

hilarity and movement (presumably including eye movement) during the compression phase due to the combined effects of warmth and nitrogen narcosis, thus assisting the flow of nitrogen-laden tears between the lens and cornea, while during decompression the chamber was, as is usual, rather cold and foggy, with the subjects relatively immobile, thus minimizing any flow of tears which might have helped to wash out the nitrogen. As the other eye was only slightly affected, it must be presumed that there was a difference in the fit, and hence in the flow of tears under the two lenses, causing either less absorption or better elimination of gas from the other eye.—I am, etc.,

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Bowel Motility and Colonic Cancer

SIR,—Recent studies¹ and comments² on cancer of the colon indicate that valuable information may be forthcoming from intensive studies of bowel motility and faeces composition in populations with contrasting prevalences of this type of cancer.

In South African Bantu age specific mortality is only a tenth of that in whites.^{3,4} In preliminary studies on this subject we have noted two points of interest. In the Bantu (children and students studied thus far) a third have three motions daily compared with only 1–2% in whites. Moreover, in terms of exposure of bowel mucosa to digesta, carmine studies have revealed that in the Bantu the mean transit time of the longest third is less than the mean time of the quickest third among whites. The finding to be stressed is that even in Bantu and whites with the same frequency of defaecation (say, one to two motions *per diem*) traces of carmine continue to be seen far longer in stools of whites than in Bantu; in whites the period is sometimes five to seven days. In addition, therefore, to the presumably vulnerable constipated moiety of population,^{1,4} there is this further moiety with regular motions, not constipated, who, unknown to themselves and undetectable clinically, have unduly prolonged times of traversal of digesta. This is the condition which conceivably provides the favourable *milieu intérieur* required for carcinogenesis, whether of exogenous or endogenous origin.

The second finding to be emphasized concerns the differing ability to produce a stool quickly on request. Eighty to ninety per cent. of rural Bantu children have this capacity, 70–80% of partially sophisticated urban Bantu, but fewer than 10% of white children. Previously^{5,6} we noted that when young white adults consumed a very high-residue Bantu-type of diet for several days they still could not produce a stool on request in the same facile manner as Bantu. Evidently, with "civilization," voluntary control of the defaecation reflex is largely lost. May not differences in physiological tone of the colon be associated with different susceptibilities to carcinogenic agents?

The critical question, of course, is whether the moiety with protracted exposure to possible carcinogens is in fact that moiety in which sufferers from bowel cancer are to be found. Elucidation of this problem will be difficult. For example, verbal questioning regarding bowel habits, etc., is often worthless; we find a poor correlation between frequency from recall and frequency by keeping a weekly chart. Further,

not recollectable to patients, their bowel habits, etc., at 50–60 years may differ markedly from those at 30–50 years.

Obviously, far more explicit data are needed on populations with contrasting prevalences of colonic cancer. In the present circumstances it would seem that only by impeding carcinogenic action may prophylaxis be envisaged. Screening centres have been advocated to detect the segment of population most prone to coronary heart disease, to detect the aglycosuric population who have abnormal glucose tolerance, etc. Would it be too far fetched to suggest that the younger adult population be screened, initially with carmine, to detect the moiety with very prolonged transit times, and that such be given dietary or therapeutic advice to accelerate excretion?—We are, etc.,

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Pigmentation in Megaloblastic Anaemia

SIR,—We have read with interest the description by Dr. N. Baumslag and Dr. J. Metz of spotty pigmentation of palms, soles, and tongue in lactating Africans with folate deficiency (21 June, p. 737). Clinicians in Ibadan are aware of the possibility of hyperpigmentation in patients with megaloblastic anaemia, as it has been seen in one Nigerian with vitamin B₁₂ deficiency, but it has not been noticed in folate deficiency, though about 200 women with severe megaloblastic anaemia associated with pregnancy are seen each year. No areas of hyperpigmentation were revealed by a detailed dermatological examination of six women with profound anaemia in pregnancy.

Failure to observe pigmentation in Ibadan may be because it has not been looked for closely enough, or it may be related to the different presentation of folate deficiency—anaemia is seen most commonly near the end of the second trimester, while the South African patients were seen during lactation. The South Africans may have been deficient for longer than the Nigerians, and shown an early stage of a skin lesion which is much more remarkable in vitamin B₁₂ deficiency,^{1,2} a condition which develops insidiously and is almost always long-standing at the time of presentation.

Biopterin is the coenzyme required for hydroxylation of phenylalanine to tyrosine, and it has been found in abnormally high concentration in the serum of folate-deficient pregnant Nigerians.³ Widespread disturbance of amino-acid metabolism has been found in pregnant Nigerians with megaloblastic anaemia, but no evidence of a failure to convert phenylalanine to tyrosine (Jacobs, S., and Fleming, A. F., unpublished observations). There is a lower than normal histidine α -deaminase activity in the skin from vitamin

B₁₂ or folate-deficient Indians with hyperpigmentation.⁴ None of these abnormalities of amino-acid metabolism help us to understand the accumulation of melanin in megaloblastic anaemia. A possible explanation is that it is the result of abnormal cell division.—We are, etc.,

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Hypokalaemia after Treatment with Duogastrone (Carbenoxolone)

SIR,—Dr. J. Forshaw's Memorandum on hypokalaemic muscle weakness complicating the use of Duogastrone (position-release carbenoxolone sodium) (14 June, p. 674) prompts me to record a similar case.

A woman of 55 developed pins and needles in the fingers of both hands while cooking one evening. This lasted only 30 minutes, but an hour later she noticed weakness of both hands and the next day her right arm was weak. Over the next 24 hours the weakness spread to both arms, the shoulders, and then to the thighs and back muscles and she had difficulty in holding up her head. She had no muscle pain, no difficulty in swallowing, and no visual symptoms. Her general health was good and there had been no diarrhoea or vomiting. She had never suffered from muscle weakness before, nor was there any family history of a similar condition. A duodenal ulcer had been demonstrated 23 years previously, but had always responded to conservative treatment. She had been taking Duogastrone, 200 mg. four times a day, for six weeks; the course of tablets had finished one day before the onset of her present symptoms.

On examination she was a fit-looking woman. General examination was negative except for a blood pressure which varied between 200/120 and 140/80, and a small nodule in the thyroid gland. There was slight weakness of jaw opening and weakness of the sternomastoids so that she had difficulty in lifting the head from the pillow. She had severe flaccid weakness in the limbs affecting proximal muscles more than distal and the arms more than the legs. There was no fasciculation or muscle tenderness, and the tendon reflexes were absent in the arms and at the ankles. The plantar responses were flexor. There was no impairment of sensation and the peripheral nerves were not thickened.

The relevant investigations were as follows: Serum electrolytes (mEq/l.): Na 149, K 1.7, Cl 101, CO₂-combining power 32. Serum enzymes (units): Aldolase 160, S.G.O.T. 244, S.G.P.T. 200. Glucose tolerance test (30 minute intervals following the ingestion of 50 g. glucose): 117, 162, 175, 206, 209 mg./100 ml.

Electromyogram (right deltoid): mean muscle action potential duration 10 msec. (normal 14.3 \pm 20%) and incidence of polyphasic potentials 16% (normal 3–12%). Maximum effort showed a normal interference pattern of reduced voltage. Conduction velocities in the ulnar and lateral popliteal nerves were within normal limits. These results strongly suggested a myopathic lesion (Dr. J. S. Chopra). Electrocardiogram: depression of ST segment in leads 1, 2, AVL, V5, and V6; QT interval 0.4 sec: prominent U waves in chest leads.