in the West Indians. Neither can they be attributed to liver disease, in which the B_{12} level may be raised.

The occurrence of a raised IgG in the West Indians suggests that the primary abnormality may be one of protein formation. It is not likely that the higher B_{12} levels are due to its binding directly to IgG, because neither of the two B_{12} binding proteins (Hall and Finkler, 1963, 1965) is a gammaglobulin. Transcobalamin I is an α1-globulin and transcobalamin II elutes from diethylaminoethanol cellulose just following the majority of γ- and β-globulins. High levels of IgG have been reported in Gambians (Rowe *et al.*, 1968), in the Congolese (Michaux, 1966), and in Nigerians (Turner and Voller, 1966). Rowe and his colleagues think that this difference may be genetic in origin. Liver disease and recurrent infections are less likely alternatives. High B_{12} levels and high levels of B_{12} binding capacity have recently been reported in Southern Nigerians by Fleming (1968). The mean serum $B_{12} \pm 1$ S.D. was 575 ± 16 $\mu\mu$g./ml.; the mean unbound serum B_{12} binding capacity was 1,802 $\mu\mu$g./ml. with a range of 1,433 to 2,083 $\mu\mu$g. Brandt and Metz (1961) and Brandt *et al.* (1963) reported high serum B_{12} levels in some of the Bantu population.

All the West Indians studied here were of African descent. Their high levels of B_{12} may be an inherited feature which is independent of the nutritional and environmental changes of their living in the West Indies and Great Britain. Similar considerations apply to the high level of IgG.

Whether the high B_{12} level is of any importance or value to the West Indians is speculative. In some conditions, particularly liver abscess, the finding of high B_{12} levels is of help in arriving at the correct diagnosis (Neale *et al.*, 1966). Clearly a high B_{12} level in a West Indian patient suspected of having a liver abscess could be misleading. If the total body stores of B_{12} are increased in West Indians this might afford some protection against a development of B_{12} deficiency.

Lowering of the B_{12} in pregnancy has previously been reported (Heinrich, 1954; Spray and Witts, 1958; Lowenstein *et al.*, 1960). Clearly West Indians are not exceptions, as the fall seen in this study was similar in the Europeans and the West Indians. The B_{12} level reaches the lowest values at the end of pregnancy. The progressive fall in the level is thought to be due to the concentration of the vitamin across the placenta by the foetus (Heinrich, 1954: Killander and Vahlquist, 1954).

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REFERENCES

Brandt, V., and Metz, J. (1961). *S. Afr. J. med. Sci.*, **26**, 1.
Brandt, V., Kerrich, J. E., and Metz, J. (1963). *S. Afr. J. med. Sci.*, **28**, 125.
Fleming, A. F. (1968). *W. Afr. med. J.*, **17**, 25.
Gottlieb, C., Kam-Seng Lau, Wasserman, L. R., and Herbert, V. (1965). *Blood*, **25**, 875.
Hall, C. A., and Finkler, A. E. (1963). *Biochem. biophys. Acta (Amst.)*, **78**, 234.
Hall, C. A., and Finkler, A. E. (1965). *J. Lab. clin. Med.*, **65**, 459.
Heinrich, H. C. (1954). *Klin. Wschr.*, **32**, 205.
Killander, A., and Vahlquist, B. (1954). *Nord. Med.*, **51**, 777.
Lowenstein, L., Lalonde, M., Deschenes, E. B., and Shapiro, L. (1960). *Amer. J. clin. Nutr.*, **8**, 265.
McCance, R. A., and Widdowson, E. M. (1960). *Spec. Rep. Ser. med. Res. Coun. (Lond.)*, No. 297.
Mancini, G., Carbonara, A. O., and Heremans, J. F. (1965). *Immunochemistry*, **2**, 235.
Michaux, J.-L. (1966). *Ann. Soc. belge Méd. trop.*, **46**, 483.
Neale, G., Caughey, D. E., Mollin, D. L., and Booth, C. C. (1966). *Brit. med. J.*, **1**, 382.
Rowe, D. S., McGregor, I. A., South, S. J., Hall, P., and Williams, K. (1968). *Clin. exp. Immunol.*, **3**, 63.
Spray, G. H., and Witts, L. J. (1958). *Brit. med. J.*, **1**, 295.
Turner, M. W., and Voller, A. (1966). *J. trop. Med. Hyg.*, **69**, 99.

Medical Memoranda

Apparent Cure of Cancer with Cyclophosphamide

Brit. med. J., 1968, **4**, 161–162

Cure of cancer of the upper oesophagus by cytotoxic drugs is a rare event. A small number of two-year survivors of cancer of the head and neck by direct intra-arterial injection of alkylating agents are reported by Harrison (1964). Rundles (1962) quoted the case of a woman with an oesophageal tumour who lived two years after cyclophosphamide therapy.

CASE REPORT

A 58-year-old man presented on 10 March 1962 with a seven-weeks history of hoarseness and pain, difficulty in swallowing, and a swelling in the neck. He had also lost 2 st. (12.7 kg.) in weight.

On examination he was thin, emaciated, pale, and anxious. There was a hard fixed mass in the left supraclavicular fossa, about 3½ in. (9 cm.) in diameter. This felt like a mass of malignant lymph nodes. A barium swallow showed a smooth stricture at the upper end of the oesophagus.

On 16 March oesophagoscopy revealed a smooth, hard stricture at 18 cm. from the upper gums, and bronchoscopy at the same time showed a right vocal cord palsy and a granular tumour projecting from the back wall of the trachea 2.5 cm. below the vocal cords. A biopsy specimen of this mass was taken and reported on as follows: "The specimen is a portion of tissue covered by squamous epithelium, which is not ulcerated in the tissue received. Beneath the epithelium there is widespread infiltration by a carcinoma composed of large pleomorphic cells, with many mitotic figures. There is heavy infiltration by polymorphs, and the neoplasm shows no evidence of differentiation. The findings are those of infiltration by carcinoma compatible with a primary origin in the oesophagus or the trachea."

No treatment was given, but nearly a month later the patient was readmitted with nearly absolute dysphagia, and a further oesophagoscopy was carried out on 14 April. The malignant stricture was now much tighter and it was dilated, and a No. 12 Mousseau–Barbin tube cut off to a suitable length was passed through the stricture and left in position. On 17 April he was given 1 g. of Endoxana (cyclophosphamide) diluted in 50 ml. of water intravenously. He had a sharp reaction with nausea and vomiting and leucopenia. He was so ill that it seemed he would very soon die, and accordingly he was allowed to go home.

On 10 August he reappeared saying that swallowing liquids caused him to cough, but he had no difficulty with solids. This statement was surprising in the circumstances, but even more remarkable was the fact that the mass in the left side of the neck had entirely disappeared, and moreover he looked remarkably well and had gained a lot of weight.

Oesophagoscopy on 15 August revealed no sign of the Mousseau–Barbin tube or of the malignant stricture. In its place were two clean punched-out holes through into the trachea, each about 5 mm. in diameter. Tracheoscopy still showed the right vocal cord palsy and the oesophagotracheal fistula.

On 17 August he developed severe right iliac fossa pain, and the Mousseau–Barbin tube was removed at operation from the caecum, where it was found to be on the point of perforating the wall.

On 6 September the oesophagotracheal fistulae were closed transoesophageally, through an incision in the right side of the neck. It was noted that a length of about 5 cm. of the right recurrent laryngeal nerve was missing, and histology of the excised edges of the fistulae showed no sign of tumour tissue.

On both 11 and 12 November he was given cyclophosphamide 0.5 g. intravenously, the idea being to consolidate the position.

On 25 February 1963 he was readmitted, as he still had a small oesophagotracheal fistula, and this was dealt with once more through the right side of the neck. Since then he has had no symptoms of any sort, apart from hoarseness, and when last examined, on 21 March 1968, there was no sign of recurrence or metastases.

Comment

The original sections have been reviewed, and there is no reason to alter the original diagnosis of anaplastic carcinoma. The malignant nature of the lesion is supported by the fact that a length of the right recurrent laryngeal nerve had disappeared, and also by the presence of a mass of typical hard malignant glands in the left side of the neck. Since no other treatment was given apart from palliation by a tube, there can be no reasonable doubt that this man's apparent cure had been occasioned by cyclophosphamide.

In my experience, though cyclophosphamide commonly gives reasonable palliation in malignant disease, a cure of this sort is unique, and can only be expected in the tiny minority of cases.

The destruction of the tumour left a gap where it had been —a fistula which was not easy to deal with. It has stimulated the speculation that if a more completely effective cytotoxic drug is developed the surgical services, far from being underemployed, will be swamped by cases requiring repair and reconstruction.

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References

Harrison, D. F. N. (1964). *Irish J. med. Sci.*, p. 151.
Rundles, W. (1962). *Cancer Chemotherapy Reports*, No. 20, p. 1.

Congenital Cytomegalovirus Infection Treated with Idoxuridine

Brit. med. J., 1968, 4, 162–163

The recent demonstration that the intravenous inoculation of idoxuridine in herpes simplex encephalitis is not as toxic as was once thought (Breedon *et al.*, 1966 ; Buckley and MacCallum, 1967 ; Evans *et al.*, 1967) led us to consider its use in congenital cytomegalovirus infection. The related drug floxuridine was used by Cangir *et al.* (1967) with marked clinical improvement in five cases of leukaemia thought to be complicated by cytomegalovirus infection. A suitable case came under the care of one of us (A. F. C.), and idoxuridine therapy was given.

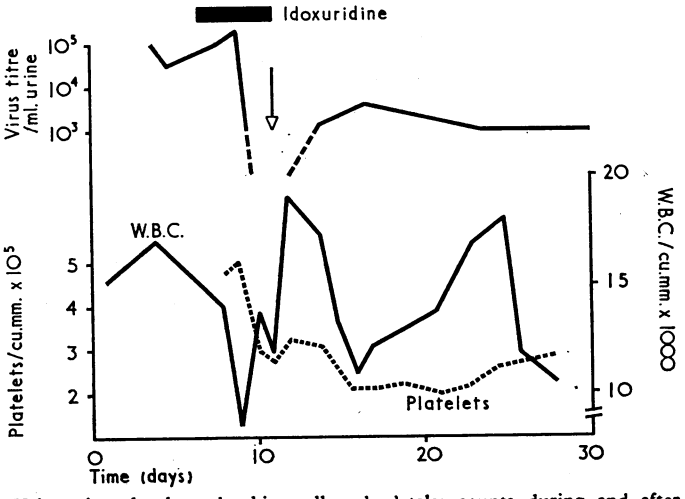
Case Report

The infant was born at home one week post-mature by dates, and was the second daughter of healthy parents. The pregnancy was uneventful and the delivery normal. At birth she weighed 3.6 kg. At the age of 7 weeks she was referred to the Derbyshire Children's Hospital because her general practitioner thought her head was small and she was not thriving. She had been irritable, fed poorly, and had not yet smiled. At that time her head circumference (33.6 cm.) was below the tenth percentile for her chronological age. The anterior fontanelle was patent and exhibited normal tension. There was no detectable chorioretinitis. The arms were held flexed at the elbows with the hands clenched, and the legs were extended ; muscle tone was increased in all four limbs. *X*-ray examination of her skull showed patchy intracerebral calcification.

Antibody studies on the mother showed complement-fixing titres of 1/320 to cytomegalovirus, and 1/32 to adenovirus, haemagglutination inhibition titre of 1/20 to rubella, and dye test titre of <1/8 to toxoplasma. Titres in the patient were 1/40, <1/8, 1/4, and <1/8 respectively.

As cytomegalovirus infection was a possibility, a sample of the infant's urine and a throat swab were obtained for virus culture. Both yielded cytomegalovirus. Treatment with idoxuridine was suggested to the parents, to whom the experimental nature of this form of therapy was explained fully, and who readily agreed to the procedure.

Treatment was begun on 18 September 1967, when the infant was 14 weeks of age. Urine samples were obtained for virus culture on two days before the institution of therapy and on each day that the idoxuridine was administered. After that further specimens were obtained at less frequent intervals. Cerebrospinal fluid obtained by lumbar puncture just before treatment showed no abnormality. Cytomegalovirus was not isolated from this specimen. Because of the cytotoxic action of the drug used, a full blood count was performed on the same days that the urine samples were taken, and on several days after treatment. The haemoglobin fell from a level of 11.6 g./100 ml. before treatment to a minimum of 9.8 g./100 ml., but returned to 10.7 g./100 ml. 12 days after treatment. Results of white cell and platelet counts are shown in the Chart. Liver-function tests were performed before and four days after the cessation of therapy. Results of serum bilirubin, alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, isocitrate dehydrogenase, thymol turbidity, and flocculation tests were all within normal limits.



Urine virus levels and white cell and platelet counts during and after idoxuridine treatment. Arrow indicates onset of staphylococcal infection (see text).

Treatment

A total of 600 mg. of idoxuridine per kg. body weight was given by intravenous infusion over a period of five days, 200 mg./kg. being given on the first day and 100 mg./kg. on the subsequent four days. A sample of each batch of prepared drug was checked for sterility on the day that it was used. The fluid was given on