been associated with use of the same syringes in more than one patient [4]. This suggests that potentially severe infection can occur in patients on propofol infusions because of lack of aseptic technique.

The authors would recommend preparation of propofol infusions under aseptic conditions, the use of separate syringes and catheters for each patient and their replacement when the infusion requires changing.

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REFERENCES


SPEED OF ONSET OF ANALGESIA OF DIAMORPHINE OR MORPHINE

Sir,—We were interested by the report that morphine has a more rapid onset of action than diamorphine [1]. The accepted wisdom is that diamorphine, being more lipophilic than morphine, acts more quickly. That the converse is true implies that our understanding of the lipid solubility of drugs and the dynamics of their transport across membranes is incomplete.

Morphine-6-glucuronide (M6G), an active metabolite of morphine, has been shown to have a greater analgesic activity than would be expected from a compound considered to be highly polar and unable to cross the blood-brain barrier [2]. It has been shown now that M6G has a lipophilirity similar to that of morphine, and much greater than expected [3]. Force field and quantum mechanical calculations indicate that M6G can exist in two conformational forms. The extended form exposes the polar groups of the molecule to the solvent and thus the form is hydrophilic. In the other form, the molecule is folded so that its polar groups are inaccessible and the molecule is lipophilic. An equilibrium exists between the two forms such that the extended hydrophilic form predominates in polar media such as water, and the folded lipophilic form predominates in non-polar media, such as biological membranes. Morphine-6-glucuronide is able, therefore, to cross the blood-brain barrier more efficiently than expected and this may explain its clinically observed analgesic effect.

Diamorphine is metabolized to morphine through 6-acetyl morphine (6AM). This metabolite is able also to cross biological membranes more readily than would be expected by its apparently polar nature. Unlike M6G, 6AM does not appear to have conformational isomers. However, the 6AM molecule is shaped so that the OH groups of the morphine moiety are effectively masked and the molecule is rendered more lipophilic.

Conventional pharmacokinetic theory answers many questions and new investigative techniques are explaining some unresolved clinical anomalies. Our understanding of the behaviour of drugs in the body is incomplete and we should not be surprised, therefore, at such findings as morphine acting more rapidly than diamorphine.

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REFERENCES


FIRST USE OF COMBINED SPINAL-EXTRADURAL ANAESTHESIA

Sir,—In the interesting review of extradural, spinal or combined blocks for obstetric surgical anaesthesia [1], Brownridge is described as the inventor of the combined spinal-extradural technique. However, Brownridge suggested it in February 1979 [2], but described its use in Caesarean section only in 1981 [3]. I had cited him as the first user of this method while describing our combined spinal-extradural needle [4]. However, Curelaru, and not Brownridge, was the first to use this technique [5], and described it in February 1979. He tested the method in 150 patients, using two vertebral punctures for the procedure, and described its advantages as the possibility of obtaining high quality conduction anaesthesia, minimal toxicity, absence of postoperative pulmonary complications and economy.

Twelve years have elapsed since that publication, which should be cited in further publications of the method.

J. Eldor  
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Sir,—Thank you for the opportunity to comment on Professor Eldor's letter. I should now agree with him that Curelaru [1] in 1979 was the first to publish a description of a combined spinal and extradural (CSE) technique which involved the insertion of the spinal and extradural needles at separate lumbar interspaces.

My article [2] was submitted for publication in February 1990 and it was not until later that year that I (and also, I understand, Professor Eldor) learned from a most interesting exchange of letters with Professor Curelaru, of the latter's publication of his description in 1979. Professor Curelaru worked on the technique while an anaesthetist in Romania, where the poor standard of equipment available at the time for both general and regional anaesthesia led to his search for a more effective and reliable technique.

While the origin of many innovations seems to lead back inevitably to Biblical times, the first description of any type of CSE technique which I can find dates only from 1937! In that year, Soresi [3] described an "episubdural technique", which comprised an extradural injection with a single needle which was then advanced through the dura mater into the subarachnoid space to perform a spinal block. The author made the unlikely claim of a duration of action of 24–48 h even with the short-acting procaine. The technique was often preceded by the author's (a surgeon, not an anaesthetist) favourite premedication of "wine proctoclysis" which now would certainly be considered to be the misplaced use of 100–250 ml of port wine—per rectum! The method (but not the premedication) was revived recently by Sprotte and colleagues using their atraumatic needle [4]. However, the technique required the patient to be left rather awkwardly with the needle in situ until the extent and efficacy of the extradural block had been assessed. The needle was pushed through the dura mater to perform additional spinal anaesthesia only if the extradural block was inadequate.

To the best of my knowledge, credit for the first CSE technique by a single interspace spinal needle through extradural needle technique should go to Coates [5], who passed a 26-gauge spinal needle through a 16-gauge extradural needle in orthopaedic patients. Mumtaz, Daz and Kuz [6] also described a needle-through-needle technique in the same journal (indeed on the same page) as the Coates letter. Another variation is to use a single vertebral interspace, but to pass the spinal alongside the extradural needle in some type of guide, after the extradural space has been identified and a catheter introduced. Professor Eldor himself was the first to describe a device of this type [7].

I shall be neither surprised nor disappointed if publication of this letter leads to further revelations concerning the origin of the combined spinal–extradural technique.

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REFERENCES