Evidence for In vivo Biotransformation of Nitrous Oxide

To the Editor:—Dr. Linde and Dr. Avram1 pose the question: “Can mammalian systems biotransform \( \text{N}_2\text{O} \)?” I think the answer must be yes. It is known that nitrous oxide can oxidize the cobalt moiety of vitamin \( \text{B}_12 \) to its bivalent form in vitro.\(^2\) It has been clearly established that methionine synthesis is inhibited when rats or humans breathe 50 per cent nitrous oxide for several hours,\(^3,4\) and there can be little doubt that this must be due to oxidation of \( \text{B}_12 \) occurring in vivo as it also happens in vitro. Demonstration of the biotransformation of nitrous oxide by this mechanism is difficult. Even if all the \( \text{B}_12 \) in the body was oxidized (and this does not appear to be the case), the quantity of nitrous oxide required would still be much less than 1 ml, and the detection of this small amount of \( ^{15}\text{N}_2 \) formed from \( ^{16}\text{N}_2 \text{O} \) would be virtually impossible in view of the substantial background level of \( ^{16}\text{N}_2 \) in the atmosphere.

Asystole after Intravenous Dantrolene Sodium in Pigs

To the Editor:—The recommended method of administering dantrolene sodium for malignant hyperthermia (MH) crisis in patients is 1 mg/kg, iv, rapidly, then continuing to 10 mg/kg if needed. Animal studies report no appreciable effect on the heart at these doses in one study\(^1\) and cardiac depression in other studies.\(^2,3\)

We have had two 35-kg MH positive pigs die from intravenous dantrolene administered during an MH crisis. One pig received a 10-mg/kg dose as a bolus; the other pig received a total dose of 30 mg (0.43 mg/kg) of dantrolene prior to arrest. Both pigs were in sinus rhythm (rate 130–140) prior to the dantrolene, but developed severe sinus bradycardia followed by cardiac arrest from asystole during the dantrolene administration. The first pig may have been given dantrolene in too high a concentration and too rapidly, but the second pig had an abrupt asystole while the dantrolene was being titrated and arrested after 30 mg was given. Neither pig was collapsing.