Tylosis and Oesophageal Carcinoma

SIR,—Some new data¹ on the association between tylosis and squamous celled carcinoma of the oesophagus is consistent with the suggestion,² based on a genetical analysis, that the gene responsible is at a single autosomal locus. There are resemblances between structure of the oesophageal mucosa (in mammalian species other than man) and the

FIG. 1.—Human thick skin (sole of foot). C=Stratum corneum, L=Stratum lucidum, and G=Stratum granulosum. H & E $\times 115$.

structure of the epidermis of those areas of skin subject to tylosis, and we suggest that both tissues may be responsive to the same functional requirement—namely, the need to provide resistance to mechanical friction.

Human epidermis can be classified into "thick" and "thin" types.³ Thick skin is found most characteristically on the palms and soles, and relative to thin skin it has a thicker stratum corneum, a more marked stratum granulosum, and a thick stratum spinosum. It also has a stratum lucidum (Fig. 1), a layer not found in thin skin, and is devoid of hair follicles. In sections of skin from the middle finger of a female cadaver it was noted that the histological appearances overlying the metacarpophalangeal and proximal and distal interphalangeal joints and distal phalanx were those of thick skin, as judged by their conformity with the features described above. The distribution

FIG. 2.—Rat oesophagus. Abbreviations as for Fig. 1 H & I $\times 460$.

of tylotic lesions was studied in members of a family subject to tylosis and carcinoma of the oesophagus. When the backs of the hands were affected the lesions were confined to thick skin areas. In one case skin over the proximal interphalangeal joints was the only part of the hand affected, though characteristic tylotic lesions were present on the feet.

We have observed that tylotic lesions seem to be closely related to exposure of thick

skin areas to an amount of friction which would not be expected to produce thickening of the skin in non-tylotic individuals. Friction also seems to be an important determinant of the structure of oesophageal epithelium. Thus it is generally thicker and shows more keratinization in animals who eat coarse vegetable diets than the epithelium of insectivorous and carnivorous mammals.⁴ The oesophageal mucosa in some herbivorous mammals has cell layers similar to those in thick skin. A stratum granulosum is found in the oesophagus of the guinea-pig, rat, and porcupine and a stratum lucidum has been described in the oesophagus of the opossum⁵ and of the rat⁶ (Fig. 2). The occurrence of a stratum lucidum in the oesophagus is of special interest, because in the human it is confined to thick skin.

We would suggest: (1) That oesophagus and thick skin have histological similarities, particularly in those mammals which eat a coarse vegetable diet. (2) That both tissues have a particular ability to respond to friction. (3) That there is an abnormal response to friction in the thick skin areas of tylotics. (4) That oesophageal friction in those tylotics at risk of developing carcinoma of the oesophagus should be kept at low level. Thus thorough mastication, swallowing small rather than large mouthfuls of food, and the maintenance of good dental health could be advocated. These measures could be instituted in addition to abstinence from alcohol and cigarette smoking—factors which are already suspected as being implicated in the aetiology of carcinoma of the oesophagus.⁷ —We are, etc.,

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Treatment of Diabetes Insipidus

SIR,—As was recently pointed out in your leading article (6 February, p. 302) chlorpropamide has an important role in the treatment of vasopressin-dependent diabetes insipidus, especially in those cases where the side effects of the widely used lysine-8-vasopressin (LVP) are so unpleasant that the patients prefer to put up with the symptoms of disease rather than taking vasopressin. Chlorpropamide, however, is not effective in all cases of vasopressin-sensitive diabetes insipidus¹ and not free from side effects.^{2 3}

We would like to call attention to a newly synthesized analogue of vasopressin, DDAVP (1-deamino-8-D-arginine)-vasopressin (Fer-

ring AB, Malmö, Sweden), which we expect will soon be available for clinical trials in the United Kingdom. DDAVP has a higher anti-diuretic potency, less pressor activity, and a longer duration of action than the natural hormone,^{4 5} and it may be administered intranasally or by injection. Because of these properties DDAVP is particularly suited for the treatment of cranial diabetes insipidus.⁴

We have tried DDAVP in a series of eleven patients (6 males and 5 females) aged 18-57 with this disease. Without treatment the patients had a urine production of 5-20 l./day. DDAVP was given intranasally in a dose of 10-15 μ g twice a day to 10 of the patients (in one case 15 μ g $\times$ 3) and at this dosage their daily urine output was reduced to 1-2 l. In six patients DDAVP was also administered intravenously. It was found that 2 μ g had an effect for 10 hours or more, compared to 1-2 hours for 2 μ g LVP. No pressor response, facial blanching, abdominal discomfort, or any other side effects have been noted after doses up to 16 μ g DDAVP intravenously. Nasal administration for more than nine months has also proved satisfactory without any deleterious effect on the nasal mucosa.

Judging from our experience DDAVP represents progress in the treatment of cranial diabetes insipidus, and its long duration of action and absence of side effects present obvious advantages over both LVP and chlorpropamide.—We are, etc.,

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Antibiotic Sensitivity Testing

SIR,—You pointed out in your leading article (22 May, p. 416) that diversity and unreliability of techniques for testing antibiotic sensitivities of bacteria had induced in some clinicians such despair that they "have expressed the view that laboratory reports on this subject are better disregarded." Such despair could become widespread if clinicians not familiar with the underlying data put a wrong (but all too obvious) interpretation on some of the words in Dr. E. Joan Stokes's letter (19 June, p. 707). This would be particularly sad because of all the hard work that Dr. Stokes has done to improve the reliability of such tests.

Dr. Stokes said in her letter that in the Association of Clinical Pathologists sensitivity test trial¹ "42 laboratories using the direct plating technique gave 64% correct results whereas 107 laboratories using pure culture techniques gave only 45% correct results." The uninitiated reader could easily take this to mean that even in a well-run trial the results of sensitivity tests are about as likely to be wrong as they are to be right. However, in context a "correct" report was one that agreed at every point, over a series of tests involving four bacterial