are trained in our schools and universities. At the same time, the Pasteur Institutes and the Institut Français de Recherche Scientifique pour le Developpement en Coopération (ORSTOM) are developing active research programmes in many endemic areas.

The combination of the well-established expertise of many groups in France in parasite epidemiology and ecology with clinical research provides our parasitologists with a unique opportunity to develop field research under optimal conditions.

However, the real question that remains is how adequate is our research potential in the face of the number and diversity of problems to tackle? In France, do we have sufficient numbers of scientists to undertake such an ambitious programme? The answer is obviously no, and the only hope is in wider international collaboration. Thus France has at European levels taken several initiatives in recent years, and played an active role in the successful development of several European Economic Community programmes, among which Science and Technology for Development (STD) I and presently STD2 are essential for parasitological research in Europe. This reflects the increasing will of French researchers to move from their nationalist traditions towards multinational cooperation. Many French laboratories actively participate in European networks and collaborative programmes, and there is no doubt that we will see a strong amplification of this process in the future.

Basic cellular and molecular studies leading to improvement of diagnosis, prevention and therapy of parasitic diseases, together with the development of field studies and operational research, and the extension of international collaboration leading to an integrated European programme, are the major trends in French parasitology that I can see developing.

Identifying trends in science does not necessarily imply an exclusive selection of priorities. I should re-emphasize how our progress in the knowledge of the fascinating world of parasites will always require a multidisciplinary approach, ranging from morphological and taxonomical studies to cellular immunology and molecular genetics, and the maintenance and support of individual expertise. Although I am personally convinced that sophisticated tools of modern biology such as DNA technology and the use of transgenic animals will be essential to our increasing understanding of parasitism, I also believe that our capacity to apply these tools for the improvement of human health will depend upon the strength of more traditional approaches in parasite biology and human epidemiology. The extraordinary evolution of biology over the last 20 years, the unifying and simplifying concepts it has raised, should not occlude the complexity presented by both parasite infections and the factors that govern their incidence, from immune response genes to socio-economics.

There is no doubt that French parasitology will continue to contribute to the successful development of a frontier science, both to its basic roots and to its application to human and animal health.

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Parasitology in France: Some Aspects of the Present

O. Bain, D. Camus and J. Prod'hon

Numerous organizations participate and cooperate on parasitological research in France including the Institut national de la Santé et de la Recherche Médicale (INSERM), the Centre national de la Recherche Scientifique (CNRS), the Institut Pasteur, the Institut Français de Recherche Scientifique pour le Développement en Coopération (ORSTOM), the Institut national de la Recherche Agronomique (INRA), the Muséum national d'Histoire naturelle (MNHN), the Universities, the Collège de France, the Ecole Pratique des Hautes Etudes (EPHE) as well as various commercial firms. Exchanges and collaborations with foreign workers are continuous and essential to the success of research on tropical diseases. Here, in their own words, Odile Bain, Daniel Camus and Jacques Prod'hon highlight some aspects of current parasitological research in France.

It was not possible to write a complete review of research in all the fields of parasitology, consequently, we have deliberately chosen to limit our account to first, the host–parasite relationship from zoological and molecular points of view and second, to the development of control strategies. In doing this, we are conscious that we neglect several interesting lines of research, including modern diagnostic clinical parasitology in spite of the successful activities developed in these fields by groups such as those of Pierre Ambroise-Thomas, Marc Gentilini, Jean-Marcel Senet, and so many others.

Phylogeny and ecology

It would be difficult to gain an accurate picture of the biology of a host–parasite association unless basic knowledge is available of phylogenetic and epidemiological relationships. Several groups in France are actively working on parasite systematics: Irène Landau has specialized in the Sporozoa[1]; Stephane Deblock and Louis Euzet on the Platyhelminths[2,3]; Alain Chabaud on the Nematodes[4], and a number of others concentrate on vector taxonomy (phlebotomines[5,6], midges[7], ticks[8] etc.).

Some of the well defined topics are discussed below.

Chaetotaxy, the distribution of sensillae on

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Box 1

Nematodes are well suitable for phylogenetic research because of known free-living ancestors. They may be indicative of evolutionary origins of hosts: for example, they argue the Ethiopian origin of caviomorph rodents, arriving into South America during early Oligocene.

cercariae, was first discovered by Josette Richard in 1968 (Ref. 9) to provide a reliable basis for trematode systematics. This method, which also allows intraspecific discrimination, has proved valuable for epidemiological investigations of schistosomes[10,11].

Alain Lambert has also used successfully chaetotaxy in his work on the oncomiracidia of monogeneans[12].

For the nematodes of vertebrates, the rules of morphological and biological processes have been well defined and a coherent classification scheme has been proposed by Chabaud[13] which has allowed an assessment of the history and evolution of parasites (Box 1). Comparative data from parasites (see for example, Figs 1 and 2) and those from hosts (host range, biogeography, paleobiogeography), show various distinct evolutionary patterns[14,15]. The coevolution of host and parasite, classically illustrated by the oxyurids[16], in fact is seldom apparent in other groups of nematodes, and what Chabaud calls 'zoologically non coherent spectra'[14] are more frequent. This classification refers to three main processes:

(1) The parasite line is associated with host animals which appeared during the same evolutionary period. For example members of Molineinae, a subfamily of trichostrongyloids, are parasites of bats, carnivores and primates, all of which are ancient hosts that evolved during the early Eocene (60 M years ago).

(2) The host range depends upon ecological conditions. For example, oxyurids of South-east Asian squirrels show host distribution patterns that are unrelated to the host-subfamilies, but rather to the preferred host niche in the forest, canopy or subcanopy[17].

(3) The parasite line evolves by transfer from one host group to another via the 'capture phenomenon'.

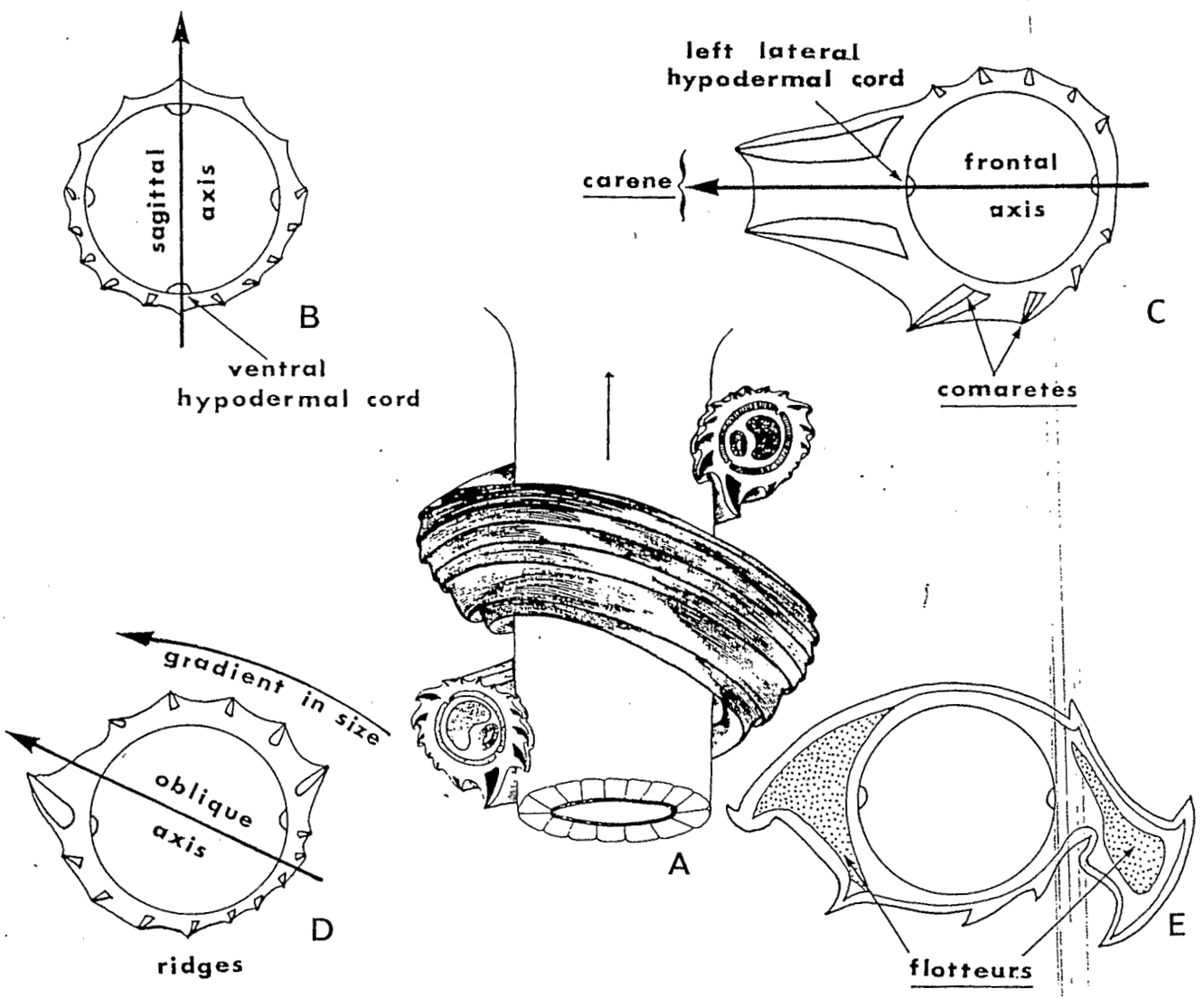


Fig. 1. In trichostrongyloids, the synlophe, ie. the cuticular ridges used for locomotion and attachment to intestinal villi (A), has been studied in more than 500 species by Marie-Claude Durette-Desset since 1964. From the basic plan of the trichostrongylid and molineid lines (B) have evolved many specialized types (C, D, E represent the different evolutionary levels of the heligmosomid line)[15].

Examples are given again by trichostrongyloids: two subfamilies (Libyostrongylinae and Cooperiinae) were successively parasites of ratites (flightless birds) in the late Paleocene, then of pliomorph rodents in the Eocene, and later expanded into lagomorphs and Bovidae during the Oligocene. The 'capture' phenomenon is a frequent evolutionary mechanism seen in groups as diverse as nematodes and fleas[18].

One of the interesting problems set by parasite evolution is the polyparasitism of one host by congeneric species, a phenomenon that careful morphological studies have shown to be a common occurrence. There are many examples, for instance Annie Petter[19] has for some years worked on palearctic herbivorous tortoises whose colons harbour 5000–200 000 individual organisms belonging to 15 different species, the majority of which belong to two genera; interestingly, the relative abundance of each species is well defined and obeys the laws established for free-living organisms. Similarly, Landau and colleagues have established that 12 species from the genus *Isospora* coexist in the intestine of the domestic sparrow[20] and it is now known that, in monopisthocotylean monogeneans, biparasitism of fish gills is the rule[21]; in men too, the common oxyurid *Enterobius vermicularis* is generally associated with another species *E. gregorii* (Hugot and Tourte-Schaeffer, 1985).

In an individual host, different spatial and temporal ecological niches may explain polyparasitism; but Chabaud and Durette-Desset[22] suggested another explanation, a temporary isolation of host populations which allowed speciation of the parasite but was not long enough to let the hosts diversify.

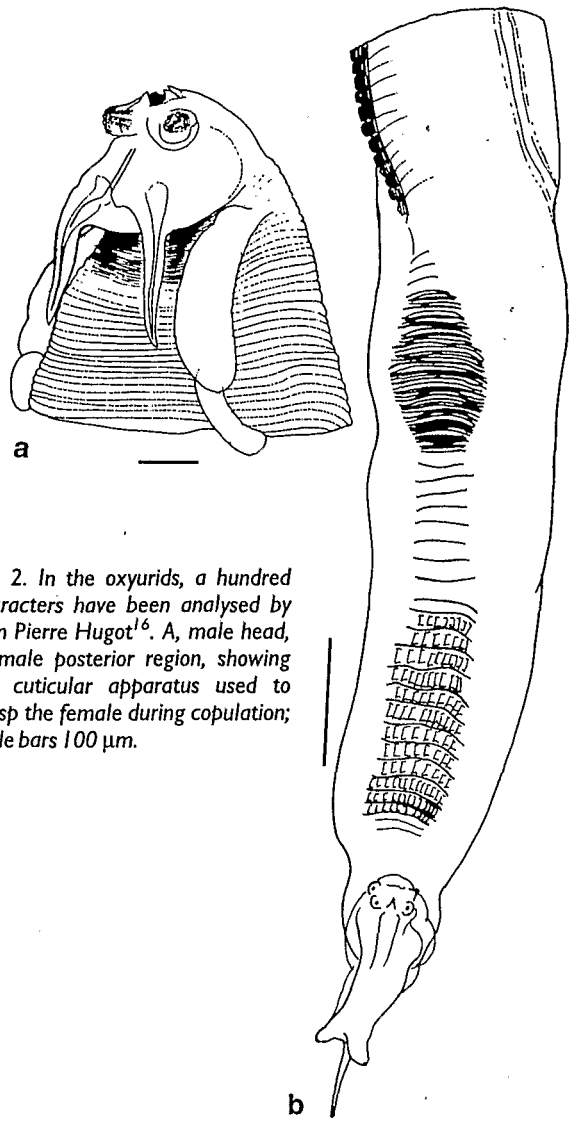


Fig. 2. In the oxyurids, a hundred characters have been analysed by Jean Pierre Hugot[16]. A, male head, B, male posterior region, showing the cuticular apparatus used to grasp the female during copulation; scale bars 100 µm.

Strategies of dispersal

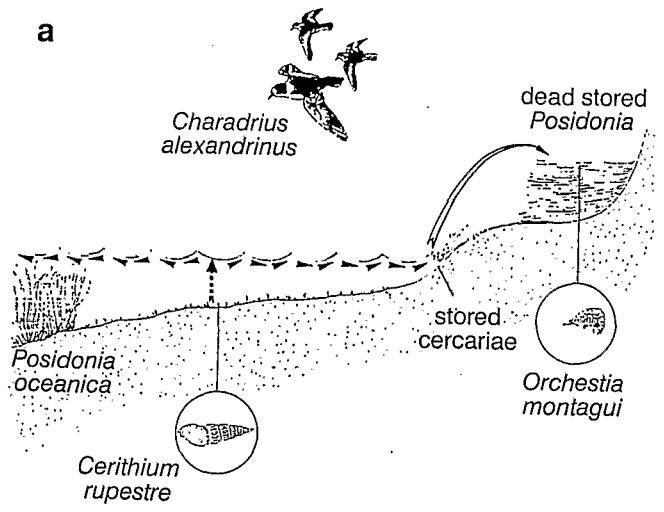
One fascinating aspect is the diversity of the transmission events which were raised in the different lines of parasites during their evolution to answer the necessity to infest new hosts; this is illustrated at any stage of the life cycle[23] by behavioural or anatomical adaptations (Fig. 3); some of these fundamental mechanisms are detailed.

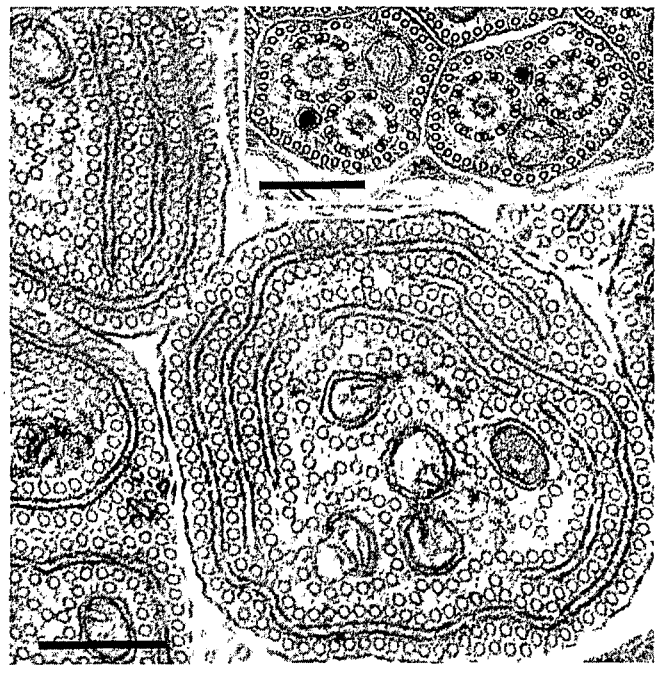
One of them is the possibility of a given species to present different morphs in response to different environmental conditions. For example, two morphs take action in the dispersal strategy of the trichostrongylid *Telardorsagia*, a parasite of sheep; one morph is characterized by an increased fertility and a clumped distribution, of high concentration in certain individuals of the host species but this morph is only frequent when favourable conditions exist, such as temperate climate and low host resistance[27].

With the refinement of identification techniques[28] has come the realization that polymorphism occurs more frequently than previously thought. By using these techniques extensive genetic analyses of Chagas disease have made it possible to identify the major clones within the taxon *Trypanosoma cruzi* and to ascertain their geographical distribution[29]. The medical and epidemiological significance of the major clones are currently being studied using specific polymerase chain reaction kDNA probes[30].

Another interesting adaptation is the timing of transmission events to match contact between parasite and host. In Guadeloupe, the chronology of release of cercariae from the mollusc vector differs between murine and human *S. mansoni*, and corresponds with the respectively nocturnal and diurnal activity of the vertebrate hosts[31]. Hybridization experiments by Alain Théron and Claude Combes resulted in the production of intermediary chronobiologic phenotypes, showing that this phenomenon is genetically controlled[32].

Vectors themselves act to regulate transmission by various mechanisms. In filariasis for example, our laboratory has found that the greatest establishment occurs when the microfilariae penetrate the stomach wall during the 12 h which follow the ingestion of the parasites by the vector species, this regulation is quite different: the proportion of microfilariae which arrive in the haemocoel may decrease (limitation) or increase (facilitation) with increasing number of ingested microfilariae this being the result of different modifications of the stomach wall in response to parasite stimulation[34]. These represent the insect's





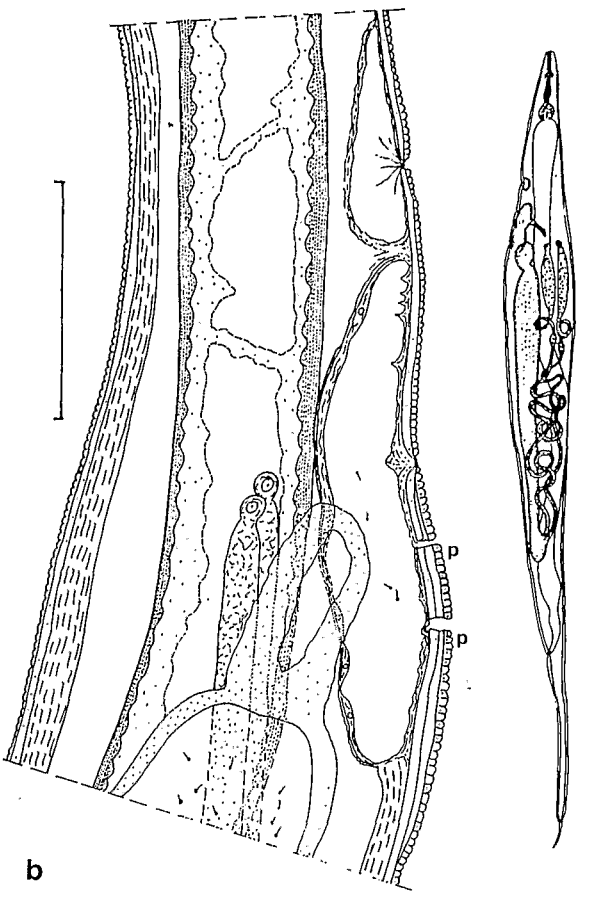


Fig. 3. Some examples of strategies of parasite dispersal. (a) Cercariae of Maritrema misensis *float near the lagoon surface; in the unsheltered lagoons they are projected by wind in water drops up to the bank where lives their second host; in calm lagoons cercariae develop in another second host which has direct contact with water[24]. (b) Oxyurid males have* n *chromosomes[95] and a shortened life span; this constraint has resulted in various adaptations; one of these is traumatic insemination, illustrated here by a young female of a rabbit oxyurid showing cuticular perforations (p) and the special pocket collecting the spermatozoa[25]; scale bar = 1.3 mm for whole worm, 250 μm for section. (c)* Diplozoan *adults are permanently fused together and they have aflagellate sperm, versus the normal biflagellate sperm of other polyopisthocotyleon monogeneans[26] (insert); both scale bars = 200 nm.*

original immune responses and it is obvious that they will have important epidemiological consequences (Fig. 4)[35].

Similarly, in the protostrongyloids of cattle that have molluscan vectors, there is a limitation or facilitation depending upon whether the reinfestations occur close together in time, or further apart; this regulation seems to be due to modification of the mollusc mucus as in the case of limitation larvae that are immobilized or destroyed by the vector's mucus[36].

Another mechanism that acts on parasite dispersal is the occurrence of dormant stages. The stages responsible for relapses or recrudescences, although more difficult to demonstrate than the acute phases, are shown to be frequent. In members of Coccidiomorpha, dormant stages are either cysts composed of sporozoite equivalents, the cystozoites, that develop in intermediate hosts which are part of a food chain (Coccidia), or schizonts which develop very slowly and produce relapses of the parasitaemia, and gametocytes (Hemosporidia). These different strategies represent two different adaptations of the parasitic cycle and have been defined by Landau[1] as the sporozoite system (eg. *Toxoplasma*) and the gametocyte system (eg. *Plasmodium*).

Animal models

The wealth of knowledge that has been gained on the phylogeny of host–parasite relationships has been particularly valuable for identifying suitable model systems for laboratory research. These are necessary to discover secret but important phases of the parasite life and to elucidate immunopathological problems linked to parasites, such as fibrosis[37]. Without these, the application of molecular techniques to test the feasibility of various vaccine and drug developments is not possible.

A great deal of work done on experimental malaria uses the animal models found during 1965–66 in the forest tree rodent, *Thamnomys*, from the Congo basin forest[38]. Since then the maintenance of numerous strains by cyclical transmission through *Anopheles stephensi* has facilitated research in many fields from drug testing in primary cultures of hepatocytes[39] (a technique also developed for *P. falciparum*[40]), to investigations on drug resistance to chloroquine. The various stages of the cycle in the blood have different degrees of sensitivity to drugs and the detailed study of the periodicity of *Plasmodium* species of *Thamnomys* revealed three different timing niches. These observations have direct chronotherapic implications. It has been shown, for example, that merozoites of the chemoresistant *P. yoelii* persist as a latent stage for long periods in rodents[41,42]; the study of the merozoite biology brings about a new biological approach and may be of great importance for the understanding of drug resistance mechanisms[42].

Three species of rodent filaria have been found by our laboratory and experimentally maintained to answer some major problems. *Monanema martini* has skin-dwelling microfilariae and induces dermal and ocular lesions similar to those of human onchocerciasis[43]; it realizes a practical model which completes the usual ones set up with bovine or equine *Onchocerca* species. *Litomosoides galizai* by its capacity of developing in the white mouse[44], is an exceptional tool to favour immunological and biomolecular studies of the filarial diseases. Jean-Charles Gantier (Faculte de Pharmacie, Chatenay-Malabry) with a third species, *Molinema dessetae*, has shown that an apparently harmless filaria is far from being innocuous for its natural host and reproduces pathology similar to that observed in human filarial disease[45].

Finally, it was discovered in the INSERM laboratory of Villeneuve d'Ascq that rabbits act as laboratory models for *Pneumocystis carinii* and conveniently need no immunosuppressive treatment to facilitate infection (Fig. 5)[46].

Molecular aspects

Medical research has mainly focused on vaccine and drug development with the goal of reducing the impact of parasitic diseases in tropical countries. Basic research has been strongly required for these projects which rapidly appeared dependent on a better knowledge of parasite biology and host–parasite relationships.

The pioneering effort in this field made by Jean Biguet and André Capron, using qualitative immunological methods, showed that fungi and parasites were composed of both specific antigens, and antigens that are common to other species, genera or even classes. These observations were important for the development of immunological assays in the diagnosis of parasitic or fungal diseases[47,48]. However, the main break-throughs have followed reports of common antigens between parasites and their hosts. These observations have led to the concept that adaptation to a parasitic mode of life could be partly dependent on mimicry and/or phyletic convergence[49–51].

Seminal immunological research on host–parasite relationships in schistosomes has revealed previously unsuspected effector and regulatory immune mechanisms. One of the most interesting series of observations has provided evidence for immunity resulting from the joint activity of multiple effector mechanisms. Antibody dependent cell-mediated cytotoxicity (ADCC) against the schistosomulum stage can be obtained *in vitro* with macrophages, eosinophils and platelets, and direct evidence also exists for the relevance of effector mechanisms with the three cell populations *in vivo*[52–55].

A major contribution from the Caprons' laboratory during the investigation of ADCC mechanisms was identifying the role of anaphylactic antibodies in parasite-killing, hitherto considered only in the context of allergic responses[52–56]. The demonstration of interactions between IgE antibodies and non-mast cells or non-basophilic populations, has led to the discovery of IgE receptors on monocytes, macrophages, eosinophils, and platelets. Another aspect of the study of ADCC mechanisms was the discovery of factors specifically produced by effector cells after IgE-dependent activations[56–58].

The evidence for the selective production of defined antibody classes during schistosome infection has raised the question of the blocking-antibody functions of isotypes not directly involved in killing mechanisms[59]. Jean-Marie Grzych's hypothesis has been corroborated by the discovery of human IgM antibodies that are able to block the eosinophil-dependent killing of schistosomula[60].

Other mechanisms may also explain how the parasite is able to modulate immune attack by the host. Among them, schistosome-derived immunosuppressive factor (SDIF) is of particular interest since it is able to enhance other parasitic infections[61,62].

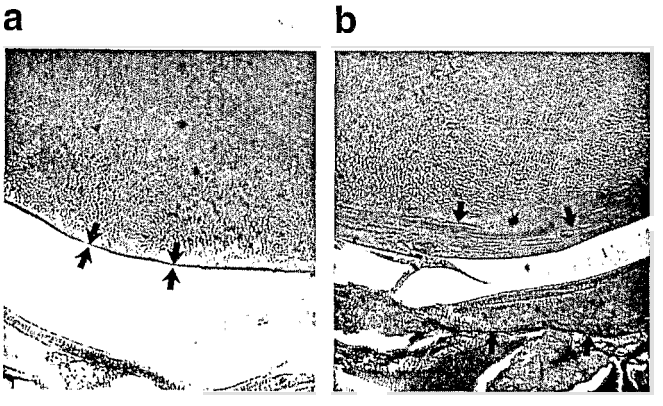


Fig. 4. In the savannah onchocerciasis region, the peritrophic membrane of the locally found Simulium sirbanum *is normally thin (a), whereas it thickens when ingested* O. volvulus *microfilariae stimulate the stomach wall (b). This results in a strong limitation as the microfilariae are prevented from penetrating into the haemocoel[35]; scale bar: 40 μm (peritrophic membrane marked by arrows; sections taken 6 h after a blood-meal).*

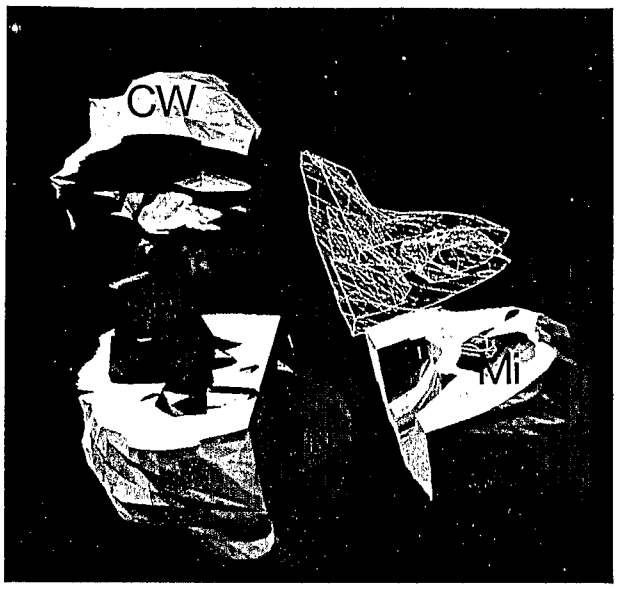


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Fig. 5. In some cases, 'high-tech' is needed when data are too complex to be analysed. One example is given by Pneumocystis carinii, *for which serial thin sectioning was ineffective in yielding the complex morphological structures of the parasite. The 3-dimensional reconstruction as well as morphometric data definitions were performed using a technology developed by aeroplane manufacturers (the Dassault system). Serial thin sections were digitized and a surface generated to define realistic structures composed of rectangles. The meshes are further shaded for better visualization, and arbitrary sections can be performed to point out particular structures: N, nucleus; CW, cell wall; ER, endoplasmic reticulum; Mi, mitochondria; overall size of* P. carinii *= 1·5 μm.*

Despite parasite-mediated regulatory and immunodepressive effects, protective mechanisms are still effective and can be elicited by vaccination. One of the most promising approaches for a schistosome vaccine is the use of a 28 kDa antigen that generates partial protection against infection after immunization in the mouse, rat, hamster, and baboon. Interestingly, Capron has shown that the protective P28 antigen of *S. mansoni* cross-reacts with *S. haematobium*, *S. japonicum* and *S. bovis*[63].

Fortunately vaccine development for *Plasmodium*, *Toxoplasma*, *Leishmania*, and *Trypanosoma cruzi* infections has also increased basic knowledge of parasite biology. One such area is the molecular basis of recognition and invasion of host cells by parasites.

In *P. falciparum* the interaction between free merozoites and erythrocytes is dependent on specific cellular ligands and parasite receptors. It appears that the parasite uses a soluble receptor as a bridging molecule between the merozoite and the sialic acid moieties on the surface of the erythrocyte[64]. The bridging mechanism is probably not strongly inhibited by specific antibodies since the immune complexes formed at the surface of the erythrocytes are quickly eliminated. The erythrocyte surface is therefore free for the binding of other bridging molecules[65].

The cellular and molecular events involved in the formation of the parasitophorous vacuole of *Toxoplasma gondii* probably reflect basic mechanisms common to many Sporozoa including *Plasmodium* spp.[66,67]. The role of rhoptries in cell invasion is now better understood and the recent report from Luis Pereira da Silva's group of an enzymatic process leading to the activation of a rhoptry antigen in *Plasmodium* has greatly advanced the knowledge of sporozoan biology[68].

Work on *T. cruzi* has corroborated another model for parasite-cell recognition proposed by Ali Ouaissi in which trypomastigotes have been found to have a receptor for host fibronectin on their membrane surface. It has been suggested that attachment involves the P85 surface protein of the parasite and the arginine-glycine-aspartic acid (RGD) sequence of fibronectin. Fibronectin receptors may also play a role in the attachment of *Leishmania* to host cells[69].

In *P. falciparum* infections, the inhibition of merozoite release from mature schizont-infected erythrocytes has been shown to be associated with the processing of the P126 molecule stored inside the parasitophorous vacuole. Patrick Delplace and colleagues have shown, from a concept developed by Alain Vernes, that *Saimiri* monkeys immunized with P126 develop a significant degree of protection against a challenge infection[70]. For *P. vivax*, potential targets for vaccine development are currently being defined against asexual and sexual stages. Peter David in collaborative work performed in Sri Lanka together with Kamini Mendis has demonstrated on *P. vivax* an extensive antigenic polymorphism and the dual activity of antibodies on the development of the parasite in the vector. These examples illustrate how a more detailed understanding of the features that appear unique to *P. vivax* among human malaria parasites should further enhance the possiblities of successful control and prevention strategies[71].

The main efforts for vaccine development in France have been developed by Pereira Da Silva's group who has selected *P. falciparum* antigens, using sera from immunized *Saimiri* monkeys that were able to transfer immunity passively. This approach has been made possible by the animal facilities developed by the Pasteur Institute in French Guyana[72]. These studies have produced some exciting data on the biology of *P. falciparum* infections:

First, it has been established, at least in *Saimiri*, that parasite neutralization by antibodies alone is not a major effector mechanism; on the contrary, the mechanism involved in protective immunity induced by passive transfer is mainly due to opsonic activity[73].

Second, it has been shown that malaria parasites expose a complex network of cross-reacting antigens that are recognized by antibodies from infected humans, and that the multiple cross reactivities between different antigen groups impair protective immunity[74]. This has resulted in the definition of a series of antigen families.

Third, amino-acid sequence homologies linked to immune cross reactions have been shown for poly-

peptide parasite antigens and host thymosin a1. Moreover, the parasite antigens share some of the biological acitvities of thymosin a1, which suggests that the parasite may be able to impair the regulation of host immune responses[75].

Fourth, protective and non-protective antibodies competing for the same antigenic determinants could help the parasites facing the host's immune response. Work in this area could lead to the definition of novel target antigens and to studies that determine how an antibody response can be elicited without inducing blocking antibodies[76].

The development of resistance of plasmodia to drugs underlines also the tremendous adaptative capabilities of the parasite. Ultrastructural investigations using immunological probes show that a chloroquine sensitive strain of *P. berghei* accumulates the drug in its endocytic vacuoles, but that in chloroquine resistant strains the drug is not localized and is scattered throughout the parasite cytoplasm[77]. This difference has been linked to an impairment in the acidification of endocytic vesicles[78]. The drug-resistance phenomenon favours also research for new malaria chemotherapy and a promising approach is based on the knowledge of the specific phospholipid metabolism which characterizes infected erythrocytes[79].

The epidemiolgy and control of major epidemics

From basic systematics, French parasitologists have extended investigations into the epidemiology of parasitic infections of which Mediterranean leishmaniasis naturally comes to the forefront in the laboratory of Jean Rioux. Sampling and identification of sandflies, prevalence analysis, and research of potential animal reservoirs permitted the elucidation of several problems in the epidemiological cycle, such as the existence of new vectors and of new vertebrate hosts, eg. the fox. Quantitative analysis of the canine reservoir was conducted concurrently with that of vectors by use of phyto-ecological indicators on a small scale: this resulted in the construction of a mathematical model giving a structural representation of an enzootic focus[80]. Analysis of leishmanian foci led to the development of biochemical techniques for identification and for phenetic and cladistic classification schemes (Fig. 6)[81].

Echinococcosis has become a by no means insignificant disease in the eastern and central regions of France with the changes of agricultural practice: this has stimulated field research with the objective of defining precisely the respective epidemiological roles of the carnivorous hosts[82] and the rodent reservoirs[83,84], together with an immunopathological investigation of the hepatic lesions[85].

The successful control strategy for schistosomiasis employed in Guadeloupe was developed by Yves Golvan from an ecological analysis of the disease with the help of several groups of specialists, such as those of Claude Combes, Jean Euzeby for the vertebrate hosts and Bernard Salvat for the mollusc vectors[86]. Infection of *Biomphalaria glabrata*, the sole vector, is linked to local contamination of water[87] by both human and murine faeces. The rodents are infected by strains of *Schistosoma mansoni* with distinctive characteristics[10,31] but whatever the strain, cercariae are released during the whole life of the infected mollusc, due to sporocyst replication[88].

Interestingly, there are a series of other trematode species, that are known to develop in *Biomphalaria glabrata* in Guadeloupe and which affect the snail's fecundity principally by blocking the secretion of a neurohormone. One of these, *Ribeiroia guadeloupensis*, has been exploited in an integrated control programme for schistosomiasis, which also involves the control of carriers and the improvement of sanitation.

French parasitologists from ORSTOM have been actively involved in the WHO Onchocerciasis Control Programme (OCP)[89]. Fifteen years after the inception of *Simulium* control by chemical larviciding in some 80% of the central OCP treated area (600 000 km^2), onchocerciasis transmission has been virtually interrupted and no recrudescence has so far been detected among the human and vector populations even after cessation of larviciding and a return of blackflies. Onchocerciasis no longer constitutes a public health problem in this part of Africa. This success is largely attributable to the long term nature of the fundamental and applied research programme. The human parasite and related species has given rise to phylogenic studies which have shown that *Onchocerca volvulus* is a 'capture' from a line particular to African savannah bovines[90], and it was demonstrated that one of these animals species develops in the human parasite vector, giving a similar L3[91]. A number of cytospecies of the *Simulium damnosum* complex have been identified, together with knowledge of their distribution, bionomics, and vectorial role[92]. The consequent need for control specificity has given an important input to

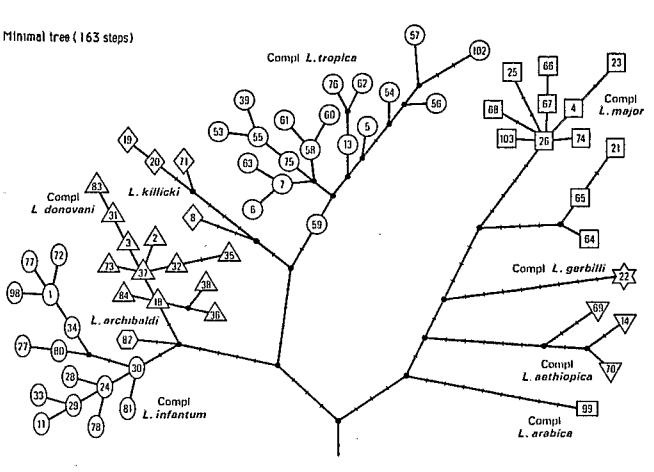

Fig. 6. Cladogram of Leishmania *of the Ancient World, using 15 characters (alloenzymes). It shows the clonal type of evolution of these parasites. In the* L. killicki *branch, two of the four zymodemes (numbers 19 and 20, from Namibia) are related to both human and hyracoid parasites and argue the zoonotic origin of the* L. tropica *complex.*

ongoing immunological and genetic research on the *Onchocerca volvulus* complex and its relationship with the vector cytospecies. The difficulties of treating, but not permanently polluting an aquatic environment, together with a need to combat resistance to insecticides has stimulated much study. Finally the accumulation of 15 years of results has allowed the construction of a statistical model for onchocerciasis transmission that has subsequently been used for prediction of infection and disease trends after vector and chemotherapy control.

Since 1987, a number of mass treatment trials by ivermectin has been undertaken. Besides countries in the OCP area, a trial has taken place in Northern Cameroon in a focus of hyperendemic savannah onchocerciasis that has never been submitted to *Simulium* control. Twenty thousand people over five years old have been treated[93]. Comparison of several treatment protocols have shown that two doses administered at six monthly intervals, followed by annual retreatments, leads to a major reduction of microfilarial loads and their further maintenance below 15–20 mfs/snip (Community Microfilarial Loads) ie. at the safety level for which onchocerciasis is no more an important ocular problem of public health. Treatment coverage was about 65% and the reduction of transmission exceeded 60%. After a first round of treatment, 20% of the people in hyperendemic villages had moderate adverse reactions, which although cured by simple drugs nevertheless required a medical monitoring two days post treatment.

Although ivermectin also acts as an insecticide, engorgement of flies on treated patients does not increase the mortality rate of the vector. However, interesting and unexpected effects on transmission are induced by ivermectin: during the first three weeks following treatment, the intake of microfilariae by blackflies fed on treated people is highly reduced compared to that fed on untreated patients having similar low microfilarial density[94] and the passage of the microfilariae to the haemocoel is also reduced.

The feasibility of mass treatment with ivermectin has thus been verified. However, target populations and a joint strategy for both mass chemotherapy and vector control still have to be defined.

The fact that only 95 references are quoted gives an imperfect view of the extremely wealthy and fructuous present. That has been built thanks to the right orientations chosen by our 'Maitres'. It emphazises the necessity to pursue the investigations in two major closely linked fields: natural history of the parasite and biomolecular host–parasite relationships.

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Parasitology in France: The Past

I. Humphery-Smith, J. Théodoridès, L. Touratier and A-M. Le-Flohic

The 'French School of Parasitology' has its roots in the thirteenth century. Since then, it has contributed much to our understanding of parasitic organisms, their biology and their role as etiological agents of disease. In many fields of parasitology, the names of members of this school remain associated with taxonomic groups or species and they include two Nobel Prize winners, yet today, the origins of these names and the efforts of these early parasitologists have too often been forgotten. Here, Ian Humphery-Smith, Jean Théodoridès, Louis Touratier and Anne-Marie Le-Flohic outline the highlights of the French contribution to our knowledge of host–parasite relationships.

Prior to the efforts of Robert Hooke (1635–1703) and Antoni van Leeuwenhoek (1632–1723) and the subsequent development of microscopy, the discipline of parasitology did not really exist. However, right back to antiquity[1–5], notions of parasites and parasitism were in evidence, although these organisms were not necessarily associated with disease before the work of Girolamo Fracastoro (1478–1553), Francesco Redi (1626–1697), Jan Swammerdam (1637–1680) and Edward Tyson (1651–1708).

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Early thoughts

The idea of parasitism was first introduced into France by a Catalan, Arnaud de Villanova (c1240–1311), who visited Montpellier in about 1285. Arnaud de Villanova taught medicine at Montpellier and used his knowledge of both Italian teachings acquired in Salerno and the strong Arab influence in that part of the world. The Islamic experience, together with the works of Avicenna and Galen, provided the basis of his writings on parasitology, but the introduction of the term 'solium' or sovereign (of worms) in association with the taenid tapeworm of man is attributed solely to him[2].

Shortly afterwards, Henri de Mondeville (1270–c1318) arrived in Montpellier, bringing with him learning gained from Guillaume de Saliceto in Italy. Mondeville in his *Chirurgia*[6] wrote in detail on the human scabies mite and associated lesions, but did not suggest any causative relationship. The renowned medieval surgeon and inventor of sutures using golden thread, Guy de Chauliac (c1290–1367), repeated much of what his colleague at Montpellier had to say on human scabies in his *Chirurgia Magna*[7]. However, he went further and spoke of the virulent and contagious nature of these organisms or 'syrones' (later 'cirons' in French), which tunnelled their way between flesh and skin. This affirmation of cause cannot be given too much credence, as it probably represents little more than an association of two phenomena brought about by a 'causative humour'. The members of this early Montpellian school are presented in Fig. 1, a–c.