COINCIDENCE OF MALARIA AND TYPHOID FEVER

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The association of malaria and typhoid fever in the same individual was a subject of discussion among medical writers as far back as the early part of the eighteenth century and the literature of the thirty-year period preceding the discovery of the malarial parasite (by Laveran in 1883) contains many papers dealing with the question. The frequency of the association and the distinctness of the clinical picture were among the topics about which there was a lack of agreement. Many physicians both in Europe and the United States insisted on giving a special name to the combined infection, the French (Grall, Marchand and others) using the term "typho-paludism", while in America "typho-malarial fever" came to be the designation.

Some observers, among whom Boudin was prominent, claimed that there was definite antagonism between the two infectious agents and denied the possibility of simultaneous infection. But Leveran and Le Dantec demonstrated in several cases the co-existence in the blood of the malarial parasite and Eberth's bacillus. While this seemed to settle the matter it was still maintained by some that a certain degree of incompatibility existed.

In America, the name "typho-malarial fever" came into general use between 1860 and 1870, and during the Civil War some 57,000 cases were reported under this designation. Later Woodward, who was one of the first to use the term, said he had not intended to indicate his belief in a distinct disease entity, but only to designate a hybrid form of fever due to the association of two infectious agents.

Following Laveran's discovery and the development of the agglutination method for the diagnosis of typhoid fever, controversial discussion diminished, the problem becoming much more clearly delimited. It was soon shown that many cases reported as typho-malarial fever were nothing more than typical examples of typhoid fever.

Regarding the frequency of concurrent infections, Deaderick (1911) said that the association was not very rare, adding that a

search of the literature revealed records of 215 cases in which laboratory methods proved the association. As respects incompatibility, Craig makes the following statement: "There is, I believe, good reason for thinking that there does exist a certain amount of incompatibility between the two infections, for it is frequently observed that when typhoid fever develops in a patient suffering from malarial fever the malarial symptoms disappear as well as the plasmodia from the peripheral blood, re-appearing during the convalescence from typhoid". All observers, however, are not agreed on this point, it being believed by some that an attack of typhoid fever may actually stir up a latent malarial infection.

In view of the fact that malaria is endemic in almost all the coastal zone of Porto Rico and that periodic outbreaks of typhoid fever are not uncommon, Dr. R. A. Lambert suggested that the writer make a study of the association of the two infections in the hope that some facts of interest might be brought to light. In the local literature the only report of cases of concurrent infection which the writer has been able to find is that of Dr. A. Torregrosa (*Boletín de la Asociación Médica de Puerto Rico*, 1921, Vol. 131).

Our plan of investigation consisted of three parts: (1) A questionnaire was sent to the 350 physicians of Porto Rico. This was followed up by visits to several communities from which cases were reported. (2) An investigation was made of recent typhoid epidemic in one of the towns (Fajardo) situated in the malarious zone. (3) The records of autopsies made by the staff of the School of Tropical Medicine during the past two years were reviewed.

Reports of Physicians.

There were 136 replies to the questionnaire, which was aimed particularly at finding out how frequently the association of malaria and typhoid fever was observed. Of the 136 physicians responding, 85 had not observed any instances of concurrent infection; 47 had seen one or more such cases, the diagnosis being established by the demonstration of plasmodia in the blood and a positive Widal reaction; four physicians reported having seen patients with a positive Widal reaction and with indications of an associated malarial infection though the latter was not proven by laboratory examination. Of the 47 cases in which the association existed the species of parasite was as follows:

P. vivax	12 or 25.5 per cent
P. falciparum	26 or 55.3 per cent
P. vivax and P. falciparum	9 or 19.2 per cent

Among the cases seen through consultation with physicians, the five following may be cited:

The first case observed by the writer was a case of L. B., a girl twenty-two years old who was taken with a chill and high fever. Blood examination revealed the presence of P. falciparum. Quinine was given in one-gram doses but the fever did not disappear, the chart showing a remittent fever. Quinine was discontinued on the twelfth day. Several later blood counts showed a leucopenia and no malarial parasites. Widal reaction became positive on the twentieth day for para-typhoid A. Hemorrhage from the bowels was noted on the 21st day. Malarial parasites were found again in a blood examination on the 37th day. Following the administration of quinine, fever disappeared. The nervous and the abdominal symptoms in this case were very severe.

The second case was a male adult in the Guánica Hospital. The patient had been treated for an infection by P. falciparum for about two weeks previous to admission. Quinine therapy was continued seven days after admission on account of the persistence of the fever and blood for Widal reaction was taken and sent to the laboratory. This showed an incomplete Widal reaction. Five days later another sample gave a definitely positive Widal. Two weeks after this there was a severe chill followed by a sudden rise of temperature. The pulse was very rapid, and the patient became very restless and ill. Two days later examination revealed numerous malarial parasites (P. falciparum). Quinine (1 gram) was given intravenously but there was a severe intestinal hemorrhage. On the following day an operation for perforation of the intestine was attempted but the patient died on the table.

The third case was reported by Dr. A. R. of Yauco. Patient was a young woman about 24 years of age. The symptoms were typical of early typhoid fever with positive Widal reaction. Toward the end of the second week patient started to have severe chills. Examination of the blood showed both P. falciparum and P. vivax. Quinine was administered liberally and while the chills ceased, the typical typhoid course continued until the 26th day when the patient succumbed with signs of severe intestinal hemorrhage and perforation.

A fourth case, a man, 34 years old, was seen in Añasco. Patient had been suffering from malaria and had improved under quinine therapy. He was up and about when he became very ill with a continuous fever. Blood was examined and found positive

for malaria. Widal reaction was also positive. A few days later there was a severe chill, with pain in the epigastrium tympanitis, rapid feeble pulse. Diagnosis of intestinal perforation was made, operation was immediately performed and patient recovered.

The fifth patient, a resident of Hato Rey, was seen by courtesy of Dr. M. Soto Rivera. Patient showed general malaise, headache and temperature of 38.2° C. Pulse was slow. On the eighth day blood culture and Widal were both reported positive for paratyphoid A. On the 18th day of illness there was a severe chill followed by high fever and sweats. Another chill occurred on the following day. Blood examination revealed a double cycle of P. vivax. After administration of quinine in 50-centigram doses intramusculary, fever came down, temperature until convalescence running a normal typhoid course.

2. Typhoid Epidemic in Fajardo.

This epidemic occurred in December, 1927, and January and February of 1928. Fajardo is situated on the coast at the eastern end of the Island. The municipality, which includes a rural district, has a population of approximately 15,000. Epidemiological investigations by the Department of Health showed that the epidemic was due to contaminated water supply. Malarial control measures, preceded by careful survey and carried out with a systematic check on all cases of fever, were begun two years before the typhoid outbreak. It was therefore possible to get considerable data on the association of the two diseases. There were altogether some ninety cases of typhoid fever on 63 of which it was possible to obtain laboratory data from the records of the Department of Health. In these cases there was both a careful study of the blood for malaria and a Widal test. In a few cases there were also blood or stool cultures.

Of the 63 cases there were 11 positive for malaria, 3 showing P. vivax, 8 showing P. falciparum and one P. vivax and P. falciparum. In our opinion it is significant that nearly 20 per cent of the cases of typhoid fever should have shown an associated malarial infection. In view of the malaria control measures it is doubtful if at the time of the epidemic the percentage of malaria positives in the general population was as high as among the group of typhoid patients. Our findings indicate at least, that there is no incompatibility between the two infections and the figures might be interpreted as favoring the view held by some, that a typhoid infection tends to stir up a latent malaria.

3. Autopsy Studies.

Up to the time of this investigation, 130 autopsies had been made by Dr. R. A. Lambert, Dr. Alice Burke and Dr. W. C. Earle of the School of Tropical Medicine. Of the 130 cases there were 4 in which typical lesions of typhoid fever were found, while 10 of the cases showed anatomical evidence of malarial infection. There were two autopsies in which evidence of both malaria and typhoid fever was found. In the first of these cases there was a history of malaria before and during the early stage of the typhoid fever. In the second case the history obtained was incomplete and there was no record of a blood examination for malaria parasites during life. It is perhaps noteworthy that the two cases of associated infection came from Salinas on the south coast where malaria has long been prevalent. A survey in 1926–27, under the direction of Dr. W. C. Earle, showed that the parasite index there was around 55, a very high rate.

CONCLUSIONS

From the foregoing studies and case observations, we may conclude that in Porto Rico it is not unusual to find a coincident infection by typhoid fever and malaria; that these cases are more frequent in the localities where malaria is endemic; that the symptoms are more severe than in simple typhoid fever; that hemorrhages are apparently more common than in uncomplicated typhoid fever, and that P. falciparum is the most frequent parasite found.