Inhaled methoxyflurane and intranasal fentanyl for prehospital management of visceral pain in an Australian ambulance service

Steven Johnston  
*Edith Cowan University*

Gary Wilkes  
*Edith Cowan University*

Jennifer Thompson  
*Edith Cowan University*

Melanie Ziman  
*Edith Cowan University*

Richard Brightwell  
*Edith Cowan University*

10.1136/emj.2009.078717

Inhaled methoxyflurane and intranasal fentanyl for prehospital management of visceral pain in an Australian ambulance service

Steven Johnston,1,2 Garry J Wilkes,1,2,3 Jennifer A Thompson,4 Mel Ziman,4 Richard Brightwell1,2

ABSTRACT

Objective This study analysed the analgesic effect and changes in vital signs associated with administration of inhaled Methoxyflurane (MTX) and/or intranasal Fentanyl (INF) for prehospital management of visceral pain. 

Method A retrospective, observational study reviewing 1024 randomly selected records of patients with presumed visceral pain administered MTX (465), INF (397) or both (162) by the Western Australian Ambulance Service between January 2004 and February 2006. Clinical variables assessed included systolic blood pressure, pulse rate, respiration rate and Glasgow Coma Scale score. Pain was assessed utilising Visual/Verbal Analogue Scale pain scores.

Results Overall effects on vital signs appeared favourable 5 min after use and at hospital arrival with either agent alone or in combination. As sole agents, MTX produced the greatest initial pain scores reduction (2.0 (1.7 to 2.2) vs 1.6 (1.4 to 1.8)) (mean (95% CI)), and INF provided greater pain reduction by hospital arrival (3.2 (2.9 to 3.5) vs 2.5 (2.1 to 2.9)). While both agents were effective, INF provided a greater pain score reduction for cardiac (3.0 (2.6 to 3.4) vs 2.3 (1.8 to 2.8)), female (3.4 (2.9 to 4.0) vs 2.5 (2.0 to 3.0)) and age 75+ patients (3.2 (2.5 to 3.8) vs 1.8 (1.0 to 2.5)). Combined use of agents was not advantageous.

Conclusions MTX and INF are effective agents for providing visceral pain analgesia in the prehospital setting. While MTX provided a more rapid onset of pain relief, INF provided superior analgesia after subsequent doses and in female, cardiac and older patients.

Although these agents are well established in local ambulance and military practice, they are not widely used elsewhere in the world with few reports regarding efficacy and safety. The aim of this study was to analyse the analgesic effect and changes in vital signs associated with administration of MTX and INF in the prehospital management of pain of presumed visceral origin in Western Australia, and to explore whether combined use is advantageous.

MTX is a volatile, fluorinated hydrocarbon used for analgesia in paediatric and adult patients since the 1960s. Reports have questioned its safety due to dose-dependent nephrotoxicity for longer-term analgesia7 and anaesthesia,8 particularly when used in conjunction with known nephrotoxins.9 MTX has been used routinely in subanaesthetic doses by ambulance services Australia-wide for prehospital analgesia for more than three decades at doses lower than those reported above where adverse events have been observed. The Therapeutic Goods Administration (TGA) has no reports of renal toxicity despite an estimated three million patient treatments (Medical Developments International, personal communication 2009). Small observational studies report it as a safe and reliable prehospital analgesic when used at analgesic doses for both adult10 and paediatric patients, with the caveat that it may lead to brief, self-limiting episodes of deep sedation in young children.11,12 Longer-term follow-up of more than 17 000 patients receiving MTX has shown no increase in adverse events (I Jacobs, unpublished data 2009).

Exposure to anaesthetic gases is measured in parts per million (ppm). Thresholds are described as a time-weighted average (TWA) (the average continuous exposure) and a ‘ceiling’ level over a single hour, generally cited as four times the TWA.13 Exposure Standards have not been established for MTX. Standards for Halothane are accepted as applicable and relevant. The TWA threshold for Halothane as a sole agent (and hence MTX) is 50 ppm.14 However, in the operating room environment, Halothane is typically administered with nitrous oxide (N₂O) at 50 times the concentration of Halothane. The TWA for N₂O is 25 ppm. Hence, in the operating room environment, the TWA for Halothane is adjusted to 0.5 ppm (and ceiling value 2 ppm) because, although this is 100 times lower than the threshold value for Halothane itself, a level of Halothane of 0.5 ppm would be associated with N₂O at its threshold level of 25 ppm.
An Ambulance commissioned study of MTX exposure found that MTX levels did not reach the 1 h peak of 2 ppm or shift average of 0.5 ppm unless oxygen was administered through the device. Ambulance Services throughout Australia have now changed Practice Guidelines to advise against routine administration of oxygen through the device (see online appendix).

Fentanyl is a potent, synthetic opioid used for analgesia since the 1960s. Previous studies favourably report its safety and efficacy as a prehospital analgesic in both paediatric and adult cases when administered intravenously or intranasally. Fentanyl has been suggested as the preferred opioid in the prehospital setting due to its rapid pain relief, short duration of action, non-histamine release (a major component contributing to hypotension) and reduced incidence of nausea and vomiting. When compared for efficacy in the prehospital setting, INF and intravenous morphine are comparable.

Within the Western Australian Ambulance Service, the most commonly used analgesic agents are inhaled MTX, introduced in the 1980s and INF introduced in 2001. Combined use has been reported by paramedics to enhance pain relief. This reported synergism, however, remains to be verified.

METHODS
We undertook a retrospective, observational review of patient care record forms encompassing patients administered MTX or INF for the prehospital management of presumed visceral pain by the Western Australian Ambulance Service between January 2004 and February 2006. For the purpose of this study, visceral pain was determined by attending paramedics as being of abdominal, renal or cardiac aetiology.

Of 14232 cases available, 10900 (76.6%) patients received MTX, and 3332 (23.4%) patients received INF. Six hundred cases had sufficient data for further analysis. Of these, 465 (45.4%) received MTX, 397 (38.8%) received INF, and 162 (15.8%) received both.

MTX is self-administered by patients via a hand-held inhalation device (Penthrox inhaler, Medical Developments International, Springvale, Australia). A single dose of 3 ml delivers MTX at a concentration of 0.2% or 0.4% depending on whether the diluter hole is open or occluded. After an initial loading dose of 10–12 breaths through the device, the patient is encouraged to take a few breaths through the device every few minutes as required thereafter. A single dose will provide analgesia for 15–20 min if oxygen is administered through the device, or up to 1 h if used intermittently (and oxygen administered separately by face mask as required). A second dose may be administered when the initial dose has been exhausted.

INF was administered by attending ambulance officers via a metered dose delivery at a concentration of 500 μg/ml in accordance with the dosing regimen in table 1.

| Table 1 | Intranasal fentanyl dose regimen |
|-----------------|-----------------|-----------------|
| **Dose chart** | **First dose** | **Subsequent at 10 min** |
| **Age** | **First dose** | | **Subsequent at 10 min** |
| <5 years | 1 × 0.05 ml (15 μg) | | 1 × 0.05 ml (15 μg) |
| 6–10 years | 1 × 0.10 ml (30 μg) | | 1 × 0.10 ml (30 μg) |
| 11–15 years | 1 × 0.15 ml (45 μg) | | 1 × 0.15 ml (45 μg) |
| Small/elderly/fragile | 2 × 0.20 ml (120 μg) | | 1 × 0.20 ml (60 μg) |
| Adult | 3 × 0.20 ml (180 μg) | | 1 × 0.20 ml (60 μg) |

The choice of analgesic agent is at the discretion of the attending paramedic. For both agents, administration is continued as needed up to hospital arrival and may be continued at the discretion of receiving hospital staff.

Data extracted from patient records included patient demographics (age, gender, aetiology of pain), vital signs (systolic blood pressure (SBP), pulse rate, respiration rate and Glasgow Coma Scale (GCS) score), and a pain assessment utilising Visual/Verbal Analogue Scale (VAS) pain scores (assessed by paramedics). The limits used to define clinically significant extremes of vital sign measurements are listed in table 2. A 1.4-point change in VAS pain score is considered clinically significant. As VAS pain scores for individual patients are assessed as whole numbers, a change of 2 points was considered clinically significant for an individual patient.

**Statistics**
Data were exported into and analysed with SPSS (version 11.5: SPSS, Chicago, Illinois). Descriptive statistics and frequencies are reported. A sample size of 600 per drug cohort was calculated to provide 80% power to detect a statistical difference with α set at 0.05. A two-way, repeated-measures analysis of variance (ANOVA) was used to test for significant differences in vital sign means over the measured intervals. The Student t test was used to compare pain score reduction and $\chi^2$ test for proportions with pain score reduction $\geq 2$ points.

**RESULTS**

**Patient demographics**
Males (584) represented 57% of the cohort, and most patients (62.3%) were over 50 years of age with a mean age of 59.1 years (female 58.7, male 59.4 years (table 3). Pain aetiology was classified by the attending paramedic as cardiac (485, 47.4%), abdominal (249, 24.5%) and renal (290, 28.3%) (table 4).

**Physiological vital signs**
SBP, pulse rate and respiration rate were recorded at three time points: prior to administration of medication, 5 min after administration and on arrival at hospital. Changes in conscious state were assessed by determining GCS prior to and 5 min after administration of the analgesic agent.

**Blood pressure**
Changes in SBP 5 min after initial analgesic dose varied considerably for individual patients (range −170 mm Hg to +70 mm Hg). Despite these large individual variations, the majority of changes were towards the normal range. Only four patients with initial SBP >100 mm Hg entered the hypotensive range (SBP <90 mm Hg). Three received INF as sole therapy for cardiac pain, and one patient received both for abdominal pain.

The reduction in mean SBP 5 min after the initial dose of MTX was 5.7 mm Hg (median 10 mm Hg) and after INF was 4.5 mm Hg (median 5 mm Hg) (table 5). Similar changes were seen on arrival at hospital, with MTX reducing mean SBP by 15.1 mm Hg (median 20 mm Hg) and INF 11.5 mm Hg (median 15 mm Hg).

| Table 2 | Vital sign parameters classified as clinically significant |
|-----------------|-----------------|-----------------|
| **Vital sign** | **Lower limit** | **Upper limit** |
| Systolic blood pressure (mm Hg) | <90 (hypotension) | >180 (hypertension) |
| Pulse rate (per min) | <60 (bradycardia) | >100 (tachycardia) |
| Respiration rate (per min) | <8 (bradypnoea) | >24 (tachypnoea) |
On hospital arrival, 10 patients with initial SBP >100 mm Hg had entered the hypotensive range. All received INF, nine with cardiac and one abdominal pain. MTX was also administered to the abdominal pain and two of the cardiac pain patients. None of these patients received nitrates or other cardiac medications. Of those who became hypotensive after treatment, no other adverse effects in physiological parameters and no fall in GCS were noted. One patient increased SBP within the hypertensive range after treatment (SBP rise from 180 to 190 mm Hg).

Pulse rate
Pulse rate changes were minimal (table 5). In the majority of cases, both agents affected pulse rate favourably towards normal values, but changes were not significant for either cohort.

Respiratory rate
Assessment of respiration indicated very little effect after administration of either agent (table 5). Overall, mean respiration declined by 1.7 rpm initially and by 2.1 rpm on hospital arrival, with median respiration rates unchanged. No patients became bradypnoeic.

GCS
Changes in GCS were negligible (table 6). Five patients had falls in GCS (maximum two points in a male with renal pain receiving INF), and four patients had increased GCS (maximum four points).

Pain scores
Pain score reduction by VAS was assessed 5 min after treatment and on arrival at hospital (table 7). A further subgroup analysis by agent, gender, aetiology and pain group was also performed (table 8). Transport times were comparable for both agents. As sole agents, MTX produced the greatest initial pain score reduction (p=0.025), and INF provided greater pain reduction by hospital arrival (p=0.007). While both agents were effective, INF provided a significantly greater pain score reduction for cardiac (p=0.025), female (p=0.020) and age 75+ patients (p=0.006) on arrival at hospital.

Analysis of the proportion of individual patients achieving pain score reductions of two points or greater by hospital arrival showed significantly higher proportions with INF overall (p=0.027) and for the subgroups of cardiac aetiology (p=0.033), female patients (p=0.021), female patients with cardiac aetiology (p=0.044) and for patients aged 45–59 years (p=0.047).

Further analysis of the patients aged 75+ years with cardiac pain showed that the difference between agents was limited to female patients in this subgroup (p=0.003) where MTX appeared to be ineffective (table 8).

Differences in pain score between agents were seen in the age groups <30 years (1.50 reduction), 75+ years (1.41 reduction) and in the subgroup of patients with cardiac pain and aged 75+ years (males 1.16, females 1.99, overall 1.95).

The patient care records in use at the time of the study did not record which agent was administered first, and so this could not be analysed. Combined use of agents was not advantageous.

For the 465 patients administered MTX, a single 3 ml dose was used in 241 patients (51.9%), a second dose was used in 195 patients (41.9%) and 29 (6.2%) received a third dose. The mean total dose of INF administered per patient was 362 μg (median 240 μg; SD ±191.74).

DISCUSSION
The objective of this study was to analyse and compare the analgesic effect and changes in vital signs associated with administration of MTX and/or INF for the prehospital management of visceral pain. Both agents proved effective with no bradypnoea.

Only one case increased SBP within the hypertensive range (increase from 180 to 190 mm Hg) which is unlikely to be clinically significant. All cases that experienced a fall in SBP from >100 mm Hg to hypotensive levels received INF either alone or in combination with MTX. However, these patients did not experience any fall in GCS or other evidence of respiratory or cardiovascular compromise. The results concur with previous studies indicating that INF is an agent with good analgesic properties.26–28 While one small study found that the rate of adverse events for patients treated with INF in a prehospital setting was 28%,28 this rate is too high for prehospital use. In this study, no adverse events were recorded.

Table 3  Age group, gender and agent administered

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Gender unspecified</th>
<th>Female</th>
<th>Male</th>
<th>Grand total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Fentanyl</td>
<td>Methoxy</td>
<td>Methoxy</td>
<td>Male total</td>
</tr>
<tr>
<td>0 to 29</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 to 44</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>45 to 59</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>60 to 74</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>75+</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unspecified</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grand total</td>
<td>4</td>
<td>226</td>
<td>162</td>
<td>48</td>
</tr>
</tbody>
</table>

Table 4  Aetiology, gender and agent administered

<table>
<thead>
<tr>
<th>Aetiology</th>
<th>Gender unspecified</th>
<th>Female</th>
<th>Male</th>
<th>Grand total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Fentanyl</td>
<td>Methoxy</td>
<td>Methoxy</td>
<td>Male total</td>
</tr>
<tr>
<td>Abdominal</td>
<td>1</td>
<td>61</td>
<td>32</td>
<td>32</td>
</tr>
<tr>
<td>Cardiac</td>
<td>3</td>
<td>107</td>
<td>99</td>
<td>99</td>
</tr>
<tr>
<td>Renal</td>
<td>58</td>
<td>11</td>
<td>13</td>
<td>13</td>
</tr>
<tr>
<td>Grand total</td>
<td>4</td>
<td>226</td>
<td>162</td>
<td>162</td>
</tr>
</tbody>
</table>


59
Following analysis of the pilot period in 2001, the initial dose for MTX was 180 mg, and the mean reported here of 362 mg per patient since initial use in 2001 to that observed here in 2004, without significant change in total dose administered per patient since introduction of the agent (Ford et al, 2001). This increased total dose administered per patient may have been influenced by the need to continue administration at the recommended intervals if pain relief is inadequate. Increased education has reinforced the need to continue administration at these intervals. MTX as a sole agent was not associated with any adverse effects, is most effective in patients with pain of traumatic origin, which has been more extensively studied. This may explain the difference between previous findings of a poor response to MTX in the prehospital environment. Further analysis of the cardiac subgroup of patients with visceral pain, they are therefore at greatest risk of cardiovascular compromise and are reassuring in this particular group who are more rapid pain relief from alfentanil was noted for relief of acute ischaemic-type chest pain in the prehospital setting as well as in hospital for paediatric patients (1.67 point reduction at 30 min postadministration). Decrease 10 min postadministration and 2.91 point reduction 30 min postadministration.31 The subgroup of patients with a history of MTX, was provided greater pain relief in pain control than the subgroup of patients with a history of MTX. MTX showed greater analgesic activity than alfentanil in patients aged 75 years and above on arrival at hospital. INF produced greater increases in pain score reduction and indicated both provide effective pain relief. MTX showed a greater pain reduction 5 min after commencement of treatment. INF showed a superior pain reduction on arrival at hospital. The results of the current study of prehospital MTX and INF conducted in a hospital environment, which report a mean reduction in VAS pain score of 0.5 point at 5 min postadministration, are reassuring in this particular group who are Systolic blood pressure (mm Hg)

<table>
<thead>
<tr>
<th>Methoxy</th>
<th>Initial</th>
<th>5 min</th>
<th>Hospital</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average</td>
<td>138.0 (96.9 to 154.2)</td>
<td>135.1 (126.7 to 143.6)</td>
<td>136.3 (127.4 to 145.1)</td>
</tr>
<tr>
<td>Pulse rate (per min)</td>
<td>85.0 (82.4 to 87.1)</td>
<td>86.0 (84.3 to 87.1)</td>
<td>83.0 (80.5 to 85.6)</td>
</tr>
<tr>
<td>Respiratory rate (per min)</td>
<td>22.3 (21.8 to 22.8)</td>
<td>20.7 (20.1 to 21.3)</td>
<td>19.9 (19.5 to 20.4)</td>
</tr>
</tbody>
</table>

Table 5 Changes in physiological parameters by agent used
pain reduction for traumatic pain (Ford, unpublished, 2004) compared with a three-point reduction found in this study of visceral pain.36

The use of MTX has changed since the time of this study. Previously, it was routine practice to administer oxygen through the device. This is now recognised to increase evaporation of the agent into the ambient air, reducing the dose delivered to the patient and limiting analgesia to 15–20 min. The current recommended technique is to administer oxygen via a separate face mask and not through the inhaler (see online appendix). Intermittent use of MTX in this manner allows a single dose to last approximately 1 h, and as a result, the need to refill the inhaler with a second dose is now exceedingly uncommon. The briefer duration of effect with oxygen administered through the device—which was common at the time of the study—may also contribute to the lesser effect of MTX with longer transports and by hospital arrival despite having a greater initial effect. With oxygen flowing through the device, exhaustion of the MTX may not have been apparent to either patient or treating officer and hence analgesic effect removed. Further analysis with the current technique and/or comparison of techniques may yield more information.

Interestingly, there was no significant difference in pain assessment scores of patients who received MTX and INF in combination, relative to INF alone. This is consistent with a previous study23 that demonstrated similar or less pain reduction when these agents were combined in patients with non-cardiac pain. One possible explanation is that a second agent has been used when the first agent is ineffective, and hence the use of both agents is apparently less as it is a group of relative ‘non-responders’ or those suffering hyperalgesia. Further studies will be required to examine the sequence and timing of agents and the effect of each individually when used in combination. It is also unknown how frequently both agents were used simultaneously from the outset. Until these issues are clarified, no firm recommendations can be made regarding routine use of both agents.

**Limitations**

The limitations of the study are consistent with retrospective, observational studies of this nature and relate to available equipment, the study population and compliance with recording procedures.

The investigation of the analgesic agents’ effect on respiration has been limited to respiratory rate and GCS. More sensitive indicators are oxygen saturation and end tidal CO2 (ETCO2) monitoring. However, oxygen saturations were not routinely measured and/or repeated at the time of this study and ETCO2 monitoring in spontaneously breathing patients requires

---

**Table 6** Glasgow Coma Scale before and after treatment

<table>
<thead>
<tr>
<th>Agent</th>
<th>Glasgow Coma Scale before agent</th>
<th>15</th>
<th>14</th>
<th>13</th>
<th>12</th>
<th>11</th>
<th>Grand total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methoxy</td>
<td></td>
<td>456</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>459</td>
<td></td>
</tr>
<tr>
<td>Fentanyl</td>
<td></td>
<td>380</td>
<td>1</td>
<td>1</td>
<td>31</td>
<td>381</td>
<td></td>
</tr>
<tr>
<td>Both</td>
<td></td>
<td>156</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>156</td>
<td></td>
</tr>
<tr>
<td>Grand total</td>
<td></td>
<td>996</td>
<td>11</td>
<td>1</td>
<td>1</td>
<td>1009</td>
<td></td>
</tr>
</tbody>
</table>

---

**Table 7** Changes in pain scores by agent used

<table>
<thead>
<tr>
<th>Pain score</th>
<th>Methoxy</th>
<th>Fentanyl</th>
<th>Both</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial</td>
<td>8.1</td>
<td>6.2</td>
<td>6.9</td>
</tr>
<tr>
<td>Hospital</td>
<td>5.6</td>
<td>5.3</td>
<td>5.4</td>
</tr>
<tr>
<td>Pain reduction</td>
<td>2.5</td>
<td>2.9</td>
<td>2.5</td>
</tr>
</tbody>
</table>

equipment not currently utilised in ambulance services in Australia. It is possible, therefore, that minor degrees of respiratory depression have not been identified. Similarly, GCS is a crude estimate of conscious status. Confusion and/or disorientation are important effects produced by both these agents but not specifically analysed in this study. Further research is required to assess the significance or otherwise of these factors.

No allowance has been made for the anaesthetic effect of nitrates and oxygen for patients with pain of presumed cardiac origin. Although the use of these confounders is routine and is assumed to be similar between subgroups, this was not specified. Statistical significance or otherwise of these factors.

While the study population encompassed all age groups, only 1.1% of patients were under 20 years of age. Paediatric patients are therefore under-represented in this study, and as such we are unable to specifically analyse the effects in this group. Finally, the analysis of patient records was hampered by incomplete data, with missing values attributed to short journey time to hospital and non-compliance with completion of the case sheets by paramedics.

CONCLUSION

The results presented in this paper demonstrate MTX and INF are effective analgesic agents for the prehospital management of visceral pain, with only a very small number of cases in the INF group associated with subsequent hypotension but no change in GCS or other evidence of cardiovascular compromise. No patients were compromised by a fall in consciousness level or impaired respiratory rate. MTX may be the treatment of choice for shorter patient contact cases due to ease of administration, but INF provided superior pain relief at hospital arrival, and achieved greater pain relief for presumed cardiac pain, particularly in older and female patients. No clinical advantage could be detected by their combined use, however measures were limited.

Acknowledgements The authors would like to thank the paramedic staff, management and patients of the St John Ambulance Australia (Western Australia) Inc. for their participation and assistance with this study.

Competing interests None.

Ethics approval Ethics approval was provided by the Human Research Ethics Committee of Edith Cowan University.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

5. Wilkes GA, Oder HFO, Johnston SN. Inhaled methoxyflurane and intranasal fentanyl provide effective prehospital analgesia. CEMEM 2006;S103.


Inhaled methoxyflurane and intranasal fentanyl for prehospital management of visceral pain in an Australian ambulance service

Steven Johnston, Garry J Wilkes, Jennifer A Thompson, et al.

Emerg Med J 2011 28: 57-63 originally published online May 13, 2010
doi: 10.1136/emj.2009.078717

Updated information and services can be found at:
http://emj.bmj.com/content/28/1/57.full.html

These include:
- References
  This article cites 29 articles, 2 of which can be accessed free at:
  http://emj.bmj.com/content/28/1/57.full.html#ref-list-1
- Email alerting service
  Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Articles on similar topics can be found in the following collections
- Coma and raised intracranial pressure (2704 articles)
- Pain (neurology) (30931 articles)
- Hypertension (12672 articles)
- Pain (palliative care) (2868 articles)
- Pain (anaesthesia) (2764 articles)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/