parts of the world, as far as documents of greater or lesser antiquity allow us to trace its movements in time and space. Its 'natural history' ist the study of such factors as the identity of the causal agent; its epidemiology; its reservoir or reservoirs; the way in which the agent circulates and is eventually released into the external environment; its adaptation to one or several species, and so on.

As a living entity, the infectious disease is more dependent on human activity than any other. Schematically, one can divide this activity into two categories. On the one hand, mankind has searched for ways to fight against infectious diseases by the study of their causal agents, by research into methods of treatment, and by prophylaxis, which may be individual (vaccination) or collective (improvements in sanitation, eradication of vectors or of animal species which act as reservoirs, etc.). The activity in question is, of course, beneficial to the human species, and it can have very striking results, like the retreat of malaria in Europe, the control of yellow fever, and the eradication of smallpox.

But, on the other hand, we are forced to recognize that human activity since the dawn of time has never ceased to work in various ways on behalf of the infectious diseases unconsciously, involuntarily but very effectively. First and foremost, we have constantly extended their area of distribution, by taking them on journeys and placing more and more rapid means of transport at their disposal. Plague provides one of the clearest examples; its 'natural history' can be summarized as the transfer of a bacterium by a flea from an infected rodent to a healthy rodent or to a human being. Limited by these conditions, even under the most favorable circumstances the disease could hardly have travelled more than a few kilometers, and could never have crossed the oceans. But the history of the plague shows us that man, and he alone, has made it possible for the disease to invade the world by offering it new and faster means of transport; at first he transported infected fleas or rodents only as fast as he could walk, but later at the speed of his transport animals; finally, sailing ships were put at the disposal of the plague – they were still slow, but they were followed by steamships and finally aeroplanes. The history of cholera shows how the destiny of the Vibrio bacterium is linked exclusively with the movements of human beings; it benefited first from railways and river-routes, and finally from air transport, which has dominated the present pandemic. The history of yellow fever, that of syphilis, according to the 'Columbus theory', and that of the leptospiroses, show how man has involuntarily provided the necessary carrier from one continent to another.

The transformation of the landscape, particularly as a result of deforestation, has gradually changed the original 'closed' environment, the forest, into an 'open' countryside, and this has modified the activities of predators; the history of rabies in Europe is correlated with large-scale deforestation. In Africa, irrigation schemes involving the construction of large dams have provided malaria and bilharzia with every opportunity for causing epidemics. A study of the relationships between man and other animals shows how far man, in satisfying his many needs – for example for food, energy and emotional satisfaction – has transformed localized infections into world-wide ones; brucellosis, melioidosis, leishmaniasis, tuberculosis.

Changes in human habits – even very minor ones – can cause a profound disturbance in the relationship between man-and-infectious agent or man-and-vector; for instance, the parallel decrease in Europe of both plague and typhus may be linked to general increase in the habit of removing one's daytime clothes during the night, thus impeding the reproductive cycles of the ectoparasite vectors. The attitude of man to water, his habitat, and urbanization have determined the evolution and epidemiology of salmonellosis, leptospirosis, viral hepatitis and poliomyelitis. We have shown how the appearance of infection with *Yersinia enterocolitica* could be connected with some recent modifications in dietary habits; changes in the composition of menus, the general use of domestic refrigerators, and the provision of meals on a large scale. The 'Legionaires' Disease' is another example of a 'new' disease caused by 'old' bacteria; by modifying his habits – often only slightly – man comes into contact with species of bacteria or viruses from which his previous mode of life had protected him.

As he gains access to more and remote territories, man gains access at the same time to reservoirs of infectious agents which he has never reached before, thus liberating, for example, the Marburg, Lassa and Eboli viruses. By modifying his internal environment for therapeutic purposes (e.g. transplants), or by upsetting his bacterial flora completely by a badly-conducted antibiotic therapy, man turns previously inoffensive organisms into opportunists. By his activities, by the development of new habits, indeed by his very existence, man modifies his relationship with microorganisms, and thus transforms their ecology, completely changes their destiny and, at the same time, that of the diseases they transmit.

Imported diseases in Switzerland

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It is not possible to have a precise idea of the real frequency of imported diseases in Switzerland. The statistics of the Swiss Tropical Institute (STI) show a steady rise of malaria cases, but since 1980 also a stagnancy of the number of other diseases.

Giardiasis and intestinal worms are most frequently observed. But it is malaria, hepatitis and acute diarrhea that preoccupy patients and doctors most. Some of these diseases present epidemiological and clinical characteristics that are misleading for the doctor.

For the correct management of the laboratory examinations, which are often the only means to make a reliable diagnosis, a good anamnesis is indispensable! In this field it is therefore essential that appropriate methods be used by a qualified and experienced staff. Thus, a certain centralization on the level of laboratory work is required.

Some tests, especially serodiagnostic tests, do not have a sensitiveness and a specifity of 100% and the discovery of a parasite does not always explain the symptoms observed with the patient. It is therefore important that the

practitioners are able to interprete their results or that they refer to a specialist.
By some examples the problems and tendancies of the parasitological diagnosis of these diseases are briefly analyzed.
As for the malaria, particular emphasis is laid on the importance of the blood examination until immunological techniques for the detection of antigenes can assure the continuation of the procedure. Unless there is no room for doubt, an examination must be repeated at the proper time. The same situation applies for the stool examinations for the detection of intestinal amebiasis and lambliasis.
Taking into account the increasing resistance of *P. falciparum* to Chloroquin, the STI has introduced routine in vitro tests. Moreover, these routine in vitro tests play a more and more important role in the diagnosis of protozoa, e.g. leishmaniasis and trypanosomiasis.
Techniques for special examinations like rectal biopsy, skin-snips, urine and blood filtration are briefly illustrated.
Blood eosinophilia is often the only objective sign for a helminth infection. It could indicate either an invasion phase (mainly ascariasis, strongyloidiasis, fascioliasis) with or without Loeffler syndrome or helminths in an impasse (toxocariasis) or even helminths that are difficult to trace without appropriate laboratory techniques (strongyloidiasis, filariasis). A comprehensive anamnesis and a serological screening, which is now possible through the ELISA technique, are the basis for the diagnosis of these eosinophilia.

Serodiagnosis of parasitic diseases

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The reliability of a serological test depends primarily on the quality of the antigen used. In contrast to most serological tests for bacterial and viral diseases, defined antigens are not readily available for the serodiagnosis of parasitic diseases. In most cases crude antigen extracts or whole organisms are used. Thus, parasite serology very often lacks specificity. The problem of specificity is especially pronounced in tests for helminth diseases, where cross reactions not only occure among related organisms but also among phylogenetically divergent species. To overcome partly this specificity problem, we developed a multi-antigen ELISA screening system, which will be described here for the example of serodiagnosis of infections with tissue dwelling helminths.
The test system is characterized by the following features which distinguish it from more conventional ELISA systems:
a) relatively short (15 min) incubation times at 37 °C for sera and conjugate (conjugate: goat anti-human IgG (H + L), IgG fraction conjugated with horseradish peroxidase, Miles No. 61-230-1).
b) relatively low serum dilution (1:160 in PBS saline, containing 0.05% Tween-20).
c) relatively high concentration of the substrate and chromogen (H_2O_2 0.03%, orthophenylene-diamine 0.1%).
d) rapide and perfectly linear enzyme-reaction (stopping time ± 3 min at 20 °C, reactions stopped with 8N H_2SO_4).
e) in each horizonal row of wells, a different antigen preparation is adsorbed on the plastic surface.
f) the patients sera are then tested vertically against the different antigens.
Thus, avoiding inter-test variations and keeping low intra-test variations, small differencies between extinction values of different reactions can be recognized for one serum in a reproducible way. Since short incubation times and low serum dilutions are used, the test may preferentially detect antibodies of higher avidity, thus increasing the specificity of the test. The short incubation time with the substrate chromogen solution leads to a test system similar to the k-ELISA, enabling better quantitative measurements.
In this ELISA system, we found that, despite the lack of specificity of some antigen preparations, homologous antibody-antigen reactions give in most cases the highest extinction values, enabling the multi-antigen approach to indicate the true infection of the patient. In addition, we observed typical reaction patterns in a given helminth infection. These reaction patterns are visualized in the figure.

1. Toxocariasis patients have antibodies directed mainly against specific metabolic antigens of *Toxocara canis* larvae II. In this regard, it is interesting to note that a high sensitivity and specificity was recorded with the toxocariasis in vitro precipitation test. Our results indicate, that the humoral response of toxocariasis patients is directed predominantly against very specific antigens released in vivo and in vitro by the *T. canis* larvae II. However, some borderline reactions (cf. fig.) between toxocaral patients sera and antigens from *Dipetalonema viteae* or *Echinococcus granulosus* can be observed when the homologous toxocariasis system reveals very high extinction values. In line with the hypothesis of a specific immune response in toxocariasis patients, crossreactions with metabolic antigens from *T. canis* larvae II are rarely observed and if, to our knowledge, predominantly with sera from filariasis patients, showing very high extinction values with *D. viteae* antigens. These crossreactions, however, never exceed extinction values over 1.0 (cf. fig.).

2. The most often observed cross reactions occur with sera from filariasis and echinococcosis patients and antigens from *E. granulosus* resp. *D. viteae*. However, the homologous antibody-antigen reactions are stronger than can be observed with the cross reacting system. Thus, in most cases a good indication for an echinococcosis infection can be obtained by just comparing the extinction values of both reactions. This is less true when estinction values with *D. viteae* antigens are considered, since virtually all sera from patients with extraintestinal helminthic infections, exhibiting high serum antibody concentrations, can crossreact with *D. viteae* antigens. This problem could not be overcome to date by using antigens from other filariae. Thus, antigens from *D. viteae* serve as a good general marker for extraintestinal helminthiasis (except toxocariasis). This is also true with antigens from *E. granulosus* at lower extinction values, since crossreactions always occur with both antigens.

3. Antibodies from patients with fascioliasis crossreact very strongly with antigens from *D. viteae* and *E. granu-*