This may be due to the presence of a third vas, division of a testicular vein in mistake for a vas, or possible recanalization. Such cases will be missed if specimens of ejaculate are not examined after vasectomy.—I am, etc.,

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Anaesthetic Safety Devices

SIR,—The anaesthetic machine is unique among medical devices in that it is hermetically sealed to the respiratory system of an unconscious patient whom it will inevitably kill if it fails to deliver oxygen, and if such failure is not relieved in some four minutes. Further, it routinely does fail as the gas in a cylinder becomes used up, whereupon the anaesthetist then turns on another cylinder. It says a great deal for the attention, skill, and reliability of anaesthetists that accidents occur so rarely. That they do happen nevertheless is shown by two recent reports.^{1,2}

There are three groups of devices on the machine which help or can help the anaesthetist to avoid the patient becoming short of oxygen.

The first group is the indicators—for example, the oxygen pressure gauge, the flow meter, and the bag. This last in fact may be the only indication that the patient is breathing at all as sometimes patients are entirely covered by sterile cloths.

The second group consists of warning devices of which the Bosun is possibly the best known and is widely used. It is connected to the low pressure nitrous oxide supply by a pipe and tap, and gives a loud and continuous warning if the low pressure oxygen supply fails. There are two situations where the Bosun will not give a warning, with potential danger to the patient. It is possible, although not very likely, that the nitrous oxide cylinder will run out shortly before the same happens to the oxygen supply. There will then be no gas pressure available to blow the alarm. The other and far more likely situation arises when someone has forgotten to turn on the tap from the nitrous oxide supply to the Bosun, and the anaesthetist awaits its warning, which never comes.

In both the cases reported the Bosun would almost certainly have saved the patient's life had it been present, as it was on at least one of the two occasions, and had it been turned on. It is difficult to understand how the designer or those who recommended the Bosun for general use in the N.H.S. could have accepted the existence of this dangerous tap by which it can be turned off. It is equivalent to the insertion of a tap between a boiler and its safety valve. Those working nearby would feel less than easy knowing that the boiler might explode if the stoker forgot to turn the tap on. This tap in the nitrous oxide supply pipe to the Bosun converts a useful warning hazard device, which has certainly saved life, into an added anaesthetic hazard. As a matter of urgency this tap on every anaesthetic machine should be turned to "on" and the boss holding the cross bar by which it is controlled sawn off. This would take about five minutes work and would undoubtedly save life in the future.

The third group consists of safety devices, and the astonishing fact, so far as I have been able to discover, is that none exist. The essentials of an ideal anaesthetic safety device are:

- (1) It must be mechanically sound.
- (2) If it is present at all it must operate under all conditions of use and be incapable of being put out of action or turned off.
- (3) It must "fail safe."
- (4) There must be some mechanism such that it is automatically tested every time the anaesthetic machine is prepared for use.
- (5) In the event of oxygen failure not only must an efficient alarm be raised but also the machine must be effectively disconnected to leave the patients breathing air alone.—I am, etc.,

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- ¹ *British Medical Journal*, 1973, 3, 302.
- ² *The Times*, 31 August 1973.

Nephrotoxic Drugs

SIR,—The combined use of more than one nephrotoxic drug is best avoided where uncertainty exists as to possible additive toxic effects. This area of concern is complicated where a drug which is usually nontoxic may potentiate the nephrotoxic effect of another. The recent report of Professor J. P. Fillastre and associates (19 May, p. 396) implicates cephalothin (which is not nephrotoxic by itself) as a possible contributory agent along with gentamycin in the acute renal failure of three patients. Cephalothin has also been found to be nephrotoxic in rats primed with a subtoxic dose of glycerol.²

Looking at a different interaction, a protective effect of probenecid against cephaloridine (which is nephrotoxic by itself¹) has been reported by Child and Dodds.³ This is of particular interest because other organic anions are also protective,³ and renal cortical cephaloridine uptake is inhibited by this group of actively secreted organic anions.^{4,5} Thus there is evidence that though cephaloridine is not secreted by the kidney to any significant degree it is still actively transported into the proximal tubule cell, where it exerts its toxic effect.^{1,5}

The possible nephrotoxic property of cephalothin and the protective effect of organic anions against cephaloridine's known toxic effect raise two conflicting considerations:

- (1) That these two cephalosporin drugs share common nephrotoxic properties which may be additive, or
- (2) That cephalothin, which is also secreted by the organic anion transport system,⁶ may protect the kidney against cephaloridine by preventing its uptake by the proximal tubule.

We therefore further studied cephaloridine's nephrotoxicity in the rabbit using single subcutaneous injections as has been previously described.¹ Animals were killed 48 hours after the injection. Their kidneys were fixed in Bouin's solution and stained with hematoxylin and eosin. Animals given a subtoxic dose of 75 mg cephaloridine per kg body weight and either 200 mg/kg cephalothin intramuscularly (100 mg in saline) or the same volume of isotonic saline showed no cellular necrosis (2 animals each). A second group of animals was given 100 mg/kg cephaloridine and either 300 mg/kg cephalothin or a like volume of isotonic

saline (2 animals each). Mild-to-moderate proximal tubular cell necrosis was seen in those animals which received cephaloridine and saline, while no necrosis was seen in those which received cephalothin at the same time.

Fully toxic doses of cephaloridine (200 mg/kg) were therefore given to 33 rabbits, which were broken down into three groups. Fifteen control animals were given intramuscular saline in the volume used to administer cephalothin to experimental animals. Two groups were given cephalothin, 1000 mg/kg intramuscularly at the same time as or 30 minutes following the cephaloridine (9 rabbits each). This dose was selected because the same quantity of benzylpenicillin was required to completely inhibit cortical cephaloridine uptake in previous studies.⁴

The results are tabulated below:

	Proximal tubule cell necrosis			
	None	Mild	Moderate	Severe
Cephaloridine alone	0	0	0	15
Cephalothin simultaneously	9	0	0	0
Cephalothin 30 minutes later	4	4	1	0

When one is choosing between cephalothin and cephaloridine as a parenteral cephalosporin the former is preferable, because of its lower toxicity compared to that of cephaloridine.¹ However, because cephaloridine is less painful and because it can be given less frequently, it is often used when an intramuscular route is chosen. Occasional circumstances may therefore lead to the two drugs being given in sequence. Though cephalothin protected against cephaloridine's nephrotoxicity in these studies, these results do not necessarily establish that a similar interaction would occur if the two drugs were given together or in sequence to man.

We only wish to emphasize another aspect of the complex interactions which drugs may exhibit and to further illustrate the importance of Child and Dodds's initial observation with probenecid. Finally, we wish to emphasize the importance of applying known biological principles to such observations. We hope these findings will stimulate further research in this area.—We are, etc.,

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¹ Perkins, R. L., Apicella, M. A., Lee, I., Cuppage, F. E., and Saslaw, S., *Journal of Laboratory and Clinical Medicine*, 1968, 71, 75.

² Linton, A. L., Bailey, R. R., and Turnbull, D. I., *Canadian Medical Association Journal*, 1972, 107, 1414.

³ Child, K. J., and Dodds, M. G., *British Journal of Pharmacology and Chemotherapy*, 1967, 30, 354.

⁴ Tune, B. M., *Journal of Pharmacology and Experimental Therapeutics*, 1972, 181, 250.

⁵ Tune, B. M., and Fernholt, M., *American Journal of Physiology*, in press.

⁶ Lee, C., Herr, E. B., Jun., and Anderson, R. C., *Clinical Medicine*, 1963, 70, 1123.

Hypotension in Tetanus

SIR,—I read with interest the paper by Dr. J. L. Corbett and others entitled "Hypotension in Tetanus" (25 August, p. 423).

In my experience, hypotension is a dramatic and sometimes fatal complication in the course of tetanus. Episodes of hypotension