response curve. However, this shift was less than half that seen with pethidine alone and it was not statistically significant. The antagonism of pethidine-induced depression provided by doxapram lasted as long as the depressant effect of pethidine. As doxapram is metabolized rapidly this finding was unexpected.

The projection of the findings of Gregoretti and Pleuvry (1977) to man is unwarranted. Furthermore the studies in man described above support this conclusion.

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Bruce, R. B., Pitts, J. E., Pinchbeck, F., and Newman, J. (1977) to man is unwarranted. Furthermore the studies in man described above support this conclusion.

REFERENCES


Sirs,—Before replying to the letter from Drs Winnie and Funderburk, I should like to restate the final paragraph of our paper (Gregoretti and Pleuvry, 1977).

"It is hoped that this interaction is murine-specific, but in view of the current vogue for morphine–doxapram mixtures and reports of doses in excess of 1 g being used in man (Newell et al., 1969) it may be advisable to limit doses until the situation has been clarified."

We have not suggested that this interaction does not occur in man. However, we do not have any evidence that it does not, and this was the reason for the note of caution in our paper.

The fact that morphine and doxapram mixtures have been used by many workers with no apparent toxic effects does not prove that our data in the mouse are necessarily irrelevant to man. The lethal dose of doxapram in mice depended upon the dose of morphine given. Thus, if our results are relevant to man, I would expect to see problems only when large doses of doxapram are used to reverse large doses of narcotic analgesics.

In their letter, Drs Winnie and Funderburk have discussed interactions between doxapram and narcotic analgesics with respect to respiration and analgesia in man. I have no evidence from my rodent studies that the site of the toxic interaction between morphine and doxapram is the respiratory system. Indeed, more recent studies in this laboratory have shown that the cardiovascular system is a more likely site of the interaction. In mice and rats morphine, by a mechanism which is as yet unclear, increases the intrinsic ability of doxapram to produce conduction defects in the heart. In sub-lethal doses these effects may be seen only by monitoring the e.c.g. The cardioxicity of high doses of doxapram has been reported also in the cat (Polak and Plum, 1964).

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REFERENCES


ANAESTHESIA WITH PROFOND HYPOTENSION FOR MIDDLE EAR SURGERY

Sirs,—I have read with interest the article on this subject by Dr A. R. Kerr (1977), but I was surprised that the e.c.g. was not used as part of the monitoring technique to detect dangerous arrhythmias, myocardial ischaemia and the onset of cardiac arrest during profound induced hypotension, even in the physically fit patient.

While the critical closing pressure of healthy coronary arteries may be as little as 15 mm Hg, which may be reduced during induced hypotension according to the Law of La Place, I do feel that some reserve should be retained and in my view the systolic arterial pressure should not decrease below 50 mm Hg at the level of the heart except for very brief periods such as to facilitate the clipping of a cerebral aneurysm.

Should the systolic arterial pressure be allowed to decrease to 30 mm Hg it will be no greater than that in the pulmonary artery or that at the arteriolar end of a capillary, and all reserve will have been lost.

In my experience, it is possible to obtain dry operating fields for middle ear surgery using halothane to produce arterial systolic pressures of 55–60 mm Hg at heart level, provided posture and IPPV are utilized and practolol used to correct tachycardia or ventricular arrhythmias.

If the very high PaCO₂ values mentioned in some of the patients in the series were higher than the arrhythmia threshold for halothane, it is possible that some patients developed dangerous ventricular arrhythmias which passed unnoticed but which could have been prevented by IPPV or treated with a cardioselective beta-blocking drug.

The total absence of morbidity or mortality in the series is commendable, but it may lead some anaesthetists into a false sense of security.

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REFERENCE