This month • elderly primigravidae • anticonvulsants • MAOI • breast cancer • lipid lowering drugs

Elderly primigravidae

THE notion of identifying 35 years as the age for a woman to become an 'elderly primigravida' apparently dates from 1958. Tuck and colleagues start from the assumption that in 1958 this age group would have included a larger proportion of women who had had difficulty conceiving than it would today; now the group is generally healthy and probably includes a larger number of women deliberately putting off motherhood for the sake of careers. The plan was to compare primigravid women over the age of 35 years, with and without a history of infertility, with primigravid women aged 20–25 years without a history of infertility.

More older women had hypertension (but not pre-eclampsia) and more had uterine fibroids. There was a marked increase in the rate of Caesarean section, both elective and emergency, in the study group, with the commonest indications being breech presentation and maternal age. Older women were also likely to have a longer second stage of labour and more preterm deliveries.

Against this rather gloomy picture there are two crumbs of comfort. The differences were brought out by careful matching of subjects and controls: the study group, as expected, contained a smaller number of smokers and a higher proportion of women from classes 1 and 2. They would therefore have been expected to have very good outcome figures, as indeed did the controls. In fact, the figures for the study group, at least for preterm deliveries and low birthweight babies, become similar to those for all Oxford residents delivered at the same hospital.

Second, the good news for the older women with a history of infertility is that the infertility does not carry any added obstetric risks over and above those of age.

(D.J.)

Source: Tuck SM, Yudkin PL, Turnbull AC. Pregnancy outcome in elderly primigravidae with and without a history of infertility. *Br J Obstet Gynaecol* 1988; **95:** 230-237.

Withdrawal of anticonvulsants

MOST general practitioners know that they have patients who take their anticonvulsant drugs irregularly or at sub-therapeutic levels. This is often an example of a therapeutic truce in which the patient is seizure free and is happy with the homeopathic therapeutic regimen while the doctor justifies the paradox by being patient centred: 'the situation is stable so why rock the boat', hoping that he or she will escape the censure of any new partner or trainee who has a touching belief in anticonvulsant blood levels.

A prospective trial now provides fresh evidence that up to a third of children and adults who have been seizure free for two years on therapy will remain seizure free after withdrawal of anticonvulsant medication. The authors found that complex partial seizures with secondary generalization carried the worst prognosis and that withdrawal of barbiturates or phenytoin is more likely to be successful than withdrawal of sodium valproate.

An actuarial life table show that after two fit-free years following withdrawal of therapy a relapse is highly unlikely.

(N.S.)

Source: Callaghan N, Garrett A, Goggin T. Withdrawal of anticonvulsant drugs in patients free of seizures for two years. *N Engl J Med* 1988; **318:** 942-946.

MAOI and wine and beer

PATIENTS on monoamine oxidase inhibitors are advised to avoid tyramine containing foods such as cheese, meat and yeast extracts and pickled herring, and also, on the basis of a few early reports, to avoid beer and red wine, which are thought to have a particularly high tyramine content. A letter in the *Lancet* reports accurate measurements of the tyramine content of various alcoholic drinks but shows no significant differences in free tyramine levels between white wine, red wine (including Chianti) and beer.

There are many variations in the recommendations about wine and beer drinking. It seems, however, that there may be no reason to avoid wine but not beer, when beer is drunk in larger quantities, and there is no evidence that red wine (even Chianti) is more dangerous than white. This may all be academic though as the Pharmaceutical Society recommends avoidance of all alcoholic drinks when taking these drugs.

(A.B.)

Source: Hannah P, Glover N, Sandler M. Tyramine in wine and beer. *Lancet* 1988; **1:** 879.

Choice of surgery for breast cancer

RECENT studies of women with breast cancer have shown similar survival rates and disease-free intervals after simple mastectomy as after side excision plus radiotherapy. This has encouraged a study of the psychological effects of different treatment for 30 patients with breast cancer. Ten were not offered a choice since the site of the tumour at that time dictated mastectomy, seven chose to have a mastectomy and 13 chose side excision plus radiotherapy. The controls were women with benign breast disease not having operations, and women having general surgery for non-malignant conditions. All patients and their husbands completed questionnaires at various stages before and 12 months after their operation.

Women and their husbands who were offered a choice showed less anxiety and depression than those not offered a choice immediately before their operations. Two to three months after the operation the same was true for the patients, but not their husbands, and the differences became insignificant thereafter. In the group offered a choice, the frequency of psychological problems was unaffected by the choice made. Those offered a choice had similar preoperative levels of psychological morbidity to those in the control groups.

The authors acknowledge the possibility that patients not offered a choice might have experienced more anxiety and depression through believing their disease to be more serious, although this is unlikely since a breast specialist nurse had specifically explained the reason for their not being given a choice. Perhaps it does not matter whether the group offered a choice do better because they feel their disease to be less serious or because they feel more in control. It is encouraging to find further pragmatic evidence to support the cause of patients' autonomy.

(D.J.)

Source: Morris J, Royle GT. Offering patients a choice of surgery for early breast cancer: a reduction in anxiety and depression in patients and their husbands. *Soc Sci Med* 1988; **26:** 583-585.

Empty vessels?

THE early 1990s seem set to focus on therapeutic approaches to risk factors for cardiovascular disease. New lipid

lowering agents are being introduced and the effect of existing cardiovascular drugs on 'lipid profiles' continues to be a subject of controversy. Two recent reports in *Nature* describe further advances of great interest.

The first concerns the results of the European Cooperative Study Group trial of tissue plasminogen activator (TPA) in myocardial infarction and a Harvard trial of TPA in pulmonary embolism. In the myocardial infarction study mortality at two weeks was reduced by 51% in patients treated with TPA compared with placebo. In the Harvard study TPA was shown to be superior to the currently-used urokinase in clot dissolution and reduction of pulmonary artery pressure. TPA is astonishingly expensive at $2200 a dose, and another new thrombolytic agent, eminase, a chemically modified form of streptokinase, is also likely to be available in the 1990s, costing a mere $1000 a dose. Despite these astronomical prices, sales of TPA during 1988 are predicted to be as high as $350 million.

The second report concerns the discovery of a new, potent vasoconstrictor peptide produced by vascular endothelial cells. Christened endothelin by the Japanese group from the University of Sukuba, it is a 21-amino acid peptide transmitter which is part of a novel cardiovascular control system. Rather like angiotensin, it is generated by an unusual proteolytic process in which an 'endothelin-converting enzyme' is involved; perhaps we will see ECE inhibitors by the year 2000?

(R.J.)

Sources: Barinaga M. Genentech's boom is boosted by new clinical trial data. *Nature* 1988; **332:** 387. Yanagisawa M, Kurihara H, Kimura S, *et al.* A novel vasoconstrictor peptide produced by vascular endothelial cells. *Nature* 1988; **332:** 411-415.

Contributors: D. Jewell, N. Stott, A. Birchard, R. Jones.

INFECTIOUS DISEASES UPDATE: AIDS

Progression of HIV infection towards AIDS

Researchers at the University of California and San Francisco, basing their findings on a three year study,[1] predict that half of those infected with human immunodeficiency virus (HIV) will develop the acquired immune deficiency syndrome (AIDS) within six years and three-quarters will develop AIDS or AIDS-related conditions.

Dr Andrew Moss, Associate Professor of Epidemiology at the San Francisco General Hospital, who has also recently spent considerable time on the epidemiology of AIDS in the United Kingdom, followed 288 men with HIV for three years to determine progression towards AIDS and AIDS-related complex (ARC). Twenty-two per cent progressed to active AIDS, 19% to ARC and another 24% had laboratory abnormalities highly predictive of AIDS or ARC. Extrapolating from those figures, the team made predictions for a six-year progression rate.

Five specific 'markers' in the blood were found to independently predict progression to AIDS; the concentration of beta 2 microglobulin (the best single predictor of AIDS), the presence of HIV p24 antigen, the haematocrit level, and both the number and proportion of T4 lymphocyctes. The researchers found that patients having abnormal values of two or more of these markers had a 57% chance of developing AIDS over the next three years; those patients who were normal on all markers had a progression rate of only 7%.

Although it is still not known if everyone infected with HIV will go on to develop AIDS, it has become obvious that being infected is more likely to be serious than was originally thought.

Suicide and AIDS

Peter Marzuk and colleagues recently reported that men with a diagnosis of AIDS are at high risk of suicide, especially during the six months after diagnosis.[2] The researchers found that men with AIDS aged 20 to 59 years were 36 times more likely to commit suicide than were similarly aged men without such a diagnosis. These findings underline the importance of pre- and post-test counselling and of physicians being aware and sensitive to the potential psychological instabilities of individuals infected with HIV.

Global AIDS data

As of 30 April 1988, the World Health Organization in Geneva has received reports from 138 countries of a total of 88 081 cases of AIDS. An additional 36 countries have reported 'zero cases'.

The distribution of cases by continent is as follows:

Africa: 10 639 cases in 42 countries
Americas: 65 464 cases in 42 countries
Asia: 238 cases in 22 countries
Europe: 10 851 cases in 28 countries
Oceania: 889 cases in 4 countries.

AIDS and HIV in the UK

The cumulative total of AIDS cases in the UK to 31 March 1988 is 1429. The distribution of cases for each country is as follows: England 1352; Scotland 52; Wales 20; Northern Ireland five.

The cumulative total of reports of HIV antibody persons in the UK to 31 March 1988 is 8443. The distribution of reports for each country is as follows: England 6861, Scotland 1436, Wales 102, Northern Ireland 44.

Transmission of HIV

Dr Kenneth Castro and colleagues at the US Centre for Diseases Control and the New York City Department of Health, conducted a follow-up study[3] of AIDS patients reported to the centre to 30 September 1987, who could not be classified as having any known risk factor for HIV transmission.

Of the 2059 patients (5%) initially not known to have any risk factors, follow-up information was obtained in 1138; 825 (72%) were ultimately shown to have risk factors and 32 (3%) were incorrectly diagnosed as having AIDS.

Of the remaining 281 (25%), risk factors could not be identified. However, for 178 of these patients who had been interviewed with a standard questionnaire, 72% reported a history of sexually transmitted diseases or sexual contact with prostitutes. It is considered that by continuing to improve the sensitivity of interviewing, even more accurate information will be uncovered.

It is therefore still correct to state that although the virus has been detected in saliva, tears and urine, no epidemiological evidence exists for believing HIV may be transmitted through these body fluids.

References

1. Moss AR, Bacchetti P, Osmond D, *et al.* Seropositivity for HIV and the development of AIDS or AIDS-related condition: three year follow-up of the San Francisco General Hospital cohort. *Br Med J* 1988; **296:** 745-750.
2. Marzuk PM, Tierney H, Tardiff K, *et al.* Increased risk of suicide in persons with AIDS. *JAMA* 1988; **259:** 1333-1337.
3. Castro KG, Lifson AR, White CR, *et al.* Investigation of AIDS patients with no previously identified risk factors. *JAMA* 1988; **259:** 1338-1342.

Contributed by Dr D. Goldberg, AIDS Surveillance Programme Scotland, Communicable Diseases (Scotland) Unit, Ruchill Hospital, Glasgow G20 9NB.