Triplets
Current Trends in Medical Use of Opioids: Morphine versus Meperidine

Reporter: 賴裕永 醫師
## Trends in Medical Use of Opioids 1990-1996

<table>
<thead>
<tr>
<th>Year</th>
<th>Fentanyl</th>
<th>Hydromorphone</th>
<th>Meperidine</th>
<th>Morphine†</th>
</tr>
</thead>
<tbody>
<tr>
<td>1990</td>
<td>3263 (1.30)</td>
<td>118 455 (47.36)</td>
<td>5 223 137 (2087.63)</td>
<td>2 172 006 (868.13)</td>
</tr>
<tr>
<td>1991</td>
<td>12 261 (4.91)</td>
<td>126 251 (50.47)</td>
<td>4 879 898 (1950.44)</td>
<td>2 327 881 (926.19)</td>
</tr>
<tr>
<td>1992</td>
<td>23 673 (9.37)</td>
<td>129 549 (51.34)</td>
<td>4 407 189 (1746.51)</td>
<td>2 483 756 (984.26)</td>
</tr>
<tr>
<td>1993</td>
<td>29 668 (11.75)</td>
<td>129 893 (51.48)</td>
<td>4 075 132 (1614.92)</td>
<td>2 733 332 (1083.18)</td>
</tr>
<tr>
<td>1994</td>
<td>28 985 (11.47)</td>
<td>133 428 (52.88)</td>
<td>3 854 929 (1527.66)</td>
<td>2 772 441 (1098.69)</td>
</tr>
<tr>
<td>1995</td>
<td>30 640 (11.47)</td>
<td>127 905 (47.94)</td>
<td>3 483 637 (1305.53)</td>
<td>2 869 876 (1075.53)</td>
</tr>
<tr>
<td>1996</td>
<td>41 371 (15.49)</td>
<td>141 325 (52.96)</td>
<td>3 380 440 (1266.86)</td>
<td>3 461 618 (1297.29)</td>
</tr>
</tbody>
</table>

| Percentage change | 1167.88 (1091.54) | 19.31 (11.82) | -35.28 (-39.32) | 59.37 (49.43) |

*Values are expressed as grams (grams/100 000 population). Data from the Automation of Reports and Consolidated Orders System.
†Data from 1991 interpolated due to reporting anomalies.
# Trends in Medical Use of Opioids 1997-2002

## Table 2

<table>
<thead>
<tr>
<th>Year</th>
<th>Fentanyl</th>
<th>Hydromorphone</th>
<th>Meperidine</th>
<th>Morphine</th>
</tr>
</thead>
<tbody>
<tr>
<td>1997</td>
<td>74,086 (27.76)</td>
<td>241,079 (90.34)</td>
<td>5,765,954 (2,160.85)</td>
<td>5,922,872 (2,219.66)</td>
</tr>
<tr>
<td>1998</td>
<td>90,618 (33.96)</td>
<td>260,009 (97.44)</td>
<td>5,834,294 (2,186.46)</td>
<td>6,408,322 (2,401.59)</td>
</tr>
<tr>
<td>1999</td>
<td>107,141 (38.57)</td>
<td>292,506 (105.31)</td>
<td>5,539,592 (1,994.45)</td>
<td>6,804,935 (2,450.02)</td>
</tr>
<tr>
<td>2000</td>
<td>138,382 (49.82)</td>
<td>336,326 (121.08)</td>
<td>5,506,981 (1,982.71)</td>
<td>7,693,640 (2,769.99)</td>
</tr>
<tr>
<td>2001</td>
<td>186,083 (66.99)</td>
<td>400,642 (144.24)</td>
<td>5,450,204 (1,962.27)</td>
<td>8,810,700 (3,172.17)</td>
</tr>
<tr>
<td>2002</td>
<td>242,027 (87.13)</td>
<td>473,362 (170.42)</td>
<td>5,412,389 (1,948.61)</td>
<td>10,264,264 (3,695.43)</td>
</tr>
<tr>
<td>Percentage change 1997–2002</td>
<td>226.68 (213.87)</td>
<td>96.35 (88.64)</td>
<td>-6.13 (-9.82)</td>
<td>73.30 (66.49)</td>
</tr>
</tbody>
</table>
Demoral 30 mg, IM
Demoral 30mg, IM
Morphine 10 mg, IM
The main clinical indications of opioids include (Rossi, 2004):

- moderate-to-severe acute pain and chronic pain
- cough (mainly codeine)
- diarrhea (mainly loperamide and diphenoxylate used therapeutically)
- relief of severe dyspnsea (e.g. lung cancer, terminal COPD)
Morphine versus Meperidine

Morphine

Natural, 1803

Meperidine

synthetic, 1939
Heroin
1. Morphine
2. Heroin, fentanyl, methadone, hydromorphone, levorphanol
3. Pentazocine, nalbuphine, buprenorphine, codeine butorphanol
4. Naloxone, naltrexone
Clinical choice of Morphine, Demoral, Fentanyl

- All produce analgesia and respiratory depression.
- Route of administration, desired onset, duration.
Morphine, Demoral, Fentanyl

- Opioid receptors: $\mu$, $\kappa$, $\delta$


- Detection and Function of Opioid Receptors on Cells from the Immune System Clinical and Diagnostic Laboratory Immunology, September 2000
Opioid receptors: $\mu, \kappa, \delta$

- **Mu** - best analgesia, bradycardia, hypotension, sedation, respiratory depression, urinary retention, vomiting, defecation, constipation
- **Kappa** receptors trigger a lesser analgesic response, and may cause miosis, sedation and dysphoria.
- **Delta** receptors modulate mu receptor activity
Possible mechanism

• Equianalgesic doses of all opioid agonists will produce about the same effect on ventilation. In this regard, no drug is any more dangerous or any more safe than morphine.
• * 中樞神經：欣快感、嗜睡、呆滯、精神紊亂與噁心、嘔吐。
• * 呼吸道：麻醉藥品止痛劑會降低呼吸中樞對二氧化碳的敏感度。
• * 心臟血管：姿勢性低血壓與頭暈。
• * 腸胃道：便祕與 Oddi 氏括約肌痙攣。
• * 泌尿道：尿滯留。
Misconceptions of meperidine

• Less respiratory depression,
• less effect on biliary pressure,
• a lower addiction potential
• the standard dogma for the use of Meperidine
Meperidine or Morphine in Acute Pancreatitis?
**Meperidine or Morphine**

- An review concluded that there is "no good evidence" to support giving priority to meperidine for acute pancreatitis and called the practice "outdated."

American family physician 2001
Meperidine Use Guidelines

• Numerous reviews of meperidine’s pharmacodynamic properties have failed to demonstrate any benefit to using meperidine in the treatment of common pain problems, including biliary colic, pancreatitis, labor, and migraine.

Meperidine: A critical review. *Am J Therapeutics*, 2002,
MEPERIDINE: Guidelines for Use

- Prevention or treatment of drug-induced or blood product-induced rigors (e.g., amphotericin B, muromonab, platelets), and treatment of post-anesthesia shivering.
- Management of pain during medical procedures
- Intramuscular (IM) absorption is erratic and IM injections are painful; therefore, they are to be used only in emergent situations where another route is not immediately available.

» the Pharmacy and Therapeutics Committee 2002
Disadvantage of Meperidine

- Short duration of action of only 2 to 3 hours
- Meperidine is a toxic, local irritant.
- Frequent injections lead to muscle fibrosis with decreased analgesic effectiveness
- The intramuscular route is inferior for pain control and should be abandoned.

J. David Daniels
Meperidine is metabolized to normeperidine

Meperidine-induced CNS Excitatory Toxicity
Restless, tremors, myoclonus, seizures, delirium
藥物與哺乳

分娩若發生在投藥一小時內，由於尚未達到最高血中濃度，對嬰兒影響較小，而如果超過3、4 個小時或連續投與，藥物本身及代謝物則易蓄積在胎兒體內

internet郵政醫院藥劑科主任 洪增陽
• At my institution explicitly prohibits the use of meperidine for any reason other than amphotericin-induced rigors or documented intolerance to alternative narcotics.

American family medicine 2001
Changing prescribers’ practice is difficult

Formulary restriction

Figure 1. Average number of parenteral opioid doses given per day, before and after the formulary restriction. Note that hydromorphone use essentially replaced meperidine use.

The American J of Medicine 2005
Conclusion I

• Analgesics, such as morphine can be given for constant pain control while staying below toxic levels, prescribing demerol is an old habit which must be ---

• Formulary restriction or taken out right away.

The American J of Medicine 2005
Conclusion II
Pharmacoeconomics

- Fentanyl 2cc ------ $ 20
- Demoral 50mg/amp----- $ 20
- Morphine 10mg/amp---- $ 16
- Tramadol 下架了
- Ketorolac 30 mg/amp— $ 80
- Morphine 20mg/amp---- $ 20
- Butaro ( nasal spray ) 10 cc---- $ 2100
  (Fentanyl 2cc --- Morphine 10mg --- Demoral 80mg)
Conclusion III
Analgesia & Sedation in critical care

Not recommended for routine use in ICU-----

◆ Meperidine (Demerol) Active metabolite, normeperidine, may accumulate and produce central nervous system excitation.

◆ NSAID No analgesic advantage over opiates
Potential risks of gastrointestinal bleeding, platelet inhibition, renal insufficiency in critical patients.

0.1 mg morphine IV per kg
謝謝你聽我的演講，沒有打呼呼！