

blood than there would be in some Puerto Rican city with a high incidence of infection.

A consideration of the history of these persons in New York is very instructive. Perhaps the majority cease to have lymphangitis; a great number have no attacks in the spring, winter or autumn; *but a certain proportion continue to have them in the summer.* The attacks however do not manifest themselves with the same regularity that they did in Puerto Rico, but show a tendency to appear only during the oppressive heat waves which occur from time to time during June, July, August and September and which last for several days.

The fact that filarial lymphangitis is not found at the higher altitudes in Puerto Rico has been discussed. At these altitudes are many persons who have gone thither because of frequent attacks of lymphangitis in the plains. They remain free from attacks at the higher levels.

The Treatment of Elephantiasis.—Nothing need be said here about operative procedure in cases of elephantiasis of the scrotum, since the methods in general use seem to meet all requirements. Experience in Puerto Rico shows that the Kondoleon operation²², even when performed by men of considerable skill, very rarely gives permanent relief. The recent operation devised by Dr. Hugh Auchincloss³⁹ seems to be a much more rational method of attack, firstly, because it attempts to remove the disease at the same time that it removes the deformity; secondly, because it can be modified or extended according to local indications; and thirdly, it can be performed on any aspect of the diseased area with special reference to the severity of the acute symptoms. This operation requires considerable experience and patience in order that sufficient depth of skin be left to insure a proper blood supply to the flaps.

Hydrocele:—The ordinary operation in use at the present time for the treatment of hydrocele (eversion) seems to be beneficial in filarial cases, and frequently there is no further collection of fluid in the tunica vaginalis after it has been performed. However, in cases of hydrocele with recurrent funiculitis this condition has been observed to recur even after the hydrocele sac has been removed. Since clinical, macroscopic and histological studies have shown that degenerating

filariae, indicated by swellings and cysts, are to be found in the epididymis or along the course of the spermatic cord below the external abdominal ring, it is advisable that during operations for hydrocele such diseased areas should be sought for and dealt with either by incision or excision, as the occasion requires.

Chyluria:—Dr. Ross Golden³⁴ is at present testing efficacy of roentgen therapy* for chyluria. His results give some hope that the condition may be cured by this means.

Difficulty of Evaluating Results of Treatment:—In evaluating the results of any method of therapy in the various filarial conditions it is necessary to bear in mind certain facts. Firstly, just as slight physiological disturbances may excite inflammatory reaction, so also various changes in the patient's condition or environment may bring about cessation of acute symptoms over periods varying from a few months to several years. One cannot, therefore, be certain of cure by any method of treatment until many years have passed. Secondly, while an area of the body containing degenerating worms may be under treatment, parasites either not yet dead or not causing inflammatory symptoms, may be present in the vicinity and may subsequently give rise to symptoms.

Patients frequently present themselves with enlarged glands of the groin requesting their removal because either these act as a starting point in attacks of lymphangitis or because more or less continual dull aching or dragging pain occurs in the vicinity. There has been a tendency in the literature to discourage the removal of such glands, in the belief that excision may give rise to sepsis or fistula, or may subsequently cause elephantiasis. Maitland, who had considerable experience in removing glands of this type, reported very few bad results from this measure of which he was a strong advocate. In Puerto Rico many cases were seen in which excision of these glands had been performed by the local surgeons without bad results. If the glands are enlarged and painful, especially in young people, or if constant irritation occasioned by their presence makes the patient's life miserable or prevents his earning a living, it seems advisable to remove them.

BACTERIA IN ASSOCIATION WITH FILARIAL INFECTION.—The infrequency with which bacteria are found in the inflamed

tissues or blood stream in ordinary cases of filarial lymphangitis has been recently discussed^{15b}. It remains to consider the circumstances in which pyogenic bacteria are found in the blood or tissues of patients suffering from filariasis.

In endemic or hyperendemic areas of filariasis the majority, if not the whole, of the population may be infected, so that it is common to find the infection in persons who are ill or have died from any complaint. Similarly, pyogenic bacteria may be found in persons with filariasis, for there is no evidence that this infection produces any immunity against these organisms. This combination seems to be an association rather than cause and effect. One would expect such association of infection to be more common in certain countries where pyogenic bacteria are known to be especially prevalent, such as British Guiana and some parts of India, where bacteria are frequently found in persons with filariasis. On the other hand where certain bacteria, notably the hemolytic streptococcus, are not so prominently associated with human pathological processes it is often impossible to demonstrate these organisms in filarial cases.

It is obvious that one with filarial lymphangitis, who through some lesion becomes secondarily infected with pyogenic bacteria, may suffer from the complication of bacterial activity. Considering the frequent recurrences of lymphangitis in a filarial patient, the number of times that bacterial complications are observed is not high. While there are innumerable ways by which persons may become infected with bacteria, the method of invasion in filarial diseases may be considered under these headings: local infections from ulcers, fungus diseases, wounds and abrasions; distant infections which enter the system, by way of the blood, from the teeth, from septic foci in the mouth, nose or pharynx, or from sinus infection or intestinal ulceration.

Bearing in mind the fact that most of the septic complications of filariasis, such as abscess, septicaemia, etc., are terminal events and frequently do not manifest themselves until convalescence from lymphangitis is either established or concluded, it is reasonable to suppose that infection through the skin may be produced by the patient's scratching with a view to relieving the very intense pruritis which accompanies convalescence.

The foregoing accounts of association and complication of bacteria with filarial infection offer no evidence that bacteria are as a rule responsible for the disease syndrome. On the contrary there is some evidence that degenerating *Wuchereria* are, *per se*, the cause of the various clinical and pathological manifestations.

ASSOCIATION OF FILARIASIS WITH OTHER DISEASES.—*Filarial Infection in Epileptics*:—It is believed by some persons in Puerto Rico that filarial infection is especially common amongst epileptics and that in some cases this infection may be responsible for the epileptic condition. Prominent physicians of the Island do not, however, hold these opinions. It does not appear that epilepsy is more common in Puerto Rico than in other countries where filariasis is non-existent. Through the courtesy of Dr. Massenet at the Manicomio (asylum for the insane) in San Juan the blood of twelve persons suffering from epilepsy was examined at night. Amongst these, microfilariae were found in the blood of two. None of the patients gave any history of filarial disease. Advanced elephantiasis of the legs was observed in one patient with epilepsy amongst the general population. The foregoing figures are too small to warrant conclusions, but the impression formed is that while epilepsy, like any other disease, may frequently be associated with filariasis, there is no evidence that the filarial parasite is in any way responsible for epileptic symptoms.

Leprosy.—Even before the parasite of filarial diseases was discovered or its association with disease understood, physicians had noticed the frequency with which leprosy and elephantiasis coexisted in the same patient. Thus Waring³⁶ found that leprosy and elephantiasis arabum coexisted in fifty-two, or 5.65 per cent, of 919 persons examined. Day³⁷ stressed the frequency with which elephantiasis arabum or elephantoid fever occurred amongst the lepers at a Cochinchina Lazaretto. Amongst 636 persons studied by Richards⁴⁰ leprosy and elephantiasis arabum were found to be associated in 6 per cent. Since the relationship between the parasite and the filarial diseases was established this association has been frequently mentioned. Thus Cobbold⁴¹ mentions a case of Bancroft's in which filariasis and leprosy occurred together, and Acton and Rao²⁴ describe the finding of a parent filaria in the lymphatic gland of a leper.

During the examination of autopsy material from Puerto Rico, ten and twenty-nine filariae were found, respectively, in the cord and testicles from two lepers. During blood and clinical study of twenty-two lepers at the Leprasarium in Puerto Rico it was found that two had microfilariae in the blood. One had recurrent lymphangitis and elephantiasis of the legs as well, while four others had definite clinical signs of filariasis. Thus seven, or 31.8 per cent, were affected with leprosy and filariasis at the same time. Of course it is not probable that there is any relation between the diseases, and it seems that their presence in the same person is merely similar to the association of filariasis with other diseases, such as tuberculosis, pellagra, schistosomiasis or septic infections; indeed, there is good evidence that this is so. On making inquiry as to elephantiasis of the lower limbs at the Leper Home of the U. S. Marine Hospital at Carville, Louisiana, where filariasis is not indigeneous, Dr. O. E. Denny writes that he has seen the condition in only a few persons who have come from definitely endemic centers of filariasis such as Charleston, South Carolina, and some islands in the West Indies, though he has often seen hydrocele in lepers.

The frequent association of leprosy and filariasis in Puerto Rico is explainable by the fact that both diseases are most prevalent amongst the poorest classes living in overcrowded quarters lacking sanitary facilities.

SUMMARY

Filariasis is an infection of areas with high temperature and humidity and is therefore common in the plains and valleys of Puerto Rico. Adequate protection of an area from wind seems to be necessary to its existence.

Filariasis is essentially an urban rather than a rural infection, and in the towns it is most prevalent in the overcrowded localities where the poor live. No class however is immune. Persons who work immediately on the shore in exposed positions or at sea are less commonly infected.

The essential factor in infection is the transmitting mosquito, *Culex fatigans*, which abounds near the habitations of the poor. In such localities there are numerous breeding places and abundant blood supply for the adult insect. The adult feeds vigorously from sundown to about 11 p.m., al-

though it may bite later. The breeding period of the insect is shorter in the summer than in the winter.

Under experimental conditions the mosquito is rarely heavily infected with larval filariae. This is probably associated with the feeding times of the insect. On the other hand heavy infections are found in wild mosquitoes; in these insects larvae of several generations may be present.

High humidity and high temperature afford ideal conditions for the development of the larval filariae in the mosquito host. During the period of this development it seems essential that the mosquito should have adequate protection from wind.

Under favorable conditions the parasite may be found in the thorax of the mosquito within twenty-four hours after an infecting meal. The parasite curves on itself about the seventh day. The fully developed larvae show a tendency to wander within the mosquito.

There is evidence that on penetrating the skin of man many of the parasites develop locally near the point of entry. Others may complete development in the afferent lymphatics. A large number of parasites reach the first chain of lymphatic glands, where the majority are arrested either in the afferents of the periglandular tissue or in the divisions of the afferents as they enter the glands. A certain number reach the interior of the gland to develop therein. It is conceivable, as suggested by Lane⁴² (O'Connor, Discussion), that after penetrating the skin, some parasites will enter blood capillaries and be carried around the body. In any case the ultimate "objective" of the parasite is lymphoid tissue. This probably explains the large numbers of parasites frequently found in the epididymis and spermatic cord. The parasites grow to maturity and the two sexes pair in the afferent lymphatic vessels or sinuses of the glands. The length of time required for this development to take place is not known.

The only demonstrable result of the presence of the living parasites in the vessels is dilatation, but this may be considerable. If there is obstruction by degenerated worms between the parasites and the nearest or most central lymphatic glands the vessels containing the parasites will be hypertrophied as well. Such hypertrophy involves mainly the

intima and media of the vessels. No marked inflammatory changes are at first observed in the vicinity of living worms, and eosinophils and polymorphonuclear leucocytes are not conspicuous. The small lymphocyte is the predominating cell in filarial pathology.

The cause of death of the parasites is not clear in all cases, but is conceivably due to injuries from outside or to histological changes in the containing lymphatic. After death the parasite becomes a foreign body, and degeneration follows. This may be calcification, beginning in the cuticle and eventually involving the entire parasite. It may be embedded in a caseating focus and may gradually disintegrate and be absorbed by giant cells. During this process calcium may be deposited in portions of the worm. With calcification small, round cells predominate in the vicinity with or without plasma cells, and giant cells are found near the worm. Eosinophils are not usually observed. When the parasite has disintegrated and become absorbed, eosinophils, in addition to the round cells, are present in enormous numbers *during the early stages*. At this time also foreign body giant cells are conspicuous. As disintegration advances eosinophils tend to disappear. The end result of these different kinds of degeneration is fibrosis (Fig. 24). When this occurs in the lymphatic vessels the latter are completely obliterated, and when it occurs in the glands these are more or less disorganized. Since in clinical cases of filariasis large numbers of parasites are present, the changes described readily explain the obstructive phenomena associated with filarial infection. It is believed that the inflammatory phenomena of filariasis are associated with degeneration of the dead filariae by absorption of the products of decomposition, the mechanism being either allergic or anaphylactic.

Examination of apparently normal persons in endemic areas indicates that practically all the inhabitants are infected with a few or with many *Wuchereria*. It will be readily understood, therefore, that persons suffering or dying from other diseases may be found to harbor filariae. In these studies filariae have been found in persons with schistosomiasis, leprosy, tuberculosis, syphilis, malaria and septic

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Fig. 24. Section near the capsule from which a worm has been absorbed. X37.

GRABADO 24. Corte cerca del epidídimo, mostrando la cápsula de la que queda el verme. X37.



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infections. This implies association, but not complication of diseases.

Microfilariae may be found in the blood of the human host at any time during the day, but they are least numerous or absent between 11 a. m. and 2 p. m. After the latter hour they begin to increase in numbers until late at night, the greatest numbers being found in the blood between 10 p. m. and 4 a. m. They may be altogether absent from the blood, but may be present in hydrocele or cystic fluids. They may not be demonstrable in any way, and yet their presence in the body may be evident from the finding in histological sections of parent females with embryos in utero. The method of their destruction is not clear in all cases, but they are undoubtedly destroyed in some instances in the nearest chains of lymphatic glands. The microfilariae can traverse the walls of hypertrophied lymphatic vessels to enter blood vessels in the vicinity; this is probably a passive process associated with raised pressure in the partially obstructed lymph vessel and not direct progression. Microfilariae probably reach hydrocele and other fluids, such as the urine, in the same way.

Bacteriological studies indicate that bacteria are not demonstrable in the majority of filarial inflammations. When present, they generally manifest themselves toward the end of the inflammatory period and are a secondary infection. All the evidence suggests that the filarial syndrome is produced by the parasites *per se*.

Clinical studies in Puerto Rico show that certain filarial diseases, e.g., lymph scrotum and varicose groin glands, so common in other filarial countries, are rare in this Island where the commonest manifestations are lymphangitis, adenitis, elephantiasis and hydrocele.

In the majority of patients the attacks of lymphangitis begin with pain. This is frequently localized either in the glands or some distal portion of the limb or appendage. In subsequent attacks the primary pain often occurs in the same locality; there may be several such areas of focal pain. During the attacks pain may be especially severe in these areas. Histological study shows that in a high percentage of cases these foci indicate the presence of parasites.

The febrile attack most commonly lasts two to three days. The redness may be purely local around the focal spot or may

ascend or descend the limb. When beginning it may occur as lines or as blotches. It appears suddenly and does not tend to spread. The margins are not raised, but gradually fade into uninflamed tissue. Swelling is more extensive than redness in the limb.

When abscess occurs it is most commonly a terminal event in the attack of lymphangitis or it may come on during convalescence or after its completion. Abscesses may be sterile, when the contents are lympho-purulent; or they may be septic, containing pus with any of the known pyogenic bacteria. Both kinds of abscess were observed in about equal numbers. Comparing the number of abscesses with the number of attacks of lymphangitis in an individual throughout many years, abscess is not a common occurrence.

Elephantiasis may be primary or secondary (Fig. 25). Primary elephantiasis is the more common. In a fair percentage of cases it has developed before the onset of inflammatory phenomena, and cannot have been caused by them. It is suggested that obstructive phenomena resulting in the imprisonment of worms in the afferents and collaterals may bring about the death of the parasites and that the lymphangitis follows their disintegration. On the other hand more complete obstruction in the neighborhood of the glands may bring about elephantiasis with or without inflammatory phenomena. In either instance obstruction is the principal cause of the condition (Fig. 26).

At the beginning of the filarial attack there is a sudden leucocytosis with polymorphonuclear predominance. This is rapidly replaced by lymphocytosis. The eosinophil cell does not seem to play an important part in the acute inflammatory phenomena.

Under present circumstances in Puerto Rico preventive measures against the mosquito seem to be well nigh impossible. The ultimate solution to this problem will be the improvement of the economic condition of the people.

The treatment of filariasis is unsatisfactory. However, in individual cases the excision of focal spots gives promise of relief. Elephantiasis can also be aided by surgery, and there is some hope that with the development of the present technique of roentgen therapy, recurrences of lymphangitis may be prevented.

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Elephantiasis may be primary or secondary (Fig. 25). Primary elephantiasis is the more common. In a fair percentage of cases it has developed before the onset of inflammatory pyaemia, and cannot have been caused by them. It is suggested that obstructive venous thromboses resulting in the imprisonment of toxins in the area of the collaterals may bring about the development of the parasites that the lymphogitis follows. The integration of the other hand more complete obstruction in the neighborhood of the glands may bring about elephantiasis with or without inflammatory phenomena. In the latter instance obstructive thrombosis of the collateral veins may be the principal cause of the condition (Fig. 26).

At the beginning of the illness there is a sudden leucocytosis, a lymphocytosis, and a marked lymphatic hyperplasia. This is rapidly relieved by the administration of a small dose of a lymphocyte inhibitor. The eosinophil cell does not seem to play an important part in the variable inflammatory phenomenon.

Under certain circumstances in Puerto Rico preventive measures against the mosquito, the principal vector, are not possible. The only solution to the problem will be the improvement of economic conditions in the tropics.

The treatment of elephantiasis is unsatisfactory. However, in individuals with the exsiccated skin spots gives promise of relief. Elephantiasis can also be aided by surgery, and there is some hope that with the development of the present technique of roentgen therapy, recurrences of lymphangitis may be prevented.

FIG. 25.

- A. Girl aged 9. Enlargement of left leg since age of five when she had abscess on instep.
 B. Boy aged 5. Right leg permanently enlarged since three years old, when he had abscess in groin and attack of lymphangitis.
 C. Boy aged 12. Elephantiasis of left leg and thigh with trophic changes at ankle.
 D. Girl aged 13. Permanent enlargement of left leg.

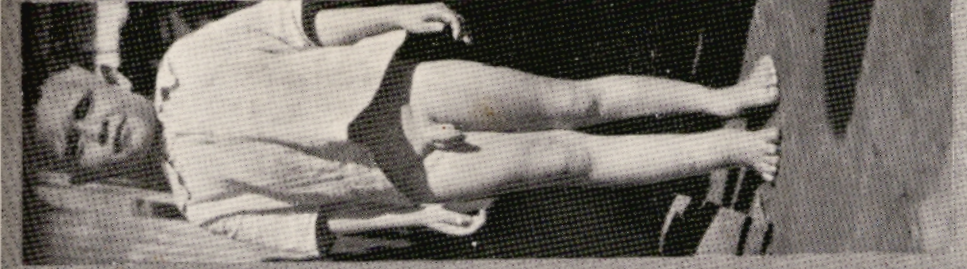
GRABADO 25.

- Elefantiasis en edad temprana.*
 A. Una niña de 9 años. El agrandamiento del miembro empezó a los 5 años con ocasión de un absceso.
 B. Un niño de 5 años. El agrandamiento del miembro empezó a los 3 años, con ocasión de un absceso de la ingle y un ataque de linfangitis.
 C. Enfermo de 12 años de edad. El agrandamiento comprende el muslo y llega hasta el tobillo.
 D. Enferma de 13 años.



A

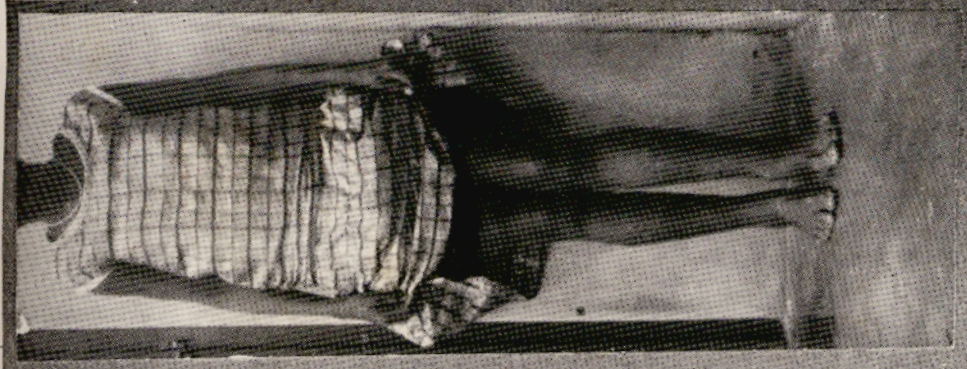
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B



C



D

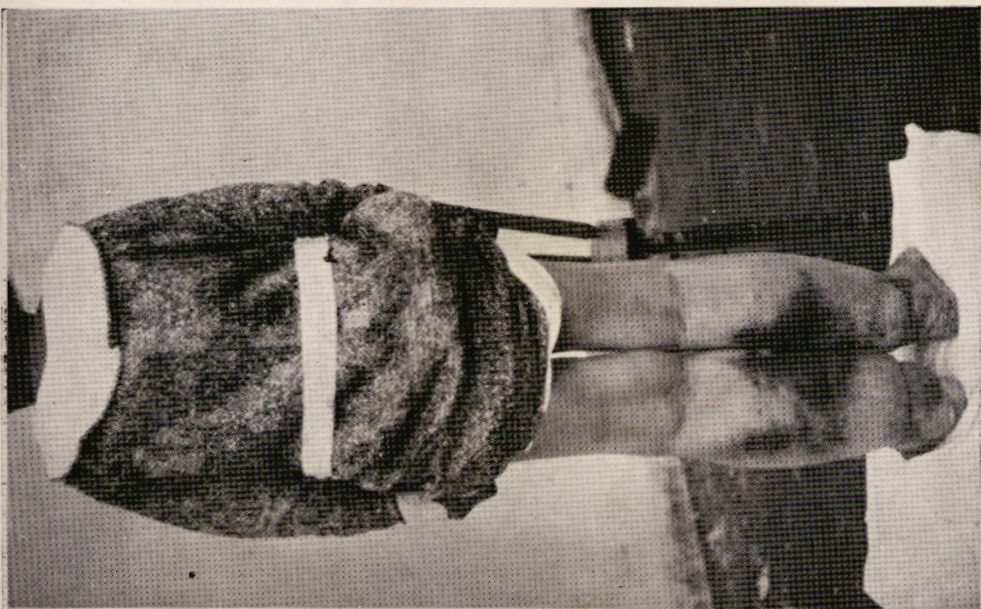
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FIG. 26. Puerto Rican female. Extensive elephantiasis with trophic changes of both legs. Convalescent from an attack of lymphangitis and the discoloration of the skin indicates the distribution of the rash during the acute attack.

GRABADO 26. *Elefantiasis extensa, con cambios tróficos en ambas piernas. Enferma convaleciente de un ataque de linfangitis. La decoloración de la piel indica la distribución del enrojecimiento en el momento agudo del ataque.*



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