

n the United States, opioid pain medications such as oxycodone and hydrocodone have become the most common drug of abuse after marijuana. That's why states are imposing laws to curb their use.

Florida, where oxycodone caused 1,185 deaths in 2009, recently passed a "pill mill" law that tightens restrictions on pain clinics and physicians who prescribe pain medication.

In Washington, deaths from accidental overdose of opioid pain medications have surpassed automobile accidents as the leading cause of injury death among people 35 to 54 years of age. As a result, the state recently passed a law requiring careful assessment of how doctors manage chronic pain.

And Project Lazarus, based in Wilkes County, North Carolina, promotes the distribution of naloxone, an antidote that can save people who overdose on an opioid drug.

MOST DEATHS DUE TO MISUSE, NOT ABUSE

While illegal consumption of opioids is certainly growing, pain experts believe that most people who die from an overdose have a legitimate prescription for the pain killer. Perhaps they took too much in an effort to quell a sudden increase in their

pain, or didn't realize that combining an opioid with alcohol, antidepressants, or sleep aids could cause them to stop breathing while they slept.

The actor Heath Ledger, for example, who died in January 2008, was found to have a lethal combination of prescription drugs in his system. On top of oxycodone and hydrocodone, he had taken diazepam and temazepam, which are often prescribed for anxiety and insomnia, the anti-anxiety drug alprazolam, and the antihistamine doxylamine, which causes drowsiness. As he slept his breathing grew increasingly shallow until it stopped.

"This is how people get into trouble—as the dose creeps up, it puts them at risk of unintentional overdose

—especially if they're taking other medications."

-GARY M. FRANKLIN, M.D.

"We call it waking up dead," says Roger A. Rosenblatt, M.D., professor of family medicine at the University of Washington School of Medicine. "These people are not suicidal. They're just on a high dose of opioids, and they take some other medication or they have too much to drink, and the opioids cause respiratory depression."

HIGHER DOSES MEAN HIGHER RISK OF OVERDOSE

Intense craving for opioids explains only a small part of the rapid increase in their use, according to pain experts. A more obvious explanation lies in the fact that chronic pain is a widespread problem affecting millions of Americans, and opioid drugs usually provide significant relief. Physicians are grateful to have such an effective tool at their disposal. Unfortunately, many apparently prescribe opioids without coaching patients sufficiently in the use of such drugs or monitoring how much patients are taking.

In 1986 Russell Portenoy, M.D., and Kathleen M. Foley, M.D., published a highly influential study, in the medical journal *Pain*, of 38 chronic pain patients who took opioids for several months without becoming addicted or developing significant side effects.

The pharmaceutical industry soon developed formulations that

made opioids easier to use and marketed the new drugs aggressively. But what really drove the rapid increase in opioid prescriptions was their effectiveness.

"Drug companies were definitely part of the reason for the rapid increase in opioids for non-cancer pain," says Dr. Portenoy, chairman of the department of pain medicine and palliative care at Beth Israel Medical Center, New York, NY. "But if there was no need, and the drugs didn't work, do you think doctors would keep prescribing them? Strong pain killers became more acceptable in the medical community because doc-

How to Take Opioids Safely

- Identify the cause of your pain and take opioids only if other treatments bring no relief.
- Try to take opioids for a limited time for acute pain only.
- If you suspect you are depressed, get evaluated.
- Give your doctor a list of all medications you are taking.
- ► Tell your doctor if you have a history of drug abuse.

tors have few other tools at their disposal, and they want to provide relief for their patients."

Over time, people who start out on 30 or 40 milligrams of an opioid for chronic pain develop tolerance for the drugs and require larger doses. On the one hand, tolerance means a reduction in side effects such as constipation, nausea, and mental fogginess. Dr. Portenoy has a 56-year-old patient with chronic hip pain who is able to work and function normally on a very high dose of an opioid medication.

"If I gave him the same dose he's

taking now when I first met him, I would have killed him after the first or second dose," Dr. Portenoy says. "Now he takes that dose three times a day, and he's completely alert and able to do complex cognitive tasks on a daily basis."

However, patients who take more than 100 milligrams a day of an opioid increase their risk of overdose by nine times, according to a 2010 study in the *Annals of Internal Medicine*.

"We have 10,000 people in Washington State now who are taking over 120 milligrams a day," says Gary M. Franklin, M.D., a neurologist at the University of Washington who has done research on opioid prescribing. "This is how people get into trouble—as the dose creeps up, it's not always possible to monitor their intake. Higher doses put them at risk of depressed breathing—the leading cause of unintentional overdose—especially if they're taking other medications."

OTHER RISKS OF OPIOIDS

The constipation produced by chronic opioid use got so bad for one man that he had to have his colon removed, Dr. Franklin says.

In addition, elderly people on opioids experience a higher rate of falls and fractures, according to a 2010 study in the *Archives of Internal Medicine*.

Pregnant women who take opioids risk giving birth to a baby addicted to the drug. "They get opioids from the mother *in utero*, so when they're born they start to get tremors as though they're coming off heroin," says Dr. Franklin.

And since most opioids are mixed with acetaminophen, people who take them can develop liver damage, especially if they also start taking cold medications, sleep aids, Tylenol, or other products that also contain acetaminophen. That's why an FDA advisory panel recently recommended removing acetaminophen from opioid drugs.

"People on pain medication may not realize that another drug also contains acetaminophen, so they end up with liver CONTINUED ON P. 15

NEUROBICS

Mental Juggling

AUDIO

LANGUAGE

his puzzle exercises your memory and your reasoning ability. Keeping a list in your head is like juggling: It takes effort to keep track of all the items without dropping anything, especially when you have to juggle the order.

SPATIAL

LOGIC

NUMBER

Memorize the shopping list below. Practice until you can recite the list perfectly from memory.

Tea
Applesauce
Mouthwash
Kiwi
Ice cream
Yogurt
Honey

- 1. Cover the list and recite the items from memory. Check your answer. If you have trouble remembering all the items, try making a humorous mental picture that includes all the items in order. For instance, you might picture a teabag steeping in a spoonful of applesauce that is in a person's open mouth.
- 2. Cover the list and recite the items in backwards order. Check your answer. This is harder than reciting the items in their original order, because you have to rearrange the list in your head. Reciting a list backwards from memory exercises your short term or "working" memory.
- 3. Cover the list and recite the items in alphabetical order. All items in the list start with different letters. This is harder than reciting the list backwards, because you must keep track of all seven items at once in order to put them in alphabetical order.
- **4.** Cover the list and recite the list in order from the item with the fewest letters to the item with the most letters. All items have different numbers of letters.
- 5. Cover the list and recite the items in an order so the last letter of each item in the list is the first letter of the next item. Hint: the first item is "kiwi."
- 6. Uncover the original list and look at it. The items are in this order for a reason. What is the reason? Hint: All's well that ends well.
- 7. Bonus question: Visualize the path you would walk in your local supermarket in order to buy all the items in one efficient circuit.

This puzzle was adapted from the book *The Playful Brain:*The Surprising Science of How Puzzles Improve Your Mind,
by Richard Restak and Scott Kim (Riverhead Books 2010).
For more information, visit theplayfulbrain.com. — Scott Kim,
scott@scottkim.com

ANSWERS ON P. 15

EWAITING ROOM

CONTINUED FROM P. 11

failure," says one member of the panel, Janet P. Engle, Pharm.D., a professor of pharmacy at the University of Illinois, Chicago.

Nevertheless, Dr. Engle voted against taking the acetaminophen out of opioid drugs. "I'm in favor of better education for prescribers and patients," she says. "As long as the patient and the prescriber are careful that no more than 4 grams a day of acetaminophen is taken, these products are fine."

While no one advocates eliminating opioids, many now recognize the importance of utilizing other forms of pain relief, such as cognitive behavior therapy, exercise, and physical therapy.

"These improve a person's perception of their pain," says Dr. Franklin, "but most insurers do not pay for multidisciplinary pain care. We say opioids can be a problem, especially at high doses, but at same time we're not providing alternatives."

NEUROLOGY NEWS

Smoking May Double Dementia Risk

igarette smoking may be associated with an increased risk of Alzheimer's disease and other types of dementia, such as vascular dementia. Smoking is a risk factor for heart disease and some cancers, but its long-term link with dementia has been controversial. Some previous research has suggested that smoking does not cause dementia. Now, a study published in the medical journal Archives of Internal Medicine in October 2010 found that heavy smoking in mid-life may increase the risk of Alzheimer's and vascular dementia in late life by as much as 100 percent. Vascular dementia is an umbrella term that describes cognitive impairments caused by problems in blood vessels that feed the brain.

Researchers in Finland, Sweden, and the United States looked at data from a group of 21, 123 people from different ethnic backgrounds. All were members of the Kaiser Permanente Medical Care Program of Northern California and participated in a survey between 1978 and 1985. Of those, 5,367 (25.4 percent) were diagnosed with dementia over the 23-year follow-up period.

"We found a two-fold increase in risk among those who smoked two packs per day, a 44 percent increase in those who smoked one to two packs, and 37 percent increase in those smoking one-half a pack per day in mid-life," says lead author Rachel A. Whitmer, Ph.D., an investigator at

the Kaiser Permanente Northern California Division of Research.

The risk might be even higher, says Dr. Whitmer, because the initial data were self-reported—and smokers often claim to be nonsmokers or underreport daily use.

"We've probably underestimated the real risk, and we don't know how many of these people quit smoking between the time of the initial survey and being diagnosed with dementia. People need to understand that these are long-term consequences from mid-life smoking," Dr. Whitmer says.

Middle-aged people who described themselves as former smokers did not appear to have an increased risk of later dementia

Smoking might increase the risk of dementia by narrowing blood vessels in the brain, which leads to increased stroke risk, says Dr. Whitmer. But even those people who did not have a stroke were at higher risk for dementia, she says.

Although the study found an association

between smoking and dementia, association does not necessarily imply causation, cautions John C. Morris, M.D., Friedman Distinguished Professor of Neurology at Washington University School of Medicine in Saint Louis, MO.

"We do not know whether it was the heavy smoking in mid-life that caused the later development of dementia. People who smoke heavily may have other attributes, such as socioeconomic background, nutritional preferences, or other factors that end up being the real culprit," Dr. Morris says.

The findings were adjusted for age, sex, education, race, marital status, hypertension, hyperlipidemia (too much bad cholesterol or triglycerides), body mass index, diabetes, heart disease, alcohol consumption, and stroke. In other words, the investigators looked for associations between these factors and dementia in order to rule them out as the real cause.

"This is not new," says Richard Mayeux, M.D., the Gertrude H. Sergievsky Professor of Neurology, Psychiatry and Epidemiology, and co-director of the Taub Institute on Alzheimer's Disease and the Aging Brain at Columbia University Medical Center, in New York, NY. "There are now three large studies demonstrating these risks. These studies have all said the same thing: Smoking increases Alzheimer's dementia risk," Dr. Mayeux says. —Michael Smolinsky

NEUROBICS ANSWERS CONTINUED FROM P. 11

1.
TEA
APPLESAUCE
MOUTHWASH
KIWI
ICE CREAM
YOGURT
HONEY

2.
HONEY
YOGURT
ICE CREAM
KIWI
MOUTHWASH
APPLESAUCE
TEA

3. 4.
APPLESAUCE TEA
HONEY HON
ICE CREAM YOG
KIWI KIWI
MOUTHWASH ICE

YOGURT

4. 5.
TEA KIWI
HONEY ICE CREAM
YOGURT MOUTHWASH
KIWI HONEY
ICE CREAM YOGURT
MOUTHWASH TEA
APPLESAUCE APPLESAUCE

ORTHE ITEMS IN THE
ORIGINAL LIST ARE
ORDERED ALPHABETICALLY
BY LAST LETTER: THE FINAL
A IN TEA COMES BEFORE
THE FINAL E IN APPLESALICF AND SO ON