the adherence of patients to tuberculosis treatment.[2] We included trials that were randomised or pseudo-randomised or examined interventions to promote compliance with curative or preventive therapy for tuberculosis, and contained at least one outcome measure of adherence. We used a comprehensive search strategy, and five studies met the prespecified inclusion criteria. Although various specific strategies seemed to work in specific situations, none of the included studies examined DOT. However, we did identify two trials in progress that assess DOT, and when the results are available we will incorporate them in future editions of the review. Only then will it be possible to substantiate or refute WHO's claim that observation of patients taking their drugs is the "breakthrough of the decade". Without adequate evaluation of the options, there is a risk that effective existing tuberculosis control programmes could be swept aside by the rhetoric around DOT. It would be helpful to identify mechanisms whereby WHO and the World Bank can draw more extensively on reliable reviews in the formulation of their policies.

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PCR analysis of Y-chromosome deletions in subfertile men

SIR—In his seminar on male infertility, D M de Kretser (March 15, p 787)[1] states that there is no screening test for Y-chromosome deletions. Several recent publications have used PCR-based techniques to screen for Y-chromosome deletions in diverse populations of infertile men.[2] Moreover, in reports cited in the seminar, techniques are described which can be used in routine screening procedures.

Over a year ago, we started screening for deletions on the Y-chromosome in subfertile men who are candidates for the intracytoplasmic sperm injection procedure. We chose to concentrate on the AZF-a, AZF-b regions as defined by Vogt and colleagues,[2] because they have also been reported by others.[3] We use two separate multiplex PCR reactions. Each multiplex contains primer pairs for STSs of all three AZF-regions, as well as primers for a control STS from a region near the Y-centromere.

In a population of 164 subfertile men, seven were found to carry a deletion in the AZF-c region. When a deletion was found, the test was always repeated at least twice, as well as on a second blood sample to confirm the initial findings. In three cases we were able to confirm that the deletions were new mutations. No deletions were found in the AZF-a or AZF-b regions. As a control group, 100 fertile men were tested in the same way. No deletions were found in this control group. Six of seven men with the AZF-c deletion belonged to a subgroup of 25 men which was characterised by severe oligospermia, a normal follicle stimulating hormone level, and normal clinical andrological findings.[4] Under the conditions described, the PCR test is easy and reliably performed, and given these results, we feel secure to offer this screening test for Y-chromosome deletions to our patients.

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Calcium-channel blockers and risk of cancer

SIR—A single epidemiological study cannot provide conclusive evidence about causality, but it is important to note emerging consistencies in published work on calcium-channel blockers (CCBs) and cancer risk. Jick and colleagues' data (Feb 22, p 525)[1] confirm others' findings[2] that the relative risk of cancer is significantly increased for uses of high doses of CCBs[2] and is not increased for users of β-blockers or angiotensin-converting enzyme (ACE)-inhibitors.[2,3] Among CCBs, the relative risk of cancer is greater with verapamil[2,3] and lower with diltiazem.[2] The distinction among individual CCBs and effects at differing doses are potentially important in accounting for inconsistencies in findings related to cancer incidence and overall CCB use.

Jick and colleagues judge their data inconsistent with a causal relation between CCBs and cancer because "... there is no increase in risk with increasing duration of calcium-channel blocker use". However, they do not measure absolute risk; case-control studies can estimate only relative risk. Moreover, increased relative risk with increased duration of exposure is no causal *sine qua non*. It is widely accepted that cigarette smoking is causally related to the development of acute coronary events. However, neither cohort nor case-control studies have recorded increasing relative risks of disease with increasing duration of smoking.[4] Epidemiological studies of exposure to tumour initiators do show increased relative risks of disease with greater duration of exposure, but it is a logical fallacy to conclude that because the data do not support one model of causality they are therefore incompatible with any model of causality.

With respect to CCB use, no increased relative risk with increased duration of use would be expected if CCBs do not initiate tumours but rather promote tumours by providing an environment in which a greater proportion of initiated tumours come to clinical attention; this is consistent with their known effect of inhibiting apoptosis.[5] Thus, consistencies in the emerging scientific evidence and the existence of a plausible biological mechanism warrant serious consideration of a causal relation between the use of some CCBs and incident cancer.

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