The Nature of Parasitism

The Relationship of Some Metazoan Parasites to Their Hosts

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Preface

A CONSIDERATION of host–parasite relationships raises a number of basic problems. What are the features of the parasite and the host that allow infection to occur? What are the physiological characters that distinguish a parasite from its free-living relatives? What are the features of the environments of parasites which affect specificity? To these sorts of questions our present knowledge provides only general answers. Until we have more precise answers we cannot begin to understand the basic features of the host–parasite relationship and the nature of parasitism.

My chief aim in writing this book has been to provoke interest in these sorts of problems; I have been concerned not so much to summarize our knowledge as to stimulate research on parasitism. Most of the book concerns metazoan parasites, chiefly nematodes and platyhelminths. I have grouped chapters in four parts which correspond roughly to different stages in the association between the metazoan parasite and its host. Part I, speculations on the host–parasite relationship, gives a general introduction and a brief statement of a hypothesis about some aspects of parasitism, especially in relation to parasitic nematodes. Part II deals largely with the stage in the association between the parasite and the host when infection occurs. The chapters here deal with factors that lead to infection, the life cycle of the parasite and the special character of the infective stage, the physiology of the free-living and infective stages, and finally, the physiology of infective processes. In Part III is discussed what I regard as the second stage in the association between the parasite and the host. Infection has occurred and the parasite now needs nutrients, oxygen and other factors from the host if it is to survive. In this part of the book these needs and the general physiology of parasitic stages are discussed. The last part of the book is concerned with factors which affect the propagation and maintenance of parasites as species; so the chapters deal with reproduction, specificity and the evolution of parasitism.

In an attempt to interest readers who may not have a detailed knowledge of parasitology I have used the more common parasites and hosts as examples whenever possible. The special language of parasitology has been avoided as much as possible, but some terms which parasitologists use in a different way from other biologists are included in the text. Thus the word "egg" is used for what might be more properly described as a "capsule", and includes the embryo, its membranes, and the shells of the egg. And the term "larvae" or "larval stages" used to denote the immature stages in the life cycle of nematodes may also be misleading to some biologists. These stages are juveniles, not larvae.

I am deeply indebted to Dr R. Dubos of the Rockefeller Institute for Medical Research who reviewed the chapters on more general aspects of parasitism, and to Dr E. Bueding of Johns Hopkins University who reviewed chapters on the physiology of parasites. Many of my colleagues at the University of Adelaide, especially Dr G. Mayo of the Department of Genetics, also gave me helpful advice for which I am most grateful. I wish also to thank the many authors whose illustrations I have used and whose work I have quoted; individual acknowledgements are given in legends.

I am most grateful to Mrs M. Ross, who is a member of the staff of the University of Adelaide, for the many drawings she prepared for me. My warmest thanks are due to my wife, Lillian Rogers, who did most of the typing and some of the drawings, who checked references and polished at least some of the rough spots in the manuscript.

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PART I

Speculations on the Host–Parasite Relationship

General Introduction

MANY parasitologists accept the view that adaptation to a life of commensalism or mutualism precedes adaptation to a parasitic mode of life, though there seems no good reason why parasitism should not develop without these intermediary conditions. The morphological changes, such as the increased development of organs for attachment to the host or the loss of digestive organs, are frequently found as adaptations to a parasitic mode of life and they tell us something about the relationship of the parasite to the host. But adaptations of this sort must have occurred after the assumption of a parasitic mode of life. The morphological characters which might be necessary for the establishment of parasitism, such as thickness of the cuticle or the nature of the feeding mechanism, are more difficult to visualize. So it must be with the physiological adaptations to parasitism. We need to know not only those characters of a parasite which determine its dependence on the host, but also those which made it possible for the ancestors of parasites to move from the environment of the free-living forms and enter the environment on or in the host and survive there.

The infective stage of modern parasites is specialized to move from one sort of environment to another. Does it represent physiologically the stage in the life cycle of the free-living ancestor which was best adapted to invade the host and so "pre-adapted" for starting a parasitic mode of life? Are the sorts of adaptations to parasitism likely to be different in different stages of the life cycle so that the relationship of the parasite to the host changes?

After entering the host the infective agent is exposed to an environment from which it must obtain the factors necessary for its growth and development. It must also overcome the toxic and damaging features of the environment. These opposing conditions, the one favourable, the other unfavourable, are the major components which must be considered in the study of host–parasite relations. But there is another factor of importance in the relationship between many metazoan parasites and their hosts. Infection often requires the hatching of the egg of the parasite, or excystment or moulting. Until this occurs the infective agent may be isolated from the host by a barrier formed of the egg-shell, the cyst-wall, or sheath. Thus the host must provide the right conditions for certain changes in the infective agent before either the favourable or unfavourable components in the environment can affect many parasites.

A parasite may influence the favourable or unfavourable features of its environment. As an isolated system the host–parasite complex may be represented as host $\rightleftharpoons$ parasite's environment $\rightleftharpoons$ parasite. Though not all changes in the environment caused by the host would affect the parasite and *vice versa* there would be considerable feedback in the system which would be more closely coupled than in most free-living systems. In the relationship between the parasite and the host, negative feedback would lead to a steady-state condition with the survival of the host and the parasite; positive feedback would lead to the death of the host or the parasite. A negative feedback system in the host–parasite relationship thus might have selective value for the parasite.

CHAPTER 1

The Study of Parasitism

THE relationship of macroscopic parasites to disease has been recognized, in general terms, from early times. As a consequence, the motivation for research in parasitology has arisen largely from the desire to cure or to prevent disease. Thus studies on host–parasite relationships have been concerned largely with pathology and immunology, and the bulk of research in parasitology, dealing with the natural history of parasites, has sought in studies on life cycles and in ecology to provide means whereby infection could be prevented. From the time of Koch's demonstration that disease in human beings could be caused by bacteria, studies on parasitic micro-organisms have followed similar lines. But because parasitic micro-organisms are of special importance in human disease, their study has been regarded as a special field outside what is conventionally called parasitology, and the organisms themselves are called pathogens, rather than parasites.

INFECTIOUSNESS AND PARASITISM

It is often implied that an understanding of virulence or pathogenicity is basic to an understanding of parasitism. This is not necessarily true. What is more important is an understanding of infectiousness—the capacity of the organism to infect the host and live as a parasite. In order to infect and live in the host the parasite must be able to counter the toxic actions of the host and it must obtain, under the right conditions, certain substances from the host. So to understand parasitism we want information about the needs of the parasite and its defence mechanisms rather than about the damage it does to the host. One way of obtaining this information is to study the metabolism of the parasite. This approach is thought to have a practical value also because it may show biochemical differences between the host and the parasite which might be exploited by selectively toxic compounds.

Studies on the Metabolism of Parasites

In discussing the contribution that studies on bacterial metabolism have made to the understanding of parasitism by micro-organisms, Dubos (1954, p. 12) said

. . . all textbooks of infectious diseases dutifully begin with chapters devoted to metabolic chemistry. But like the religious convocation which opens political or other lay gatherings, this chapter has little to do with, and is never mentioned in, subsequent proceedings. In practice metabolic knowledge is not used in the analysis of reactions between host and bacteria. The reason is simply that despite the spectacular advances during the past three decades, the science of bacterial metabolism has contributed but little to the understanding of infectious processes.

Has this statement any special significance to those who study metazoan parasites? I think it has. By and large our research on the biochemistry of animal parasites has shown that the basic ground plan of their metabolic processes is similar to that in other sorts of animal cells. Surely this is not surprising. Long before the free-living ancestors of metazoan parasites appeared the most efficient and adaptable basic metabolic pattern for cellular function must have evolved. We might expect that this ground plan would be modified only in minor respects in different sorts of animals or even in different sorts of tissue. It may be, however, that some parasites have lost the power to synthesize coenzymes or other substances which are important in metabolism and so they become dependent upon the host for the supply of these substances. As yet no evidence to this effect has come from studies on metazoan parasites.

If it is difficult in studies on the basic metabolism of parasitic bacteria to discover the mechanisms of infectiousness as Dubos suggests, it is likely to be even more difficult with metazoan parasites. From an evolutionary point of view these animals are much more closely related to their hosts than are parasitic bacteria. Moreover, they seldom multiply within the host. On the other hand, the greater complexity of metazoan parasites should provide wider avenues for biochemical research which might lead to an understanding of infectiousness, but these I believe must be based on a deeper knowledge of the biology of parasitism than we have at present.

An example from outside parasitology may best explain what I mean here. The problem, let us say, is to discover the essential biochemical differences between muscle and liver. We might start, without any knowledge of the biology of these tissues, by studying their basic metabolism—aerobic and anaerobic respiration, the general processes of nitrogen catabolism and the mechanisms of synthesizing new tissue. The results would show that different parts of the basic ground plan of metabolism would have different emphasis in the different tissues as well as other minor variations. Even the synthetic mechanisms would probably be basically the same though the substances synthesized would differ. Gradually, however, information would accumulate which the inspired biochemist could interpret to show that the essential biochemical differences were those which concerned the contractile function of muscle and the storage function of the liver. Would this information have come more quickly if we had started with our biological knowledge about the functions of liver and muscle? I think so. This may seem a gross exaggeration of the situation of research on parasitism. But one must agree, for instance, that more information on the biology of infectiousness and the host as an environment for the parasite is needed as a basis for biochemical studies on parasitism.

One of the ways in which information about infectiousness and the requirements of metazoan parasites from their hosts might be found is the study of the biochemistry of the life cycle of parasites and the processes which lead to infection of the host. There is a wide background knowledge of the natural history of life cycles and the experimental biologist has also entered this field so that some of the problems are open to biochemical investigation. Problems of this sort are comparable with those in which the parasite has lost some power of synthesis and so becomes dependent on the host for a coenzyme or essential metabolite. Consider, for instance, the parasite in which the infective stage is an egg. Part of the mechanism which causes hatching of the egg has been lost and the parasite becomes dependent on the host to make good this loss.

This approach to the study of parasitism has been used to suggest a hypothesis about the relationship of nematode parasites to their hosts which will be discussed later.

Studies on the Culture of Parasites in vitro

It is the hope of most parasitologists that the culture of metazoan parasites *in vitro* will provide opportunities for great advances in our knowledge of parasite physiology from which will come an understanding of infectiousness and parasitism. Though this has not proved true in work on parasitic bacteria (Dubos, 1948) the differences between parasitic bacteria and metazoan parasites are so great that parasitologists generally have remained hopeful. Now that two specialized nematode parasites, *Nippostrongylus muris* and *Haemonchus contortus*, have been cultured through their whole life cycles from egg to adult (Weinstein and Jones, 1956; Silverman, 1959), the value of this approach should soon appear. These two parasites are closely related taxonomically so it is not surprising that the same basic medium serves for their cultivation. But the host preferences and life cycles are quite different. *Haemonchus contortus*, a parasite of ruminants, has a histotrophic larval stage in the walls of the abomasum and the adult lives on the host blood and tissues of the mucosa of the same organ. *Nippostrongylus muris* has a life cycle which takes it via the blood stream to the lungs and thence up the trachea and down the œsophagus to the small intestine. The adult, a parasite primarily of rodents, lives on blood and tissue of the mucosa of the small intestine. In view of the differences between these two parasites it seems that it may be possible to alter the basic medium so tha. it would support one but not the other. This may give information on specificity. But the difficulty here is that many aspects of specificity may not depend on nutrition. Thus the nutritional needs of *Nippostrongylus muris* and *Haemonchus contortus*, blood and mucosal tissue, may well be the same. But the environments are quite different: the one highly acid, containing pepsin and the fermentation products from the rumen which are undergoing peptic digestion; the other weakly acid or alkaline, containing the juices from intestinal cells, the bile, pancreatic secretions and the partly digested products from the stomach of an omnivore. The physical organization of the habitat *in vivo* is such that the parasites can live in one medium and feed on something quite different. Specificity and infectiousness may depend more on the total environment, physical as well as chemical, than on the nature of the nutrients, especially for endoparasites.

This problem may be posed in another way. To explain infectiousness and parasitism it is not only necessary to demonstrate what factors in the environment the host must provide for the parasite; it is necessary also to show what prevents the saprophytic form from living in such an environment (Rogers, 1954). It may be asked then if the medium in which parasites like *Nippostrongylus muris* and *Haemonchus contortus* will grow *in vitro* will support the growth of saprophytic nematodes. As for bacteria it may prove that most saprophytes will grow as well as the parasite *in vitro* and that factors other than those directly concerned with nutrition are important in determining infectiousness. Thus the parasitic habits of nematodes which live in the alimentary canal may be determined by their resistance to the action of the gut contents as much as by nutritional demands.

The properties of the gut contents that limit infectiousness may not be the same as those that function in other parts of an animal's body or in plants. A general statement on this subject has been made by Lewis (1953) who suggested that parasitism is the result of a balance in the host's capacity to provide substances which favour the growth of parasites and those which inhibit. Such substances commonly occur among the metabolites of many different species. Though the examples which Lewis gives are drawn from bacterial and fungal parasites there seems no reason why his hypothesis should not apply to animal parasites as well (see Chapter 8).

Studies on the cultivation of metazoan parasites *in vitro* may be used to examine the "balance hypothesis". Presumably the role of more complex inhibitors, antagonists and antibodies, which form part of the more established theories of resistance and susceptibility, and which are important in acquired as well as natural immunity, can also be studied in this way.

The Relationship between Nematode Parasites and Their Hosts

Most of the detailed discussion in this book concerns nematode parasites and chiefly nematode parasites of the gut. Other metazoan parasites are referred to, but generally in less detail. I have selected nematode parasites because they, especially those which live in the alimentary canal, are the animals which I have studied in my own research work. But there are other reasons:

(a) Nematodes are very successful animals; free-living forms, plant and animal parasites are common and widely distributed and show little morphological specialization. The basic physical organization of nematodes (Harris and Crofton, 1957) seems to be suitable for a variety of environments, and parasitism has not given rise to specialization to the degree found in other groups. Physiological specialization may not be as great either. This certainly applies to the physiology of digestion and absorption. In any case, information about physiological specialization may be sought by comparing free-living and parasitic forms. This may be especially useful in comparing, for instance, the capacity of saprophytic and parasitic forms to live in special media *in vitro*. This would not be possible with many other groups of metazoan parasites in which free-living species suitable for comparison often cannot be obtained.

(b) Because there are a large number of species which are parasites of the gut it seems reasonable to suppose that this organ presents less formidable barriers to the establishment of parasitism than many other organs. In some groups the adults are found only as parasites of the alimentary canal. The alimentary canal has features which are not commonly found in other environments and which give a starting point for the study of parasitism.

(c) The processes of reproduction and the life cycles of nematode parasites are generally relatively simple and similar to those of free-living forms. This again suggests that the parasitic forms are relatively unspecialized as compared with the Trematoda and Cestoda, for instance.