siivity. Furthermore, it is hardly possible to draw clear conclusions from the rather fragmentary data reported for man (see cases reviewed in the Addendum by Ablitt, case report by Wilson, and review by Green), which are greatly complicated by polypharmacy and grave illness, particularly tetanus and leukemia. There appears to be a lack of information about the safety of prolonged exposure to nitrous oxide under other conditions in man, and it may be that we are overlooking a drug that would be valuable in preventing needless suffering in patients undergoing prolonged artificial ventilation. The problem will be resolved only by careful study of patients under the relevant clinical conditions.

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In reply:—It is a pleasure to respond to the letter of Drs. Nunn and Sturrock. Their studies of the cellular effects of anesthetics have established the standard for all workers in this exciting field. They raise three concerns: The first is the lack of details in our recent publication on the use of intermittent nitrous oxide. In that paper, we cited our earlier publication as a reference for the method. The second concern relates to our citation of their paper suggesting an effect of nitrous oxide on the growth of bone marrow stem cells in culture. After rereading their paper, I remain with the impression that cell suppression by nitrous oxide alone was nearly significant, suggesting a subthreshold concentration for this model. Thus, when mixed with subthreshold halothane, the occurrence of an additive effect was not surprising. Nevertheless, I will accept their statement that “nitrous oxide, 75 per cent, had no significant effect on growth.” The third relates to fear, possibly needless, of prolonged use of nitrous oxide in man. Some of our experiences regarding its safety for prolonged use as an analgesic in man were previously reported. We concur that the safety of nitrous oxide for prolonged use should be reviewed.

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References


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Anesthesia Does Not Cause Metabolic Stress

To the Editor:—In their otherwise excellent review, Drs. Blackburn, Maini and Pierce state that: “the induction of anesthesia initiates the (metabolic) response to injury, while most surgical procedures 60 to 90 min in duration do not augment this stress further.” We believe that this statement is not correct. First, the documentation given for the above statement is incorrect, since the article referred to deals with the extent and composition of postoperative weight loss. Second, several studies have shown that anesthetic
agents *per se* play only a minor role in the observed hormonal changes seen during surgical procedures 60 to 90 min in duration. Existing evidence would suggest that anesthesia is not an important initiator of endocrine-metabolic alterations during or after surgical stress.

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Hypovolemia and Hypotension with Carcinoid Syndrome

To the Editor:—We have read with great interest the case report of the anesthetic care of a patient with carcinoid syndrome by Drs. Patel et al. We have had considerable experience anesthetizing patients with carcinoid syndrome and would like to call attention to one very important aspect of anesthetic care, namely, the preoperative treatment of dehydration and hypovolemia. Hypotension is the greatest problem for the anesthetist during and after operations on patients with carcinoid syndrome. Some decrease in blood pressure occurs in all patients owing to the vasodilator effects of virtually all anesthetics. Preoperatively, these patients often have severe diarrhea as well as hypertension, both of which will promote dehydration and extreme hypovolemia. The clinical findings of hypovolemia are poor tissue turgor, slow capillary refill, and a marked decrease in the amount of urine per 24-hour period. Fluctuations in blood pressure may occur during handling of the tumor, but these do not necessarily lead to hypotension when there is a sufficient circulating blood volume, ensured by vigorous preoperative fluid therapy.

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REFERENCES


Dose Limits to Acute Nitroprusside Therapy Challenged

To the Editor:—We wish to comment on a letter by Professor Katz. Our suggestion for a maximum dose of sodium nitroprusside (SNP) of 1.5 mg/kg was made on the basis of reported blood cyanide levels in cases of deliberate cyanide poisoning and SNP overdosage. We concluded from these cases that plasma cyanide levels of about 10 μmol/l could be lethal and levels below this might well prove toxic during the inevitably prolonged exposure to cyanide during SNP infusion. Indeed, the fact that *in vitro* the terminal respiratory enzyme cytochrome oxidase is inhibited by 50 per cent by 1.5 μmol cyanide/l makes a lower toxic plasma level very likely. It is probable that there would be a concentration gradient between plasma and tissue, and an upper limit to plasma cyanide levels of 3 μmol/l was suggested. Work in patients demonstrated a correlation between total dose of SNP and plasma cyanide levels, and extrapolation of these results indicated that 3 μmol cyanide/l plasma could result from a total dose of 1.5 mg SNP/kg for hypertensive anesthesia of short duration. Our work in dogs, soon to be reported, indicates that this