confirmed and cholecystectomy carried out. Operative cholangiography was normal and an explanation for the chronic pelvic pain was provided by the finding of bilateral hydro-salpinges.

On reviewing the limited literature concerned with opioid-induced biliary colic, it would appear that case reports relating to this problem all concern patients who have had or are about to have biliary surgery [1–3]. This raises the possibility that opioid-induced colic is not a pharmacological response, but rather biliary tract pathology is a pre-requisite for it to occur. Biliary pressure studies have demonstrated biliary hyper-tension and spasm of the sphincter of Oddi as a common consequence of opioid administration. The results of these studies may be misleading as, by necessity, the measurements are made during the course of cholecystectomy (i.e. there is proven biliary disease) and, furthermore, pressures are measured by cannulation of the cystic duct (after the gall bladder has been removed), which is not a particularly physiological situation [4–6]. This view point is endorsed by canine studies which revealed that biliary pressures did not change in healthy dogs following administration of opioids unless the gall bladder had previously been removed [7]. This raises the possibility that the gall bladder is functioning as a pressure valve and limiting opioid-induced effects. On the basis of these observations, we would suggest that it is perhaps only those patients with an absent or non-functioning gall bladder who are at risk of opioid-induced colic. It may be, therefore, prudent to investigate the biliary tract in such patients rather than to dismiss the problem as a pharmacological response.

N. J. Saunders
C. J. Levy
Sheffield

REFERENCES

SUXAMETHONIUM AND INTRAOCULAR PRESSURE

Sir,—After reading the paper on the changes in intraocular pressure changes during induction and intubation associated with the administration of thiopentone or propofol [1], I felt that an important result of the study was rather ignored.

The results in table II clearly show that the combination of induction and suxamethonium did not cause a significant increase in intraocular pressure in any group when compared with baseline values. However, the authors preferred to use the post-induction values of intraocular pressure, and to state—in the summary—that there was a significant increase in intraocular pressure following suxamethonium. Yet the authors used baseline intraocular pressure as their reference point to comment on the lack of a significant increase in intraocular pressure with the combination of a second dose of propofol and intubation. (The use of the “post second dose induction value” of intraocular pressure, a reference point similar to that used when stating the significant increase in intraocular pressure with suxamethonium, would of course have given the result of a significant increase in intraocular pressure.)

Surely, the authors should be consistent (with reference points) when using statistics to conclude the possible beneficial effect of certain therapeutic measures. If it is “true” that a second dose of propofol protected against the increase in intraocular pressure secondary to intubation, then it is also “true” that suxamethonium did not cause an increase in intraocular pressure.

When considering the problem of how to maintain a stable intraocular pressure during induction and intubation, surely both these facts are equally important.

L. EDMONDSON
London

REFERENCE

Sir,—Thank you for giving me the opportunity to reply to Dr Edmondson’s letter. While Dr Edmondson is correct in pointing out that we used the post-induction value intraocular pressure (IOP) for comparing the increase in IOP after suxamethonium administration, it was clearly stated in the text that, even after suxamethonium administration, the IOP was never significantly greater than the baseline value. The use of post-induction values after suxamethonium was used purely to show the increase that occurs in IOP following suxamethonium. Yet the authors preferred to use their baseline IOP as their reference point to comment on the lack of a significant increase in IOP after suxamethonium administration. Further, it was stated in the results section of our paper, that intubation did increase the IOP in all groups, although the IOP in the supplementary-dose propofol group did not exceed the baseline value.

R. K. Mirakhur
Belfast

ANTI-NEOPLASTIC SYNERGISM OF NITROUS OXIDE AND METHOTREXATE

Sir,—The review article by Nunn [1] mentioned a suggestion by Ueland and co-workers [2] that the side effects associated with methotrexate could be increased, and the efficacy of leucovorin rescue be decreased, by anaesthetic regimens in which nitrous oxide is used. They further suggested that, until these possibilities have been rejected “... nitrous oxide should be used with caution in patients receiving methotrexate”.

Nunn went on to suggest that this theoretical problem has not been investigated. However, there is some work which indicates that, far from causing problems in association with
methotrexate, nitrous oxide may well have a positive synergistic action. For instance, it has been shown in vitro that a combination of nitrous oxide and methotrexate was more effective in depleting functional folate than either agent alone, indicating the possibility that these agents might act synergistically as anti-neoplastic agents in vitro [3]. Furthermore, whilst the rescue effect of 5-methyltetrahydrofolate is diminished following exposure to nitrous oxide, this was not the case with 5-formyltetrahydrofolate (folinic acid) [4].

Such a finding is not unexpected, since both nitrous oxide [1, 3, 5] and methotrexate [3, 4, 6] appear to disrupt steps in folate metabolism only before the formation of folinic acid. It is, therefore, not surprising that, according to Ueland and colleagues [2] the "rescue therapy seems to work in children exposed to nitrous oxide". Indeed, this rescue effect of adequate doses of folinic acid has been shown quite clearly to prevent megaloblastic bone-marrow changes in most human subjects following extended analgesic and anaesthetic exposures to nitrous oxide [1, 7]. It would appear, therefore, that the presence of nitrous oxide is unlikely to have an effect on the rescue effect of leucovorin, whilst possibly having a positive anti-tumour action through its synergism with methotrexate [3].

Therefore, far from decrying the use of nitrous oxide in conditions sensitive to folic acid antagonists (such as methotrexate), the possibility of using these agents in combination with the gas should be further investigated. Such investigations could lead to better disease control or reductions in the doses of methotrexate used. Apart from its synergistic anti-neoplastic effect in this context, nitrous oxide would have the further advantage of being an excellent analgesic [8].

M. A. GILLMAN
Johannesburg

REFERENCES


CATHETER EROSION OF VESSEL WALLS

Sir,—Recently, I observed an interesting series of events in a cachectic elderly male patient suffering from chronic pancreatitis. He had been admitted to an Intensive Therapy Unit on account of pulmonary oedema, and for parenteral nutrition to improve his condition in anticipation of further surgery. A 16-gauge Teflon catheter was sited in the left internal jugular vein (after blockage of a catheter in the right side). Approximately 48 h later, the patient complained of chest pain; this was mainly central, but with some associated discomfort in the left shoulder. Clinical examination was normal, as were an ECG, chest radiograph and arterial blood-gas tensions. Dextrose 50% was being infused through the central venous catheter, from which blood could be freely obtained by gravitational reflux.

Pulmonary embolism or myocardial ischaemia was suspected. Sublingual glyceryl trinitrate was given, and the patient’s pain appeared less. He was instructed to bite, and retain orally, a capsule of nifedipine, but this provided no further benefit. Morphine was then given slowly i.v. until he was comfortable (total 17 mg). He slept for the remainder of the night, during which time Intralipid as well as dextrose was given through the internal jugular catheter.

A chest radiograph obtained the following morning, approximately 12 h after the onset of pain, showed a large left-sided pleural effusion (fig. 1). This was tapped and 200 ml of milky fluid obtained. Although blood could still be aspirated from the central venous catheter, it was removed. A chest drain was inserted, from which over 900 ml of milky fluid drained during the following 24 h. There were no further complications.

This report demonstrates that the ability to aspirate blood from a central venous catheter is not an absolute guarantee that a subsequent injection or infusion will be i.v. Presumably, the tip of the catheter eroded the vein, so that the catheter opening lay partly within the vein and partly within the pleural space.