

# "Subutex in Finland"



**BUPRENORPHIN,  
AN ABUSED  
OPIOID**

**Prof. Erkki Vuori**

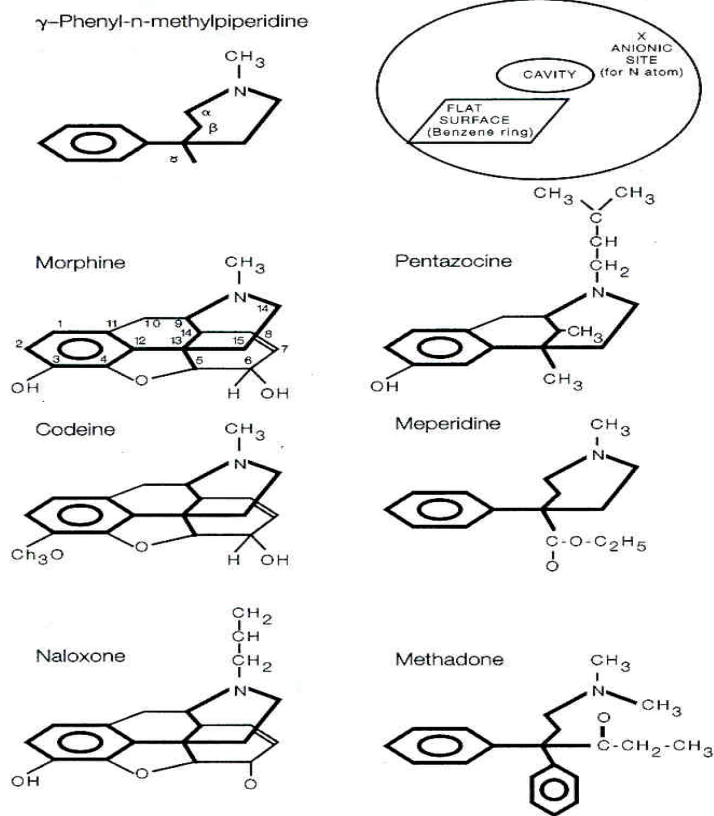
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**Department of Forensic Medicine, University of Helsinki**

# OPIOIDS ARE IMPORTANT DRUGS IN MEDICINE AND IN FORENSIC MEDICINE

- **Opioids are needed as centrally active analgesics, especially in the treatment of severe pain**
- **Opioids are also badly abused**
- **Dealing in abused opioids is linked with organized crime**
- **The usual way to abuse opioids is by injecting, which involves health risks**
- **All opioids share a common mechanism of action via  $\mu$ -receptors:  $\mu$ -1 for analgesia,  $\mu$ -2 for respiratory depression**
- **All opioids can cause sudden death**

# OPIOIDS AND $\mu$ -RECEPTORS



**Figure 25-1** Structural formulas of some opioids. **Top left:** Note that  $\gamma$ -phenyl-*N*-methylpiperidine forms the common chemical "backbone" in all the compounds shown, although in some, for example, methadone, the piperidine ring has been opened. **Top right:** shows the main features of the opioid receptor. The main topographic features of the receptor are shown and by mentally transposing the formula of, for example, pentazocine over the diagram, it becomes evident how the main parts of the chemical structure relate to the key areas of the receptor. (From Thompson JW. Clinical pharmacology of opioid agonists and partial agonists. In: Doyle D, ed. *Opioids in the Treatment of Cancer Pain*. International Congress and Symposium Series No. 146. London: (Royal Society of Medicine Services, 1990: 17-38.)

# ADVERSE EFFECTS OF OPIOIDS

- **Pinpoint pupils (miosis)**
- **Confusion, dizziness**
- **Respiratory difficulty (failure to respond to increased CO<sub>2</sub>)**
- **Cardiovascular changes: hypotension**
- **Gastrointestinal symptoms (nausea, constipation)**
- **Hypothermia**
- **Bronchial constriction**
- **Convulsions**
- **Coma**

# OPIOIDS

- **Agonists**
  - natural: morphine, codeine**
  - semi-synthetic: heroine, oxycodone, ethylmorphine**
  - synthetic: methadone, propoxyphene, fentanyl, tramadol**
- **Antagonists**
  - naloxone, nalophine, naltrexone**
- **Partial agonists/antagonists**

# BUPRENORPHINE 1

- **Is a semi-synthetic opioid derived from thebaine**
- **First synthesized in the USA in 1973**
- **Buprenorphine (Temgesic, Subutex, Suboxone) is:**
  - **as an analgesic 25-40 times more potent than morphine**
  - **as an antagonist equivalent to naltrexone**
- **Has a ceiling effect – higher doses do not produce greater effects**
- **Has low oral bioavailability, but can be taken sublingually**
- **Has an active metabolite, norbuprenorphine**

# BUPRENORPHINE 2

- **For treatment of pain the usual dose is 0.3-0.6 mg parenterally or 0.2-0.4 mg sublingually every 6-8 hours**
- **For maintenance therapy high strength tablets are available (2 and 8 mg), dose up to 16 – 24 mg**
- **The duration of action is long, up to 72 h**
- **Withdrawal symptoms appear slowly**
- **High-dose buprenorphine treatment for**



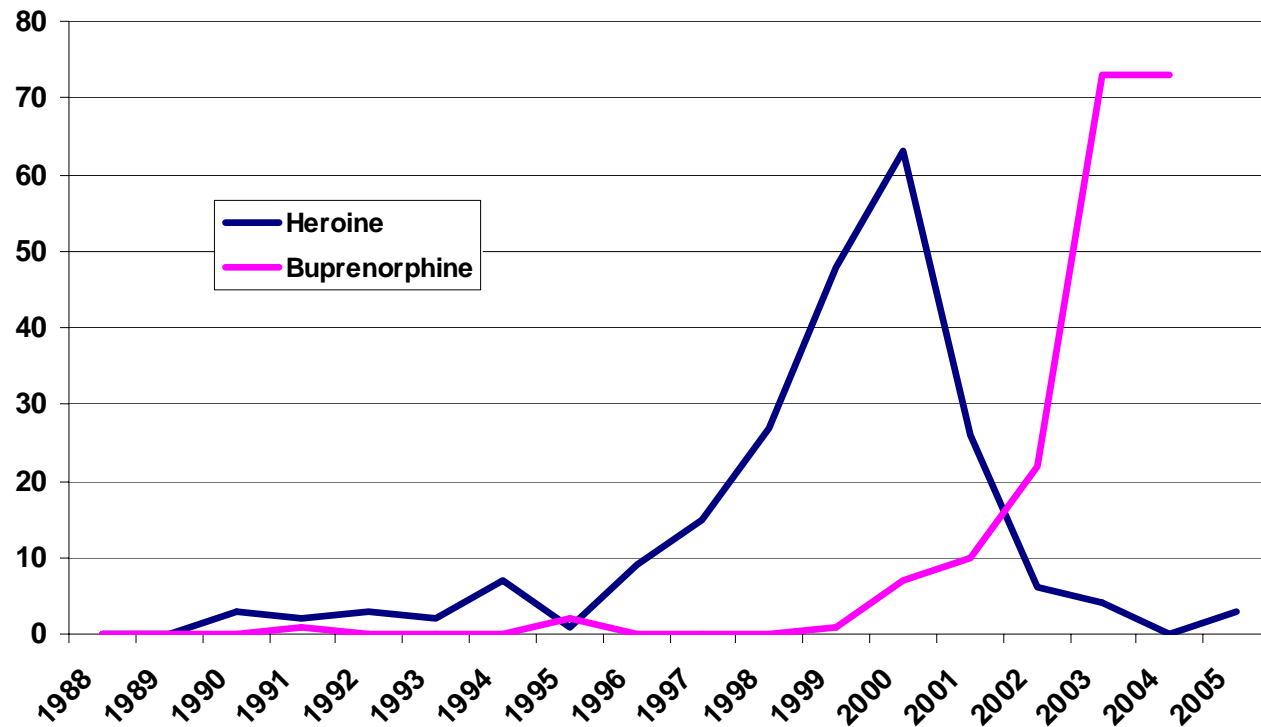
# BUPRENORPHINE 3

- **Abusers take it sublingually, intravenously or by snorting. The typical intravenous dose is about 1 mg 2-3 times a day, sublingual dose up to 24 mg day**
- **Sublingual bioavailability is 50% and oral 16%**
- **Therapeutic blood level is up to 10 µg/l**
- **Drug levels in fatalities are 1.1-29 µg/l, average 8.4 µg/l!**
  - **”There is no safe therapeutic concentration for opioids.”** (Drummer 2001)
- **Typical fatal combination:**
  - **Buprenorphine**
  - **CNS-acting agents:**

# **WHAT IS THE USE OF BUPRENORPHINE (SUBUTEX) COMMON IN FINLAND?**

- **Good reputation: Subutex is manufactured by a pharmaceutical company**
- **It is a simple tablet, not a hazy powder**
- **The quality is high and quantity is consistent, tablets are easy to divide and dose**
- **It can be used via several routes: sublingually intravenously or by snorting**

# HEROIN AND BUPRENORPHINE IN POST MORTEM FORENSIC TOXICOLOGY IN FINLAND



# ABUSED BUPRENORPHINE, FINDINGS AND DEATHS IN

Age groups	2000	2001	2002	2003	2004
15-19	1	2	4	6	6
20-24	3	3	11	23	15
25-29	2	0	2	19	20
30-34	0	4	4	9	9
35-39	1	1	1	8	13
40-44	0	0	0	5	5
45-49	0	0	0	2	4
50-	0	0	0	1	1
N	7	10	22	73	73
<b>Deaths</b>	<b>3</b>	<b>2</b>	<b>13</b>	<b>33</b>	<b>36</b>

# BUPRENORPHINE 4

- **In Finland the legal use is strictly controlled and is foolproof**
- **Illegal buprenorphine first came from France, but now comes mostly from the Baltic countries**
- **We have a drug tourism problem:**
  - **1-day trips**
  - **local general practitioner gives the prescription**
  - **possibility of contacts with several doctors**
  - **extra drugs are sold in Finland**
  - **trafficking trips are organized**
- **The result: buprenorphine is at present the main injected opioid in Finland and in many cases the first opiate used by young abusers.**