Pain relief for labour is freely available in the United Kingdom, principally because of the widespread use of systemic agents, like pethidine, and self-administered inhalation analgesia. These methods have enabled midwives, who, after all, deliver the majority of babies, to provide a substantial degree of pain relief for most mothers associated with an impressive record of safety (Arthure et al., 1969). But there remains a substantial minority of mothers who are not satisfied with their pain relief. Although other procedures are available, it is by improvements in these basic methods, and their application, that there lies most hope of a rapid improvement in results. This article mainly describes advances which have appeared since previous reviews (Crawford, 1965; Crawford, 1966a; Utting and Gray, 1968; Bonica, 1969).

**INHALATION ANALGESIA**

Inhalation analgesia does not provide complete relief of severe pain with retention of consciousness except in a minority of patients. If it did it would be used in this way during surgery. However, it can give a substantial and useful degree of pain relief to the majority in labour while the mother is still able to co-operate with the midwife or obstetrician.

**Methoxyflurane.**

Methoxyflurane (Penthane) is the most recent addition to the inhalational analgesics used for obstetrics (Boisvert and Hudon, 1962). After controlled clinical trials in Cardiff, from 1965 to 1969, methoxyflurane was approved by the Central Midwives Board in 1970 for use by unsupervised midwives.

The trials were designed to discover whether this new drug had anything special to offer in obstetrics and also whether it was acceptable to midwives. The first trial, using a new method of assessment, screened methoxyflurane to find out if it was any better than, or as good as, those agents already available. The comparison was made with trichloroethylene because it too has somewhat similar characteristics, including a smell. Since the correct concentration of methoxyflurane for intermittent administration was unknown, an anaesthetist administered both drugs continuously, altering the inhaled concentration according to certain objective criteria of the mother’s behaviour (Major, Rosen and Mushin, 1966). The mother’s response to each contraction, her level of consciousness, and whether she was restless, or not, between each contraction, was graded. The percentage of time for which all three factors were simultaneously “satisfactory” during the labour was calculated (fig. 1). The agents were then compared, since both were given at the optimum concentrations for each patient, and any differences arising from individual response were minimized. Methoxyflurane gave better pain relief and less restlessness than trichloroethylene. From the recorded concentrations it was possible to determine the optimum concentration of methoxyflurane likely to be required for intermittent use, which was 0.35 per cent. Trials showed that 0.25 per cent gave significantly poorer analgesia than 0.35 per cent. On the other hand, 0.45 per cent was too strong (Major, Rosen and Mushin, 1967).

Two further trials compared nitrous oxide/oxygen with methoxyflurane. When both were given continuously with an anaesthetist varying the inhaled concentration there was little to choose between them (Jones et al., 1969a). However, when administered intermittently methoxyflurane 0.35 per cent was superior to 50 per cent nitrous oxide in oxygen (Entonox) (Jones et al., 1969b), probably because 50 per cent is not the optimum concentration for nitrous oxide when used in this way.

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Finally, in eight obstetric units, a field trial was organized in which methoxyflurane (0.35 per cent in air), nitrous oxide/oxygen (50 per cent) and trichloroethylene (0.5 and 0.35 per cent in air) were compared (Rosen et al., 1969). From the patient's point of view there was little difference between any of the agents as regards the percentage of mothers who thought pain relief was "complete" or "considerable" (table I). However, of multiparae asked to compare their previous labour with the present one, 55 per cent of those receiving methoxyflurane thought the present labour was better compared with 42 per cent receiving trichloroethylene and 35 per cent of those receiving nitrous oxide. These differences were significant.

The midwives reported that 14 per cent of the mothers who received methoxyflurane had

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**Table I**

<table>
<thead>
<tr>
<th>Number of mothers</th>
<th>Methoxyflurane</th>
<th>Nitrous Oxide</th>
<th>Trichloroethylene</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mother's opinion of pain relief</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>How much did it help?</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Completely</td>
<td>11.5</td>
<td>11</td>
<td>12</td>
</tr>
<tr>
<td>Considerably</td>
<td>59</td>
<td>61</td>
<td>60</td>
</tr>
<tr>
<td>Total</td>
<td>70.5</td>
<td>72</td>
<td>72</td>
</tr>
</tbody>
</table>

"excellent" pain relief, compared with 7 per cent who had nitrous oxide and 11 per cent trichloroethylene. On the other hand, they considered more patients who received methoxyflurane were "drowsy" than after the other two
drugs; but there were negligible differences between the drugs when the unsatisfactory grades of “too drowsy”, “asleep”, and “unco-operative” were compared. This probably occurred because patients who have methoxyflurane frequently close their eyes and appear to be asleep, although responding immediately to conversation and instruction. This appearance of tranquillity is a feature of successful methoxyflurane analgesia. Sometimes patients volunteer that they feel detached from the pain and that it is somewhat like the effects of alcohol. Midwives not used to this sign were probably unsure how to grade the patient. It is important that midwives be instructed to distinguish between this harmless, common effect and overdosage.

The patients who had methoxyflurane without pethidine were judged less restless than those who had the other agents without pethidine. When pethidine had been given, there was no difference in restlessness between any of the drugs. This may make it useful for short labours when pethidine is contraindicated.

Only a minority of midwives (35 per cent) found the smell unpleasant as compared with 42 per cent who found trichloroethylene objectionable. However, methoxyflurane proved generally acceptable to the midwives, most of whom said they would welcome its introduction into their practice. They considered it especially useful in apprehensive patients and in those in whom labour was progressing rapidly.

As a result of these investigations, approval was given by the Central Midwives Board to the administration of methoxyflurane by midwives. Generally, similar results have been reported with methoxyflurane analgesia for labour in this country (Bodley et al., 1966) and in the United States (Kortis et al., 1967; Smith and Moya, 1968; Barber, Barnett and Williams, 1969).

**Accumulation of methoxyflurane.**

Calculations, based on solubility factors, suggest that progressive accumulation should occur if methoxyflurane is inhaled intermittently for a period of time (Mapleson, 1969; Waud and Waud, 1970). A typical computed uptake based on available data illustrates this (fig. 2). However, measurements of arterial blood concentrations of methoxyflurane, made during intermittent inhalation of 0.35 per cent, indicate that this is not usually the case. The calculated uptake was based upon the premise that the mother breathes in a regular pattern both during and between inhalations of methoxyflurane. Continuous recordings of ventilation showed, in a longer labour, that the mother actually reduced her intake of methoxyflurane by breathing less of it as she approached delivery, so maintaining a relatively steady blood level (Latto, Molloy, and Rosen, 1971). Moreover, although it has been assumed that recovery from an overdose would be slow, in practice rapid falls in blood levels occurred, related mainly to ventilation. It is clear that a large measure of control can be achieved, either by encouraging the mother to breathe more methoxyflurane or by taking away the mask and encouraging her to hyperventilate (Latto, Molloy and Rosen—in preparation). This has considerable practical importance since the number of mothers who considered the pain relief complete in the large clinical trial (Rosen et al., 1969) was less than in two smaller trials in which there was an anaesthetist present (table II). In
The mothers' opinion of the pain relief. A comparison between two trials of intermittent inhalation of methoxyflurane and one of nitrous oxide/oxygen supervised by an anaesthetist.

<table>
<thead>
<tr>
<th></th>
<th>Methoxyflurane</th>
<th>Nitrous oxide</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Major, Rosen and Mushin, 1967</td>
<td>Jones et al., 1969b</td>
</tr>
<tr>
<td>Number of mothers</td>
<td>23</td>
<td>25</td>
</tr>
<tr>
<td>Mother's opinion of</td>
<td></td>
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<tr>
<td>pain relief</td>
<td></td>
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<tr>
<td>How much did it help?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Completely</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Considerably</td>
<td>65</td>
<td>60</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>88</td>
</tr>
</tbody>
</table>

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<tr>
<th></th>
<th>Major, Rosen and Mushin, 1967</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Number of mothers</td>
<td>23</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Mother's opinion of</td>
<td></td>
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</tr>
<tr>
<td>pain relief</td>
<td></td>
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</tr>
<tr>
<td>How much did it help?</td>
<td></td>
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</tr>
<tr>
<td>Completely</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Considerably</td>
<td>65</td>
<td>60</td>
<td>64</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>88</td>
<td>76</td>
</tr>
</tbody>
</table>

both cases (tables I and II) midwives supervised the inhalation. Although the presence of a doctor might be expected to add emotional reinforcement to the analgesia this cannot be the complete answer, since there was virtually no difference between the results with nitrous oxide/oxygen in a similar comparison (tables, I and II). Probably, the midwives felt safer with a doctor present, and encouraged the mothers to breathe more methoxyflurane.

Nitrous Oxide.
The optimum intermittent concentration of nitrous oxide for pain relief during labour has been reported as not 50 per cent, but nearer to 70 per cent (McAneny and Doughty, 1963). Calculations from the concentrations found necessary during the continuous administration of nitrous oxide indicated that a concentration of 74 per cent by intermittent inhalation would be best (Jones et al., 1969a). The results from a large clinical trial of intermittent inhalation (Report to the Medical Research Council, 1970) also confirmed that 70 per cent was better than 50 per cent nitrous oxide. However, it has been noted that some mothers became semiconscious quite suddenly with higher concentrations of nitrous oxide (Jones et al., 1969a) and that a small but significantly higher proportion of patients became unconscious with intermittent 70 per cent nitrous oxide (Report to the Medical Research Council, 1970). The risk that this complication would occur was not considered to be acceptable for unsupervised midwives. The undoubted advantage in some cases of using a higher concentration of nitrous oxide must, therefore, be reserved for occasions when it can be given under medical supervision.

It would seem logical if pain relief is inadequate with one inhalational agent to change to another. In a trial (Seward, 1949) in which two agents—nitrous oxide 50 per cent (in air) or 75 per cent (in oxygen), or trichloroethylene 0.5 per cent—were given alternately in the same labour, many mothers indicated a preference; but the trial did not compare these mothers with others having only one agent, so establishing whether the results over all could be improved. Another trial of intermittent inhalation analgesia showed that a mixture of nitrous oxide and methoxyflurane produced better pain relief than either alone (Shnider, Steffenson and Margolis, 1969).

The Baby.
Inhalational agents easily pass the placental barrier (Schultz, 1970); nitrous oxide does so rapidly (Marx, Joshi and Orkin, 1970) and so does methoxyflurane (Siker et al., 1968; Clark et al., 1970). Clinical studies showed no significant differences between the inhalation analgesics when Apgar scores at birth were compared, provided the durations of administration were similar. Nor was there any difference between the agents when pethidine had been given, but significantly better Apgar scores were obtained when the inhalation agent was used without pethidine (Rosen et al., 1969).

Is Additional Oxygen of value during Inhalation Analgesia?
Animal and human experiments indicate that, providing the placental foetal circulation is functioning, a change in the mother's arterial oxygen tension is soon reflected in the foetus. In lambs, severe maternal hypoxia caused a fall in umbilical venous and arterial oxygen tensions, associated with a fall in uterine blood flow (Dilts et al., 1969). An increase in maternal oxygen tension, both in the ewe and the mare, increased oxygen levels of the foetus (Comline and Silver, 1970), although this effect is limited by placental oxygen consumption, by maternal oxygen carriage (the mother's blood is already nearly saturated at normal inspired tension), and by uneven distribu-
INHALATION AND SYSTEMIC ANALGESIA

Inhalation of placental flow (Dawes, 1963). Similar results have been found in women in labour both when the maternal arterial oxygen was increased (Newman et al., 1967; Gare et al., 1969) or decreased (Newman et al., 1967), the latter consistently causing changes in the foetal heart rate (John, 1965). This relationship has been confirmed when the mother is having inhalation drugs as general anaesthetics (Davey et al., 1967; Rorke, Davey and DuToit, 1968; Baraka, 1970). However, in one study, although foetal oxygen tension rose with increases in maternal inspired oxygen up to 66 per cent, 100 per cent oxygen caused a slight fall in foetal oxygen tension suggestive of a reduction in placental blood flow. Even so, the umbilical venous oxygen tension was still higher than when the inspired oxygen concentration was 33 per cent (Rorke, Davey and DuToit, 1968).

In normal labour, the maternal arterial oxygen tension is higher than when it is measured in the puerperium (Andersen and Walker, 1970), and there seems to be no evidence indicating any advantage in administering oxygen unless there is foetal distress. Then, although the inhalation of added oxygen, as with nitrous oxide/oxygen or methoxyflurane/oxygen mixtures, must have some effect on maternal arterial tension, it is probably not of much value to the foetus when breathed for such brief intermittent periods. To be fully effective the additional oxygen should be inhaled continuously.

Is Hyperventilation harmful during Inhalation Analgesia?

Morishima and colleagues (1965) hyperventilated pregnant guineapigs and produced foetal acidosis which they ascribed to uterine vasoconstriction. Experiments in ewes have shown that the umbilical venous oxygen tension is correlated with maternal PaO₂, so that maternal hypocapnia results in a low umbilical venous oxygen (Motoyama et al., 1966, 1967). This relationship has been confirmed with pregnant ewes and mares (Comline and Silver, 1970). Conversely, hypercarbia can increase the umbilical venous oxygen tension in ewes (Dawes, 1968).

Parer and associates (1970) in a study of macaque monkeys subjected to hyperventilation found neither uterine vasoconstriction nor diminution in uterine blood flow. Although there was a fall in foetal arterial oxygen tension the total oxygen uptake by the placenta and foetus showed no decrease. They considered that the foetus could compensate for hyperventilation, at least for a time.

Some investigators believe that this relationship exists in humans (Moya et al., 1965; Rorke, Davey and DuToit, 1968; Sailing and Ligdas, 1969) but others do not consider it proved (Crawford, 1966b; Coleman, 1967; Baraka, 1970). All the patients studied by these authors, except those of Saling and Ligdas (1969), were under general anaesthesia.

In 86 conscious mothers in labour, Lumley and his colleagues (1969) could not find any relationship between maternal PaCO₂ and foetal scalp oxygen tension. In a review of other studies up to that date they suggest that perhaps general anaesthesia was also necessary before hypocapnia affected foetal oxygenation. They pointed out that only two of Crawford's (1966b) patients had evidence of severe hyperventilation; that Coleman's (1967) patients had lower PaCO₂ levels (mean 15.7 mm Hg), and, although the induction to delivery time was short (mean 13.1 min), re-analysis of his data showed that there was a marked metabolic acidosis in the majority of the babies. Then Baraka (1970) in a later study of 15 mothers having Caesarean section under general anaesthesia, was not able to confirm any relationship between hyperventilation of the mother and foetal oxygenation; but only one mother had a PaCO₂ below 28 mm Hg. Low, Boston and Cervenko (1970) found lower umbilical venous and arterial oxygen tensions when mothers had a low carbon dioxide tension, but no evidence of foetal metabolic acidosis indicating that the total oxygen uptake by the babies remained adequate.

It seems that more information is required to resolve whether, and how, maternal hyperventilation affects foetal oxygenation. This is especially important in the light of recent findings by Fadl and Uting (1969) with inhalation analgesia. Mothers who had intermittent nitrous oxide/oxygen (Entonox) at the end of the first stage had lower carbon dioxide tensions while breathing the mixture than the mothers who received narcotics, epidurals, or no treatment. They
reported three instances of foetal distress, when mothers had been breathing nitrous oxide, each associated with low maternal carbon dioxide tensions (22.7, 13, and 12.5 mm Hg respectively), and advise discretion in encouraging hyperventilation when using nitrous oxide/oxygen. There is no direct evidence yet whether hyperventilation occurs to such an extent with the other inhalational analgesics, but it is more likely if pain relief is inadequate. Maternal ventilation was significantly greater while breathing intermittently the weaker, 0.25 per cent, concentration of methoxyflurane than with the more effective 0.35 per cent (Major, Rosen and Mushin, 1967).

Unlike Fadl and Utting (1969), Andersen and Walker (1970) found that patients having systemic analgesics also commonly had a fall in arterial carbon dioxide tension during contractions. This difference is most probably due to variations in the dose, and therefore the effectiveness, of the analgesics. Although the situation is not absolutely clear, it would seem wise to discourage prolonged, severe, maternal hyperventilation, passive or active, during labour.

Renal toxicity.

Occasional cases of renal failure associated with tubular damage have been reported following prolonged methoxyflurane anaesthesia although there has been no instance reported of this complication in obstetric patients having inhalation analgesia or anaesthesia. A study of 125 patients after methoxyflurane analgesia and a similar number who had nitrous oxide/oxygen showed no evidence of renal dysfunction after either agent (Rosen et al., in preparation).

Apparatus.

Methoxyflurane.

The Cardiff Penthrane inhaler is designed to give 0.35 per cent methoxyflurane, and is a development from the Tecota Mark 6 trichloroethylene vaporizer. It has a special, non-interchangeable, filling mechanism designed to prevent spillage of liquid methoxyflurane, overfilling, or the introduction of the wrong agent. A production batch of the vaporizers was examined in detail (Jones, Molloy and Rosen, 1971) and found to be consistently satisfactory within the standards laid down by the Central Midwives Board for a trichloroethylene vaporizer. It delivers a single concentration of methoxyflurane, 0.35 ± 0.07 per cent in a wide variety of circumstances, since an alternative lower concentration was found to be unnecessary (Rosen et al., 1969). Investigation at extremes of environmental temperature showed that if a vaporizer is suddenly removed from a hot environment, such as a warm cupboard or sunny windowsill, and then given directly to the mother it delivers a higher concentration (about 0.5 per cent). The vaporizer should not be kept in a warm store, or, if it is, it must be brought into the room for about an hour before use.

A fixed-volume reservoir which can be fitted round the top of the inhaler enables up to 50 per cent oxygen to be given to the mother, dependent on the fresh gas flow and the mother’s minute volume ventilation. If no oxygen is available, or the supply runs out, the one-way valve of the vaporizer prevents rebreathing.

The use of a mouthpiece in place of a mask might be preferred for some patients during inhalation analgesia. However, one new hazard has occurred with the mouthpiece; some patients retain it between their teeth when too drowsy (Marx, Chen and Tabora, 1969).

Vaporizers which are not compensated for changes in ambient temperature or flow are used in the United States but are not approved by the Central Midwives Board in this country for use by midwives. One of these, the Analgizer (not available in the United Kingdom), has a superficial attraction because of its simple construction, small size, and the fact that it is disposable. It is used with a mouthpiece and consists of a polypropylene sponge in a polyethylene cylinder (Romagnoli, Busque and Power, 1970). It is not temperature-compensated and does not give a constant concentration when tested in laboratory conditions (Jones and Rosen, unpublished data). Furthermore, although disposable, it is not really cheap since it requires about 15 ml of expensive methoxyflurane to fill it.

Nitrous oxide.

In 1968, the Minnitt nitrous oxide/air apparatus ceased to be authorized for use by midwives. It is noteworthy that little harm was
ever recorded from such regular incidents of hypoxia inflicted on millions of mothers; hypoxia which must have been severe indeed since certain machines gave much lower concentration than 10 per cent (Cole and Nainby-Luxmoore, 1962).

The use of oxygen and nitrous oxide as premixed nitrous oxide/oxygen 50 per cent (Tunstall, 1961) was introduced into general use for midwives in 1965. The Entonox apparatus for administering the premixed gas has been described in recent reviews in this journal (Tunstall, 1968; Cole, 1968). Additional recommendations for nitrous oxide/oxygen apparatus have been drawn up by a committee under the aegis of the Medical Research Council both for separate cylinder apparatus (e.g. Lucy Baldwin) and premixed nitrous oxide/oxygen apparatus (Entonox) designed to supplement British Standards specifications BS.4272, parts 1 and 2 (1968) (Cole et al., 1970). However, only the Entonox apparatus with premixed gases is at present authorized by the Central Midwives Board for use by unsupervised midwives.

Separation of the premixed gases can occur below -7°C (Cole, 1964) but after rewarming, conversion to a single phase can be achieved simply by inverting the cylinder three times (Tunstall, 1968).

**Apparatus resistance.**

It is important that resistance to breathing should not be excessive or the mother may reject the apparatus. There is, generally, a lack of data about what should be the resistance of the apparatus offered to women in labour. Cole and associates (1970) have made a useful start in proposing resistances for premixed and separate-cylinder apparatuses. They based their choices, at least partly, on *maximum* peak inspiratory flows measured during labour, either when inhaling air, or premixed nitrous oxide/oxygen through a demand valve (Crawford and Tunstall, 1968). Their recommendations are compared (in table III) with the specifications for trichloroethylene and methoxyflurane vaporizers and the mean resistance, experimentally determined, of a number of Cardiff Penthrane inhalers. Clearly the specifications for both trichloroethylene and methoxyflurane inhalers should include more than one point. The measured resistance of the methoxyflurane vaporizers is greater at higher flows, but rather less at lower flows when compared with the recommendations for nitrous oxide apparatus. Although in clinical use the peak inspiratory flow may exceed 200 l./min, mothers neither refuse to use the vaporizer nor complain about it (Jones, Molloy and Rosen, 1971). The recommendations of Cole and associates (1970) may be stricter than necessary at higher inspiratory flows.

**Table III**

<table>
<thead>
<tr>
<th>Pressure (mm H₂O)</th>
<th>Flow (L/min)</th>
<th>Nitrous oxide/oxygen apparatus</th>
<th>Trichloroethylene and methoxyflurane vaporizers</th>
<th>Cardiff Penthrane inhaler</th>
</tr>
</thead>
<tbody>
<tr>
<td>Separate cylinders</td>
<td>Premixed cylinders</td>
<td>Inhalers</td>
<td>Inhalers</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>25</td>
<td>12.5</td>
<td>5</td>
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</tr>
<tr>
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<td>50</td>
<td>10</td>
<td></td>
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<tr>
<td>300</td>
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</table>

**SYSTEMIC ANALGESICS**

**Pethidine.**

Pethidine is still the most widely used systemic analgesic for relieving pain during childbirth. Although continuous intravenous administration of large doses has been employed—up to 600–800 mg in 24 hours (Jeffcoate, Baker and Morton, 1952)—Scott (1970) has now described an apparatus operated by the mother enabling her to administer a dose intravenously when she feels the need for more pain relief. With this method 50 of 55 patients reported the pain relief “good” or “very good”. Despite giving a mean dose of 448 mg pethidine (0.41 mg/kg/hr), Scott (1970) surprisingly reported no untoward foetal depression. A more sophisticated apparatus, although not yet used in obstetrics, has been described for self-administration of intravenous drugs by patients. With this apparatus the frequency of increments and the total dose can be preset (Forrest, Smethurst and Kienitz, 1970).
Such a demand system has certain attractions since it should satisfy the patient's anxiety about whether she is going to get enough pain relief when she wants it and yet a safe dosage cannot be exceeded.

If the intravenous route is chosen for its more rapid effect it would seem wise to use small increments well diluted. Crawford and Rudofsky (1965) have shown that with an intravenous "slug" there is a much greater transfer of pethidine to the foetus than with an intramuscular injection.

Although it is difficult to be precise about the ultimate cost in foetal morbidity and mortality there is no doubt now that the use of pethidine in labour is associated with more respiratory depression of the newborn baby (Shnider and Moya, 1954; Crawford, 1966a; Rosen et al., 1969). This is not an argument for giving up the use of pethidine but for trying to minimize these effects. The timing of a dose is particularly important. Shnider and Moya (1964) concluded that with intramuscular pethidine an interval of 2-3 hours before delivery was critical, and no depression was evident in less than 1 hour. It seems wiser, therefore, to avoid the use of pethidine within 3-4 hours of delivery and to use an inhalational analgesic at an earlier stage of labour if there is any doubt.

Most authorities agree that a mixture of pethidine with a narcotic antagonist such as nalorphine or levallorphan given to the mother before delivery has not proved effective as a prophylactic against respiratory depression while retaining equivalent pain relief (Telford and Keats, 1965; Bonica, 1967; Lind, 1970). Recent double-blind studies in volunteers did not show any difference between the respiratory depression caused by pethidine alone and when combined in various ratios with levallorphan (Rouge, 1969). Although the use of a narcotic antagonist has also been described (Crawford, 1965, 1966a, 1969) as "the way to safety", it would seem at present that these agents should be reserved for cases exhibiting obvious respiratory depression (either maternal or foetal) due to opiates.

**Pentazocine.**

Pentazocine (Fortral) is a recently introduced powerful analgesic (Keats and Telford, 1964) which only rarely causes drug dependence. The Central Midwives Board has now accepted its use by midwives in doses of 30–45 mg (Prescott, 1970). Its pharmacological and clinical features have been reviewed (Potter and Payne, 1970) and its use in labour has been reported by Filler and Filler (1966), who initially gave a dose of 30 mg intramuscularly which they subsequently increased to 45 mg. In 18 (72 per cent) of mothers, pain relief was described as "excellent" or "good" and remarkably rapid in onset. Only one patient vomited. Moore, Carson and Hunter (1970) in a double-blind comparison between pentazocine 40 mg, pethidine 50 mg and pethidine 100 mg, giving repeated doses when required, concluded that the pain relief with pentazocine was comparable with pethidine 100 mg. However, the duration of action of pentazocine, being about 2 hours, was shorter than that of pethidine, which confirms the observations of other investigators (Filler and Filler, 1966; Hamilton, 1969).

Mowat and Garrey (1970) in a double-blind trial compared pentazocine 20 mg and pethidine 50 mg repeated 3-hourly as necessary and found little difference between them as regards pain relief and sedation, but there was less vomiting with pentazocine.

Although psychotomimetic reactions have been described with narcotic antagonists and might have been expected with pentazocine, Hamilton and his colleagues (1967) predicted that they would be absent in clinical doses. Indeed, the only cases of hallucinations in the study of Moore, Carson and Hunter (1970) occurred in mothers who had received pethidine 100 mg!

Pentazocine crosses the placenta (Beckett and Taylor, 1967), although the foetal/maternal ratio does not appear to be as high as that of pethidine (Duncan, Ginsberg and Morris, 1969). The clinical importance of this finding seems uncertain since none of the trials showed any important differences between the Apgar scores of the babies, whether the mother had received pethidine or pentazocine.

In equivalent analgesic doses pentazocine depresses ventilation just as much as the other narcotics (Jennett, Barker and Forrest, 1968). The specific opiate antagonist Naloxone, which is not available in this country, might be of value.
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to reverse this effect (Kallos and Smith, 1968). In
the adult, non-specific antagonists such as methyl-
phenidate (Telford and Keats, 1965) or niketha-
mide (Doran and Burt, 1970) have been recom-
mended. However, there appears to be only one
record, with vanillic acid diethylamide (Vandid),
of experience with such drugs in the newborn
(County Borough of Reading Midwifery Service,
1969).

The risk of dependence developing from
short-term treatment with a narcotic analgesic is
slight. Nevertheless this is an advantage of
pentazocine, especially reducing any temptation
which exists for the administrator. However, the
principal claims of pentazocine over pethidine are
that for equal analgesia there is a more rapid
onset of effect, less nausea and vomiting—
perhaps half the incidence (County Borough of
Reading Midwifery Service, 1969; Moore, Car-
son and Hall, 1970; Mowat and Garrey, 1970)—
and possibly less sedation.

Although there has been some doubt it now
appears clear that in the commonly used doses,
neither pethidine nor pentazocine slows estab-
lished labour (Filler and Filler, 1966). Indeed
pethidine may increase uterine contractions
(Lindgren, 1969; De Voe et al., 1969). Con-
fusion in the past probably arose because the
stage of labour studied was not clearly defined
(Bonica, 1967).

Other systemic analgesics.

Many other drugs have been tested although
few have proved to have any real advantage over
pethidine. Slom (1968), however, compared
dihydrocodeine, in a double-blind trial, with
pethidine. He reported that an equally effective
analgesic dose of dihydrocodeine caused signifi-
cantly less depression of the newborn Apgar
scores at 1 minute.

Analgesics and tranquillisers.

Combinations of phenothiazines, such as
promazine, promethazine, and propiomazine,
with pethidine are widely used (Crawford, 1965;
Bonica, 1967). They are given to produce seda-
tion, especially early in labour, and to reduce the
incidence of nausea and vomiting. They all
potentiate the central effects of narcotics, the
dose of which must therefore be reduced.
McQuitty (1967), in a double-blind trial, has
thrown some doubt on their value since he could
find no evidence to suggest that they conferred
any clear benefit over the use of pethidine alone;
indeed some side effects were more frequent.

Diazepam.

Diazepam was introduced as a tranquillizer
and sedative for psychiatric practice (Randall et
al., 1961). Its pharmacology and use for pre-
medication, for the induction of general anaes-
thesia, and as a sole agent for cardioversion,
endoscopy, and dentistry have been reviewed
recently (Dundee and Haslett, 1970). A wide
interest in diazepam has been paralleled by
investigations in the United States into its value
in the delivery room (Bepko, Lowe and Waxman,
1965). It appears to provide good sedation with
a low incidence of nausea and vomiting and little
evidence of maternal or neonatal depression.
Other trials (Niswander, 1969; Flowers, Rudolph
and Desmond, 1969; Friedman, Niswander and
Sachtleben, 1969) agree upon the general
efficacy of diazepam. All these have followed the
same general pattern; either diazepam (up to 20
mg) or a placebo were given intravenously,
repeated 3-hourly as required in smaller doses.
Pethidine 12.5 mg, as an intravenous increment,
as administered if the mother did not relax
between contractions. Conduction anaesthesia
was used for delivery. Although these trials were
intended to be double-blind, the authors
acknowledge that it was impossible to conceal
the effects of the active agent from the
administrator.

The average dose of pethidine was signifi-
cantly less when it was combined with diazepam
than with the placebo (table IV). There was also
a significantly higher percentage of those who
had diazepam who did not require any pethidine
at all in comparison with the placebo group.
More mothers who had diazepam thought the
pain relief was “excellent” or “good” than those
who had placebo. One mother had a drop in
blood pressure (unspecified degree), and a few
became “uncontrollable”.

Diazepam does not appear to slow labour and
may even speed up the first stage although the
difference from the control group was not statis-
tically significant (Friedman, Niswander and
The blood level of diazepam in the baby is in equilibrium with that of the mother within a few minutes (Bepko, Lowe and Waxman, 1965; Mothers not evidenced of the latter by the next day (Flowers, Apgar scores and hypotonicity have been reported at delivery although there was no complications. In a very careful study lower Apagar scores and hypotonicity have been reported at delivery although there was no evidence of the latter by the next day (Flowers, Rudolph and Desmond, 1969). Other investigators did not report such complications.

CONCLUSIONS

If presently available drugs are used properly about a third of mothers claim “complete” pain relief with inhalation and systemic analgesics and nearly all “considerable” relief. Even if no new agents were to appear scope for improvement seems possible through the systematic investigation of better methods of administration, and of the optimum interactions between the tranquilizers, the systemic, and the inhalational analgesics.

ACKNOWLEDGEMENT

Figure 2 was published through the courtesy of Farbwierke Hoechst AG.

REFERENCES


TABLE IV

<table>
<thead>
<tr>
<th>Trial</th>
<th>Placebo</th>
<th>Diazepam</th>
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<tbody>
<tr>
<td>Niswander, 1969</td>
<td>73.1</td>
<td>25.4</td>
</tr>
<tr>
<td>Flowers, Rudolph and Desmond, 1969</td>
<td>58.6</td>
<td>18.5</td>
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</tbody>
</table>

No. of mothers:

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<td>Niswander, 1969</td>
<td>94</td>
<td>95</td>
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<tr>
<td>Flowers, Rudolph and Desmond, 1969</td>
<td>101</td>
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Mean dose pethidine intravenous (mg):

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<td>58.6</td>
<td>18.5</td>
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Mothers not requiring pethidine (%):

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<tr>
<td>Niswander, 1969</td>
<td>15</td>
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<td>Flowers, Rudolph and Desmond, 1969</td>
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Mother’s opinion of pain relief:

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<tr>
<td>Niswander, 1969</td>
<td>33</td>
<td>57</td>
</tr>
<tr>
<td>Flowers, Rudolph and Desmond, 1969</td>
<td>44</td>
<td>76</td>
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</tbody>
</table>


In the paper "The change in calf muscle blood flow in the ischaemic limb during anaesthesia with pancuronium bromide" by G. J. J. Fuzzey and J. C. Edwards in the August 1971 number of the Journal, the second line of the second column on page 756 which reads \( t=1.819 \) and \( P<0.5 \) should read: \( P<0.05 \).