expected in patients who are conscious after overdosage of nitrazepam.

I find this quite confusing, and as a clinician who prescribes both nitrazepam and methaqualone I cannot see how judgements as to "safety" in overdosage can be equated with "preference," presumably as such preference must take into account the effectiveness of a drug in normal dosage for a specific purpose—in this case induction of sleep.—I am, etc.

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Groote Schuur Hospital,
Cape Town, S. Africa.

REFERENCE

- Oswald, I., *Nature*, 1969, 233, 893.

Susceptibility to Aspirin Bleeding

SIR,—Your leading article (23 May, p. 436), which accompanied the paper of Dr. D. J. B. St. John and Mr. F. T. McDermott (23 May, p. 450), refers to the controversial nature of the role of acid in aspirin-induced gastrostaxis, but fails to point out the equally controversial nature of some of your other statements. Thus, the opening sentence implies that aspirin is a proved and primary cause of a substantial proportion of acute gastrointestinal bleeds. In fact, the evidence is not strong enough to support such an unequivocal statement. Some publications certainly suggest that such may be the case, but the evidence adduced is circumstantial, with the major references quoted as "proof" resting their case on the finding that patients admitted to acute medical wards with haematemesis and melaena had somewhat more commonly taken aspirin during the preceding week than patients admitted to the same units for other reasons. Valman *et al.*¹ are typical in that 56% of their cases with an acute bleed had taken some aspirin, while aspirin had been taken by only 32% of the control group. There are many reasons for not jumping to the too obvious conclusion. For example, the vague symptoms of discomfort and malaise with which a developing bleed may be associated would tend to cause many people to seek relief with their old standby, aspirin. Smith² stated that a history of higher incidence of recent ingestion of aspirin is not proof that aspirin is the causal agent of massive haemorrhage, and Waterson³ could find only three patients out of 165 where aspirin could possibly be incriminated as the cause of bleeding. More recently, Halmagyi in Ontario⁴ was unable to find any causal relationship between drugs and upper gastrointestinal haemorrhage in his series of 425 cases.

Among difficulties in the way of accepting the hypothesis that aspirin is a direct cause of acute bleeds are: the non-reproducible nature of the phenomenon in the same subject⁵; the numerous controlled studies which indicate that the increase in faecal blood loss due to repeated large doses of aspirin is distributed about a mean of 3-4 ml./day, and the lack of evidence to justify extrapolation to the high figures associated with haematemesis and melaena; and the fact that in cases of massive aspirin overdosage obvious blood is rarely, if ever, found in the gastric aspirates.

Again, your statement that 10-15% of

persons taking aspirin continually lose enough blood to develop iron-deficiency anaemia is not well supported by the world literature (and not supported at all by the reference you quote). Baragar and Duthie⁶ concluded that the great majority of patients with rheumatoid arthritis can tolerate regular aspirin without serious blood loss or development of anaemia. This is not surprising since the average man replaces red cells equivalent to 40 ml. of blood daily, and has the ability, when the need arises, to increase this rate 6 to 9 fold. There is enough iron in the normal daily dietary intake to permit the generation of 23-29 ml. of blood.

With respect to the use of aspirin in people with bleeding diatheses involving platelets, such as von Willebrand's disease, there is mounting evidence that even moderate doses of the drug may prolong bleeding time.⁷ However, this effect does not so far appear to bear any relationship to the sort of gastric bleeding referred to in your leading article.⁸⁻⁹ Leonards and Levy¹⁰ state that gastrostaxis is a local effect and is not related to the prolongation of bleeding time produced by aspirin.

Progress is being made towards aspirin formulations with less risk of adverse effects on the gastric mucosa, and recent sophisticated studies have established that extra blood loss on administration of plain aspirin is approximately halved by substitution of a soluble preparation.⁹

It is important that a balanced view be taken with regard to the deficiencies of aspirin therapy. Here is a rare example of an efficacious drug which has been proved to be relatively safe, whether taken sporadically as self-medication for aches, pains, and fevers, or when prescribed for the treatment of certain common and crippling rheumatoid diseases where dosage is high and continuous.—We are, etc.,

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GORDON R. FRYERS,

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REFERENCES

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**We disagree with Drs. Blane and Fryers that there is not enough "proof" that aspirin can be a clinical problem, in terms of both acute and occult bleeding. In the study by Valman and others¹ the incidence of aspirin ingestion among patients admitted for haematemesis and melaena was greater than among patients admitted to a general medical ward with pneumonia,

fever, and chest pain. The difference was highly significant ($P < .001$). The control group had as much, if not more, cause for taking aspirin for symptomatic relief as had the patients who were bleeding. In view of the welter of evidence, dating from Douthwaite and Lintott's observations in 1938,² that aspirin has a direct haemorrhagic effect on the human gastric mucosa, the most reasonable conclusion from these data is that aspirin caused the erosions. This is not to deny that other factors are involved. Excessive blood loss is the single most important cause or iron deficiency.³ Patients with rheumatoid arthritis are commonly anaemic and aspirin-induced occult bleeding is likely to be an important factor in some of them.⁴

Drs. Blane and Fryers imply that easier gastric absorption of aspirin will result in less mucosal damage. In fact it is formulations that are not absorbed in the stomach but are absorbed lower down, such as enteric-coated aspirin, that cause less occult bleeding. Aspirin is a very useful drug but it does cause trouble, and research into an aspirin preparation free from gastric side-effects would be welcomed.—ED., B.M.J.

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Pseudo-obstruction of the Large Bowel

SIR,—I see that yet another clinical entity has emerged. I refer to the condition of "Pseudo-obstruction of the Large Bowel" described under Current Practice by Mr. P. K. Caves and Dr. H. A. Crockard (6 June, p. 583).

Large bowel obstruction is a clinical syndrome characterized by abdominal distension, constipation, colicky lower abdominal pain, and with the typical x-ray findings of dilated large bowel. A careful analysis of the case histories of the four examples of "pseudo-obstruction" described in this paper reveal that they all had the criteria of large bowel obstruction, and indeed they all underwent laparotomy for this condition, though no mechanical cause for obstruction could be found at operation. There is therefore no case for labelling this condition "pseudo-obstruction" simply because no mechanical cause could be found. The patients were undoubtedly suffering from functional obstruction of the colon, but the obstruction was real enough.

The pathogenesis of functional obstruction of the intestine has until recently been poorly understood. There are two known mechanisms: vascular and neurogenic. A vascular aetiology can apparently be excluded in these patients, so we are left with a neurogenic cause, or, as it is more popularly called, paralytic ileus. Ileus is a sympathetic reflex which may affect the intestinal tract in whole or in part,¹ and the colon is the portion of the intestinal tract under the greatest influence of the sympathetic nervous system and with the least parasympathetic contribution. The colon therefore will be maximally affected by a sympathetic reflex, the small intestine

escaping initially due to its high level of parasympathetic tone.²

Ileus has for many years been known to occur as the result of a variety of conditions, many of them remote from the gastrointestinal tract, and I would submit that the patients described as suffering from pseudo-obstruction of the large bowel were in reality suffering from paralytic ileus.—I am, etc.,

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REFERENCES

- 1 Neely, J., M.S. Thesis, *London University*, 1968.
- 2 Neely, J., and Catchpole, B. N., *Gut*, 1967, 8, 230.

Evaluation of Simpson

SIR,—The recent correspondence (30 May, p. 541, and 13 June, p. 668) following the interesting article by Mr. E. Gaskell (16 May, p. 414) does not mention that chloroform plus spirits of wine—chloric ether—was first administered at St. Bartholomew's Hospital by Mr. Holmes Coote, to a patient of Mr. Lawrence, on the recommendation of Mr. M. C. Furnell, in the spring of 1847. This was some months before Sir James Young Simpson introduced and popularized undiluted chloroform.—I am, etc.,

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REFERENCE

- 1 Sykes, W. S., *Essays on the First Hundred Years of Anaesthesia*, Edinburgh, Livingstone, 1960.

SIR,—In his spirited denial of Sir James Young Simpson's varied achievements, Dr. W. B. Gough (30 May, p. 541) unfortunately ignores several important aspects of Simpson's career, notably his lifelong campaign against hospital cross-infection.¹ His work was based on detailed epidemiological studies, which remain the models in this field. These investigations were combined with a remarkable appreciation of the role of animate contagion long before the "germ theory" had been formulated by Pasteur and others. Simpson's revelations of the horrifying mortality from surgical sepsis in our great hospitals resulted in a barrage of abuse and vituperation from the leaders of the medical profession, but this by no means deterred him.

Dr. Gough saw fit to compare Simpson adversely with various medical pioneers including Lister. The enormous importance of Lister's work on antiseptic surgery is self-evident. However, it is interesting to note that Lister was either unaware of or chose to ignore in his original papers the previous work on antiseptics. This included, in particular, the work of two predecessors in Edinburgh. The first of these, Sir John Pringle, in 1750 had actually invented the term "antiseptic" and had carried out the initial experiments on this group of substances.² The second, Sir James Simpson, advocated ten years before Lister's first paper on the subject "in the prophylaxis of surgical fever . . . acid, chlorinated or other antiseptic applications."

In this centenary year of Simpson's death it is essential that his extraordinarily diverse

achievements are placed in true perspective. I am, etc.,

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REFERENCES

- 1 Selwyn, S., *Medical History*, 1965, 9, 241.
- 2 Selwyn, S., *Medical History*, 1966, 10, 266.

Disposing of "Disposables"

SIR,—While sailing on the Thames recently, I was surprised to see a disposable colostomy bag floating by. Most probably this had arrived via the sewerage system.

It would appear that the instructions given to colostomy patients do not adequately stress the results of disposing of the bag by a seemingly innocuous route. Through the medium of your columns may I point out the hazards of polyethylene's near indestructibility which are encountered by veterinary surgeons and navigators of power craft. These are ingestion by farm animals leading to intestinal obstruction, fouling of propellers, and blockage of cooling-water intake pipes.—I am, etc.,

E. H. COMPTON.

London W.10.

Cost of Treatment

SIR,—There is no doubt that Kabikinase (pure streptokinase) may be considered an expensive form of treatment. Kabi Pharmaceuticals Limited recognizes this and fulfils most of Mr. A. P. J. Ross's suggestion (30 May, p. 543) by specifically instructing its representative staff to draw attention to cost. The order department does the same when receiving urgent telephone requests from hospital pharmacists (who also have been sent a price list) for this material. However, expense is a relative matter; the conditions for which pure streptokinase are used are potentially lethal, and its cost clearly is less than, for example, that of renal dialysis. One may ask "What is the cost of not using streptokinase?"

Mr. Ross has constructed his argument

Authors	Average No. Vials*	Cost (£)
<i>Venous Thrombosis</i>		
Browse <i>et al.</i> (21 September, 1968, p. 717)	13	215
Kakkar <i>et al.</i>	26	430
Kakkar <i>et al.</i> (29 March, 1969, p. 806)	31	512
Mavor <i>et al.</i>	6	100
Robertson <i>et al.</i>	13	215
<i>Pulmonary Embolism</i>		
Hirsh <i>et al.</i> (21 December, 1968, p. 729)	11	182
Miller <i>et al.</i> (29 March, 1969, p. 812)	7	116
Gibson ¹	13	215
Average per Thrombolytic Course . .	15	248

*600,000 i.u. vials per thrombolytic course.

from the early work by one investigator. Had he reviewed the recent literature, he would have found estimated costs of treatment as follows:

Moreover, the recommendations in the company's handbook on thrombolytic thera-

py suggest the usual thrombolytic course to be 600,000 i.u. as an initial dose and 100,000 i.u. hourly for about 72 hours. It commonly is found that 12 vials of 600,000 units are supplied and found sufficient—a cost of £200. This cost is only one-third of that cited by Mr. Ross, who disclaims a wish "to restrict the freedom of the pharmaceutical industry with regard to advertising." It is to be hoped that the extreme example he has quoted will not restrict the freedom of decision to use pure streptokinase when indicated, since its therapeutic efficacy in suitably selected cases is not only well-proved but perhaps life-saving.—I am, etc.,

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REFERENCES

- 1 Kakkar, V., *et al.*, *British Journal of Surgery*, 1969, 56, 178.
- 2 Mavor, G. E., Ogston, D., Galloway, J. M. D., and Karmody, A. M., *British Journal of Surgery*, 1969, 56, 564.
- 3 Robertson, B. R., Nilsson, I. M., and Nylander, G., *Acta Chirurgica Scandinavica*, 1970, 136, 173.
- 4 Gibson, R., *Practitioner*, 1970, 204, 262.

Primary Medical Care

SIR,—I am writing to you as a general practitioner and a member of the Association ever since my student days.

I have become a general practitioner not as a failed consultant but out of choice, because I find that this is the type of work which corresponds most closely to my ideal of a doctor helping the sick. It was thus somewhat of a shock to read in the *B.M.J.* (30 May, p. 493) that my care is well-nigh useless, that I am not competent to deal with obstetric problems (although I have the D.Obst.), and that I know less about skin conditions and acute E.N.T. infections than a houseman qualified a few days before taking up his post. I thought then seriously that if this is the opinion of the B.M.A. our ways must obviously part.

On top of this I see today that members of Council who are comfortably off and busily engaged in various forms of private practice call on me to resign from the National Health Service "even if it means starving some time in the future." Perhaps surprisingly, my feeling is that the National Health Service, with all its shortcomings, is satisfactory for the population as a whole, and it should be satisfactory for the doctors if they will put into it as much as they hope to get out of it.

In short, I feel with a number of your correspondents that we should accept the not ungenerous award and should try to work, possibly even harder and possibly without a review body, to better the conditions of both the patients and ourselves.

It should have become obvious by now that we are in the fortunate position of not being able to withhold our services under any circumstances, and it would certainly not inconvenience the Government if we resign and then carry on normally. We should, however, become the laughing stock of the country.—I am, etc.,

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