data show that the most striking improvement was a reduction in deaths from cardiogenic shock. This may well have occurred because of poor matching of the placebo and treatment groups. The treatment group were younger and had a lower prevalence of previous ischaemic heart disease than the placebo group.

The idea that intravenous magnesium could be beneficial by causing coronary vasodilatation is interesting, but to our knowledge there are no trials in vivo comparing the use of magnesium with intravenous nitrates.

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1 Rasmussen HS, Norregard P, Lindene O, *et al.* Intravenous magnesium in acute myocardial infarction. *Lancet* 1986;i:234-6.

Cervical cytology screening

SIR,—Mr John A Giles and others (16 April, p 1099) have suggested that the prevalence of cervical intraepithelial neoplasia may be as high as 11%. The time has come to try to distinguish important cervical abnormality from that which is of lesser or no importance.

Important abnormality, in the context of a screening programme, must be defined as that which is detectable and destined to progress to invasion in the absence of intervention. Its prevalence can be inferred by multiplying its plausible duration by the incidence of invasive disease. For the sake of simplicity we may begin by assuming the duration to be 10 years. The incidence of invasive disease has not differed substantially from 30 per 100 000 women per year since data on cervical cancer became available separately. The prevalence of important cervical abnormality must be about 300 per 100 000 women.

If screening procedures are detecting apparently important abnormalities in much more than 300 per 100 000 women examined there are four possible explanations. Firstly, the incidence of the invasive disease may be about to rise remarkably (to explain the claimed detection rate would require an increase of nearly 40 times, and cervical cancer would outnumber all other cancers combined). Secondly, the duration of the detectable abnormality may be much longer than our preliminary assumption (in fact it would need to last for nearly 400 years). Thirdly, screening may be selectively reaching a subset of the population which is at exceptionally high risk (all the evidence suggests that the opposite is the case). Fourthly, we may be unable to distinguish the one important abnormality from the 40 in which the cytological or histological appearance appears to be abnormal.

It is absurd to conduct a screening test in such a way that nearly 40 women are referred for an expensive and possibly hazardous procedure for every one who is at risk of developing serious disease. We need common sense and a more discriminatory assessment of the results of screening tests.

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SIR,—Dr David S Grimes (14 May, p 1363) comments on the fear engendered among women by the publicity surrounding cervical cancer and cervical cytology screening. The finding that women whose smears are negative are, in general,

reassured is not surprising, but his study does not attempt to assess the impact that a result other than negative may have.

Of the smears reported in the Grimsby laboratory about 5% are inadequate, 13% show some sort of inflammatory change, and about 3% are positive for dyskaryosis. This means that 21% of smears will not be reported as negative, and we think that this is typical of most laboratories.

The way in which the disease has been publicised has left many women with the impression that it is common, rapidly progressive, and invariably fatal.¹ In the desire to simplify the explanation of the role of cervical cytology we often hear the smear referred to as a test for cervical cancer. We are, therefore, concerned that in some women the fact that their "cancer test" is not negative will cause much anxiety. The increasing workload engendered by the call-recall systems will mean that doctors will probably have less time to spend with patients to explain fully the implications of every non-negative report. There may, therefore, be ample opportunity for anxiety to develop into fear.

The medical profession should do its best to ensure that all publicity makes it clear that cervical cancer is a relatively uncommon cause of death. The link between cervical cancer and sexual behaviour should be more firmly emphasised so that women may take positive action to avoid exposure to known risk factors and, hopefully, prevent any abnormality of the cervix from occurring. More emphasis needs to be placed on the fact that cervical cytology screens for a precancerous abnormality and that this is harmless and likely to remain so for many years. It is presumably only this fact that explains the proven efficacy of well run screening programmes² given the recently reported insensitivity of the test.³

If the correct balance can be achieved fear may be replaced by knowledge. This would enable women to make choices that may prevent (rather than just detect) cervical abnormalities and to realise when they are truly at risk. Otherwise, women may not respond to call-recall systems through fear,¹ and those women whose smears are not reported as negative may become increasingly anxious, causing appreciable morbidity which may result in further pressure on diagnostic and counselling services.

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1 Nathoo V. Investigation of non-responders at a cervical screening clinic. *Br Med J* 1988;296:1041-2.

2 Anderson GH, Boyes DA, Benedet JL, *et al.* Organisation and results of the cervical cytology screening programme in British Columbia, 1955-85. *Br Med J* 1988;296:975-8.

3 Giles JA, Hudson E, Crow J, *et al.* Colposcopic assessment of the accuracy of cervical cytology screening. *Br Med J* 1988;296:1099-102.

Graves' disease

SIR,—Dr T W A de Bruin and others (7 May, p 1292) suggest that HLA-DR4 is significantly associated with remission after treatment with antithyroid drugs in Graves' disease and with the absence of antibodies to the receptor for thyroid stimulating hormone. They acknowledge that the statistical values given are not corrected for the number of variables tested.

In a series of 65 patients we found no association of HLA-DR4 with outcome.¹ Twenty (31%) patients were HLA-DR4 positive, of whom nine relapsed and 11 entered remission ($\chi^2=0.21$,

Number (%) having each thyroid autoantibody for HLA-DR4 positive and negative patients

	HLA-DR4 state	
	Positive (n=20)	Negative (n=45)
Thyroid stimulating antibody	19 (95)	43 (96)
Thyroglobin antibody	13 (65)	30 (67)
Microsomal antibody	18 (90)	44 (98)

$p>0.1$ when compared with HLA-DR4 negative patients.) Moreover, the distribution of thyroid autoantibodies was the same when patients were divided according to HLA-DR4. Thus our results do not confirm those of Dr de Bruin and others, although our follow up was only for one year after stopping treatment.

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1 Weetman AP, Ratana Chai Yavong S, Middleton GW, *et al.* Prediction of outcome in Graves' disease after carbimazole treatment. *Q J Med* 1985;59:409-19.

SIR,—Dr T W A de Bruin and colleagues (7 May, p 1292) conclude that HLA-DR4 predicts remission in Graves' disease.

Antithyroid drugs have both a direct action on the thyroid cell, inhibiting the organification of iodide, and an indirect immunosuppressive action.¹ Five patients in this study were positive for antibody to the thyroid stimulating hormone receptor at the end of treatment, and four of these relapsed within a few weeks. These patients should be regarded as immunological non-responders rather than as true relapsers. The authors' statement that antibody to the thyroid stimulating hormone receptor at the end of treatment is not associated with long term relapse is based only on the observation of one such patient. Thyroid stimulating hormone receptor antibodies are markers of active autoimmune disease rather than predictors of relapse. The response to antithyroid drugs may itself be genetically determined.

In our series of 53 patients with Graves' disease the median thyroid stimulating hormone receptor antibody index in 22 HLA-DR2 positive patients was 25.2 compared with 17.5 in 31 other patients ($p<0.05$, normal index less than 9.0). The index of the antibody to the thyroid stimulating hormone receptor in seven HLA-DR2 homozygotes was 36.2 compared with 19.9 in the 15 heterozygotes ($p<0.01$). The antibody indices were measured monthly during treatment with carbimazole in eight HLA-DR2 positive patients and 16 HLA-DR2 negative patients (figure).

Both groups were clinically and biochemically euthyroid within two months, but antibody to the

Serum concentrations of thyroid stimulating hormone receptor antibodies during treatment with carbimazole in eight HLA-DR2 positive (●) and 16 HLA-DR2 negative (○) patients with Graves' disease.