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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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. Smith[2] 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 Waterson[3] could find only three patients out of 165 where aspirin could possibly be incriminated as the cause of bleeding. More recently, Halmagyi in Ontario[4] 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 subject[5]; 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 Duthie[6] 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 Levy[10] 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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**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 others[1] 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