these were mild, in eight moderate, and in three severe. Two patients with severe symptoms were pale and sweating, with almost unrecordable diastolic pressures, and the clinical picture suggested peripheral blood pooling with low cardiac output. The mean maximum erect pressure reduction was 63/48 mm Hg (from 165/112 mm Hg) at a mean of 90 min after the dose. Mean pulse rate rose 10/min. Postural hypotension lasted up to four hours in 11 patients and up to seven hours in three. Two severe reactors had had no previous drug therapy. Subsequently 22 additional patients were studied in the same manner with a single dose of 0.5 mg, 11 of them in a double-blind within-patient crossover study with placebo. There were no significant postural symptoms in this group and there was a mean maximum fall in erect diastolic pressure of approximately 25 mm Hg.

These observations indeed confirm that initial symptoms of postural hypotension after the first dose of prazosin are dose-dependent and that the initial dose should not exceed one 0.5-mg tablet. Many of these patients were subsequently treated with prazosin. Doses of thiazides and beta-blocking agents were not increased and in some cases were reduced. Our preliminary observations suggest that the therapeutic response may be better and the dose of prazosin required may be lower in those patients in whom the hypotensive response to the first dose is abrupt. We believe that a significant initial postural fall in blood pressure may be indicative of a subsequent satisfactory response to this very useful drug.

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Possible association of Madelung's deformity with Huntington's chorea

SIR,—Recently correspondents have discussed in your columns (3 July, p 46; 14 August, p 420) the desirability of publicity directed at the lay public concerning Huntington's chorea. As a direct result of this publicity a member of a Huntington's chorea family has approached me for assistance in clarifying their family history. A diagnosis of Parkinson's disease had been made in a member of the family who would have had to have Huntington's chorea to substantiate the subsequent diagnoses. On studying this family it became apparent that a wrist deformity (possibly Madelung's deformity) was also inherited as a dominant condition. It also appeared that the wrist deformity was inherited only by those members who went on to develop Huntington's chorea.

Although the members of this family have not been seen in person, considerable correspondence has taken place with them and their medical practitioners and it was felt that the family needed to be investigated more thoroughly as there was a possibility of a linkage between the wrist deformity and Huntington's chorea. To this end a request was inserted in the latest newsletter of the Association to Combat Huntington's chorea for news of any people in choreic families who also had a wrist deformity. To date there has been one reply from a young woman in such a family who states that she has Madelung's deformity which was successfully operated upon some years ago. Although Madelung's

deformity is very unlikely as a genetic link in all cases of Huntington's chorea, there appears to be a strong possibility of it being linked in the family originally investigated. The next step must therefore be to trace the family of the young woman with Madelung's deformity to see if she is related to the original family, and a continuing search must be made for other patients in whom these dominant diseases coexist. Madelung's deformity sometimes shows up only radiographically, so it is hoped that x-ray films of the wrists of all members of these families will be undertaken.

In the meantime we must again look at the question of ethics with regard to counselling such a family. Should this link prove to be predictive, could it in all fairness be used when we have nothing in terms of treatment to offer the unfortunate carriers of the gene? This was the problem the levodopa provocation test produced some years ago, as discussed in the *BMJ*.¹ The majority solved this problem by not using levodopa. An obvious wrist deformity is much less easy to ignore.

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¹ *British Medical Journal*, 1972, 3, 540.

Immunofluorescent sperm antibodies in virgins

SIR,—Your recent leading article on antibodies to spermatozoa (2 October, p 774) appeared to recommend the use of immunofluorescent techniques and staining patterns to distinguish between normal and pathological autoantibodies.

From previous studies on infertile patients¹⁻³ I cannot share this enthusiasm, as a large number of positives were not only found in infertile couples but also in control groups with no particular pattern or titre appearing significant. There are, however, potential errors in the use of serum from pregnant or previously pregnant patients as control. To allay any such criticisms serum from virgins was tested for sperm antibodies by the indirect immunofluorescent technique on the rationale that females who have never had contact with spermatozoa should not have circulating sperm antibodies.

Serum from 66 informed virgin volunteers aged between 18 and 45, obtained from random sources, was tested for the presence of antibodies against sperm at a titre of 1 in 25 by the indirect immunofluorescent technique, with and without methanol fixation.¹ From table I it can be seen that positives were

TABLE I—Immunofluorescent sperm antibodies: virgin serum

Total No	No positive
66	20 (30%)

TABLE II—Positive immunofluorescence patterns: virgin serum

Equatorial	Tail	Postnuclear cap	Mid-piece	Achrosomal	More than one pattern
21%	29%	8%	0	41.6%	20%

obtained from 20 (30%) of these virgins, which surely is indictment enough of any method. From table II it would also appear that examination of the staining pattern is of little help, for all patterns were found to be present, except mid-piece, with achrosomal the most common. Indeed, more than one pattern was present in 20%.

This high number of positives in a group of subjects who should be negative reflects the intrinsic weakness of the method. False-positives may occur due to cross-reaction with bacterial antibodies,⁴ non-specific binding of immunoglobulins,⁵ or involvement of antibodies from beneath the cell membrane of the sperm.⁶

It would therefore appear that the indirect immunofluorescent test is of little value as a measure of sperm antibody presence, and, although it may be a more acceptable immunological test than some of the others available, the question of the significance of sperm antibodies as a cause of infertility cannot be answered by its use.

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¹ Wall, J R, et al, *American Journal of Obstetrics and Gynecology*, 1975, 121, 198.

² Wall, J, et al, *Fertility and Sterility*, 1975, 26, 1035.

³ Harrison, R F, et al, *Reproduction*, 1976, 2, 338.

⁴ Hansen, K B, and Hjort, T, *Clinical and Experimental Immunology*, 1971, 8, 9.

⁵ Petrunia, D, Taylor, P, and Watson, J, *Fertility and Sterility*, 1976, 27, 655.

⁶ Hansen, K B, *Acta Obstetrica et Gynecologica Scandinavica*, 1974, 53, 69.

Teaching of anatomy

SIR,—Having read with keen interest your leading article on this subject (11 September, p 603), I wonder whether I could give my views as an anatomist teaching in Germany.

I have just returned from a most stimulating meeting on "computerised axial tomography" in London (11-15 October). This meeting and the enormous progress made by British inventiveness offer a very stimulating challenge to the anatomist who teaches clinical or topographical anatomy. Axial tomography has enlarged the scope of anatomy teaching enormously, a subject which can only be taught in its clinical implications by medically trained lecturers. Clinical students, clinicians, and radiologists have now to know more anatomy, not less, and have to adapt their teaching to the new demands of axial tomography, demanding more anatomy from a clinical diagnostic point of view. But your leading article clearly points out that anatomy is taught on a very much reduced scale in Britain. In Germany standards have been very significantly and drastically cut—for example, dissection of the body has been reduced to one winter term only. Altogether the preclinical curriculum has been reduced from five terms to four—two summer terms and two winter terms. Two terms account for about 5½ months of one year. While term work has thus been reduced, new subjects

such as sociology, psychology, and bio-mathematics have been added.

In anatomy preclinical students *have to attend* courses on histology (52 h), dissection of the body (104 h), and dissection of the brain (8 h), giving a total of 164 h of practical work. They *can attend* lectures on macroscopic anatomy (65 h), histology (65 h), macro-anatomy (52 h), and embryology (26 h), totalling 208 h. There is thus a potential total of 372 h of anatomy teaching, but for the past two years a sharp reduction in lecture attendance has been noted as local university examinations have been abolished and by this any feed-back between teacher and student; only written examinations conducted by a central examination board on the basis of multiple-choice questions can be taken. This type of question is highly unsuitable for a subject like anatomy, makes it unnecessary for a student to visualise body relations and to gain tactile experience or convey a spatial knowledge of the human body to an examiner.

The action of the EEC in allowing free exchange of doctors forces every national health authority to compare and evaluate the relative standards of medical education of member countries. I wonder which body or bodies are dealing with this real and very urgent problem. What is the educational background of a medical doctor in each of the EEC countries and is the training sufficient both in quality and quantity?

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Administration of diazoxide

SIR,—The article by Dr J C Petrie on the treatment of hypertension (7 August, p 359) recommends that intravenous diazoxide should be given in a dose of 300 mg over 10 s. It is not generally recognised that this dose may be halved so that 150 mg is given intravenously over 5 s, thus producing a less dramatic fall in blood pressure. If the reduction in blood pressure is not of sufficient magnitude a further 150 mg may be infused over 5 s. The above method of giving intravenous diazoxide has the advantage of allowing a rough titration of the reduction in blood pressure.

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A further endoscopy problem solved?

SIR,—Mr J S Martin's letter (16 October, p 946) provides a reminder that a syndrome of temporomandibular symptoms may follow peroral endoscopy and other oral surgery. Owing to the prolonged depression of the mandible into an unusual phase of opening there is a tendency, on release, to a backward displacement of the meniscus in the temporomandibular joint if any slackness is present. Unless corrected this will affect the first phase of opening for normal use—speaking and chewing—and of the second phase—opening to accept a spoonful of food. This causes a wide range of symptoms varying from an overt click with or without trismus or pain to simple, often obscure, tensions in the muscles of mastication, of facial expression, and of the pharynx and to "earache," "toothache," and

temporal headaches with wider repercussions and false inferences.

A simple, safe, and painless self-manipulation, specifically designed for the purpose, has cured hundreds of such cases in my experience in general practice over the past 20 years. Momentary distraction of the temporo-mandibular joint at the affected phase of movement using a suitable prop between the molars as a fulcrum for the lever of the mandible is all that is required. The patient bites on the prop, consisting of a wooden or plastic rod of suitable thickness (a pencil or toothbrush handle, for example) placed transversely between the front molars, and presses the point of the chin down into the cup formed between thumb and first finger of a clenched fist. He or she then gives a firm upward jab with the base of the palm of the other hand striking up under the first fist, which acts as a buffer. This is usually repeated some six times as a first treatment and generally gives immediate relief.

Any residual symptoms or recurrence can equally easily be self-treated at any time, even by the most nervous individuals.

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Urinary amyloid fibrils in the absence of amyloidosis

SIR,—The detection of urinary amyloid fibrils by electron microscopy as a non-invasive diagnostic method for amyloidosis was put forward by Mr P Nimmo and others (31 July, p 284), who confirmed data reported by Derosena *et al*¹ and Neale *et al*.² Continuing the discussion I would like to add a few points as a note of caution against the assumption that urinary amyloid can be taken as a reliable indicator for renal amyloidosis.

To begin with, Limas *et al*³ found amyloid in renal casts in 15 out of 35 patients with multiple myeloma. At necropsy, however, only eight of these 35 revealed amyloidosis, suggesting that amyloid may be present in casts from patients without concomitant amyloidosis. Our own studies⁴ have demonstrated that a substance having the essential properties of amyloid could be generated from the urine of a patient with Bence Jones proteinuria without amyloidosis at necropsy. This was simply done by incubating at pH 3.5 and 37°C for over an hour without adding any enzyme. When, however, the purified Bence Jones protein (BJP) of this patient was treated identically the amyloid-like precipitate was found only after the addition of fresh urine. This experiment suggested to us the presence of amyloidogenic enzymic activity in the urine, particularly since the precipitate was composed of N-terminal fragments of the intact BJP similar to those fragments present in amyloid fibrils in primary and myeloma-associated amyloidosis.⁵ In support of these findings is the report⁶ of a "proteolytic factor" cleaving BJP in two. Fibrillar amyloid-like precipitates may also be obtained by treating BJP with kidney extracts.⁷ These findings are in line with the experiments of Glenner *et al*,⁸ who showed for the first time the in-vitro formation of amyloid-like fibrils from some BJPs after digestion with pepsin.

Furthermore, when amyloid disease is experimentally induced in mice by casein injections a severe amyloidosis with renal

involvement usually ensues. Yet in such mice amyloid could not be found in the urine, even though penetration of amyloid fibrils into the urinary space in two out of five animals was detected by electron microscopy.⁸ This observation confirms for the mouse model what Derosena *et al*¹ had reported in man and indicates that in spite of the presence of amyloid in the renal urinary space the amount of amyloid excreted into the urine may be too small to detect, particularly when other insoluble substances are simultaneously present in high amounts.

In conclusion I suggest that urinary amyloid fibrils need not necessarily be derived from tissue amyloid but may also be formed by digestion of excreted light chains of immunoglobulins in patients without amyloidosis by an "amyloidogenic factor" in the urine.

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¹ Derosena, R, *et al*, *New England Journal of Medicine*, 1975, **293**, 1131.

² Neale, T J, *et al*, *New England Journal of Medicine*, 1975, **294**, 444.

³ Limas, C, *et al*, *American Journal of Medicine*, 1975, **54**, 166.

⁴ Linke, R P, *et al*, *Journal of Immunology*, 1973, **11**, 10.

⁵ Glenner, G G, *et al*, *Science*, 1971, **174**, 712.

⁶ Solomon, A, and McLaughlin, C L, *Journal of Biological Chemistry*, 1969, **244**, 3393.

⁷ Epstein, W V, *et al*, *Laboratory and Clinical Medicine*, 1974, **84**, 107.

⁸ Linke, R P, and Merker, H, Unpublished observations.

Cramp in the elderly

SIR,—Your expert, answering a question about night cramp in the elderly (9 October, p 861), mentions a number of drugs in addition to quinine sulphate.

Imipramine 10 mg three or four times a day had been by far the best remedy I have tried since I had to give up daily quinine because of its ototoxicity about a year ago. I took it in the first place for nasal "catarrh," then realised that it, with quinine, had ended cramp completely, though with quinine only there was still a fair amount of cramp.

Could your expert please let me know if there are likely to be any long-term side effects? I have experienced none in about 18 months except a welcome relief from catarrh as well as cramp. My age is 66 and I have suffered from severe cramp since adolescence.

H B LEE

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*.*Our expert writes: "I was most interested to hear of your correspondent who can keep cramp at bay with 10 mg of imipramine four times a day. Although there have been some cardiac deaths, usually associated with arrhythmias, in acute overdosage from imipramine there are, so far as I am aware, no records of chronic toxicity with this drug so far as the heart is concerned. The Committee on Safety of Medicines records show that from 1964 to 1971 approximately 1.4 million prescriptions were written each year for the drug. The number of cardiac deaths was in single figures and some of these may have been fortuitous. If your correspondent is fortunate enough to have found a drug which relieves cramp he may continue to take it with confidence. It is perhaps worth adding that most physicians now see little point in the administration of imipramine at frequent intervals. A single dose at night is often satisfactory."