ORAL MEDICATION BY SOBISMINOL IN THE TREATMENT OF SYPHILIS

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Towards the end of the era of mercurial therapy in the treatment of syphilis there was entertained and freely expressed a decided preference for the parenteral rather than the oral route of administering the drug. It was insisted that with the oral method there was no uniformity of absorption and that gastro-intestinal disturbance was more often encountered. The prejudice thus established against the oral administration of antisyphilitic remedies still persists. Although there has been no backward swing of the pendulum, an inclination towards further exploration of the possibilities of the oral route has certainly been manifested recently. Nabarro (1941) has strongly advocated the use of ingested stovarsol, a pentavalent organic arsenical, in the treatment of congenital syphilis in infants; and several American publications have described experiences with an orally applied bismuthial—sobisminol—in the treatment of acquired syphilis in adults. The present article deals with a small series of cases treated with sobisminol (sodium bismuthate soluble), "a complex organic bismuth compound the chemical structure of which has not been established."

Methods of Administration Compared

The advantages and disadvantages of the oral treatment of syphilitic infections may here be briefly recapitulated. Only a small proportion of patients fail to become accustomed to "the needle" after the first few injections. Efficient injection technique is attended with very little immediate pain, but when several injections a week are given (e.g., two or three intravenous arsenicals and two intramuscular bismuthials), and especially when the intramuscular injections cause tenderness and stiffness, as occurs with oil-soluble bismuth, then many patients would appreciate a period of relief from "that pincushion feeling." Also, especially in women with fat-infiltrated hips, it may be difficult to prevent the bismuth forming pockets, from which absorption is slow, or seeping back along the needle track to form tender subcutaneous nodules. Moreover, some women are averse to receiving hip injections during a menstrual period. Also, especially at the present time, seafaring men on long voyages may be delayed in reaching a port where injection treatment could be continued, and may find regular visits to V.D. clinics impossible. In these and similar cases a potent drug for oral administration would satisfy a real need in anti-syphilitic therapy. In the present emergency an important consideration is the saving of time, and the taking of a drug by mouth exacts but a small fraction of the time required for visits to a clinic or a doctor.

On the other hand an oral medicament may vary in its degree of absorption, and therefore of potency, in different individuals and in the same individual under different conditions—e.g., of bowel activity. The use of this route may cause gastro-intestinal irritation, leading to nausea, anorexia, vomiting, and diarrhoea, with, of course, lessened absorption or enforced cessation of administration. The regular use of an oral medicine, too, depends upon the mentality and co-operation of the patient, and carelessness

and forgetfulness are special attributes of V.D. patients. A simple and easy treatment is regarded as much less important than the injection visit, and may lead to an erroneous impression as to the seriousness of the disease. The major disaster to be avoided is that the patient should come to believe that the control of treatment is within his or her own competence: oral medication tends to propagate this fallacy, and self-treatment by the patient is absolutely inadmissible. All orally administered antisyphilitic remedies should be scheduled at once and be obtainable on prescription only.

The manufacturers state that, given orally, sobisminol is reputed to have an antisyphilitic effect comparable to that produced by other soluble compounds of bismuth given intramuscularly. It is further averred that a daily dose of from six to nine 0.75-gramme capsules (each representing 150 mg. of bismuth) will produce a satisfactory concentration in the blood stream in most patients, and that probably the optimum dose is six capsules a day.

The small series of cases now to be discussed comprised twelve male and three female patients, all of whom were admitted to hospital in order to facilitate close observation.

Sobisminol Treatment: Male Cases

Of the male patients eleven had primary genital chancres and one had a primary chancre of the lower lip. In all cases before starting treatment *Spirochaeta pallida* was demonstrated in serum from the primary lesion and a blood Wassermann test was made. Thereafter treatment with sobisminol was begun and the chancre dressed with saline, serum from it being examined daily for *S. pallida*. The blood Wassermann test was repeated at the end of the course. Immediately the administration of sobisminol orally was stopped intensive routine antisyphilitic treatment with intravenous "914" or stabilarsan and intramuscular bismuth was begun.

Particulars of the eleven primary genital cases are given in Table I.

TABLE I

Case No.	Blood Wassermann at Outset	No. of Capsules per Day	Total No. of Capsules given before Arsenicals Started	<i>S. pallida</i> Absent After	Blood Wassermann at End of Course
1	+++	6	42	4 days	+++
2	+++	6	38	3 "	+++
3	+++	6	54	2 "	+++
4	+	6	67	8 "	+++
5	—	6	66	8 "	±
6	+++	9	33	3 "	+++
7	+++	9	36	2 "	+++
8	±	9	45	<i>S. pall.</i> present at end of 5 days	+
9	—	9	51	3 days	+
10	—	9	54	4 "	+
11	—	9	39	4 "	—

In the twelfth case dark-field examination of serum showed dead *S. pallida* only, as this patient had been applying antiseptics to the erosion. His wife, however, was admitted to hospital with a lip primary chancre, less well developed, which showed living and active *S. pallida* on dark-field examination. The husband's blood Wassermann reaction was strongly positive. Treatment with six capsules of sobisminol daily was started, and was continued for twelve days, during which time the lesion increased in size and was covered with a crust. On the twelfth day an early macular rash was visible on the trunk; thereupon sobisminol was stopped and intravenous "914" begun.

Commentary.—The average number of days before the dark-field serum tests became free of spirochaetes was 4.2. At the end of the course three cases which at the outset of treatment showed a negative blood Wassermann reaction became seropositive, and in two other cases the intensity

of the blood Wassermann reaction was increased. One patient developed a secondary macular eruption after eleven days of treatment. These last clinical findings may seem to infer that the undoubted antagonistic influence of oral sobisminol on primary syphilis is yet not strong enough to prevent the generalized systemic extension of the disease. Nevertheless it is commonly observed in the routine treatment of early syphilis that a positive blood Wassermann reaction may increase in intensity after each injection of "914" ("provocative" effect), and the first injections may accentuate or accelerate the appearance of an early rash.

Female Cases

Particulars of the three female patients are given in Table II.

TABLE II

Case No.	Blood Wassermann at Outset	No. of Capsules per Day	Total No. of Capsules given before Arsenicals Started	S. pallida Absent After	Blood Wassermann at End of Course	Bismuth Excretion
1	+++	6	108	6 days	+++	11.52 mg. per day after 18 days
2	+++	6	68	3 days (serum from condylomata)	+++	
3	+++	6	88	6 days (serum from condylomata)	+++	12.5 mg. (5th day); 5.04 mg. (10th day); 4.29 mg. (12th day)

Clinical Observations.—The oral sobisminol, given alone, achieved rapid resolution of the syphilitic manifestations, whether primary sore, condylomata lata, or mucous patches. In the first two cases an early examination of the cerebrospinal fluid was carried out, on the twelfth and the sixteenth day respectively, and in both cases all the tests, including the cell count, globulin estimation, Wassermann, and gold sol, were negative. In all three cases the sobisminol was continued after an arsenical (stabilarsan) had been introduced, and altogether totals of 212, 512, and 142 capsules were given. In the first case, an early secondary, the blood Wassermann reaction became negative after only three intravenous injections, each of 0.2 gramme, of stabilarsan. In the second case, a late secondary with condylomata lata, the Wassermann reaction was negative after eight intravenous injections of stabilarsan (2 of 0.15 gramme and 6 of 0.3 gramme), given twice weekly. If any deduction were permissible, it would be that the oral sobisminol had acted as a powerful adjuvant of the injected arsenical.

Toxic Effects

Only two of the male patients complained of any upset. In both cases the symptoms were "indigestion" and nausea, which were relieved by a sedative powder.

Two of the female patients experienced untoward effects before the arsenical injections were started. The first had severe abdominal pains during the fifth night, but they were not accompanied by nausea or diarrhoea. The following day she complained of a sore tongue, but the abdominal pains subsided and the glossitis gradually abated, although the capsules were continued in unreduced dosage. Later there was some soreness of the throat and the fauces were slightly red, but the gums remained healthy. The second patient developed a stomatitis on the eighth day and sobisminol was withheld for one day. Thereafter it was found possible to resume the capsules, although slight gingivitis and blue

discoloration of the gums persisted. This patient received a total of 512 capsules in less than three and a half months. The third patient received 88 capsules before the arsenical was started, and without untoward incident; but after three small intravenous injections of stabilarsan (two of 0.2 gramme and one of 0.1 gramme) she had nausea and vomiting: these symptoms passed off in a few days and the capsules were continued until a total of 142 had been taken.

In general the toxic manifestations were not severe; they were mainly referable to the alimentary system, and sometimes subsided when the drug was continued. There was no evidence of cumulative toxic effects after the drug had been administered every day for many weeks.

Summary and Conclusions

The results are reviewed of the oral exhibition of sobisminol in twelve male and three female cases of early syphilis. Suggestions are made as to the province of sobisminol in antisiphilitic therapy.

Deductions from such a limited experience as is afforded by this small series may not be regarded as acceptable, but the object of this paper is to suggest a sphere of usefulness for oral sobisminol without attempting to draw hard-and-fast conclusions.

Our results do not justify the use of oral sobisminol alone in cases of early syphilis, particularly in wartime, when it is essential to render the patient non-contagious as soon as possible. It would appear, however, that sobisminol can and should have a place in the treatment of the following classes of patients: (1) those who cannot attend regularly for injection therapy—e.g., long-distance seamen; (2) those who are intolerant of arsenic and in whom for any reason injection therapy is contraindicated; (3) those who show persistently positive serological tests in spite of long-continued parenteral treatment: in these cases oral sobisminol might be a logical and valuable alternative to the time-honoured mercury pills. One of us (R. C. L. B.) has in mind a tertiary case in which sobisminol provided a most useful stopgap during a long voyage from the East. This female patient realized that regular visits to the ship doctor might excite comment and inquiry.

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REFERENCE

Nabarro, D. (1941). *Brit. J. vener. Dis.*, 17, 87.

MENTAL HEALTH IN WARTIME

The subject of mental health, states the annual report of the National Council of Mental Hygiene, has received an impetus denied to it in the leisurely times of peace. The war has not so far produced any appreciable increase in nervous disorders, but the great changes in national life are bringing to the fore persons suffering from nervous and emotional reactions. Many such cases are encountered in shelters, rest centres, and first-aid posts. Evacuation has also brought its own problems, especially among nervous and difficult children, the subnormal, epileptics, and neurotics of old standing, and a good deal of emergency psychiatry has become necessary. The Council, now in its eighteenth year, has organized lectures on practical methods of dealing with nervous manifestations under war conditions, has produced a film on the prevention and treatment of fear, has compiled a directory of out-patient clinics for functional mental and nervous disorders, and has given attention to mental testing in the Services, psychological problems among enlisted women, and wartime mental health propaganda, among other subjects. Lord Alness, who has been associated for some time past with the Tavistock Clinic, has accepted the chairmanship of the Council, vacant by the resignation of Mr. Walter Roch, and Dr. H. Crichton-Miller the treasurership.