antibodies to the recipient's tissue cells by the marrow graft. That this has not been found in the present case may be due to the close relationship, and the fact that the donor is known to possess all the blood-group antigens found in the patient.

Summary

A patient is described who suffered from acute bone-marrow failure due to chemotherapy for Hodgkin's disease. She was treated with a bone-marrow transfusion from her sister. Evidence is presented to show that the bone-marrow graft survived for more than six months, responsible for the production of an increasing proportion (now 24%) of the patient's erythrocytes. A skin graft was undertaken between the donor of the marrow and the patient, but it was not successful.

[ADDENDUM.—We repeated the haematological investigation on this patient on September 26, 1959. Rh-positive cells are still present in her circulation. Titration studies indicate that approximately 40% of her circulating erythrocytes are Rh-positive. Woodruff and Lennox have recently published (*Lancet*, 1959, **2**, 476) further details of the results of the skin grafts in blood-group chimeras.]

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In his Annual Report for 1958 Dr. I. GORDON, medical officer of health of Ilford, comments on the difficulty of assessing radiation dangers. Medical officers of health, he writes, are worried that they and their staffs are not competently trained to evaluate radiation hazards, and feel that the Ministry of Health is showing unnecessary reluctance in providing this training. He continues: "We hope that the Ministry will shortly make it possible for local authorities to take an active part in controlling and evaluating this potential hazard, but the experience of the Essex County Council with regard to their own scheme does not give rise to optimism. It is true that if a hazard is suspected the medical officer of health can obtain a trained expert from the Ministry who will visit, inspect, and advise, but how can one even suspect a hazard which is only demonstrable with special instruments that one doesn't possess, or how can suspicion be aroused by industrial or medical use of radioactive materials when information with regard to supply of these materials is withheld?"

MAINTENANCE TREATMENT OF PERNICIOUS ANAEMIA BY MASSIVE PARENTERAL DOSES OF VITAMIN B_{12} AT INTERVALS OF TWELVE WEEKS

BY

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Parenteral vitamin B_{12} is now generally recognized as the treatment of choice in pernicious anaemia. Once full clinical and haematological remission has been obtained, various regimes have been recommended to provide adequate maintenance therapy (Mollin and Dacie, 1950; Blackburn *et al.*, 1952; Conley *et al.*, 1952; Davis and Brown, 1953; Hemsted and Mills, 1958). The dosage advised has been of the order of 20 to 100 μg. every two to four weeks.

If massive doses of vitamin B_{12} of the order of 1,000 μg. or more could be given every three months for the maintenance treatment of pernicious anaemia, this would be a distinct advantage to the patient if it were to prove entirely safe.

The cost of the larger dose would be slightly more, and, as most of the injected vitamin B_{12} is excreted in the urine within a short time of administration (Conley *et al.*, 1951; Mollin and Ross, 1953; Reisner and Weiner, 1953), there would be greater wastage. However, ample compensation would be obtained by the reduction in the number of injections required and the consequent saving of both the patient's and the general practitioner's time.

The effectiveness of large doses of vitamin B_{12} parenterally at intervals of over six weeks in the maintenance treatment of pernicious anaemia has been studied in only a small number of patients (Conley *et al.*, 1952; Walker and Hunter, 1952; Reisner and Weiner, 1953).

The purpose of this paper is to report the results of a trial in which 112 treated cases of pernicious anaemia were changed from orthodox maintenance treatment to maintenance treatment with 1,000 μg. of vitamin B_{12} parenterally every 12 weeks, most of them being kept on this regime for a period of two years.

Material and Methods

The diagnostic criteria observed for inclusion of patients in the trial were a macrocytic anaemia, megaloblastic bone-marrow, histamine-fast achlorhydria, and a clinical and haematological response to the administration of vitamin B_{12} or liver extract.

Of 155 patients with pernicious anaemia who had been fully treated and were attending hospital regularly for supervision, 112 were considered suitable for inclusion in the trial. Of the remaining 43, 30 were regarded as unsuitable because of other complicating disease: 9 had early subacute combined degeneration, 6 had incapacitating cardiovascular disease, 8 were elderly arthritic patients, 2 had cirrhosis of the liver, 2 had polycythaemia vera, and 3 had other illnesses. Eight patients were unable to attend because of their employment, and five were partaking in another research trial.

The 112 patients selected consisted of 85 women and 27 men; their ages ranged from 31 to 85 years, the

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average being 59. Every patient was requested to attend for supervision at intervals of four weeks. Injections of 1,000 μg. of vitamin B_{12} ("cytamen") were given once every 12 weeks. The haemoglobin and red-cell count were estimated at least every 12 weeks, and more often if the levels were not entirely satisfactory.

Serum vitamin B_{12} assays were performed on the majority of patients, using the method described by Ross (1952) modified by Hutner *et al.* (1956) using *Euglena gracilis* 3 strain as the test organism. Samples were obtained at 18 months at random intervals of one, two, or three months after vitamin-B_{12} administration.

Results

To determine whether or not there was any deterioration in the haematological values during the course of the trial the mean of the first three and the mean of the last three red-cell counts and haemoglobin estimations were compared. The haematological levels at which it was considered desirable to maintain patients were:—for men: haemoglobin 100%, red-cell count 5,000,000/c.mm.; for women: haemoglobin 90%, red-cell count 4,500,000/c.mm.

During the course of the trial three patients died from other diseases and nine were withdrawn owing to intercurrent illness or inability to attend.

Of the remaining 100, 87 were maintained in the trial throughout a two-year period of study and showed no deterioration in their red-cell counts or haemoglobin values. Seventeen of these, however, were maintained with red-cell counts slightly under the desired levels, and two required intermittent oral iron therapy to maintain their haemoglobin levels.

Thirteen patients were withdrawn from the trial at intervals varying from 9 to 16 months (mean 14 months) on account of unsatisfactory red-cell counts, though none were below 4,000,000/c.mm., and in these cases the dosage of vitamin B_{12} was increased to 1,000 μg. monthly in an effort to determine whether or not an improvement might be obtained. Of this group, one patient had, after 12 months in the trial, developed paraesthesia of the hands and feet, which did not clear up until the dosage of vitamin B_{12} had been increased to fortnightly. Three patients were known to have other disease: one had mild rheumatoid arthritis, one had been under out-patient treatment for a year for pulmonary tuberculosis, and one had a probable bronchial carcinoma. These four patients had the lowest haematological values in the whole survey.

Eleven of these 13 cases showed a rise of the red-cell count of 100,000–400,000/c.mm. (mean 300,000/c.mm.) following the more intensive vitamin-B_{12} therapy. These must be accepted as failures of the regime.

Serum vitamin-B_{12} assays performed on the first group of 87 patients after 18 months showed satisfactory levels in all cases except in one performed three months after her last vitamin-B_{12} injection, which gave a borderline result though her haematological values were normal. Facilities were not available for carrying out assays on the 13 patients of the second group at the time at which they were withdrawn from the trial.

Summary and Conclusions

One hundred treated cases of pernicious anaemia were maintained on a two-year trial to assess the adequacy of the maintenance therapy of 1,000 μg. of parenteral vitamin B_{12} every 12 weeks.

Throughout the period of study 87 patients showed no deterioration as judged by their haematological values (haemoglobin and red-cell count) and serum vitamin-B_{12} assays.

Thirteen patients showed unsatisfactory red-cell levels after 9 to 16 months, and in 11 of these improvement was obtained by increasing the vitamin B_{12} dosage to 1,000 μg. monthly.

It is concluded that one injection of 1,000 μg. of vitamin B_{12} every 12 weeks provides adequate maintenance therapy for most patients suffering from pernicious anaemia. However, as this dosage is inadequate in a small number of patients it cannot be recommended as a general routine measure.

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DIETHYLCARBAMAZINE IN TROPICAL PULMONARY EOSINOPHILIA

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Tropical pulmonary eosinophilia, which is widespread in India, is now recognized as a major cause of respiratory illnesses. It is increasingly regarded as an eosinophilic disorder in which bone-marrow, blood, lungs, liver, and probably other viscera may be involved. So far, its aetiology is mainly speculative, though allergy, parasitic infection, and viral infection have all been incriminated.

Until recently, arsenic was the sheet anchor in its treatment. Antimony and bismuth (D'Abrera, 1946), sulphonamides (Joseph, 1946; Chaudhuri *et al.*, 1954), chloroquine, and chlorbetamide ("mantomide") (Ganatra and Lewis, 1955) have all given disappointing results. Chaudhuri (1950) and Prasada Rao and Krishnan (1952) reported encouraging results with chlortetracycline, but antibiotics have not proved effective in the hands of Misra *et al.* (1958), Reeder and Goodrich (1952), and Diaz Rivera *et al.* (1950).

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