Methadone: evidence of accumulation

SIR,—We have recently been exploring the possibility of producing a controlled-release methadone tablet for the treatment of pain in patients with terminal cancer. We have used a controlled-release tablet that we have previously shown to provide a satisfactory bioavailability pattern, with a strong correlation between in-vitro and in-vivo release with aminophylline.[1] This controlled-release tablet formulation has also been shown to provide an effective method of drug delivery for papaverine[2] and glyceryl trinitrate.[3]

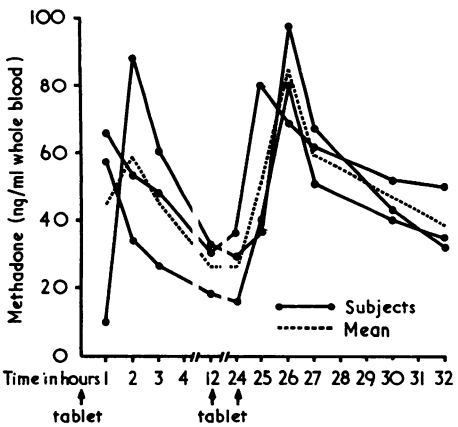
Methadone created unexpected practical difficulties since, although the drug is an effective analgesic for only some 4 h, the plasma half life has been variously reported to be 15 h[4] and 25 h.[5]

Our controlled-release methadone tablets containing 10 mg of methadone hydrochloride were prepared and a satisfactory in-vitro release pattern obtained. Three healthy volunteers were given one 10-mg tablet at 0, 12, and 25 h. Plasma methadone levels were measured at 0 hours and at 1, 2, 3, 6, 8, 12, 24, 25, 26, 27, 30, and 32 h.

Plasma methadone levels were determined after extraction on a Perkin Elmer F17 gas liquid chromatograph, using a 3% OV-17 on Gas Chrom Q column, with dieldrin as internal standard. Standard reference solutions used were methadone base and dieldrin at 20 ng/ml and 40 ng/ml respectively. This was modified from a method kindly provided by the Guy's Hospital Poisons Unit. (Further details of the method are available from the address below.)

As can be seen from the accompanying figure a satisfactory plateau level was obtained from the third hour onwards. However, marked peaking occurred 2 h after the third dose and, as can also be seen, there was firm evidence of accumulation. This would suggest that Inturrisi and Verebely[4 5] in their original estimates of the half life had considerably underestimated. Indeed, since we completed our study these authors have produced further work on the subject in which they suggest that methadone has a "slow secondary life" of 54·8 h.[7]

For these various reasons we have now abandoned the project. However, we felt that we should briefly publish our findings since methadone is widely used as a cough linctus in addition to its use as a narcotic analgesic and in the weaning of heroin addicts.



Blood methadone concentrations in three volunteers after repeated administration of controlled-release tablets each containing 10 mg of methadone.

Consequently we thought it important to bring this problem of accumulation to the general notice of the profession since it does not appear to be widely appreciated and could give rise to problems in clinical practice.

We have been encouraged to publish our findings by Dr R Twycross and by Professor D Vere and his colleagues Dr T B Binns and Dr A Herxheimer, and we wish to express our gratitude to them for their help and advice and also to Dr D Robinson for his assay method.

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[1] Boroda, C, *et al*, *Journal of Clinical Pharmacology*, 1973, **13**, 383.
[2] Miller, R B, *et al*, in preparation.
[3] Ikram, H, *Current Medical Research and Opinion*, 1976, **3**, 719.
[4] Inturrisi, C E, and Verebely, K, *Clinical Pharmacology and Therapeutics*, 1972, **13**, 923.
[5] Inturrisi, C E, and Verebely, K, *Clinical Pharmacology, and Therapeutics*, 1972, **13**, 633.
[6] Robinson, D, personal communication.
[7] Verebely, K, *et al*, *Clinical Pharmacology and Therapeutics*, 1975, **18**, 180.

Future of child health services

SIR,—It would be unfortunate if many people were to be misled, as have the Court Committee,[1] by faulty interpretation of the evidence. Dr M A P S Downham (22 January, p 227) is quite incorrect in his belief that epidemiological evidence supports their principles and proposals. Indeed, their use of a comparison of the rate of fall of infant mortality in England and Wales with those of Japan, France, Sweden, and Finland in such a way as to cause the unwary reader to infer that our slower rate of improvement is due to less adequate services is questionable.

The countries selected have enjoyed more rapid economic growth than has the UK. They have not had their infant mortality statistics inflated by substantial contributions from immigrants who have brought with them the mortality rates related to the dietary and cultural practices of their native lands. It may well be that if even half the resources needed to implement the proposals of the Court Committee were spent on improving nutrition (or preventing malnutrition) in girls of reproductive age we might see a greater reduction in perinatal and infant mortality due to a fall in incidence of low birth weight. Even if we accepted that this was a proper aim it has not been proved that "integration of preventive and curative services" contributes in any way to reducing mortality, nor that "continuity of health surveillance from fetal to adult life" would achieve this. Many of the suggestions made in the report have already been tried out in various places and found wanting, but the committee conveniently omits mention of these unpalatable facts.

Many people, however, would dispute their tacit assumption that reductions in perinatal and infant mortality are proper aims. There are good humanitarian grounds as well as sound economic reasons for rejecting them and substituting the "minimising of handicap" as our objective. This would be more appropriate to the needs of society and meet the wishes of most potential parents. The salvaging of damaged babies is an expensive way of imposing a continuing burden on parents, education and social service departments, the NHS, and the taxpayer, and is currently done in ways which impose additional handicaps on the child.

It is a great pity that this long-awaited report contains so many flaws. Its main recommendations are unsound and impossibly expensive; they are never likely to be implemented in full. Very many of the minor recommendations which are scattered (in italics) through the report are sound and wise. It would be unfortunate if the contempt earned by the rest of the report led to the rejection of the good as well as the bad.

Adoption of some of the minor recommendations combined with encouragement to authorities to experiment with alternative methods of developing and improving their existing service would permit considerable improvement in our services without any massive increase in cost and without the problems which a revolutionary change would inevitably throw up.

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[1] Committee on Child Health Services, *Fit for the Future*. London, HMSO, 1976.

SIR,—I read your leading article (25 December, p 1524) with great interest and found myself wondering how the proposals for the appointment of general practitioner paediatricians would affect my own work as a single-handed rural practitioner. Professor Donald Cout's report[1] suggests that I and two or three neighbouring practitioners would be joined by a GPP who would be responsible for the developmental supervision of the children in our practices.

As the care of these young patients is one of the delights and interests of our everyday work I would bitterly oppose such a move, for I would fear that the next logical step would be to relieve me of the care of my elderly patients and that general practitioner geriatricians will be appointed to assist me look after these equally interesting and rewarding patients.

If our standards of care are not up to those deemed proper by Professor Court's committee, surely an easier way to attack the problem is to train or encourage existing practitioners to raise their standards—after all, that is what is suggested for those chosen or who choose to become GPPs.

The attraction of general practice to most of us is that it is truly general and includes the whole family, if not from birth, at least from the cradle to the grave. Any new grade of practitioner would be detrimental to the general practitioners' role in the community and should. I would submit, be resisted.

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[1] Committee on Child Health Services, *Fit for the Future*. London, HMSO, 1976.

Rarity of non-accidental penetrating injury in child abuse

SIR,—Penetrating non-accidental injury as part of the syndrome of child abuse is extremely rare.

A 13-month-old child was admitted with no pulse or blood pressure and not responding to painful stimuli. Bleeding had stopped from a 2-cm stab