to belittle Harvey's great contributions to the discovery of the circulation of the blood, but is it not time that we in Britain stopped perpetuating what at least is an oversimplified claim, that it was Harvey and Harvey alone who made this great discovery?

It would be most interesting, especially to me, to learn the views of professional medical historians—British, Italian, and Dutch.

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- ¹ Harvey, W, *Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus*. Frankfurt, 1628.
² Mettler, C C, *History of Medicine*. Toronto, Blackiston, 1947.
³ *Encyclopaedia Britannica*, 1963, vol 11, p 236.
⁴ Caesalpinus, *Quaestiones Perpetuarum*, libro V. Florence, 1571.
⁵ Fabricius (Fabrizio d'Acquapendente), *Tractatus de Respiratione ejus Instrumentis*, libro II. Padua, 1615.
⁶ Malpighi, M, *De Pulmonibus, Epistolae II, ad Borellium*. Bologna, 1661.

Erosive duodenitis during cimetidine treatment

SIR,—We were interested to read the case report by Dr J Webster and others (7 January, p 20) in which erosive gastritis and duodenitis were ascribed to a side effect of cimetidine treatment. We too have observed a case of erosive duodenitis occurring during cimetidine treatment.

A 46-year-old man presented with a history of epigastric pain for one month with no previous history. Endoscopy showed an ulcer on the posterior wall of the duodenal bulb with no evidence of duodenitis or duodenal deformity. Cimetidine treatment was started at 1 g/day and three days later the pain disappeared. During treatment he took a normal diet with no alcohol or coffee and he stopped smoking. No other drug was given. One month after starting treatment the patient was still free of symptoms and further endoscopy showed the duodenal ulcer to be healing; nevertheless, the duodenal mucosa showed intensive and widespread hyperaemia and oedema with several areas of punctate erosion. The appearance of the oesophagus and stomach was normal. Renal (blood urea, serum creatinine, and creatinine and urea clearance) and hepatic (serum transaminases, serum bilirubin, and bromsulphalein excretion) function was normal before and after the 30 days' treatment. Basal acid output and maximum acid output (pentagastrin test) before treatment were 12.7 mmol/h and 44.8 mmol/h and two days after stopping treatment they were 13.2 mmol/h and 49.1 mmol/h respectively. Cimetidine treatment was not resumed. A month later endoscopy showed a slight improvement in the punctate erosive duodenitis, but without the healing. A third pentagastrin test showed no significant variation from the previous ones. We have followed up 32 other patients with duodenal ulcer treated with cimetidine (1 g/day for one month and then 400 mg/day for six months) and also 18 patients with duodenal ulcer treated with an antacid (Maalox) in high dosage for one month followed after healing by small doses at night. All these patients were included in a randomised controlled trial carried out by our unit and we did not observe any further cases of widespread punctate erosive duodenitis.

The report by Dr Webster and his colleagues, together with ours, might suggest that the appearance of punctate erosive duodenitis or gastritis during cimetidine treatment is due to side effect of the drug. Nevertheless, it is not clear why, once the treatment is stopped, no significant improvement of the erosive duodenitis occurs even after as long as four months' suspension of treatment.

Since we deem it very important to determine the true incidence of this possible side

effect we would appreciate any further observations.

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SI, moles, and drugs

SIR,—I was interested, but somewhat disturbed, by your leading article under this title (18 March, p 668), which seems to have been inspired, at least in part, by your experience in converting drug concentrations from mass concentrations to substance concentrations. Having recently been involved in the conversion to SI units (at University College Hospital, London) I can confirm that the conversion of drug concentrations did provide some problems. However, your leading article does little to clarify the matter and indeed may cause further confusion. The mathematics of conversion is not the main difficulty (though care is needed); nor is failure to understand the exact nature of the substance being measured (though it may be of some importance). The most important source of error is failure to identify the primary standard used in the assay.

In practice most measurements are made by comparing the reaction of the test solution with that of a standard solution in an assay procedure. In drug measurements, as you point out, a number of related substances may be present and their reactivity may well vary. This is a fundamental problem in clinical chemistry, not merely in drug assays. It is unrelated to SI and cannot be fully eliminated. All that can be done is to define a standard and make the simplifying assumption that test and standard react equally in the assay.

Having defined a standard it is easy to convert results to SI units, using the molecular weight of the standard; and theoretically there is some justification for doing so. The activity of the reacting molecules is more likely to be related to their number than to their weight. The importance of identifying the primary standard was amply demonstrated by your experience with chlormethiazole, where both 513.5 mg of chlormethiazole edisylate and 161.65 mg of chlormethiazole base provide 10 mmol of chlormethiazole (as edisylate or base).

Only if the exact composition and molecular characteristics of the standard are uncertain or unknown is conversion unsafe or impossible. Total protein is a special case where the assay commonly employed quantifies peptide bonds and not protein itself.

While I do not readily defend SI, the problems thrown in its path are problems that it has not caused but merely drawn to our attention.

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Expression of complex symbols

SIR,—Your leading article "SI, moles, and drugs" (18 March, p 668) refers to the undesirability of using, for example, $\text{mg}\cdot\text{kg}^{-1}\cdot\text{d}^{-1}$ to avoid the ambiguity of $\text{mg}/\text{kg}/\text{d}$. Unfortunately ambiguity will always exist

when the complex symbol is in a field of medical science outside one's own.

In a relatively simple expression such as the above negative indices are not essential and ambiguity may be avoided by using parentheses.¹ In $\text{mg}/\text{kg}/\text{d}$, if the numerical values are 12/4/2, then $(\text{mg}/\text{kg})/\text{d}$ or $\text{mg}/(\text{kg}\cdot\text{d})$ equals 1.5 and $\text{mg}/(\text{kg}/\text{d})$ equals 6.

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¹ *Units, Symbols, and Abbreviations*, 3rd edn, ed D N Baron, pp 5-6, 41. London, Royal Society of Medicine.

* * Surely in clinical medicine "mg/kg/d" is used as an expression of daily dosage, not of total dosage, so that the ambiguity to which Professor Baron refers does not arise.—Ed, *BMJ*.

Typhoid and its serology

SIR,—Your leading article (18 February, p 389) on the use and limitations of serological tests in the diagnosis of typhoid fever is timely, especially as in the majority of cases reported in Britain the infection has been contracted abroad. Brodie¹ is to be congratulated on such painstaking and useful work in following up so many patients for so long after the outbreak of typhoid fever at Aberdeen in 1964. These serological tests have also been used for many years to "screen" waterworks staff and potential employees for possible carriage of *Salmonella typhi* and thus aid the detection and exclusion of typhoid carriers.² The limitations of typhoid serology for this purpose are also illustrated by Brodie's results.

The recent creation of water authorities with responsibility for water supply, sewerage, and river management—previously administered by separate bodies—has necessitated consideration of the multifunctional use of staff as well as the need to reassess the value of screening tests for them. The Public Health Laboratory Service Standing Committee on the Bacteriological Examination of Water Supplies has therefore recently reviewed the epidemiology of waterborne infectious disease in Britain since 1937—the year of the large outbreak at Croydon—as well as the role of serological screening tests.³ The committee concludes, in view of the current low incidence and changes in the natural history of typhoid fever—quite apart from improvements in water treatment and examination since 1937—that the continued mass use of serological screening tests is no longer justified in Britain. Since typhoid fever is not the only potential hazard, however remote, the committee recommends that examination of waterworks staff and potential employees for carriage of agents of potentially waterborne disease should be done selectively by appropriate laboratory tests, preferably in consultation with medical microbiologists, and then only when indications for them are revealed by medical assessment. Indeed, this accords with advice issued by the Department of Health and Social Security⁴ for employees in the food and catering services, where the potential microbiological hazards are probably very much greater than with water supplies. The role of codes of practice and of education in simple applied hygiene⁵ previously mentioned in your columns,⁶ cannot be too strongly