SCIENCE

VOL. 75 FRIDAY, FEBRUARY 26, 1932 No. 1939

SCIENCE: A Weekly Journal devoted to the Advancement of Science, edited by J. MCKEEN CATTELL and published every Friday by

THE SCIENCE PRESS

New York City: Grand Central Terminal
Lancaster, Pa. Garrison, N. Y.
Annual Subscription, $6.00 Single Copies, 15 Cts.

SCIENCE is the official organ of the American Association for the Advancement of Science. Information regarding membership in the Association may be secured from the office of the permanent secretary, in the Smithsonian Institution Building, Washington, D. C.

HOW THE OTHER HALF LIVE[1]

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THE title of my address this evening was called for by our secretary eight months ago; this made it necessary for me to select a title broad enough to cover anything I might wish to say. I was quite certain at the time that I would talk about parasites. I might equally well have chosen the title "How the Neglected Half Live" instead of "How the Other Half Live," since very few zoologists seem to realize what a large part of the animal kingdom consists of parasites. Those of us who have selected parasitology as a field of research know that every species of animal that has been studied carefully harbors within it one or more species of parasites. Man, for example, is known to be parasitized by about 25 different species of protozoa, 85 different species of worms and an uncertain number of different species of arthropods, the exact number depending on one's definition of a parasite. Many of these parasites appear to exist only in man. A similar condition prevails among domesticated animals and common wild animals and probably is universal. Hence it would appear that there are at least as many species of animal parasites as there are species of animal hosts for them to live in.

The number of individuals belonging to various species of parasites is astounding. The number of ciliates in the stomach of a cow, or cecum of a horse, the number of flagellates in the cecum of a guinea-pig, the number of malaria parasites in the blood of a human being suffering from malaria, and the number of amoebae in a dysenteric patient mounts into the billions.

Parasites have attracted more attention in recent

[1] Address of the vice president and chairman of Section F, American Association for the Advancement of Science, presented at the Zoologists' dinner in New Orleans on December 30, 1931.

years than formerly, but I believe zoologists in general still feel that there is some fundamental difference between free-living and parasitic animals and that the latter are of no particular importance as material for teaching purposes and research. This seems clear from the relatively small amount of space devoted to parasitology by teachers of zoology who have recently published text-books to fit their courses. For example, the "Invertebrate Zoology" used in the course at Woods Hole includes outlines for the study of 97 species of animals, only 5 of which are parasites. A text-book designed for courses in college zoology and written by well-known zoologists at the University of Missouri contains accounts of only three parasites and devotes eleven of a total of 585 pages to parasites and parasitism. A biology prepared for college students by a professor at Yale University contains 501 pages; two sections of this book comprising 22 pages are devoted to parasites. In a book on ecology written by a professor of zoology at Duke University, the subject of parasitism is relegated to the next to the last chapter and occupies 21 of a total of 417 pages. I feel free to criticize others for neglecting parasites in their text-books, since I have been guilty of the same offense.

Every one, I think, will agree with me that such a vast assemblage of animals deserves to be treated more fully than these statistics indicate is now being done. I should like to detail to you at some length the many advantages parasites present for biological study; how easily they may be obtained in large numbers; how interesting are their relations to their environment; how numerous are the problems of fundamental biological significance offered by them; and what great opportunities they give us, especially for the study of experimental evolution. However, because of lack of time, I will limit myself to a discussion of one group of parasites in a single host, namely, the protozoa of man.

For hundreds of years investigators have been studying the structure and physiology of the human body, and no other animal has ever been subjected to such careful and exhaustive examination. However, when all this knowledge has been assembled, it represents only half of the story. What is lacking is a knowledge of the fauna that use the human body as a residence, a food supply and a common carrier.

When one observes a relative or a colleague he may think he is seeing an individual, whereas, as a matter of fact, he is really looking at a menagerie. The human body may appropriately be compared to a zoological garden closed for the winter. The animals are there but one can't see them because they are kept concealed behind closed doors. Similarly the protozoan parasites of man are concealed from view because they all live inside of the body. But a proper examination will reveal them and I propose this evening that we take a peep through the keyhole into this marvelous assemblage of animal life.

The protozoan parasites of man may conveniently be divided into two groups on the basis of habitat. One group live in the digestive tract and are commonly known as intestinal protozoa. The other group live in the blood stream and are known as blood-inhabiting protozoa. These protozoa do not wander all over the body at will, but each of the 25 species that occur in man is definitely localized in some particular region of the body, just as free-living animals occupy definite habitats on the surface of the earth.

It is surprising to most people to learn that about one half of the general population are infected with a mouth-inhabiting amoeba. This organism lives in the tartar around the base of the teeth. It has been accused of being the causative organism of pyorrhea but has not been definitely incriminated. Transmission from one person to another no doubt takes place by contact. The logical conclusion is that those who are not infected have never been kissed. Human nature being what it is, there is no known method of preventing the spread of this amoeba. The other protozoon that lives in the mouth is a flagellate that is also probably non-pathogenic, although it occurs more frequently in diseased than in healthy mouths.

The two species of protozoa that live in the small intestine must be able to maintain themselves there against the rapid movement of food from the stomach to the large intestine. One type is a flagellate which possesses a sucking disc, by means of which it attaches itself to the intestinal wall to prevent being swept away. The other type is a coccidium which maintains itself by penetrating the cells of the intestinal wall. Coccidia are all pathogenic but are very rare in man.

The ten different species of protozoa that live in the large intestine are all more or less similar as regards their life histories. Most of them live in the lumen of the intestine and are harmless; but two of them, an amoeba and a ciliate, are responsible for the production of dysentery and are often lethal. Although 10 per cent. of the general population is infected with the dysentery amoeba, most of those infected are in the carrier condition, that is, although the organism is present, the human body is able to repair the damage caused by it so rapidly that no symptoms appear. This pathogenic amoeba is particularly prevalent in tropical countries and is responsible for thousands of deaths every year. Fortunately, several drugs specific for this organism have been discovered, and whereas formerly patients were almost certain to die in agony, now proper treatment just as certainly restores the patient to health.

The ciliate that causes dysentery in man is of considerable interest because we share it with monkeys and pigs; probably 80 per cent. of the pigs in this country have intestines swarming with this ciliate. Apparently they do not injure the pigs in any way, but the cysts that they produce are sometimes swallowed by susceptible human beings in whom they bring about dysenteric conditions. Most people are evidently not susceptible to this ciliate, since our food and drink must frequently be contaminated. A study of the cases that do occur reveals the fact that the patients had been associated in some way with pigs or had eaten insufficiently cooked pork products.

The other protozoan inhabitants of the large intestine of man are all supposed to be non-pathogenic, although certain protozoologists claim that several species of flagellates bring about intestinal disturbances. From about 5 to 50 per cent. of the general population may be infected with these intestinal protozoa. Inasmuch as no antagonism exists among these organisms and one person may be infected with the entire job lot assortment, it is probable that all but a very few of us have been unconsciously furnishing a residence and a food supply for several of these parasites and were totally ignorant of it. As a matter of fact, the material used in my laboratory at the Johns Hopkins University for the study of these protozoa is almost all furnished by the laboratory staff.

There is an interesting relation between these intestinal protozoa and the character of our diet. Meat-eating animals are not ordinarily infected with them, but vegetarians are very highly parasitized. This situation led to some experimental work which has demonstrated the effectiveness of animal proteins in preventing infection and of carbohydrates in intensifying infections. Casein seems to be the best of the proteins. A diet consisting largely of casein soon brings about a decrease in the number of certain organisms and often leads to their total elimination. Starch, on the other hand, provides a favorite article of food and results in an enormous increase of certain of these protozoa. The fact that rats fed on a high protein diet lost their intestinal protozoa suggested at once the treatment of human infections by modifying the diet. A series of menus were prepared in which animal proteins predominated, but which included such items as pickles and strawberries to make the food more palatable. The results when applied to human patients suffering from digestive disturbances due to certain protozoa were very striking; in many cases the protozoa disappeared along with the symptoms within a week. Two objections to this treatment have been reported; one patient was unable to get strawberries and another patient just couldn't eat pickles.

The blood-inhabiting protozoa of man are local in their distribution. The leishmanias, which cause kala-azar and oriental sore in the Far and Near East, and cutaneous ulcer in South America, are flagellate protozoa, all pathogenic and some of them very dangerous. The organism of kala-azar destroys thousands of human lives every year in Asia. Oriental sore is a disease that is called Delhi boil by the inhabitants of Bagdad, and Bagdad sore by the natives of Delhi. It is not a fatal disease, but leaves permanent scars in its wake. It is apt to occur on the face, being transmitted by a biting sand-fly. One attack gives immunity, hence it is the custom in certain eastern regions to inoculate children on some part of the body other than the face much as we vaccinate against smallpox. The resulting infection is mild, gives immunity and hence insures against facial disfigurement. It is becoming increasingly more difficult, however, because of modern styles of dress, to find a part of the body for vaccination that is not exposed.

Trypanosomes that are responsible for African sleeping sickness are also flagellates. They live in the blood stream and are transmitted from one host to another by tsetse flies. They are able to live not only in human beings but also in game animals, especially antelope; hence the flies have a constant reservoir from which they may become infected. Large sections of Africa are uninhabitable because of the presence of these protozoan organisms. Drugs have been developed in Germany, France and the United States that are effective against sleeping sickness if administered in the early stages of the disease. African sleeping sickness should be distinguished from Encephalitis lethargica, a type of sleeping sickness that occurs in this country and is an entirely different disease, the causative organism of which is still unknown.

Perhaps the most interesting of all the protozoa that live in man is the malaria organism. Malaria is undoubtedly the most important disease in tropical and subtropical regions and in some respects is the most important of all human diseases, since it is responsible for preventing the colonization of vast areas in the most fertile regions of the earth. As you all know, only female mosquitoes are able to transmit the disease, and even the female is quite innocent of any harmful intention, since she doesn't know the blood she sucks into her stomach is loaded. When she bites she regurgitates juices from her salivary glands into the blood stream of her victim, and in this salivary secretion are suspended the infective stages of the malaria organism. Malaria could easily be eradicated therefore, if we could teach mosquitoes not to spit. Malarial organisms occur in birds, monkeys and other animals as well as in man, but the bird malaria parasites are unable to set up in-

fections in human beings. We are not yet certain whether the parasites of man and monkeys are capable of setting up cross infections.

Much can be done to control malaria by killing mosquitoes, but there are still many problems unsolved. One of the most important of these is the problem of relapse. Quinine and the new drug plasmochin destroy most of the parasites in a patient and give relief from symptoms, but they do not ordinarily eliminate all the parasites and the host is thus in the carrier condition and liable to suffer a relapse at any time. What we need more than anything else to aid us in eradicating malaria is a drug that will destroy all the parasites in an infected person and thus prevent relapses. Many chemists and zoologists are now engaged in studies directed toward the discovery of such a drug.

Even if all the parasites are destroyed, we are in constant danger of reinfection. You probably all know about the student who was once asked to name a famous parasitologist of the past. "Milton," he replied, "because Milton wrote 'Parasites Lost' and 'Parasites Regained.'" The problem of reinfection must be solved by those who are in charge of our public health activities. As every one knows, the most conspicuous successes in the field of public health have been the campaigns for the eradication of such diseases as malaria and yellow fever. In fact, the residents of the Panama Canal Zone call a policeman if they are attacked by a mosquito.

Sometimes one type of parasite preys upon another type of parasite. An interesting and important case of this so-called hyperparasitism that has attracted wide-spread attention during the past decade is that of the effects of malaria on general paralysis or paresis. Malarial organisms, when inoculated into patients suffering from general paralysis, bring about a distinct improvement in the course of the disease. Patients are allowed to go through eight or nine malarial chills and fever and are then treated with quinine to check the malaria. The results of investigations of this type carried on in various parts of the world have almost all been favorable.

This review of the protozoan parasites that live in man may serve to refresh your memory regarding these interesting animals, but to determine satisfactorily how the other half live it is necessary to follow their entire life cycle from the invasion of a host to the escape of the offspring from that host. Much research is necessary to work out life cycles and the view-points of investigators working in several different fields must be combined before a satisfactory ensemble is attained. Zoologists are primarily interested in the taxonomy, morphology, physiology and development of the parasite; medical men are more interested in the reactions of the host than they are in the parasitic organisms that cause the diseases; and students of hygiene and public health emphasize those phases in the life cycle that have a bearing on the transmission of the parasite from one host to another.

I have attempted to combine the view-points represented by these three types of investigators into one program which I call "Host-Parasite Relations." In this program the events in the life cycle of the parasite, the reactions of the host to the invasion of the parasite, and the transmission of the parasite from one host to another are arranged in logical order beginning with the exogenous existence of the organism. Such a program may be compared with the study of a free-living protozoon involving the investigation of its life cycle, the interactions between it and the environment and its geographical distribution. There is no real difference between free-living and parasitic protozoa except that of environment, and the environment of parasites appears to be remarkably similar to that of free-living animals when the two are analyzed carefully.

Perhaps the best stage with which to begin a study of host-parasite relations is that during which the organism is transmitted from one host to another. Among human protozoa this is accomplished either by an intermediate host, for example by mosquitoes in malaria or tsetse flies in sleeping sickness, or by cysts that are swallowed in contaminated food or drink as in amoebic dysentery. It can not be too strongly emphasized that the parasite is passive and the host active during transmission and that consequently we are responsible for our own infections, either because we fail to prevent mosquitoes or other blood-sucking insects from biting us or because we allow our food and drink to become contaminated with fecal material containing protozoan cysts.

After gaining entrance to the body the protozoa are distributed to the primary sites of infection either in the blood stream or by the movements of the alimentary canal. This distribution is brought about almost entirely by the physiological activities of the host, the parasite remaining passive. The site of infection, whether the red blood cells, blood plasma, endothelial cells, muscle cells, mouth, duodenum or colon, is no doubt largely determined by the reactions of the different parasites to various stimuli; just as free-living protozoa become localized in particular types of habitats in a pond or in the ocean.

During the period when a protozoan parasite is becoming established in the human body there is a struggle going on between host and parasite. The host exhibits a natural resistance to infection which the parasite must overcome. For example, the acid condition of the stomach contents is detrimental to active protozoa; this obstacle is overcome by intes-

tinal protozoa by the production of cysts whose walls resist the action of the digestive juices and enable the organism to pass through the stomach unharmed. To a zoologist who has attempted to rear pure lines of free-living protozoa, one of the most remarkable features involved in the life cycles of parasitic protozoa is their ability to remain vigorous for an indefinite number of generations in a medium that is practically constant in temperature, density, chemical composition and food content. For example, the parasite of bird malaria with which we have worked in my laboratory for the past twelve years was obtained by Dr. Eugene Whitmore from an English sparrow in Brooklyn, N. Y., in 1913 and has lived in canaries ever since, multiplying once per day by asexual reproduction without the intervention of sexual reproduction or endomixis and without any perceptible loss of vigor. During this period these parasites have passed through over 6,600 asexual generations.

The interactions of host and parasite result in various changes in both organisms. If the host does not successfully resist the parasite it suffers injury, as evidenced by the appearance of symptoms which may lead to death. Or the host may build up resistance against the parasite, thus becoming immune and recovering from the attack. Often an equilibrium is established between host and parasite, the injuries of the host being repaired as rapidly as inflicted; the host thus becomes what is known as a carrier. Any change in the host that lowers its resistance and any change in the parasite that increases its virulence upsets this equilibrium, and the attack of the parasite again brings about the appearance of symptoms.

One of the most interesting phases of our program is that of host-parasite specificity. In many cases a particular species of host is parasitized by species of protozoa that occur in no other species of animal. Thus the 25 species of protozoa known to live in the human body are rarely found in lower animals. The rat, for example, which is so closely associated with man and lives on a somewhat similar diet, is parasitized by at least seven species of protozoa that belong to seven genera represented among human protozoa; these seven species, however, are morphologically different and may easily be distinguished from species belonging to the same genera in man. This is not true when the protozoa of man and monkeys are compared. Of the 25 species that live in man, 20 indistinguishable from them have been reported from monkeys and only 3 species have been recorded from monkeys that are not known to live in man. The assumption is reasonable that animals whose parasites resemble each other closely are near of kin. If this is true, we may add the species identity of parasitic protozoa to the other types of evidence that lead us to believe in the close kinship between monkeys and man.

The protozoan parasites that I have described this evening are considered to be normal inhabitants of the human body, and all of us probably serve as hosts for one or more species. The expression "we all" often applied by Southerners to a single person appears, therefore, to be quite appropriate. In many regions, where such diseases as malaria occur, every human being is infected from soon after birth until death. Fortunately for us, most of our protozoan parasites are not destructive, and we carry them about with us unharmed. It isn't pleasant, however, to realize how many millions of creeping microbes use our bodies as a protozoan universe, and it is natural for us to want to do something about it. Much has been done and is being done. Malaria, amoebic dysentery, sleeping sickness and other protozoan diseases of man have lost much of their terrors because therapeutic agents and methods of control have been discovered and put into practice.

However, protozoology needs more publicity than it has at present; probably not one person in a carload even knows that such creatures as protozoa exist. Perhaps, in course of time, biologists may be able to defaunate the human body and thus initiate a race of supermen. Modern facilities for rapid transit are, however, making this continually more difficult. Disease-producing organisms may be transported from one locality to another and for long distances either by human carriers or by intermediate hosts. The intermediate hosts of protozoan parasites are usually flies and bloodsucking insects; these are frequently transported from one country to another. It is usually not necessary, however, to take drastic action for the purpose of preventing the importation of animal parasites into the United States because of their complicated life-histories. For example, trypanosome diseases can not be transmitted in a locality where certain species of tsetse flies are absent, even if animals with trypanosomes in their blood are present in large numbers.

One field in which the study of the protozoa of man has taken a leading rôle is that of rendering the tropics as habitable for man and his domesticated animals as are the temperate regions of the earth. Such conquests as that of malaria and yellow fever in Havana and the Panama Canal Zone have a distinct bearing upon one of the greatest problems before mankind at the present time—the problem of population. Statistics show that the world's population has increased about two and one half times during the past century. Many methods of preventing further increases in population have been suggested, but no one can predict what the future may have in

store for us in this direction. We must, however, face the problem that confronts us to-day. In tropical countries large areas of land exist that are now sparsely inhabited and unproductive. That these tropical regions can be made healthful to men from the colder regions of the earth has been proved again and again by various nations that have founded colonies in the torrid zone. To do this it has only been necessay to control certain diseases, and these diseases have been for the most part due to animal parasites or their transmitting agents.

My remarks this evening may lead you to believe that we think we really know something about the protozoa of man. This, however, is far from the truth. One has only to look back to the situation that existed 30 years ago to realize our own position to-day. Zoologists in 1900 believed that they were living in an enlightened age, but now we know that they were densely ignorant. It seems probable that in 1960, 1931 will likewise be considered among the zoological dark ages. Hence, although we have made a good beginning in the study of parasitic protozoa we must continue our efforts until we are able to escape from the humiliating condition that exists at the present time and man ceases to be held in bondage by his invisible fauna.

OUR DEBT TO FARADAY'S EPOCH[1]

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ONE hundred years ago the first third of the nineteenth century was drawing to a close, as now is the first third of the present century. You may reflect that the stated facts are obvious and that the whole statement is a platitude. I center your attention on them with the clearly defined purpose of emphasizing the debt which we, in this first third of the present century, owe to discoveries originating in that significant first third of the immediately past century.

Using that first third as a landmark: James Watt, the founder of mechanical engineering, had already proved the usefulness of his conception of the steam engine; Lavoisier, the father of modern chemical thought, had just been guillotined by the revolutionists in Paris. Science and engineering had taken on new aspects, and the spirit of inquiry was abroad in a newly felt freedom.

Exclusive of those features of sentiment and religion, which must be dealt with independently because they are primarily of intellectual and spiritual moment, rather than pertaining to the physical conditions of health, comfort and convenience of the body, we are primarily dependent in our present-day living methods on a few great modern developments. Preventive medicine, sanitation, sound food preservation, transportation by water, rail and highway, electric quick communication, ready transmission of power, convenient artificial illumination, largely determine our relatively great assurance of health and comfort in life compared with the conditions of a couple of centuries ago.

I wonder whether any of you express to yourselves and associates doubts regarding the relative advantages in favor of our present status measured in health, comfort and opportunities for all men and women in the democratic countries, compared with the conditions of the common people of the great countries of a few generations ago. If you do, I assure you that it is because you have failed to study the effect of the changes of conditions; or, having studied them, you have failed to accurately interpret their meaning. When I speak thus in comparative favor of our own times I refer not only to average opportunities for health, comfort and happiness in life, but also to the conditions available particularly for those who are little favored with influence or money.

If you wish a bit of my meaning more fully illustrated, I invite you to drive through the Värmland and Dalecarlia provinces of Sweden, as my wife and I did last summer in a pigrimage to the birthplace, school place and tomb of John Ericsson. And then compare, feature by feature, the present comfortable, well-supplied life of the present dwellers, living secure in that community, with the sordid hardships of the life there several generations ago, which are identically described by Selma Lagerlöf in her distinguished saga of Gösta Berling. I am sure that the sordidness and hardships of the older life and the relatively healthful, comfortable and happy conditions of the present life in the area will impress you. The changes are revolutionary and heavily favorable to the present. Food is now certain for all. Children are born under sanitary conditions and with suitable medical aid. The sick are properly cared for. Products of the farms, forests and mines are of definite value. Reasonable periods of sleep and recreation are within command of all. Shelter and clothing are assured. This makes a deep-seated contrast with the

[1] Address delivered at the celebration of Faraday's life held in New York on November 18, 1932, by the New York Museum of Science and Industry.