ulcer and certainly no place in 1972 for treating any odd lesion in the bladder without a biopsy. As you rightly point out, "Hunner's ulcer" in a man often turns out to be cancer, infiltrating or in situ.—I am, etc.,

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New Salicylates

SIR,—It is generally accepted that aspirin is the drug of choice in the treatment of rheumatoid arthritis, particularly in the early stages. Unfortunately, the administration of aspirin has the disadvantage that it may cause troublesome gastric irritation. For this reason, much time and money has been spent in attempting to produce a new formulation which would be free from this serious side effect.

Brennan and Sripathy,[1] reporting the results of a clinical trial of a new enteric-coated aspirin preparation, Safprin (each tablet contains 300 mg aspirin, as a central enteric-coated core, surrounded by 250 mg paracetamol), claimed that it was free from gastric irritation, and that it did not cause overt gastrointestinal bleeding. This trial was conducted in a series of 54 geriatric patients suffering from either rheumatoid arthritis or osteoarthritis.

During the past 18 months, Safprin has been prescribed in this unit for more than 50 patients suffering from rheumatoid arthritis. In the first instance, a short clinical trial was organized in which Safprin was compared with indomethacin. The results appeared to confirm that Safprin was relatively free from gastric irritation, and that it appeared to control joint symptoms in an acceptable percentage of patients.

Subsequently, a further 40 patients suffering from rheumatoid arthritis have received Safprin and been observed as an "open study." Twenty-four of these patients gave a history of dyspepsia while on other analgesic preparations. Four patients continued to complain of dyspeptic symptoms while on Safprin, but the remaining 20 patients claimed to be trouble free. The majority found the preparation effective in controlling joint pain, although four claimed that they had derived no relief of joint pain, even when taking three tablets 5 times daily (4·5 g aspirin).

From this somewhat limited experience, it would appear that Safprin is a useful alternative preparation in the long-term treatment of patients suffering from rheumatoid arthritis, particularly in those patients with a previous history of dyspepsia.—I am, etc.,

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1 Brennan, J. B. and Sripathy, S., *British Journal of Clinical Practice*, 1970, **24**, 263.

SIR,—Many currently available salicylates cause gastrointestinal bleeding (10% in arthritis patients and 7% of patients overall); acetylsalicylic acid (aspirin) in particular has been associated with nearly 50% of cases of acute gastrointestinal haemorrhage.[1] The development of a salicylate free from such side-effects would clearly be a therapeutic advance.

Meglumine salicylate has been selected for the present study because it is freely water soluble, relatively non-hygroscopic, and has a near neutral pH in 1% and 10% aqueous solutions (6·47 and 6·60 respectively). The study involved the effects on the bleeding time and in vitro platelet aggregation in humans, and on the gastric mucosa of rats.

TABLE—*Effect of Placebo (Lactose) or Meglumine Salicylate on Bleeding Time, Platelet Aggregation Rate, and Platelet Reaction time following Addition of Collagen.*

	Bleeding time (mean of 3 readings, min) 20 normal subjects		Reaction time* (sec) 18 normal subjects**		Rate of aggregation* (arbitrary units) 18 normal subjects**	
	pre	post	pre	post	pre	post
Placebo	3·8 (2·6-7·0)	3·9 (1·2-14·1)	52·4 (35·1-71·0)	58·5 (29·1-96·0)	8·6 (2·2-12·3)	8·0 (4·4-11·5)
Meglumine salicylate	3·8 (1·9-5·8)	3·7 (2·0-5·2)	56·2 (38·1-82·5)	55·6 (30·0-84·6)	7·7 (5·1-15·2)	8·8 (4·2-14·5)

* Mean of two readings for each subject.
** Although 20 normal subjects were studied, platelets obtained from two did not react to collagen, so that the figures for in vitro platelet studies refer to 18 subjects only. Figures show the mean result and range in each group.

Ivy bleeding times were determined for 20 normal subjects before, and two hours after, the ingestion of two gelatin-coated capsules containing either 1·2 g meglumine salicylate (equivalent to 650 mg aspirin) or placebo (lactose); all tests were performed double-blind. The mean bleeding time from three stabs was recorded in each case,[2] and the bleeding time two hours after ingestion of the capsules was determined on the opposite arm at a symmetrically equivalent site.

In vitro platelet function tests were carried out using platelet-rich plasma (P.R.P.) prepared from venous blood taken immediately before each bleeding time estimation. Aggregation studies were carried out using a EEL aggregometer[3] linked to a Vitatron UR 400 pen recorder. All samples were tested within 45 minutes of their collection.

"Collagen" was prepared from human Achilles tendon by its homogenization and suspension in 0·05M Tris buffer pH 7·2 at 21°C after filtration through coarse nylon mesh. The suspension was stored at −21°C. After prewarming aliquots of P.R.P. to 37°C in the aggregometer, 1/10 volumes of collagen suspension were blown in and aggregation slopes were obtained. All samples were tested twice; in each case the reaction time of the mixture was taken to be the first definite decrease in optical density following the addition of collagen, and the rate of aggregation was obtained from the slope of the tangent of the curve when aggregation appeared to be most rapid.

Results are shown in the Table. No difference could be ascertained between meglumine salicylate and placebo with respect to bleeding times, reaction times, or rates of platelet aggregation.

Comparative effects of three salicylates on the gastric mucosa of rats were also studied. Three groups of 25 rats were fasted for 18 hours and then given an oral toxic insult dose (1 g/kg salicylate equivalent) of aspirin, buffered aspirin, or meglumine salicylate. One of the rats given aspirin was found dead after treatment. The remaining animals in all three groups were killed 16 hours after treatment and the stomach mucosae examined macroscopically for evidence of bleeding. In the aspirin-treated group, "slight" to "massive" bleeding was found in all 25 animals, including the one found dead. "Slight" to "considerable" bleeding was found in 10 of the 25 animals given buffered aspirin, and "slight" bleeding was found in three of the animals given meglumine salicylate.

These results show that meglumine salicylate may be a "safer" drug than aspirin because of the absence of a demonstrable effect on platelet function, and, at least in rats, there is little or no gastrointestinal bleeding. The effect in man of meglumine salicylate is so far unknown, and further study in this respect may therefore be warranted.—We are, etc.,

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1 Muir, A., in *Salicylates, an International Symposium*, ed. A. St. J. Dixon, p. 230, Boston, Little, Brown, 1963.
2 Leslie, J., and Mason, D. Y., *Journal of Clinical Pathology*, 1970, **23**, 526.
3 Born, G. V. R., and Cross, M. J., *Journal of Physiology (Lond.)*, 1963, **168**, 178.

"Cot Deaths"

SIR,—I was especially interested in the excellent contribution by Dr. John L. Emery (4 March, p. 612) concerning families involved in cot deaths. His article shows a rare understanding and grasp of the subject. A month ago my granddaughter, aged three months, was found dead in such circumstances.

When I read that one in every 400 babies dies in this way I am prompted to say that surely some more active steps are overdue in trying to trace the cause or at least in determining common factors. My suggestions are:

(1) A central registry be set up to which all such cases are referred.

(2) Every family so afflicted be invited for interview or at least to fill in a questionnaire. This should be exhaustive and should deal not only with details of birth, management, feeding, and medical history but such items as clothing, snuffles, sleeping position, even baby care preparations and decorating materials. In the generation between my children and grandchildren, which seems to be the period in which these "cot deaths" have become highlighted, we have seen many changes in baby management. Nappies are applied differently, babies are placed in the prone position, and the use of plastics, detergents, and chemical sterilization of utensils are but a few of the changes that have become commonplace. I do not suggest any of these is responsible but all should be taken into account in the search for common denominators.

(3) Families should be kept in touch from time to time with a newsletter mentioning