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In reply:—Dr. Skacel and co-workers have drawn attention to methodologic problems related to deoxyuridine (dU) suppression test. They note that the use of autologous serum in the incubation of marrow cells may produce conflicting results, depending whether the serum used was obtained before or after the administration of folate to the patient. We encountered this difficulty particularly in the present study since we were comparing patients before and after folate administration. To combat this methodologic difficulty, we did not use autologous serum, but rather used Hank's solution throughout our investigations. By doing this, we sacrificed a degree of sensitivity in order to obtain consistency in the test. Experiments done in our laboratory have confirmed that Hank's solution gives the same trends as does autologous serum. Although the overall results were lower, the diagnostic value of the test was maintained since each dU suppression test is controlled internally.

Skacel *et al.* have been unable to confirm our findings that folic acid given before prolonged nitrous oxide (N₂O) anesthesia prevents the development of megaloblastic hemopoiesis. We have no explanation for their results. The marrow slides derived from our patients who were given prophylactic folic acid which were

reported blind by one of us (S. McC) showed no evidence of megaloblastosis following 24 h N₂O anesthesia. Whatever the methodologic problem associated with the dU suppression test in such sequential experiments, such should not be the case for the presence or absence of megaloblastic changes in the marrow. In view of the very clear-cut nature of our results in this regard with six patients, it would seem difficult to explain this group's result on their one long-term N₂O-treated patient. We await with interest to see if they find megaloblastic changes in other patients pretreated with folic acid prior to N₂O anesthesia.

H. O'SULLIVAN, B. SC.
F. JENNINGS, M.B.
S. R. MCCANN, M.R.C.P.I.
K. WARD, M.R.C.P.I.
J. M. SCOTT, PH.D.
D. G. WEIR, M.D., F.R.C.P.I.
*Department of Gastroenterology
Federated Dublin Voluntary Hospitals
Sir Patrick Dun's Hospital
Dublin 2, Ireland*

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