METHADONE

Methadone Mortality Working Group
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Methadone

- Background
- Pharmacology
- Toxicity
- Diversion, Toxic Exposures, Mortality data
- Methadone Distribution (ARCOS data)
- Methadone Initiative
Methadone - Background

- In late 1940s - marketed as pain reliever ("analgesic"), but not extensively used.
- In the 70s - shown to be effective as once-daily medication for narcotic (opioid) addiction treatment.
- In the US - Established as the standard for treatment of narcotic (opioid) addiction.
- From late 1990s - methadone is being increasingly used in pain management.
Methadone – an Opioid

- Methadone belongs to pharmacological class called “Opioids”

- **Opioids** are among the most potent analgesic drugs and are widely used

- **Opioids** are used in the management of acute and cancer-related pain, and chronic non-cancer pain
Opioids are of either **natural** origin or **semisynthetic**, or **synthetic**

- **Natural**: e.g., Morphine from opium poppy
- **Semisynthetic**: e.g., hydrocodone (Vicodin), oxycodone (Percocet, OxyContin)
- **Synthetic**: e.g., Methadone (Methadose), meperidine (Demerol), fentanyl (Duragesic) etc.
Opioid Actions on Brain and Spinal Cord

- **Pain relief**: Acts on pain pathways in brain and Spinal cord to relieve pain

- **Abuse and Addiction**: Acts on brain reward pathways to produce “high”

- **Widely abused**
New Drug User Patterns

Source: Prescribing Opioids for Chronic Pain, SAMHSA-CSAT: Clinical Challenges in Prescribing Controlled Drugs
Methadone goes well with OJ
Deaths per 100,000 related to unintentional overdose and annual sales of prescription opioid pain relievers by year, 1990-2006

Source: Paulozzi, CDC, Congressional Testimony, 2007
Poisoning Deaths in the U.S

% Increase

% Increase in deaths

2000 2001 2002 2003 2004 2005

-100 0 100 200 300 400 500

Source: CDC

- All poisoning deaths
- Methadone
- Other opioid
- Other synthetic narcotics
- Cocaine
- Heroin
Methadone Related Deaths (% of all Poisoning Deaths)

Source: CDC

Graph showing the increase in methadone-related deaths as a percentage of all poisoning deaths from 1999 to 2005.
Methadone - Pharmacokinetics

- Well absorbed (>80%) taken orally.
- Body eliminates methadone (half-time up to 59 hrs) slowly, while methadone’s pain relieving action lasts much shorter (4-8 hrs).
- Patient may feel the need to repeat dose at intervals shorter than body can handle.
- Repeated dosing may lead to accumulation in the body and result in serious toxicity.
Methadone Single Dose Effects


Source: Resource Manual for CME course entitled “Prescribing Opioids for Chronic Pain” - Offered by the New England Chapters of the American Society of Addiction Medicine with support from CSAT, SAMHSA
Toxic Effects of Multiple Methadone Doses

Source: Resource Manual for CME course entitled “Prescribing Opioids for Chronic Pain” - Offered by the New England Chapters of the American Society of Addiction Medicine with support form CSAT, SAMHSA
Examples of Substances – May Enhance Methadone Effects

- These reduce elimination of methadone by body
- Some antidepressant drugs – e.g., Prozac, Paxil, Zoloft etc.
- Depressants (e.g., alcohol, anesthetics, benzos, some sedatives, other opioids)
- Some drugs used for fungal infections
- Some antibiotics – e.g., Erythrocin
- Grapefruit juice
Examples of Substances - May Reduce Methadone Effects

- These upon *prolonged* exposure reduce methadone effects
- Anti-seizure drugs – Tegetrol, Dilantin
- Sedatives (barbiturates) – e.g., Amytal, fioricet, fiorinal, etc.,
- HIV/AIDS drugs
- Drugs used to treat Tuberculosis
- Cocaine
- Smoking
Methadone Deaths—Two Major Mechanisms

- **Respiratory depression**
  - Major hazard (Similar to other opioid analgesics)
  - Respiratory depression typically occurs later and persist longer than its peak analgesic effects

- **Toxicity on heart**
  - Not shared by other opioids
  - Shared by LAAM, a previously marketed addiction treatment drug.

(SPECT Brain scan from Brainplace.com, Dr. Daniel Amen)