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STUDIES ON SCHISTOSOMIASIS IN PORTO RICO

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Under this title two interesting contributions appeared in the PORTO RICO REVIEW OF PUBLIC HEALTH AND TROPICAL MEDICINE, Volume III, number 6, articles which had already been read by title on behalf of their authors, Doctors R. A. Lambert and W. A. Hoffman, in the twenty-third meeting of the American Society of Tropical Medicine, in Boston, on October 23, 1927.

I can not pass over these articles without bringing forward some objections to that of Lambert and correcting manifest errors which appear in that of Hoffman; especially since the latter affect a matter which may be designated as my scientific property.

Hoffman cites one of my monographs entitled "Investigations on the Prevalence and Clinical Features of Intestinal Bilharziosis (*Schistosomiasis mansoni*) in Porto Rico" (1). In spite of the fact that in this article I enumerate my previous publications on the subject and relate in detail the history of the disease in the region, the above-named author commits a manifest error.

His error is that he attributes the credit for the first report of the presence of schistosomiasis in the country to the Porto Rico Anemia Commission, basing his statement on the statistics contained in the report *which was made public by this organization in December 1904.*

This error appears to take from me a mark of distinction which no one shared with me and one which was and is exclusively mine; because in February, 1904, I had the good fortune to discover the first two cases, the opportunity to report them to the local press and subsequently to publish the first study of "La Bilharziosis en Puerto Rico" (2). On April 3, 1904, this study was read before the Annual-Meeting of the Medical Association. At that time the

Anemia Commission did not exist, the project was only in the embryonic stage and was being developed within our legislature. Furthermore this same article, assuredly mentioned in the bibliographic notes of the report of which Hoffman makes use, *appeared one month before the distinguished members of the Commission opened their dispensaries in Utuado on May 9, 1904* (3).

It might be possible to question my priority in the discovery of *Schistosomiasis mansoni* as an endemic disease in America, for in the search of the literature it is quite possible that some previous authentic report may have escaped me, in spite of the fact that in the extensive and minute review made by J. R. Rizquez (4) no author appears prior to myself.

Even though the chronological data given are sufficient to clear up Hoffman's error, the following information constitutes supplementary evidence:

1. The testimony of the members of the first Anemia Commission, especially Doctor Gutiérrez Igaravídez, active investigator and author of the Spanish editions of the valuable reports of the Commission.

2. The testimony of the Medical Association of Porto Rico, in the records of which the dates and nature of my communications are established.

3. In the United States, copies of my monograph "La Bilharziosis en Puerto Rico", published April 3, 1904, are to be found in the Congressional Library, the library of the Army Medical Museum and in that of the Hygienic Laboratory.

In foreign countries copies are to be found in the principal schools of tropical medicine of that time.

4. The testimony of investigators of such high standing in the medical world as Doctors Rosenau, Stiles, and Catto. Doctor M. J. Rosenau, then Director of the Hygienic Laboratory, in acknowledging receipt of the monograph said:

"Referring to your letter of August 13th, addressed to Dr. Stiles, I have the honor to acknowledge, on his behalf, the receipt of your interesting publication on *'Bilharziosis in Porto Rico'* and a mounted specimen of eggs of Bilharzia Hematobia; August 23rd, 1904."

Dr. John Catto, of the Pathological Department, Great Northern Central Hospital, London, writes:

"I beg to acknowledge the receipt of your work in Bilharziosis and thank you for the *worms* you kindly sent me. I must apologize for my *dilatory reply*, but I hope to be able to send you a copy of my work. I have shown *your worms and papers* to Sir Patrick Manson and he is also very interested." December 15, 1904.

All of this was written, therefore, before the publication of the first report of the Porto Rico Anemia Commission.

5. Quotations from monographs and authoritative works which are devoted wholly or in part to the diseases of warm countries. Among others the following: "*Precis de Parasitologie*" by E. Brumpt, Professor of Parasitology in the University of Paris (5), in dealing with schistosomiasis mansoni, says on page 391:

"As the result of epidemiologic studies of P. Manson (1903), of González Martínez (1904), zoological studies of Sambon, Piraja da Silva, Flu, Leiper, —the identity of the parasite which causes ordinary intestinal bilharziasis is now admitted by all authors. This affection is found in its pure state in America where it has been reported from almost all of the West Indies (Manson, Letulle, *González Martínez*, Noc.)."

The *Noveau Traité de Médecine* published under the direction of Rogier, Widal, and Tessier contains an article by Brumpt in which he makes statements similar to those just given (6).

John Catto, in his monograph entitled "*Schistosoma cattoi, a New Blood Fluke of Man*", which was published January 7, 1905 (7) cites my study on bilharziasis in Porto Rico in his bibliography. And finally J. R. Rizquez, in a monograph which received a prize from the Academy of Medicine of Caracas, the most thorough and complete study of the many which have been published on this disease in America, which is entitled "*La Bilharziosis Mansoni en Venezuela*", commenting on my investigations says on page 16:

"During the same month, April 1904, I. González Martínez of Porto Rico read before the general assembly of the Medical Association of the island a report demonstrating the presence in that island of bilharzia infection, discovered by him in February of the same year."

And further, page 38:

"Puerto Rico—*Here bilharziasis was studied for the first time in America in February, 1904, by I. González Martínez*" (4).

Another error committed by Hoffman which should be corrected is that of considering himself the discoverer of the intermediate

host of our schistosomes. Nothing is more incorrect. Before him, between 1917 and 1922, Iturbe of Venezuela and Brumpt of Paris, respectively, had already pointed it out as such. *The Journal of Tropical Medicine* of London, Volume XX, 1917 number 11, page 130, in abstracting Iturbe's monograph entitled *"Intermediate Host of Schistosoma mansoni in Venezuela"* says:

"The colour of those *(Planorbis guadelupensis)* gathered in the creeks near Caracas is a yellowish brown, and of a paler hue than those found in Porto Rico."

A similar reference is found on page 83 of number 114 (1917),

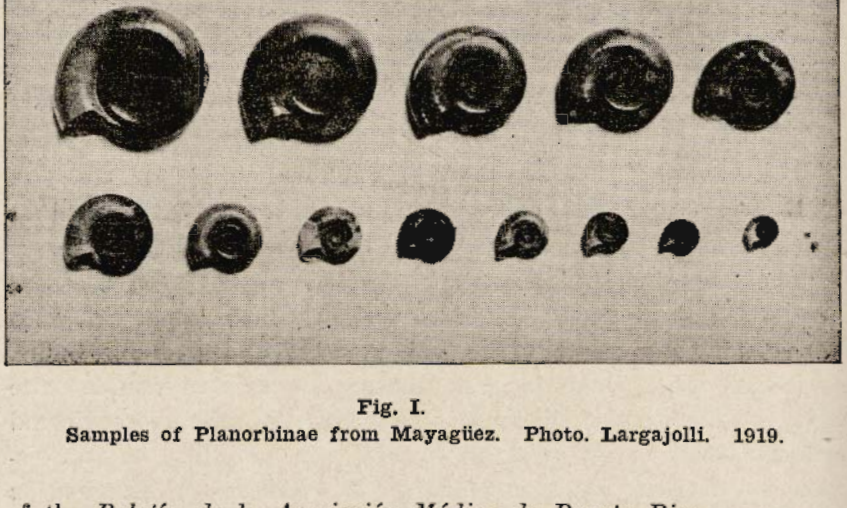

Fig. I.
Samples of Planorbinae from Mayagüez. Photo. Largajolli. 1919.

of the *Boletín de la Asociación Médica de Puerto Rico.*

This opinion was immediately accepted by all of us who were working in the Institute of Tropical Medicine. The logic of the conclusion was incontrovertible: if, as the Venezuelan investigator had shown, *Planorbis guadelupensis* was one of the most favorable intermediate hosts of *Schistosoma mansoni,* then, whenever both the disease and this snail were found, the role of principal vector had to be ascribed to the latter. In Porto Rico schistosomiasis existed and the presence of *Planorbis guadelupensis* had been pointed out; then it followed logically that this mollusc must be one of the intermediate hosts.

Lest this should not be sufficient, we had a large number of them collected and had a number of specimens photographed by the photographer of the Institute, (Figs. I and II) Señor Largajolli who died in 1920. We were then about to make a trip to Europe and we took a dozen of them with us. In the Laboratory of Parasitology in Paris, Professor Brumpt and his assistant, Langeron, identified them as *Planorbis guadelupensis*. On account of this, Brumpt, in discussing the intermediate host in his *Precis de*

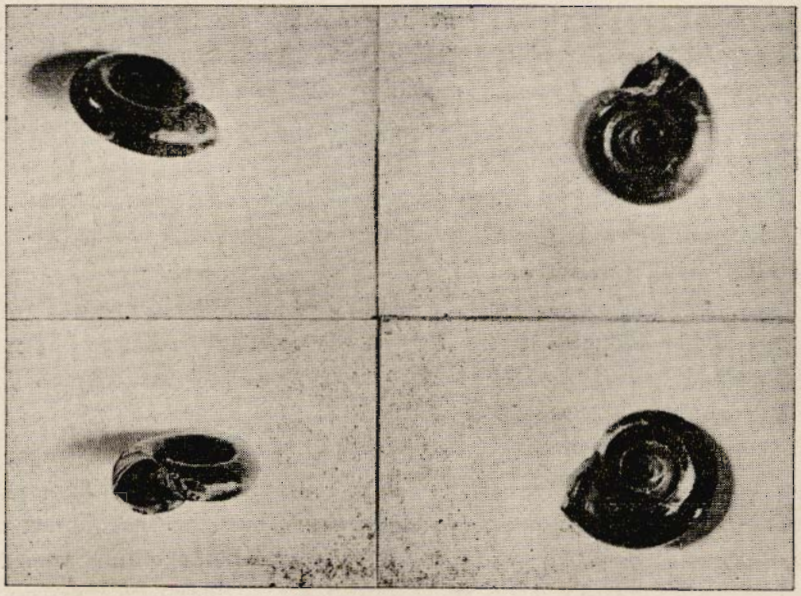

Fig. II.
Shells of Planorbis Guadeloupensis collected in Mayagüez (1919), giving ventral, dorsal and side views. Photo. Largajolli.

Parasitologie, says on page 390: "in Venezuela and the West Indies it is *Planorbis guadelupensis* (Iturbe and González, Brumpt)". In order to avoid any misinterpretation it must be pointed out that here he refers to Eudoro González, who collaborated with Iturbe.

On my return I found that Doctor Iturbe had sent to Doctor Gutiérrez Igaravídez specimens of planorbis with the liver full of cercariae. My distinguished colleague turned them over to me for

comparative study with indigenous specimens, a task to which I devoted myself at once, requesting several colleagues in the Island to send snails to me, for which purpose I took care to provide them with dry specimens. Doctor Blanes of Mayagüez was the first to respond, sending several hundred. The examination of this collection showed that a large number were infested but I did not determine the percentage because we lost more than half of them on account of the lack of facilities in the laboratory for keeping them alive during the entire period of the investigation. The same difficulties, together with the lack of subjects, interfered with efforts to bring about experimental infection. In Caguas and Río Piedras we collected snails personally and in one hundred we found two infested. In Bayamón the collection was in charge of one of our assistants; no specimen showed cercariae.

The planorbis of Mayagüez were collected from Marina Septentrional and Marina Meridional, and from Quebrada de la Salud, near the slaughter house.

We have given these facts simply to show that if Doctor Hoffman, contrary to what was expected from the clinical findings, did not find infected snails in Mayagüez, his failure was due only to defective methods of collection.

That Lambert's report is far-reaching and is the more importtant of the two there can be no doubt; it constitutes a skillful and fruitful effort to obtain a correct estimate of the endemic index of our schistosomiasis, an unknown quantity which the author tries to determine by searching systematically for the characteristic lesions of the disease in a considerable group of autopsies on bodies coming from different hospitals and municipalities. Notwithstanding the justifiable criticism which might be brought forward against the preliminary statistics of an investigation which requires, for conclusions approaching the true result, the execution of thousands of autopsies wisely distributed throughout the Island, I said that the attempt was fruitful because bilharziasis is a chronic disease which leaves indelible traces in the viscera and we must agree that the method chosen by Lambert is very suitable, superior to clinical criteria and excelled only by intensive and systematic fecal examination in the districts where *Planorbis guadelupensis* is found.

It cannot be denied that the result of Lambert's inquiry in his

first hundred autopsies contributes most interesting data to our regional pathology. An important fact which it demonstrates, though he does not state it, is that I was not exaggerating twenty-two years ago, in my second communication to the annual meeting of the Medical Association of Porto Rico (8) on July 2, 1905, in holding that in our plains the incidence of intestinal bilharziasis was about 7.8 per cent, nor was I dreaming years later when in my paper of 1916 (1) at the American Society of Tropical Medicine, I raised this index to 8.4 per cent for certain severely infested localities like Mayagüez.

It is to be regretted that the brevity of Lambert's note prevents him from presenting a complete study of the pathological anatomy of schistosomiasis as it occurs in this country. Nevertheless he affirms categorically that its lesions are due essentially to the irritative action of the ova in the tissues and *not to the presence of the parasite*. This old theory has been overturned by the work of Letulle in 1905 and by later investigations, among which are those of J. R. Rizquez (4), of Venezuela and my own (1, 9, 10), demonstrating that in intestinal bilharziasis the lesions have three origins, namely: the irritative action of the egg, the sclerosis produced by the chemical action of a phlogogenic toxin secreted by the adult parasite and by its ciliated embryo; and, finally, the endovascular traumatic effects of the adult parasites, producing not a thrombotic but a vegetative endophlebitis, pathognomonic of our schistosomiasis.

So long as the distinguished professor of the School of Tropical Medicine does not present better arguments than his simple negative, we shall continue to believe and to defend the former theories, in favor of which there are such formidable proofs, such as the lesions in the tissues, and the alterations in the blood and in the humoral reactions.

In 1920, dealing with the pathological anatomy of this disease in one of my lectures before the Faculty of Medicine of Barcelona, I described it as follows on the basis of my personal investigations and the authoritative studies of Letulle, Maden, and J. R. Rizquez:

"*Pathological anatomy.*—The prolonged presence of *Bilharzia mansoni* in the mesenteric veins and the passing of the eggs through the intestinal coats provoke a series of pathological changes in the large intestine and in the cellular

tissues of the pelvic basin, which should be considered, to a certain degree, as specific of this parasitic disease.

"It was believed and maintained for a long time by a number of authors that the adult worm, male or female, was in itself inoffensive and that the anatomic changes observed and the corresponding functional disorders should be attributed to the sharp spicules of the eggs. But the discovery of like lesions in Japanese schistosomiasis which parasite, however, lays eggs without spicules and the investigations of Maurice Letulle proving that the numerous and extensive traumatisms produced by the suckers and dorsal papillae of the male, and by the suckers and tail of the female are capable of creating inflammatory reactions in the veins which are specific of bilharziosis mansoni overthrew the foundation

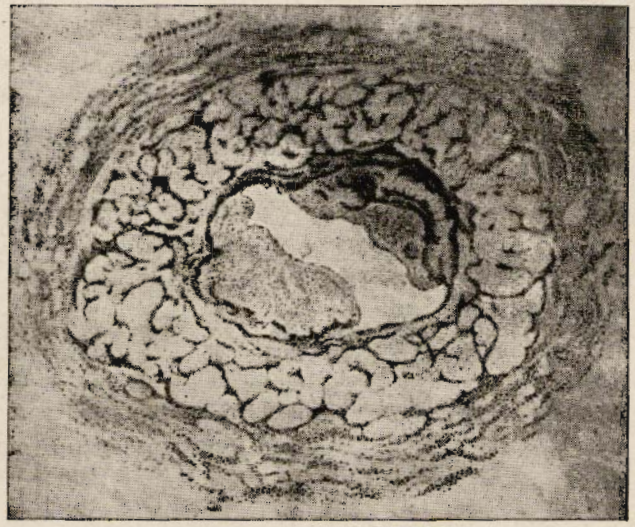

Fig. III.
Section of a vein in Bilharziosis Mansoni showing peculiar endophlebitis (after Maurice Letulle).

on which such belief was raised.

"The different coats of the intestine, and some viscera, such as the liver and lungs, at times infested with embolized eggs, besides the irritating stimulus of numerous injuries produced by the spicule of the egg, suffer also from the phlogogenic action of some toxin discharged by the worm. There is no reason to doubt the existence of such toxin. The extensive diffusion of the chronic inflammatory process and the evident alterations in the blood picture which will be later described are convincing proofs.

"The anatomical lesions produced by *Schistosome mansoni* should be chiefly

investigated in the lower third of the large intestine, especially the rectum and sigmoid flexure. In these locations they are most often encountered and show all their distinctive microscopic characteristics, although they are to be found in other sections of the colon and have even been reported in the appendix.

"Anatomical changes are commonly present in the liver, in the mesentery of the colon and rectum, in the pelvic cellular tissue, and in the mesenteric glands. They rarely occur in the spleen or the pancreas.

"The macroscopic appearance of the bilharzia—infested intestine is that of hypertrophied and sclerotic organ: The thickened walls are harder and less flexible than normally; their lumen becomes diminished; and the normal mobility of one coat on the other is hindered by the abundance of fibrous tissues. The

Fig. IV
Egg and embryo of Schistosoma Mansoni between Lieberkuhm glands.
I. González Martínez.

peritoneal folds or mesenteries and the pelvic cellular structures also show evident signs of diffuse fibrosis in their interstitial connective tissue. The inner surface of the rectum and often of the colon, give signs of anatomical changes so characteristic that it is impossible, with the naked eye, to mistake them for those of any other disease of the digestive tract. During the first stage of infestation, it is scarcely possible to detect any modification in the intestinal mucous membrane off scarcely possible to detect any modification in the intestinal mucous membrane. At most it reveals only a coating of gray mucus covering segments of congested velvety membrane. When the process is more advanced, vegetations appear, some-

times pedunculated and at other times sessile of a bright brownish red hue, round in form and verying in size from that of a millet seed to a hazel nut. They are generally discrete but at times confluent, distributed irregularly over the mucous membrane, which is often swollen, exuberant and reddish, but occasionally of a normal macroscopic appearance. These eminences of warty vegetations are soft in consistency, very vascular, and bleed at the slightest touch. When attached to the intestinal wall by means of a pedicle, a necrotic ring is often to be seen at its base which causes the loosening of the polypoid vegetation leaving in its place an ulcer with ragged edges, excavated base, and covered with gray material. These ulcers and the warty protuberances constitute the most common and characteristic lesions in the intestinal mucous membrane caused by *Schistosoma mansoni*.

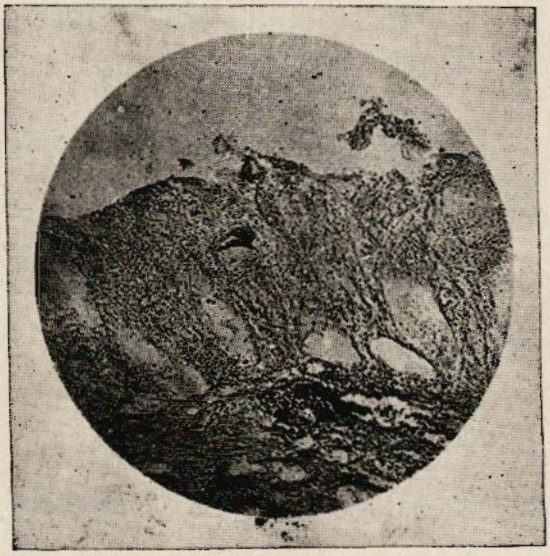

Fig. V.
Egg of the Schistosoma Mansoni in the intestinal mucosa.
I. González Martínez.

"The liver, though enlarged in some cases, usually retains its normal size. It frequently shows thickening of the Glisson's capsule and when cut with a knife, the cut surface usually displays irregular white spots corresponding to the portal spaces, measuring as much as one centimeter in diameter (Symmers).

"The mesenteric glands appear enlarged and congested. The spleen has occasionally been reported enlarged. In my autopsy series it has always been normal in size. However in *Schistosoma mansoni* infested patients, free from malaria or anemia, without fever or leukocytosis, and with a blood picture greatly resembling that of bilharziosis I have observed marked splenomegaly. Explora-

tory puncture in these cases did not disclose the presence of protozoa in the splenic pulp.

"The mieroscopic study of organs invaded by *Schistosoma mansoni* reveals the fact that the fundamental anatomical changes are hypertrophy and sclerosis. These alterations are due to two different causes, the one mechanical, the traumatism engendered by the worms and their eggs; the other chemical, a phlogogenic toxin.

"The traumatisms of the worm, limited to the veins in which it resides temporarily or habitually, give rise to a peculiar endophlebitis, chronic and fibroid, which Letulle considers pathognomonic of bilharziosis. This endophlebitis is not

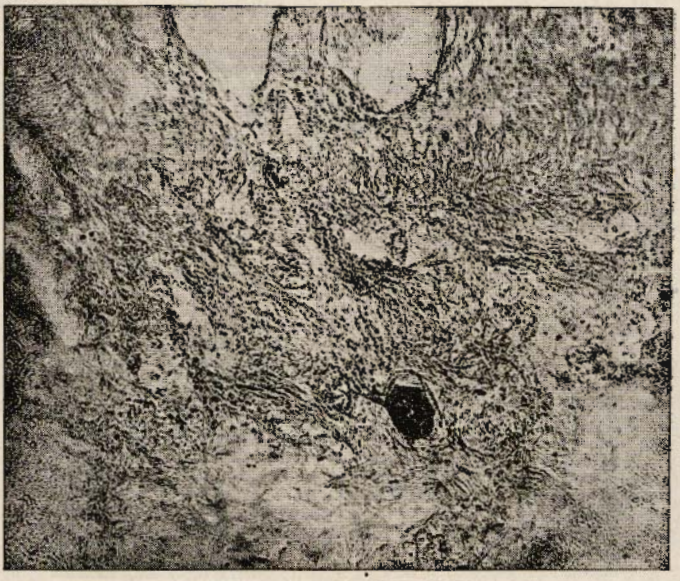

Fig. VI.
Egg of the Schistosoma Mansoni in the submucosa.
I. González Martínez.

of thrombotic origin, for *Schistosoma mansoni*, doubtless on account of the toxin it secrets, prevents the coagulation of blood in the veins; it is characterized by the complete integrity of the endothelium, and the extensive hyperplasia of the intima and of the subendothelial connective tissue. This proliferation pushes the endothelium toward the interior of the vein, forming voluminous, irregular protuberances that reduce the lumen of the vessel and may even obstruct it entirely. The endophlebitic process, which at times attains considerable degree, is not widespread in the submucous coating of the large intestine, but develops to a greater or less degree in the subserous portion, in the peritoneal folds and in the pelvic

cellular tissue. It is quite probable that in its genesis there is, besides local traumatism, the diffuse action of phlogogenic toxin. (Fig. 3.)

"Microscopic examination frequently discloses the presence of coupled pairs of worms within the large veins of the mesenteries, rectum, colon, or the finer ones of the submucosa.

"The traumatic action produced by the spicules of the eggs principally affects the mucous and submucous coats of the intestines, but it also appears in the hepatic parenchyma and in the mesenteric glands into which the eggs are carried as venous and lymphatic embolisms.

"Anatomic changes in the intestine, though due to the same fundamental process of generalized hyperplasia, differ as they are studied in the mucosa or submucosa.

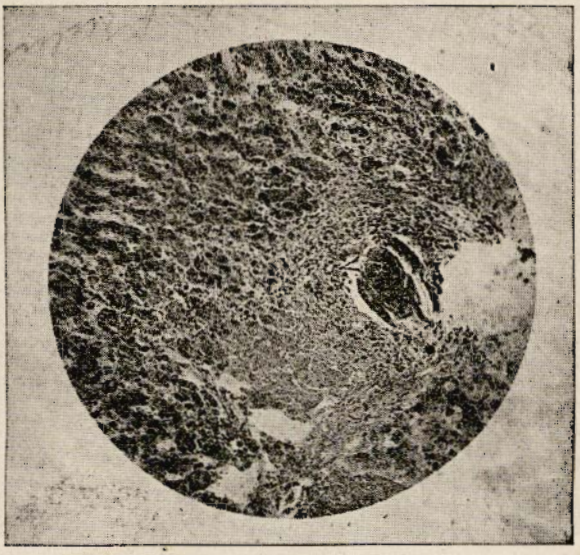

Fig. VII.
Egg of Schistosoma Mansoni in the periportal space surrounded by leucocytic infiltration.—I. González Martínez.

"In the mucous membrane, the macroscopic inspection revealed to us two kinds of lesions of quite opposite appearance, verrugous proliferations and superficial ulcerations.

"The verrugous eminences are, as Letulle says, the result of a defensive process. They constitute true parasitic adenomas in which the hyperplastic growth is to be seen in full play. The vascular connective tissue of the mucosa attains an enormous development. The glands of Lieberkuhn hypertrophy and become hyperplastic to considerable size, and frequently are transformed into ramified glands, (Fig. 4.) Between these glandular elements and in the connective tissue are of

the polypoid masses, the characteristic eggs of the Schistosoma mansoni are often found accompanied by scattered centers of round cell infiltration. (Figs. 5 and 6.)

"The bilharzial adenoma is a benign neoplasm that does not pass the limits of the muscularis mucosae, nor does it show a tendency to malignant degeneration.

"With reference to the ulcerations, the anatomic changes appear to be different and, to a certain point, just the opposite: the glands of Lieberkuhn are atrophied, disintegrated, or are entirely lacking; the epithelium of the mucosa has disappeared, and the connective tissue stroma, invaded by mononuclear leukocytes, proliferates and becomes granulation tissue. To the destruction of the tubular glands is later added the action of the microbic flora of the intestines

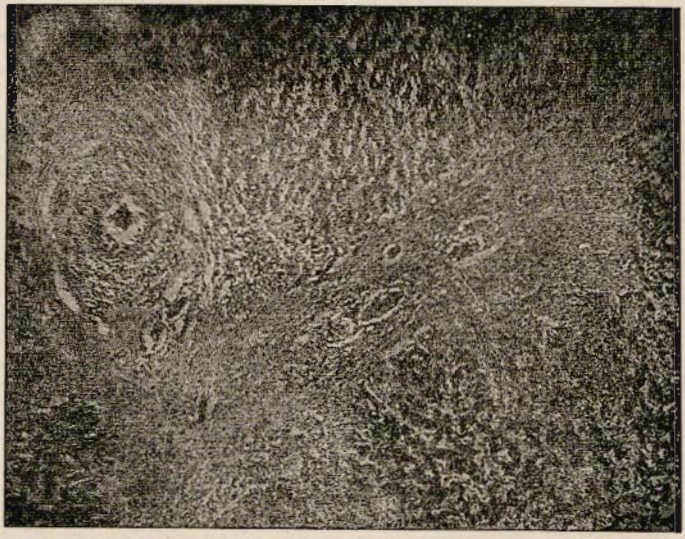

Fig. VIII.
Another aspect of the cirrhotic process of the liver in Schistosomiasis Mansoni. I. González Martínez.

which hastens the disintegration of the mucosa. The ulcerative process, however, is invariably checked before reaching the muscularis mucosae, a feature which differentiates it from the true dysenteric ulceration. The closed follicles are that they never arrive at the suppurative stage as occurs in dysentery. Neither is the interstitial thrombosis, so common in bacillary dysentery found in bilharzial ulcerations. On the other hand some sparsely scattered *Schistosoma mansoni* eggs are frequently encountered in the vicinity of the ulcers, though not so much as in the adenomatous tumors.

"In the submucosa of the large intestine, which is the place selected by the female for laying her eggs, it is to be observed, besides the vegetative endo-

phlebitis of which we have spoken, a diffuse sclerosis with dense proliferation of the connective tissues and disappearance of the adipose cells.

"In the liver, the lesions generally correspond to those of a discrete cirrhosis scarcely recognizable in the leukocytic infiltration; but it is an important fact of the insular type. The periportal spaces show proliferation of the connective tissue and accumulation of mononuclear leukocytes in the vicinity of the egg. I have also been able to corroborate the presence of the inflammatory nodules described by Letulle and Nattan Larrier. They are found disseminated through the hepatic parenchyma and are composed of a conglomeration of mononuclear leukocytes enveloping Bilharzia eggs. (Figs. 7 and 8.)"

SUMMARY

1. We have proved that Hoffman commits an error in attributing the discovery of schistosomiasis (*S. Mansoni*) in Porto Rico to the Anemia Commission.

2. We present evidence that no investigator appears in medical literature prior to myself in the study of intestinal schistosomiasis as an endemic disease of America.

3. We have demonstrated that, before Hoffman, Iturbe and Brumpt had designated Planorbis guadelupensis as intermediate host of the trematode in the Island; a fact confirmed by our investigations in 1921.

4. The geographical distribution of bilharzia infestations of planorbis indicated by Hoffman's map is erroneous in so far as the region of Mayagüez is concerned. In 1921 I found there a high proportion of snails infested with cercariae of schistosomes.

5. The theory of Lambert that the lesions produced by *Schistosoma mansoni* are due essentially to the irritative action of the ova and not to the adult parasite cannot be sustained. It was long ago overthrown by pathologic, hematologic, and humoral evidence.

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