digits, and, in association with the letter, specifies the tablet exactly (e.g., "P 5" for the 30 mg. phenobarbitone tablet). With the aid of the Co-Tabs code index, which is a simple list of the code letters and numbers for all members of the range, identification of an individual Co-Tab is a matter of seconds. A tablet could carry two identifying letters instead of one; and the coding system can, of course, be used freely by any manufacturer for any kind of tablet. Indeed, as it will make possible the identification of 70,000 separate kinds of tablet and is believed to be the only system of its kind in operation anywhere in the world, international, as well as national, usage may be looked for. Details of the code have been made available to all the appropriate official bodies in this country.

Some means of ready identification of tablets has been suggested by many individual doctors in the past, and it has more than once been the subject of a resolution at the Association's Annual Representative Meeting. It has been pointed out that widespread usage of coded tablets would prove of very great value in connexion with cases of attempted suicide, when patients are transferring from one doctor to another, in preventing tablet wastage, etc. In the past, however, various difficulties attendant on tablet coding have also been mooted. Now happily, with the introduction of Co-Tabs, these difficulties have largely been overcome, and coded tablets exist and are in everyday use.—I am, etc.,

S. BRADSHAW,
Medical Adviser,
Arthur H. Cox and Co., Ltd.,
Continental Laboratories Ltd.

Amersham, Bucks.

¹ Co-Tabs are manufactured by Arthur Cox and Co., Ltd., of Brighton, and distributed by their associated ethical house, Continental Laboratories Ltd.

"Rule of Three"

SIR,—I attended the press conference at which the Minister enunciated the "rule of three." The Minister made it quite clear, repeatedly, that drivers must be advised not to drink before driving. He then went on to emphasize that neither the public nor the courts appeared to be fully aware of the effect of the Road Traffic Act, 1962, which had made it an offence for a person to drive when his ability to drive properly was impaired as a result of his having taken alcohol. He referred to the B.M.A.'s report that "a concentration of 50 mg. of alcohol in 100 ml. blood while driving a motor vehicle is the highest that can be accepted as entirely consistent with the safety of other road users" and he indicated that anyone who exceeded this concentration whilst driving might be regarded as committing an offence. In practice any adult who follows the "rule of three" will not exceed this concentration, and the Minister was quite correct in stating that, as the law is at present, a driver who kept to the "rule of three" would be unlikely to commit this particular offence.

The following is a quotation from the Ministry's memorandum on the subject:

"The only completely safe rule is not to drink at all before driving. The next best thing is not to drink more than the amount which can produce the potentially dangerous concentration of 50 mg./100 ml. This amount is 1½ pints of beer or 3 single

whiskies. Anyone who drives after drinking more than this amount may be increasing his risk of having an accident. Anyone who drives after drinking more than double that amount will almost certainly do so. In some circumstances (e.g., on an empty stomach or for a person who is not accustomed to drink) even 1½ pints or 3 single whiskies may increase the accident risk."

It is unrealistic to believe that everyone who drives will take no alcohol at all, and it is surely better to give some advice on the maximum amount which can be taken without exceeding the concentration of 50 mg./100 ml. mentioned in the B.M.A.'s report.—I am, etc.,

EDWARD WAYNE,
Chairman,
Alcohol and Road Accidents Committee,
British Medical Association.
London W.C.1.

T.A.B. Reaction

SIR,—Correspondents have been commenting on local reactions to intradermal T.A.B. Experience shows that the same dose of vaccine will produce a different amount of local reaction depending on the site used. If given on the forearm severe reaction with erythema and induration in the region of 10×8 cm. is quite common, but if given high up on the upper arm is much less so.

For some years I have given intradermal T.A.B. to nurses and others on a site on the back between the shoulder-blades, and during this time no nurse has been off duty because of local reaction. This variation in reaction with site appears to be similar to the phenomenon seen with smallpox vaccination, where there is increased chance of virus growth on the partial immune (revaccination) as the site becomes more peripheral.—I am, etc.,

C. W. DIXON.

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University of Otago Medical School,
Dunedin, New Zealand.

Cerebrovascular Accidents and Oral Contraception

SIR,—Dr. K. J. Zilkha's report (31 October, p. 1132) of two cases leads me to record two other instances of cerebrovascular disturbances while taking oral contraceptives in healthy women with no hypertension or any other evidence of cardiovascular disorder and with no history of any previous thrombosis.

One was a woman aged 32 who had been taking Conovid E (norethynodrel and mestranol) cyclically for 22 months and suddenly developed a typical lateral medullary syndrome, with severe vertigo and vomiting, ataxia, diplopia, a right Horner's syndrome, and loss of sensation over the right side of the face and the left half of the body. A gradual improvement took place during the next two months, leaving only a slight residual defect. This must have been caused by a thrombosis of a vertebral or a posterior inferior cerebellar artery.

The other, aged 46, experienced the sudden onset of vertigo and unsteadiness, causing her to lurch and even fall to the right, visual discomfort on looking to the right without closing one eye, and excessive drowsiness. Both plantars were extensor. No appreciable headache. She gradually recovered over the next few

weeks and it was considered that there had been an ischaemic disturbance of the brain stem. This patient had a history of migraine since childhood with an aura of patchy vision and numbness of the lips and one or other arm followed by headache behind the eyes, making her lie down for an hour. She had been taking Ovulen on 20 days each month for six months.

I am indebted to Dr. C. J. W. Hunter, of Searle & Co., Ltd., for referring me to two similar cases recorded in the U.S.A. in 1962.¹ He also knows through a personal communication of a third case in Newcastle.

The report of these few cases and those of Dr. Zilkha does not prove any causal relationship between the lesions and the oral contraceptives. Such cerebrovascular incidents are known to occur on rare occasions spontaneously without any apparent cause in this age group, and it has been estimated that 1,300,000 in the U.S.A. in 1962² and perhaps 250,000 women at the present time in Britain³ have been taking these preparations.

These cases, however, add emphasis to the importance of carefully planned prospective studies into the incidence of thromboembolism in a series of women taking these hormones compared with an untreated control group. They suggest that attention should be directed to cerebrovascular disturbances in addition to the more common thrombophlebitis of the legs and pulmonary embolism forming the basis of previous investigations which have been retrospective.—I am, etc.,

Hove, Sussex. A. M. STEWART-WALLACE.

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- ¹ *Thromboembolic Phenomena in Women*. Proceedings of a Conference, 1962. Searle, Illinois.
- ² Final Report on Enavid by an Ad Hoc Committee to the Food and Drug Administration of Health, Education, and Welfare, U.S.A., 1 November 1963.
- ³ *Brit. med. J.*, 1964, 2, 1089.

Steroid Addiction in Ulcerative Colitis

SIR,—Your editorial statement (10 October, p. 894) "Perforation of the colon is the outstanding risk . . . but experience at Oxford did not support the impression of other workers that steroid therapy increases the danger, often only suspected because of a sudden deterioration in general condition" accepts the statistical tables of Edwards and Truelove,¹ which imply that the prognosis in ulcerative colitis has improved. On this question the "impression of other workers" has been ignored. The "steroids-for-colitis" men in Britain and America have never replied to criticism but have accepted as "normal" the 12 deaths in 92 patients of Truelove and 11 helpers.² In America the four deaths in 52 patients of Zetzel and Korelitz³ is as disturbing as the steroid death rates in a dozen authoritative papers by Palmer and Kirsner.⁴

When I looked into this question I discovered that none of the steroid protagonists has given a straightforward comparison of death rates in colitis before and after steroids. Zetzel and Atin⁵ said that their 4 out of 52 deaths in two years (8%) was better than their previous 51 deaths in 244 patients (20%). But the 51 deaths were spread over 24 years (1930–1954); the true annual death rate before steroids was less than 2% per year.

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.,

MICHAEL KELLY.

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Melbourne, Australia.

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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.,

London W.1.

NORMAN C. TANNER.

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-