blurred vision as a result of oral omeprazole, but no data are presented for these. The other cases had been found by the experts of the Committee for Proprietary Medicinal Products to have ischaemia resulting from their primary disease, not from omeprazole. It is not possible to determine the cause of anterior ischaemic optic neuropathy in the new cases (6 and 7) from the data presented by Schönhöfer et al. That this neuropathy is unilateral shows that it is not related to a systemic drug, which would be expected to affect both eyes.

The authors attempt to relate these cases to a role of the acid pump of the stomach in vascular smooth muscle. The gastric potassium-hydrogen ATPase is present in the stomach in large quantities and in the distal renal medulla at very low levels, but no other location for this pump has been found, even with modern molecular biological techniques. The reference quoted as providing evidence for the gastric potassium-hydrogen ATPase in vascular smooth muscle used various pharmacological agents before these more modern methods were available and drew incorrect conclusions. Schönhöfer et al say that inhibition of the pump supposedly present in the vasculature would result in intracellular acidification. The sodium-hydrogen exchanger would prevent such acidification even if the pump were present.

The amino acid target, cysteine 813 of the catalytic subunit of the gastric potassium-hydrogen ATPase, is absent from other ATP driven ion pumps. The action of omeprazole depends both on accumulation due to a highly acidic space and on acid catalysed conversion to the active drug. These factors are absent in the vasculature. Hence, neither the target molecule nor the mechanism necessary for an action of omeprazole is present at the site suggested by Schönhöfer et al as explaining the anterior ischaemic optic neuropathy.

The ocular events reported in cases 6 and 7 are probably not related to omeprazole. The absence of causality between the use of proton pump inhibitors and visual disturbances continues to hold true.

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1 Schönhöfer P, Werner B, Tröger U. Ocular damage associated with proton pump inhibitors. *BMJ* 1997;314:1805. (21 June.)

Author's reply

Editor—Riordan-Eva and Sanders miss a diagnostic differentiation between anterior ischaemic optic neuropathy and demyelinative optic neuritis. All patients had computed tomography or nuclear magnetic resonance imaging, or both, to exclude demyelinative or other diseases. Furthermore, linking anterior ischaemic optic neuropathy to gastrointestinal ulcers does not explain why the neuropathy was not seen in patients treated with other anti-ulcer drugs. Our hospital based monitoring system would certainly have signalled such cases, as it did with proton pump inhibitors.

Lessell regards our hypothesis of omeprazole induced optic neuropathy as ill founded. However, he stated in a letter to Merck in 1994 that case 1 "might well be a toxic drug-effect of intravenous Antra." It is surprising that the experts of the Committee for Proprietary Medicinal Products changed the diagnosis in case 6 from anterior ischaemic optic neuropathy to demyelinative optic neuropathy without contacting the hospital and checking the clinical records, which clearly argue against these experts' interpretation.

Arteritis, also in nervous tissue, was described in toxicological studies with lansoprazole in dogs and discussed with respect to similar findings with other substituted benzimidazols.[1] Various effects of omeprazole on human brain function are described.[2] Vasoconstriction and disturbance in transcellular transport mechanisms may be involved due to inhibition of ATPases. Therefore, irreversible visual disorders (anterior ischaemic optic neuropathy, for example) may arise from ischaemia in the distribution territory of endarterioles and capillaries in the optic nerve tissue.

Sachs reiterates what he has often said at Astra's press conferences. Drug companies and their experts use lack of causality in defending a product and to discredit reports of adverse effects. There is no causal explanation for the antidepressant effect of tricyclic agents, the antipsychotic effect of neuroleptics, or the sedative effect of barbiturates; there is only an association between the drugs and the desired result. This is sufficient to grant therapeutic efficacy. The same applies for unwanted effects. Visual disturbances and anterior ischaemic optic neuropathy occur in patients treated with proton pump inhibitors but not in those treated with other anti-ulcer drugs. This association does not disappear simply because experts declare that the events are not related causally. Such causality rating is misused as a bureaucratic safety measure.

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1 Schlaeppi B, Roncari G, Zahn P. Vascular toxicity in dogs associated with overdoses of a novel benzodiazepine receptor partial agonist. *Arch Toxicol* 1991;65:73-80.
2 Meeuwisse EJM, Groen FC, Dees A, Smit GH, Ottervanger JP. Lethargy with omeprazole. *BMJ* 1997;314:481.

Reducing morbidity from insertion of chest drains

As few sharp objects as possible should be used on entering pleural space

Editor—Peek and Firmin's letter about attempted drainage of the pleural space raises a pertinent point: that an expanded lung is at risk of injury from any sharp object in its proximity.[1] But two caveats must be borne in mind. Just because a lung is subject to positive pressure ventilation does not mean that it is expanded, and a lung removed from positive pressure ventilation may be perilously close to an oncoming scalpel, forceps, or trocar.

Lung collapsed due to proximal airway blockage or compressed by effusion or tension pneumothorax may well not be subject to the volume change that a normal lung undergoes with positive pressure ventilation. Furthermore, lung encased in a pleural space containing organising blood or adhesions due to infection may never collapse away from the chest wall on release from positive pressure ventilation.

The main lesson would seem to be to use as few sharp objects as possible on entering the pleural space. In addition, operators should become experienced in using a finger in clearing away lung from the site of insertion of the chest drain once the pleura has been breached.

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1 Peek GJ, Firmin RK. Reducing morbidity from insertion of chest drains. *BMJ* 1997;315:313.(2 August.)

Disconnecting patient from positive airways pressure is not always possible

Editor—Peek and Firmin state that "it is essential to disconnect the patient from positive airways pressure as the pleura is breached" during insertion of a chest drain in ventilated patients.[1] This may not always be practical.

Patients who develop pneumothoraces while ventilated often have precarious oxygenation, with critical levels of inspired oxygen and positive end expiratory pressure. Even transient disconnection from the ventilator may lead to profound hypoxia, which may not simply respond to reconnection. The reintroduction of positive end expiratory pressure to predisconnection levels has to be titrated to minimise distension of alveoli (hyperinflating non-compressed lung and hence increasing physiological dead space) and reduce the incidence of further barotrauma.[2] This may take several minutes and render the patient profoundly hypoxic. The reduction in the risk of lung injury may not therefore offset the gas exchange problems generated by the procedure. Similar considerations apply if the patient is being treated with inhaled nitric oxide.

One alternative is to keep the patient connected to the ventilator and manually pause the ventilatory cycle during expiration. Thus achieves the desired effect of allowing the lung to fall away from the pleura but without disruption of the gas supply or positive end expiratory pressure.

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1 Peek GJ, Firmin RK. Reducing morbidity from insertion of chest drains. *BMJ* 1997;315:313. (2 August.)
2 Burchardi H. New strategies in mechanical lung ventilation for acute lung injury. *Eur Respir J* 1996;9:1063-72.