Pricing of orphan drugs

The Lancet’s leader on solutions to the research and development crisis for neglected diseases (Nov 22, p 1784) warns of a problem with the cost of orphan drugs, but this is already a reality.

An inherited defect of N-acetylglutamate synthetase was first described by Bachmann in 1981. N-acetylglutamate is an allosteric activator of carbamyl phosphate synthetase, the first step in the urea cycle. The disorder is very rare, although more cases have been diagnosed since the gene was identified. Bachmann introduced treatment with N-carbamylglutamate in 1982. The treatment is highly effective and must be continued for life.

N-carbamylglutamate is now licensed as an orphan drug, but the price has risen sharply. The current price of the unlicensed product is £11 (US$15) per g whereas the price of the licensed one is £262.90 ($367.30) per g. If the licensed preparation is used, the annual cost for a 10 kg child increases from £4015 ($5611) to more than £95 000 ($132 774). The reasons for the high price are not clear. Since the compound was already being used for this purpose, albeit unlicensed, the expenditure on research and development must be less than developing a medicine from scratch. When questioned informally by one of us (JVL), a company employee cited the cost of licensing and the small number of patients being treated.

The price of N-carbamylglutamate is now so great that patients risk being denied full treatment. It is clear that a robust mechanism is needed to set the price of orphan drugs, otherwise patients will be the ultimate losers.

Gulf war illnesses

In your Editorial of Nov 29 (p 1856) you repeat the conclusion of the “Binns committee” report, sponsored by the US Veteran’s Administration, to the effect that those who served in the 1991 Gulf war are at increased risk of ill health, and that it is unequivocally the result of injury to the brain or to the peripheral nervous system. The former conclusion is hardly new, and the latter is far from certain. We were the first to confirm, in this journal, that service in the 1991 Gulf war affected the subjective health of some UK service personnel, even though this effect did not amount to a new illness per se.

However, if either pyridostigmine bromide or pesticides were indeed associated with ill health, one would have expected a new “Iraq war syndrome” in UK Armed Forces as of 2003, since pyridostigmine bromide was again issued, and used, by 73% of UK forces during the invasion of Iraq, as it was in the 1991 Gulf war. Likewise, pesticides were again used to combat the threat of insect-borne disease. Yet despite the use of both agents by UK personnel, we found no evidence that history did repeat itself. The evidence implicating organophosphate agents in the cause of ill health in UK military personnel who deployed to the Gulf is far from compelling. We have found no evidence of peripheral neuropathy in UK personnel.

We agree with the Binns committee that psychological disorders are not the most plausible explanation for Gulf war illness. Given that there is no dispute that Iraq has proven to be a longer, harder, and more dangerous campaign than Gulf 1991, if frank mental health disorders were a major causative factor, then we would have found the opposite results to those that we reported. NG is a full-time active member of the Royal Navy. SW is partly funded by the South London and Maudsley NHS Foundation Trust/Ipswich Institute of Psychiatry NIHR (National Institute of Health Research) Biomedical Research Centre. However this submission was prepared independently and not subject to alteration by the Ministry of Defence or NIHR. We declare that we have no conflict of interest.

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