

# PAIN TOPICS

## Meperidine--What's all the Fuss?

Thomas E. Quinn, MSN, RN, AOCN  
Project Director, MGH Cares About Pain Relief

This article first appeared in *Pain Relief Connection* Vol 2 #2, February 27, 2003 p 3-6. "Pain Topics" and *Pain Relief Connection* are services of MGH Cares About Pain Relief, <http://www.massgeneral.org/painrelief>

### Introduction

The title of this essay was borrowed from Dr. David Weissman's "Fast Fact"<sup>1</sup> of the same name, one of many short reviews of issues in pain and palliative care on the End of Life Physician Education Resource Center ([EPERC](#)) web site.

Meperidine (Demerol<sup>®</sup>) was first synthesized in 1939. For both practical and "naïve"<sup>2</sup> reasons it became the most widely prescribed opioid analgesic in the United States in the 2<sup>nd</sup> half of the 20th century.<sup>3</sup> Meperidine was introduced in a solution conveniently available in single dose ampules or multidose vials at a time when morphine was only available as an injectable hypodermic tablet (it had to be crushed and dissolved).<sup>4</sup> Furthermore, it was initially thought that meperidine did not have the same toxicities as morphine, including respiratory depression, constipation, and the potential for chemical dependence. Meperidine has been used extensively as a preoperative medication, frequently combined with a phenothiazide such as hydroxyzine (Vistaril); as a postoperative analgesic, historically ordered IM every 4-6 hours PRN; as an IM analgesic for migraine and sickle cell pain; as the drug of choice for biliary colic; and to palliate rigors associated with anesthesia, amphotericin, and blood or biologic products.

However, by the 1990's clinical guidelines<sup>5,6</sup> were discouraging the use of meperidine as first line therapy for moderate to severe pain. Several major institutions have reported removing it from formularies<sup>7</sup> or severely restricting its use.<sup>8</sup> Some anti-meperidine advocates have used relatively inflammatory language to call attention to its problems and overuse or misuse, even referring to it as a "monster"<sup>9</sup> or declaring "Demerol Free Zones."<sup>10</sup>

The reasons for the dramatic rise and fall of the reputation of meperidine are as complex as opiophobia (the irrational fear of addiction) and as common as habit. Pain management is one of the most difficult arenas in which to change clinical behavior. Physicians, nurses, and pharmacists tend to persist in old practices and beliefs in spite of evidence that those practices or beliefs are either erroneous or harmful. An examination of several opioid actions and toxicities finds that meperidine has no advantages over other opioids, but several disadvantageous characteristics.

In early 2002 a team led by Kenneth Latta, a Clinical Pharmacist at Duke University Medical Center, published an extensive review<sup>2</sup> of meperidine. The team examined every paper previously published on this drug. By today's standards studies of meperidine and other opioids have frequently been of poor design. The preponderance of evidence, however, does not support the wide spread use of this drug.

### Analgesia

Meperidine is relatively less potent than other opioids, but perhaps more importantly it has a short duration of analgesia, 2 - 3 hours compared to morphine's approximately 4 hours. The more severe the pain, the less effective it is at the published equianalgesic doses. Some equianalgesic references use a 1:7.5 morphine:meperidine ratio,<sup>6</sup> while others,<sup>5</sup> and several studies,<sup>2</sup> suggest that 1:10 is more clinically appropriate. In one study cited by Latta et al, 50 mg of IM meperidine was no more effective than placebo. In another, meperidine 50 mg was no more effective as a preoperative medication than hyoscine, a phenothiazide with no analgesic properties. IM meperidine is variably absorbed and IM injections are painful. Problems inherent in IM administration and differences in duration of action would seem to be overcome if both drugs are administered by IV patient-controlled analgesia (PCA). When meperidine and morphine were compared in this fashion, analgesia was similar when patients were at rest, but morphine was superior during movement, when pain was assumed to increase in severity.<sup>2</sup> Oral meperidine is poorly absorbed, having a 1:3 parenteral:oral equivalency. In itself this would not appear to be problematic, but one source reports patient reluctance to take what appears to be large amounts of medication:<sup>11</sup>

oral meperidine is available in 50 mg tablets, each of which is larger than standard morphine and hydromorphone tablets. Oral meperidine 50 mg has been reported to be no more potent than 650 mg of aspirin or acetaminophen.<sup>12</sup> Much more importantly, the toxic metabolite of meperidine, normeperidine, accumulates more rapidly with oral dosing, as will be discussed below.

Meperidine IM has been very commonly used for migraine and for sickle cell pain crisis. There has been no advantage shown compared to other opioid analgesics and its short duration of action would seem an inherent limitation in both indications. Indeed, one study showed that continuous infusion morphine was superior to intermittent scheduled injections (IV or IM) of meperidine, morphine, or codeine for sickle cell vaso-occlusive pain crisis.<sup>13</sup>

### **Local reactions**

Meperidine is too irritating to give subcutaneously. Given intramuscularly, historically the most common route, local irritation is common. Patients describe it as a burning sensation. Repeated IM dosing can cause induration and scarring. The intravenous route appears to be the most appropriate route of administration.

### **Smooth muscle relaxant**

Meperidine was theoretically proposed and then identified early on in animal studies as a smooth muscle relaxant. It was enthusiastically embraced, and in many settings persists, as the preferred opioid for abdominal pain presumed related to spasm of smooth muscle such as biliary colic. Subsequent study has shown that meperidine has local anesthetic properties, and when applied topically to smooth muscle does cause relaxation. This is a rare clinical scenario, however. Meperidine has been shown to be no more effective as an analgesic for biliary colic, and may actually not be as effective as morphine.

### **Toxicity**

The major cause for concern among critics of meperidine is the rapid accumulation of the neuroexcitatory metabolite, normeperidine. While all opioids have the capacity to cause neuroexcitability, most require prolonged use at high doses. With meperidine, subtle changes can be seen in a matter of hours, and significant toxicity within 2 days or less. Initial signs may include fear, anger, and anxiety, whereas morphine tends to be anxiolytic. Mood changes may progress to shaky feelings, tremors and twitches, myoclonus, and even grand mal seizures. Fortunately, few people these days are on MAO inhibitors, since these antidepressants can precipitate neurotoxicity; concurrent use of MAO inhibitors and meperidine is contraindicated. Normeperidine accumulates very rapidly in renal failure, and meperidine should not be used in that setting. Normeperidine accumulates more rapidly when meperidine is taken orally. The analgesic effect of meperidine is reduced when taken orally, but the same amount of normeperidine is produced, milligram for milligram of meperidine, no matter the route. Normeperidine is not an opioid. Therefore, if neurotoxic symptoms develop, opioid antagonists such as naloxone do not reverse the symptoms. Indeed, they are reported to worsen.

### **Indications for meperidine**

Meperidine is not a "monster." It has been widely overused and misused for many years. It has no advantages as an analgesic over any other opioid. However, its rapid onset and short duration of action make it a potentially useful drug for short procedures that do not cause severe pain. Used in conjunction with appropriate sedatives, it can be used for conscious sedation. In the United States, it probably has no equal in palliating the rigors (shivering) associated with anesthesia, amphotericin, and certain biologic agents. For this indication, 25-50 mg by slow IV injection may be used. Outside the United States nefopam and parenteral tramadol appear to be effective for this indication.

### **References**

1. End of Life Physician Education Resource Center. Requires free registration. Source of many pain and palliative care resources, including "Fast Facts" a series of short reviews of pertinent topics. Notable among them is "Fast Fact and Concept #71: "Meperidine: what is all the fuss?" and Fast fact and Concept #69: "Pseudoaddiction."<http://www.eperc.mcw.edu>
2. Latta KS, Ginsberg B, Barkin RL. Meperidine: A Critical Review. *American Journal of Therapeutics* 2002;9(1):53-68
3. Ibid.
4. Ibid.

5. Acute Pain Management Guideline Panel (1992). *Acute Pain Management in Adults: Operative or Medical Procedures and Trauma*. Administration for Health Care Policy and Research. Rockville, MD Pub # 92-0032
6. American Pain Society. *Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain*. 4<sup>th</sup> Ed. May be ordered through the APS web site, <http://www.ampainsoc.org/pub/principles.htm>
7. Daniels JD. "DFZ." <http://ruralnet.marshall.edu/pain/dfz.htm> (accessed 28 Jan 2003)
8. Gordon D, Jones HD, Goshman LM, Foley DK, Bland SE. A quality improvement approach to reducing use of meperidine. *Journal of Quality Improvement* 2000 Dec; 26(12):686-699.
9. Hoyer KA. Slaying the Meperidine Monster: Building Awareness and Changing Practice. *Pain Management* (Oncology Nursing Society Special Interest Group Newsletter) 2001 Nov;11(3):1,4.
10. Op cit. Daniels
11. Antonopoulos J, Bollinger K, Goshman L. Guidelines for Use of Meperidine. University of Wisconsin Hospitals and Clinics. 1999.
12. McCaffery M & Pasero C. (1999) *Pain: Clinical Manual*. St. Louis: Mosby, Inc.
13. Robieux IC, Kellner, JD, Coppes MJ, et al. Analgesia in children with sickle cell crisis: comparison of intermittent opioids vs continuous infusion of morphine and placebo-controlled study of oxygen inhalation. *Pediatric Hematology Oncology* 1992 Oct-Dec;9(4):317-326
14. DeWitte J & Sessler DI. Perioperative Shivering. *Anesthesiology* 2002;96(2):467-484