

In conclusion, in 17 patients with advanced bronchial carcinoma we have failed to confirm the optimistic results described by Price and Goldie in their preliminary report.—I am, etc.,

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<sup>1</sup> Price, L. A., and Goldie, J. H., *British Medical Journal*, 1971, 4, 336.

### Chemotherapy of Candidiasis

SIR,—The paper on "Relevance of Antigenicity of *Candida albicans* Growth Phases to Diagnosis of Systemic Candidiasis," by Mr. E. G. V. Evans and others (13 October, p. 86) is most timely indeed, not only because of the increasing frequency of iatrogenic systemic candidiasis, as stated in the paper, but even more so since several promising antifungal agents have become available.

We have had the opportunity to use an injectable solution of miconazole, one such agent, which was made available to us for investigational use. Miconazole, 1-[2, 4-dichloro- $\beta$ -(2, 4-dichlorobenzoyloxy) phenethyl] imidazole, is a synthetic chemotherapeutic agent which is active against most pathogenic fungi, yeasts, and Gram-positive bacteria.<sup>1</sup> Miconazole has proved its therapeutic usefulness in dermatomycosis<sup>2</sup> and vaginal candidiasis.<sup>3</sup>

We have used miconazole in 14 patients with systemic candidiasis proved by positive bronchial sputum, urine, or blood culture. Treatment was successful in all at the dose of 200-400 mg thrice daily for 5-30 days given intravenously or occasionally, as indicated by the primary site of the infection, also by such routes as direct instillation into the trachea, bladder, or renal pelvis. Treatment must be continued until the relevant cultures have become completely negative. The most striking advantage of miconazole has been its excellent local tolerance and the absence of renal, liver, or blood toxicity.

We also treated seven cancer patients with a persistent fever of unknown origin which was resistant to broad-spectrum antibiotics, on the assumption that the fever could have been due to candida infection though blood cultures were negative. Necropsy on such patients may reveal nidi of candida infection which could not be demonstrated during life.<sup>4</sup> Miconazole given intravenously at a dose of 600 mg per day made five of the seven patients subfebrile within three days, but even prolonged treatment did not change the febrile state of the other two patients.

Clearly for this category of patients accurate and fast diagnosis of candidiasis would be most desirable since effective therapy could then be started immediately.—We are, etc.,

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- <sup>1</sup> Van Cutsem, J. M., and Thienpont, D., *Chemotherapy*, 1972, 17, 392.
- <sup>2</sup> Bruggmans, J., Van Cutsem, J. M., Thienpont, D., *Archives of Dermatology*, 1970, 102, 428.
- <sup>3</sup> Godts, P., Vermeylen, P., and Van Cutsem, J. M., *Arzneimittel-Forschung*, 1971, 21, 256.
- <sup>4</sup> Taschdjian, C. L., Kozinn, P. J., and Toni, E. F., *Annals of the New York Academy of Sciences*, 1970, 174, 606.

### Pyomyositis in London

SIR,—I would agree with Dr. P. E. T. Isaac's view (27 October, p. 235) that the interesting case of gluteal abscess described by Dr. D. W. Rogers (29 September, p. 679) falls into a different category from that of tropical pyomyositis. Denial by the patient is no guarantee that there has been no recent injection in this site, the lapse of memory being sometimes genuine and sometimes—for a variety of reasons—feigned. Tropical pyomyositis, first described by Scott in the West Indies in 1912,<sup>1</sup> has been reported with such frequency since then from areas confined to the tropical belt which encircles the world, that it must surely be associated with some common factor (such as parasites) encountered in these areas.

However, I would disagree with Dr. Isaac's assertion that the lesions of tropical pyomyositis are always multiple. Buxton, in his classic monograph on the disease,<sup>2</sup> did not make this distinction. In a personal series of 65 cases reported from Nigeria<sup>3,4</sup> there were 55 single abscesses, while in only 10 cases were three multiple abscesses.

In this series nematode larvae in large numbers were demonstrated in the pus from intramuscular abscesses. The following aetiological hypothesis was advanced: (1) From initial nematode infestation (ancylostoma, dracunculus, etc.) shoals of larvae migrating through the systemic circulation break out through capillaries to be deposited in skeletal muscle, causing a local allergic inflammation (tropical myositis) similar to that which occurs in visceral larva migrans or in ascarid pneumonitis. (2) Subsequent autogenous infection of the lesion—for example, by staphylococci—would produce pyomyositis. These abscesses therefore differ from those caused by adult worms (such as *Dracunculus medinensis* or filaria), which inhabit subcutaneous planes or lymphatics.

Nematode infestations of differing varieties are heavy in all areas in which tropical pyomyositis is endemic. Numerous attempts have been made before and since the above hypothesis was advanced to explain the aetiology of this disease, but no other offers a factor which is common to every area in which tropical pyomyositis is endemic.—I am, etc.,

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- <sup>1</sup> Scott, H. H., *Journal of Tropical Medicine and Hygiene*, 1912, 15, 97.
- <sup>2</sup> Buxton, P. G., *Researches in Polynesia*, Memoir No. 2, London School of Hygiene and Tropical Medicine, 1928.
- <sup>3</sup> O'Brien, D. D., *Journal of the Royal Army Medical Corps*, 1963, 109, 43.
- <sup>4</sup> O'Brien, D. D., *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 1963, 57, 313.

### Nicotine Availability as a Factor in Tobacco Consumption

SIR,—Dr. M. A. H. Russell and others (1 December, p. 512) suggest that a cigarette

could be less harmful if it had "a low tar and carbon monoxide yield but a high, rather than low, nicotine yield." The high correlation between the tar and nicotine yields of cigarettes in the current "league table" precludes the likelihood of such a cigarette being obtainable.

However, there do exist cigarettes in which the nicotine availability is potentially high though the tar content remains relatively low. Nicotine is absorbed more readily in the form of a free base, as it exists in an alkaline smoke, than in the form of a stable salt, as it would be in an acid smoke.<sup>1</sup> English cigarettes, which are made of flue-cured tobacco of high sugar content, give rise to an acid smoke (about pH 4). It has been pointed out by Elson and Betts<sup>2</sup> that "in the smoke of 'reduced tar and nicotine' cigarettes made of high sugar tobacco not only is the nicotine low but its 'pharmacological availability' is also low because of the progressive increase in acidity during smoking. Is there not some danger therefore that the smoker of these cigarettes, in order to achieve his 'nicotine satisfaction' will smoke more, or, what is perhaps more serious, will increase his tendency to inhale?"

In contrast to this the smoke of cigarettes made mainly from air-cured low sugar content tobacco such as those popular in France and other European countries, and of cigars, becomes progressively more alkaline (to pH 8 or 9) during the course of smoking. Thus "nicotine satisfaction" should be achieved in smoking of fewer cigarettes and with less tendency to inhale. The annual cigarette consumption per head in France over the years 1930 to 1965 averaged about 900, while in the United Kingdom it was over 2,000. The death rate from cancer of the lung, bronchus, and trachea in France is less than half that in England and Wales.

The inference would seem to be that for compulsive smokers an indication toward less harmful smoking lies in the direction of decreased tar and nicotine content of the smoke together with a reduced acidity, so that a reasonable degree of "nicotine satisfaction" can be achieved with minimum lung cancer risk from inhalation of carcinogenic<sup>3</sup> tar. Reduced acidity of the smoke can be achieved by replacing part, at any rate, of the flue-cured tobacco by air-cured tobacco of low sugar content or by the synthetic "substitute smoking materials" now being developed, which presumably contain no sugar or nicotine. With the latter however, a sufficient degree of alkalinity of the smoke may not be achieved. A further or additional possibility<sup>1,2</sup> is the use of tobacco additives which give rise to an alkaline vapour at the usual temperature of combustion of cigarettes.—I am, etc.,

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- <sup>1</sup> Elson, L. A., Betts, T. E., and Passey, R. D., *International Journal of Cancer*, 1972, 9, 666.
- <sup>2</sup> Elson, L. A., and Betts, T. E., *Journal of the National Cancer Institute*, 1972, 48, 1885.

### Co-trimoxazole Resistance

SIR,—The occurrence of mutants lacking in thymine (thy) has been recently described<sup>1,2</sup> and led Dr. R. W. Lacey and Mrs. Evelyn L. Lewis (20 October, p. 165) to the assumption that significant quantities of thymidine are present in body tissues and that therefore