In his review of my book (3 September, p 629) Professor T J Hamblin stated, "In [Fleming's] view a device to perfuse a human head might lead to his reputation, and he has developed a fendish plan to prevent one being developed." That is incorrect. As stated in the book, the technology for perfusing a severed head has important potential advantages, for research and for prolonging life in a conscious and communicative state with, probably, less pain than many dying people suffer today. The difficult question is whether the advantages outweigh the disadvantages and dangers. Therefore, instead of trying to stop the research, let us propose a system where any scientist or surgeon who wants to try the experiment in America, on either animals or humans, will need to consult three independent review panels that already exist at every university: animal care committees, which control experiments on animals; institutional review boards, which must approve experiments on human subjects; and institutional biosafety committees, which control genetic engineering projects.

Some review panels are likely to approve such proposals, since perfusing intact heads will allow researchers to study the brain and sensory organs in ways that cannot be accomplished otherwise. This chemistry and medical technology could be the basis for open debate, moderated and judged by impartial experts who have nothing to gain personally from the research.

The reviewer also suggested that only one experiment had been done to keep a severed head alive. In fact, many such experiments have been reported in scientific journals. In the experiments by White et al transplanted monkey heads remained fully conscious for 36 hours.1 They died because of hepatic overuse, a problem which can be overcome today using an extracorporeal hepatic remover. Research is being done today on intact brains which continue to generate brain waves after the severed organs and the skull have been cut away.

It is far more difficult to obtain a prophetic patent in America than Professor Hamblin suggests. Such patents usually must be limited to mechanical systems, since mechanical components are more predictable than chemical reactions or experimental drugs. Every component must be publicly available and the inventor must describe explicitly how to assemble and use them. If I hadn’t been a patent attorney specialising in biomedical and medical technology, I would have killed the idea.

It isn’t spent hundreds of hours researching each component and consulting surgeons and biochemists I couldn’t have obtained the patent. You left out the other part of the question: Would anyone want the operation? I have been contacted by half a dozen people who want to know how soon the operation will be available and how much it will cost. Some are dying; others are paralysed. Most said that if they were given the chance to have their head brought back, they would take it. They would remember, see, read, hear, and talk if the operation leads to numbness rather than pain below the neck then they would want it.

Drug Points

Phenytoin interaction with rifampicin

Dr F J ARAJO and others (Hospital del Insalud “La Paz,” Madrid) followed closely a 68 year old man being treated with phenytoin 600 mg daily and ethambutol 1200 mg daily for pulmonary tuberculosis as admitted to hospital. He had a history of idiopathic focal seizures, which had been successfully treated with combined phenytoin and phenobarbitone. As he had been virtually free of seizures for two years, however, the treatment had been withdrawn nine months before admission. Phenytoin treatment was restarted as monotherapy, and the patient was counselled to obtain adequate control. Serum concentrations of phenytoin ranged from 17.3 mg/l to 18.2 mg/l (therapeutic range 10-20 mg/l) as measured by the enzyme multiplied immunosorbent technique (coefficient of variation between days was <6%).

Two weeks before completing his treatment for tuberculosis, when he had been taking 400 mg the phenytoin for eight weeks, the dose of phenytoin was reduced to 375 mg. The serum phenytoin concentration fell from 44.4 mg/l but it rose to 22 mg/l in the second week. The ethambutol dose was then reduced to 350 mg, but the serum concentration continued to rise, reaching values above the therapeutic range (22.1 mg/l). Reversal of treatment was proposed.

Dr CF TAY, Edinburgh

Delirium induced by atenolol

Dr N ARBER and others (Belinim Medical Centre, Peta Tisqa, Israel 49100) write: Psychiatric disturbances have rarely been associated with atenolol treatment.1 We report an acute episode of delirium in a patient taking atenolol that was completely reversed after the treatment was withdrawn.

An 85 year old woman who did not have a psychiatric history was admitted with rapid atrial fibrillation. She had had angina that was stable and chronic atrial fibrillation. She was treated with atenolol 50 mg twice a day, isosorbide mononitrate 20 mg twice a day, and diltiazem hydrochloride 30 mg four times a day. Physical examination disclosed an irregular heart rate (120 beats/minute) and a blood pressure of 135/80 mm Hg. The urine culture was negative; the 83 year old patient had a body temperature of 36.4°C; her mental and haematochemical state were normal on examination. Atenolol was increased to 100 mg twice a day. Eight hours later she became violent and confused; she had visual hallucinations and paranoid thoughts. Consultation by an psychiatrist suggested that the diagnosis was delirium induced by the drug. A metabolic cause could not be found for the change in her mental state, she was haemodynamically stable, and findings on electroencephalography and brain computed tomography were normal. Atenolol was replaced by amiodarone, and within one day her mental state had returned to normal. She subsequently refused rechallenge with atenolol.

Delirium is usually associated with infections, drug reactions, metabolic changes, drug withdrawal, compensation, trauma to the head, or cerebral insufficiency, especially in the elderly.2 β Blockers, especially propranolol, cause the organic brain syndrome.3 Penetration of the blood-brain barrier by atenolol is limited because of its hydrophilic nature, therefore its untoward effects on the system should be fewer compared with other β blockers. In this case the sequence of the development of the behavioural change after administration of a double dose of atenolol, rapid improvement after its withdrawal, and the absence of any evidence of other possible causes strongly suggest that atenolol may have played a part in the development of the delirium.

We know of only two other cases of the organic brain syndrome induced by atenolol,4 and in both the clinical features were similar to those in our case. Our report suggests that atenolol at high doses, despite being hydrophilic, must be considered among the drugs that may cause the organic brain syndrome. The phenomenon may be more common in the elderly as overdose induced by drugs is much more prevalent in this age group.


Fatal triazolam poisoning

Dr J J O'DOUGHLIN (East Glamorgan General Hospital, Pontypridd, Mid Glamorgan), P P SPARG, and A ROTA (Llandough Hospital, Vale of Glamorgan) write: Dr J P SUNTER and others (17 September, p 719) report three cases of death due to triazolam poisoning. We have recently seen a similar case in South Wales.

A 58 year old woman was being treated for depression and taking 0·25 mg triazolam at night. She had threatened to commit suicide by overdose; the previous night she had taken 10 mg and on the day of her death she ran into a neighbour's house and stated that she had taken 70 tablets. She collapsed, became unconscious, and died shortly after reaching the accident and emergency department.

A postmortem examination showed mild athero- sclerotic lesions in the anterior descending coronary artery with minimal narrowing of the left circumflex artery. The rest of the postmortem examination showed normal results, and therefore no anatomical lesion accounting for death was found. Toxicological tests showed a blood triazolam concentration of 870 nmol/l, a blood alcohol concentration of 105·0 mmol/l, and a serum creatinine of 130 mg/100 ml. The peak plasma therapeutic concentration of triazolam is reported to be 0·5 mmol/l.

This woman showed no gross or histological cause for her death, but she had taken an overdose of triazolam and had an alcohol concentration about one and a half times the legal driving limit. The balance of evidence in this postmortem was therefore judged as suicide, and death was therefore ascribed as a result of triazolam overdose associated with alcohol consumption.

It is often said that benzodiazepine poisoning is comparatively safe, but we would agree with Dr Sunter and others that patients who have taken an overdose of triazolam should be carefully monitored and that death can result from an overdose of this drug. We thank Mr A Davies, the coroner for Mid Glamorgan, and the southern district, for permission to report this case.


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