history—namely, Bellergal (belladonna alkaloids with ergotamine and phenobarbitone), amitriptyline, Stelabid (isopropamide and trifluoperazine), orphenadrine, and phenytoin. Two patients had been on a combination of Bellergal and amitriptyline. All of these drugs have an anticholinergic effect and will produce a decrease in bladder contractility. There were seven patients with a slow stream. Their aetiology is shown in the table; one of them has gone into retention but subsequently has been relieved. Of the total cases, 15 were found to have a neurological component—namely, multiple sclerosis, prolapsed intervertebral disc, laminectomy, tethered cord, and ependymoma of the spinal cord. I am unable to support your contention that hysteria is not a common cause as six patients were found to be suffering from this.

Aetiology*	Acute retention (8)	Chronic retention (12)	Slow stream (7)
Drug	2	2	1
Neurological	6	6	3
Hysteria	2	4	
Other		1 pelvic exenteration 1 diabetes mellitus	1 distal urethral stenosis 1 following vaginal surgery 1 No abnormality found

*Some patients had a multiple aetiology

I would like to place greater emphasis on the early diagnosis of these conditions by the use of voiding pressure and flow rate studies aided by electromyography of the external urethral sphincter and the use of pharmacological agents (for example, carbachol and alpha-blocking drugs such as phenoxybenzamine) to determine subsequent treatment.

STUART STANTON

Department of Obstetrics and Gynaecology,
St George's Hospital Medical School,
London SW17

¹ Doran, J, and Roberts, M, *British Journal of Urology*, 1976, 47, 793.

² Fox, M, Jarvis, G J, and Henry, L, *British Journal of Urology*, 1976, 47, 797.

SIR,—I was interested to read your leading article on this subject (26 June, p 1554), the references of which are misquoted.

For many years¹⁻⁴ I have stressed how common urinary troubles, including obstructions, are in women. The female bladder and its mechanisms are heir to all the disorders affecting the male. This is not surprising as embryologically both have the same origin. Every structure present in the one is represented in the other, either fully matured or rudimentary according to the genetic sex. Both in lectures and articles I have tried to spread the gospel of the truth of the significant incidence of urinary obstruction in the female and discussed the causes, differential diagnosis, and treatment.

Many of the obstructions occur at the bladder neck and simulate the common prostatic obstructions in the male. All the various male syndromes, including acute and chronic retention of urine, chronic retention with overflow, secondary infection, haematuria, latent uraemia, etc, also occur in the female. Recently⁵ I reviewed 84 such cases, mostly treated by perurethral resection of the obstructing tissue.

Some years ago in one family I removed the grandfather's, his son's, and his daughter-in-law's prostate with equally satisfactory results.

I would hope the profession is now much more aware of the frequency of retention of urine in women than your leading article would suggest.

THOMAS MOORE

Manchester

¹ Moore, T, *Proceedings of the Royal Society of Medicine*, 1953, 46, 558.

² Moore, T, *Lancet*, 1960, 1, 1305.

³ Moore, T, *Congrès de la Société Internationale d'Urologie*, 1961, vol 2, p 363.

⁴ Corrin, B, Mayor, D, and Moore, T, *Journal of Urology*, 1963, 90, 434.

⁵ Moore, T, *European Urology*, 1975, 1, 32.

* * * We regret the errors in our references to which Mr Moore refers. In each case the date of publication should read 1975, not 1976 as printed.—Ed, *BMJ*.

Amoxycillin, talampicillin, and ampicillin

SIR,—I hope you will permit me to reply to the various points raised by Dr D A Leigh (24 July, p 232) in response to the views I expressed (10 July, p 106) on the propriety of prescribing new derivatives of ampicillin in preference to the original drug.

(1) Dr Leigh gives the impression that the *British National Formulary* (p 104) restricts its preference for amoxycillin over ampicillin to circumstances in which high blood levels are important. In fact, the relevant passage reads, "It [amoxycillin] should therefore replace ampicillin, especially when high blood levels are important."

(2) Evidence that amoxycillin penetrates bronchial secretions more readily than ampicillin, and that this is not dependent on the level of purulence, in no way proves that it is more effective than ampicillin in the treatment of bacterial infections of the respiratory tract. Similarly, although higher peak serum levels can be obtained with amoxycillin and talampicillin than with ampicillin, this cannot and should not be regarded as a valid reason for prescribing the more expensive ampicillin derivatives unless there is incontrovertible evidence that they are superior in therapeutic effect to ampicillin itself. I would challenge Dr Leigh to cite any such evidence.

(3) With regard to relative costs, I note that Dr Leigh equates 500 mg 4 times daily of ampicillin with 250 mg 3 times daily of amoxycillin and talampicillin. In fact, it was shown in one of the articles¹ he quoted in his letter (admittedly reporting an uncontrolled clinical trial) that "the overall success rate with ampicillin (250 mg 4 times daily) was 96% and with talampicillin (250 mg 3 times daily) was 94.8%." If he accepts the validity of these figures, the cost comparison he should have made was with 250 mg 4 times daily of ampicillin. On that basis one day's treatment with amoxycillin would cost three times as much, and talampicillin more than twice as much, as one day's treatment with ampicillin.

(4) Dr Leigh chided me for not referring to the articles^{1,2} he quoted in support of his contention that the clinical use of talampicillin "should be associated" with a lower incidence of diarrhoea than ampicillin. Both articles, however, reported "open" uncontrolled clinical trials, the scientific reliability of which must always be open to question. There is, as far as I know, no reported evidence of a significantly lower incidence of diarrhoea with amoxycillin than with ampicillin.

To be frank, my contretemps with Dr Leigh is something of a side issue. The main purpose of my last letter was to draw attention to the irresponsible attitude of the *British National Formulary* in stating that amoxycillin "should replace oral ampicillin" when there is no

evidence that ampicillin is not equally effective in those clinical circumstances where amoxycillin is now being prescribed. In 1975 the National Health Service was spending over £10 million on ampicillin. The highly successful advertising campaign now being promoted to popularise amoxycillin and talampicillin could at a very conservative estimate increase the bill for this group of antibiotics by £5 million. For all we know a similar situation may exist in respect of a large number of other drugs, and the squandering of money on expensive new derivatives of drugs which are not demonstrably superior in therapeutic effect to the original product may well be depriving the National Health Service of resources it could use much more profitably for other purposes.

IAN W B GRANT

Northern General Hospital,
Edinburgh

¹ Knudson, E T, and Harding, J W, *British Journal of Clinical Practice*, 1975, 29, 255.

² Jaffe, G, et al, *Practitioner*, 1976, 216, 455.

Effect of salicylates on creatinine clearance

SIR,—In their interesting article (3 July, p 16) Drs H C Burry and P A Dieppe have shown that in some patients with rheumatoid arthritis and in some normal subjects salicylates raise the serum creatinine level and reduce the creatinine clearance, but they incline to reject the idea that a change in glomerular filtration rate is responsible. Earlier this year we reported this change in serum creatinine in five subjects (four with systemic lupus erythematosus and one normal) in a study protocol of the hepatic effects of aspirin.¹ In our patients, however, the blood urea nitrogen was affected as well as the creatinine. We have now extended our observations to a substantial number of patients with lupus or rheumatoid arthritis and found similar effects. Furthermore, we have established that inulin clearance is reduced in parallel with creatinine clearance, strongly suggesting that glomerular filtration is indeed altered.

In view of the known effects of salicylates on prostaglandin synthesis and the role of prostaglandins in regulating renal blood flow the mechanism for these effects on glomerular filtration probably involves prostaglandins. In accord with that possibility we have observed similar effects on creatinine clearance by two other non-steroidal anti-inflammatory drugs, indomethacin and naproxen, which also inhibit prostaglandin synthesis, and studies on fenoprofen² suggest that it too may cause a similar change. It is not clear from Drs Burry and Dieppe's study or from ours whether or not there is attenuation of the changes with time.

Since the observed changes in serum creatinine and creatinine clearance do appear to be caused by changes in renal function we believe that the statement that "clearly the creatinine clearance test is not suitable for assessing renal function in patients suffering from rheumatoid arthritis" might be better phrased to suggest that renal function ought to be assessed with caution in patients taking drugs that may alter it, such as salicylates or other non-steroidal anti-inflammatory drugs.

Although now and then there are new things under the sun, both Drs Burry and Dieppe and we appear to have rediscovered renal effects

of aspirin described by Hanzlik and his colleagues in a series of papers published in 1917.³

PAUL PLOTZ
ROBERT KIMBERLY
JOHN R GILL JUN

National Institutes of Health,
Bethesda,
Maryland

WILLIAM SEAMAN

Veterans Administration Hospital,
San Francisco,
California

¹ Seaman, W E, and Plotz, P H, *Arthritis and Rheumatism*, 1976, **19**, 155.

² Huskisson, E C, et al, *British Medical Journal*, 1974, **1**, 176.

³ Hanzlik, P J, Scott, R W, and Thoburn, T W, *Archives of Internal Medicine*, 1917, **19**, 1029.

Superficial carcinoma of the stomach

SIR,—We have read with interest the article by Dr G Machado and others (10 July, p 77). Since the introduction of fiberoptic endoscopy at St Luke's Hospital, Malta, in October 1975 we have diagnosed two cases of superficial gastric carcinoma in a total of 120 patients subjected to gastroscopy. In both cases the endoscopic appearances were not impressive and in one case there was a long history of dyspepsia with negative barium studies. This has stimulated us to perform biopsy on any lesion or irregularity of gastric mucosa, no matter how insignificant the appearance, with a view to the early detection of gastric carcinoma.

FF FENECH
A CARUANA GALIZIA

Royal University of Malta,
Medical School,
Guardamangia,
Malta

Aplastic anaemia and hair dye

SIR,—One must take exception to Dr A J Jouhar's contention (1 May, p 1074) that the fatal case of aplastic anaemia described by Drs P J Toghil and R G Wilcox (28 February, p 502) "was probably if not definitely due to either oxytetracycline or penicillin and that it is doubtful that the hair dye in question was causal."

There appear to be no published case reports of aplastic anaemia unequivocally associated with penicillin, and the report cited by Dr Jouhar for oxytetracycline appears to be unique. Agreed, isolated cases have been privately communicated to drug safety committees, but the significance of these is often compromised by inadequate reporting and follow-up. Even so, the Panel on Hematology, Registry on Adverse Reactions of the Council on Drugs of the American Medical Association, between 1 July 1963 and 31 December 1966 tabulated only two cases with penicillin alone and one case each with penicillin and oxytetracycline combined with other presumably innocuous drugs.

On the other hand there are four apparently valid published cases and two Registry cases associated with hair dyes. In addition to the case reported by Drs Toghil and Wilcox and the one reported more recently by Drs S Hamilton and J G Sheridan (3 April, p 834) there are two earlier cases published by Baldridge¹ and Thompson.² In the first of these one of the hair dyes was specifically identified as *para*-phenylenediamine. In all

four there was a definite temporal relationship between exposure and clinical symptoms. An additional two unpublished cases involving hair dyes, rinses, and tints were reported to the Panel on Hematology, Registry on Adverse Reactions of the Council on Drugs of the American Medical Association, between 1 July 1963 and 30 June 1964.

R J HANS

Medical Affairs Division,
Parke, Davis and Co,
Detroit, Michigan

¹ Baldridge, C W, *American Journal of the Medical Sciences*, 1935, **189**, 759.

² Thompson, S J, *Nursing Times*, 1965, **61**, 12.

Compulsory seat belts

SIR,—Dr W A Fraser-Moodie (17 July, p 178) expresses the hope that the public would respond to legislation to make them wear seat belts, but his own figures show that only half of those who have suffered injury from not wearing a belt are now regular wearers. So what hope has legislation? His cases, like those I see, were mostly cuts from windscreen glass, which presumably would not have happened if the windscreen had been laminated. The fitting of such windscreens can be effectively enforced by law, at least on all new cars, yet Britain still churns out cars with unlaminated ones. Even when specifically requested I was not given what I wished and I know of others who have had similar difficulties.

In Australia (Dr John Knight, 5 June, p 1391) it seems that injuries, although reduced by seat belts, still happen and laws restricting personal freedom are difficult to enforce. Without a breakdown of the figures to show whether more injuries are from lack of seat belts or lack of laminated windscreens and also what are attributable to the wearing of belts or to having laminated windscreens statistics are of little value. But a law that cannot be enforced and that the police do not like is a bad law and will continue to be flouted. One recent patient with a perforating eye injury with traumatic cataract from broken windscreen glass, when asked about seat belts, was quite adamant that she would continue to be a non-wearer.

I think one can expect the young especially to continue to drink, to drive, and to value their freedom rather than their safety in spite of any legislation.

JOHN PRIMROSE

Regional Eye Centre,
Oldchurch Hospital,
Romford, Essex

Tuberculosis of the colon

SIR,—Over the past few years there appears to have been an increase in the incidence of tuberculosis affecting the large bowel. This increase is not wholly confined to immigrant populations and consequently the diagnosis may not be initially considered. We have recently seen two patients, one thought to have a carcinoma and the other Crohn's disease, who illustrate different presentations of the disease.

Case 1—A 56-year-old Englishwoman who had never been abroad presented with a microcytic hypochromic anaemia. During investigation a barium enema examination revealed a stricture in the ascending colon suggestive of a carcinoma. At

laparotomy a narrowed ring lesion was found in the distal right colon with nodes in the meso-colon. A right hemicolectomy was performed and she made an uneventful recovery. Histological examination showed a constricting lesion consisting of caseating giant-cell granulomas with mucosal ulceration. Acid-fast bacilli were present. There was no other evidence of tuberculosis either in the chest or urinary tract. She has been started on a course of antituberculosis treatment (isoniazid, rifampicin, and streptomycin) and is progressing well.

Case 2—A 43-year-old male Pakistani who had been resident in Britain for 18 years presented with typical small-bowel obstruction. At laparotomy a large hard mass was found in the caecum and an initial diagnosis of Crohn's disease was made. A right hemicolectomy was performed and he made an uneventful recovery. Histological examination showed mucosal ulceration and fissure formation in the caecum with caseous granulomas within the large bowel and lymph nodes. Acid- and alkali-fast bacilli were identified in the granulomas. There was no evidence of active tuberculosis elsewhere and he has been started on antituberculosis therapy.

In both these cases it is most probable that the lesions occurred as a result of post-primary activation of previously acquired foci. Frequently one finds no evidence of tuberculosis elsewhere, either active or old,¹ and this should not distract one from the diagnosis.

We feel bound to comment also on the very real increase in the incidence of Crohn's disease affecting the large bowel which has also occurred in recent years.

I TAYLOR
P BROOMAN

Royal Hospital,
Sheffield

¹ Kaufman, H D, and Donovan, I, *Journal of the Royal College of Surgeons of Edinburgh*, 1974, **19**, 377.

Sacroccygeal teratoma and "non-immunological" hydrops fetalis

SIR,—Hydrops fetalis due to rhesus blood group incompatibility is becoming progressively less common and fetal hydrops from other causes (sometimes referred to as "non-immunological" or "idiopathic") attracts increasing interest. A number of conditions associated with the latter have been reported with varying frequency; these include instances of anaemia due to haemoglobinopathy (Hb Barts),¹ anaemia due to transplacental leakage (feto-fetal or feto-maternal^{2 3}), congenital leukaemia,⁴ fetal heart disease (for example, endocardial fibroelastosis,⁵ premature closure of the ductus arteriosus,⁶ premature closure of the foramen ovale⁷), cystic malformation of the lungs,⁵ intrauterine infections,⁵ chromosomal aberrations,⁵ and, last but not least, haemangiomas of the placenta.⁸ This is by no means a complete list. Mechanisms by which one or the other of these associations can cause hydrops have been suggested, but clarification of many problems is still being awaited.

Recently I had the opportunity of observing a stillborn fetus which was undoubtedly hydropic, even though macerative changes were superimposed. The placenta too was hydropic and this was confirmed by histological examination. The common type of blood group incompatibility was excluded by routine antenatal tests. Post-mortem examination did not suggest other forms of blood disorder; in particular, the liver and spleen were of appropriate size. A large sacroccygeal teratoma measuring approximately 20 cm