\$24 100.¹ The difference between this figure and the estimate quoted in my editorial is attributable to the inclusion of additional charges for extended acute hospital care and different assumptions about the life expectancy of survivors (5 v 10 years). Even so, the cost of HA-1A still compares favourably with that of many other widely accepted medical interventions.

I find it difficult to reconcile the results of these careful calculations with Sheppard and Kelly's unusual methods of estimating cost effectiveness. Part of the difficulty is their surprisingly low local mortality for Gram negative bacteraemia. As their data have not been published they are difficult to interpret, but the authors have probably included patients who would not fulfil clinical criteria for the diagnosis of sepsis or septic shock and therefore would not qualify to receive HA-1A. Similarly, it is impossible to judge the validity of their assumptions regarding the proportion of their patients with severe underlying illness in whom HA-1A might be inappropriate.

Although current evidence suggests that HA-1A is likely to be cost effective (provided it is not used indiscriminately), I agree with Sheppard and Kelly that confirmatory studies are required and the drug's mechanism of action needs to be clarified to establish beyond doubt that it has a place in sepsis.

C J HINDS

St Bartholomew's Hospital,
London EC1A 7BE

- 1 Hinds CJ. Monoclonal antibodies in sepsis and septic shock. *BMJ* 1992;304:132-3. (18 January.)
- 2 Taylor D. Centoxin—birth of a budget buster. *BMJ* 1991;302:1229.
- 3 Ziegler EJ, Fisher CJ, Sprung CL, Straube RC, Sadoff JC, Foulke GE, et al. Treatment of Gram-negative bacteremia and septic shock with HA-1A human monoclonal antibody against endotoxin. *N Engl J Med* 1991;324:429-36.
- 4 Schulman KA, Glick HA, Rubin H, Eisenberg JM. Cost-effectiveness of HA-1A monoclonal antibody for Gram-negative sepsis. *JAMA* 1991;266:3466-71.

Detecting congenital heart disease prenatally

SIR,—We have a long standing interest in research on the usefulness of symptoms, signs, and investigations. Although not radiologists, we are concerned about the presentation of data in Reuwen Achiron and colleagues' paper on using extended fetal echocardiography to detect cardiac malformations in low risk pregnancies.¹

The authors state that the extended fetal heart examination was completed in 4812 cases, but in the description of the diagnostic accuracy of the test (table III) the specificity is calculated as 5323/5324. Unsuccessful attempts to perform the extended examination seem to have been treated as having yielded true negative results. This seems to be a dangerous assumption (although it does not alter the specificity or predictive value greatly in this case). Perhaps editors should require authors to publish their original 2x2 tables to avoid any confusion.

The authors have clearly acquired great skill at interpreting ultrasonographic images. Before they so strongly recommend using this test, however, they should consider that others may not be as skilled. Sackett *et al* refer specifically to ultrasonography as being a test in which the quality of the results may vary greatly,² and they show the effects of a small change in sensitivity or specificity on predictive value at low prevalences.

Before concluding that a test should be incorporated into routine procedure investigators should consider its resource effectiveness. This may require a formal cost-benefit analysis. In this case, seemingly, an additional 1310 hours of testing was required to detect 18 cases of congenital heart disease—that is, 73 hours a case. The authors' recommendations may therefore need further

scrutiny, especially as a positive finding does not always alter management.

PAUL KINNERSLEY
PENNY OWEN

University Department of General Practice,
Health Centre,
Llanedeyrn,
Cardiff CF3 7PN

- 1 Achiron R, Glaser J, Gelernter I, Hegesh J, Yagel S. Extended fetal echocardiographic examination for detecting cardiac malformations in low risk pregnancies. *BMJ* 1992;304:671-4. (14 March.)
- 2 Sackett D, Haynes R, Tugwell P. *Clinical epidemiology: a basic science for clinical medicine*. Boston, Toronto: Little, Brown, 1985.

SIR,—In Reuwen Achiron and colleagues' study of using extended fetal echocardiography to screen prenatally for congenital heart disease a positive result seemed generally either to result in termination of the pregnancy or to determine the nature and site of delivery.¹ At least one specific feature of the treatment of certain forms of congenital heart disease in infants might be improved by prenatal diagnosis.

In several forms of congenital heart disease the neonatal circulation depends on persistent patency of the ductus arteriosus, either to sustain systemic or pulmonary blood flow or to permit adequate systemic venous mixing. Closure of the ductus in neonates with these diseases may be lethal. These conditions are treated with intravenous prostaglandin E₁, which is a potent dilator of the ductus. It often dramatically improves the clinical condition of affected infants, allowing the defect to be investigated and elective or semielective surgery planned.²

E series prostaglandins dilate the ductus by a direct relaxant effect on ductal smooth muscle³ and by inhibiting its response to vasoconstrictors such as noradrenaline.⁴ Constriction of the vessel in neonates desensitises the vessel to the dilator effect of prostaglandin E₂.⁵ In infants with pulmonary atresia the cross sectional area of the vessel during infusion of prostaglandin E₁ is directly proportional to that before infusion. It follows, therefore, that in infants with these defects the earlier in neonatal life that prostaglandin E₁ is started the more effective it will be.

Prenatal diagnosis of congenital heart disease in which the neonatal circulation depends on the patency of the duct would allow prostaglandin E₁ to be given immediately after birth, before loss of endogenous circulating prostaglandin E₂ and subsequent constriction of the vessel. This should optimise ductal patency in these neonates.

GORDON C S SMITH

Department of Midwifery,
Queen Mother's Hospital,
Glasgow G3 8SH

- 1 Achiron R, Glaser J, Gelernter I, Hegesh J, Yagel S. Extended fetal echocardiographic examination for detecting cardiac malformations in low risk pregnancies. *BMJ* 1992;304:671-4. (14 March.)
- 2 Freed MD, Heymann MA, Lewis AB, Roehl SL, Kensey RC. Prostaglandin E₁ in infants with congenital heart disease. *Circulation* 1981;64:899-905.
- 3 Coccani F, Olley PM. The response of the ductus arteriosus to prostaglandins. *Can J Physiol Pharmacol* 1973;51:220-5.
- 4 Smith GCS, McGrath JC. Prostaglandin E₂ and fetal oxygen tension synergistically inhibit response of isolated fetal rabbit ductus arteriosus to norepinephrine. *J Cardiovasc Pharmacol* 1991;17:861-6.
- 5 Clyman RJ, Mauray F, Roman C, Heymann MA, Payne B. Factors determining the loss of ductus arteriosus responsiveness to prostaglandin E. *Circulation* 1983;68:433-6.

Melanoma in people aged 65 and over

SIR,—Pamela M McHenry and colleagues report a disturbingly high rate of thick melanomas with a poor prognosis in the elderly Scottish population.¹ They suggest that health education has failed to

reach this group. We have tried to identify other factors that might be responsible for the late presentation of this potentially curable cancer.

We examined the records of patients who had presented to St George's Hospital with thick primary cutaneous melanoma since 1986. Thick lesions were defined as lesions with a Breslow thickness >3.5 mm.² We identified 24 patients over the six years, of whom 14 had died (10 male, 14 female; age range 22-79, median 61.5). This compares with 168 patients with invasive melanoma less than 3.5 mm thick (age range 12-85, median 46; Mann-Whitney U test, p<0.02).

Circumstances that could have accounted for a delay in diagnosis were noted. Nineteen lesions were nodular³; six were amelanotic; and 11 occurred in or on poorly visualised sites—the back (six), buttock (one), axilla (one), sole (one), and vulva (one), with one amelanotic lesion developing within a tattoo. Four patients had clearly documented evidence of a phobia about doctors or hospitals, one of whom had attempted suicide. Two had chronic schizophrenia, one suffered from agoraphobia, and one misused alcohol. One patient was blind, and another was Greek with no understanding of English. Although some patients had a combination of these factors, only one had none of them.

Therefore, many unavoidable factors could have accounted for delayed referral, including the tumours being amelanotic or occurring at sites that were hard to see, psychiatric illness or phobia about hospitals, and visual or language problems. Most lesions were nodular, perhaps being intrinsically aggressive, rapidly growing lesions.³

Patients in our series tended to be elderly. Other workers have shown a higher proportion of thick melanoma in elderly people.^{1,4,5} Biological factors, such as atrophy or impaired immune function associated with aging skin, may be relevant. We think, however, that delay in presentation is more likely to be due to some of the clinical reasons outlined. Despite the promotion of rapid screening clinics many patients may present too late. Nevertheless, our results support the conclusions of McHenry and colleagues. A specific educational programme directed towards the elderly population is required.

C C HARLAND
R A MARSDEN

Department of Dermatology,
St George's Hospital,
London SW17 0QT

M E FALLOWFIELD

Department of Histopathology,
St George's Hospital

- 1 McHenry PM, Hole DJ, MacKie RM. Melanoma in people aged 65 and over in Scotland, 1979-89. *BMJ* 1992;304:746-9. (21 March.)
- 2 Breslow A. Thickness, cross sectional area and depth of invasion in the prognosis of cutaneous melanoma. *Ann Surg* 1970;172:902-8.
- 3 Clark WH, From L, Bernardino EA, Mihm MC. The histogenesis and biologic behavior of primary human malignant melanoma of the skin. *Cancer Res* 1969;29:705-26.
- 4 Loggie B, Ronan SG, Bean J, Das Gupta TK. Invasive cutaneous melanoma in elderly patients. *Arch Dermatol* 1991;127:1188-93.
- 5 Rivers JK, Kelly MC, Kopf AW, Welkovich B, Bart RS. Age and malignant melanoma: comparison of variables in different age groups. *J Am Acad Dermatol* 1989;21:717-22.

Changing lifelong habits of elderly people

SIR,—Keith Beard and colleagues question whether elderly people are able to change lifelong habits.¹ We recently studied this issue.

Patients aged over 70 admitted to the coronary care unit at John Radcliffe Hospital with suspected myocardial infarction during 1990 were studied with the agreement of Central Oxford Research Ethics Committee. There was no age limit for admission to the unit. After their discharge sur-