its height. As your leader implies, the long-term follow-up has considerably diminished this enthusiasm and a conservative policy is now rightly more frequently adopted.

I believe that stenotic mitral valves should almost never be replaced, that patients with some degree of mitral incompetence may have little disability for many years after commissurotomy, and that even heavily calcified mitral valves can be successfully treated by simple valvotomy.²

Lastly, although the relevant merits of open and closed valvotomy have not yet been firmly established, the risk of unnecessary valve replacement with all its attendant evils must be increased when an open operation is done.

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¹ Belcher, J R, *Thorax*, 1973, 28, 608.

² Smith, G H, and Belcher, J R, *British Heart Journal*, 1970, 32, 198.

Uniform style for biomedical journals

SIR,—I wonder whether Mr Roger Hole (3 June, p 1483) was objecting to “unpublished work” or “personal communications” rather than “in press” papers. The first two should certainly be barred from reference lists. Professor W B Jennett (24 June, p 1699) is, of course, right about “in press” papers being perfectly acceptable. If the journal’s name can be given (and preferably the title of the paper) any interested reader can eventually find a paper of this kind. But referees should perhaps examine reference lists of manuscripts they are reviewing and then ask to see copies of papers listed as being “accepted” or “in press”—as suggested by Professor S Saxov at a recent conference of editors (Editerra Fourth General Assembly, joint meeting with ELSE).

MAEVE O’CONNOR

*.*Since “in press” implies that the paper has definitely been accepted for publication in a specific journal the name of that journal should always be given in such references. But since, as pointed out by Professor Jennett, the interval between acceptance and publication is often long, the date and volume number cannot be given without risk of inaccuracy.—ED, *BMJ*.

SIR,—In response to your leading article (20 May, p 1302) I have the following comment and proposal to make. One great advantage of the Harvard system is that creditability of a quoted observation can be readily assessed. Thus I find myself frequently having to look at the list of references to see just who proved what and when when reading the journals using the number system. The Harvard system saves a great deal of time and also refreshes my memory of important observations made by others. As such, it more closely reflects a scientific discussion between colleagues or at “grand rounds,” where one quotes Harvey, Osler, Salk, etc, but never 13, 41, 57, and so forth. To be continually reminded by the Harvard system by whom a certain observation was made is a positive learning experience which I believe we cannot afford to lose for sake of uniformity. The argument that the head of a unit’s name might appear too far down the list and may be deleted in subediting

may be dealt with by placing the head of a unit’s name in a constant position (for instance, second or third position) or alternatively by limiting the number of authors for any given article.

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*.*The placing of the name of the head of a unit at the end of a list of authors is often deliberate, indicating that he exercised only a supervisory role while the previously named authors bore the chief responsibility for the work reported and should be given the credit for it. Neither the Harvard nor the numerical system, however, rules out the possibility of mentioning by name the head of the unit (“Professor Smith’s team (Jones, Brown, Robinson, *et al*, 1977) . . .”) or the department (“at St Swithun’s¹⁰ . . .”).—ED, *BMJ*.

Standardisation and safety

SIR,—Among the benefits of standardisation, we are told, not the least is that of safety. How safe then is a new anaesthetic apparatus recently supplied to this department by a well-known manufacturer? The gauges are calibrated as follows:

Oxygen, high pressure	..	kPa × 100
Oxygen, low pressure	..	lb/in ² and kg/cm ²
nitrous oxide, low pressure	..	lb/in ² and kg/cm ²
nitrous oxide, high pressure	..	“full at varying temperatures”
vacuum	..	kPa and mm Hg
blood pressure	..	mm Hg
Manley ventilator, pressure	..	cm H ₂ O
Manley ventilator, tidal volume	..	ccs
Rotameters	..	cc/min
Cylinders, tested to	..	2000 lb/sq in (psi)
nitrous oxide	..	900 litres, of which 100 gallons weighs 30 oz
oxygen	..	1360 litres
carbon dioxide	..	450 litres, of which 100 l weighs 0.182 kg (6½ oz)

No sane comment seems possible, but do other specialties enjoy such variety?

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Drug treatment card

SIR,—Experience with the use of this card in the way described in my article on the Aldeburgh record system (10 September 1977, p 683) has suggested that the division of drugs into those for maintenance therapy and those for episodic treatment is impracticable. It is better to enter all drugs in chronological order, ignoring the division between those for short- and long-term use. Each drug should carry a reference number, which can then be used on the repeat prescription card or the continuation notes if appropriate.

Any drug given for long-term use should be recorded on the flow sheet described in the article. This will make it clear whether the patient is currently on any long-term therapy and if so in what dose. In due course the design of the drug treatment card will be amended; meanwhile the present card can be used as suggested above.

Those seeking information about the record system or “starter pack” of background data cards and questionnaires should now contact

the Central Information Service for General Medical Practice, 14 Princes Gate, London SW7 1PU (*not* the Cardew Stanning Foundation as stated in the article). Those wishing to purchase cards can still do so from: F W Pawsey and Son, Dales Road, Ipswich, Suffolk.

IAN TAIT

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Oesophagitis as a side effect of emepromium

SIR,—I read Mr S L Stanton’s article on drugs acting on the bladder and urethra (17 June, p 1607) with interest but was disappointed that oesophagitis was not mentioned as a possible side effect of emepromium bromide. This adverse reaction to the drug is now well recognised and has recently been highlighted by the Committee on Safety of Medicines.¹

Two patients have recently been admitted to this hospital with severe oesophagitis causing complete dysphagia. Both had been taking emepromium 200 mg thrice daily at the time of onset of their symptoms, both had endoscopically proved mid and distal oesophagitis, and one had an ulcer at 30 cm. Whether the oesophagitis is due to direct mucosal injury by the drug or a result of increased gastro-oesophageal reflux by an anticholinergic mechanism is not certain.

Three other patients treated with emepromium in this department have developed dysphagia of such severity that treatment has had to be stopped. I would therefore suggest that this drug be used with caution.

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¹ Committee on Safety of Medicines, *Current Problems*, No 3, 1978.

Genital infections and cervical carcinoma

SIR,—In your leading article (1 April, p 807) you discuss the significance of herpes simplex virus infections in cervical carcinoma and its prevention. Although herpesvirus has been considered carcinogenic and shown to be a common genital infection, the possible significance of other accompanying infections should be borne in mind.

In the past five years herpesvirus cultures from cervical mucus have been performed from patients admitted to our venereological clinic for vaginal infections. Thirty-seven patients with positive cultures were followed up with vaginal smears. Cytological findings were negative in 35 of the women and atypical in one. Biopsy in this atypical case produced no evidence of cervical carcinoma stage 0. These figures do not exceed what can be found in large mass examinations.¹ However, the observation time of 1–5 years is short and cytological and clinical manifestations might require a longer time to develop.

We also followed up another series of 162 patients who had been infected with neisseriae in 1954–5 and were still residing in the receiving area of the hospital. These patients were all traced in the gynaecological cytology register. Patients with positive smears had been referred for gynaecological examination

and could be traced in the records of the department of gynaecology. Of the 162 patients, 29 had cervical carcinoma stage 0 as diagnosed at conisation of the cervix and five had invasive cervical carcinoma stage I-II. One hundred and seventy-two age-matched controls were selected from the registers of births, marriages, and deaths and followed up in the same way as the patients. Seven cases of carcinoma of the uterine cervix stage 0 were found and one case in an invasive stage. The frequency of carcinoma was thus 20% in the patients compared with 5% in the controls—that is, four times higher in the patients who had previously had infection with *neisseriae*.

The results are in agreement with the general opinion that genital infections predispose to cervical neoplasia. Neither in the *neisseria* group nor in the controls was the frequency of herpesvirus infection known. We feel that estimation of the significance of herpesvirus infection and of the importance of possibly carcinogenic metabolites of bacterial origin requires well-planned long-term studies. Attention must be given also to other micro-organisms known to be of importance in genital infections, such as *Mycoplasma hominis*² and *Chlamydia trachomatis*.³

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- ¹ Bjerre, B, *Acta Obstetrica et Gynecologica Scandinavica*, 1969, **48**, suppl 6.
² Mårdh, P-A, and Weström, L, *British Journal of Venereal Diseases*, 1970, **46**, 179.
³ Mårdh, P-A, et al, *New England Journal of Medicine*, 1977, **296**, 1377.

Epidemic myalgic encephalomyelitis

SIR,—From Dr H G Easton's letter (24 June, p 1696), I can only conclude that he ignored all the evidence at the symposium on myalgic encephalomyelitis at the Royal Society of Medicine that did not fit in with his theories. If he had stayed to the end, when a vote was taken, he would have found himself the only person present still in favour of the "conversion hysteria" theory.

Dr Pampiglione, for example, referred to the electroencephalographic abnormalities—which were quite different from those seen in an acute encephalitis or liver failure with encephalopathy. The abnormalities were also different from those in chronic psychiatric patients. The cerebral cortex appeared to be disturbed by an insidious illness which was worthy of further investigation. Dr Peter Behan said that lumbar puncture performed on different days could give different results. Abnormal lymphocytes had been found by Dr Dillon, and reference was also made to anticomplementary activity in the serum and the ability of lymphocytes to live in vitro for an extended period, as is found with lymphocytes from patients with known viral diseases.

Dr Easton's "vapour and virus" remarks are hardly worth serious attention. Failure to isolate a virus does not rule out the possibility of a viral illness, because viruses that are of low antigenicity could become non-detectable if they were incorporated into the host cell's DNA. I would suggest that before putting pen to paper again he talks to some of the nurses (who have never been adequately followed up)

permanently disabled as a result of the Royal Free Hospital outbreak. He might then discover how much unnecessary anguish the "conversion hysteria" theory had added to their mental and physical suffering. Or perhaps he would prefer to talk to some of the patients affected in the recent Essex outbreak, originally diagnosed as multiple sclerosis. Your leader admirably demonstrated the similarity between the two conditions. Perhaps Dr Easton thinks that multiple sclerosis is also hysterical in origin, since many of the symptoms, like those in myalgic encephalomyelitis, cannot be proved to be of organic aetiology.

Dr Peter Behan said at the symposium that he thought the disease was an immunological reaction triggered off by a virus. It would be helpful if more doctors, instead of pursuing outdated theories, seized the ample opportunities which study of this illness offers for research, a point which you rightly make in your leader.

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Leukostasis in chronic myeloid leukaemia

SIR,—In his recent paper (6 May, p 1169) on leukostasis in acute myeloid leukaemia (AML) Dr A L Harris draws attention to an important, avoidable cause of early death which is also relevant to other types of leukaemia. We have recently seen a similar event in a patient with chronic myeloid leukaemia (CML).

The patient was a 26-year-old man who presented with sudden deterioration of vision in one eye. Examination revealed several deposits with surrounding haemorrhage in both fundi and splenomegaly of 10 cm. Blood and bone marrow examination showed CML; his haemoglobin concentration was 6.8 g/dl, leucocyte count $500 \times 10^9/l$ ($500\,000/mm^3$) with a typical differential count, and platelet count $75 \times 10^9/l$ ($75\,000/mm^3$). Neutrophil alkaline phosphatase activity was absent and the Philadelphia chromosome was present. He was treated initially with busulphan 4 mg daily, but his condition deteriorated, with malaise, fever, pain in the splenic area, and some confusion. It was thought that these features reflected the very high leucocyte count, now $630 \times 10^9/l$ ($630\,000/mm^3$) and he was therefore transferred for leukapheresis (Hemonetics model 30). A blood count immediately before the procedure was as follows: haemoglobin 6.1 g/dl, leucocyte count $770 \times 10^9/l$ ($770\,000/mm^3$), platelets $100 \times 10^9/l$ ($100\,000/mm^3$). The leucocyte count immediately after leukapheresis had fallen to $560 \times 10^9/l$ ($560\,000/mm^3$) and a transfusion of 5 units of blood and 2 units (10 donations) of platelets was given. The following day the leucocyte count had not changed significantly ($550 \times 10^9/l$ ($550\,000/mm^3$)) and a second leukapheresis was carried out. Within 4 h the clinical features of a subarachnoid haemorrhage developed. The leucocyte count at this time was $300 \times 10^9/l$ ($300\,000/mm^3$). The patient's condition deteriorated and he died shortly afterwards. Permission for necropsy was not obtained.

Although no positive proof was obtained the clinical features and course of this patient were sufficiently similar to those described by Dr Harris to make cerebral leukostasis and haemorrhage the likely cause of death. It is evident that transfusion must be approached cautiously in any patient with a very high leucocyte count and preferably postponed until the count has been reduced to a level which does not significantly affect whole-blood viscosity. This can be achieved within a few days in AML but may take several weeks in

CML with traditional treatment. In these circumstances more vigorous chemotherapy or leukapheresis may be needed. Although in this case each leukapheresis produced a fall of over $200 \times 10^9/l$ ($200\,000/mm^3$) the leucocyte count still remained high enough for leukostasis to result from the combined haemodynamic effects of transfusion and the rapid blood volume changes inherent in the leukapheresis technique.

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Treatment of ulcerative colitis

SIR,—We wish to reply to the remarks made by Mr P G Bevan about the problems of colitis patients being treated in fever hospitals (3 June, p 1459). As a group associated with a so-called "fever hospital" we feel that the discipline of infectious diseases has a contribution to add to the subject of inflammatory bowel disease (IBD).

It is not widely appreciated that salmonella infection by itself can produce a severe inflammatory colitis with persistent bloody diarrhoea¹ and even, on occasions, toxic dilatation of the colon,² so it would be true to say that the distinction from IBD on clinical grounds is not possible. In fact the differentiation between IBD and salmonellosis in an acutely ill patient may not be readily solved by sigmoidoscopic or barium x-ray appearances or even by biopsy findings.³ We find that it is only by repeated assessment and repetition of the major investigations over a period of time that the diagnostic puzzle can be resolved, with all its implications for the management of the patient. To make matters worse, there are occasional patients in whom IBD of acute onset and salmonella infection coexist, and in these all the problems are compounded.

We feel that the specific bowel infections should be considered as part of the spectrum of IBD and, as in the case of ulcerative colitis and Crohn's disease, to produce good results it is necessary to have close co-operation at senior level between physicians and surgeons with experience of the problem.

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- ¹ Mandal, B K, and Mani, V, *Lancet*, 1976, **1**, 887.
² Schofield, P F, Mandal, B K, and Ironside, A G, *British Journal of Surgery*. In press.
³ Day, D, Mandal, B K, and Morson, B M, *Histopathology*, 1978, **2**, 117.

Spontaneous remission of nephrotic syndrome in amyloidosis

SIR,—I have read with interest the article by Drs J Michael and N F Jones on spontaneous remissions of nephrotic syndrome in secondary renal amyloidosis (17 June, p 1592). Spontaneous remission can also occur in primary amyloidosis. Indeed I have observed