dilettante and will only discover something new by accident.

Your "single brilliant or lucky scientist" is my man from the start, provided that he will allow for the fact that years and years of conscientious painstaking endeavour are almost certain to result in a prejudiced approach. The whole history of the progress of mankind is witness to the fact that where a breakthrough has been made, it has come about through a combination of fortuitous circumstance and insight.

For this reason I cannot agree that to confirm researchers for life in a career structure would be an advance. In fact I believe that because "doctors and scientists undertake research during their progress to other posts" they are much more likely to have new ideas than those who enter research as a life-time occupation. There are plenty of these devoted workers who today can look back on 30 or 40 years of conscientious endeavour without having had a single new idea. This situation is inevitable if research is conducted by a vertical approach alone.—I am, etc.,

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1 De Bono, Edward, *The Mechanism of Mind*, London, Jonathan Cape, 1969. *The Use of Lateral Thinking*, London, Jonathan Cape, 1967.

Tumbu Fly

SIR,—The fascinating accounts of dermal myiasis to tumbu fly (1 April, p. 58, and 15 April, p. 164) prompt me to report a further unexpected locus of the larvae. While working in East Africa a consultant surgeon produced a "worm" which he had removed by simple expression of a swollen healing appendicectomy wound.

The patient was a young girl of 16 years, and both she and her surgeon were somewhat alarmed to find the parasite. Her wound healed without further difficulty. The larva was duly fixed in methanol, and a quick reference to Ashe and Spitz's excellent treatise on *Pathology in the Tropics*[1] made recognition simple.—I am, etc.,

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1 Ashe, J. E., and Spitz, S., *Pathology of Tropical Diseases*, Philadelphia, Saunders, 1945.

Urinary Candidiasis after Renal Transplantation

SIR,—We wish to report the use of the synthetic antimycotic agents 5-fluorocytosine and clotrimazole in the successful treatment of urinary candidiasis in a patient who had received a renal homograft.

A 32-year-old man received a renal homograft from his father. The graft functioned well although further operations were necessary to relieve ureteric obstruction. Gentamicin was then given to offset the effect of any bacteria introduced into the urinary tract by the passage of urethral and ureteric catheters, strains of *Klebsiella aerogenes* sensitive to gentamicin but resistant to ampicillin and carbenicillin having been repeatedly isolated from the perineal area before operation.

The urine, which was cultured daily, remained sterile until the 25th post-transplant day when *Candida albicans* was isolated. On the 30th day the urine contained more than 10^5/ml. The organism was also isolated from the mouth and throat although there were no clinical signs of infection. Because of its nephrotoxicity the use of amphotericin B was considered inadvisable. The patient was given 5-fluorocytosine 10 g daily in divided doses, reducing to 2 g on the third day, by which time the urine was sterile. On the sixth day, however, urine cultures were again strongly positive for *C. albicans*. Treatment was stopped for two days because of an operation to maintain urine drainage, but was recommenced with 2 g daily and continued for a further 10 days. Urine cultures for *C. albicans* remained strongly positive and the yeasts by now were shown to be resistant to 5-fluorocytosine. Three days later clotrimazole therapy, 100 mg/kg body weight was started. After five days urine cultures for *C. albicans* were negative. On the ninth and tenth days the patient was excessively drowsy and disorientated. Treatment with clotrimazole was stopped and his mental state rapidly improved.

There has been no recurrence of candiduria over the ensuing 10 months. The patient remains well and the graft is functioning satisfactorily.

The minimum inhibitory concentrations of the antimycotics for most of the candida isolates were measured. Serum and urine levels of 5-fluorocytosine and serum levels of clotrimazole were assayed. Yeast morphology agar (Difco), a cytosine-free medium, was used for all the sensitivity tests and assays. A sensitive strain of *Candida pseudotropicalis* was used for the assays of both drugs.

Mycological Findings During 5-Fluorocytosine Treatment

Day	*C.albicans*/ml	Levels (μg/ml)	
	Urine	Serum	Urine
0 ..	$>10^5$ (0·25)*	0	0
2 ..	10^3	5	100
4 ..	0	24	200
6 ..	10^4 (⩾1000)	28	200
9 ..	$>10^5$ (⩾1000)	1	60
11 ..	$>10^5$ (⩾1000)	5	100
17 ..	$>10^5$ (⩾1000)	6	150

*Mean Inhibitory Concentration for isolate in μg/ml.

The Table summarizes the mycological findings during treatment with 5-fluorocytosine. Candida initially isolated were sensitive to 0·25 μg/ml 5-fluorocytosine but were replaced by organisms resistant to more than 1,000 μg/ml. Serum levels varied from 1 to 28 μg/ml and urine levels from 60-200 μg/ml. The sensitivity of isolates was also determined by disc diffusion using discs containing 1 μg 5-fluorocytosine. Further examination of the initial isolate showed that it was not uniformly sensitive. Repeat disc sensitivity tests incubated at 37°C for 24 hours showed clear zones round the discs but when these were incubated at 30°C for the same time, colonies grew up to the discs. The minimum inhibitory concentration of clotrimazole for all the isolates tested was between 1 and 2 μg/ml. In the sera examined the levels never exceeded 0·6 μg/ml.

Liver function was assessed by measuring the serum levels of bilirubin, alkaline phosphatase alanine aminotransferase, and lactic dehydrogenase. During treatment with 5-fluorocytosine, there was a rise in the alkaline phosphatase level and isoenzyme studies showed that the increase was in the liver fraction. There was no disturbance of liver function during treatment with clotrimazole. Neither drug had an adverse effect on renal or bone marrow function.

Broad-spectrum antibiotics and immunosuppressive drugs are recognized factors in the aetiology of severe candida infections.[1,2] Both were given to this patient. Although gentamicin therapy had stopped before the candida was first isolated from the urine the antibiotic had probably selectively encouraged growth of the yeast. The failure of 5-fluorocytosine to eradicate the candida was disappointing. Strains of *C.albicans* resistant to clotrimazole have not been reported and attempts to induce resistance have failed.

Both these drugs are potentially useful in the treatment of systemic candida infections but are not free from toxic side effects. Disturbances of the bone marrow and liver function associated with 5-fluorocytosine have been reported previously.[3,4] The disturbances were transient but in patients dying from the underlying disease toxic necrosis of the liver was demonstrated at necropsy by Record *et al.* (30 January 1971, p. 262).

The early trials have shown that as in this patient mild disturbances of the mental state may be associated with clotrimazole therapy. There are no reports of irreversible toxic effects associated with treatment with either drug.

We wish to thank Dr. J. Garrod, Roche Products Ltd. for supplies of 5-fluorocytosine, Mr. J. Dixon and Mr. C. S. Good, F.B.A. Pharmaceuticals Ltd., for supplies of clotrimazole, Miss M. McCready for the isoenzyme studies, and Dr. B. Moore for his encouragement and help.

—We are, etc.,

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1 Folb, P. I., and Trounce, J. R., *Lancet*, 1970, 2, 1112.
2 Symmers, W. St. C., in *Symposium on Candida Infections*, ed. H. I. Winner, and R. E. Hurley, p. 3. Edinburgh and London. Livingstone. 1966.
3 Grunberg, E., Titsworth, E., and Bennett, N., in *Antimicrobial Agents and Chemotherapy*, p. 566. Ann Arbor, American Society of Microbiology, 1964.
4 Tassel, D., and Madoff. M. A., *Journal of the American Medical Association*, 1968, **206**, 830.

Research in Psychiatry

Sir,—Your leading article (8 April, p. 61) makes no mention of the contribution of general practitioners to this field. Yet their situation in the community can enable them to elicit both clinical and social data that are accurate and meaningful.

The article stresses the need for research "to be directed towards early ascertainment of the vulnerable." May I cite an instance of this? A pilot study to determine whether puerperal depression can be predicted from factors presenting in pregnancy has been devised and carried out by a consultant psychiatrist. three general practitioners, and a social worker. The findings, which were obtained from a series of 112 pregnancies and reported in the *Journal of the Royal College of General Practitioners*,[1] indicated four factors statistically significant by the χ^2 test:

(1) Low tolerance to suffering at previous birth;

(2) low tolerance to suffering associated with dysmenorrhoea;

(3) husband away at time of birth; and

(4) an ambivalent attitude towards, or an inability to accept, the pregnancy in the middle trimester.