


It should be noted that Dr. Simpson's review on perioperative blood loss was commissioned originally as part of a Postgraduate Educational issue, devoted to various aspects of haematology. Some 10-11 articles were commissioned and some of these would have dealt in great detail with the other methods of decreasing blood loss, referred to above by Dr. Appadu. Unfortunately, however, most of these reviews failed to materialize and it was not possible to produce a single issue. Thus Dr. Simpson's article covered only the area requested of him by the Editor of Educational Reviews.

**PRE-EMPITIVE EXTRADURAL ANALGESIA**

Sir,—In their letter, Dr. Wilder-Smith and colleagues [1] ask an important question which neither they nor the replying letter [2] address. Why do yet further studies fail "to produce the results expected from previous experimental work" [3]? In relation to pre-emptive analgesia?

This previous experimental work with the concept of "pre-emptive analgesia" and related concepts such as "wind-up" were derived in neurophysiological laboratories in which stimuli are applied to (often neonatal and often decerebrate) animal spinal cord preparations [4], and responses such as the spinal output of neurons including ventral horn (motor) cells [4] measured. In order to obtain the so-called pre-emptive analgesia in rats "low-dose" morphine (0.5 mg/kg) is used, as opposed to larger doses (5 mg/kg) needed to suppress this effect when the drug is given after the stimulus [5]. Such industrial doses have no relevance to the study of pain or the response of analgesics in man. Pain is measured. In our study, there was a wide variation in the metabolic response within groups, but there was no significant difference between the two groups. As a result of a different assay technique, our IL-6 results are substantially greater and cannot be compared directly with those of Joris and colleagues. Furthermore, in our study, the CRP response after laparoscopic cholecystectomy was more than twice that found by Joris and colleagues. Given that there is wide variation in the magnitude of the metabolic response to surgery, it is not surprising that studies with small patient numbers can produce such different results. In the study of Joris and colleagues, patients were not allocated randomly to groups. Patient selection bias may, therefore, account for the difference in findings.

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