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TROPICAL DISEASE INVESTIGATIONS IN AFRICA

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Even today, in the age of the hydrogen bomb and supersonic flight, much of Africa remains wild and primeval. In many parts of the continent, wild animals such as the elephant, giraffe, hippopotamus, and others still abound. Over large areas, man still lives a primitive existence in much the same way as did his forebears. Civilization has left little imprint upon him and he still carries on his daily occupation in accordance with his ancient customs.

In vast areas in Africa there are countless persons suffering from many strange and exotic diseases, some of which are found nowhere else in the world. Some of these diseases are swift killers, while others leave their victims permanently incapacitated until death finally intervenes. These diseases greatly interfere with the economic development of the tropical countries and hamper the exportation of enormous reservoirs of material resources so much needed by the free world. Furthermore, there's a constant threat of the spread beyond the tropics by means of today's rapid transportation systems.

Research in the field of tropical medicine is of more than academic or altruistic concern to the people of the United States, because our own economy is involved. 60 percent of our imports come from the tropical countries, including many of the strategic materials which we lack.
Before one can hope to control or eliminate these various diseases, it is necessary to study them in the areas in which they are prevalent. To do this, scientists must make their way into the heart of the endemic areas by whatever means are available. Shown here is a National Institutes of Health research team working as a part of the Point Four program, leaving for a field survey in the Liberian hinterland.

Field investigations are especially important in arriving at methods for the prevention and control of tropical diseases. Tropical medicine is not a static science and the tropics cover vast areas of the globe. Methods employed to combat a particular disease in one part of the tropics may not be equally applicable elsewhere. All aspects of tropical medicine, however, cannot be studied in the field but must be investigated at special research centers. Not only in the tropics, but also in the more advanced areas where specialized equipment and qualified personnel are more readily available. This film will show how aspects of some of the more important tropical diseases of Africa, with special reference to conditions in Liberia, West Africa. Together with some of the research work being done not only in that area, but also at the National Institutes of Health of the United States Public Health Service.

MALARIA

HEAVILY ENDEMIC
MODERATELY ENDEMIC
LIGHTLY ENDEMIC

Malaria is an acute, recurring, febrile disease caused by protozoan parasites of the genus Plasmodium which are transmitted by and undergo part of their life cycle in certain anopheline mosquitoes. This disease is one of the main obstacles to successful settlement in many warm countries. The part it plays in general world morbidity and mortality is hard to judge, but it is thought to be responsible for more illness and death per year than any other transmissible disease.

The prevalence of malaria parasites in a population group can best be ascertained by means of microscopic examination of thick blood smears. While the parasites are more abundant in the blood of infants and children before the development of immunity, it is not uncommon in hyper-endemic areas to demonstrate them in 80 to 90 percent of adults examined. Thick blood smears are used primarily in surveys and for case findings because of high concentration of parasites provided by this technique.
Thin blood smears are more suitable when exact species determination is required or when morphological studies are desired.

In order to gain a complete picture of malaria in any region, it is necessary to study the mosquitoes that transmit it. Larvae and pupae of anopheline mosquitoes are sought in the field in order to locate their breeding areas and to study the conditions under which they multiply. Adult mosquitoes can be captured in traps placed over windows of huts. The study of these mosquitoes will show, among other things, which species are the most important vectors in a given locality. This is done by demonstrating sporozoites, the infective stage of the malaria parasite, in the salivary glands of the mosquito. These glands are easily dissected from the mosquito and when gently crushed under the cover slip, the sporozoites are expelled and can be readily seen under the microscope.

Only a small portion of the mosquitoes captured are found infected. But in view of the vast numbers which feed on unprotected individuals in the tropics, even a small percentage of infected mosquitoes is sufficient to maintain a high incidence of infection in the population.

The clinical diagnosis of malaria is frequently difficult. It may be confused with many diseases, both cosmopolitan and tropical. This is inevitable in view of the pathology which consists mainly of mechanical interference with the vascular supply in many organs of the body. Among the tropical diseases with which it may be confused are kala-azar, amoebic liver abscess, relapsing fever, and yellow fever. Among the cosmopolitan diseases, it may simulate typhoid fever, tuberculosis, brucellosis, influenza, myelitis, and other septic conditions as well as certain diseases of the central nervous system.

Great strides have been made in recent years in developing new drugs for the suppression and treatment of malaria by testing thousands of compounds against the malarias of lower animals, such as chicks. The drug being tested here is administered orally to the infected chick. Blood smears are prepared before and at intervals after treatment. The anti-malarial effect of the compound is then determined by the presence or absence of the malaria parasite.

An essential part of all research concerns the publication of the results. Shown here is a monograph in which data on nearly four thousand compounds are analyzed to show the relationship between chemical structure and anti-malarial activity.

The final evaluation of any anti-malarial drug must of course be made against human malaria in endemic areas.

ONCHOCERCIASIS

Onchocerciasis is a form of filariasis transmitted by gnats of the genus Simulium. The adult worms live in subcutaneous nodules, while the larvae, or microfilari, migrate within the layers of the skin. These microfilari frequently penetrate into the structures of the eye so that a variable proportion of the population in the endemic area suffers from partial or complete blindness. Blindness due to this disease usually affects less than 1 percent of the population. However, in scattered foci, the incidence may be extremely high. The subcutaneous nodules, which contain the coiled up adult worms, are the most characteristic lesions of onchocerciasis.

Ocular changes usually occur only after long and repeated exposure. These changes bear no relation to the anatomic location of the nodules but rather are associated with the development of sensitivity to antigenic substances produced by the parasite or its product.

The most widely distributed vector of onchocerciasis in Africa is the gnat Simulium damnosum, which breeds in cataracts and waterfalls of rapidly flowing streams where the larvae and pupae may be found attached to submerged stones and vegetation.

The other principle vector is Simulium neavei, which is found primarily in East Africa and parts of the Congo. It was only after years of diligent search that the larvae and pupae of this fly were found to live only on the carapace and legs of a freshwater crab, Potamon niloticus. The discovery of the ecology of the larval and pupal stages of this gnat has greatly simplified the control and eradication of onchocerciasis in the areas in which Simulium neavei is the sole vector.

The Simulia are daytime feeders which have a painless bite and are not easily disturbed after they have started feeding. The incidence of infection in these flies is determined by searching for developing stages of the worm onchocerca in nets captured while feeding on natives serving as human bait. The ingested larvae, or microfilari, leave the stomach of the fly and penetrate the thoracic muscles where they grow into the so-called 'sausage stage'. After six days or more of development, the elongated infective larvae travel to the labium of the fly. When the insect bites another person, the larvae escape and penetrate into the skin. The microfilari live in the dermis of the skin and can be demonstrated easily in skin biopsies which consist of thin slices of skin placed in drops of normal saline. This method is satisfactory only where onchocerca is the only filarid encountered, since microfilari, which are characteristically found in the blood, occasionally occur in skin biopsies.

All species of microfilari can be readily demonstrated and identified in scarification smears which are prepared by making several superficial incisions in the skin with a scalpel and squeezing out the blood and tissue juices.
This material can be examined fresh for motile microfilari, but must be examined as a thick blood smear stained with hematoxylin to determine the species.
Wuchereria bancrofti microfilari have a sheath and the nuclei extends farther forward than do those of the Onchocerca volvulus which have a somewhat bulbous head and no sheath.

TRYPANOSOMIASIS

Trypanosomiasis is an acute and chronic disease produced by protozoan parasites of the genus Trypanosoma. American trypanosomiasis, or Chagas disease, is caused by Trypanosoma cruzi which is transmitted by bugs of the genus Triatoma.

TRYPANOSOMA CRUZI

African trypanosomiasis, or sleeping sickness, is caused by Trypanosoma gambiense in the western and equatorial parts of Africa and Trypanosoma rhodesiense in the eastern part of the continent.

TRYPANOSOMA CRUZI
TRYAPANOSOMA GAMBIENSE
TRYPANOSOMA RHODESIENSE

Both are transmitted by various species of Glossina or tsetse flies. It has been said that the economic future of equatorial Africa depends largely upon the issue of the struggle of science against the scourge of trypanosome diseases which affect both man and domestic animals. The sleeping or somnolent stage of Gambian trypanosomiasis begins with apathy associated with tremors, shuffling gait, and incoordination from which it proceeds to true coma and eventually death. The latter is usually due to malnutrition or intercurrent infection.

When the trypanosomes are ingested by the tsetse fly, they undergo a cyclical development in the digestive tract. After 18-34 days, infective trypanosomes reach the salivary ducts and enter the bite wound at the next feeding. Glossina palpalis, the tsetse fly which transmits Gambian sleeping sickness, frequents the dense undergrowth bordering water courses. The pregnant female produces a single, large, fully developed larvae at intervals of about ten days. The larva burrows into the ground to a depth of about two inches and immediately pupates. The pupa hatches into an adult fly in three to 12 weeks. Tsetse flies of the Glossina morsitans group which transmit Rhodesian sleeping sickness are less dependent upon water and are found in wooded savanna country that provides moderate shade. Cover is more or less essential and suitable breeding grounds largely determine the location of the fly belt.

With drugs now available, it is possible to cure the majority of sleeping sickness patients, provided they are treated before invasion of the central nervous system by the parasite. All individuals in an endemic area are examined for evidence of the disease, such as enlarged posterior cervical lymph nodes, which is called Winterbottom's sign. And for the presence of the parasite in blood smears. Nodule aspiration is useful in diagnosing the Gambian form of the disease.

A study of the spinal fluid will determine whether the central nervous system is involved. An increase in the amount of protein or in the cell count indicates such involvement, in which event, the patient must be treated with one of the more toxic, arsenical compounds such as tryparsamide or arsabal.

Due to the rather ineffective methods of diagnosing sleeping sickness, attempts are being made to develop tests which will detect the disease in early stages. Fractions of protein derived from trypanosomes are purified by various procedures

including dialysis and then concentrated by evaporization and lyophilization. Drying is completed under vacuum while the material is still frozen. The resulting product is then used in various types of serologic tests.

Information gleaned from basic research on the physiology and metabolism of the trypanosome contributes to knowledge of the parasite and may lead to the development of a drug that will destroy them regardless of their location in the human body.

COMPARATIVE STUDIES ON THE METABOLISM OF THE CULTURE FORM AND BLOODSTREAM FORM OF TRYPANOSOMA GAMBIENSE

SCHISTOSOMIASIS

Schistosomiasis, a chronic disease caused by blood flukes of the genus Schistosoma, is characterized by inflammatory and proliferative lesions of the liver, genital urinary, and lower intestinal tracts.

Several species of schistosomes are capable of infecting man but only three are important clinically: Schistosoma mansoni and the more virulent Schistosoma japonicum primarily involve the intestinal tract, while Schistosoma hematobium affects the genital urinary tract.

SCHISTOSOMA MANSONI
SCHISTOSOMA JAPONICUM
SCHISTOSOMA HEMATOBIUM

Schistosomiasis is one of the most widespread and serious of all the diseases produced by animal parasites. The disease is estimated to affect 115 million people in the world and seems to be spreading in the Near East and Brazil. Shown here is a district health clinic in the Liberian hinterland staffed by a U.S. Public Health Service physician under the foreign technical assistance program. Nearly half of the patients attending this clinic have urinary schistosomiasis. Symptoms of this infection are caused by small ulcers in the bladder and consist of hematuria, burning on urination, and supra pubic or perineal pain.

The prevalence of schistosomiasis varies considerably from place to place, even in the same endemic area, and hence surveys are necessary to evaluate its local importance.
The ova of Schistosoma haematobium in the urine are concentrated by centrifugation. The supernatant is decanted and the sediment is examined under the microscope for the eggs.

When the schistosome egg reaches fresh water, a ciliated larva, or miracidium, is free and must find and penetrate a suitable snail host in order to continue the life cycle. Only a few species of snails are capable of serving as intermediate hosts for the schistosomes. In the snail, the parasite undergoes a two-phase process of development ending in four to seven weeks with the production of tens of thousands of free swimming, infective forms called cercariae.
When an individual wades or works in infested waters, the organisms become attached to the exposed skin and penetrate within a few minutes. Slow-moving streams clogged with vegetation and high organic content are particularly favorable habitats for the snails which transmit schistosomiasis. In such advantageous surroundings, these snails frequently are found in enormous numbers. Man himself contributes to their welfare and to the spread of the disease when he disturbs natural conditions and constructs new ponds, alters the course of streams, or introduces irrigation systems.

Colonies of snails that serve as vectors of schistosomiasis in many parts of the world are maintained at the National Institutes of Health and are utilized in research on prevention and control of this disease.
The molluscicide effect of numerous compounds has been determined in the laboratory by mixing various concentrations of the substance being tested in small aquaria. The vector snails are then added to the treated water and after a stated interval of time, the snails are removed and the lethal action of the compound is determined by noting the proportion of dead and live snails.
Using this or some other techniques, it has been shown that sodium pentachlorophenate is an effective molluscicide, and numerous field tests have been made with this compound. Shown here is a report on an experiment to compare the effect of this chemical on different laboratory strains of the same vector species.

Studies to determine the mechanism of action of sodium pentachlorophenate have been made on various species of snails.

Shown here is an experiment in which a suspension of cells is prepared by comminuting the liver of a snail followed by differential centrifugation. Various concentrations of a molluscicide are added to this suspension and the effect on the metabolism of the cell is observed.

These studies indicate that the molluscicidal property of sodium pentachlorophenate is due at least in part to its ability to inactivate certain enzyme systems and thus prevent the cell from utilizing the energy available from the metabolic breakdown of nutriments.

Comparative studies on the physiology and metabolism of the same species of vector snails from different geographical areas, such as the anaerobic carbon dioxide production experiment shown here, have demonstrated much differences in what appear to be identical snails. This helps to explain why snails in different areas do not always react similarly to identical control measures.

The schistosomacidal activity of numerous drugs has been tested in mice. These animals have been infected by inserting their tails into water containing live cercariae. After the infection has developed the mice are treated with a test compound, and after suitable intervals are autopsied to determined the schistosomacidal effect of the drug.
Untreated mice, or those treated with ineffective compounds, have adult worms in their mesenteric and portal veins and evidence of innumerable eggs in the liver.
Mice treated with effective drugs have few eggs in the liver and show remains of dead worms in the liver tissue. Furthermore, all adult worms have disappeared from the mesenteric and portal veins.
In this experiment, antibiotic complexes of antimony trichloride were found to be active orally against Schistosoma mansoni, but no more active than plain antimony trichloride or tartar emetic.

It is hoped that eventually an effective and nontoxic drug will be found to aid in the control of what the World Health Organization considers to be one of the world's most important health problems. During the past half-century, great strides have been made in our knowledge of tropical diseases. However, only a few of these diseases have been adequately controlled. Because of their public health and economic importance, they must be studied more intensively both in the laboratory and in the field. If these maladies can be further checked and ultimately eradicated, Africa need no longer be referred to as the "dark continent". Equal benefits will redound to other parts of the globe where many of these scourges also take their toll.

THE END

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