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Long Acting Medications for Opioid Addiction

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It's been long known that having to use medication daily is fraught with more problems and worse outcomes compared to when it can be taken less frequently. Methadone and buprenorphine/naloxone for opioid addiction are two of those that must be used daily to be most effective. Patients on methadone are required to attend a clinic daily at first but then can earn unsupervised take homes. Those on buprenorphine/naloxone are also required to see their provider frequently at first but even more quickly begin receiving unsupervised doses. This lack of supervision lends itself to missed doses and the potential for medication diversion, misuse, or being stolen. Thus, providers need to search for long acting medications.

The first medication approved that did not require daily administration was the methadone metabolite Levacetylmethadol (LAAM). Approved in the 1990's, LAAM required dosing 3 days per week on average. But this medication was abandoned because of concern over a black box warning it received several years after approval due to its potential to increase the QT interval (time between heartbeats) and risk Torsades de Points (sudden cardiac death from an abnormal heart rhythm).

Then came Vivitrol, the depot injectable (injection of a substance in a vehicle that tends to keep it at the site of the injection so absorption can occur over a prolonged period) form of naltrexone (the opioid antagonist) that could be given once a month. First approved for alcohol dependence, it is now also used for opioid dependence. Its main drawback is that it is a large injection of 4cc that can cause pain at the site of injection, however, it is quite effective at blocking the effects of illicit opioid use.

On the horizon, and in trials but not yet approved in the United States, are the naltrexone implants. These are currently available in Europe for 3, 6, or 12 month implantable durations.

The newest implantable opioid treatment is probuphine, which was approved by the FDA in May of 2016. Probuphine is a form of the drug buprenorphine that releases buprenorphine at a constant rate over time. These are small 1mm x 26 mm rods of which 4 are implanted subcutaneously in the arm to equal a dose of 8mg of buprenorphine/naloxone a day for 6 months. It's found to be well tolerated and greatly reduces the risk of diversion, being stolen, misuse or missed doses.

The phase III safety and efficacy 6 month double blind, double dummy trial included 177 opioid addicts randomized between receiving dummy implants + sublingual buprenorphine/naloxone or probuphine implants + dummy sublingual strips. They were previously stabilized on 8mg or less of buprenorphine/naloxone a day. The results showed that 96% of those on probuphine compared to 87% stayed sober for at least 4 months of the study. Furthermore, the study showed that 88% of those on probuphine stayed sober for all 6 months vs. 72% of those on the sublingual buprenorphine/naloxone.

Opioid addiction has been said to be at epidemic proportions in the United States and death rates from overdoses and complications of intravenous use continue to rise. These new modalities should provide more tools by which we can treat patients. Combined with psychosocial interventions and participation in community recovery programs they should make significant strides to reducing the problem.

??? Did You Know ???

The adoption of recovery by behavioral health systems in recent years has signaled a dramatic shift in the expectation for positive outcomes for individuals who experience mental and/or substance use conditions. Today, when individuals with mental and/or substance use disorders seek help, they are met with the knowledge and belief that anyone can recover and/or manage their conditions successfully. The value of recovery and recovery-oriented behavioral health systems is widely accepted by states, communities, health care providers, peers, families, researchers, and advocates including the U.S. Surgeon General, the Institute of Medicine, and others.
Source: SAMHSA

Question of the Month

Question: My patient is positive for methadone and negative for methadone metabolite. Is this result acceptable?

Answer: The only physiological state in which this result *may* be acceptable is pregnancy. If a patient is taking, and keeping in their body, a dose of greater than 30 mg of methadone per day, and the urine sample is from the patient, their result should always be positive for BOTH methadone and methadone metabolite.