

should become febrile it is most likely that he would consult a physician or perhaps, under exceptional circumstances, take additional chloroquine. It seems unlikely that this would happen other than very rarely, and I cannot see that it would add significantly to his intake of chloroquine over a period of years.

The expert's statement that "airline pilots may develop malaria in Africa but are unlikely to do so elsewhere" is a most questionable assumption. I have just returned from India, where malaria is highly endemic again, even in the capital city, and I would be not in the least surprised to learn that a number of aircrew taking their rest periods in one or other centre in that country became infected with malaria if they follow your advice.

I also take issue with the claim of your expert that Maloprim, two tablets weekly, is an effective prophylactic "anywhere in the world" (my italics). The comments on this made by Professor Bruce-Chwatt are highly relevant. Your expert's suggestion that an airline pilot "might fly to malarious areas for about 30 years," the implication here being that he must take chloroquine throughout each entire year, seems to me to be equally unrealistic. I would be interested to know what the airlines themselves say about this likelihood.

I certainly support the suggestion that malaria should be considered and looked for in any aircrew who become ill when they have recently been in an endemic area. They also may be suffering from a late relapse or a delayed onset of *Plasmodium vivax* malaria that has been adequately suppressed but not completely prevented by standard chemoprophylaxis.

I do not wish to enter into the dispute concerning alcoholism, since I am not an authority in that field. My sympathies, however, would go out to all aircrew if the airlines ruled that every pilot must be a complete teetotaler. Without entering into the question of airline pilots who become alcoholic, I cannot help but feel that pilots would greatly regret not being permitted to take at least an occasional drink to help themselves unwind after a long and arduous flight.

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<sup>1</sup> Peters, W, *British Medical Journal*, 1971, 2, 95.

**Medical moralising**

SIR,—I have delayed writing to protest at what appears to be a most unfair book review, thinking that others would already have made comment. Dr William Thomson's new book *A Dictionary of Medical Ethics and Practice* is severely criticised by the Rev Dr A V Campbell (5 November, p 1208).

Dr Thomson is a renowned medical editor and writer who has achieved a singular distinction in this field. His contributions are always a delight to read, well informed, wise, pungent, and often witty. This book excels in this respect. But the point at issue is whether medical ethics should, as far as is possible, be presented by firm belief and clearly stated principles or whether it should be taken under the smothering mantle of academic disputation. Surely, once we become involved in "styles of argument in philosophy, law, theology, and the social sciences," we may lose our way and fail to find any coherent ethical answers at all. Of

course, we need to study our problems in depth, getting all the help we can from other disciplines of thought, but what is not possible is to get a satisfactory synthesis from a variety of world views which are, in many aspects, contradictory.

Dr Thomson is exceptionally well informed medically and is aware of the issues involved in decision-making. He writes strongly. His approach is broad-minded and is based on the traditional Judaeo-Christian understanding of man and his place in the world. Such has been the foundation of medical ethics in the Western World over the past thousand years. Many of us believe it is still the surest guide to the doctor and in the best interest of the patient—even (perhaps especially) in the complexities of modern practice.

Yes, Dr Thomson's book is "biased." But then so are the contributions of, say, the modern humanist, for he too quite naturally "moralises" by saying what he thinks is right and wrong when a particular problem is under discussion. All ethical decision-making in medicine depends ultimately on what we believe about man and his place in the world.

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**Bromocriptine and uterine neoplasia**

SIR,—Dr M S Rose and Drs H S Jacobs and J D Hutton (3 December, p 1475) inquire as to the proportion of rats developing uterine tumours with bromocriptine. Detailed results of the two-year rat toxicity study will be published elsewhere; however, the salient features can be summarised as follows.

Two hundred male and 200 female rats were divided equally into four groups and given bromocriptine for 100 weeks mixed in their feed at concentrations which provided mean daily drug intakes of zero, 1.7, 9.8, and 44 mg/kg. At the low dose level there was a reduction in the incidence and severity of periarteritis (a known age-related process in rats), an increased incidence of inflammatory, hyperplastic, and metaplastic changes in the uterus, and a significant reduction in the total number of tumours in females (see table).

At the mid and high dose levels there was a significant decrease in mortality of males due to delayed onset and decreased severity of chronic progressive nephropathy, another age-related disease of rats. Inflammatory, hyperplastic, metaplastic, and neoplastic changes were seen in the uterus. There was a significant decrease in the overall number of tumours in females at both doses (fewer mammary tumours) and in males at the high dose level (fewer adrenal tumours). On the other hand the incidence of uterine neoplasia was increased (see table).

Most of these effects can be regarded as being beneficial—decreased mortality, decreased periarteritis, decreased chronic nephropathy, and decreased mammary and adrenal tumours. However, the increase in uterine tumours clearly re-

quired further investigation. A series of additional experiments showed that, owing to its prolactin-inhibiting action, bromocriptine prevents the pseudopregnancy periods (prolonged dioestrus) which normally occur with increasing frequency as rats age and correspondingly increases the incidence of the alternative situation, persistent vaginal cornification. Plasma oestradiol and progesterone levels in rats from the 100-week study showed that bromocriptine administration inhibited the rise in progesterone levels associated with the state of pseudopregnancy normally seen in old female rats, although basal progesterone levels were unaffected. There was no evidence of a drug effect on the oestradiol levels in rats at any time during the study or on the progesterone levels of young rats—that is, those examined early in the study. Progesterone:oestradiol ratios correlated well with uterine histology, low progesterone levels being associated with endometrial metaplasia or uterine neoplasia.

Since in aging rats, in contrast to women, the cyclicity of reproductive function is lost owing to hypothalamic changes in the presence of responsive ovaries, one of two alternative stable conditions pertains: pseudopregnancy (progesterone dominance) or persistent vaginal cornification (oestrogen dominance). The former is prevented by the prolactin-inhibiting action of bromocriptine, thereby favouring the occurrence of the latter. The fundamental differences in the aging process between female rats and women make it clear that the effects produced by bromocriptine in rats cannot occur in women—either they have cyclic menstrual activity or, after the menopause, involution of both the ovaries (with corresponding diminished oestradiol production) and the uterus. In hyperprolactinaemic women with disturbed menstrual cycles bromocriptine restores cyclicity rather than prevents it.

Although these arguments appear cogent, we agree with Professor G M Besser and his colleagues (1 October, p 868) that women receiving bromocriptine for prolonged periods should have gynaecological assessments at regular intervals as an additional precautionary measure until sufficient results have accumulated to show that this is no longer necessary.

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**"Curing" minor illness in general practice**

SIR,—May I comment on Dr G N Marsh's statement (12 November, p 1268) that "something in the order of £10m could have been saved in one month by general practitioners" by general adoption of a policy of non-prescribing for minor self-limiting illness?

If we accept the figure of 17 000 quoted in the local press as the size of the practice population of Dr Marsh and his partners, the adoption of the policy will have reduced his prescribing costs per patient from £1 to 84.5p, a saving of 15.5p. But the average cost

*Deaths and tumours in rats given bromocriptine in their food for 100 weeks*

	Controls		Low dose		Mid dose		High dose	
	Male	Female	Male	Female	Male	Female	Male	Female
Rats in study	50	50	50	50	50	50	50	50
Dead by 100 weeks	36	32	28	25	21*	24	19*	32
Rats with tumours	28	44	30	29*	28	26*	19	20*
Benign mammary tumours	—	37	—	14*	—	10*	—	8*
Malignant mammary tumours	—	3	—	1	—	0	—	0
Benign adrenal tumours	19	2	12	2	14	1	3*	1
Benign uterine tumours	—	0	—	0	—	1	—	0
Malignant uterine tumours	—	0	—	2	—	7*	—	9*

\*P<0.01 v control group (one-sided Fisher's exact test).