Professor Wright in their patients with carpal tunnel syndrome than in the controls be due to the fact that they were not matched for occupation and that the former group were more active manually?

T C BEER
N MEMON

Department of Rheumatology,
General Hospital,
Kettering, Northants

[1] Brian, W R, Wright, A D, and Wilkinson, M, *Lancet*, 1947, **1**, 277.
[2] Kendall, D, *British Medical Journal*, 1960, **2**, 1633.
[3] Birkbeck, M Q, and Beer, T C, *Rheumatology and Rehabilitation*, 1975, **14**, 218.
[4] Gunn, C C, *British Medical Journal*, 1974, **3**, 624.

Bromocriptine and breast cancer

SIR,—In the light of recent articles concerning bromocriptine your leading article "Hormone receptors and breast cancer" (10 July, p 67) raises the possibility of the use of this drug to suppress the growth of prolactin-dependent breast tumours since, as you say, "the main peptide hormone implicated in promoting the growth of breast tumours is thought to be prolactin."

The theoretical and to some extent substantiated fear of oestrogens and other hormones as carcinogenic agents should, however, perhaps now be extended to include other drugs which interfere with man's delicately balanced endocrine functions—for example, phenothiazines, methyldopa, and even indeed bromocriptine, which is used to suppress puerperal lactation, a physiological state which in itself affords some protection against breast cancer.

PHILIP A KNOWLES

Department of General Practice,
Hackney Hospital,
London E8

Eggs and hypercholesterolaemia

SIR,—I was interested to read Professor V Lindén's comments (10 July, p 109) on the case report by Dr H P Rhomberg and Professor H Braunsteiner (15 May, p 1188). He suggests that the excessive hypercholesterolaemia following a daily intake of 8-12 eggs daily extending over a period of 3½ years can be mainly ascribed to the high vitamin D content in the yolk of eggs. Evidence is quoted which indicates that an excess of vitamin D raises the serum cholesterol level, thus leading to a significant relationship between a high intake of vitamin D and the incidence of myocardial infarction.

However, an excess of vitamin D also leads to increased calcium absorption and to an increased serum calcium level. In extensive animal experiments Selye *et al*[1] have shown that an acute heavy overdose of vitamin D compound leads to general metastatic calcification. The chronic administration of less massive doses of vitamin D causes calcification which is almost entirely confined to the aorta and its main branches and to the coronary arteries. Many pathologists and my own investigations[2] suggest that calcium deposits in the media of the large human arteries are one of the essential preliminary processes in atherogenesis. A high serum cholesterol, whether of endogenous or exogenous origin, seems to have an accelerating effect on atheroma formation when the ground has been prepared by ageing processes in the arterial wall.

In the case referred to a return to a balanced diet led to the disappearance of the skin deposits consisting mainly of lipids. The same response is less likely to occur in the case of atheromata.

A ELKELES

Prince of Wales's Hospital,
London N15

[1] Selye, H, Strebel, R, and Mikulaj, L, *Journal of the American Geriatric Society*, 1963, **11**, 1.
[2] Elkeles, A, *Journal of the American Geriatric Society*, 1976, **24**, 58.

High-dose corticosteroids in severe acute asthma

SIR,—The comparison of different corticosteroid regimens in acute asthma by Dr M G Britton and others (10 July, p 73) deserves further comment. The use of three different corticosteroids given by four different routes hinders easy comparison between the three groups. The fact that only one group received an intravenous infusion introduces a further difficulty.

The variability of the results in the small groups examined makes it difficult to come to any confident conclusions about the findings. The authors correctly use standard errors for comparing peak flow, REV_1 and FVC. However, the values quoted are very high and back-calculation of the standard deviations gives negative values well within the lower end of two standard deviations. It is patently absurd for any individual to have a negative value for a lung function test, and clearly a correction for skewness is required. Even if this is made, variations about the mean will probably still be large and the only likely conclusion should still be that the small patient numbers used in multiple patient groups give results which are very variable so that, taken overall, no statistically significant difference can be detected and likewise no useful clinical difference is detectable. The wide variation within each group is also likely to obscure any minority of patients failing to respond to smaller steroid doses. It may well also be true that high-dose steroids confer no extra benefit, but clear proof is still lacking.

J B MACDONALD

City Hospital,
Nottingham

Rubella antibody tests in pregnancy

SIR,—The letter from Drs D A McSwiggan and C E D Taylor (17 July, p 174) is timely and highlights some of the difficulties encountered in using the results from testing pregnant women for rubella antibodies to best advantage.

For several years this laboratory has made these tests on all blood samples submitted from antenatal clinics and more recently those women with no evidence of immunity to rubella have been offered vaccination against rubella in the immediate postnatal period. Since general practitioner records do not appear to hold this information readily available it was hoped that the women themselves would be made aware of their immune status. In this way the intense anxiety which many experience when they are pregnant and come into contact with a case of presumed rubella would be avoided and the number of sera submitted for this reason would be reduced. Experience has shown that this optimism was not justified, for the number of women seen because of this is as high as ever. If the first baby was born in our catchment area our own records or a single telephone call reveals the result of any previous test and usually offers immediate comfort to the anxious patient, though the serum is still tested in parallel with any previous sample which might still be frozen in store.

In this area we have therefore adopted the practice of giving all women who have had their babies in the maternity units a notice which gives dates and identification details and goes on:

Rubella titre:.....
You are immune to rubella (German measles)

If there is no evidence of immunity to rubella and vaccine has been given the second line of the notice is deleted and the administration of vaccine is recorded on the slip. It is hoped that this, and the explanation given, will enable the women themselves to know and perhaps remember this information.

In recent weeks an encouraging number of sera have been submitted from family planning clinics. It is to be hoped that the number will increase and the patients will be informed of and understand the significance of the test. There remain groups who, surprisingly, are unaware of their immune status and who should know before they become pregnant. These are schoolteachers, play-group helpers and supervisors, district nurses and midwives, nursery nurses, social workers, and housemothers at council homes. Efforts to get these groups to be tested have been unrewarding so far, but wider publicity from general practitioners—for example, by notices in surgery or health centre waiting rooms—might be effective.

W R G THOMAS

Department of Microbiology,
Croydon Health Area Laboratories,
Mayday Hospital,
Thornton Heath, Surrey

Nitrazepam and diazepam

SIR,—Dr F O Wells (3 July, p 48) advocates the use of diazepam in place of nitrazepam as a safe, effective, and infinitely cheaper product. While this may well be accepted in the young and middle-aged adult, I venture to suggest that in the elderly patient with a failing autonomic nervous system the occurrence of postural hypotension with diazepam is a very real and serious risk. Falls from bed (these usually mean falls on getting up to go to commode or lavatory) are all too frequent in the elderly, often resulting in severe bruising and shock and sometimes in fractures of the femur and elsewhere.

Over the past two years it has been routine in this unit to measure the blood pressure in the erect as well as the supine position in all patients who have had falls or who complain of vertigo when standing. The prevalence of severe postural hypotension found has been quite staggering, and diagnoses of vertebrobasilar ischaemia, drop attacks, and transient ischaemic attacks have been correspondingly reduced, the first to an almost negligible level. The vast majority of these cases were clearly due to drugs, as the blood pressure stabilised completely or substantially within a few days of stopping them. Of the drugs responsible, excluding levodopa in Parkinson's disease, one-third were legitimate hypotensives perhaps

unnecessarily given to the over-65 age group, one-third hypnotics and tranquillisers, and one-third antidepressants (imipramine, amitriptyline, and protriptyline) and the so-called cerebrovascular dilators (cyclandelate, isoxsuprine, naftidrofuryl, pentifylline, and thymoxamine). In the hypnotic and tranquilliser group the following drugs were considered to be responsible, listed in descending order of frequency of occurrence: prochlorperazine, chlordiazepoxide, diazepam, dimenhydrinate, chlorpromazine, chlormethiazole, promazine, thioridazine, trifluoperazine, and meprobamate. No cases were found among patients taking chloral hydrate and analogues, glutethimide, or nitrazepam. Prescription of barbiturates and methaqualone hypnotics are infrequent in this area but again postural hypotension was not recorded with either.

Until such time as a simple and reliable test of autonomic nerve function comes into use, we should do well to ignore much of the advice of our enterprising pharmaceutical industry and select and administer vasodilators and antidepressant and sedative drugs to the elderly with extreme caution.

S L O JACKSON

Geriatric Unit,
Harold Wood Hospital,
Romford, Essex

Raynaud's phenomenon as side effect of beta-blockers

SIR,—We note the comments made by Drs C W Marsden and P F C Bayliss (17 July, p 176) concerning our study of Raynaud's phenomenon in patients taking beta-blockers (19 June, p 1498). We accept that the incidence of side effects obtained with specific questionnaires may be an overestimate. Equally, side effects may be missed when spontaneous reporting by patients is awaited.[1] We reported the results of observations made in clinical practice. The study was retrospective and consequently it would have been impracticable to have had a placebo-treated group and a double-blind design.

The mean doses of the three beta-blockers and the effect of dose on development of Raynaud's phenomenon are shown in table I. The relationship between the presence of cold extremities and blood pressure control for patients on beta-blockers is shown in table II. While there are clear differences in the doses used in the three groups, there is no relationship between dose and development of Raynaud's phenomenon. Similarly, degree of blood pressure control was not associated with cold extremities. These facts, therefore, do not detract from the possibility that there are true inter-drug differences in causing this side effect. Such differences can be verified only by prospective studies.

ANDREW MARSHALL
D W BARRITT
C J C ROBERTS

Bristol Royal Infirmary,
Bristol

[1] Alexander, W D, and Evans, J I, *British Medical Journal*, 1975, **2**, 501.

TABLE I—*Mean dose ± standard deviation (mg/day)*

Drug	Whole group	Raynaud's phenomenon	
		Present	Absent
Oxprenolol	536 ± 303*	453 ± 120	560 ± 336†
Atenolol	180 ± 120*	157 ± 113	192 ± 125†
Propranolol	280 ± 200*	242 ± 163	334 ± 240†

*Significantly different from other treatments ($P < 0.025$)
†No significant difference between presence and absence of Raynaud's phenomenon ($P > 0.05$)

TABLE II—*Results (mm Hg) for whole group on beta-blockers. Mean ± standard deviation*

	Raynaud's phenomenon		Student's *t* test
	Present	Absent	
Treated diastolic BP	92 ± 17	95 ± 13	NS
Treated systolic BP	157 ± 34	163 ± 23	NS
Change in diastolic BP	28 ± 17	28 ± 20	NS
Change in systolic BP	41 ± 27	39 ± 31	NS

NS = not significant

Alternatives to barbiturate hypnotics

SIR,—There is an obvious advantage in prescribing nitrazepam as a hypnotic because with this drug overdose is less likely to be fatal. It is certainly less dangerous than barbiturates and indeed other non-barbiturate compounds mentioned in your leading article (12 June, p 1424). However, another aspect of nitrazepam deserves a mention. It has been shown[1] in a double-blind placebo controlled design to be more persistent than amylobarbitone. In this study single doses of 5 and 10 mg of nitrazepam and 100 and 200 mg of amylobarbitone were given at bedtime to normal subjects. They were tested the following afternoon with psychomotor tasks and an electroencephalogram (EEG) was recorded some 18 hours after the test substances had been given. The recording was assessed "blind" in terms of drowsiness and sleep. Both the psychomotor tasks and the EEG showed significant changes after nitrazepam in terms of slowing of performance and increased amounts of drowsiness and light sleep on the EEG. Even more important was the fact that the subjects were unaware of any persistent drug effects. Anxious patients in a similar study[2] showed the same trends but the effects were less marked.

Of course these findings do not entirely negate the current trend away from prescribing barbiturates but emphasise the fact that no drug is ideal.

D F SCOTT

EEG Department,
The London Hospital (Whitechapel),
London E1

[1] Malpas A, *et al*, *British Medical Journal*, 1970, **2**, 762.
[2] Malpas, A, Legg, M J, and Scott, D F, *British Journal of Psychiatry*, 1974, **124**, 482.

Child-resistant containers and child poisoning

SIR,—Accidental poisoning in childhood results in some 30 000 admissions to hospital in England and Wales each year and salicylates are a major contributor to this total. The most effective measure in controlling this problem in the USA has been found to be the use of child-resistant containers, and since 1 January 1976 all aspirin and paracetamol manufactured for children in the United Kingdom has had to be packaged in child-resistant containers.

We report the preliminary findings of an ongoing survey of accidental poisoning in children and compare the total numbers of children under the age of 6 years who were admitted to hospital either in Newcastle upon Tyne or in South Glamorgan with accidental salicylate poisoning during the first six months of 1975 and 1976.

	Newcastle	S Glamorgan	Total
Jan-March 1975	10	21	31
April-June 1975	9	25	34
Jan-March 1976	5	10	15
April-June 1976	4	13	17

Thus a total of 65 children were admitted between January and June 1975 compared with 32 during the same period of 1976; the difference between these is statistically significant ($P < 0.002$).

Many children are still being poisoned with aspirin which has not been dispensed in child-resistant containers, the manufacturers and retailers still working through old stocks, but the significant downward trend in poisonings should continue when these are exhausted. We report our early findings to give encouragement to those campaigning for better safety for children in the form of more widespread use of child-resistant containers.

A W CRAFT
R H JACKSON

Department of Child Health,
Royal Victoria Infirmary,
Newcastle upon Tyne

J R SIBERT

Department of Child Health,
University Hospital of Wales,
Cardiff

Priorities in the NHS

SIR,—In your leading article on this subject (12 June, p 1425) you made the interesting, indeed provocative, comment that "If a diagnostic aid or a new drug or procedure has been proved to make a substantial difference to mortality or morbidity then the doctors working in the specialty will not be content until they use the new treatment on their patients." This assertion was subsequently challenged by Professor A L Cochrane (3 July, p 41) who pointed out your failure to supply evidence to support the statement. In reply you listed six specific procedures, etc, in which financial constraints have caused doctors to operate a rationing system. One of these examples was the use of fibre endoscopes in the management of upper intestinal haemorrhage.

While I agree that a large number of articles have shown the diagnostic superiority of endoscopy compared at least with the conventional barium meal (rather than the double-contrast technique), I would suggest that there are few data to prove that it has made a "substantial difference to mortality or morbidity." Indeed, the authors of some well-controlled prospective studies[2-3] have actually shown that it apparently makes no such difference at all. Even the much quoted retrospective study by Hoare[4] found that the difference in mortality rates between the group of patients having routine endoscopy and the group of patients having selective endoscopy was not statistically significant at the 5%