In their later papers, Truelove, Korelitz, and Palmer have consistently cited Palmer-Kirsner as the supreme authority but shut their eyes to the presteroid death rate in colitis of less than 2% per year.⁷⁻⁹ Patients seldom died from colitis; nearly the biggest worry was the possibility of cancer of the bowel.

From the introduction of steroid therapy physicians^{10, 11} and surgeons^{12, 13} have reported many deaths from perforation, anaesthetic shock, and infections; many patients with colitis became addicted to steroids. Later, surgeons were still more emphatic¹⁴⁻¹⁷; Brooke¹⁸ has written six condemnatory papers since 1956. Of Sauer's¹⁹ 52 patients after 10 years nine are addicted and four others went insane.

Lately Kellner²⁰ has reported three post-operative deaths in 21 patients treated with steroids compared with no deaths in 21 patients not treated in this way. Ross,²¹ a surgeon who is not in favour of steroid treatment, has had no deaths in 132 colitis patients; four developed peptic ulcers, "surely another argument against the indiscriminate use of steroids."

A recent semi-official pronouncement by Truelove²² says, "Corticosteroid therapy has been shown in a number of controlled clinical trials to increase the chance of obtaining a rapid clinical remission." A more relevant statistic for most doctors would be the addiction and death rates of patients who have had steroids.—I am, etc.,

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*. Most of the figures quoted by Dr. Kelly are extremely difficult to evaluate; the only analysis with significant meaning is that which relates to patients admitted or treated for their first attack of colitis and then followed up subsequently. This has been done in this country both by Truelove and Edwards,¹ and by Kellock² at Central Middlesex Hospital. Their findings convincingly demonstrate that ulcerative colitis in the pre-steroid era was far from being the

negligible threat that Dr. Kelly implies. He quotes a pre-steroid death rate of about 2% per year, yet this is not only several times the expected value but also overlooks a mortality rate greatly in excess of 2% in patients with a first attack within one year of referral to hospital.

Since 1952, when cortisone was first introduced into treatment at Oxford, Truelove has found a notable improvement in the fatality rate and several controlled trials have confirmed the beneficial effects of steroids. Such treatment certainly carries its own risks, not the least of which is the steroid servitude mentioned by Dr. Kelly, but the application of these methods appears to have provided a much more hopeful prognosis than formerly existed.—ED., *B.M.J.*

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Local Analgesics

SIR,—In your interesting article in "To-day's Drugs" on local analgesics (28 November, p. 1380) your contributor says that lignocaine "falls short of the ideal because . . . serious, even fatal, side-effects can result from overdosage." Surely all local analgesics have a toxic effect, especially on nerve tissue, and it is difficult to imagine any such drug without side-effects when used in excess dosage.

In this connexion, it is remarkable that local analgesics such as lignocaine can produce convulsions in overdosage, and that the same drugs given as an intravenous infusion can terminate existing convulsions such as those occurring in status epilepticus. The same effect has been shown in cats and monkeys when the exposed cerebral cortex was stimulated electrically to cause convulsions. This apparent paradox has been known for many years, and it would be interesting to hear a reasonable explanation.—I am, etc.,

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SIR,—In your expert's review of local anaesthetics, under "To-day's Drugs" (28 November, p. 1380), it is stated that lignocaine is the nearest available approach to an ideal local anaesthetic drug and that there is little reason to use the newer local analgesics.

To my mind, amethocaine has many advantages over it. One of these is that a large volume of effective fluid can be injected, even feeble subjects tolerating over 400 ml. of 1/2,000 solution with adrenaline. This is a distinct advantage if an abdominal operation such as gastrectomy is to be carried out—or a radical mastectomy, or a thoracotomy—and there are occasional indications for local anaesthesia for these procedures. The latent period before anaesthesia develops is short, for if the surgeon, having finished the injection, prepares and towels the part, the operation can be started at once. The duration of anaesthesia is such that I have on one occasion injected the amethocaine solution, then gone away for lunch, and returned to

carry out a radical gastrectomy for cancer without further anaesthesia of any sort being required.

With regard to toxicity, we have used the drug as a 2% solution or as a tablet for every gastroscopy for over 25 years, certainly more than 12,000 times, without any reaction. In addition we have used it in a 1/2,000 solution for abdominal-wall anaesthesia and for thoracotomy well over 4,000 times without any reaction. The only reaction I have seen from the drug was when a non-sterile 2% solution was injected into the tissues by a new house-officer unfamiliar with the drug, but of course most local anaesthetics are dangerous if given in 40 times the correct strength.

Its only disadvantage is its instability in solution. This is, in fact, an advantage, for we keep it as a dry powder, 100 mg. per ampoule, and make up each solution fresh in normal saline. The ampoules are extremely convenient for use abroad. They are much more portable than flasks of lignocaine.

I regret very much that the English drug firms are giving up the manufacture of this safe and useful drug, and that we are compelled to explore abroad for it.—I am, etc.,

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Cephaloridine in Typhoid

SIR,—By courtesy of Professor J. W. S. Blacklock and Dr. J. P. Currie of Glaxo Research Limited, five patients with typhoid fever in this year's epidemic in Aberdeen were treated with the new broad-spectrum antibiotic cephaloridine (Dr. P. W. Muggleton and his colleagues, 14 November, p. 1234; Dr. J. McC. Murdoch and his co-workers, 14 November, p. 1238). The minimal inhibitory concentration *in vitro* for the organism (phage-type 34) causing the epidemic lay between 5 and 6 µg./ml., at which level there was virtually 100% kill (Dr. Currie, personal communication).

Three patients with moderate or severe typhoid were started on cephaloridine in the recommended dosage within an hour or two of admission, one was treated with it for a second relapse, and one at the end of a seven-weeks illness which had shown no lasting response to either chloramphenicol or ampicillin.

The first patient, a woman aged 26 admitted in her third week of illness, was one of the relatively few patients in the epidemic who were dangerously ill. On admission her temperature was 104° F. (40° C.), her abdomen distended and tender, and toxæmia severe. Cephaloridine 0.5 g. intramuscularly was given twice on the first day, and on the second day increased to 0.5 g. six-hourly. Fluids were given intravenously. On the afternoon of the third day, when 4 g. of cephaloridine had been given, her temperature was 103° F. (39.9° C.) and her condition had worsened; blood culture, reported later, was positive. Persistence with an untried drug was obviously not justified and she was started on chloramphenicol 3 g. daily with an intravenous loading dose, and intravenous hydrocortisone six-hourly for two days. She improved steadily and was afebrile on the sixth day of chloramphenicol. Convalescence was uneventful.

A woman aged 49 was admitted at the end of her first week, moderately ill with a temperature of 104.6° F. (40.3° C.). Cephaloridine was given in a dose of 0.5 g. six-hourly. On the fourth day of this treatment, when 6 g. of cephaloridine had been given, her temperature was 104° F. (40° C.), and her condition if any-