Preliminary Communications

"1314" in Pulmonary Tuberculosis

We have been concerned in the early clinical trial of a new substance, alpha-ethylisonicotinic thioamide ("1314"), synthesized by Libermann *et al.* (1956). This compound is not a derivative of isoniazid, but, like isoniazid, a derivative of isonicotinic acid. Its use in tuberculosis is being explored because Rist *et al.* (1958) showed that it was active *in vitro* against isoniazid-resistant tubercle bacilli and that cross-resistance apparently did not occur.

Brouet (1958) treated with 1314 alone 18 patients who had minimal disease and a positive sputum. Organisms resistant to the drug emerged in three patients at the end of three months' treatment. Loss of sensitivity to 1314 was not recorded when it was combined with isoniazid, streptomycin, and other antibiotics, though detailed information is awaited.

In an attempt to delay the development of resistance we combined 1314, 1 g., with tetracycline, 4 g., both in two divided doses daily. Tetracycline was used because it has only very slight antituberculous activity but may delay the emergence of resistance to certain antituberculous drugs (Stewart *et al.*, 1954; Murdoch and Stewart, 1956). We were therefore able to assess the antituberculous activity of 1314 more accurately than if it had been given in combination with a more effective drug.

Seven patients with chronic advanced pulmonary tuberculosis whose bacilli were known to be resistant to streptomycin, para-aminosalicylic acid, and isoniazid were treated with the combination of 1314 and tetracycline. The trends of sputum positivity were studied by weekly viable counts. The sputum became negative on culture in one patient after five weeks' treatment, and has remained so during a subsequent 27 weeks' follow-up. This patient had had a positive sputum for at least seven years. A second patient showed a marked decrease in sputum positivity, but occasional positive cultures have been obtained up to 17 weeks; no resistance has yet been demonstrated. An initial reduction in sputum positivity occurred in a further four patients, but there was a subsequent rise in positivity while still on treatment. In all four cases organisms resistant to 1314 were detected after 5, 7, 8, and 18 weeks' treatment. The seventh patient showed a reduction in sputum positivity, but resistant organisms were detected at the third week and the patient died three weeks later.

Drug intolerance in the form of nausea and sometimes vomiting proved troublesome in six out of the seven patients. In several it necessitated reduction of dosage or even temporary cessation of treatment.

CONCLUSION

Our preliminary bacteriological evidence suggests that 1314 is an effective antituberculous drug but that tetracycline will prove relatively ineffective in preventing resistance to it. On present dosage nausea and vomiting are likely to prove troublesome in a number of patients.

We suggest that at this stage it would be inadvisable for physicians to hazard their patients' future by premature use of a potentially powerful drug. The

result may be a few weeks' improvement at the expense of permanent drug-resistance. Further studies, now being planned through the Clinical Trials Committee of the British Tuberculosis Association, may establish a better tolerated but effective dose and also indicate drug-combinations which will prevent resistance. A wider use of the drug in patients with bacilli resistant to standard chemotherapy may then be justifiable.

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A. R. SOMNER, M.D., M.R.C.P.Ed.
J. D. ROSS, M.B., F.R.C.P.Ed.
H. M. MACLEOD, M.B., M.R.C.P.Ed.
S. M. STEWART, B.Sc., Ph.D.
N. W. HORNE, M.B., F.R.C.P.Ed.
J. W. CROFTON, M.D., F.R.C.P., F.R.C.P.Ed.

Department of Tuberculosis and Diseases of the
Respiratory System, University of Edinburgh.

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Medical Memoranda

A Case of Twin Pregnancy in a Double Uterus

The patient, aged 39, presented herself at my antenatal clinic on September 19, 1956, with a history of amenorrhoea since May 23, 1956, and early morning sickness and enlargement of the breasts.

Previous Obstetric History.—1943: Spontaneous delivery of a 4-lb. (1,800-g.) boy of 36 weeks' gestation. Severe blue asphyxia due to the cord being round the neck. He responded to treatment and is alive and well. 1945: Spontaneous delivery of a 5-lb. (2,270-g.) boy of 40 weeks' gestation. Precipitate labour. Alive and well. 1949: Miscarriage at 4½ months. 1954: Miscarriage at 10 weeks.

Menstrual History.—Onset at 11, 5-6/25-26; regular.

On examination she was clinically anaemic. A soft systolic murmur was audible all over the praecordium. There was no cardiac enlargement. Her pulse was 76 a minute, blood pressure 120/80. The urine was normal. The uterus was enlarged to three fingerbreadths above the umbilicus. A distinct groove was felt down the anterior wall of the uterus. Movements had not been felt nor could they be heard. Vaginal examination revealed a roomy pelvis with an outlet of more than four knuckles and an internal conjugate of more than 4½ in. (11.4 cm.). Two cervixes were present lying side by side. Her blood was group O, rhesus positive. No antibodies were present. The Wassermann and Price reactions were negative. Her haemoglobin was 59% (8.76 g./100 ml.); R.B.C., 3 millions; M.C.H., 29 µµg.; P.C.V., 28%; M.C.H.C., 31%; M.C.V., 93 cubic microns. A diagnosis of twins in a double uterus and anaemia was made. She was treated with "ferromyn," one tablet three times a day after food, and rest in bed at home. On examination a month later it was obvious that the two foetuses were lying a long way apart; this was confirmed on subsequent x-ray examination.