

Forum

THE QUARTERLY NEWSLETTER FOR CLINICAL HEALTH CARE PROFESSIONALS ON ADDICTION TREATMENT

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Methadone Overdose in MMT

What to know. How to prevent it. What to do if it happens.

Managing inherent risks of methadone to prevent overdose is everyone's responsibility and it begins with better education.

Risk Management Begins with Education

An overdose of any drug can occur when a harmful (toxic) amount, alone or in combination with other agents, overwhelms the body. Overdose often is thought of as a sudden, life-threatening event; however, with methadone, overdose is a relative condition ranging from the mild 'high,' nodding-off, or other effects of overmedication to the passing out and stopped breathing of a full blown medical emergency. And, methadone overdose can take several days to occur since its effects build over time.



Because of methadone's complex pharmacology and the varieties of individual patient responses to it, incidents of overmedication in some patients may be unavoidable. Knowing this, and the signs/symptoms of overmedication that might lead to overdose, can prevent an occasional occurrence from becoming a medical emergency.

Therefore, managing inherent risks of methadone therapy during MMT begins with educating all clinic staff. These professionals should then be able to train and counsel patients, as well as their close relatives and friends, on methadone overmedication and overdose concerns. This special-focus edition of *AT Forum* provides helpful information for achieving those ends. (Reference resources consulted are listed at the end, with Internet links to full documents in many cases.)

Methadone – An Essentially Safe & Valued Medication

Since the mid-1960s, methadone maintenance treatment (MMT) has been highly valued for helping to reduce the ravages of heroin and other opioid addiction. Yet, during this past decade, overdoses and deaths associated with methadone have gained it a reputation as being "widely abused and dangerous." This came largely from sensational news stories claiming inherently harmful effects of methadone, rather than more accurately stressing that most tragedies were the result of methadone being either misprescribed, misused, or abused in some way.

However, methadone is indeed a very potent opioid medication, and fatal overdoses have been reported ever since it was first used, as a pain-reliever, in the 1940s. At that time, the most severe risks of death were associated with excessive amounts of methadone being prescribed.

According to all recent accounts, methadone-associated emergencies, over-

doses, and deaths have steadily increased. While the evidence suggests that methadone prescribed outside of MMT clinics as a pain reliever is the greatest source of problems, methadone in general is being portrayed as a threat to individual and public health.

Yet, *when prescribed and used properly, methadone has been consumed safely by millions of patients worldwide during its more than 40-year history in MMT.* And, increasing numbers of individual patients have now been maintained on methadone for several decades or more without incident or physical harm.

All cause mortality in MMT patients is typically many-fold lower – as much as 15 times lower – than in untreated opioid addicts in the community. Some researchers have observed that the all-cause fatality rate among MMT patients is around 1%; whereas, the rate increases

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Events to Note

For additional postings, including international meetings, see: www.atforum.com

October 2007

AATOD (American Association for the Treatment of Opioid Dependence) Conference

October 20-24, 2007
San Diego, California
Contact: 212-566-5555 or www.aatod.org

Amer. Society of Addiction Medicine (ASAM) State of the Art in Addiction Medicine

October 25-27, 2007
Washington, DC
Contact: 301-656-3920 or www.ASAM.org

November 2007

American Public Health Association 135th Annual Meeting and Exposition

November 3-7, 2007
Washington, DC
Contact: 202-777-2742 or www.apha.org/meetings/

2007 United States Conference on AIDS

November 7-10, 2007
Palm Springs, California
Contact: 202-483-6622 or <http://www.nmac.org>

Association for Medical Education and Research in Substance Abuse (AMERSA) 31st National Conference

November 8-10, 2007
Washington, DC
Contact: 401-243-8460 or www.amersa.org

Southeast Conference on Alcohol & Drug Addiction (SECAD 2007)

November 28-30, 2007
Atlanta, Georgia
Contact: 717-392-8480 or <http://www.naatp.org/secad/>

American Academy of Addiction Psychiatry (AAAP) 18th Annual Meeting & Symposium

November 29 – December 2, 2007
Coronado, California
Contact: 401-524-3076 or <http://www.aaap.org>

December 2007

2007 National HIV Prevention Conference

December 2-5, 2007
Atlanta, Georgia
Contact: 800-772-8232 or www.2007nhpc.org/backgroundinfo.asp

2007 Intl. Drug Policy Reform Conference

December 5-8, 2007
New Orleans, Louisiana
Contact: 866-219-4582 or <http://www.drugpolicy.org>

[To post your event announcement in AT Forum and/or our website, fax the information to: 847-392-3937 or submit it via e-mail from www.atforum.com]

Straight Talk... from the Editor

Overdose in MMT: Better Safe Than Sorry

This is the first-ever theme edition of *AT Forum* and it focuses on a topic of critical importance – methadone overdose. Surprisingly, federal regulations and current guidelines on methadone maintenance treatment (MMT) fail to thoroughly address how methadone overdose happens, how to recognize it, and what to do about preventing or overcoming it.

A Spoiled Reputation

Today, more than ever, methadone's reputation is in jeopardy. It seems that whenever methadone is involved in a tragic incident news media eagerly feature the story with headlines condemning "killer methadone" or similar fear-provoking messages.

Spurred by that, petitions have been circulated via the Internet and to the FDA by angry citizens – many of them relatives of persons who allegedly died from taking methadone. They want to stop the deaths by more severely restricting methadone's use or banning it entirely.

Much, but not all, of the uproar over methadone has involved its application and distribution as a pain reliever. Still, many cases of abuse or death involve methadone from MMT clinics, and watchful eyes in Washington, DC have been following the increasing trend of methadone-associated deaths.

As a consequence, if the safe prescribing and use of methadone in MMT cannot be assured, regulators may have no choice but to place further restrictions on clinics and methadone distribution.

Personal Responsibility Critical

Even more important, as folks at the Chicago Recovery Alliance have written: "Dead addicts never recover." That's a raw but irrefutable truth. And, among the greatest threats to life during MMT are the misprescribing, misuse, or abuse of methadone – all of which are preventable.

Methadone safety is everyone's responsibility. This begins with clinic staff, but also extends to patients and their close relatives and friends.

As long as even a tiny proportion of patients who come into MMT continue abusing alcohol and other drugs, and possibly abuse or divert methadone for illicit purposes as well, safety-conscious clinics will need to err on the side of caution. It is unfortunate, but this may sometimes translate into what are perceived by many

Clinics need plans for overdose emergencies just as they do for natural disasters.

patients as unreasonably rigid and restrictive clinic rules.

For example, take-home methadone doses must be denied to patients who cannot be relied upon to

safeguard the medication from improper or illicit use. Some reports of tragic and inexcusable deaths have occurred in children accidentally poisoned by their relative's take-home methadone.

The obligation to be safe rather than sorry when it comes to methadone is of prime importance. Just as MMT clinics should have a plan for dealing with natural disasters, they should have procedures and training for handling personal medical disasters, such as methadone overdose.

All clinic staff and patients (and, ideally, their families) should be participants in overdose preparedness activities. Hopefully, this edition of *AT Forum* will be helpful in that endeavor.

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NEW SURVEY: Overdose in MMT

As a followup to this special edition on methadone overdose, *please respond to the following survey questions:*

1. Are patients provided written instructions on recognizing signs/symptoms of methadone overmedication or overdose?
 Yes; No; Don't Know.
2. Does your MMT clinic provide training on handling methadone overdose emergencies? Yes; No; Don't Know.
3. Is naloxone for reversing methadone overdose available in your MMT clinic?
 Yes; No; Don't Know.
4. Are you responding as an MMT patient, or MMT clinic staff member or other?

There are several ways to respond to AT Forum surveys: A. provide your answers on the postage-free feedback card in this issue; B. write, fax, or e-mail [info above]; or, C. visit our website to respond online. As always, your written comments are important.

to 10% or greater in those who are discharged or voluntarily discontinue methadone maintenance for addiction. Other studies have found that the death rates in addicts who are merely detoxified from opioids can be 22 times greater than in MMT patients.

Within the controlled and regulated environments of MMT programs, most if not all of the overdoses related to methadone can be prevented. And, if opioid overdoses do occur, they need not be fatal if proper training and safety procedures have been implemented.

Anatomy of an Overdose

There are 3 primary reasons why methadone overdose may occur during MMT:

1. A new patient who is not sufficiently accustomed to opioids (tolerant) is prescribed an excessive amount of methadone, or the person supplements safely prescribed methadone with illicit methadone outside the clinic.
2. Once started on methadone, the amount is increased too rapidly, leading to a harmful build-up of the drug.
3. There is a methadone-drug interaction resulting in an unexpectedly excessive level of methadone, or methadone is combined with other drugs that harmfully affect the patient's breathing, nervous system, and/or heart function.

Opioid-related overdose deaths, especially with long-acting opioids like methadone, rarely occur immediately and there usually are warning signs of overmedication (see *Table*). Sometimes, MMT clinic staff, and patients, refer to this as being "loaded" on methadone.

In overdose, the primary mechanism of death is suffocation — breathing slows (respiratory depression), resulting in a lack of oxygen (hypoxia), until breathing stops completely and the victim lapses into a coma. Along the way, depressed breathing may cause fluid to fill the lungs (pulmonary edema), or the victim may inhale their own vomit or saliva (aspiration pneumonia), which further inhibits lung function.

Excessive methadone also can slow heart rate and lower blood pressure, but breathing is most typically affected first and causes the death. Patients with a history of breathing problems — sleep apnea, asthma, emphysema, congestive obstructive pulmonary disease — or heart problems can be at special risk.

Methadone overdose rarely is seen right in the MMT clinic; rather, it typically occurs many hours after dosing when methadone levels have peaked and the patient is asleep, or has passed out, at home. *Patients do not die from opioid-induced respiratory failure while they are awake and alert.*

Methadone patients, as well as family members or friends, need to know the warning signs and symptoms of overmedication or overdose to take action before it is too late (see *Table*). By knowing what to watch for patients themselves can be alerted to seek help before they become ill or lose consciousness. But, if this happens, others must seek emergency help as necessary and care for the patient until help arrives (see *Handling Emergencies* below).

Methadone Safety Starts on Day One

Induction Cautions

"All substances are poisonous; only the amount differentiates a poison from a remedy," said the 16th Century physician Paracelsus. Indeed, all opioids, including methadone, can be poisonous in excessive amounts.

Therefore, based on the principles of opioid tolerance (*discussed below*), care in dosing must be taken when starting new patients on methadone as well as when dose increases are prescribed for existing patients. Numerous reports have commented on overdose hazards especially during the startup stage of methadone maintenance — the induction period.

"Safely Starting Methadone in MMT" for high risk and low risk patients was the subject of an extensive article in *AT Forum* last fall (*see reference at end*), and guidance is presented in that document. Of most significance, in any patient the risk of fatal overdose is many times greater during the first 2 weeks after starting MMT than in patients who have stabilized on the medication.

Increased death rates during induction are largely due to difficulties in assessing the opioid-dependence status and, consequently, the expected opioid tolerance of new patients. For example, some individuals who claim to be regular and heavy users of heroin or other opioid drugs actually may be occasional users or even opioid-naïve with minimal opioid tolerance.

US Federal Regulations recommend a *maximum* first-day dose of 30 mg methadone in *opioid-tolerant* patients, with another 5-10 mg allowed if opioid withdrawal persists (maximum of 40 mg). However, it must be remembered that methadone levels in blood and tissues build from day to day, and some reports have noted that starting oral methadone doses during MMT at 20 mg/day or even much less can be fatal after several days unless the patient has sufficient opioid tolerance.

What is Opioid Tolerance & Why Does it Matter?

Unfortunately, there is no laboratory test to objectively assess opioid tolerance. If patients are started in MMT at doses in excess of their established tolerance it can lead to dire consequences, and the mere presence of opioid in a urine or blood screen is no indicator of tolerance.

All opioids have desirable and undesirable (eg, respiratory depression) effects. Normally, frequent opioid users become tolerant to those effects; that is, they grow accustomed to or adapt to them to some extent. Over time, this means that the dangers of respiratory depression — the key hazard in fatal overdose — become of less concern, provided the development of tolerance to this effect can keep pace with any ongoing increases in opioid dose.

However, tolerance to methadone's respiratory-depressant effect develops more slowly than tolerance to other effects. So, increasing the methadone dose too soon or too rapidly can risk causing overdose.

Individuals who have tolerance to the effects of one opioid (eg, heroin) have

What to Watch For – Signs/Symptoms of Overmedication/Overdose

Overmedication Warning*

- Unusual sleepiness, grogginess, drowsiness (oversedation, somnolence).
- Mental confusion, slurred speech, intoxicated behavior.
- Slow or shallow breathing.
- Pinpoint pupils (miosis).
- Slow heartbeat, lowered blood pressure.
- Unusual snoring while asleep.
- Difficulty arousing the person from sleep.

Overdose Emergency

- Face extremely pale, clammy.
- Fingernails, lips turning blue/purple.
- Body is limp.
- Vomiting or gurgling noises.
- Cannot be aroused or unable to talk.
- Very little or stopped breathing.
- Very slow or stopped heartbeat.

* An often unrecognized symptom of methadone over-medication is unusual feelings of excess energy with or without euphoria. As methadone levels drop the other signs/symptoms may emerge.

Handling Emergencies – Taking Immediate Action

If sign/symptoms of methadone overmedication or overdose are identified (see Table above), taking prompt action can be lifesaving. Patients and their close family or friends should know when to call the MMT clinic about possible overmedication, when to call for emergency help, and what to do while waiting for help to arrive.



If there are possible signs/symptoms of overmedication or overdose, determine if the victim is responsive. Shout their name, pinch their ear, rub your knuckles on their breastbone to arouse them. If they can be fully aroused, keep them awake and call the MMT clinic for instructions on what to do.

If the victim cannot be aroused,
call for emergency help immediately.
In the United States, dial 911 (this may differ in other countries)



Overdose... continued from page 3

some immediate tolerance to effects of any other opioid (called "cross-tolerance"); however, this is usually incomplete. Even individuals who have been consuming significant amounts of opioid daily for a long time may not be tolerant to all effects of methadone.

Depending on the amount and type of opioid previously used, initial tolerance to methadone's respiratory-depressant effect may be quite low. So, in a new patient, start-up methadone doses can cause life-threatening respiratory depression if the person is not already sufficiently opioid-tolerant and/or they continue to abuse other drugs or alcohol in combination with methadone.

It is also important to consider that since tolerance to the respiratory-depressant effect of methadone may develop slower than tolerance to other effects, even long-term MMT patients can be at risk of overdose if there is a sudden and large increase in methadone levels via prescribed dose or abuse, or due to interaction with other drugs. This is *not* to say that higher doses of methadone are in themselves harmful, provided such dose levels are achieved gradually. In fact, research has demonstrated significantly lower rates of accidental overdose deaths in patients receiving higher rather than lower methadone dosing during long-term MMT.

Finally, reduced methadone tolerance resulting from a period of diminished use or abstinence can result in much greater effect per given dose of methadone if/when it is resumed. That is, a methadone dose that previously caused minimal respiratory depression may be life-threatening if restarted at that same level. If only a couple of days dosing are missed, a temporary dose reduction might be appropriate; if more than 5 days are missed the patient may need to be reinduced on methadone as if starting from day 1 (at 30 - 40 mg/day).

Beware of "Poison Cocktails"

Taking methadone along with unauthorized drugs is severely hazardous. Researchers long ago called attention to the "poison cocktail" resulting from the intake of multiple drugs such as alcohol, sedatives or tranquilizers (benzodiazepines), hypnotics, and/or other opioids *in addition* to methadone. When used alone, many of these substances are relatively moderate respiratory depressants; however, when combined with methadone their effects can be magnified and add up to become lethal.

Overdose risks decline substantially after stabilization on methadone, along with reductions in illicit drug and/or alcohol use during successful participation in MMT. Yet, when methadone-associated deaths occur during later stages of MMT non-prescribed drugs are almost always detected at autopsy.

Furthermore, care must be taken regarding prescription medications that patients may be taking when entering MMT or those prescribed later. Many drugs are known to interact with methadone, producing higher than expected serum methadone levels (SMLs). During methadone induction, such interactions might cause unanticipated signs/symptoms of methadone overmedication requiring dose adjustments of either methadone or the other drugs. When medications are newly prescribed in stabilized MMT patients, the possibility of an interaction should be taken into account. Potentially interacting drugs are listed in the *AT Forum* paper "Methadone-Drug Interactions" (see reference at end).

It must also be noted, however, that SMLs *alone* are not an indicator or a predictor of overdose. SMLs considered as therapeutic during MMT commonly overlap those reported in methadone-associated deaths. For example, methadone concentrations claimed as fatal by various investigators have ranged from 60 to 4,500 ng/mL; however, methadone levels within that range also have been observed in persons taking methadone who died of non-drug-related causes, and the lowest (trough) therapeutic SML range during MMT is considered to be 150 to 600 ng/mL, with peak levels at twice that amount.

Strategies for Reducing Overdose Deaths

Potential safety risks associated with methadone should be an essential ingredient of clinic communications with and education of patients, as well as their close relatives or friends. All MMT staff should have CPR training, and clinics should provide (or arrange for) at least basic life-saving skills training for patients and adults who live with them. It is critically important to include these other persons, with the patient's permission, because they will probably be the first responders in an emergency.

Vital information on dealing with methadone overmedication or overdose situations should be provided *in writing* – including who to call and when. MMT clinics should arrange to have a trained staff member reachable by telephone at all times to respond to urgent calls.

Here are some points to stress with patients and their close relatives/friends:

- Methadone is a very strong and long-lasting opioid medication. Patients, and their close relatives or friends, need to be on their guard for any indications – signs/symptoms – that the patient is not responding well to treatment.
- Any signs/symptoms of possible methadone overmedication or overdose should be taken seriously, and help called immediately.

(Continued on page 6)

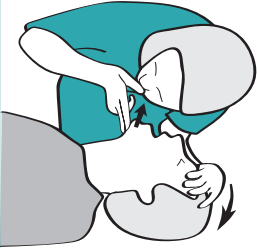
Handling Emergencies – While Waiting for Help to Arrive



CAUTION: The following life-saving procedures are provided here for informational purposes and require training to be done properly. This is available from Red Cross chapters around the world, and training programs offered by the American Red Cross may be found at: http://www.redcross.org/prepare/trained/trained_2.asp.

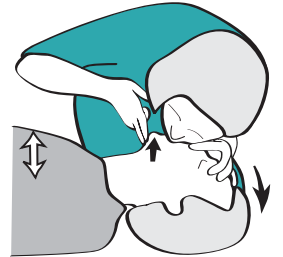
Rescue Breathing...

With the victim flat on their back, preferably on a hard surface like the floor, determine if there is breathing. Tilt the head back to open the airway and make sure the mouth is clear. Lean close to feel on your cheek and hear if there are breaths. If there is no breathing, brain damage can occur within 3-5 minutes, so immediately perform rescue breathing.



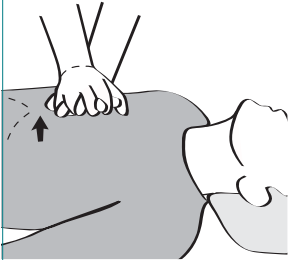
For mouth-to-mouth rescue breathing, first pinch the victim's nostrils together between your thumb and first finger. Make a good seal around their lips with your mouth and blow steadily until the chest rises, then take your mouth away and let the chest sink back down.

Give 2 breaths every 5 seconds. Always support the victim's chin to keep their head tilted back and airway open.



CPR (Chest Compressions & Rescue Breathing)...

If both breathing and heartbeat stop (that is, there is no pulse), CPR (cardiopulmonary resuscitation) is the only hope of sustaining life until emergency help arrives.

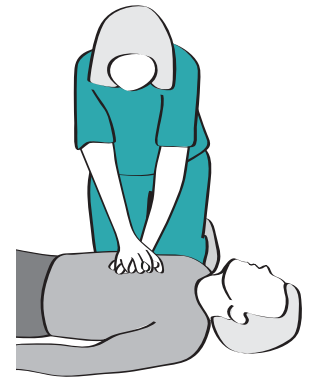


First, measure two fingers up from where the ribs meet the breastbone (arrow). Just above where your fingers are, place the heel of one hand on the breastbone and put the other hand on top of this hand, locking fingers together.

Next, keep your shoulders above the center of the victim's chest, arms straight, and press down on their chest by about 1 to 2 inches. Rapidly release the pressure, but keep your hands where they are.

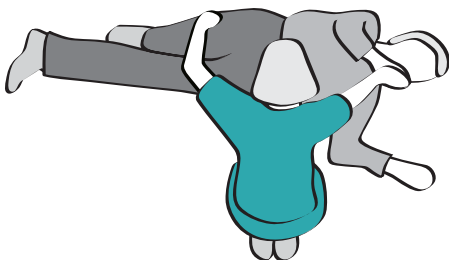
It is necessary to do 15 rapid chest compressions every 10 seconds followed by 2 breaths of rescue breathing – repeat this cycle until help arrives.

If the heart starts beating, and the person's normal color comes back, stop chest compressions but continue rescue breathing unless the person regains consciousness.



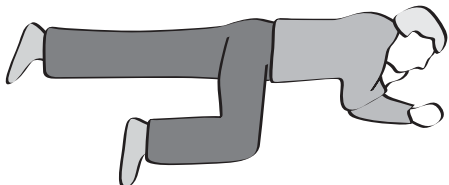
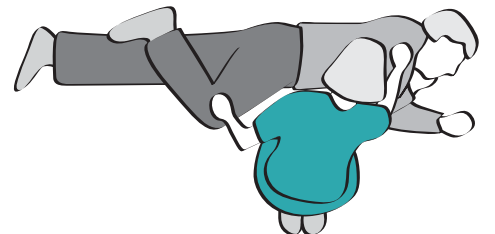
Recovery Position...

If the person is breathing, with a heartbeat, the "recovery position" will help them breathe better, without choking, and prevent further harm until help arrives.



First, tilt the victim's head back to open the airway and straighten the legs. Put their arm nearest to you at right angles to their body. Pull the arm farthest from you across victim's chest and place the back of the hand against the cheek nearest to you to support the head.

Next, pull up on far leg just above knee and roll the victim toward you and onto their side.



Finally, place the leg closest to you at right angles to prevent the person from rolling over further. Be sure the back of their hand is supporting the cheek and the head is tilted back for easier breathing. Make sure the airway is clear.

Monitor the person's breathing and heartbeat, and do not leave them alone until help arrives.

Many patients would prefer to be somewhat overmedicated with methadone, rather than experience the discomfort of any opioid withdrawal – which can be hazardous.

(Overdose... continued from page 4)

- Patients need to know and understand that consuming *any* unauthorized drugs or alcohol while on methadone is dangerous and may lead to overdose and death. Also, cocaine is cardiotoxic and may cause heart failure.
- Patients who lie about their opioid or other drug consumption or how they are feeling on methadone risk not being properly medicated – that is, being given too little or too much – and/or dying from overdose if the methadone amount is excessive for the particular patient.
- During startup of methadone, it is *not* normal for the patient to be nodding off to sleep or unsteady on their feet.
- A patient who feels or acts overmedicated should *not* just "sleep it off." The person should stay awake and MMT clinic staff called.
- Signs/symptoms of overmedication or overdose may take time to develop – a methadone dose that does not completely control withdrawal during the first day or two may cause overdose by day 3 or 4.
- If overdose is suspected, immediately call for emergency help without delay and then begin rescue procedures (*see pages 4-5*). When calling for help, tell the responder that an opioid overdose is suspected and that they should be sure to bring naloxone (*discussed below*).

Along with the above, it must be considered that many patients would prefer to be somewhat overmedicated with methadone, rather than experience the discomfort of any opioid withdrawal. Clinic staff should explain how methadone works – eg, builds up in the body with time – and that adequate methadone dosing will be eventually achieved, but safely

What NOT To Do For A Methadone Overdose

There are many "street myths" about how to deal with an opioid overdose, including from methadone. All of the alleged "remedies" take precious time away from getting real help, and they all can be harmful rather than helpful. Here are several precautions for patients and their relatives/friends to know about...

- Do *not* slap the victim or walk/drag them around to wake them up – if they cannot be roused by shouting, rubbing knuckles on the sternum (center of rib cage), or pinching their ear they are unconscious. Further stimulation will not help and may cause injury.
- Do *not* put the person into a cold bath or shower – they could fall, go into shock, or drown.
- Do *not* inject the person with any substance (salt water, "speed," heroin, etc.) – the only antidote for an opioid overdose is naloxone (*see below*).
- Do *not* try to make the victim vomit orally ingested opioids – they may choke or inhale the vomit into their lungs causing fatal damage.

The most important thing is to call the MMT clinic for advice regarding overmedication or, in the event of overdose, to call emergency medical services for urgent help. And, call sooner rather than later.

NALOXONE – Overdose Antidote

Rapid, Effective, Safe

In cases of life-threatening opioid overdose, there is fortunately an antidote that acts rapidly, effectively, and safely. Naloxone (brand name, Narcan®) has been used for decades by emergency medical services (EMS) personnel for reversing opioid overdose and reviving victims who otherwise would have died.

Naloxone is an opioid antagonist, meaning that it bumps opioid drugs, including methadone, off of their receptors in the brain and protects the person for a period of time from further action by the opioids. It is an unscheduled drug with no overdose or abuse potential and can be prescribed by any licensed practitioner.

Naloxone's only physiological activity is opioid blockade; therefore, it is not of benefit in reversing effects of alcohol, benzodiazepines, cocaine, or other drugs. In opioid-dependent persons, full reversal of opioid effects by naloxone will cause moderate to severe withdrawal, which is unpleasant but obviously preferable to death. Other adverse reactions to naloxone are very rare, but have included agitation, seizures, pulmonary edema, and heart rhythm disturbances. Finally, naloxone is quite inexpensive, with the generic formulation costing as little as 25-cents per dose.

Easily Controlled Action

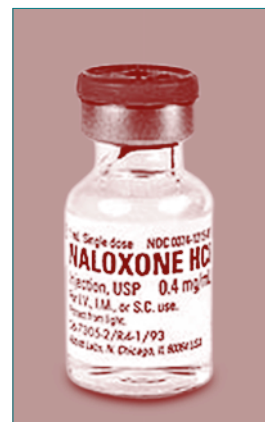
The overdose reversal effects of naloxone are easy to control because it is short acting, exerting its opioid-blocking action for only about 20 to 45 minutes. Depending on how much naloxone is given and how often, it can fully reverse a life-threatening overdose of opioid or be used merely to relieve milder respiratory depression, sedation, or low blood pressure resulting from opioid overmedication.

Naloxone is available in several concentrations: 0.02 mg, 0.4 mg, and 1 mg per mL. It can be administered via intravenous infusion, or intramuscular or subcutaneous injection. An intranasal naloxone spray also has been successfully tested, but is not currently commercially available.

For opioid overdose, an initial naloxone dose of 0.4 mg is typically administered intravenously (preferred) or intramuscularly. It usually takes 2 to 3 minutes for it to take effect, and adequate breathing is usually restored in less than 10 minutes. Higher naloxone doses (1.0 - 2.0 mg) can be given if there is no response or for severe overdose from longer-acting opioids (eg, methadone, buprenorphine, OxyContin®, etc.). Initial doses can be repeated until the victim has received a total of 10 mg. Since naloxone's effects completely wear off in 40 to 60 minutes, the victim will need to be monitored for signs of returning breathing problems and then more naloxone administered as necessary.

For methadone overdose, individual doses of naloxone range from 0.4 to 2.0 mg depending on the apparent severity of respiratory depression. Since methadone is very long acting, the victim might need to be monitored for an extended period of time and repeated doses of naloxone given if severe overdose signs/symptoms reappear. However, complete reversal of methadone effects in MMT patients, resulting in full withdrawal, would not be necessary or desired in most cases.

In MMT patients merely overmedicated on methadone, very small doses of naloxone – 0.05 to 0.1 mg – have been used by emer-



(Continued on page 7)

(Overdose... continued from page 6)

gency medicine specialists to boost breathing rate and reduce sedation. This can be a vital intervention when opioid tolerance is overestimated and excessive methadone is prescribed during the induction phase of MMT.

Naloxone in the Community

Besides its use by EMS teams worldwide, some harm-reduction organizations – starting in Europe, then in Australia and the United States – have provided prescription naloxone directly to injection drug users. As a life-prolonging effort, to help curtail opioid overdose deaths most usually from heroin injection, these individuals are provided training in recognizing overdose, basic life-support techniques (eg, rescue breathing, recovery position, etc.), and how to administer naloxone. Participants are typically provided a container of naloxone and one or more syringes for intramuscular injection of the drug. They are encouraged to share this information with drug-user peers so they can assist each other in an emergency.

Although these programs have been controversial, successes have been well-documented. According to one report, as of early 2006 harm-reduction programs in 5 US communities, beginning in Chicago in 1999, had trained and distributed naloxone to 8,450 participants resulting in more than 980 documented episodes of life-saving overdose reversal with naloxone.

Fears that naloxone-prescription programs would encourage increased opioid abuse by making an antidote for overdose readily available have not been supported by any evidence to date. Therefore, experts have recommended further evaluation and expansion of such programs.

Naloxone in MMT?

For MMT clinic staff and patients – it is important to know how naloxone works and that it is available as a safe emergency treatment to deal with methadone overmedication or overdose. At the least, it would make sense for MMT clinics to have naloxone on hand for emergencies or to reduce sedation and respiratory depression in cases of severe methadone overmedication.

MMT medical staff should know the proper protocol for naloxone administration, and they should also understand how other depressant drugs – eg, alcohol, benzodiazepines – might complicate the situation.

Providing MMT patients with take-home prescriptions of naloxone for emergency use has not been formally reported, but might be worthwhile. This would be an "off label" application of naloxone, just as it is for harm-reduction programs mentioned above, and local laws may differ regarding allowing the prescription of naloxone to individuals to have on hand for administration in an emergency. MMT programs would need to explore pursuing this approach in consultation with appropriate authorities.

At the least, MMT clinic staff could make sure that EMS teams in the community carry naloxone and that local emergency departments also have it on hand at all times. MMT medical staff can serve as an educational resource helping to instruct emergency medical personnel on the nature of methadone and the proper use of naloxone for methadone poisoning. For example, due to its long-acting pharmacology, reversing methadone effects may take multiple administrations of naloxone over many hours, and the patient would need to be observed for signs of rebound respiratory depression.

In sum, methadone and other opioid toxicity can be easily reversed by naloxone. However, this only works if the patient receives competent help in time and naloxone is readily available.

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Survey Results: Guarding Heart Health in MMT

The Winter 2007 edition of *AT Forum* (Vol. 16, No. 1) featured an article discussing a new FDA advisory cautioning that oral methadone may influence life-threatening changes in heart rhythm. Such possibly harmful cardiac effects of methadone in relatively small numbers of patients were known and previously addressed in *AT Forum*.

The FDA advisory and an associated new "black box" warning on methadone packaging raised questions about what methadone maintenance treatment (MMT) programs should be doing to help protect the heart health of their patients. The Winter *AT Forum* article presented guidance for optimizing cardiac safety during MMT, and a followup reader survey examined some current practices.

Cardiac Screening Neglected

There were 87 responses to the survey, roughly equally divided between MMT patients and clinic staff. This is a significantly lower response rate than on past surveys, which might suggest that the subject is either confusing or of less concern than it should be.

One of the recommendations from *AT Forum* was that all MMT patients should have basic screening for heart-health risks as part of their assessments for methadone therapy. When asked about this in the survey, a 52% majority of respondents said their clinics did *not* do cardiac screening and 18% said they did not know (which should be equivalent to a 'no' answer, since not knowing means it is unlikely being done). Overall, then, the cardiac status of 7 out of 10 MMT patients is not assessed by clinics, see **pie graph**.

ECGs Unavailable at Clinics

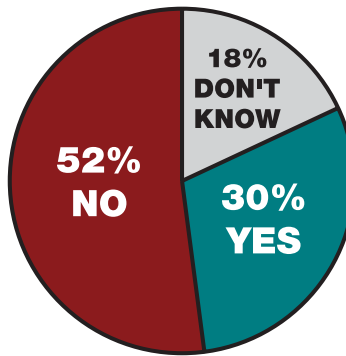
Furthermore, *AT Forum* advised that electrocardiograms (ECGs) should be considered when cardiac health risks are detected during screening. Survey respondents were asked where such ECGs are performed, if they are ordered.

Only 15% of respondents indicated that ECGs were performed right in the MMT clinic. Most, were done at an outside facility (56%) or other location (29%), with primary-care physician offices mentioned most frequently.

Patient Education Minimal

Finally, readers were asked if MMT patients were educated on identifying signs and symptoms of heart problems. Nearly three-quarters of survey respondents overall answered either 'no' (60%) or 'don't know' (14%).

Heart Health Screen?



It is interesting to note that about 45% of clinic staff said patients do receive such education, while nearly 90% of patient respondents said they *do not*. Clearly, if there is any education going on in this regard patients are not perceiving it as such. Understanding what might indicate a heart problem – such as fainting or racing heartbeat – would encourage patients to seek medical assistance before early warnings become crisis situations.

Much Room for Improvement

Due to the low response rate, results of this survey must be considered cautiously. However, if the indications are accurate it would appear that MMT clinics typically overlook assessments of patients' heart health, only a small proportion of clinics are equipped to do further testing via ECGs if problems are detected, and patient education is insufficient.

The alleged effects of methadone on cardiac rhythm are somewhat controversial and require further study. However, helping to protect the health of patients in recovery from addiction would make good sense from a medical best-practices perspective and MMT programs appear to have room for improvement when it comes to this.

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