Fentanyl Abuse: A fatal attraction

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What is fentanyl?

- Fentanyl is an opioid pain killer in the same class as codeine, morphine & oxycodone
- In patch form, fentanyl is released slowly over 3 days for sustained pain relief
- Fentanyl is an important medication for people with severe pain (cancer-related, surgical, end of life)
- Access to prescription forms of fentanyl is well-controlled, but diversion can still occur

Effects of opioids in brain & body

- Operate painkills can have effects similar to heroin and morphine, especially when prescribed by a doctor
- Your skin may feel flattened and numb
- Your vision may blur
- Your breathing can slow and cause increased anxiety, wheezing, or even death
- Your heart rate can decrease
- You may develop a tolerance, meaning the next dose you need more to produce the same effect
- You may become sick
- You may develop a depression
- You'll begin to feel that the effects of 15mg or less will manifest on their own and last longer
- High doses of fentanyl can be lethal
- Access to prescription forms of fentanyl is well-controlled, but diversion can still occur
How does it compare with other opioids?

- Fentanyl is a very potent drug – up to 100x stronger than morphine & 50x stronger than heroin
- There are members of the “fentanyl family” in current medical and/or veterinary use that are much stronger than fentanyl.
  - Sufentanil (used in palliative care) is up to 10 times stronger than fentanyl
  - Carfentanil is up to 100 times stronger than fentanyl
- Newer opioid-like drugs emerging in the illicit market may be even stronger than the fentanyl analogues (e.g., W-18)

**Opioid Comparison**

<table>
<thead>
<tr>
<th>Relative Strength of Opioids in Morphine Equivalents</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Weak Opioids</strong></td>
</tr>
<tr>
<td>Codeine</td>
</tr>
</tbody>
</table>

**Relative Strength of Opioids in Morphine Equivalents**

<table>
<thead>
<tr>
<th>Weak Opioids</th>
<th>0.1</th>
<th>0.15</th>
<th>0.6</th>
<th><strong>Strong Opioids</strong></th>
<th>1</th>
<th>1.5</th>
<th>2-4</th>
<th>5</th>
<th>7.5</th>
<th>40</th>
<th>75-100</th>
<th>10,000-100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Codeine</td>
<td>Hydrocodone</td>
<td>Methadone</td>
<td>Hydromorphone</td>
<td>oxycodone</td>
<td>Methadone (chronic)</td>
<td>Buprenorphine</td>
<td>U47700</td>
<td>Heroin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**NOTE:** This chart represents a rough approximation of relative potencies of common opioids. Many environmental or individual factors could affect the relative potency of an opioid in a specific situation. The person's characteristics — age, health status, nutritional status, etc. — and the drug characteristics — dose, purity, other substances used concurrently, etc. — will have a significant impact on that person’s experience.
How do people use fentanyl?

- There is a market for fentanyl as a drug of abuse, where it is used orally, smoked, snorted, or injected.
- Fentanyl patches may be diverted from medical sources (either new or used) and cut up for sale as “chicklets”
  - Enough drug may remain in a section of the patch to be potentially lethal
- There is an growing trend towards a powdered form that is illegally imported from international sources (mostly China)
- Because of the extremely high strength of pure fentanyl powder, it is very difficult to dilute appropriately. This leads to a mixture that may be far too strong and very dangerous.

How do people use fentanyl?

- Fentanyl is often added to other drugs without the user’s knowledge.
  - Traces have been found in other recreational drugs including cocaine, Xanax, MDMA & heroin.
- Fentanyl is sometimes sold as heroin, often leading to overdoses.
  - Many fentanyl overdoses are initially classified as heroin overdoses
  - The mixture of fentanyl & heroin is known as "magic" or "the bomb", among other names, on the street
- Organized crime groups press the powder form into fake OxyContin tablets (“greenies”).

Is fentanyl adulteration of other drugs really a problem?

- Fentanyl has been found in 2,503 drug samples submitted by Canadian law enforcement agencies so far in 2016 (Health Canada, 2016).
  - This is a 43 per cent increase from the 1,749 drug samples submitted in all of 2015.
  - In Manitoba, 26 drug samples containing fentanyl have been identified by Health Canada so far this year, compared with 20 in all of 2015.
- This is a problem because people think they are using a particular drug, and are not prepared for the life-threatening effects of fentanyl.
- Emergency first responders may not administer naloxone (the drug that counteracts overdose with opioids) if they are not aware fentanyl has been ingested.
Is fentanyl addictive?

- If you are prescribed fentanyl and use it as directed you are not likely to become addicted.
  - About 10-15% of people taking prescribed opioids become addicted to their medication
  - This figure may be higher for strong opioids like fentanyl
- If you use fentanyl to get “high” there is a greater risk of becoming addicted over time
  - Many factors contribute to addiction, and it is impossible to predict who will or won’t become addicted
  - Many users don’t have the chance to become addicted
- Those addicted to fentanyl have the same treatment options & expectation for success as those who use other opioids.

The new frontier: Designer opioids

- Fentanyl itself is a potent synthetic opioid.
- Many other related compounds – designer opioids or fentanyl analogues – have appeared in North America.
  - These compounds include acetylfentanyl, 6-butyrfentanyl and 3-methylfentanyl. All three have been detected in drug-related fatalities in Canada, although no specific numbers are available.
  - The United States DEA reported at least 52 confirmed fatalities involving acetylfentanyl between 2013 and 2015.
- Furanylfentanyl has appeared in Canada in the last six months.
  - In the U.S. at least seven deaths were caused, at least in part, by furanylfentanyl since mid-December.
  - Fentanyl analogues are noteworthy due to their toxicity
  - Many are significantly more toxic than fentanyl.
Fentanyl analogues

- Fentanyl (left) and 3-methylfentanyl (right) differ by only a methyl (CH$_3$) group. This slight alteration makes 3-methylfentanyl 100 x stronger than fentanyl.
  - There are 18 other places on the fentanyl molecule where a second methyl group could be added, resulting in potentially 18 new drugs.
  - Adding a third methyl group would lead to hundreds of new drugs.
  - Adding other atoms/groups could lead to millions of new drugs.

Fentanyl analogues?

Endless possibilities...

Potency of fentanyl analogues

<table>
<thead>
<tr>
<th>Substance</th>
<th>Potency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meperidine (Demerol)</td>
<td>0.10</td>
</tr>
<tr>
<td>Anileridine</td>
<td>0.25</td>
</tr>
<tr>
<td>Morphine (comparison)</td>
<td>1</td>
</tr>
<tr>
<td>W-15</td>
<td>5</td>
</tr>
<tr>
<td>Alfentanil</td>
<td>10-20</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>50-100</td>
</tr>
<tr>
<td>Remifentanil</td>
<td>300</td>
</tr>
<tr>
<td>Sufentanil</td>
<td>500-1000</td>
</tr>
<tr>
<td>Carfentanil / W-18 / 3-methylfentanyl</td>
<td>10,000</td>
</tr>
</tbody>
</table>
The new kid on the block: Carfentanil

- Fentanyl is a powerful and dangerous drug – carfentanil is about 100 times more potent than fentanyl.
- Carfentanil was never intended for use in humans. Its most common use is to tranquilize very large animals in veterinary practice. It is known as the “elephant tranquilizer.”

![Fentanyl and Carfentanil Structures](image)


![Opioid Potency Chart](image)


As little as 10 mg carfentanil would be needed to sedate – or even kill – an elephant

How dangerous is the fentanyl family?

- The risk of overdose and death are the greatest concerns about fentanyl/related drugs.
- Fentanyl is a very potent drug – a very tiny amount about equal to 2 grains of salt can be lethal.
- The effects of fentanyl occur very quickly after use
  - Intoxication and overdose can occur before the user is aware something is wrong.
- The difference between an effective dose and a lethal dose is very small – fentanyl is not a very forgiving drug in overdose situations.
A deadly dose of fentanyl is 2 mg, which is equal to just 2 grains of salt.

How much is in your pill?

#FentanylKills

A deadly dose of carfentanil may be as small as 20 micrograms (0.02 mg)

A single snowflake weighs about 30 micrograms


Why doesn’t everyone die?

Question:
“Why doesn’t everyone die?”

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#FentanylKills

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A single snowflake weighs about 30 micrograms


Why doesn’t everyone die?

Question:
“If a potentially fatal dose of fentanyl is so small, why are there not more deaths from fentanyl poisoning?”

Answer:
Tolerance to opioids develops with repeated use.

AND

The dose of street fentanyl is impossible to predict.

• Someone who hasn’t used opioids before – or only used them rarely – is called “opioid naïve”
  – These are the people most at risk of dying from an overdose.
  – They have no “resistance” to the effects of opioids.

Tolerance

• Frequent users of opioids develop tolerance – they can withstand much larger doses, even of fentanyl.
• Tolerance develops fairly quickly to certain opioid effects:
  – Euphoria
  – Sedation
  – Pain relief
  – Nausea/vomiting
  – Mental clouding
  – Respiratory depression
• Little or no tolerance develops to some effects, like pupil constriction, constipation, convulsions
• As tolerance continues to develop, the person needs more and more of the drug to get the same effect.
• Ultimately, so much is needed that it causes an overdose.
What does an overdose look like?

- There are different severities of opioid overdose
  - Ranges from drowsiness/slurred speech to coma & possible death

- **Early signs** of an overdose include:
  - Severe sleepiness
  - Slow heartbeat
  - Trouble breathing
  - Slow, shallow breathing (<12 breaths/minute) or snoring
  - Cold, clammy skin
  - Trouble walking (i.e., stumbling)
  - Slurring words
  - Pinpoint pupils

- If any of these signs are present, call 911 immediately.
- Naloxone may be administered while waiting for an ambulance (once kits are widely available)
How do we treat an overdose?

- Treatment focuses on supportive care with airway protection & respiratory assistance.
- Co-ingestions with other drugs should be considered.
- **Naloxone** – an opioid antagonist or “blocker”
  - reverses the effects of an opioid overdose, restoring breathing & preventing death – is **NOT** a safety net!
  - does **NOT** last as long as most opioids!!
  - may cause abrupt withdrawal symptoms
- Up to 6x the usual IV dose of naloxone might be required for fentanyl & other synthetic opioids
  - This is because these newer drugs are much more toxic & have unpredictable amounts of opioid in each tablet/etc.

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**How antagonists work**

<table>
<thead>
<tr>
<th>Agonists</th>
<th>Drugs that occupy receptors and activate them.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antagonists</td>
<td>Drugs that occupy receptors but do not activate them. Antagonists block receptor activation by agonists.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Agonist alone</th>
<th>Agonist + antagonist</th>
<th>Antagonist alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full activation</td>
<td>Less activation</td>
<td>No activation</td>
</tr>
</tbody>
</table>

**Source:** [http://physiologicalmechanismsofopioids.weebly.com/](http://physiologicalmechanismsofopioids.weebly.com/)
Messaging about fentanyl/analogues

• Messages (flyers, posters, etc.) should avoid language that might be attractive to users, such as “potent,” “strong,” or “more powerful”

• Better alternatives are “toxic,” “dangerous,” or “lethal” – terms that imply harm.

• Any messaging should be clear that the potency/toxicity of fentanyl is not the only danger. The variability of the dose from one tablet/powder to the next is just as important in increasing the risk of overdose.

The bottom line:
What you need to know about fentanyl

1. It’s Dangerous - Using fentanyl to “get high” is very dangerous. It only takes a tiny amount (about equal to two grains of sand) to result in overdose and death.

2. It’s Addictive - Fentanyl can be highly addictive when used to get high. It is very strong and fast acting, making it one of the more addictive drugs.

3. It’s Strong - Fentanyl is a very potent drug – up to 100 times stronger than morphine and 20-50 times stronger than heroin.

4. It’s Fast-Acting - Fentanyl effects occur very quickly after use, meaning intoxication and overdose can occur before a person is aware something is wrong.

5. You Might not Know It’s There - Fentanyl can be added to other drugs without the user’s knowledge. There is no way for an average person to tell if fentanyl has been added to another drug.

What can we do?

• In terms of prevention, our best weapon is information!

• The best people to have the conversations with young people are their parents/guardians. – Having open conversations about drugs and drug abuse is one of the most effective prevention strategies.

• Reassure anyone abusing fentanyl that successful recovery is possible, and that several options are available.

   Manitoba Addiction Helpline:
   1-855-662-6605
   MBAddictionsHelp.ca