

The physiology of trematodes **Second edition**

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The physiology of trematodes

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SECOND EDITION

CAMBRIDGE UNIVERSITY PRESS

CAMBRIDGE

LONDON NEW YORK NEW ROCHELLE

MELBOURNE SYDNEY

Published by the Press Syndicate of the University of Cambridge
The Pitt Building, Trumpington Street, Cambridge CB2 1RP
32 East 57th Street, New York, NY 10022, USA
296 Beaconsfield Parade, Middle Park, Melbourne 3206, Australia

First edition © J.D. Smyth 1966
Second edition © Cambridge University Press 1983

First published by Oliver & Boyd 1966 and W. H. Freeman 1966
Second edition published by Cambridge University Press 1983

Printed in Malta by Interprint Limited

Library of Congress catalogue card number: 82-12961

British Library Cataloguing in Publication Data

Smyth, J.D.

The physiology of trematodes. - 2nd ed.

I. Trematoda

I. Title II. Halton, D.W.

594.1'22041 QL391. T7

ISBN 0 521 22283 4 hard covers 2nd edition

ISBN 0 521 29434 7 paperback 2nd edition

Preface to the second edition

Since the first edition of this text was published (1966), the impact of modern biological techniques, especially electron microscopy and cytochemistry, have revolutionised our ideas regarding the structure and ultrastructure of trematodes. Parallel advances in biochemistry and immunology have also greatly expanded our understanding of the host-parasite relationship of the group. The result is that much more information on the physiology of trematodes is available. In this edition an attempt is made to review the progress in this field up to about 1980. We are fully aware, however, of the rate at which biological concepts are changing and of the mass of material being published even while this volume is going to press. Perhaps some idea of the explosion in the volume of research in this field is reflected in the fact that the first edition of this book had 365 references, whereas this edition quotes some 1200. We have attempted a world-wide coverage of the literature and where translations are available (especially from the Russian) this has been indicated (by an asterisk) in the References. The Figures include more than 60 new diagrams and some photographs have also been added.

Although a great deal of physiological research has concentrated on trematodes of veterinary or medical interest, it is stressed that, for studying many physiological problems, species outside these categories may serve as more suitable models. The physiology of a wide range of species is thus dealt with in this volume. Data likely to be of more interest to the specialist than the general student are given in smaller type. One of us (D. W. H.) was responsible for Chapters 2, 3, 10, 11 and 12 and the other (J. D. S.) for the remaining Chapters.

March 1982

J. D. SMYTH
D. W. HALTON

Preface to the first edition

The aim of this book is to give an account of the physiology of the Trematoda from the egg, through the developmental stages, to the adult worm. Although the Trematoda have been extensively studied, as far as the writer is aware, an account of the physiology of the group has not hitherto appeared in any language. This text is an attempt to produce a general picture of trematode physiology; it is not a detailed survey of all the physiological work which has been carried out on individual species.

Several difficulties arise in attempting to cover this field. First, most of the physiological studies have been carried out on species of trematodes of medical, veterinary or economic importance. Although this position is understandable, it does not necessarily follow that the species studied have been those most suitable for experimental work; indeed, this approach has undoubtedly resulted in the neglect of other trematode species which have special advantages for certain kinds of physiological investigations. The domination of parasitological research by pragmatic considerations reflects to some degree the historical development of the biological disciplines, at least until the last decade. Fortunately, the value of any parasitic organism as an experimental model *per se* is becoming increasingly appreciated and there is now a strong wave of interest in parasitism as a biological phenomenon, quite apart from any consideration of possible effects on the economy caused by the species of host or parasite.

A second difficulty is that many of the biochemical or biophysical techniques which have proved most valuable in studying physiological phenomena in free-living organisms have been developed as precise tools only within recent years. Hence, so far as the parasitic platyhelminths are concerned, the data based on these methods are very limited. In some areas of the biology of the trematodes, then, much early work may have been carried out with methods or techniques for which more sophisticated techniques are now available. This is, of course, a common state of affairs in scientific work and one which constantly confronts workers in every field.

It is now widely recognized that the advance of biological research has become so rapid and the amount of published work so vast that the 'half-life' of any scientific text is inevitably shortening by the time it is published. This text is unlikely to be exceptional in this respect and advanced workers are therefore advised to supplement its contents by reference to recent published work, most of which can be found conveniently listed in Helminthological or Biological Abstracts.

October 1965

J. D. SMYTH

Acknowledgements

We are grateful to the following, who have read and commented critically on various sections of the text: Mrs N. J. Barrett, Dr J. L. Bennett, Dr J. A. Clegg, Dr C. Davies, Dr R. V. Gotto, Dr R. E. B. Hanna, Dr J. B. Jennings, Dr G. C. Kearns, Dr D. J. McLaren, Dr D. P. McManus, Dr D. Lane, Mrs M. M. Smyth and Professor L. T. Threadgold.

Most of the illustrations have been redrawn from original sources to conform to a uniform style and we are grateful to the skill of Mrs N. J. Barrett and Miss F. C. M. Craig in this respect. Mrs Smyth also contributed several illustrations, and helped at every stage in the preparation of this text. Mrs Barrett was largely responsible for the final form of the illustrations and we are grateful for the meticulous care and patience with which she carried out this task. We are also indebted to the following who contributed original drawings or photographs: Dr M. K  ie, Dr P. F. Basch, Dr M. J. Howell, Dr C. Davies and Dr D. J. McLaren.

The typing of the chapters of one of us (J. D. S.) and all the references was carried out by Mrs G. Adams in London and we are indebted to her skill and patience and for her generous assistance to both of us in numerous other ways. Mrs E. J. Purdy, in Belfast, was responsible for typing the remaining chapters (by D.W.H.) and her skilful help is gratefully acknowledged.

We are grateful to numerous authors and to the following editors or publishers for permission to use material:

Academic Press Inc. (London) Ltd.; Adam Hilgar Ltd.; Acad  mia Nyomda; American Elsevier; American Society of Parasitologists; American Society of Tropical Medicine and Hygiene; Birkh  user Verlag; Blackwell Scientific Publications; *Canadian Journal of Zoology*; *Central African Journal of Medicine*; Elsevier Scientific Publishing Company; George Allen & Unwin Ltd.; *Journal of Helminthology*; Liverpool School of Tropical Medicine; Marine Biology Laboratory, Helsing  r, Denmark; *M  moires du mus  um national d'histoire naturelle, Paris*; New York Academy of Science; Pergamon Press; Springer-Verlag; *Zoomorphologie*.

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Digenetic trematodes: general considerations

GENERAL ACCOUNT

Basic biology and life cycles

Adult digenetic trematodes, with very rare exceptions, occur exclusively in vertebrate hosts, where they are found typically in the major viscera such as the bile ducts, lungs and alimentary canal; one major group, the schistosomes, occurs exclusively in the blood system. Less favoured sites are the coelom, the urinogenital system, the swim bladder of fish, various sinuses or spaces and such aberrant sites as the eye.

A habitat which permits survival of an adult trematode must, in general, satisfy at least four criteria: (a) it must possess a connection with the outside world to enable the eggs to pass out of the body of the host (e.g. in faeces, sputum, blood or urine); (b) it must present a surface to which attachment, by means of suckers, is possible and on which feeding can take place; (c) it must possess an environment with a nutritional level sufficiently high to satisfy the enormous demands for energy and synthetic materials required for maturation and egg production; (d) it must be sufficiently well supplied with blood vessels so that (possibly toxic) waste products of metabolism may be rapidly removed from the vicinity of the worm.

With the exception of the alimentary canal, which is briefly considered (Chapter 3), it is not intended here to deal with the properties of the various habitats in which trematodes occur, but it is important that the properties of these be borne in mind when the physiology of a particular species is being considered. As far as vertebrates are concerned, the nature of some habitats has been dealt with in some detail by a number of workers, the best documented being the alimentary canal (222-225, 707, 736, 738, 1026, 1031) with only limited data being available (571, 1031) for tissue and other habitats such as muscles, lungs, liver, body cavity, kidneys and cerebrospinal fluid.

The digenetic trematodes differ from other groups of parasitic worms in that the first larval stages develop in intermediate hosts from the same

phylum, namely, the Mollusca. It is difficult to account for this extraordinary relationship between digenetic trematodes and molluscs other than by concluding that trematodes were originally parasites of molluscs and secondarily developed an association with vertebrate hosts.

Pearson (844a) has drawn up a possible evolutionary sequence which envisages the ancestor as being a rhabdocoele ectoparasitic on snails, whose eggs fell to the bottom and from which ciliated, free-swimming larvae emerged. In the next evolutionary stage, the rhabdocoele became endoparasitic, but left the snail as a tailed adult in order to disperse eggs by swimming. The ciliated larva (now a miracidium) which hatched from the egg became adapted to penetrate the snail. Post-miracidium parthenogenesis developed, perhaps in response to added difficulties in the life cycle. A tailed stage (= cercaria) leaves the snail and becomes initially gravid but, by degrees less so, until the 'adult' makes contact with another (vertebrate) host in which it eventually becomes mature and the life cycle is thus extended.

This phylogenetic explanation receives some support from the fact that certain free-living flatworms, notably dalyellioid rhabdocoeles, are commensal with molluscs and echinoderms and are clearly tending towards parasitism. The trematode redia also possesses certain rhabdocoele characteristics such as doliiform pharynx, sac-like intestine, paired protonephridia with separate pores, and surface muscle sheaths. It can be easily visualised that when vertebrates evolved, the digenetic trematodes – perhaps in an encysted form – became ingested and adapted to vertebrate hosts (with the accompanying selective advantages of greater food resources and wider distribution), while retaining their connection with their original molluscan hosts in which they now undergo polyembryony. Although this is the hypothesis generally put forward, the retention of the invertebrate phase in the trematode life cycle indicates that a molluscan intermediate host must have some selective advantage for the trematodes, an advantage probably related to the enormous reproductive capacity of this stage.

No clear ecological or physiological explanation can be put forward to account for the extremely complex larval stages formed in the Digenea. In addition to the molluscan intermediate host, a second intermediate host and, more rarely, a third intermediate host, as well as the definitive host, may be involved. This may result in a trematode being exposed to a range of habitats having widely different physico-chemical properties and exhibiting a range of nutritional levels. The genetical implications of this are considered later (p. 4). There is abundant evidence from many groups that parasites may undergo a diapause and may utilise the different

properties of such environments to 'trigger' the next stage of development when a new habitat is reached. Thus, the egg of the blood fluke (*Schistosoma mansoni*) is inhibited from hatching within its human host by the high osmotic pressure of the body fluids, the high body temperature and the absence of light; when it is passed to the outside world, it is stimulated to hatch rapidly by the lowering of osmotic pressure and temperature and the presence of light (545, 1050). The eggs of *Gorgoderina vitelliloba* in the bladder of *Rana temporaria* similarly hatch immediately on entering the water (1034). Many other examples could be quoted.

BASIC PHYSIOLOGICAL PROBLEMS

Trematodes as experimental material

The trematodes as a whole provide superb material for many biological studies. The examination of at least three organisms is involved: the parasite, its definitive host and its intermediate host(s). Quite apart from the anatomy of the hosts, which must be known in order to locate the parasite initially, it is also important to have data on those physiological and biochemical factors which frequently play an important role in controlling trematode development or maturation.

Again, the actual structure of the boundaries of the habitat (such as the intestine) and the physico-chemical and nutritional characteristics of its environment frequently reflect the type of trematode parasites which could successfully adapt to these conditions. To obtain information on the nature of this complex interrelationship requires analysis at ultrastructural, cytochemical and biochemical levels so that a multi-disciplinary approach becomes essential. Basic processes in biology which lend themselves to study by the use of trematodes include uptake of materials (especially amino acids and sugars) by various transport mechanisms (p. 55), cellular differentiation (p. 207), photobiological phenomena (e.g. egg-hatching p. 105), metabolic pathways (p. 71), neurosecretion (p. 44), hormone action (p. 212), and protein stabilisation (e.g. egg-shell formation p. 94). Trematode material is particularly useful for enzyme studies at the cytological level.

In analysing the host-parasite relationship, it is further necessary to have a knowledge of immunological reactions of the definitive hosts at a tissue and a humoral level, and investigation of these leads into the fields of immunology and serology - areas in which an enormous amount of work has been carried out in recent years (Chapter 13).

Genetics of the host-parasite relationship

The host-parasite relationship in trematodes is clearly a complex one involving at least three genetical systems; those of the parasite, the intermediate host and the definitive host. The trematode must be suitably adapted over a wide spectrum of its characteristics – morphologically, biochemically, physiologically, immunologically and ecologically – in order to survive. Unfortunately, speciation in trematodes has been largely defined in morphological terms and it has only been appreciated within recent years that (a) the morphology of a species can vary in different hosts and (b) in order to obtain an integrated picture of the true phenotype the study of all aspects of trematode biology (physiological, biochemical, behavioural, ecological and morphological) should be taken into account.

It is important to recognise that trematodes have characteristics (shared with some other invertebrates, e.g. cestodes (1031)) which makes it theoretically possible for them to produce 'strains' adapted to a new species or strain of host. These characteristics are (a) that they are hermaphrodites, and thus an unexpressed recessive mutant gene from one generation will appear in both male and female germ cells at the same time in the next generation; (b) that self-fertilisation may occur in some cases, or if cross-fertilisation does occur, it is likely – on ecological and behavioural grounds – that mating individuals will have closely related (if not identical) genotypes. Thus, a *single* mutation could theoretically give rise to a homozygous double recessive and an 'instant' mutant could appear. To these considerations may be added, (c) the fact that, in the molluscan host, trematodes multiply by polyembryony (i.e. multiplication of the original embryo), so that the mutant multiplies very rapidly.

These reproductive mechanisms could result in a large number of genetically identical individuals, i.e. a *clone* (in microbiological terms) developing from a single mutant. Thus a new 'strain' (or 'race') of a trematode, adapted to new 'strains' of intermediate or definitive hosts and perhaps having distinct physiological characteristics, could arise. Chinese, Formosan and Japanese strains of *Schistosoma japonica*, for instance, are well known, although in this case, since the organisms are unisexual, the hermaphrodite factor outlined above does not apply. According to Wright (1193) this process may happen within two or three generations; in this way *S. haematobium* appears to have become broken up into a multiplicity of local strains which differed in parameters such as growth rates, egg production, maturation time and pathology. Physiological strains of the strigeoid trematode, *Posthodiplostomum minimum*, in fish have also been reported (828).

Problems of the life cycle

Some of the basic physiological problems which arise when the life cycle of a trematode is considered are shown in Fig. 1.1. Within recent years, there has been a great upsurge of interest in analysing the physiological processes involved in the various stages of the life cycles of many trematodes, especially those of medical, veterinary or economic importance (e.g. *Schistosoma*, *Fasciola*). It must be emphasised, however, that these may not, in fact, be the best models for such studies and that the life cycles of other species may prove to be more rewarding from the point of view of investigating basic parasitological phenomena. Thus a bird schistosome (Fig. 8.11) matures more rapidly (9 days) and is much less dangerous to handle than the much-investigated *S. mansoni* which requires 34 days to reach maturity and is, of course, a dangerous pathogen. In many ways the bird schistosome provides the better model for experimental work and probably even more suitable species could be found.

Many basic physiological problems in trematode life cycles remain unsolved. Thus, the metabolism has been examined in detail only in a limited number of genera (e.g. *Dicrocoelium*, *Fasciola*, *Schistosoma*) and yet a knowledge of this is fundamental to the understanding of basic trematode biology as well as being important in chemotherapeutic control of diseases of trematode origin. The chemistry of egg-shell formation has been fairly extensively studied at least as far as the tanned form of egg-shell is concerned (p. 97), and yet little appears to be known of the keratin-type egg-shell which occurs in some species (especially amphistomes). A fairly substantial amount of work has also been carried out on the hatching of the egg (Chapter 5), and yet most of these studies have been concerned with those eggs which hatch *outside* the host (e.g. those of *Fasciola*, *Schistosoma*) and the processes in eggs which hatch *inside* the snail host (e.g. those of *Haematoloechus*) have been largely neglected (1034).

Turning to the larval stages, the way in which miracidia find a host has been increasingly investigated (Chapter 6) and the physiology of the cercariae has been actively examined (Chapter 7). On the other hand, the physiology of the intra-molluscan stages has again been largely neglected and little, for example, is known regarding metabolism or the processes controlling differentiation of sporocysts or redia or the mechanism by which the snail host may undergo parasitic castration as a result of the presence of trematode larvae. The neurophysiology of all stages – both adult and larval – has been very little studied, a position probably related to the difficulties of investigating this experimentally. Related to this are the fields of neurosecretion and endocrinology, about which almost nothing is known with respect to trematodes.

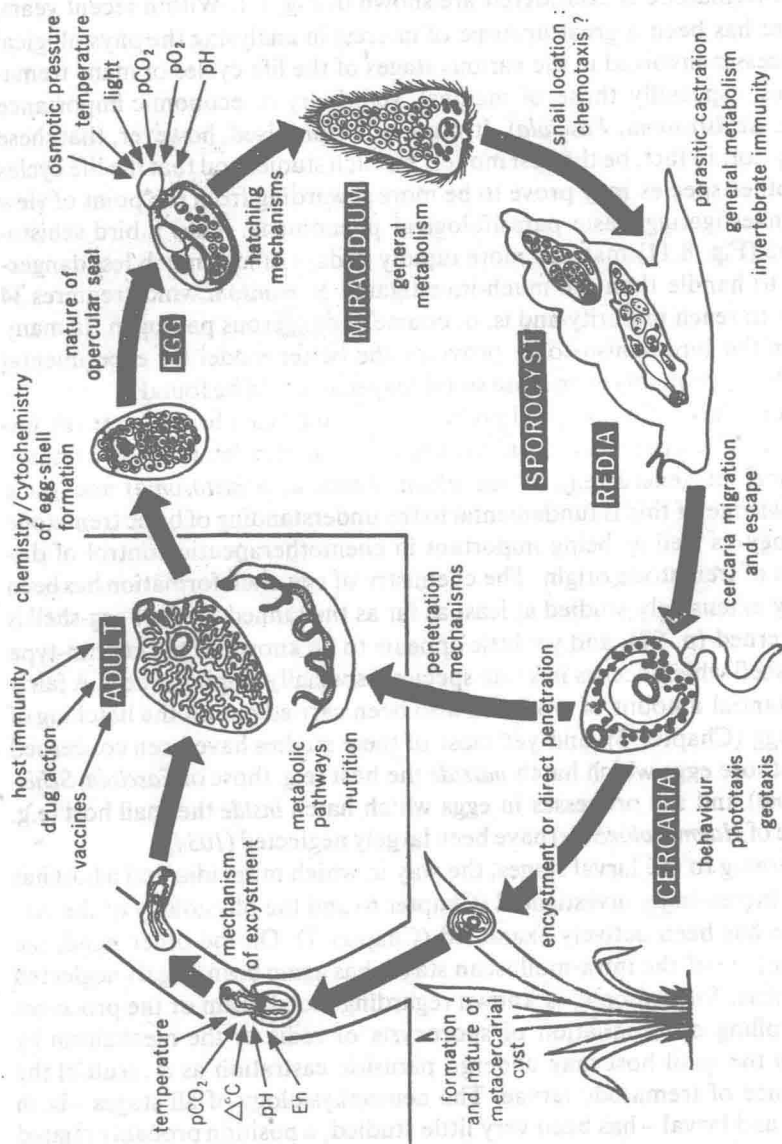


Fig. 1.1 A generalised diagram of a trematode life cycle, based largely on *Fasciola* and partly on *Schistosoma*, to illustrate some of the physiological processes involved. In many species a second or, more rarely, a third intermediate host is utilised.

The adult trematode – functional morphology

GENERAL REMARKS

The general pattern of trematode anatomy is illustrated in Fig. 2.1 and comprehensive accounts of the organisation and biology of trematodes

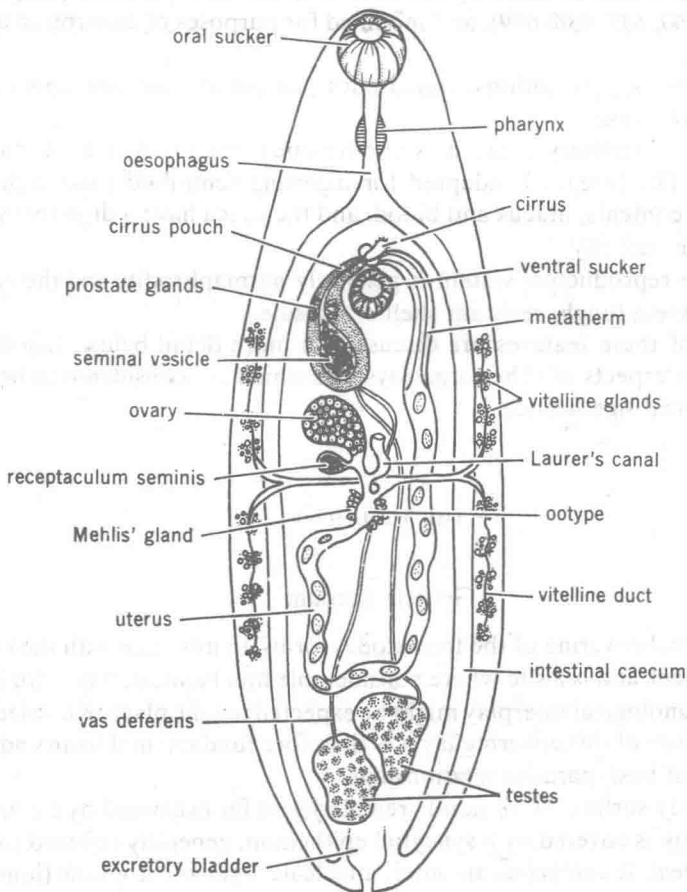


Fig. 2.1. A generalised diagram of trematode anatomy. (Modified from Cable, 1940.)