

LETTERS TO THE EDITOR

Osler's disease is not a telangiectasia but a tumour

SIR,—I have read with great interest the instructive article by Zentler-Munro *et al*¹ about an association of vascular abnormalities and hepatic fibrosis in Osler's disease. Above all, I was impressed by their photographs. In Figure 3, there are dilated vascular spaces practically devoid of erythrocytes and still other ones full of red blood cells. I covered the latter by white stain and looked with astonishment how few hepatocytes remained from original hepatic tissue. To all appearances, a tissue of hepatic lobules was almost destroyed by vessels the aggressive character of which reminds of tumoral growth instead of telangiectases.

As we believe that hyperplastic capillaries are involved in a pathogenesis of fibrosis, I looked for them in the article of Zentler-Munro *et al*.^{1,2} Having been unable to identify them, I turned to other articles concerning Osler's disease. I found them in an article by Tedesco *et al*³ who had described an angioma in the submucosa of a stomach and telangiectases associated with fibrosis in the liver.

Further, I was attracted by an article by Nödl⁴ who had studied cutaneous telangiectases. His outstanding photographs of pathological vessels surrounded by nonhaemato-poietic mesenchymal cells (Figs 2, 3, 4, 5, 6, 7, 8) reminded me immediately of similar vessels that I had observed when I studied cutaneous vascular tumours.^{5,6} At that time, I described hyperplastic capillaries composed of epithelioid undifferentiated endothelial cells and situated in the vicinity of a capillary haemangioma, a haemangiopericytoma, and an angioleiomyoma. The capillaries were so similar to sweat glands that a careful morphological analysis was needed in order to distinguish these two structures. These hyperplastic capillaries could give rise: (a) to long narrow strips of smooth muscle tissue by an *in situ* differentiation of their cells into smooth muscle cells; (b) to pathological muscular vessels by a short distance centrifugal migration and a differentiation of their cells into vascular wall muscular cells; and (c) to ectatic capillaries surrounded by fibroblast-like cells by a migration of their cells into the extravascular space and their differentiation there.¹

A similarity between the vessels described by Nödl⁴ and the vessels I have observed suggests that Nödl described in reality tumoral lesions. I looked, therefore, for hyperplastic capillaries in his article. I found them in Figs 3, 4, 6c, 6d, 7, 8. Nödl does not mention them because he considers them to be sweat glands. Why I believe that at least some of these structures are hyperplastic capillaries: (1) a number, a location, and a morphology of pathological muscular vessels indicate that they are not formed by remodelling pre-existing normal vessels; (2) some of them are collapsed and undergoing involution suggesting their high turnover; (3) there are structures clearly recognisable as mesenchymal but similar to sweat gland tubules (Figs 3, 4, 6d—in the middle, 7—a large tubule on the right side, 8—on the right side); (4) referring to my previous observation,⁵

endothelial cells in the 'sweat glands' often degenerate, most probably because of hypoxia, and their nuclei form clusters leaving empty space in their vicinity (Fig 7—in the upper right corner); (5) endothelial cell nuclei often possess an elongated form. When they are oriented longitudinally hyperplastic capillaries manifest histopathological patterns incompatible with genuine sweat glands (Fig 7—in the upper right corner). Finally, there is a remnant of an original hyperplastic capillary composed of several layers of undifferentiated epithelioid endothelial cells (Figs 9, 10). Because there is no other pathological process present, the remnant is not a reactive hyperplasia but a manifestation of tumoural growth.

If Osler's disease is a vascular tumour anti-angiogenesis¹⁰ may be tried in its therapy. This proposition is supported by a successful treatment of this disease by medroxyprogesterone acetate,¹¹ an angiostatic steroid.¹²

There are several other diseases which present themselves as telangiectases but derive from hyperplastic tumoural capillaries. They are the senile haemangioma, *Cutis marmorata telangiectatica*,⁵ the vascular spider,¹³ and generalised essential telangiectasia (unpublished personal observation).

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- Zentler-Munro PL, Howard ER, Karani J, Williams R. Variceal haemorrhage in hereditary haemorrhagic telangiectasia. *Gut* 1989; **30**: 1293-7.
- Beranek JT, Masseyeff R, Desmet VJ. Hyperplastic capillaries and their possible involvement in the pathogenesis of fibrosis. *Histopathology* 1986; **10**: 543-51.
- Tedesco FJ, Hosty TA, Sumner HW. Hereditary hemorrhagic telangiectasia: presenting as an unusual gastric lesion. *Gastroenterology* 1975; **68**: 384-6.
- Nödl F. Zur Histopathogenese der telangiectasia hereditaria hämorrhagica Rendu-Osler. *Arch Klin Exp Dermatol* 1957; **204**: 213-35.
- Beranek J. *Activités enzymatiques des hémangiomes cutanés. Étude histologique et histoenzymologique.* Mémoire pour le Titre d'Assistant Etranger. Faculté de Médecine de Paris, 1970: 128.
- Beranek JT. Remembrance of Dr Hermann Pinkus. *Am J Dermatopathol* 1986; **8**: 451-2.
- Gans O, Steigleder GK. *Histologie der Hautkrankheiten. Vol II.* Berlin-Göttingen-Heidelberg: Springer Verlag, 1957: 468-72.
- Stout AP. Solitary cutaneous and subcutaneous leiomyoma. *Am J Cancer* 1937; **24**: 435-69.
- Beranek JT. Antiangiogenesis comes out of its shell. *Cancer J* 1988; **2**: 87-8.
- Beranek JT. Transformation of capillaries into interstitial tissue: further evidence in favour of the angiogenic hypothesis of repair and fibrosis. *Br J Plast Surg* 1989; **42**: 725.
- Richtsmeyer W, Weaver G, Streck W, Jacobson H, Dewell R, Olson J. Estrogen and progesterone receptors in hereditary hemorrhagic telangiectasia. *Otolaryngol Head Neck Surg* 1984; **92**: 564-70.
- Fujimoto J, Hosoda S, Fujita H, Okada H. Inhibition of tumor angiogenesis activity by medroxyprogesterone acetate in gynecologic malignant tumors. *Invasion Metastasis* 1989; **9**: 269-77.
- Beranek JT. Histogenesis of vascular spiders. *Hepatology* (In press).

Oesophageal carcinoma in Sri Lanka

SIR,—With reference to the article by Sagar (*Gut* 1989; **30**: 561-4), I wish to add that Sri Lanka was a transit point in the old silk route between China and Rome. Marco Polo also stopped over in Sri Lanka (then identified by him as Seilan) on his return from China.^{1,2} On the diet of the natives of the northern region of Ceylon, seven centuries ago, Marco Polo wrote,

'They have no grain other than rice. They have sesame, from which they make oil. They live on milk, flesh and rice and have wine made from trees'.

The wine he referred to, is known as 'kallu' in Tamil language, and is produced from the palmyrah palm *Borassus flabellifer*.

Stephen and Uragoda³ have reported that cancer of the oesophagus is the commonest among the patients admitted to thoracic units in Ceylon, and Ceylon is one of the few countries with a high incidence of both oral and oesophageal carcinoma. In China,⁴ the male-female ratio of patients with oesophageal cancer is reported as 2:1. But in Sri Lanka, the incidence of oesophageal carcinoma is higher among women than men.⁴

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- Yule H. *The book of Ser Marco Polo, the Venetian, concerning the kingdoms and marvels of the east*. New York: Airmont Publishing, 1969: 249-50.
- Latham R. *The travels of Marco Polo*. Middlesex: Penguin, 1987: 258-9.
- Stephen SJ, Uragoda CG. Some observations on oesophageal carcinoma in Ceylon, including its relationship to betel chewing. *Br J Cancer* 1970; **24**: 11-15.
- Khojasteh A, Kraybill WG. Cancer of the esophagus: the environmental connection. *South Med J* 1988; **81**: 878-82.

Ranitidine nocte (Rhs) v ranitidine mane and nocte (Rbid)

SIR,—We wish to comment on the abstract by Dobrilla *et al* (*Gut* 1989; **30**: A726) stating that there is no significant difference between Rhs and Rbid healing rate at two weeks but the authors did not mention which statistical test and significance level they used.

We found, however, using the χ^2 test, without Yates correction, a significant difference between the two treatments at two weeks ($\chi^2=5.2$ resulting in a p value<0.05).

It would be interesting to know why according to the authors the difference in healing rate was not significant at two weeks.

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Reply

SIR,—With regard to the letter of VanWilder and Jan Plas, the comment of these authors is correct but there is an error in our abstract.

In fact, while the reported ranitidine bid healing percentage by week two is correct (64.2%), the absolute figures are 102/159 and not 107/159, as indicated. Using the χ^2 test on the correct number of patients, the difference between the two treatment groups proves to be statistically not significant.

Further details can be found in the full paper which now has been published. (*Clin Trial J*) 1989; **26**: 153-62.

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H pylori and duodenal ulcer

SIR,—Dr Carrick and colleagues are to be congratulated on quantifying in their 137 subjects the strength of the risk factor for duodenal ulceration (relative risk=51) of duodenal infec-