### Kaiko 1982
**USA**
**Inpatient**
**Prospective cohort 1977-78**
**Purpose:** To assess the relationship between plasma levels of meperidine and normeperidine and signs and symptoms of CNS excitation in patients receiving meperidine for postoperative pain or chronic pain from cancer. Additionally these patients were compared to similar patients receiving other narcotic analgesics.

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| Kaiko 1982 | USA | N = 56 meperidine  
Phase 2  
n = 47 meperidine  
n = 29 other narcotic analgesic | n = 19 asymptomatic meperidine patients  
Mean age 50 (3.9) | Days of meperidine administration  
Mean (SE; range)  
1.2 (0.1; 1-2) | There were no significant differences between the groups of symptomatic patients |
| | | Rate of administration (mg/d)  
170 (18; 75; 75-380) | Meperidine; normeperidine (ng/ml)  
270 (28; 117-465); 56 (12; 6-190) | The variation in intensity of CNS excitation was directly associated with normeperidine plasma level and the ration combined. |
| | | Meperidine/normeperidine plasma level | | The normeperidine level contributed considerably more to this association than did the ratio. |
| | | n = 37 symptomatic meperidine patients  
Mean age 46 (3.7) | Days of meperidine administration  
Mean (SE; range)  
8.0 (1.2; 1-22) | There was no structural basis in the patients with multifocal myoclonus or grand mal seizures |
| | | Rate of administration (mg/d)  
350 (52; 59-1080) | Shaky feelings  
Tremors/twitches  
Myoclonus/grand mal | Neurological symptoms cleared slowly (3 to 5 days) following cessation of meperidine |
| | | Meperidine/normeperidine plasma level  
420 (72; 42-1220); 422 (53; 128-1290) | Mean age 46 (7.0) | Improvement in neurological signs was not associated with any measured change in blood chemistry values or renal function |
| | | n = 9 tremors/twitches  
Mean age 38 (4.4) | Shaky feelings  
Tremors/twitches  
Myoclonus/grand mal | Renal dysfunction can promote the accumulation of normeperidine in plasma. |
| | | n = 8 myoclonus/grand mal  
Mean age 46 (7.0) | Shaky feelings  
Tremors/twitches  
Myoclonus/grand mal | No significant differences for patients receiving other narcotic analgesics |

### Conclusion:
Routine use of meperidine for postoperative pain does not appear to correlate with objective signs of CNS excitation but is associated with mild negative alterations in various elements of mood. Chronic administration of increasing doses of meperidine results in the accumulation of normeperidine and may be associated with the appearance of adverse objective effects, particularly in patients with renal dysfunction. The intensity of CNS excitation is highly associated with the accumulation of normeperidine in plasma. Normeperidine toxicity is not reversed by naloxone and may be exacerbated by it.