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Opiates: A Look Back (And Forward)

Luther F. Cobb, M.D.

It has been said that the four most dangerous words in Economics are "This Time It's Different". I think this could equally well be applied to society's approach to the use of opiates for medical and other purposes.

The opium poppy has been known to have effects since before history was written. Images of opium poppies have been found in ancient Sumerian artifacts of about 4000 years BC (or BCE, if you prefer). The ancient Minoan civilization of Crete were aware of its use, and it has been more or less ubiquitous ever since.

Crude preparations of raw opium were smoked or ingested in multiple civilizations, but it is thought that Morphine was the first isolation of an active ingredient from a plant, and thus basically the foundation of modern pharmacology; this occurred in the first decade of the 19th century. It was marketed commercially by Merck in 1827. It came under wider use in the 1850's following the invention of the hypodermic syringe.

This was just in time for the US Civil War (or the War of Northern Aggression to die-hard Southerners). So many men came home from the war after surviving the dreadful conditions of military medical care of that era that addiction to morphine became known as the old soldier's disease (although apparently there is some controversy about this).

Given that there was some concern about the prevalence of this problem, plus the increasing sophistication of organic chemists of the latter part of the century, the German pharmaceutical company Bayer, having triumphed with the acetylation of salicylic acid to produce Aspirin (originally a patented trademark, now of course generic), tried their hands at treating other compounds and came up with a diacetylated derivative of morphine that they trademarked "Heroin", from the German "Heroisch" equivalent to the English "Heroic", after its supposed lack of addictive potential. It was marketed as an over the counter medication in 1895 as a cough suppressant principally, and it was touted as a non-addictive alternative. It was also promoted as useful for the relief of the pain of teething in infants.

It was soon found to be otherwise, mainly on account of the fat solubility of the acetylated moiety that allowed the drug to cross the blood-brain barrier much more readily and thus exert its euphoriant effects in a more prompt and potent way. After a few years it was recognized as such, but it was not until 1924 that the US Congress passed a law banning its manufacture, importation, or sale. It has been since then considered a Schedule 1 narcotic, illegal for any use. The Health Committee of the League of Nations followed suit in 1925, although it was not implemented for over 3 years. Meanwhile, one of the more minor consequences of the Treaty of Versailles of 1919 was that Bayer lost its trademark rights to the drug.

After that, medical use remained mainly of morphine and hydromorphone (Dilaudid), meperidine (Demerol) and codeine, although many other opioids have been synthesized and marketed, both licit and illicit, including quite a few with both agonist and antagonist actions. Pretty much each time a new drug was marketed, it was bruited as being better pain relief but with fewer side effects, in particular the most feared one, addiction.

Fast forward, as they say, to the 1990's, when longer acting opioids were marketed as being safer and "virtually" free of addictive potential, the most salient (and notorious) being Oxycontin. (There is a fascinating, if depressing, article on the subject of Oxycontin and its producer, Purdue Pharma, and the Sackler family that owns the concern, in the New Yorker of October 30, 2017, and I strongly commend it to your attention). This became such a blockbuster drug in part because we practicing physicians were being told that we were ignoring the "Fifth Vital Sign" of pain, and that untold numbers of patients were being deprived of proper treatment of that important measure. It became necessary for the nursing staff of a hospital to inquire at every encounter of the success, or lack thereof, of a patient's control of pain on a 10 point scale (and who hasn't heard that "my pain is at least 15"?). It was also claimed, without really any legitimate data, that this formulation was safe, where others had not been, due to its extended-release formulation.

This concern reached such levels that court cases were filed for elder abuse due to lack of proper control of pain, and since such cases in this state did not fall under the MICRA limitations on non-economic (so-called "pain and suffering") damages, there was no limit on potential jury awards. The California Legislature, in its wisdom, decreed that all physicians in the state (with a few exceptions) had to take a 12 hour course of continuing education on the proper management of pain so that we would not fail in this essential task in the future. I have fond memories of taking that course, in my copious spare time.

The upshot of course was that not only was the control of pain deemed a vital sign, it became almost a civil right, and our

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failure to conquer the pain with whatever medications were necessary was simply unacceptable.

To make a very long story short, people started dying from overuse, misuse, or misunderstanding of the power of these drugs. So now we face a situation where every physician is being held to account for our failure to recognize and obviate this crisis. Once again, the gentle hand of government is being used to alter medical practice, and to cut off the source of the scourge by limiting the supply of drugs. This has the unintended (at least I hope unintended) consequence that hospitals are now finding it impossible to find the opiates that we legitimately use for routine care, and meperidine, morphine, and hydromorphone are in short supply, if available at all, and there appears to be no light at the end of the tunnel for these shortages.

The pendulum swings back, hard.

It has been said that every thorny problem has a solution that is simple, easy to implement, and wrong, and I fear that in both directions of this situation this has been the case. Clinicians need to have medications that we can use for the proper treatment of pain, and patients deserve to have care that is safe, effective, and readily available.

But I think we are still a long way from achieving that balance, and in fact I wonder, given the experience of history, if we ever will. I do know that we are all going to have to apply one solution in the very near future, which is logging into the CURES system when we prescribe anything from Schedule 2 through 4, with very limited exceptions. This is being implemented in October. It has the laudable goal of preventing doctor-shopping for opiates and other medications susceptible to diversion or abuse, which is a worthy goal. CMA has a primer (Penny has copies and they are available online) on how to comply, and we all need to get familiar with this because it is the way it is going to be for the foreseeable future, and probably forever. It is a lot less Draconian than many other "solutions" that have been proposed, and does have logic behind it.

Maybe this time it WILL be different, but forgive me if I have my doubts.

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