Routine gargling had no effect in reducing the carrier rate during the epidemic.

A comparison is made with a similar type of outbreak which occurred in an American Army camp.

I wish to tender thanks to Dr. N. Crowley for the help she gave me in the bacteriological investigation of throat swabs, etc.

TREATMENT OF RHEUMATOID ARTHRITIS WITH BISMUTH

BY

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The use of gold against active rheumatoid arthritis has fully justified itself in spite of the faulty premisses which led to its introduction. Analysis of my last 200 cases indicates that it results in the disappearance of symptoms and signs of activity in 70%, but relapse within six months occurs in the majority of those subjected to only one course of injections—usually 0.8 g. Four courses in two years appear to eradicate the disease in 55%, but the possibility of recurrence, even 15 years later, forbids the use of the word "cure." The great objection to gold treatment is the high incidence of toxic reactions. In the early days it was as much as 45%, but with decreased dosage, and the use of the less toxic calcium aurothiomalate, the figure has fallen to 10 in the last 60 arthritics so treated—i.e., approximately 16%. Immediate interruption of treatment at the first sign of any one of the numerous reactions which may arise will almost invariably be followed by a slow but complete disappearance of the toxic effect. I have seen one case of agranulocytosis recover after five months, and one of gold nephrosis with oedema recover after three months. In each case instructions as to dosage, choice of preparation, and watch for toxic signs had not been observed. The commonest and most persistent reaction is seen in the skin, in which various irritating rashes are produced. It is this which has led to such fear of gold.

It seems probable that gold acts by virtue of its being a heavy metal, and not from any specific effect on the infecting agent responsible for the arthritis. In order to see whether it were possible to obtain the same effect with a less toxic substance, I started, late in 1942, administering bismuth. This substance was chosen because pharmacologically it acts similarly to heavy metals, it is easily procurable in injectable form, and its toxicity is low.

Method

Twelve consecutive patients with active rheumatoid arthritis were treated with weekly intramuscular injections of injectio bismuthi (9) or injectio bismuthi salicylatis (3). One mil of the former and 2 mils of the latter contain 0.2 g. of bismuth and bismuth salicylate respectively. These quantities were used for 10 injections, giving a course-dose of 2 g.

Clinical Material.—Ten females, two males; aged from 24 to 63 years. With the exception of one who had suffered for 19 years, they gave histories of 9 years (2), 8 (2), 4 (4), 2 (1), 1 year (1), 1/2 year (1). Eleven patients had had one or more courses of gold in the past; in three only had it failed to do any good. The others had relapsed, usually within 6 months of finishing the course.

Signs of Activity.—In all cases there were pain and swelling of many joints, a recent extension of the disease to joints previously spared, and a raised E.S.R.: in one hour the figure limits (Westergren method) were 22 mm. to 100 mm.

Results

The effect of treatment was classified as:

Group 1.—*Very good* if at the end of the course pain and swelling (not due to old deformity) had disappeared, and if the E.S.R. was below 7 mm. for one hour. Only four patients qualified for this category, the initial and final E.S.R. figures being 22/2, 23/5, 70/5, 23/5.

Group 2.—*Good* was the classification of those patients whose clinical signs had improved as in the former group but in whom the final E.S.R. for the first hour was between 7 and 15 mm. There were two of these with E.S.R. figures of 52/11 and 50/11.

Group 3.—*Moderate improvement:* those patients whose pain decreased and whose ability to perform certain movements—e.g., making a fist and walking—improved beyond doubt. Two fell into this category, with a noteworthy inertia of sedimentation rate. The initial and final figures were 40/22, 35/49.

Group 4.—*Failure*—i.e., those arthritics whose symptoms and signs showed no improvement. Of these there were four. The corresponding E.S.R. figures were 55/34, 38/35, 31/26, 100/110.

None of the patients has been under observation for less than 9 months or more than 1½ years from the beginning of bismuth treatment.

For practical purposes Groups 1 and 2 may be taken together as showing good results and Groups 3 and 4 as being failures. This gives improvement in half of a small series. There was no relation between the duration of the disease and the age of the patient with regard to the effect, or absence of effect, of bismuth on the activity of the arthritis. The two males were failures. Three patients who had had gold previously and obtained no relief provided three bismuth failures.

Relapses.—In Group 1 there has been no relapse. In Group 2 both have relapsed within 2 months of the end of treatment. In Group 3 both members relapsed within 7 weeks.

Toxicity.—There were no toxic reactions.

Difference of Preparation.—Bismuth salicylate provided two failures and one good result. It is probably immaterial whether bismuth or the salicylate is employed. The bulk of the former is less.

Control.—Six rheumatoid arthritics were given weekly intramuscular injections of 1 mil of sterile water. At the end of six weeks this was stopped because no objective improvement was seen, and in only one case did the patient declare herself to suffer less pain.

Conclusion

(1) Bismuth by intramuscular injection appears to be capable of exerting a beneficial influence on the course of rheumatoid arthritis. (2) It compares unfavourably with gold in this respect, the probability of lasting benefit being less than half that expected from gold. (3) Relapse appears to occur more quickly than that following gold. (4) Gold-resistant arthritics are unlikely to benefit from bismuth.

Bismuth is indicated only for rheumatoid arthritics who show intolerance, whether physical or mental, to gold.

Medical Memoranda

Trypanosomiasis in a European treated with Pentamidine

As cases of early trypanosomiasis may occasionally be seen at the present time among Europeans returning from tropical Africa, an account of the treatment of such a case with 4,4-diamino-diphenoxypentane (pentamidine, or M & B 800) is topical. An extensive trial of this drug on natives in Uganda was reported by Lawson (1942), and a fatality, possibly attributable to it, by McComas and Martin (1944).

CASE HISTORY

The patient, a Polish officer aged 32, had been stationed in a tsetse-fly area in Sierra Leone from April, 1942, to May, 1943. He thinks that he was bitten several times, but remembers particularly an occasion in Jan., 1943, when he had what he took to be a tsetse fly inside his trousers. Apart from malaria he was well until May, 1943, when he had a brief attack of pain and swelling of the glands in the neck, axillae, and groins. In June, 1943, he returned to the United Kingdom, and noticed occasional headaches, fever, and swelling of the face in the mornings. In the middle of September he reported sick with what he thought was malaria; scanty trypanosomes were found in thick blood films, and he was admitted to a military centre for tropical diseases.

Examination revealed the following: Irregular pyrexia to 100.5°; pulse rate almost constantly 100 to 110 a minute; mental state apparently normal; puffy swelling of lower eyelids and adjacent face; slight enlargement of occipital, axillary, and inguinal glands; no rash; spleen not palpable. A blood count showed: red cells, 3.7 millions per c.mm.; haemoglobin, 78%; white cells, 12,500 per c.mm.—neutrophils 70%, eosinophils 5%, monocytes 4%, lymphocytes 21%. Very scanty rings of *Plasmodium falciparum* were found in thick blood films, and, on two occasions, scanty trypanosomes in blood films and in juice from a cervical gland.

Treatment was begun in Sept., 1943, with 100 mg. of pentamidine dissolved in 5 c.cm. of sterile distilled water, given intravenously