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Further Experiences in the Treatment of Filariasis with Hetrazan.

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In 1947, *Santiago Stevenson, Oliver Gonzalez,* and *Hewitt* (1) reported that 1-diethylcarbamyl-4-methylpiperazine hydrochloride (Hetrazan) had brought about disappearance or marked reduction of microfilariae of *Wuchereria Bancrofti* from the peripheral blood of 26 Puerto Rican patients.

The administered dose of Hetrazan varied from 0.5 mg. to 2 mg./kg. body weight three times a day over a period of 13 to 22 days. Allergic or toxic reactions (increased eosinophilia, fever, headache, general malaise, lumbago, anorexia, nausea, vomiting, swelling of lymph nodes, testicular pain, arthralgia, skin reactions) occurred very seldom and practically only in these cases treated with the highest dose.

50 per cent of the patients were reported to have negative blood smears for microfilariae from 8 to 83 days after treatment and 15 months later 56.5% (13 of 23 patients) were found free of the infection, while the remaining 43.5% had much lower counts than before treatment (2).

The present work was carried out in order to determine the effects of higher doses of Hetrazan given during a shorter period of time.

17 Puerto Rican patients with Filariasis Bancrofti were hospitalized for the study, 15 males and 2 females, whose ages varied between 11 and 39 years. A complete history and thorough physical examination were recorded for each patient. The number of microfilariae in 60 cmm. of blood was determined the night before the onset of the treatment.

Besides a careful physical examination made every day, the following laboratory work was performed in each patient: blood serology; CBC and differential; daily eosinophile count; NPN; urea N twice weekly; urinalysis daily.

The drug was administered at the dosage of 2, 3, and 5 mg./kg. body weight three times a day and depending upon the dose used the number of patients can be subdivided into three groups.

1. The first group consists of 5 patients treated with the dose of 2 mg./kg. body weight three times a day. The duration of the treatment was for 3 patients 10 days, for the 2 others 14 and 21 days respectively.

The allergic or toxic reactions were mild and the same as reported previously.

Therapeutic results: 4 patients had negative smears for microfilariae the day after the treatment was finished. 3 of them have remained negative up to this date, while the fourth patient could not be followed up. One of the patients treated during 10 days became free of microfilariae only 3 months after treatment. His blood is still negative.

2. The 5 patients forming the second group received 3 mg./kg. body weight three times a day, two of them during 7, the other 3 during 3, 8, and 10 days, respectively.

Toxic reactions: 2 patients presented fever (maximum 100.8° F.), headache, general malaise, and testicular pain of medium intensity. These phenomena

appeared the second day of treatment. Anorexia, nausea, lumbago, arthralgia, swelling of lymph nodes, debility and skin reaction appeared mostly the third and fourth day of treatment, occurred at the frequency of 1 to 5 and had an irregular distribution over the 5 patients. None of these clinical findings were of such an intensity as to interrupt treatment.

Laboratory work. Blood picture: The eosinophilia varied before treatment from 5% to 22% and was not related to the heaviness of the filarian infestation. The dosage of 3 mg./kg. body weight three times a day produced in 3 patients a definite rise in the eosinophilia. In 3 cases leucocytosis with absolute lymphopenia was observed. There was no change in the blood count of 2 patients.

Blood chemistry: The only change observed was a slight and temporary lowering of the NPN in 3 cases.

Urine: One patient presented microhematuria (250 RBC p.h.p.f.) during the 3 first days after onset of medication.

Therapeutic results: 4 patients with 7, 8, and 10 days of medication had negative smears the day after treatment. Only the one treated for 3 days remained with a positive smear. 3 patients with 7 to 10 days of medication still have negative smears at this writing (24 months after treatment). 1 patient could not be followed up.

3. 7 patients received the highest dosage of 5 mg./kg. body weight three times a day, 5 of them during 10, and 2 for 8 and 9 days, respectively.

Toxic reactions: Fever (maximum 100^0 F.) and arthralgia were observed in 5 cases, while 4 patients presented headache, lumbago, and swelling of lymph nodes. 3 patients complained of general malaise, debility, anorexia, and nausea. In 2 cases abdominal pain and vomiting were registered. Mild skin reaction and testicular pain occurred only in 1 of 7 cases. All these manifestations appeared the first day of treatment and were of short duration (an average of 2 days) except the testicular pain and swelling of lymph nodes which were observed the third and fourth day and also lasted longer.

Laboratory work. Blood picture: The treatment provoked in all 7 cases an increase of the initial eosinophilia. 5 patients also had a temporary leucocytosis with lymphopenia. The RBC and Hgb remained unchanged.

Blood chemistry: Temporary lowering of the NPN in 2 cases.

Urine: 1 case presented microhematuria (30 RBC p.h.p.f.) the third day of treatment and lasting 2 days.

Therapeutic results: 6 of the patients had negative blood smears for microfilariae the day after treatment and remained with negative smears up to this date (20 to 24 months after treatment). The one patient who still presents microfilariae in his peripheral blood was treated during 8 days only.

In 3 cases Pyribenzamine was administered together with Hetrazan, with a remarkable decrease in the allergic and toxic reactions.

References.

1. *Santiago-Stevenson, D., Oliver-Gonzalez, J.,* and *Hewitt, R.* (1947). Treatment of Filariasis Bancrofti with 1-Diethylcarbamyl-4-Methylpiperazine Hydrochloride ("Hetrazan"), J.A.M.A., vol. 135, p. 708-712.
2. *Oliver-Gonzalez, J., Santiago-Stevenson, D.,* and *Maldonado, J. F.* (1949). Treatment of Filariasis Bancrofti with Hetrazan, J.A.M.A., vol. 139, p. 308-309.