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Methadone Rises as a Painkiller With Big Risks

By ERIK ECKHOLM and OLGA PIERCE

Correction Appended

Suffering from excruciating spinal deterioration, Robby Garvin, 24, of South Carolina, tried many painkillers before his doctor prescribed methadone in June 2006, just before Mr. Garvin and his friend Joey Sutton set off for a weekend at an amusement park.

On Saturday night Mr. Garvin called his mother to say, “Mama, this is the first time I have been pain free, this medicine just might really help me.” The next day, though, he felt bad. As directed, he took two more tablets and then he lay down for a nap. It was after 2 p.m. that Joey said he heard a strange sound that must have been Robby’s last breath.

Methadone, once used mainly in addiction treatment centers to replace heroin, is today being given out by family doctors, osteopaths and nurse practitioners for throbbing backs, joint injuries and a host of other severe pains.

A synthetic form of opium, it is cheap and long lasting, a powerful pain reliever that has helped millions. But because it is also abused by thrill seekers and badly prescribed by doctors unfamiliar with its risks, methadone is now the fastest growing cause of narcotic deaths. It is implicated in more than twice as many deaths as heroin, and is rivaling or surpassing the tolls of painkillers like OxyContin and Vicodin.

“This is a wonderful medicine used appropriately, but an unforgiving medicine used inappropriately,” said Dr. Howard A. Heit, a pain specialist at Georgetown University. “Many legitimate patients, following the direction of the doctor, have run into trouble with methadone, including death.”

Federal regulators acknowledge that they were slow to recognize the dangers of newly widespread methadone prescribing and to confront physician ignorance about the drug. They blame “imperfect” systems for monitoring such problems.

In fact, a dangerously high dosage recommendation remained in the Food and Drug Administration-approved package insert until late 2006. The agency has adjusted the label and is now considering requiring doctors to take special classes on prescribing narcotics.

Between 1999 and 2005, deaths that had methadone listed as a contributor increased nearly fivefold, to 4,462, a number that federal statisticians say is understated since states do not always specify the drugs in overdoses. Florida alone, which keeps detailed data, listed methadone as a cause in 785 deaths in 2007, up from 367 in 2003. In most cases it was mixed with other drugs like sedatives that increased the risks.

The rise of methadone is in part because of a major change in medical attitudes in the 1990s, as doctors

accepted that debilitating pain was often undertreated. Insurance plans embraced methadone as a generic, cheaper alternative to other long-lasting painkillers like OxyContin, and many doctors switched to prescribing it because it seemed less controversial and perhaps less prone to abuse than OxyContin.

From 1998 to 2006, the number of methadone prescriptions increased by 700 percent, according to Drug Enforcement Administration figures, flooding parts of the country where it had rarely been seen.

But too few doctors, experts say, understand how slowly methadone is metabolized and how greatly patients differ in their responses. Some prescribe too much too fast, allowing methadone to build to dangerous levels; some fail to warn patients of the potential dangers of mixing methadone with alcohol or sedatives, or do not keep in contact during the perilous initial week on the drug. And some patients do not follow the doctor's orders.

"Those problems were not soon recognized," said Dr. Bob Rappaport, a division director at the Food and Drug Administration. He added: "Methadone is an extremely difficult drug to use, even for specialists. People were using it rather blithely for several years."

Dr. James Finch, an addiction specialist in Durham, N.C., said, "In the clinical and regulatory communities, everyone is trying to run and catch up with and deal with the causes of methadone overdoses."

This year the federal government started sponsoring voluntary classes that teach doctors the elaborate precautions they should take with methadone, like inching upward from low starting doses and screening patients for addictive behavior. (While Robby Garvin's doctor could argue that the dosage he was taking was reasonable — one to two 10-mg tablets, three times a day — and he was cleared by his state medical board, many specialists would have started him on a lower dose.)

In what critics call a stunning oversight, the F.D.A-approved package insert for methadone for decades recommended starting doses for pain at up to 80 mg per day. "This could unequivocally cause death in patients who have not recently been using narcotics," said Dr. Robert G. Newman, former president of Beth Israel Medical Center in New York and an expert in addiction.

The F.D.A. says that in the absence of reports of problems by doctors or surveillance systems, "we would have no reason to suspect that the dosing regimen" might need to be adjusted.

In November 2006, after reports of overdoses and deaths among pain patients multiplied and The Charleston Gazette reported on the dangerous package instructions, the F.D.A. cut the recommended starting limit to no more than 30 mg per day. "As soon as we became aware of deaths due to misprescribing for pain patients, we began the process of instituting label changes," Dr. Rappaport said.

Methadone, which is made by Roxane Laboratories Inc. of Columbus, Ohio, and Covidien-Mallinckrodt Pharmaceuticals of Hazelwood, Mo., creates dependency and is sometimes sought by abusers who say they experience a special buzz when mixing it with Xanax.

While the greatest numbers of methadone-related deaths have occurred among the middle-aged, the fastest growth — an elevenfold jump between 1999 and 2005, to 615 — occurred among those age 14 to 24, which experts say may be mainly a result of pill abuse.

Pain experts say the country is seeing a reprise of the abuse and tragedies that followed the introduction of OxyContin, a time-release form of oxycodone that was heavily marketed in the late 1990s. It became a factor in hundreds of deaths and a focus of law enforcement.

OxyContin is still widely prescribed, but a survey of Medicare plans in 2008, by the research firm Avalere Health LLC, found that many did not even include OxyContin on the list of reimbursable drugs. Critics like Dr. June Dahl, professor of pharmacology at the University of Wisconsin, fault the insurance companies for favoring methadone simply because of its monetary cost. “I don’t think a drug that requires such a level of sophistication to use is what I’d call cheap, because of the risks,” Dr. Dahl added.

Yet for the right patients, methadone can be a godsend. Alexandra Sherman, a patient of Dr. Heit’s at his Fairfax, Va., clinic, suffered for years from hip and shoulder pain that “felt like somebody stabbing me with a knife,” she said. Pain began to rule and ruin her days.

Dr. Heit gave her OxyContin and later, because it seemed to work better and because of the expense, switched her to methadone. Her insurance at one point covered only $500 in prescriptions, which paid for just one month’s worth of OxyContin, compared with methadone’s cost of $35 a month.

Methadone “has given me my life back,” Ms. Sherman said.

But Dr. Heit did not just throw drugs at her problem. He told her that she would also have to try physical therapy as well. They signed a contract listing mutual obligations — she would follow directions, he would be on call. He starts patients at low doses, makes them bring in their pill bottles so he can count how many are left, and may give urine tests to deter mixing drugs.

Some doctors, like Dr. Theodore Parran of Case Western Reserve University, also require methadone patients to give them the names of relatives or friends they can call from time to time.

But not all doctors have taken such precautions. Tony Davis, a contractor in Victorville, Calif., had just turned 38 in 2004 when, after years of migraines and back pain, he saw a new pain doctor in his Kaiser Foundation Health Plan. The doctor, who had already given him the sedative Xanax, prescribed methadone because of his continued pain.

The second day on the two medications, Mr. Davis said, “I’m feeling really weird,’ ” recalled his wife, Pebbles Davis. The two lay down for a nap and when she woke up, her husband was dead.

Ms. Davis recalled that the coroner had told her, “Given the medicines he was on, his brain forgot to tell his heart to beat and his lungs to pump.” The case went to an arbitrator, who ruled that although Mr. Davis had overused his drugs in the past, the doctor had failed to warn him about the new risks of starting methadone together with Xanax and that the care was substandard. Ms. Davis was awarded more than $500,000. “I never had any idea of the risk nor did my husband,” she said.

Another source of danger has been the conversion tables that doctors use when switching patients from one opioid to another — telling, for example, how many milligrams of methadone would be equivalent to the level of morphine a patient had been taking. These charts, until recently, indicated dangerously high doses for methadone. Newer ones suggest lower levels but many experts say these may be useless because

methadone affects patients so variably.

Now, as the government is making new efforts to teach methadone's challenges, some officials and doctors would go further, requiring prescribers to take a course before using methadone.

But many physicians and patient groups are wary of any steps that would slow access to pain treatments.

As early as 2003, alarmed by the rise in methadone-related deaths, the Substance Abuse and Mental Health Services Administration made an urgent call for more systematic and detailed state and national reporting about opioid deaths — a call that still goes unanswered.

Misuse by abusers was first seen as the problem, but now, said Dr. H. Westley Clark, director of the Center for Substance Abuse Treatment of SAMHSA, "We know that a significant share of the methadone deaths involve doctors making well-intended prescriptions."

A majority of victims also used large quantities of alcohol or benzodiazepine sedatives but few would have died without an opioid as the primary culprit. "You can take a lot of benzodiazepines without dying," said Dr. Charles E. Inturrisi of Weill Cornell Medical Center, who said they strengthen the depressive effect of methadone.

Some doctors prescribe to patients who may be expected to court danger, like Anna Nicole Smith, who died from a drug cocktail including the sedative chloral hydrate and three benzodiazepines.

Last February, Margaret Moore, 54, who lived alone in South Pasadena, Fla., with a history of alcoholism, depression and chronic back pain from a car accident, was found dead at home. Her doctor had prescribed methadone and valium and, he told investigators, warned her to stop drinking.

Her body was surrounded by empty vodka bottles and a host of pills including bottles of methadone tablets and sedatives. Her death was declared an accident from methadone toxicity.

Since April, SAMHSA has sponsored nine voluntary training courses on the safe prescribing of opioids, and many more are planned, though they will only reach a fraction of prescribers. The agency is also contracting with the American Society on Addiction Medicine to set up a mentoring program, through which prescribing physicians can receive expert advice. The State of Utah has a plan to educate every doctor and pain patient in the state about safe use of methadone and other opioids.

Nancy Garvin, Robby's mother, is one of many relatives of victims who, in the absence of a national registry, have started educational and pressure groups to fight bad prescribing and abuse of the drug.

Still, the death rate appears to be rising, raising the question of what more may be necessary, in law enforcement and in doctor training.

"Methadone can be important for patients when other drugs don't work," said Dr. Inturrisi, "but unless the doctor has the training and resources to manage the patient properly, he's going to get in trouble at a rate that's unacceptable."

This article has been revised to reflect the following correction:

Correction: August 24, 2008

An article last Sunday about concerns over the expanding prescription use of methadone for various injuries erroneously included a drug among those that killed the television personality Anna Nicole Smith in 2007. The medical examiner ruled that she had died as a result of an accidental overdose of the sedative chloral hydrate and three benzodiazepines. The drug cocktail did not include methadone, though traces were found in her system.