities they fail to encounter an item sufficiently often to enable recognition of it as a potential food source. At high densities, frequent encounters enable rapid recognition to occur and hence generate active hunting behaviour. The fish used in our experiments had all gained prior experience of the prey species *D. magna* and hence our observed type II responses are consistent with the observations of Murdoch & Oaten (1975) and Ivlev (1951).

Predation and infection operating concomitantly

The experimental results and theoretical framework described in the preceding section form a template for considering the dynamics of concomitant predation and infection processes. In this section we describe the nature of the functional response of *Brachydanio rerio* to changes in the density of *Transversotrema patialense* cercariae and how this response influences the infection of the fish by larval digenean parasites. The fish plays the part of both predator and host while the larval digenean acts as both prey and parasite infective agent.

The results of a series of experiments, in which records were kept of both the number of larvae eaten by the fish and the number which managed to establish themselves as ectoparasites on the surface of the host, are illustrated in Fig. 4. The predation functional response of *Brachydanio rerio* to changes in cercarial density (Fig. 4(a)) is of the type II pattern and similar to that recorded in Fig. 1. The net rate of infection of the host appears from Fig. 4(b), to be approximately directly proportional to cercarial exposure density. The number of parasites establishing in the scale recesses varies almost linearly with larval density.

Model of predation and infection dynamics

The model outlined in the previous section (eqns (5) and (6)) based on the concept of predator satiation, can be expanded to incorporate a description of the dynamics of concomitant infection.

For reasons associated with exploring certain stochastic aspects of infection, which are detailed at a later stage in this paper, we define $P(t)$ and $I(t)$ as the number of prey eaten and parasites established per *five fish*, per unit of time (Fig. 4). We assume, for simplicity, that the instantaneous rate of infection b per five fish, per cercaria, per unit of time is constant and unaffected by changes in cercarial density. The net rate of infection is therefore assumed to be directly proportional to the density of *Transversotrema patialense* larvae in an experimental arena.

The model of the rate of change of $P(t)$ and $I(t)$ with respect to time is obtained by modifying eqns (5) and (6) in the manner

$$\frac{dP(t)}{dt} = a(1 - P(t)/K)\, C(t) \tag{8}$$

$$\frac{dI(t)}{dt} = bC(t) \tag{9}$$

$$\frac{dC(t)}{dt} = -\left[\frac{dP(t)}{dt} + \frac{dI(t)}{dt}\right] \tag{10}$$

where

$$C_o = I(t) + P(t) + C(t). \tag{11}$$

The variable F, the number of fish, is excluded from the equations since the rates a and b and the parameter K are defined per five fish in order to mimic the experimental design used to obtain the results represented in Fig. 4. Equations (8), (9), (10) and (11) yield the solution

$$P(t) = K[1 - \exp(-\mathrm{I}(t)\mathrm{a}/(bK))]. \tag{12}$$

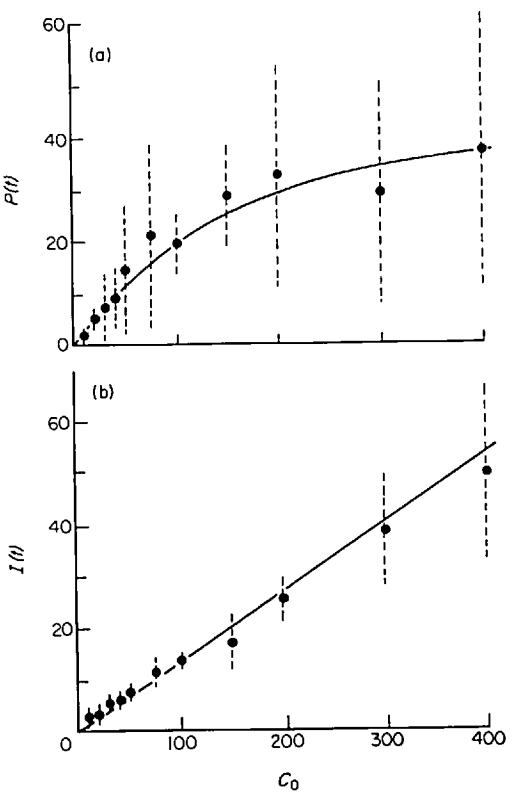

FIG. 4. Concomitant predation and infection. Graph (a): the functional response of *Brachydanio rerio* to changes in the density of *Transversotrema patialense*. P(t) represents the number of prey items consumed per 5 min period by five fish and C_0 the initial prey density. Graph (b): the relationship between the number of cercariae attaching to *Brachydanio rerio* and infective stage density. $I(t)$ represents the number of parasites attaching per five fish. Solid circles: observed means; dashed vertical lines: 95% confidence limits (five replicates); solid line: prediction of predation/infection model (eqns (8) and (9)). $K = 40{\cdot}26$, $a = 0{\cdot}329$, $b = 0{\cdot}157$.

This model provides a good fit to the experimental results recorded in Fig. 4 as shown in Fig. 5(a) where $P(t)$ is plotted against values of $I(t)$. The robustness of the model to changes in experimental design is demonstrated in Fig. 5(b), where the observed values of $P(t)$ and $I(t)$ were obtained from a series of experiments utilising single fish per arena which had been starved for 24 h prior to experimentation. Parameter estimates of K and a/b were obtained by a non-linear least squares technique.

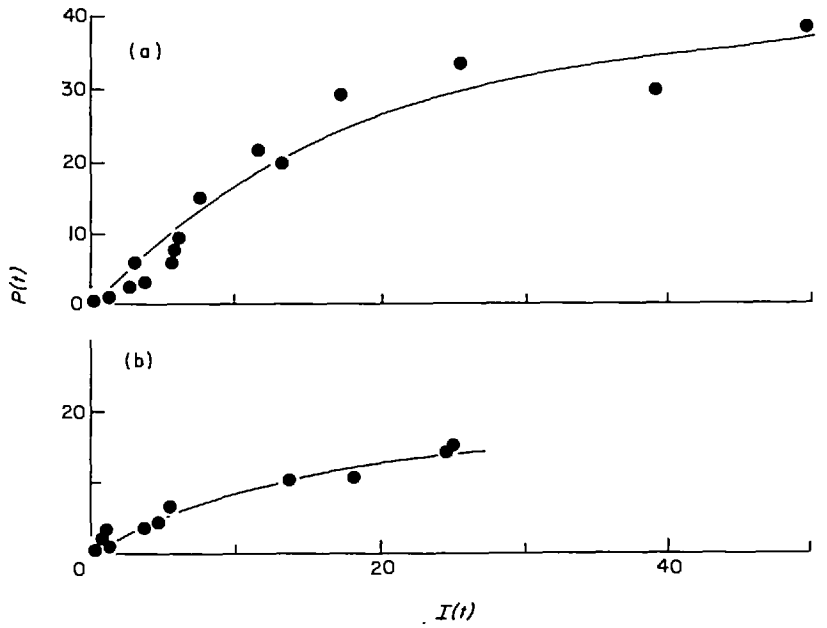

FIG. 5. The relationship between the number of cercariae predated, $P(t)$, and the number of larvae which attach to the surface of the host, $I(t)$. Graph (a): $P(t)$ and $I(t)$ defined per five fish with C_0 density ranging from 0–400 cercariae per 1000 ml. $K=40{\cdot}26$, $a/b=2{\cdot}088$. Graph (b): $P(t)$ and $I(t)$ defined per fish with C_0 density ranging 0–220 cercariae per 1000 ml. $K=16{\cdot}69$, $a/b=1{\cdot}22$. Solid circles: observed means; solid lines: model predictions (eqn (12)).

It has not proved possible to obtain explicit expressions for $P(t)$ and $I(t)$ in terms of the parameters a, b and K and the time variable t. Equations (8), (9) and (10), however can be solved numerically provided estimates of a, b and K are available. Equation (12) yields estimates of K, the maximal ration, and a/b the ratio of the instantaneous predation rate divided by the instantaneous infection rate. A method for obtaining separate estimates of a and b is outlined in the Appendix.

Numerical solution of eqns (8), (9) and (10) (given estimates of a, b and K) yields the model predictions illustrated in Fig. 4. Theoretical predictions closely mimic both the dynamics of the predator-prey functional response (Fig. 4(a)), and the host-parasite infection process (Fig. 4(b)). The relationship between $I(t)$ and C_0, predicted by the model, appears to be approximately linear in Fig 4(b). This relationship, however, is not absolutely linear due to the effects of predation on the pool of infective stages. These effects vary as C_0 changes due to the influence of fish satiation at high cercarial densities. The good agreement between predicted and observed results supports the realism of the biological assumptions incorporated in the model. In particular, it is interesting to note that the instantaneous infection rate b appears constant over a wide range of infective

stage densities. To our knowledge, this is one of the first experimental verifications of the commonly made assumption in theoretical studies that the rate of infection of a host is directly proportional to the density of infective stages within a habitat.

In the absence of predation ($P(t)=0$ for all values of t) eqn (9) predicts that a plot of $I(t)$, the number of parasites establishing on the surface of the fish versus initial cercarial density (C_0) would be linear with slope β and intercept zero. In a single unit of time ($t=1$),

$$\beta=[1{\cdot}0-\exp(-b)]. \tag{13}$$

When predation and infection are occurring concurrently the predicted and observed pattern of infection (Fig. 4(b)) deviates from linearity due to the influence of predation losses on the pool of infective stages. This feature of concomitant predation and infection is illustrated more clearly in Fig. 6. Here the functional responses of the number of prey eaten and number of parasites established, in relation to changes in prey/infective stage density, are compared with model predictions of predation occurring in isolation from infection (Fig. 6(a), and infection occurring in isolation from predation (Fig. 6(b)).

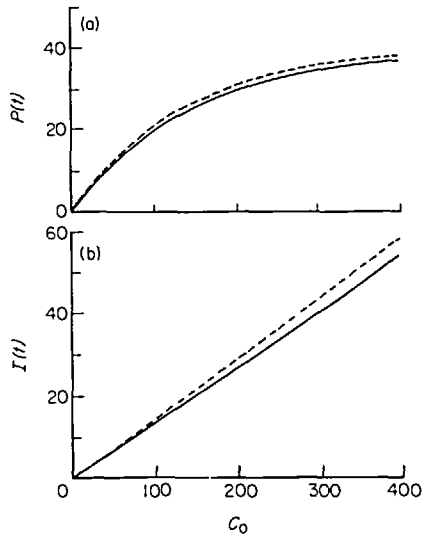

FIG. 6. The relationship between the number of cercariae predated ($P(t)$—graph (a)), and the number of larvae which attach to the surface of the host ($I(t)$—graph (b)), with the initial cercarial density (C_0). A comparison of the predictions of the model fitted to the observed results (eqn (12)) where infection and predation occur concomitantly (solid line) and model predictions of the two processes acting in isolation (dashed line). Graph (a): predation acting in isolation from infection. Graph (b): infection acting in isolation from predation.

A more pronounced deviation from a linear relationship between $I(t)$ and C_0, than that portrayed in Fig. 4(b), would occur if the functional response of the predator to changes in prey density is of the type III form, where the predation rate increases as prey density rises. The model can easily be modified to illustrate this point and a set of predictions are shown in Fig. 7. These results were obtained using a model in which the predation rate was assumed to rise to an upper asymptote as prey density increases (see Hassell, Lawton & Beddington 1977). When cercarial density (C_0) is low infection losses from the prey/infective stage pool ($C(t)$) are proportionately greater than predation losses. However, when the predation rate increases as prey density rises, predation losses overtake infection

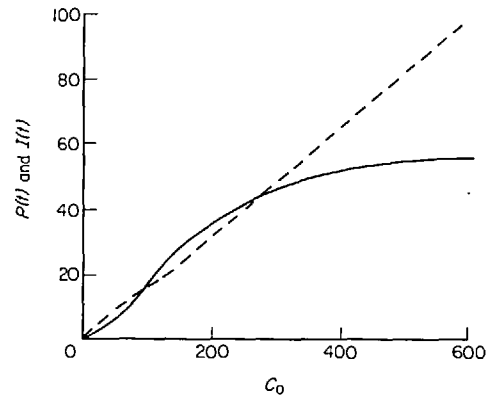

FIG. 7. The effect of a type III functional response, where the predation rate, a, is a function of prey density (see text) on the relationship between $P(t)$ and $I(t)$ with C_0. $P(t)$, $I(t)$ and C_0 as defined in Fig. 6); dashed line—$I(t)$, solid line—$P(t)$.

losses. Once satiation occurs (as $P(t)$ approaches k) infection again overtakes predation and continues to increase in a linear fashion with C_0.

Stochastic elements in the infection process

Heterogeneity between fish

Chance elements play an important role in infection processes and their independence, or lack of, determine to a large extent the nature of the frequency distribution of parasite numbers per host.

As explained previously, the experimental design used to obtain the results recorded in Fig. 4(b), entailed the use of five fish per experiment (all placed in the same arena). At each density of cercariae, five replicate experiments were performed. This procedure produced at least twenty-five individual records, for each value of C_0 (exposure density), of the number of parasites attached per host. The frequency distributions of parasite numbers per fish for each initial exposure density of cercariae are recorded in Figs 8 and 9. The results are interesting, since the form of the frequency distribution changes as cercarial density rises. The pattern is underdispersed at low exposure densities (Fig. 8(a)–(c)), random at intermediary levels (Fig. 8(d)–(g)) and overdispersed at high densities (Fig. 8(h), Fig. 9(a)–(f)). The positive binomial distribution provides a good empirical fit to the underdispersed patterns, the Poisson to the random distributions and the negative binomial to the overdispersed patterns. The goodness of fit of these theoretical probability distribution models to the observed data are shown in Figs 8 and 9.

The underlying generative processes creating the observed distribution patterns appear to be essentially random in nature at low cercarial densities. The tendency to underdispersion at very low densities is due to the finite nature of the maximum number of parasites that can attach to a single fish within the experimental time period. The generative mechanism underlying underdispersed distributions are essentially random as in the case of the Poisson model. The interesting feature of these results, however, is the tendency to overdispersion at high exposure densities.

It has not proved possible to obtain an analytical solution to the stochastic analogue of the model defined in eqns (8)–(10). Numerical results, however, are obtainable by means of simulation studies based on the model framework. A pseudo-random number genera-

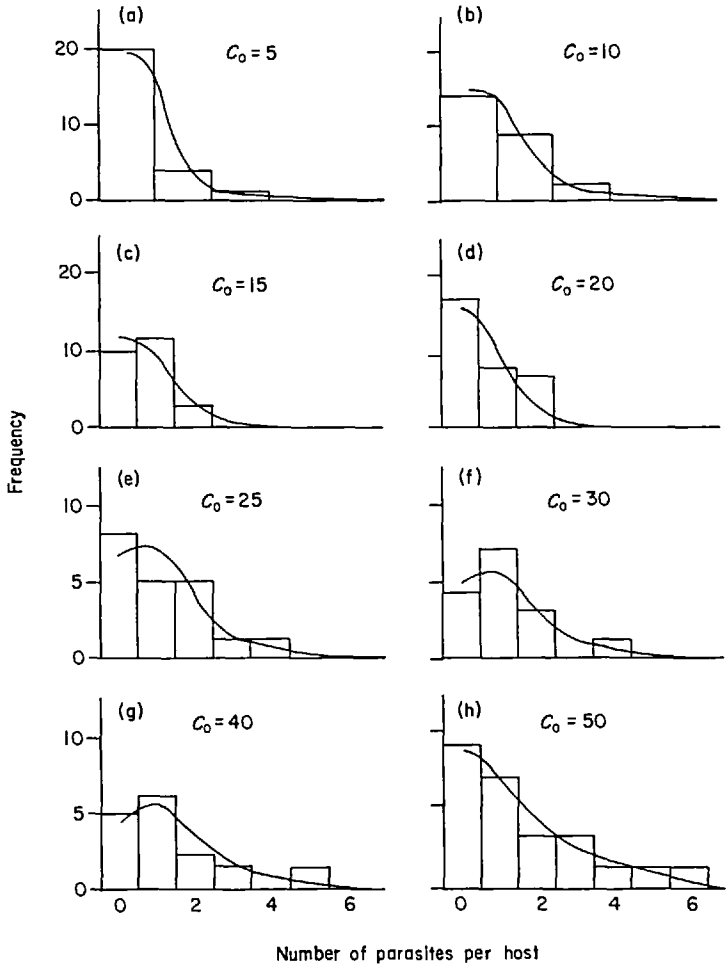

FIG. 8. The relationship between the frequency distribution of number of parasites attached per fish and C_0 the initial prey density. The histograms represent observed frequencies while the solid lines represent the predictions of various theoretical probability distribution models. The nature of the distribution changes as C_0, the initial prey density, varies. The positive binomial distribution is a good empirical model for the observed results in graphs (a), (b) and (c) where C_0 is 5, 10 and 15 respectively. The Poisson distribution is a good empirical model for the observed results in graphs (d), (e), (f) and (g) where C_0 is 20, 25, 30 and 40 respectively. The negative binomial distribution provides a good fit to the observed patterns in graph (h) where C_0 is 50.

tor can be used to estimate the time to an event (i.e. successful infection or consumption of a prey item) and which of the two types of event occurs at this point in time (see Pielou 1969). A large number of simulation runs were performed and a frequency distribution of the number of parasites per host constructed for the range of cercarial densities used in the experiments (Fig. 4(b)). The stochastic simulation model predicts a Poisson distribution of parasite numbers per host for all but the lowest cercarial densities where a tendency to underdispersion is apparent. The observed and simulated variance to mean ratios of the number of parasites per host are illustrated in Fig. 10.

A stochastic model of a pure infection process (in the absence of predation), based on the experimental design used to obtain the results detailed in Fig. 4(b) predicts a Poisson

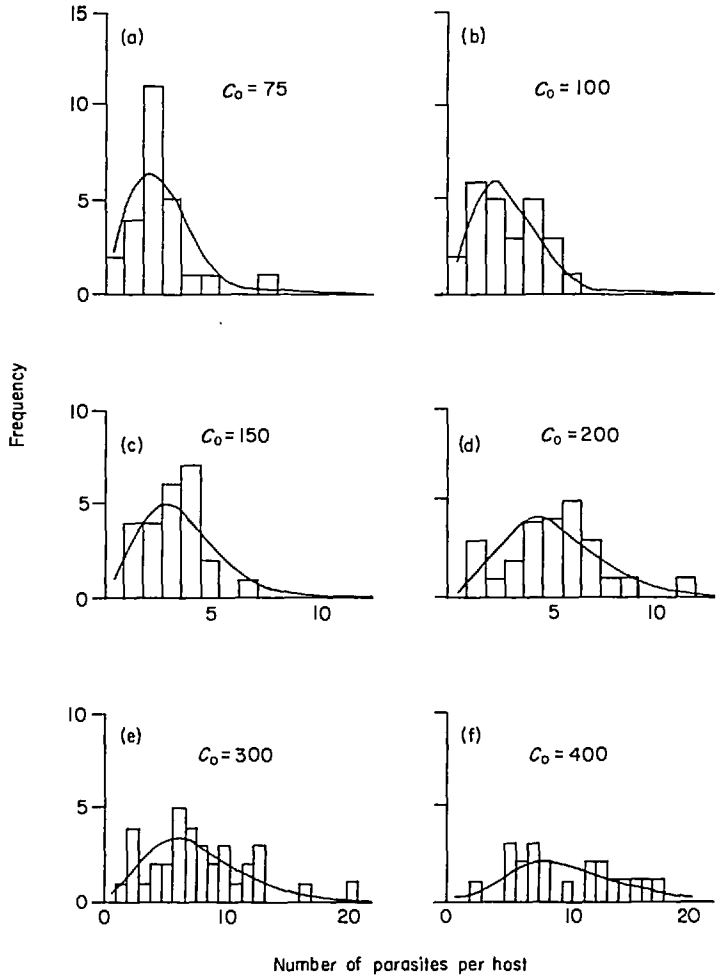

FIG. 9. The axes of the graphs are as defined in Fig. 8. The negative binomial distribution provides a good empirical model for all the patterns shown in this figure. Graph (a) $C_0 = 75$; graph (b) $C_0 = 100$; graph (c) $C_0 = 150$; graph (d) $C_0 = 200$; graph (e) $C_0 = 300$; graph (f) $C_0 = 400$.

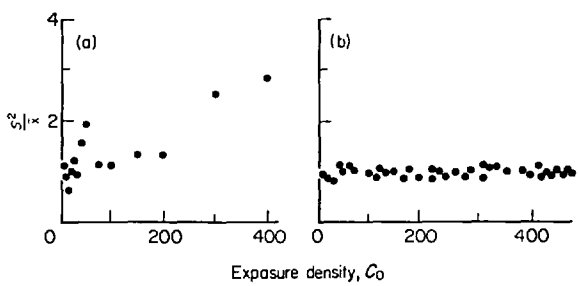

FIG. 10. Graph (a): the observed relationship between the variance to mean ratios ($S^2/\bar{x}$) of parasite numbers per host and cercarial exposure density (C_0). Graph (b): the relationship between the variance to mean rates of parasite numbers per host and C_0 predicted by the stochastic simulation model.

distribution of the number of parasites per host (Anderson 1976a). The basic assumption in this type of model is that the instantaneous infection rate b, is constant and unaffected by changes in infective stage exposure density or the number of parasites already attached to a host. The simulation results of demographic stochasticity in the concomitant infection and predation process predicts a similar pattern (Fig. 10(b)). The discrepancy between theoretical predictions and observed patterns strongly suggests heterogeneity in the behavioural patterns within the population of fish used in our experiments. Such heterogeneity could be generated by a variety of behavioural mechanisms. For example, the host behavioural response elicited by the presence of large numbers of attached parasites may vary widely between fish. Alternatively, activity levels of individual fish, when placed in experimental arenas may also vary widely. Stationary or slow moving hosts may present easier targets for infective stages, or, conversely, very active fish which traverse large volumes of water may come into contact with larger numbers of cercariae. Behavioural hypotheses to account for the observed patterns in parasite numbers per host must take into account the marked trend for increased heterogeneity as cercarial exposure rises. In other words, behavioural heterogeneity within a fish population must itself increase with infective stage density. This suggests that predation activity may play an important role. To pinpoint exactly the generative mechanisms creating behavioural changes, further detailed experimental work is required.

Heterogeneity in time

The dimension of time is inextricably linked with all infection processes. Within our previous experimental designs we have artificially constrained the infection process, from moving to completion, by terminating all the experiments at a fixed point in time (5 min). We now consider the question of how time itself influences the distribution of parasite numbers per host.

A series of experiments were carried out in which the initial cercarial density (C_0) was held constant (200 cercariae/1000 ml) and the experiments were allowed to continue for varying periods of time. Each experiment utilized five fish in a single arena and was repeated five times. The observed frequency distributions of the number of parasites per host, illustrated in Fig. 11, demonstrates an interesting trend. As the period of exposure to the infective stages increases, the distribution of parasite numbers per host becomes more and more overdispersed. At 2·5 min the pattern is random, the Poisson distribution being a good empirical model. At 5·0, 7·5, 10·0 and 15·0 min, however, the patterns are overdispersed, the negative binomial model adequately fitting the data (the 5·0 min result is a direct replicate of the distribution shown in Fig. 9(d) which is also over-dispersed in nature). The value of k, the parameter of the negative binomial which inversely measures the degree of aggregation or heterogeneity, decreases as the time parameter increases. However, as recently pointed out by Taylor, Woiwod & Perry (1978) the variance to mean ratio (see inset in Fig. 11) is probably a better measure of the degree of aggregation due to the difficulty in ascribing a biological interpretation to the value of k.

The patterns are most probably generated by the combined influences of two distinct processes. First, as already discussed, heterogeneity between fish will tend to create an underlying pattern of overdispersion (see Fig. 9(d)). More importantly, however, the changing density of infective stages ($C(t)$) through an experimental period, due to removals created by predation and successful infection, will generate differing mean net rates of infection ($b\,C(t)$) at each point in time. The final observed pattern of parasite numbers per host will be created by a series of Poisson events through time each occurring

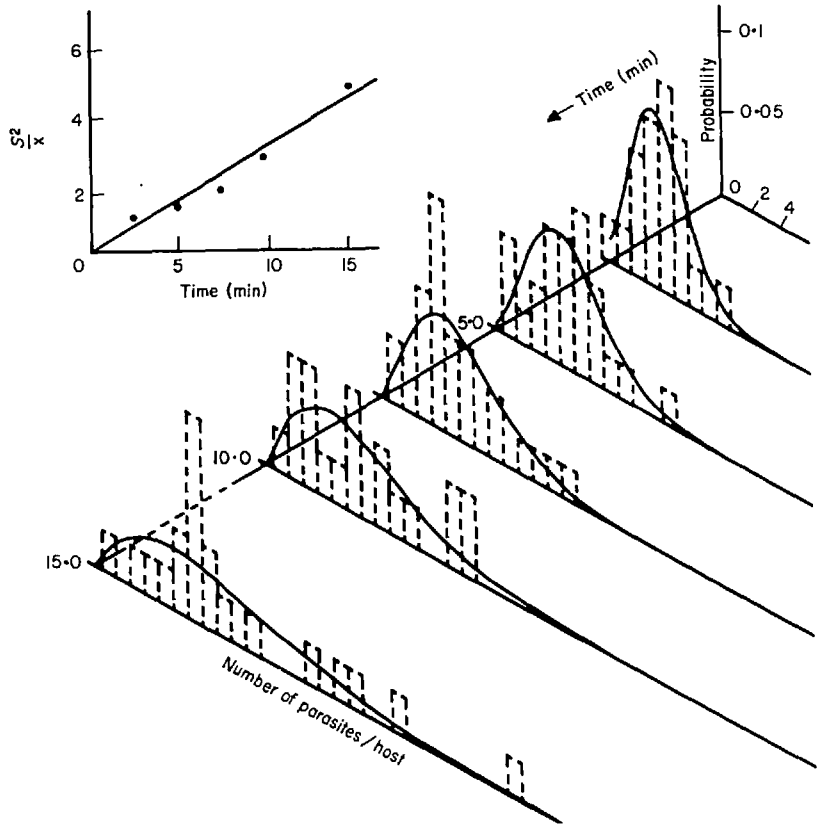

FIG. 11. The relationship between the frequency distribution of parasite numbers per host and period of exposure to the larval parasites. The histograms represent observed frequencies while the solid line presents the predictions of various theoretical probability distribution models. At 2·5 min, the Poisson model provides a good empirical model while at 5·0, 7·5, 10·0 and 15·0 min the negative binomial model closely approximates observed results. The initial prey density, C_0, equals 200 cercariae for all time periods. The *inset* graph shows the relationship between the observed variance to mean ($S^2/\bar{x}$) ratios and length of host exposure period to the infective larvae. Solid circles—observed values; solid line—best fit linear model ($S^2/\bar{x} = Z$ t, $Z = 0{\cdot}247$).

at a different mean infection rate. The compounding of a series of heterogeneous Poisson distributions generates overdispersion which may under certain circumstances, relating to the distribution of the Poisson means, be of the negative binomial form (Pielou 1969). The longer the time course of an experiment the greater the degree of compounding of Poisson means leading to higher degrees of overdispersion (see Fig. 11). The validity of this hypothesis is supported by simulation studies, where overdispersion can be generated by running simulation experiments over longer time periods than reported previously (see Fig. 10(b)). In such experiments, provided the time parameter is large enough, overdispersion can be generated over a wide range of initial cercarial densities (C_0).

One final point of importance concerns the use of the negative binomial distribution as a descriptor of the overdispersed or aggregated patterns of parasite dispersion. We have used this distribution simply for empirical convenience. The adequacy of this model in describing our data is not in itself informative due to the many biological mechanisms that can generate patterns which appear to be of the negative binomial form (see Taylor, Woiwood & Perry 1978 for a detailed discussion of this point). The significance of our

results lies in the change of the dispersion pattern from random to aggregated as both the time of exposure to infection and infective stage density increase.

DISCUSSION

The work described in this paper forms part of a continuing study of the population biology of the ectoparasitic digenean *Transversotrema patialense*. The concomitant predation and infection processes constitute a single component in the complex indirect life cycle of this parasite. The component is, however, of major importance since it contains one of the two infection processes occurring within the cycle. The second infection sequence occurs at the miracidial-snail interface, through which the parasite gains entry to its intermediate molluscan host (*Melanoides tuberculata*).

Predation is important to the dynamical properties of the life cycle of *Transversotrema patialense* in the degree to which predation losses suppress the size of the cercarial population in a given habitat. In addition, however, predation plays a further ecological role. Predatory behaviour of small fish species (many of which are potential hosts) serves to enhance the chances of contact between cercariae and host. There is a trade off in the dynamics of the parasite life cycle, between the gains of bringing potential hosts into close proximity of the larvae and losses due to predatory activities.

How important are these losses in natural habitats? This question is difficult to answer without a detailed knowledge of firstly, how attractive the larvae are in comparison with other food sources and secondly, the range of species which actively predate the cercariae. This last point is important since it is probable that not only a wide range of fish predators, both surface, mid-water and bottom dwellers, eat the larvae but also a range of invertebrate predators are likely to find cercariae an attractive food source. In a given habitat, therefore, the structure of the aquatic animal community, in terms of the number and abundance of predatory species will influence the size of the free-living pool of infective stages.

The attractiveness of the larvae in relation to other food sources, such as planktonic crustacea and other small invertebrates, is an obvious area for experimental investigation and will be examined in a future publication.

Assuming for the present that the larvae are an important food source for certain fish species, how will the nature of the functional responses of the predators to changes in prey density influence the dynamics of the parasite life cycle? Our experiments suggest that the functional response is of the type II form in the absence of other, perhaps larger and hence more attractive food sources. Since the predation rate is constant in relation to changes in cercarial density, such functional responses do not have a regulatory influence on the dynamics of predator-prey interactions. In contrast, however, if the response is altered to the type III form, in the presence of other prey species, the fish being stimulated to feed on the larvae only when they are very abundant, then such a response is potentially regulatory in nature. A type III response, in which the predation rate is an increasing function of cercarial density, will tend to stabilize the size of the prey population provided the equilibrium level falls in the region of prey densities in which the predation rate increases with rises in cercarial density (Murdoch & Oaten 1975; Hassell, Lawton & Beddington 1976). Once satiation levels have been reached the predator ceases to regulate prey population growth.

This form of predation in parasite life cycles can, under certain conditions, act as a density dependent constraint within the dynamics of the cycle, preventing unregulated

growth of parasite populations. Only one such constraint is required within extremely complex parasite life cycles, involving many host and parasite populations, to achieve regulated growth within the complete cycle (Anderson 1976b).

The infection process in the host-parasite association between cercariae and fish is somewhat analogous, in dynamical terms, to a component within the functional response of the predator-prey interaction. We can, therefore, term the relationship between the number of parasites established on a host and infective agent density the infection functional response. It is worth noting that the manner in which parasite burden influences the death rates of individual hosts is also a major component in the 'parasite functional response'.

Our experimental results, aided by the theoretical model predictions, strongly suggest that the instantaneous infection rate is constant and unaffected by changes in cercarial density. From a biological point of view this result is intuitively sensible and lends support to the often made assumption in theoretical studies of host-parasite associations, that the net rate of infection is directly proportional to infective agent density (Lotka 1925; Kostitzin 1934; Anderson 1974). Our observations, however, are restricted to a specific range of exposure densities (5–400 larvae/1000 ml). They therefore do not preclude the possibility that at extremely high cercarial densities, either interference between larvae on the surface of the host or irritation to the host itself, may generate a decrease in the rate of infection. Ultimately, of course, a fish of given size only possesses a finite number of scales and hence can only harbour a finite number of parasites. At this end of the infection spectrum, density-dependent effects resulting from intraspecific competition for a finite resource, will limit infection rates.

The dynamics of the infection functional response will also be influenced by the density of hosts within a given habitat. For example, within an experimental arena high host densities coupled with low infective stage density will lead, in a finite period of time, to exhaustion of infective agents and hence decreasing infection rates through time. This type of mechanism will also occur in natural habitats since a pool of infective stages is always susceptible to exhaustion provided the host population is large enough.

Demographic stochasticity plays an important role in the dynamics of concomitant predation and infection processes. In this paper we specifically considered the influence of cercarial density and duration of host exposure to infection, on the distribution of parasite numbers per host. Overdispersion was created by two distinct biological mechanisms, one behavioural and the other associated with changes in the density of infective stages through time. Overdispersed distributions of parasite numbers per host play an important role in the dynamics of host-parasite associations. In the life cycle of *T. patialense* their importance will be associated with the influence of the adult parasite on the natural intrinsic growth rate of its host population. We believe, for example, that the adult stage of the parasite is capable of increasing the mortality rate of its host if present in large enough numbers. More specifically the rate of parasite induced host mortality will be some function of parasite burden for a given size class of host. It is therefore apparent that the statistical distribution of parasite numbers per host will determine the net rate of parasite induced host mortalities within the host population.

Furthermore, the form of this statistical distribution determines not only the regulatory influences of the parasite on host population growth but also the stability of the host-parasite interaction. This area of the dynamical properties of host-parasites has recently been explored by Anderson & May (1978). These authors note that the literature on the dispersion of parasites within host populations is dominated by reports of overdispersed

distributions. The experimental results reported in this present paper suggest generative mechanisms of such patterns which appear to be of wide importance in host–parasite associations where infection is achieved by a free-living larval stage.

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APPENDIX

This Appendix outlines a method of estimating the instantaneous predation (a) and infection (b) rates.

Once a predator has become satiated with prey and reached the maximal ration level K in the functional response (see Fig. 4(a)) infection proceeds unhampered by the effects of predation. In such circumstances a plot of number of parasites established on the surface of the fish versus cercarial exposure density will yield a straight line of slope β where

$$\beta = [1{\cdot}0 - \exp(-b)] \tag{A1}$$

(see text eqn (13)).

By linear regression methods the instantaneous rate of infection b per unit of time can be estimated using eqn (A1) where

$$b = -\ln(1{\cdot}0 - \beta). \tag{A2}$$

In Fig. 4 of the main text it can be seen that the functional response of *Brachydanio rerio* to changes in density of *Transversotrema patialense* is rapidly approaching an asymptote (K) around densities exceeding 200 larvae/1000 ml.

In Fig. 4(b), therefore, the slope of the infection functional response will approach β after densities of 200 larvae/1000 ml and such a line with this slope will have an intercept of K on the cercarial density axis (C_0). These points are illustrated graphically in Fig. 12.

The dotted straight line with slope β has an intercept of K on the C_0 axis. In order to approximately estimate β, a linear regression model can be constructed to pass through

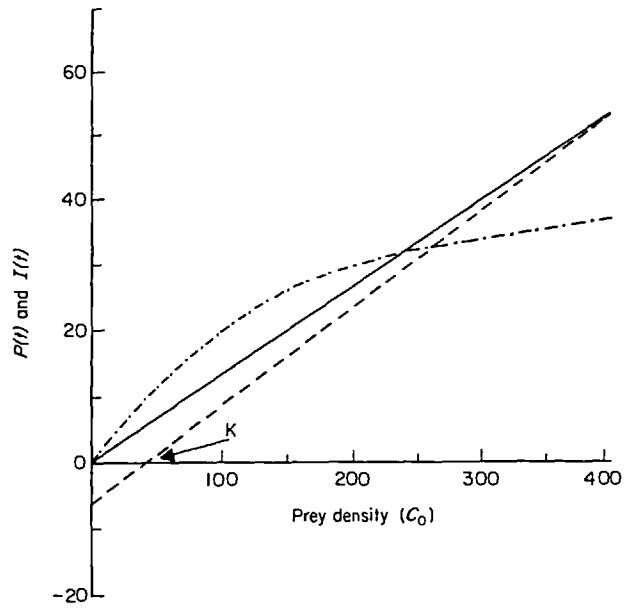

FIG. 12. Estimation of the instantaneous predation (a) and infection (b) rates. The curved dotted line represents the functional response of the fish predator (number of prey items consumed $P(t)$) to changes in prey density (C_0) as predicted by eqn (8). The solid line represents the relationship between $I(t)$, the number of parasites attached to the fish and C_0 as predicted by eqn (9). The dotted straight line has slope β (see text of Appendix) and intercepts the C_0 axis at the point K.

the point $(K,0)$. The observed points used for the regression analysis should be those values of $I(t)$ (number of parasites attached to the five experimental hosts) which occur in the region of the C_0 axis where the functional response curve approaches K. In Fig. A1 this occurs at a value of C_0 of approximately 200. The regression model constrained to go through the point $(K,0)$ gives the following estimate of

$$\beta=\left[\frac{\Sigma C_0 I-K\Sigma I}{K^2-2K\Sigma C_0+\Sigma C_0^2}\right]. \tag{A3}$$

Using eqns (A2) and (A3) an approximate value of b can be obtained. Given b an estimate of a is available, since the ratio a/b has already been estimated (see main text).

It is important to note that this method of estimation is crude and tends to underestimate the value of b and conversely overestimate the value of a. This bias is created by the gradual approach of values of $P(t)$ to K as C_0 increases. The corresponding values of $I(t)$ are thus too low and hence the value of the slope β, estimated from the regression passing through these points, is too small.

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With 5 figures in the text

The dynamics of infection of *Tribolium confusum* by *Hymenolepis diminuta*: the influence of infective-stage density and spatial distribution

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SUMMARY

The mean parasite burden of a population of *Tribolium confusum* is shown to rise to a plateau as the exposure density of infective eggs of *Hymenolepis diminuta* increases. The level of this plateau is shown to be dependent on the nutritional status of the host population, being depressed from approximately 18 cysticercoids/beetle in hosts which have been starved prior to experimentation, to approximately 2 cysticercoids/beetle in satiated hosts. A simple model is used to describe the shape of this infection functional response in terms of the predator–prey interaction between hosts (*T. confusum*) and parasite infective stages (*H. diminuta* eggs). The distribution of successful infections/host is shown to be over-dispersed, even when hosts are exposed to infective stages arranged in a uniform spatial pattern. The over-dispersion of parasite numbers/host is shown to become more severe as the spatial pattern of infective stages changes from under-dispersed, through random, to over-dispersed. Experimental results are discussed in relation to the dynamics of parasite–host interactions, in which infection takes place by host ingestion of a free-living infective stage.

INTRODUCTION

The transmission of parasites from host to host is often achieved by means of a free-living infective stage. In such cases, the rate of encounter between prospective hosts and infective stages will be influenced by both the densities of the organisms concerned and their respective spatial distributions (Crofton, 1971*a*; Anderson, 1978*a*).

Recent studies have explored the impact of infective-stage density on the dynamics of parasite transmission from host to host, in associations where infection takes place by means of either parasite attachment to the surface of the host (Anderson, Whitfield & Dobson, 1978) or direct penetration of the host epithelial layers (Anderson, 1978*b*).

The present paper examines the dynamics of parasite transmission where infection is achieved by the ingestion of infective stages by the host. Processes of this form are directly comparable to predator–prey interactions. The host, in

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its role as predator or grazer, either actively consumes the parasite, or ingests it passively as a contaminant of other items of prey.

We report the results of a series of laboratory experiments designed to display the influence of infective-stage density and spatial distribution on the dynamics of infection of a specific host–parasite interaction; namely, the infection of the intermediate arthropod host, *Tribolium confusum*, by the tapeworm, *Hymenolepis diminuta*. Specifically, we consider the impact of (*a*) infective-stage density on the rate of parasite establishment within the host/unit of time and (*b*) the influence of infective-stage spatial distribution on the distribution of successful infections within a population of intermediate hosts.

We discuss the relevance of our experimental results in the context of the overall population dynamics of host–helminth parasite associations.

MATERIALS AND METHODS

Parasite maintenance and collection

H. diminuta was routinely maintained in the laboratory in albino rats and *T. confusum* beetles. Faeces from rats with tapeworm infections of known age and density were collected over a 6-day period and the tapeworm eggs were recovered using the sucrose gradient method described by Lethbridge (1971). (Preliminary experiments had shown that eggs maintained in rat faeces at room temperature retain their infectivity for periods of up to 60 days.) The concentration of the resulting egg suspension was estimated by standard haemocytometric methods. The beetles used in the infection experiments were of approximately uniform age (20–24 days) and, except where otherwise stated, had been starved for 6 days prior to experimentation. Infection experiments were carried out at 30 ± 1 °C and 70% rel. hum.

Experiments to assess age-dependent infectivity of H. diminuta *eggs under experimental conditions*

Infection experiments were carried out in circular arenas measuring 13 cm^2 in area. By pipetting a known volume of egg suspension onto filter paper lining the base of the arena, an estimated density of 3000 parasite eggs was introduced into each of 7 arenas. Thirty beetles were introduced into each arena after periods of 0, 15, 30, 60, 90, 120 and 195 min from the introduction of the egg suspensions. The beetles were removed from each arena after an exposure period of 24 h and the number of parasites established/host was measured by beetle dissection after a period of 2 weeks.

Infective-stage density experiments

Infection arenas (base area 13 cm^2) were set up as described previously, containing estimated egg densities of 6000, 3000, 2400, 1800, 1200, 600, 500, 300, 180 and 60/arena. Immediately after introduction of the egg suspensions, beetles (30/arena) were placed in each arena for a period of 24 h. Two separate series of experiments were performed. In the first series the beetles were starved for 6

days prior to introduction into the arena. In the second series, the beetles were maintained in food medium until introduction into the infection arena. After a period of 2 weeks the beetles were dissected and counts made of the number of larval parasites/beetle.

Infective-stage spatial distribution experiments

Arenas of basal area 200 cm^2 were lined with filter paper on which were delineated ten 4×5 cm quadrats. Four different spatial patterns (each replicated twice) were created by pipetting known volumes of egg suspension into each quadrat of the infection arenas. These patterns ranged from uniform (undispersed) with a variance to mean ratio of eggs/quadrat approaching zero, to extreme spatial aggregation (over-dispersion) with a variance to mean ratio of eggs/quadrat of 2700. The two intermediate distributions had variance to mean ratios of eggs/quadrat of 300 and 540 respectively. The total egg density/arena was maintained at a constant initial level of 230 eggs/13 cm^2 (i.e. 3000 eggs/arena), irrespective of the egg spatial distribution. Beetles were placed into the arenas (30/arena) immediately after the introduction of the egg suspensions, for a period of 3 h, after which they were removed, fed and dissected 2 weeks later to assess parasite burdens.

RESULTS

Age-dependent infectivity of eggs

The rate of acquisition of larval parasites by hosts within an infection arena will depend not only on the density of eggs present and the feeding behaviour of the host, but also on the survival and infectivity of the parasite transmission stages. Non-feeding, motile infective stages, such as miracidia and cercariae of digeneans, have short life-spans measured in hours rather than days. Invariably, the duration of the period in which a successful infection can occur, if contact with a potential host is made, is shorter than the expected life-span of the larval parasite (Anderson & Whitfield, 1975). Cestode eggs are non-feeding and non-motile, relying on passive transfer from host to host. They tend to have fairly long expected life-spans in the free-living environment, although the duration of this life-span is critically dependent on the environmental conditions prevailing in the free-living habitat.

The experimental conditions under which *T. confusum* was exposed to infection by *H. diminuta* were non-optimal for parasite survival. This point is clearly illustrated by the results displayed in Fig. 1. The rate of acquisition of larval parasites declined rapidly as the period in which eggs remained on the dry filter paper linings of the infection arenas lengthened. The infectivity of the eggs declined almost to zero in the space of 3 h. This is in contrast to the retention of infectivity of eggs maintained in rat faeces, which, as mentioned earlier, was shown to last for periods of up to 60 days. In natural habitats, egg viability will depend critically on the water content of the rat faeces, which will itself depend on the humidity of the external environment.

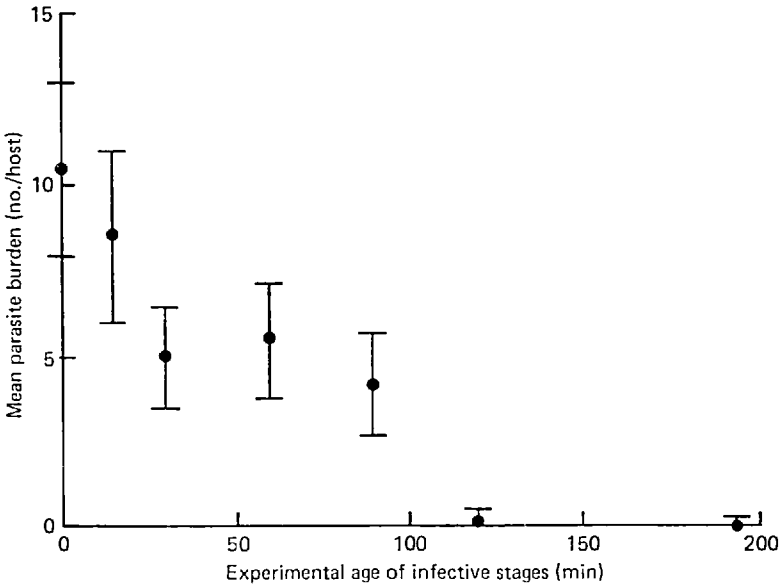

Fig. 1. The relationship between the mean number of parasites/host and the length of time the eggs had been present in the infection arena prior to exposure to the hosts.

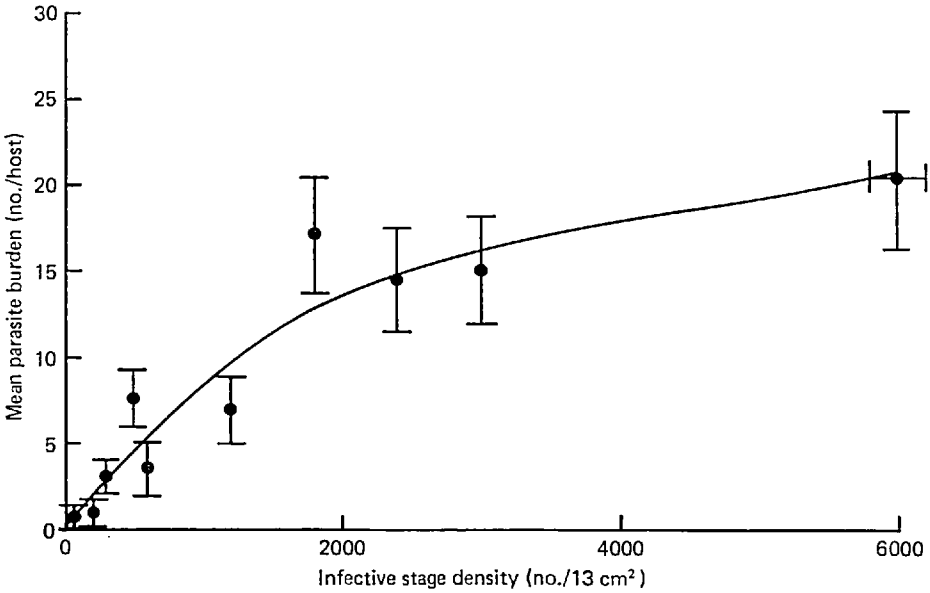

Fig. 2. The relationship between the mean number of parasites/beetle (P_t/H) and the density of infective stages to which the beetles were exposed (E_0), using beetles which had been starved for 6 days prior to experimention. The solid line represents the predictions of the functional response model defined in equation (3) and the solid circles are observed means. The horizontal bar represents the 95% confidence limit of the estimated egg density. (t_h = 0·026 days, α = 0·011/day, T = 1 day.)

The influence of infective-stage density on the rate of parasite establishment

The acquisition of the parasite by *T. confusum* results from the ingestion of the infective egg stage. Starved beetles, when placed in experimental arenas with no alternative food source, actively search for and consume the eggs of *H. diminuta*.

The relationship between the mean parasite burden/host and the density of *H. diminuta* eggs to which the starved hosts were exposed is portrayed in Fig. 2. It is clear that the relationship is non-linear; the mean number of larval parasites/host rising to a plateau of between 15 and 20 larvae/beetle as egg exposure density increases. This pattern differs markedly from that observed in studies of the relationship between parasite burden and infective-stage density, where the infective agent (cercaria or miracidium) is *not* ingested by the host, but attaches to, or penetrates through, the body wall of the host. Such studies have revealed linear relationships between the numbers of parasites established/host and infective-stage density (Anderson *et al.* 1978; Anderson, 1978*b*).

The non-linear pattern portrayed in Fig. 2 could be generated by 2 distinct types of biological mechanism; namely, (*a*) density-dependent constraints on parasite population growth within individual hosts, or (*b*) limitations on the rate of acquisition of infection imposed by the feeding behaviour of the beetle.

Density-dependent constraints

Hosts of a given age and hence size will only be able to harbour a finite number of parasite larvae due to physical constraints imposed by the size of the parasites' micro-environment (coelom of the beetle) within the exoskeleton of the host. Competition for other resources, in addition to space, may also generate density-dependence in parasite population growth within a single host. For example, available food resources may limit parasite survival, growth and infectivity. In addition, density-dependent constraints may also result from host responses to parasitic invasion (Anderson & May, 1978). It is well established that density-dependent processes act to reduce the rate of larval growth within the intermediate host when the density of parasites is high (Voge & Graiwer, 1964; Soltice, Arai & Scheinberg, 1971). However, it is not established as yet whether density-dependent mechanisms reduce either the rate of establishment of *H. diminuta* in the body cavity of *T. confusum* or the survival of the cysticercoids within the host.

We do not consider density-dependent constraints to be a causal mechanism for the plateau in Fig. 2 for two reasons. In the first place, strong evidence against the density-dependent hypothesis is provided by the observation that starved beetles acquire much higher parasite burdens than their well-fed counterparts (Figs 2 and 3). Secondly, much higher mean worm burdens/beetle than those recorded in Fig. 2 can be created by repeatedly exposing beetles to infection.

Limitations on the rate of acquisition of infection imposed by the feeding behaviour of the host

As a result of the predatory behaviour of *T. confusum*, the dynamics of infection is to a large extent controlled by the dynamics of the predator–prey interaction

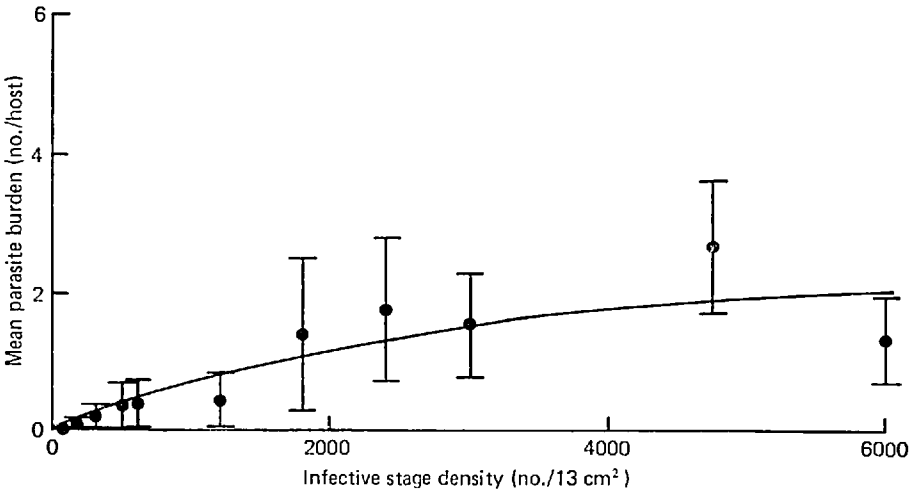

Fig. 3. The relationship between the mean number of parasites/beetle (P_t/μ) and the density of infective stages to which the beetles were exposed (E_0), using beetles which were satiated prior to experimentation. The solid line represents the predictions of the functional response model defined in equation (3) and the solid circles are observed means. (t_h = 0·485 days, α = 0·0005/day, T = 1 day.)

between the beetle host and tapeworm egg. A clear indication of this point is provided by the experimental results displayed in Figs 2 and 3. Starved beetles acquired much higher average worm burdens than their well-fed counterparts. This pattern is undoubtedly associated with the differing predatory activities of the starved and satiated hosts.

A well-documented feature of predator–prey associations is the so-called *functional response* of predators to changes in prey density (see Holling, 1965; Hassell, Lawton & Beddington, 1976). The number of prey items consumed by a predator/unit of time rises to a plateau as prey density increases (such a pattern is clearly illustrated in Figs 2 and 3). The generative mechanisms of such non-linear relationships are associated with the tendency of predators to become satiated in the presence of an unlimited supply of food and the constraints imposed within a finite period of predatory activity by the amount of time required by a given predator to handle and consume a prey item (commonly referred to as *handling time*).

As a broad generalization, within the literature on arthropod predation, handling time is usually envisaged as the generative mechanism creating the upper asymptote of the functional response (the relationship between number of prey items consumed and prey density) (Hassell *et al.* 1976). In the corresponding literature on vertebrate predation, causality is usually ascribed to satiation effects (Ivlev, 1961). Both concepts are obviously closely interrelated.

The dynamics of ingestion of H. diminuta *eggs by* T. confusum

We may consider the dynamics of infection within the framework of a predator–prey interaction incorporating the concept of a finite 'handling time' (t_h). This parameter is assumed to reflect the average time taken by an individual beetle to handle and consume an egg of the tapeworm parasite.

Two differential equations can be formulated to mimic the dynamics of predation within our experimental design. These equations describe the rate of change, with respect to time, of $E(t)$, the number of eggs left in the arena at time t, and $P(t)$, the number of eggs ingested by time t. Since our experimental design excludes the addition of eggs after time $t = 0$ (the start of the infection experiment) the initial egg density E_0 is related to $E(t)$ and $P(t)$ for all values of t where

$$E_0 = E(t) + P(t).$$

We assume that the instantaneous egg ingestion rate, α, (/egg/beetle/unit of time) is constant and unaffected by changes in egg density. The net rate of ingestion (or predation) is thus assumed to be directly proportional to egg density ($E(t)$) and beetle (host) numbers (H). The differential equations have the form

$$\frac{dP(t)}{dt} = \alpha E(t) H, \tag{1}$$

$$\frac{dE(t)}{dt} = -\frac{dP(t)}{dt}. \tag{2}$$

If the experimental time period in which beetles are allowed to ingest eggs is of length T time units and the handling and consumption of an egg takes an average t_h time units, then the solution of equations (1) and (2) is obtained by integrating over the time interval 0 to $(T - t_h P(t))$ and is of the form

$$P(t) = E_0 (1 - \exp(-\alpha H(T - t_h P(t)))). \tag{3}$$

The integration limits (0 to $(T - t_h P(t))$) define the amount of time available to a beetle, within the total experimental time period (T), for searching for eggs (prey). This period of time is obviously determined by the amount of time taken up by the handling and consumption of 'discovered' eggs ($t_h P(t)$). Equation (3) is well documented in the ecological literature and was originally described by Rogers (1972), although here it is derived in a different manner. The equation predicts that the number of eggs ingested/beetle ($P(t)/H$) will rise to an asymptote (value T/t_h) as the egg density to which the beetle is exposed increases.

The functional relationship between $P(t)/H$ and E_0 predicted by equation (3) is identical to the patterns displayed in Figs 2 and 3. The model can be fitted to these observed patterns by the use of a non-linear least squares method (Conway, Glass & Wilcox, 1970) and comparisons of observed and predicted values are shown in Figs 2 and 3. The goodness of fit of the model to the observed data strongly supports the assumption that the observed relationship between parasite burden and egg density is determined by the predatory behaviour of the host.

It is important to note, however, that the estimates of α and t_h obtained by

fitting the model (equation (3)) do not accurately reflect the true rates of egg ingestion and egg handling time within our experimental arenas. The observed number of parasites established/host is not an accurate measure of the number of eggs ingested. A large number of tapeworm eggs fail to hatch in the intestine of *T. confusum* and pass through the gut with the faeces of the host to the external environment. Voge & Berntzen (1961) and Berntzen & Voge (1965) have demonstrated that a pre-requisite for egg hatching is physical disruption of the egg-shell wall. Such disruption results from mechanical damage by the mouthparts of the host during egg ingestion. Even if the eggs hatch successfully in the gut of the host, the midgut tissue wall of the beetle presents a formidable barrier to the penetrating hexacanths and hence many parasites become trapped within the gut wall and eventually die (Voge & Graiwer, 1964; Lethbridge, 1971; Anderson & Lethbridge, 1975). It is apparent, therefore, that the number of parasites that successfully establish in the beetle represents only a proportion of the total number ingested. The number that establish within the host, however, is likely to be a constant proportion of the number ingested. It appears unlikely that the density of eggs ingested will influence the proportion of eggs that hatch and the proportion that successfully penetrate the gut wall. This point, however, requires experimental verification.

A second factor which will tend to decrease the net rate of parasite acquisition by the hosts through time is loss of egg infectivity. However, egg mortalities during the course of an infection experiment are *not* responsible for generating the plateau in the functional response of parasite burden versus egg density (Figs 2 and 3). More specifically, if the instantaneous egg death rate is constant and the infective egg population exhibits exponential decay through time (as shown by Fig. 1), then, at a given point in time during the course of an infection experiment, the density of viable eggs will decrease in direct proportion to the density of eggs introduced at time $t = 0(E_0)$.

The important point to emerge from the experimental results portrayed in Figs 2 and 3 is that the rate of infection of the beetle is *not* simply proportional to infective-stage density, but conditional on the feeding behaviour of the host. Host behaviour imposes a maximum rate of infection/unit of time, irrespective of the density of infective agents to which *T. confusum* is exposed. The magnitude of this maximum rate is critically dependent on the nutritional status of the host as indicated by the observations displayed in Figs 2 and 3 of the rate of acquisition of parasites by starved and well-fed hosts. It is important to note, however, that this maximum rate will also depend on other factors. Dunkley & Mettrick (1971), for example, have demonstrated that the rate of acquisition of infection was dependent on temperature, days of beetle starvation before exposure to infection, duration of exposure to eggs and the age (and hence size) of the host. These authors concluded that food intake controlled the action of these factors.

The influence of the spatial distribution of infective stages on infection

The dynamics of any infection process is influenced by the relative spatial distributions of infective agents and hosts as well as their respective average

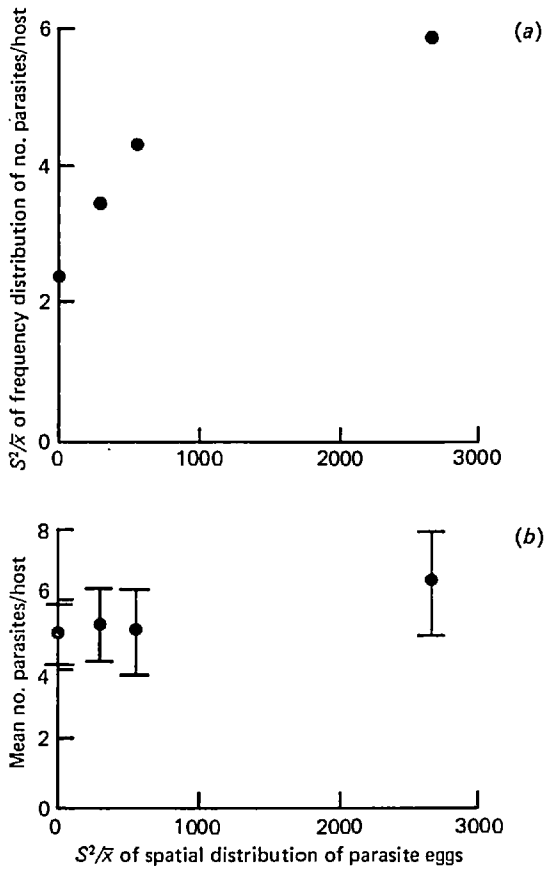

Fig. 4. (a) The relationship between the variance to mean ratio ($S^2/\bar{x}$) of the frequency distribution of the number of parasites/host and the variance to mean ratio of the spatial distribution of eggs in the infection arena. (*b*) The relationship between the mean parasite burden of the host population and the variance to mean ratio of the spatial distribution of eggs in the infection arena. The vertical bars represent the 95 % confidence limits of the means.

densities/unit area. The relevance of these spatial distributions to infection processes has often been alluded to, but never investigated experimentally. Crofton (1971*b*), for example, suggested that spatial clumping of infective stages was a contributary factor to observed patterns of over-dispersion in parasite numbers/host. Such patterns are commonly observed within natural host–parasite associations (Anderson, 1978*a*).

The impact of egg spatial distribution on the rate of acquisition of cysticercoids of *H. diminuta* by *T. confusum* was tested by varying the distribution of tapeworm eggs within the experimental infection arenas.

As portrayed in Fig. 4*b*, the average rate of parasite acquisition (measured by the mean cysticercoid burden/beetle) remained approximately constant for all the spatial patterns tested. The slope of the regression line of mean parasite burden (dependent variable) against variance/mean ratio of egg density/quadrat

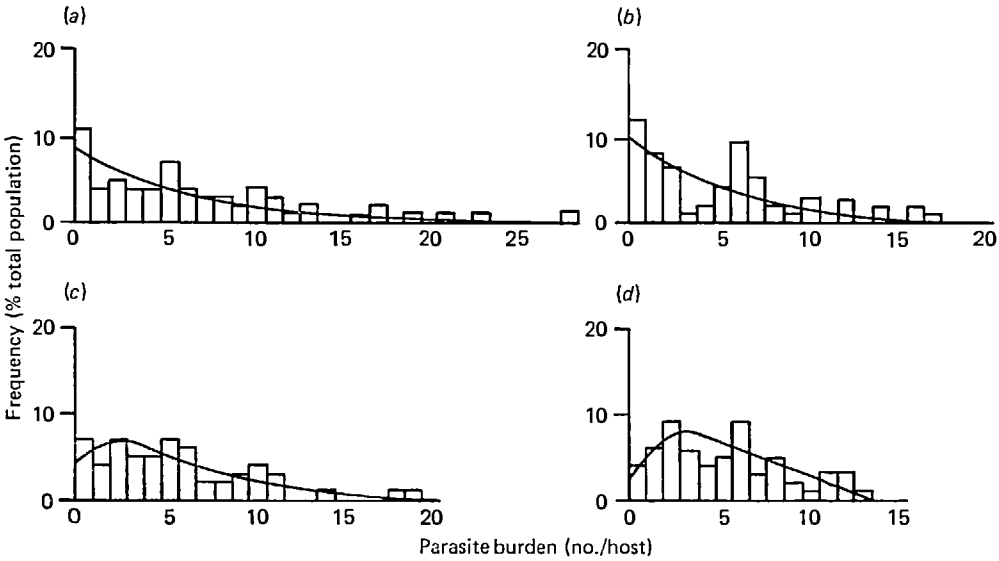

Fig. 5. The relationship between the frequency distribution of the number of parasites/host and the spatial distribution pattern (as defined by variance to mean ratio, $S^2/\bar{x}$) of the eggs to which the population was exposed. The histogram bars represent observed frequencies (as percentage of total host population) while the solid line curve represents the predictions of the negative binomial probability distribution model. (*a*) $S^2/\bar{x} = 2700$, $k = 1{\cdot}04$, $\chi^2_{17} = 11{\cdot}92$; (*b*) $S^2/\bar{x} = 540$, $k = 1{\cdot}02$, $\chi^2_{13} = 24{\cdot}58$; (*c*) $S^2/\bar{x} = 300$, $k = 1{\cdot}81$, $\chi^2_{13} = 11{\cdot}42$; (*d*) $S^2/\bar{x} = 0$, $k = 2{\cdot}88$, $\chi^2_{11} = 13{\cdot}06$.

(independent variable) was not significantly different from zero (D.F. = 2, P ($t = 2{\cdot}69$) > 0·1). The frequency distribution of parasite numbers/host, however, changes dramatically (Fig. 5). Even when the eggs were uniformly distributed within the infection arenas, the distribution of cysticercoids/beetle was over-dispersed or aggregated in form (Fig. 5*d*). As the spatial distribution changes via random to aggregated, the frequency distribution of parasite numbers/host becomes more over-dispersed or contagious (through Figs 5*c* and 5*b* to Fig. 5*a*).

The negative binomial probability distribution, a model defined by 2 parameters, the mean and a parameter k which varies inversely with the degree of over-dispersion, provides a good empirical description of the observed distributions of parasites/host (Fig. 5). Interestingly, a plot of the variance to mean ratio of parasites/host (a direct measure of over-dispersion) against the variance to mean ratio of egg density/quadrat suggests that the degree of over-dispersion in parasites/host tends to an upper asymptote as the distribution of eggs becomes highly aggregated (Fig. 4*a*).

Two important points emerge from these results. First, a degree of over-dispersion in parasite numbers/host is generated even when the spatial distribution of eggs is uniform. The generative mechanisms of such patterns are probably associated with heterogeneity in predatory behaviour between members of the beetle populations used in the infection experiment. Heterogeneity in host

behaviour (within a population of hosts) has been shown to be an important determinant of the frequency distribution of parasite numbers/host by other experimental studies of infection dynamics (Anderson *et al.* 1978; Anderson, 1978*b*). Second, spatial heterogeneity in infective-stage distribution accentuates these differences but interestingly does not appear to alter the average rate of parasite acquisition within a population of hosts.

CONCLUSIONS

The experimental results reported in this paper reveal two population mechanisms which are of some considerable significance to the overall population dynamics of *H. diminuta* within its two-host life-cycle.

Many parasitic species traverse adjacent links in community trophic webs by means of predator–prey links. Undoubtedly, such links have played an important role in the evolution of complex multi-host parasite life-cycles. Their frequency, however, amongst helminth parasite life-cycles suggests that the dynamical constraints on parasite flow through a life-cycle imposed by predator–prey links must not be disadvantageous to the stability and persistence of parasite populations.

The results displayed in Figs 2 and 3 reveal a regulatory constraint on the flow of *H. diminuta* through its life-cycle. Even when parasite egg density is very high within a specific habitat, the rate of acquisition of parasites by the intermediate host will reach an asymptote as egg density rises as a result of the feeding behaviour of the host. Where alternative and more desirable food sources are available to *T. confusum*, undoubtedly this maximum rate of parasite intake will be low (as suggested in Fig. 3). Hence where parasite transmission depends on a predator–prey link, either between infective agent and host or intermediate and final host, the functional response of the predator to changes in prey density acts as a density-dependent constraint on parasite population growth within the host (predator) population. In the life-cycle of *H. diminuta* 2 such predator–prey links exist; between egg and beetle and between beetle and rat. The combined action of both associations will provide a strong regulatory force on the population growth of the parasite.

Predator functional responses will also influence the impact of the parasite on its host populations. Cysticercoids of *H. diminuta* act to reduce the survival and reproductive capabilities of the beetle intermediate host in a manner directly related to the number of parasites harboured/host. As such, the parasite depresses the growth of its intermediate host population. Functional responses of the type displayed in Figs 2 and 3 will act to reduce the impact of the parasite on its host by restricting the rate of build up of parasite populations within individual hosts under conditions of high egg density.

The spatial distribution of tapeworm eggs also influences the overall transmission dynamics of *H. diminuta* and the interaction of the parasite with its intermediate host population. It appears from Fig. 4*b*, that this distribution does not affect the average rate of parasite acquisition within a population of beetles. However,

the change in the frequency distribution of parasite numbers/host has important consequences for the host and parasite populations. As mentioned previously, cysticercoids of *H. diminuta* act to reduce host survival and reproduction in a manner related to parasite burden/host (Anderson, 1978*a*). (Further details of the impact of *H. diminuta* on the survival and reproduction of *T. confusum* will be described in a further publication). The net effect of the parasite on its intermediate host population will, therefore, be critically dependent on the statistical distribution of parasite numbers/host. In the first place, over-dispersion is a strong stabilizing influence on host–parasite population associations (Anderson & May, 1978). The important point to note, however, is that the more aggregated or over-dispersed this distribution is, the less is the impact of the parasite on the growth of its host population, since the majority of parasites are harboured by a small proportion of hosts (Anderson, 1979).

In natural habitats, the spatial distribution of *H. diminuta* eggs will tend to be highly aggregated due to the manner of egg release from the mammalian host. As a direct consequence, the frequency distribution of parasites/beetle in natural populations will also be extremely aggregated. Such patterns have recently been reported for *H. diminuta* in wild populations of *Tenebrio molitor*.

In general terms, therefore, the degree of depression of intermediate host population growth by *H. diminuta* infections in natural habitats will tend to be reduced as a consequence of the over-dispersed nature of infective-stage spatial distribution.

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The influence of *Hymenolepis diminuta* on the survival and fecundity of the intermediate host, *Tribolium confusum*

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SUMMARY

An experimental study of the effects of parasitism by *H. diminuta* on the intermediate host, *Tribolium confusum*, is described. No density-dependent constraints on parasite establishment within individual hosts are evident, although a reduction in cysticercoid size at high parasite burdens is demonstrated. The relationship between parasite burden, host mortality and host fecundity is investigated. Host mortality is linearly related to parasite burden, whereas the relationship between parasite burden and host fecundity is non-linear. There is no difference in viability between eggs from infected and uninfected females. The generative causes of these effects are not investigated experimentally, although it is postulated that survival is related to the degree of damage to the midgut wall caused by parasite penetration, and fecundity to the biomass of parasites harboured by the host. The significance of these effects is discussed in relation to the overall dynamics of the host–parasite association.

INTRODUCTION

The rat tapeworm, *Hymenolepis diminuta*, is normally regarded as an example of an organism which is well adapted to the parasitic mode of life, since it appears to be non-pathogenic in the healthy rat host (Insler & Roberts, 1976). Several authors have, however, described an immune response generated by the rat in response to the presence of the parasite, which suggests that the relationship between host and tapeworm may not be entirely commensal in nature (Harris & Turton, 1973; Andreassen, Hindsbo & Hesselberg, 1974; Befus & Threadgold, 1975). The effect of parasitism by *H. diminuta* on the rat is as yet unclear. It may be noted, however, that another 'non-pathogenic' parasite, *Trypanosoma duttoni*, has been found to cause high mortality in its mouse host when stress is induced by starvation and low temperature (Sheppe & Adams, 1957).

The present paper reports the results of experiments designed to investigate the level of pathogenicity of *H. diminuta* in the intermediate host, *Tribolium confusum*. The impact of parasitism on both the survival and fecundity of the beetle is considered, and the relevance of the experimental results is discussed in the context of the overall population dynamics of the host–helminth association.

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MATERIALS AND METHODS

H. diminuta was routinely maintained in the laboratory in Sprague–Dawley rats and *T. confusum* beetles. The methods used for beetle infection are as previously described by Keymer & Anderson (1979).

The relationship between the number of exposures to infection, and the number and size of the parasites harboured/host

An estimated density of 1500 parasite eggs was introduced into each of 6 circular arenas (13 cm^2 in basal area). Populations of 30 beetles of uniform age which had been starved for 6 days, were immediately introduced into each arena for an exposure period of 3 h, after which they were removed and fed. At weekly intervals, the infection process was repeated, omitting 1 group of beetles on each successive week. Throughout the experiment, all populations were exposed to the same regime of feeding and starvation. After 6 weeks, groups of beetles which had been exposed to *H. diminuta* infection 1 to 6 times, respectively, were available. After a further 2 weeks (to allow development of the cysticercoids arising from the most recent infection) the beetles were dissected and their parasite burdens determined. Groups of 10 cysticercoids from hosts with differing infection levels were measured (length from anterior to posterior including tail) to assess the relationship between parasite burden and cysticercoid size.

Experiments to assess the influence of parasite burden on host fecundity

The repeated infection process described above was carried out using groups of male and female beetles which had been sexed at the pupal stage, to give single sex populations with 0–5 infections respectively, where an 'infection' is as described in the previous section. The uninfected group was used as a control. Two weeks after the last infection had been carried out, beetles with the same level of infection were paired (4–6 pairs at each of the 6 infection levels), and each pair was placed separately in a specimen tube with 1 g of flour–yeast medium. At three 24-h intervals, the medium in each tube was passed through a 150 μm sieve to determine the number of eggs laid. (It is assumed that the rate of cannibalism is negligible over the experimental range of egg densities (Rich, 1956; Howe, 1962).)

Eggs from infected and uninfected beetles (5 replicates of 10 eggs each) were placed in flour–yeast medium and left to hatch. The percentage hatch was assessed at the larval stage.

Experiments to assess the influence of parasite burden on host survival

Two separate series of experiments were carried out.

Series A

The repeated infection process was used to produce groups of 50 beetles with 0–5 infections respectively. After the 5th infection, all groups were fed for 12 h and then starved. Dead beetles were removed daily and the proportion surviving in each group was monitored.

Series B

Six groups of 50–60 beetles were exposed to a known level of infection. After infection, the beetles were fed and left for 2 weeks to allow cysticercoid development to take place. All 6 populations were then starved. The first group was dissected immediately and the parasite burdens of the beetles determined. The survival of the other 5 populations was monitored daily. They were sacrificed and dissected sequentially, when approximately 5/6, 4/6, 3/6, 2/6 and 1/6 of the population remained alive. Both the parasite burdens of the dissected beetles and the time of dissection (measured as hours post-starvation) were monitored.

This experimental process was then repeated 4 times at different initial levels of infection.

RESULTS

The relationship between the number of exposures to infection and the number and size of the cysticercoids harboured/host

Since cysticercoids of *H. diminuta* develop in the haemocoel of the intermediate host, there are 2 principal mechanisms which might generate density-dependence in parasite population growth within a single host. First, reactions mounted by the host in response to parasitic invasion might serve either to prevent cysticercoid establishment or to reduce the survival potential of established larvae. However, although encapsulation reactions in insects are well documented (Nappi, 1975), both Heyneman & Voge (1971) and Lackie (1976) have reported that no such reaction is mounted by *T. confusum* against cysticercoids of *H. diminuta*. In addition, the presence of a possible defence mechanism against beetle haemocytes (in the form of branched, secretory, microvilli) has been postulated by Ubelaker, Cooper & Allison (1970). These authors conclude that there is no effective host resistance to the establishment of the parasite.

The second mechanism, competition for food or space between developing parasites, has never been conclusively tested, although it is established that cysticercoids take up host glucose (Voge, 1959), move actively within the host (Voge, 1975) and continue growth throughout life (Prescott & Voge, 1959). Reports on the manifestation of the crowding effect vary considerably. Soltice, Arai & Scheinberg (1971) state that the effects of crowding cannot be demonstrated, whereas other authors report that heavy infections lead to a reduction in cysticercoid size (Schiller, 1959; Dunkley & Mettrick, 1971). Although Voge & Heyneman (1957) state that the reduction is due to variation in tail length, rather than scolex size, there are, to date, no quantitative results available.

The present experiments show that the relationship between the number of exposures to infection and the mean parasite burden of the exposed host population is linear (Fig. 1), thus indicating that, over the experimental exposure range, there are no density-dependent constraints on parasite establishment within the host.

Fig. 2, however, shows that the size of established cysticercoids declines as

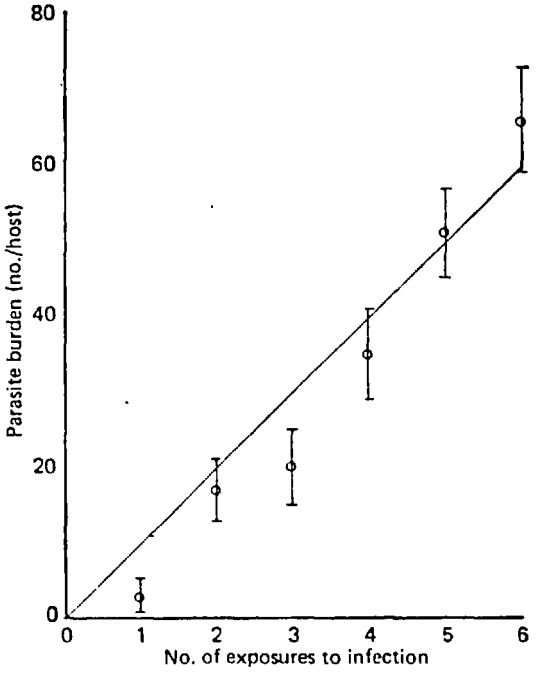

Fig. 1. The relationship between the number of exposures of a *Tribolium confusum* population to infection by *Hymenolepis diminuta*, and the resultant mean parasite burden of the exposed host population. The line indicates the best fit linear model and the points are observed values. The vertical bars represent the 95% confidence limits of the means.

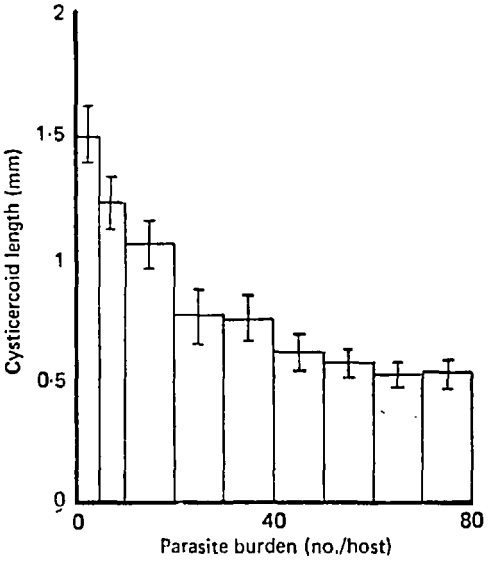

Fig. 2. The relationship between the size of a parasitic infection and cysticercoid length. The histogram bars represent the means of 10 values, and the vertical bars represent the 95% confidence limits of the means.

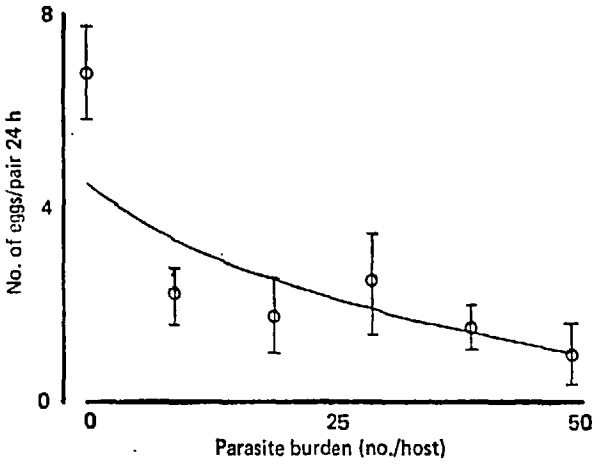

Fig. 3. The influence of parasite burden on host fecundity. The solid line represents the best fit exponential model, and the points are observed means. The vertical bars represent the 95% confidence limits of the means.

parasite burden increases, indicating that competition for nutrient resources, or, more probably, for space, is operative once the parasites are established within the coelom.

The number of exposures to infection was chosen as the experimental variable, rather than the exposure density of infective eggs, since it has already been established that, during a single exposure to infection, the mean parasite burden/host rises to a plateau due to limitations on the rate of acquisition of infection imposed by the feeding behaviour of the beetle (Keymer & Anderson, 1979).

Since the relationship between the number of infections and the resultant mean parasite burden/host (Fig. 1) is linear, a factor of proportionality of 9·85 (i.e. the gradient of the graph shown in Fig. 1) may be used to replace the observed number of infections by an estimated mean parasite burden/host, in the analysis of the results of the remaining experiments recorded in this paper.

Experiments to assess the influence of parasite burden on host fecundity

Changes in host reproductive potential, as a result of parasitic invasion, are commonly associated with parasitic infections in invertebrate hosts (Lanciani, 1975; Frye & Olson, 1974; Milner, 1972), and the degree of reduction in fecundity is often dependent on the burden of parasites harboured (Anderson, 1978; May & Anderson, 1978).

The relationship between the mean number of eggs laid/female *T. confusum*/24 h and the estimated parasite burden/beetle is shown in Fig. 3. Host fecundity decreases markedly as the mean parasite burden/host is increased, and the form of the numerical relationship may be empirically described by an exponential model.

In some host–parasite relationships, there may be a parasite-induced reduction in the survival potential of the offspring from infected parents, which, together

with the possible decrease in fecundity, contributes to the parasite-induced reduction in the reproductive potential of the host population (Weatherly, 1971).

In the *H. diminuta–T. confusum* association, the viability of eggs from infected and uninfected females was compared. There is no significant difference in the percentage hatch of eggs from uninfected beetles ($90 \pm 5{\cdot}5\,\%$) and eggs from infected beetles ($86 \pm 13{\cdot}1\,\%$) (D.F. = 8, $P(t = 0{\cdot}5) > 0{\cdot}5$).

Experiments to assess the influence of parasite burden on host survival

One of the first descriptions of parasitism as a population phenomenon was made by Crofton in 1971. It was suggested that, for each host–parasite association, there exists a specific parasite burden (the lethal level) at which host mortality becomes inevitable. More recently, examination of the results of experimental studies of many host–parasite interactions has shown that there exists a range of possible functional relationships between parasite burden and host mortality, of which the lethal level concept represents one extreme. Examples of linear relationships, as well as more complex, non-linear patterns have been described (Anderson, 1978; Anderson & May, 1978).

The determination of the precise influence of parasitism on host survival is difficult in the *H. diminuta–T. confusum* system, since the parasite burden may only be determined by destructive sampling of living hosts. It has proved necessary, therefore, to use experimental techniques which allow indirect methods of determination to be employed.

The results of the experimental series A are shown in Fig. 4. It can be seen that the populations with the higher parasite burdens tend to survive less well than those with lower parasite burdens. As before, a linear proportionality between the number of infections given and the resultant mean parasite burden has been assumed.

Assuming that the *per capita* instantaneous host death rate/unit of time (μ) is constant through time (t), the temporal change in the number of living hosts (H_t) may be described by the differential equation

$$\frac{dH_t}{dt} = -\mu H_t. \tag{1}$$

Given the initial condition that the number of hosts alive at the beginning of the experiment is H_0, equation (1) has the solution

$$H_t = H_0 \exp(-\mu t). \tag{2}$$

From equation (2), the host mortality rate, μ, may be estimated from the experimental data where

$$\mu(t+0{\cdot}5) = -\ln \frac{H_{t+1}}{H_t}. \tag{3}$$

(In the survival experiments described in this paper, t is measured in hours.) The relationship between the instantaneous host mortality rate and the parasite burden is shown in Fig. 5. From this rather crude estimation procedure, there is an

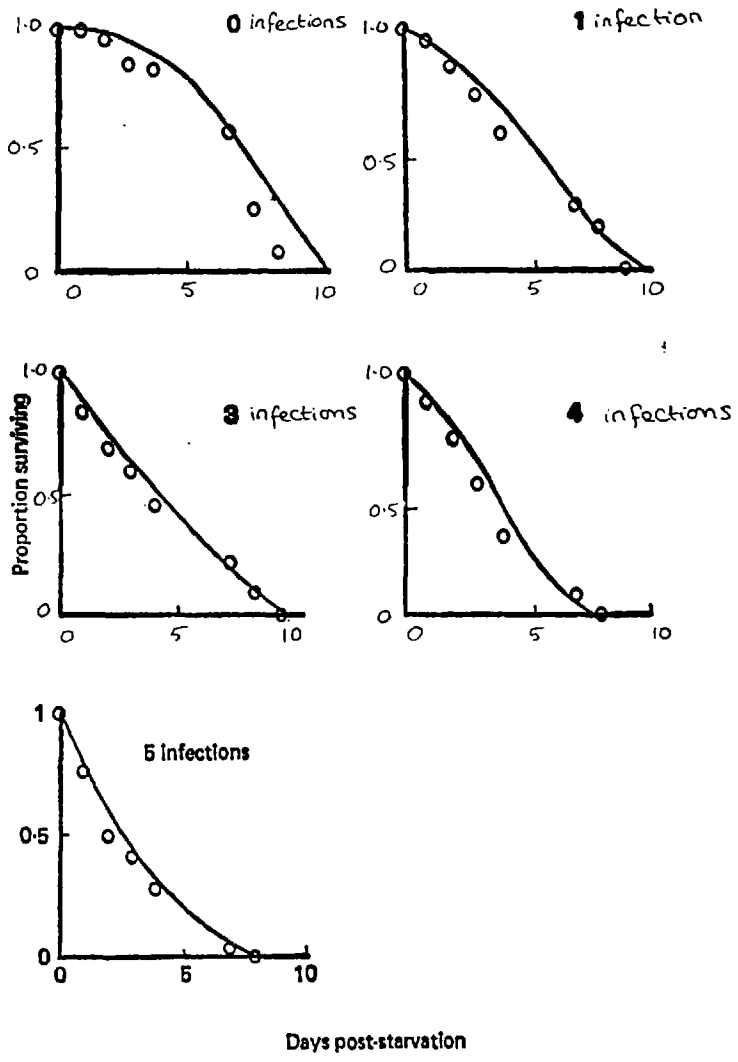

Fig. 4. The influence of parasite burden on host survival. The lines represent the predictions of an age-dependent survival model (Anderson & Whitfield, 1975) and the points represent observed values.

indication of linearity in the relationship between host mortality and parasite burden, which serves as a hypothesis for further investigation.

The second series of experiments (series B) yielded a much more detailed set of data, from which an independent estimate of the relationship between host mortality and parasite burden may be derived, for comparison with the results given above.

The experimental design was such that the change in the frequency distribution of parasites/host through time was available for 5 different initial infection levels ((i)–(v)). The frequency distributions for 1 of the 5 experiments (initial infection level (i)) are shown in Fig. 6. It can be seen clearly that the frequency distribution

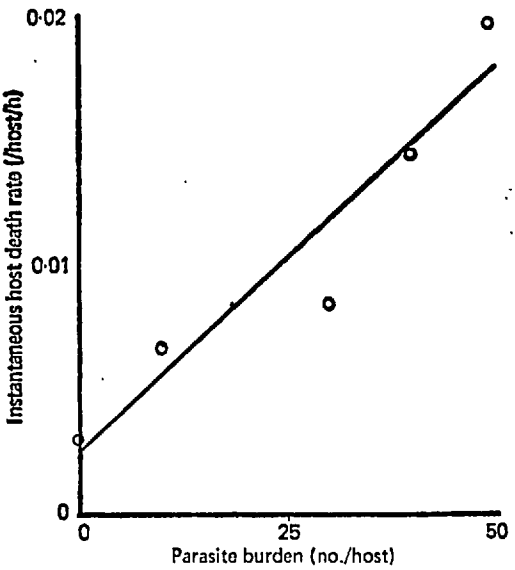

Fig. 5. The relationship between instantaneous rate of host mortality and parasite burden/host. The line indicates the best fit linear model and the points represent observed values.

of parasites/host becomes less over-dispersed as time proceeds (and the population dies). This gives a clear indication that individual hosts with high parasite burdens tend to die more quickly than those harbouring fewer parasites, and thus that there is a direct relationship between host mortality and parasite burden.

The total set of data obtained from these experiments may be conveniently summarized by representing each frequency distribution by its mean and variance. The change in the mean parasite burden of the host population through time, for initial infection levels (i) to (v), is shown in Fig. 7. The decrease of the mean parasite burden through time, together with the relationship between the initial infection level and the duration of population survival, again reinforce the hypothesis that the parasite burden of the host has a distinct influence on its death rate.

In addition to these qualitative observations, the data obtained is amenable to a more detailed investigation of the causes of mortality occurring in the population. The overall observed host mortality is a composite parameter with two distinct components. First, there is the instantaneous rate of natural mortality/host/unit of time, b, which would occur in the absence of parasitism, and the second component is the additional host mortality which is induced by the presence of the parasites. Indirect methods are necessary in order to examine the relationship between parasite burden and host mortality, and to separate these effects from the natural mortalities occurring in the population. The precise functional form of the relationship may be most easily derived by testing the experimental data against a model incorporating an assumption of linearity between the parasite burden, i, and the instantaneous rate of parasite induced

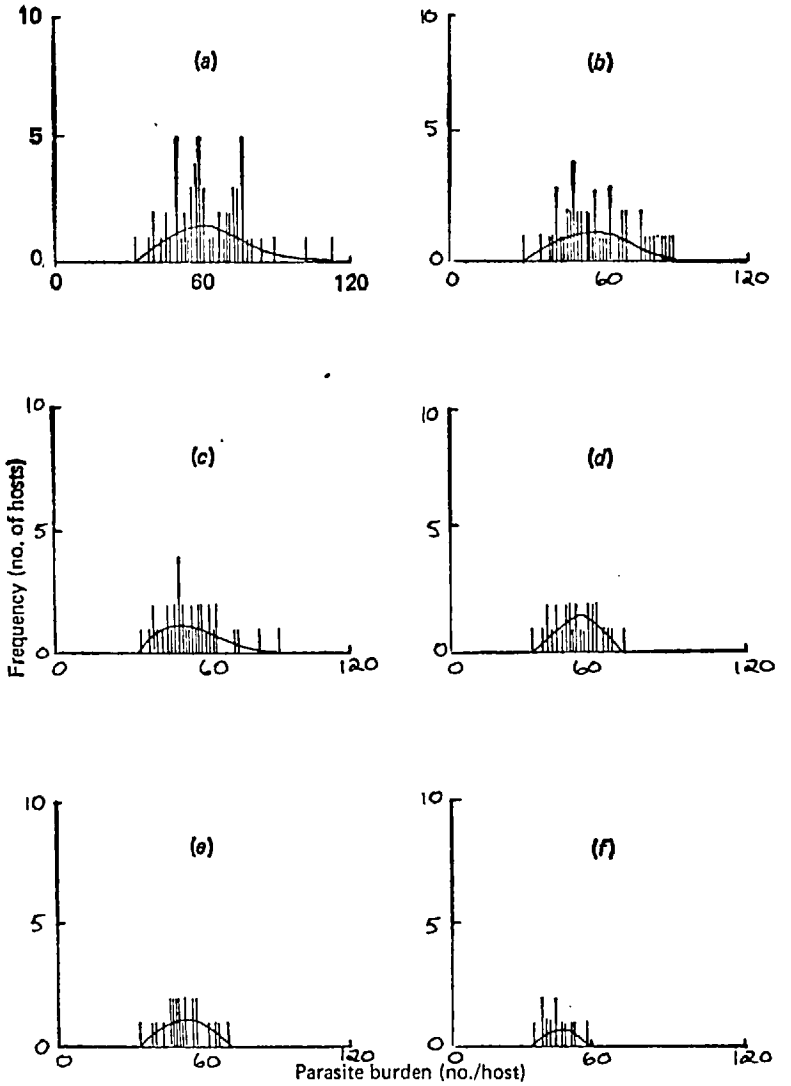

Fig. 6. The change in the frequency distribution of parasite numbers/host with time (for initial infection level (i)). The solid lines represent the predictions of the best fit probability distribution model (negative binomial for graphs a, b and c; Poisson for graphs d, e and f), and the histogram bars represent observed frequencies.

(a) 0 h; post-starvation; $s^2/\bar{x} = 3{\cdot}55$, $k = 22{\cdot}68$, D.F. = 39, $\chi^2 = 52{\cdot}11$.
(b) 12 h; $s^2/\bar{x} = 3{\cdot}42$, $k = 23{\cdot}43$, D.F. = 34, $\chi^2 = 36{\cdot}59$.
(c) 20 h; $s^2/\bar{x} = 2{\cdot}61$, $k = 29{\cdot}07$, D.F. = 27, $\chi^2 = 22{\cdot}19$.
(d) 36 h; $s^2/\bar{x} = 1{\cdot}50$, D.F. = 18, $\chi^2 = 12{\cdot}61$.
(e) 44 h; $s^2/\bar{x} = 1{\cdot}05$, D.F. = 13, $\chi^2 = 8{\cdot}94$.
(f) 48 h; $s^2/\bar{x} = 0{\cdot}63$, D.F. = 6, $\chi^2 = 7{\cdot}09$.

host mortality/*parasite/unit of time*, α, (for a host containing i parasites the instantaneous rate of parasite-induced host mortality is thus αi). If this assumption is valid, the values of α calculated from the experimental data should be constant (allowing for experimental variation) and independent of the initial mean parasite burden of the host population.

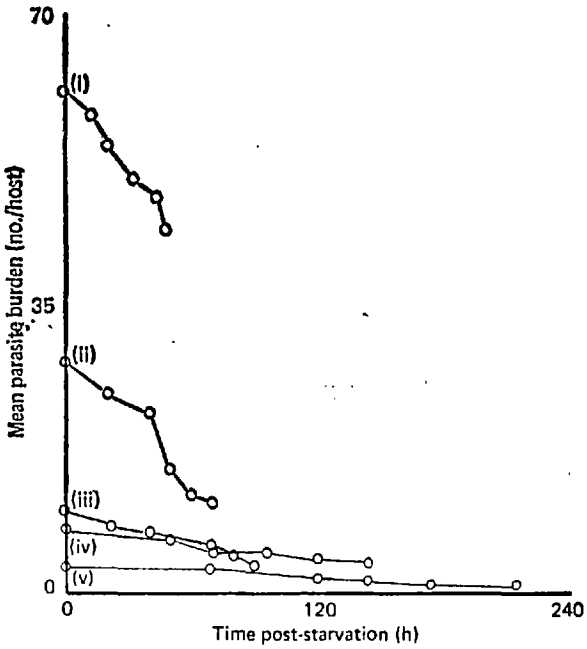

Fig. 7. The change in the mean parasite burden of an infected population with time. (i)–(v) represent different initial levels of infection and the points represent observed values.

Since the death rate of individual hosts depends on the number of parasites they harbour, the overall observed host mortality in the population will be critically dependent on both the mean parasite burden and also the statistical distribution of parasites within the host population. The latter is almost always over-dispersed (Anderson, 1978) and has recently been found to be extremely contagious, possibly due to heterogeneity in infective-stage distribution, host behaviour and host susceptibility, for both laboratory (Keymer & Anderson, 1979) and field (Rau, 1979) populations of *H. diminuta* in the intermediate host.

Assuming that the pattern of parasites/host may be empirically described by the negative binomial distribution (Bliss & Fisher, 1953), and that the degree of intrinsic over-dispersion remains constant, the following expression may be used to calculate values of α from the experimental data

$$\alpha = 1/t\left[\frac{-\ln QM}{R(M+k)}\right], \tag{4}$$

where M is the initial mean parasite burden of the host population, k is an inverse measure of the degree of over-dispersion of parasite numbers/host, $R = M/k$ and $Q = 1+R$. The derivation of equation (4) is detailed in Appendix 1.

Five values of α may be calculated from the data obtained from series B; one for each of the initial infection levels (i)–(v). These are shown in Fig. 8. It can be seen that the value of α is independent of the initial mean parasite burden of the host population, thus supporting the hypothesis that the relationship between host mortality and parasite burden is of linear form, (D.F. = 3, $P(t = 0{\cdot}8) = 0{\cdot}5$).

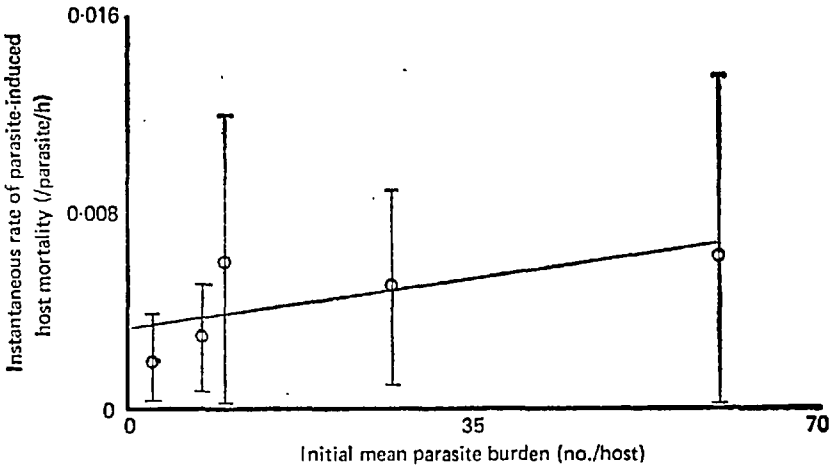

Fig. 8. The relationship between the instantaneous rate of parasite-induced host mortality and parasite burden. The solid line represents the best fit linear model and the points represent observed means. The vertical bars indicate the 95% confidence limits of the means.

To gain a more accurate estimate of the overall rate of observed host mortality, (μ/h/host), we may substitute the expression for H_t derived in Appendix 1 (which incorporates the assumption of a linear relationship between α and i) into equation (3). This leads to the expression

$$\mu = b + \frac{k}{t} \ln (Q - Re^{-\alpha t}). \qquad (5)$$

(Further details of this derivation are provided in Appendix 2.)

From equation (5) it is clear that the rate of mortality observed in a host population is a function, not only of the mean parasite burden, but also of the distribution of the parasites within the host population. The relationship between μ (overall instantaneous rate of host mortality), and k (inverse measure of the degree of dispersion) for a constant mean parasite burden is shown in Fig. 9. It can be seen that the rate of observed host mortality reaches a maximum as k increases in magnitude (when $k > 8$, the parasites are virtually randomly distributed within the host population). When the value of k is decreased (and the distribution of parasites is more over-dispersed or contagious), the observed rate of mortality in the population is also decreased, since the proportion of hosts harbouring parasites is lower, and so the effect of parasite-induced host mortality on the population is less severe.

A second point of major interest is apparent from the structure of equation (5). If the parasites are over-dispersed within the host population, then a linear relationship between the rate of parasite-induced host mortality/parasite/unit of time (α) and the parasite burden/host (i), will not generate a linear relationship between *observed host mortality* and *mean parasite burden*. This is shown in Fig. 10, where observed host mortality is plotted against the mean parasite burden of the host population, for 4 different values of k. In all cases, when the population is

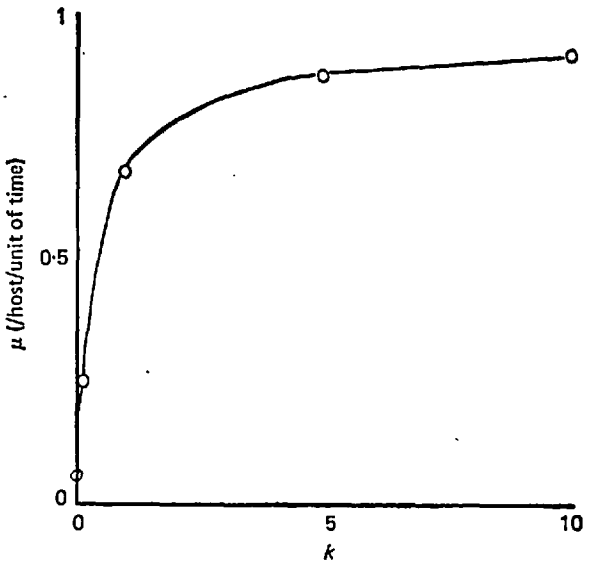

Fig. 9. The relationship between the instantaneous rate of host mortality, μ, and the degree of over-dispersion in the distribution of parasite numbers/host, as indicated by the negative binomial parameter, k (b = 0·01, M = 10, α = 0·1, t = 1).

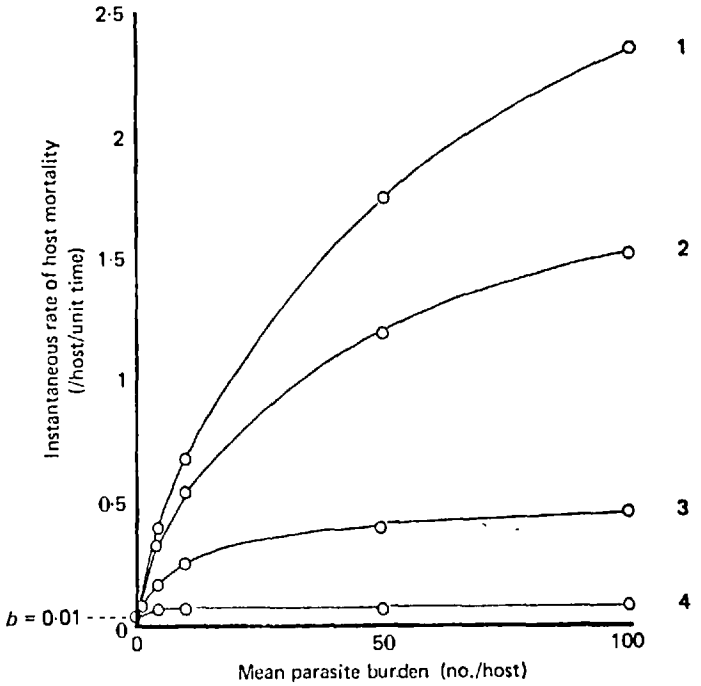

Fig. 10. The relationship between the instantaneous rate of host mortality, μ, and the mean parasite burden of the host population, M. (b = 0·01, α = 0·1, t = 1.) (1) k = 1; (2) k = 0·5; (3) k = 0·1; (4) k = 0·01.

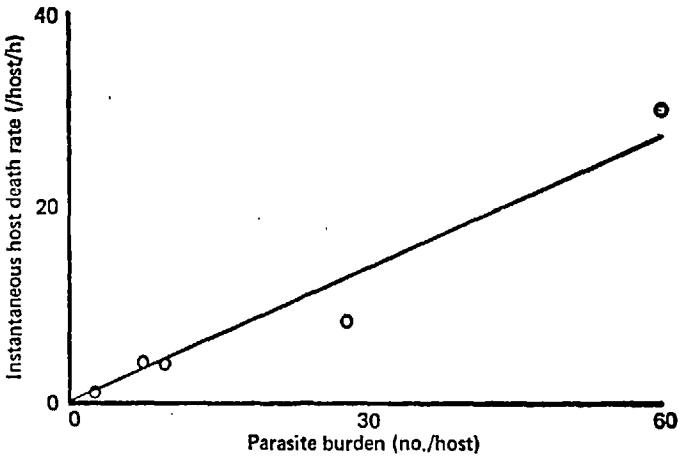

Fig. 11. The relationship between the instantaneous rate of host mortality, μ, and the mean parasite burden of the host population (series B). The solid line indicates the best fit linear model, and the points represent observed values.

parasite free, the rate of mortality observed in the population is equal to b (the rate of natural mortality/host/unit time). As the mean parasite burden is increased, however, the observed mortality rate (including both natural and parasite-induced effects), does not increase proportionately, because of the effects of contagion in the parasite distribution. A linear relationship over the complete range between host mortality and parasite burden (reflecting the direct proportionality between the rate of parasite-induced host mortality and the parasite burden/host) is only observed in populations in which the parasites are randomly distributed.

Equation (5) may be used to obtain estimates of μ from the data in experimental series B. The relationship between μ and the mean parasite burden of the host population is shown in Fig. 11. In contrast to the theoretical relationships derived above, it is of approximately linear form. This discrepancy between observed results and theoretical predictions most probably occurs because the experimental infection range represents only the lower part of the theoretical range shown in Fig. 10. Further experimental work is required in order to investigate the form of the relationship over a higher range of parasite burdens.

Figs 5 and 11 represent the relationships between host mortality and parasite burden as obtained from 2 series of experiments. The magnitude of the estimates obtained, however, are not comparable; the host death rate being much higher in series B than in series A. The only difference in experimental design which may explain this discrepancy is that the host populations were starved 12 h after infection in series A, whereas in series B, starvation did not commence until 2 weeks post-infection. Thus, in series B the beetles had already harboured the parasites for 2 weeks and had a correspondingly higher death rate when stress induced by starvation commenced.

CONCLUSIONS

The experimental results reported in this paper reveal that cysticercoids of *H. diminuta* have severe deleterious effects on both the survival and the fecundity of the intermediate host, *T. confusum*.

Cysticercoids develop in the beetle after infective hexacanth eggs are ingested. Following physical disruption of the outer egg-shell wall on ingestion, and enzyme activity together with hexacanth motility in the midgut, the eggs hatch and burrow through the midgut wall (Voge & Berntzen, 1961). Development to the mature cysticercoid occurs in the haemocoel, infectivity to the final host being achieved after a pre-patent period of 10 days at 28 °C.

The results reported in this paper reveal that there is direct proportionality between the reduction in host survival caused by the presence of the parasite and the number of parasites harboured/host. It is pointed out, however, that due to the effects of over-dispersion in the distribution of parasite numbers/host, this may not result in a linear relationship between *observed* host mortality and parasite burden. It is suggested that host survival is related to the number of parasites which penetrate through, and cause damage to, the midgut wall.

In contrast to host survival, the relationship between the reduction in host fecundity and parasite burden is clearly non-linear (Fig. 3), and is, therefore, not directly related to the *number* of hexacanths entering the haemocoel. However, the relationship between parasite burden and parasite size (Fig. 2) indicates that parasite *biomass* increases non-linearly to a plateau as parasite burden increases (assuming that parasite length may be used as an approximate estimate of parasite biomass). It is therefore suggested that host fecundity is affected by the biomass of parasites harboured by the host (and therefore the amount of resources utilized by the parasites) rather than by the absolute numerical value of the parasite burden.

Thus, although it appears rather inocuous in the adult phase, *H. diminuta* does exert adverse effects on the reproductive fitness of its intermediate host. This life-history strategy is common to many cestodes, where the main reproductive potential is invested in the long-lived adult worm, which tends to compensate, in terms of evolutionary fitness, for the low probability of successful transmission between hosts, combined with the high pathogenicity of the larval stages.

The overall consequences of parasitism by *H. diminuta* on the population dynamics of *T. confusum* will obviously depend critically on both the mean parasite burden, and also the statistical distribution of the parasites within the host population. Under laboratory conditions, where the mean parasite burden is high, and the degree of over-dispersion relatively low, the effects of parasitism on the survival and fecundity of individual hosts accrue to result in a depression in the equilibrium population level of *Tribolium* of up to 50 %. (The long term effect of the parasite on the intrinsic growth rate of the host population will be described in a further publication.)

Under natural conditions, the degree of over-dispersion in the frequency distribution of parasite numbers/host is likely to be extremely high (Rau, 1979). This,

together with the relatively low levels of parasitism which might be expected under natural conditions, will tend to reduce the regulatory impact of the parasite on the growth of its host population, since the majority of the parasites will be harboured by a small proportion of the hosts.

The experimental results reported in this paper illustrate the potential of *H. diminuta* to act in a regulatory manner on the population growth of the intermediate host, *T. confusum*. Whether this potential is realized in natural communities will be critically dependent on the observed values of the population parameters relating to other sectors of the life-cycle. More importantly, however, the results displayed in Figs 3 and 11 reveal density-dependent constraints on the flow of *H. diminuta* through its life-cycle. The tendency for host density to be reduced by high levels of parasitism by *H. diminuta* in the population will provide a strong regulatory force on the population growth of the parasite.

APPENDIX 1

Assuming that the instantaneous rate of parasite-induced host mortality/parasite/unit of time, α, is directly related to the parasite burden/host, i, the rate of change of the number of hosts harbouring i parasites at time t, (H_{it}), may be described by the differential equation

$$\frac{dH_{it}}{dt} = -(\alpha i + b)\, H_{it}, \tag{A1}$$

where b is the *per capita* instantaneous rate of natural host mortality in the absence of parasitism, assumed to be age-independent over the experimental time period.

Given the initial condition that the number of hosts harbouring i parasites when $t = 0$, is H_{i0}, equation (A1) has the solution

$$H_{it} = H_{i0} \exp\,(-(\alpha i + b)\, t). \tag{A2}$$

The initial number of hosts harbouring i parasites (H_{i0}) may be replaced by the product of the total number of hosts present, H_0, and the probability of a host harbouring i parasites, p_i, to give

$$H_{it} = H_0 p_i \exp\,(-(\alpha i + b)t). \tag{A3}$$

An expression for the total number of hosts at time t, H_t, may then be derived by summing equation (A3) over all values of i. It is assumed that the pattern of parasite numbers/host follows a negative binomial distribution, where the probability generating function is defined as $\pi(z) = (Q - Rz)^{-k}$ (see Pielou, 1977). Then

$$H_t = \mathrm{e}^{-bt}\, H_0\, (Q - R\mathrm{e}^{-\alpha t})^{-k} \tag{A4}$$

where k is an inverse measure of the degree of over-dispersion, R is the probability of a successful infection, and $Q = 1 + R$.

Similarly, an expression for the total number of parasites present at time t, P_t,

is given by the product of the number of hosts harbouring i parasites at time t' H_{it}, and the parasite burden, i, summed over all values of i

$$P_t = \sum_{i=0}^{\infty} i\, H_{it} = \mathrm{e}^{-bt}\, H_0\, \mathrm{e}^{-at}\, Rk\, (Q - R\mathrm{e}^{-at})^{-(k+1)}. \qquad \text{(A5)}$$

An expression for the mean number of parasites/host ($M_t = P_t/H_t$), may then be derived by combining equations (A4) and (A5) to give

$$M_t = \frac{\mathrm{e}^{-at}\, kR}{(Q - R\mathrm{e}^{-at})}. \qquad \text{(A6)}$$

The rearrangement of equation (A6) leads to equation (4) in the main text which is used to obtain estimates of α from the experimental data.

APPENDIX 2

From equation (2), the overall rate of host mortality, including both natural and parasite-induced effects is described by the expression

$$\mu = -1/t \ln \left[\frac{H_t}{H_0}\right]. \qquad \text{(A7)}$$

By substituting equation (A4), this may be rewritten as

$$\mu = b + \frac{k}{t} \ln (Q - R\mathrm{e}^{-at}), \qquad \text{(A8)}$$

which may be used to gain estimates of μ from experimental data.

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