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FAST FACTS AND CONCEPTS #95

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Background Physical dependence is a normal and predictable neurophysiological response to regular treatment with opioids for more than 1-2 weeks duration. Continuous or near continuous opioid blood levels are required (one oxycodone-acetaminophen tablet per day will not lead to physical dependence). Physical dependence is characterized by a withdrawal syndrome when the opioid is abruptly discontinued, if an opioid antagonist (naloxone) is given, or when drug blood levels fall below a critical level. Withdrawal can also be caused by administration of a mixed agonist-antagonist (e.g., buprenorphine, butorphanol, nalbuphine, pentazocine). Physical dependence is not a defining condition of addiction (see below and *Fast Facts* #68 and #69).

Important definitions

- Tolerance: state of adaptation in which exposure to a drug induces changes that result in diminution of one or more of the drug's effects over time.
- Physical dependence: state of adaptation manifested by a drug class-specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug and/or administration of an antagonist.
- Addiction / psychological dependence: a primary, chronic, neurobiologic disease, with genetic, psychosocial, and environmental factors. Characterized by one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving.

Signs and symptoms of the opioid withdrawal syndrome include yawning, sweating, lacrimation, rhinorrhea, anxiety, restlessness, insomnia, dilated pupils, piloerection, chills, tachycardia, hypertension, nausea/vomiting, cramping abdominal pains, diarrhea, and muscle aches and pains. Unlike withdrawal from alcohol or benzodiazepines, opioid withdrawal is not life threatening. Emergence of withdrawal symptoms varies with half-life of the particular opioid; within 6-12 hours after the last dose of a short-acting drug or 72-96 hours following methadone (see *Fast Facts* #75, 86). Duration and intensity of withdrawal are related to clearance of the drug such that withdrawal is shorter (5-10 days) and more intense for opioids like morphine and less severe and more protracted with methadone.

Prevention Opioid withdrawal syndrome should always be prevented. Patients treated with opioids for more than one to two weeks should be instructed to gradually reduce the opioid before discontinuing use. In general, **dose reductions of about 20-25% every day or two** will allow a tapering schedule that will prevent signs and symptoms of withdrawal. An alternative recommendation is to give half the previous dose for the first 2 days and then reduce the dose by 25% every 2 days. When the dose reaches the equivalent of approximately 30 mg/day of oral morphine, this dose is given for 2 days, and then the drug is discontinued. It is important to continue to provide around-the-clock opioids to prevent withdrawal in the patient at end-of-life who is no longer able to communicate or take oral opioids.

Treatment Clonidine 0.1-0.2 mg PO Q 4-6 hours PRN or by transdermal patch (clonidine transdermal 0.1 mg/24hour patch which provides 0.1 mg a day for 7 days) can be used to treat autonomic hyperactivity symptoms. It will not relieve insomnia. The major drawback of clonidine therapy is the tendency to cause

hypotension in some patients. Other agents used for control of withdrawal symptoms include: diphenoxylate/atropine (Lomotil), hydroxyzine, trazodone, and dicyclomine hydrochloride (Bentyl). For patients still in pain who have abruptly stopped their opioids (because they ran out, lost their prescription, or stopped because of side effects) reinstating opioid therapy may be appropriate to treat both their withdrawal symptoms and ongoing pain. Depending on how long a patient has been without opioids it may not be safe to reinstate the full opioid dose immediately (especially for long-acting opioids). In this case patients should go through a dose-titration phase with short-acting opioids to safely achieve analgesia.

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