Daily stool weights in this community average over 400 g.

Whereas appendicitis and diabetes have been postulated to result from two different aspects of food refining, diverticular disease and varicose veins have both been attributed to changes in faecal viscosity and volume which not only cause increased intracolonic pressure but also increased intra-abdominal pressure during straining a stool. A positive correlation between these two diseases has been reported in individual patients.¹

Professor Corridan and his colleagues are to be congratulated on their study for it is just such a search for associations between diseases in individuals which can be so informative and which is so neglected. It is hoped that others will follow their commendable example and look for other disease correlations.

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¹ Latto, C, Wilkinson, R W, and Gilmore, O J A. *Lancet*, 1973, 1, 1089-1090.

Raised mean cell volume and *Mycoplasma pneumoniae* infection

SIR,—I am writing to correct the impression given by Dr R R Khaund (7 May, p 1220) that a raised mean cell volume (MCV) together with an abnormally raised mean corpuscular haemoglobin (MCH) is "almost diagnostic of the presence of cold agglutinin." It is usual to find a raised MCH with a raised MCV whatever the cause. A more specific clue sometimes seen with a cold agglutinin is a raised mean corpuscular haemoglobin concentration (MCHC). This is due to a falsely low computation of the packed cell volume (PCV) by the Coulter S counter. The passage of agglutinates of two or more red cells at a time through the counting orifice results in a fall in the measured red cell count. This should be compensated by an equal increase in measured MCV, but loss of linearity at the very high MCV figures presumably diminishes this effect. As Dr Khaund points out, warming the specimen corrects these artefacts.

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Arthritis in Flemish paintings

SIR,—Hanging the weightiest of theories on the flimsiest of evidence is a favourite pastime of art historians, but should medical history follow their example? Professor J Dequeker's five cases of rheumatoid arthritis are surely nothing of the sort (7 May, p 1203).

The fingers of the Rombauts Christ are a bit floppy, but then someone has driven a six-inch nail through them; and besides, what would be the motive for such a debasement of the Holy Image? (as Holmes would have asked his medical colleague). Surely painting Christ with rheumatoid arthritis would end the painter's career. The Gossaert hands are, as the author suggests, probably merely a mannerism of style, and the few hurried penstrokes in the Van Eyck are hardly enough to hang a diagnosis on.

The other two pictures do seem to show real pathology, but is it rheumatoid? The girl in

the Jordaens grips so easily with her other hand that it is difficult to believe that she has as bad arthritis as it might seem. I suspect that it was not the painter's intention to make the metacarpophalangeal joints appear swollen but merely to bring out their contour for artistic reasons, to contrast with the expanse of white in the ruff. The Van Gent portrait is so frank that the abnormal joint must be taken at face value and, perhaps more specifically, nose value! The man obviously has congenital syphilis. Could the joint not be explained on this basis?

If these are the only examples of joint disease to be found in Flemish painting, it seems good evidence that rheumatoid arthritis was every bit as rare as we thought.

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Coronary heart disease and the menopause

SIR,—You confuse three issues in your leading article on this subject (2 April, p 862). These are: the relationship of a premature menopause to premature coronary heart disease (CHD); the relationship of a normal menopause to changes in CHD prevalence postmenopausally; and the effects that hormone replacement therapy given during a normal menopause might have on the incidence of CHD. It is necessary to separate them.

The evidence that a premature menopause can lead to premature CHD is stronger than you imply. Two long-term follow-up studies, one of patients with bilateral ovariectomy versus those with unilateral ovariectomy¹ and the other of women with a spontaneous menopause under the age of 40,² showed a higher than expected incidence of CHD 10-20 years later (see table). The Swedish study of women aged 50-54 showed that 76% of women with myocardial infarction had their menopause before 50 compared with 48% of healthy women.³ Further support has come from the finding that 20% of 145 women who had CHD before the age of 45 were postmenopausal,⁴ and the new Framingham evidence⁵ is also supportive although based on small numbers, as you emphasise. This applies to all these studies, since CHD is still uncommon in young and middle-aged women.

Effect of menopause on incidence of CHD

Groups	Age range (years)	Total Nos	Patients with CHD	
			No	%
Spontaneous premature menopause: ²				
6-10 years later	36-45 (mean 38)	10	0	—
11-15 years later	40-47 (mean 43)	13	2	15
16-20 years later	43-55 (mean 48)	12	3	25
Ovariectomy: ¹				
Bilateral	37-58 (mean 51)	35	9	25
Unilateral without hysterectomy (control group)	42-58 (mean 52)	31	1	3
Edinburgh group				
general practice	35-39	681	7	1.8
(5-year cumulative prevalence)	40-44	444	8	1.0
	45-49	487	14	2.9
	50-54	464	15	3.2
Framingham study ⁵				
(8-year cumulative prevalence)	30-39	1000*	1	0.1
	40-49	1000*	20	2.0
	50-59	1000*	67	6.7

*Standardised incidence per 1000 population.

But, as you say, the evidence that a menopause occurring at a normal age puts women at an immediate greater risk for CHD is not strong. Yet this does not contradict the first premise because the studies relating a premature menopause to CHD showed that there was a 15-20 year delay before an increase in incidence was evident. If the analogy were true for normal women it would be around 65 years that a higher incidence might be expected. At this age there are so many compounding influences that it is probable that the effect of a normal menopause would not be discernible and studies of mortality data would not be contributory.

Then the effect of hormone replacement therapy is an altogether different question. In discussing hormonal protection of women against CHD you comment, "Surely it is most unlikely that the same hormones could both protect from and predispose to the same disease." This is illogical. They are not the same hormones. Premature cessation of ovarian function does not lead solely to withdrawal of oestrogenic and progestational hormones but has sudden and profound effects during reproductive viability on androsterone, adrenal and pituitary function, and on lipid and carbohydrate metabolism. Replacement treatment during a normal menopause in order to maintain the physiological premenopausal hormonal balance has not been tested so far as I am aware. I agree, however, with your assessment that artificial delay of the menopause by oestrogenic compounds is unlikely to prevent CHD and, indeed, they may actually increase the risk in women who are already at risk for other reasons.

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¹ Oliver, M F, and Boyd, G S, *Lancet*, 1959, 2, 690.

² Szajderman, M, and Oliver, M F, *Lancet*, 1963, 1, 962.

³ Bengtsson, C, *Acta Medica Scandinavica*, 1973, suppl 549.

⁴ Oliver, M F, *British Medical Journal*, 1974, 4, 253.

⁵ Kannel, W B, et al, *Annals of Internal Medicine*, 1976, 85, 447.

⁶ Dawber, T R, et al, *Proceedings of the Royal Society of Medicine*, 1962, 55, 17.

Streptokinase, cerebral vascular disease — and triplets

SIR,—Your leading article on streptokinase (9 April, p 927) states that there are no reports of its use in cerebrovascular disease. May I refer you to a study of cerebral vascular disease in pregnancy¹ which included a case report of a patient with triplets who developed an occlusion of the left middle cerebral artery at 29 weeks. Repeated episodes of paresis and dysphasia over the next four weeks suggested recurrent embolism of the left middle cerebral artery. After considering the options it was decided to treat the lesion by anticoagulation.

Streptokinase was infused directly into the left internal carotid artery in a total dose of 40 000 U over six hours. Treatment was then continued with intravenous heparin. At five hours the patient was speaking clearly and a carotid angiogram was normal. Nine hours after the start of the streptokinase infusion the patient went into labour and one hour later was delivered of male triplets weighing 1.7 kg, 1.5 kg, and 1.7 kg, the first two of whom survived. Total blood loss was 500 ml despite full heparinisation throughout labour and

delivery. The patient was maintained on oral warfarin for six months. The hemiparesis and dysphasia rapidly disappeared in the puerperium. At seven months the patient reported a few brief attacks of diplopia, but there were no abnormal physical findings. She remained well 10 years later.

From the obstetric viewpoint it is possible that circulating plasminogen activated by streptokinase might have been responsible for the onset of premature labour, but there seems little doubt that anticoagulation was justified to treat a major and disabling cerebral vascular lesion.

The circumstances of this case were unique but serve to illustrate your contention that streptokinase, despite its hazards, remains a valuable drug for use in carefully selected patients.

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¹ Amias, A. G. *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1970, **77**, 312.

Glibenclamide and nocturia

SIR,—The report by Dr P L Yap and others (30 April, p 1137) concerning the treatment of inappropriate ADH secretion draws attention to the diuretic effect of the oral hypoglycaemic agent, glibenclamide. In a recent analysis of the symptoms of treated diabetics¹ we observed a significant increase ($P < 0.01$) in the incidence of nocturia in patients on glibenclamide compared with other treatment groups (see table).

Percentage of patients with nocturia (total numbers in parentheses)

Group	Age < 60	Age ≥ 60
On glibenclamide	90% (20)	90% (29)
On chlorpropamide	60% (47)	77% (64)
On insulin or diet alone	55% (89)	83% (41)

Nocturia increasing with age is a common complaint in diabetics, but the table confirms the diuretic effect of glibenclamide although not supporting the antidiuretic effect of chlorpropamide.² It would appear that up to 30% of young patients taking glibenclamide may have nocturia as a result of treatment, but this proportion falls to only about 10% in patients over 60.

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¹ Shaw, K. M., Bulpitt, C. J., and Bloom, A. *Journal of Chronic Diseases*, 1977, **30**, 39.

² Moses, A. M., and Miller, M. *Annals of Internal Medicine*, 1973, **78**, 541.

"Non-responsive" coeliac disease

SIR,—We were interested to read the observations on jejunal mucosa from patients with coeliac disease made by Drs P E Jones and T J Peters (30 April, p 1130), but it is difficult to interpret their use of the term "non-responsive coeliac disease" without more information—for example, clinical and other laboratory

response, length of time on gluten-free diet, change in epithelial and lamina propria cell counts, etc. Indeed, if the patients showed no improvement in their jejunal histology after gluten withdrawal, then by the Hammersmith definition they did not have coeliac disease.¹ However, our own definition of the disorder is less restrictive,² while Rubin *et al*³ claim only a flat mucosa on biopsy and a "dramatic clinical improvement" on gluten-free diet.

Clinical and morphological improvement after gluten withdrawal do not necessarily run parallel. We have encountered six patients (8% of our series) who have made an excellent clinical response to a gluten-free diet (average time on diet 12 years) but whose jejunal mucosa has nevertheless remained flat, although the cellular infiltration has diminished. Conversely, in seven poor clinical responders the histological appearances have improved to near normal. Furthermore, patients with a flat mucosa on biopsy but without evidence of malignancy or other complication who show steady deterioration irrespective of what treatment is given are excessively rare.

We believe that it would be regrettable if the term "non-responsive coeliac disease" were allowed to creep into an area where terminology is already greatly confused.

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¹ Booth, C. C. *British Medical Journal*, 1970, **3**, 725.

² Cooke, W. T., and Asquith, P. *Clinics in Gastroenterology*, 1974, **3**, 3.

³ Rubin, C. E., Eidelman, S., and Weinstein, W. M. *Gastroenterology*, 1970, **58**, 409.

Paget's disease of bone in 14 British towns

SIR,—Though I am no longer in radiological practice, Paget's disease, that most mysterious of bone conditions, retains its fascination for me and so I was interested to read the article by Dr D J P Barker and others (7 May, p 1181) in which they confirm the wide variation in its prevalence even in a small country like ours. I was only sorry that they were not able to include any data from Scotland.

At the time when I was recording information that formed the basis of the article they quote of 20 years ago¹ I was told by one of my then registrars, Dr P F J New, who is now at the Massachusetts General Hospital, that the prevalence in Aberdeen, where he had then been recently working, was considerably greater than in north-west London. A comment from such an acute observer would be worth checking even though it was made 25 years ago.

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¹ Pygott, F. *Lancet*, 1957, **1**, 1170.

Confidentiality and the three wise men

SIR,—I was disappointed to read the view of your legal correspondent (14 May, p 1291) that he deplored the decision of a court to compel the disclosure of documents relating to a previous "three wise men" investigation.

The public must be seen to be protected from the ministrations of unfit doctors. The "wise men" procedure works well in practice and I hope it will continue. However, in the interests of justice their findings must be admissible as evidence in any future legal action. If I were an unstable doctor—an alcoholic or drug addict for example—I would most certainly not be deterred from collaborating voluntarily with a panel of colleagues; plainly it would be in the interests of my patients and myself to do so.

Furthermore, were I a member of such a panel future possible exposure of our proceedings would in no way deflect me from my duty, and in such circumstances I hope I would always conduct myself objectively.

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Advice to senior registrars

SIR,—I am a newly appointed consultant on the first point of the incremental scale. To take up my present post I have had to accept a cut in salary of 25%.

In view of this may I be allowed to offer some financial advice to senior registrars? Do not apply for a consultant post until you are forced to. Not only are you likely to earn considerably more as a senior registrar than as a newly appointed consultant, but as age is a factor in the granting of discretionary increments by your employing authority, the older you are on appointment the more likely you are to be granted these increments. So if you are doing well as a senior registrar, stay put.

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Professional indemnity

SIR,—Dr G Russell (14 May, p 1287) is quite right when he describes the absurd situation whereby doctors are expected to provide their own insurance against possible errors for services performed upon behalf of their employers. This must surely be almost unique, although it is in the long tradition of doctors carrying little for each other's working conditions.

The situation becomes more absurd when individuals like myself, a full-time research student, decide to work for three or four weeks per year as locums to pad out the student grant. The medical insurance of £40 per year then becomes no less than £10 per week. This disincentive hardly helps to reduce the chronic shortage of locums. What is required is not, however, reduced rates for part-time doctors (any more than increased rates for doctors in particularly vulnerable specialties such as neurosurgery) but rather for insurance to be paid by the NHS to the defence societies, the total amount being simply calculated on the basis of the total number of doctor-weeks worked for the Service. Such a system would also encourage doctors to work for the Health Service, as presumably those working in private practice would have to obtain their own cover for this work.

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