THE JOURNAL OF THE MINNESOTA MEDICAL ASSOCIATION

MINNESOTA MEDICINE

APRIL 2014

Medicine OR Menace?

What we know about **medical marijuana**

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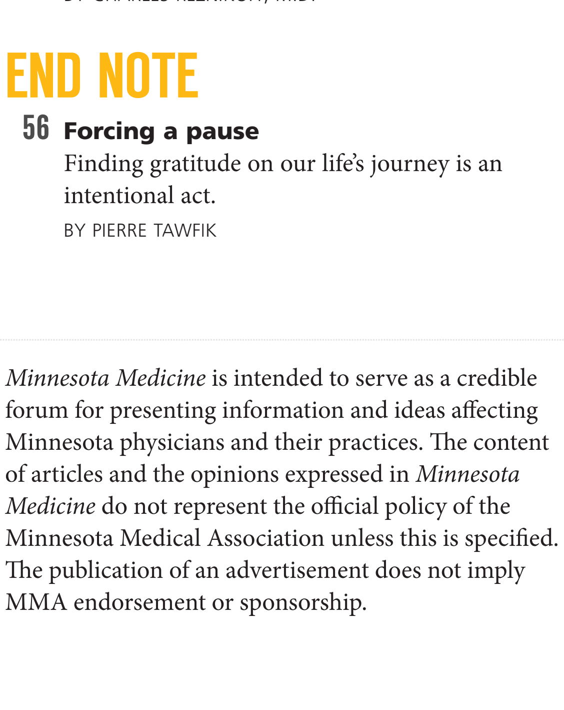

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Charles R. Meyer, M.D., Editor in Chief

How could something that was spoken of only *sotto voce* among friends in the '60s vault into such legitimacy in the 21st century?

The marijuana debate

I went to college during the early counterculture years—when long hair and beards were scary to the older generation, when rejection of the Vietnam War was merging with rejection of society, when Bob Dylan was growling out the mantras for the hip generation and when most college campuses had a pungent haze hovering over them. In many ways, the source of that haze, marijuana, became a symbol of the rebellion students were embracing. Enticing, enjoyable and illegal, smoking pot was what you did when you abandoned your parents' world. I never quite joined the counterculture. My hair was longish but never hippie-grade. My politics were liberal but to the right of the Students for a Democratic Society. And although I tried it (yes, Bill, I did inhale), I never quite got into pot.

So for a product of the '60s like me, the recent legalization first of medical marijuana and then of recreational marijuana in some states seems like a bit of a trip. How could something that was spoken of only *sotto voce* among friends in the '60s vault into such legitimacy in the 21st century? Did the tuned-out generation and their musical gurus have a lock on truth that staid society is only now discovering?

Mary Jane's journey to legality has been and continues to be rocky. Since 1970, when the Food and Drug Administration placed marijuana in Schedule I, where it keeps company with heroin, federal efforts to suppress usage and distribution have been couched in military jargon. The heat of the war on drugs that lumped Colombian drug lords with possessors of dime bags of grass has varied from the torrid efforts of the Reagan administration to the lukewarm dabblings of the Clinton years.

Despite President Obama's hints that some relaxation of federal prosecution of marijuana offenders might occur, users, growers and distributors continue to be caught and prosecuted. This triggers a tricky balancing act in the states that have legalized pot for medicinal use and in Colorado and Washington, which have approved it for recreational use. As Alyson Martin and Nushin Rashidian explained in their recent book *The New Leaf: The End of Cannabis Prohibition*, the United States has "four distinct stances on cannabis within its borders. Seventeen states have decriminalized simple cannabis possession and use. Twenty states and Washington, D.C., have legalized cannabis for medical use alone. Colorado and Washington have legalized and regulated cannabis for general use by adults 21 and over. And finally, the federal government maintains that cannabis possession for any purpose is a crime in every state."

Even though pot smoking has achieved a social acceptability in some circles to the point that a recent *New York Times* article suggested that we needed an Emily Post to "codify" the etiquette of pot smoking at parties, the debate is far from over even in states with legalized marijuana. Is the drug safe or at least safer than alcohol? What will easier availability do to the black market? Will it be a "starter drug" for young people and fuel the use of harder drugs? After considering these and other complex questions, the MMA Board recently voted not to support legalization for medicinal purposes or the bill that would legalize medicinal marijuana that appears to be stalled in the Minnesota Legislature.

So perhaps Mary Jane is no longer counterculture, but it remains as controversial as it was when Dylan was singing "everybody must get stoned." **MM**

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Marijuana for PTSD study inches closer

A researcher at the University of Arizona may soon begin studying whether marijuana is effective in treating post-traumatic stress disorder (PTSD) among veterans.

The study by Sue Sisley, M.D., will look at whether smoking or vaporizing marijuana can help reduce PTSD symptoms in 50 veterans who have not been helped by medication or psychotherapy. Sisley will test five different potencies of the drug in a placebo-controlled, triple-blind, randomized crossover pilot study funded by the Multidisciplinary Association for Psychedelic Studies (MAPS).

In March, the Department of Health and Human Services became the second government agency to give approval for the study, allowing for the purchase of research-grade marijuana from the federal government's only marijuana farm at the University of Mississippi.

According to a timeline on the MAPS website (www.maps.org), the study received approval from the Food and Drug Administration in 2011. Researchers must still get approval from the Drug Enforcement Agency before testing can begin.

Gateway to smoking?

Young people who use e-cigarettes are more likely to smoke conventional cigarettes, according to a study published March 6 in the *Journal of the American Medical Association Pediatrics.*

Researchers from the University of California, San Francisco, analyzed data on teenagers who completed the 2011 and 2012 National Youth Tobacco Survey.

Among the findings, use of e-cigarettes was associated with higher odds of being a current or past cigarette smoker. The authors stated: "Use of e-cigarettes does not discourage, and may encourage, conventional cigarette use among U.S. adolescents."

Source: Dutra LM, Stanton AG. Electronic cigarettes and conventional cigarette use among U.S. adolescents. JAMA Pediatr. Published online on March 6, 2013. Available at: http://archpedi.jamanetwork.com/article.aspx?articleid=1840772. Accessed March 7, 2014.

Parents unaware of kids' drug use

A survey commissioned by the Hazelden Betty Ford Foundation has found U.S. parents are not concerned enough about the potential for their children to use or abuse drugs and alcohol.

Nearly 60 percent of parents of youths ages 12 to 24 years said they were not concerned about their children's possible abuse of alcohol or other drugs. One in four said their homes have prescription painkillers in unlocked cabinets and 54 percent said they have alcohol out in the open.

Respondents also said they wouldn't know whom to contact if their child had a drug problem. Only 20 percent said they would seek help from a primary care physician.

The survey of 2,454 parents was conducted by Q Market Research.

Source: A matter of concern: Survey finds parents underestimate risks of alcohol or other drug use. www.hazelden.org/youth.

A 52-week, double-blind, double-dummy, active-controlled, parallel-group, multicenter study. Patients with type 2 diabetes (N=745) were randomized to receive once-daily Victoza® 1.2 mg (n=251), Victoza® 1.8 mg (n=246), or glimepiride 8 mg (n=248). The primary outcome was change in A1C after 52 weeks.

The change begins at **VictozaPro.com**.

Indications and Usage

Victoza® (liraglutide [rDNA origin] injection) is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Because of the uncertain relevance of the rodent thyroid C-cell tumor findings to humans, prescribe Victoza® only to patients for whom the potential benefits are considered to outweigh the potential risk. Victoza® is not recommended as first-line therapy for patients who have inadequate glycemic control on diet and exercise.

Based on spontaneous postmarketing reports, acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis has been observed in patients treated with Victoza®. Victoza® has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for pancreatitis while using Victoza®. Other antidiabetic therapies should be considered in patients with a history of pancreatitis.

Victoza® is not a substitute for insulin. Victoza® should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings.

Victoza® has not been studied in combination with prandial insulin.

Important Safety Information

Liraglutide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures in both genders of rats and mice. It is unknown whether Victoza® causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as human relevance could not be ruled out by clinical or nonclinical studies. Victoza® is contraindicated in patients with a personal or family history of MTC and in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Based on the findings in rodents, monitoring with serum calcitonin or thyroid ultrasound was performed during clinical trials, but this may have increased the number of unnecessary thyroid surgeries. It is unknown whether monitoring with serum calcitonin or thyroid ultrasound will mitigate human risk of thyroid C-cell tumors. Patients should be counseled regarding the risk and symptoms of thyroid tumors.

Do not use in patients with a prior serious hypersensitivity reaction to Victoza® or to any of the product components.

Postmarketing reports, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis. Discontinue promptly if pancreatitis is suspected. Do not restart if pancreatitis is confirmed. Consider other antidiabetic therapies in patients with a history of pancreatitis.

When Victoza® is used with an insulin secretagogue (e.g. a sulfonylurea) or insulin serious hypoglycemia can occur. Consider lowering the dose of the insulin secretagogue or insulin to reduce the risk of hypoglycemia.

Renal impairment has been reported postmarketing, usually in association with nausea, vomiting, diarrhea, or dehydration which may sometimes require hemodialysis. Use caution when initiating or escalating doses of Victoza® in patients with renal impairment.

Serious hypersensitivity reactions (e.g. anaphylaxis and angioedema) have been reported during postmarketing use of Victoza®. If symptoms of hypersensitivity reactions occur, patients must stop taking Victoza® and seek medical advice promptly.

There have been no studies establishing conclusive evidence of macrovascular risk reduction with Victoza® or any other antidiabetic drug.

The most common adverse reactions, reported in ≥5% of patients treated with Victoza® and more commonly than in patients treated with placebo, are headache, nausea, diarrhea, dyspepsia, constipation and anti-liraglutide antibody formation. Immunogenicity-related events, including urticaria, were more common among Victoza®-treated patients (0.8%) than among comparator-treated patients (0.4%) in clinical trials.

Victoza® has not been studied in type 2 diabetes patients below 18 years of age and is not recommended for use in pediatric patients.

There is limited data in patients with renal or hepatic impairment.

In a 52-week monotherapy study (n=745) with a 52-week extension, the adverse reactions reported in ≥ 5% of patients treated with Victoza® 1.8 mg, Victoza® 1.2 mg, or glimepiride were constipation (11.8%, 8.4%, and 4.8%), diarrhea (19.5%, 17.5%, and 9.3%), flatulence (5.3%, 1.6%, and 2.0%), nausea (30.5%, 28.7%, and 8.5%), vomiting (10.2%, 13.1%, and 4.0%), fatigue (5.3%, 3.2%, and 3.6%), bronchitis (3.7%, 6.0%, and 4.4%), influenza (11.0%, 9.2%, and 8.5%), nasopharyngitis (6.5%, 9.2%, and 7.3%), sinusitis (7.3%, 8.4%, and 7.3%), upper respiratory tract infection (13.4%, 14.3%, and 8.9%), urinary tract infection (6.1%, 10.4%, and 5.2%), arthralgia (2.4%, 4.4%, and 6.0%), back pain (7.3%, 7.2%, and 6.9%), pain in extremity (6.1%, 3.6%, and 3.2%), dizziness (7.7%, 5.2%, and 5.2%), headache (7.3%, 11.2%, and 9.3%), depression (5.7%, 3.2%, and 2.0%), cough (5.7%, 2.0%, and 4.4%), and hypertension (4.5%, 5.6%, and 6.9%).

Please see brief summary of Prescribing Information on adjacent page.

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Victoza® (liraglutide [rDNA origin] injection)
Rx Only
BRIEF SUMMARY. Please consult package insert for full prescribing information.

WARNING: RISK OF THYROID C-CELL TUMORS: Liraglutide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures in both genders of rats and mice. It is unknown whether Victoza® causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as human relevance could not be ruled out by clinical or nonclinical studies. Victoza® is contraindicated in patients with a personal or family history of MTC and in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Based on the findings in rodents, monitoring with serum calcitonin or thyroid ultrasound was performed during clinical trials, but this may have increased the number of unnecessary thyroid surgeries. It is unknown whether monitoring with serum calcitonin or thyroid ultrasound will mitigate human risk of thyroid C-cell tumors. Patients should be counseled regarding the risk and symptoms of thyroid tumors *[see Contraindications and Warnings and Precautions]*.

INDICATIONS AND USAGE: Victoza® is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. **Important Limitations of Use:** Because of the uncertain relevance of the rodent thyroid C-cell tumor findings to humans, prescribe Victoza® only to patients for whom the potential benefits are considered to outweigh the potential risk. Victoza® is not recommended as first-line therapy for patients who have inadequate glycemic control on diet and exercise. Based on spontaneous postmarketing reports, acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis has been observed in patients treated with Victoza®. Victoza® has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for pancreatitis while using Victoza®. Other antidiabetic therapies should be considered in patients with a history of pancreatitis. Victoza® is not a substitute for insulin. Victoza® should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings. The concurrent use of Victoza® and prandial insulin has not been studied.

CONTRAINDICATIONS: Do not use in patients with a personal or family history of medullary thyroid carcinoma (MTC) or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Do not use in patients with a prior serious hypersensitivity reaction to Victoza® or to any of the product components.

WARNINGS AND PRECAUTIONS: Risk of Thyroid C-cell Tumors: Liraglutide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors (adenomas and/or carcinomas) at clinically relevant exposures in both genders of rats and mice. Malignant thyroid C-cell carcinomas were detected in rats and mice. A statistically significant increase in cancer was observed in rats receiving liraglutide at 8-times clinical exposure compared to controls. It is unknown whether Victoza® will cause thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as the human relevance of liraglutide-induced rodent thyroid C-cell tumors could not be determined by clinical or nonclinical studies. In the clinical trials, there have been 6 reported cases of thyroid C-cell hyperplasia among Victoza®-treated patients and 2 cases in comparator-treated patients (1.3 vs. 1.0 cases per 1000 patient-years). One comparator-treated patient with MTC had pre-treatment serum calcitonin concentrations >1000 ng/L suggesting pre-existing disease. All of these cases were diagnosed after thyroidectomy, which was prompted by abnormal results on routine, protocol-specified measurements of serum calcitonin. Five of the six Victoza®-treated patients had elevated calcitonin concentrations at baseline and throughout the trial. One Victoza® and one non-Victoza®-treated patient developed elevated calcitonin concentrations while on treatment. Calcitonin, a biological marker of MTC, was measured throughout the clinical development program. The serum calcitonin assay used in the Victoza® clinical trials had a lower limit of quantification (LLOQ) of 0.7 ng/L and the upper limit of the reference range was 5.0 ng/L for women and 8.4 ng/L for men. At Weeks 26 and 52 in the clinical trials, adjusted mean serum calcitonin concentrations were higher in Victoza®-treated patients compared to placebo-treated patients but not compared to patients receiving active comparator. At these timepoints, the adjusted mean serum calcitonin values (~1.0 ng/L) were just above the LLOQ with between-group differences in adjusted mean serum calcitonin values of approximately 0.1 ng/L or less. Among patients with pre-treatment serum calcitonin below the upper limit of the reference range, shifts to above the upper limit of the reference range which persisted in subsequent measurements occurred most frequently among patients treated with Victoza® 1.8 mg/day. In trials with on-treatment serum calcitonin measurements out to 5-6 months, 1.9% of patients treated with Victoza® 1.8 mg/day developed new and persistent calcitonin elevations above the upper limit of the reference range compared to 0.8-1.1% of patients treated with control medication or the 0.6 and 1.2 mg doses of Victoza®. In trials with on-treatment serum calcitonin measurements out to 12 months, 1.3% of patients treated with Victoza® 1.8 mg/day had new and persistent elevations of calcitonin from below or within the reference range to above the upper limit of the reference range, compared to 0.6%, 0% and 1.0% of patients treated with Victoza® 1.2 mg, placebo and active control, respectively. Otherwise, Victoza® did not produce consistent dose-dependent or time-dependent increases in serum calcitonin. Patients with MTC usually have calcitonin values >50 ng/L. In Victoza® clinical trials, among patients with pre-treatment serum calcitonin <50 ng/L, one Victoza®-treated patient and no comparator-treated patients developed serum calcitonin >50 ng/L. The Victoza®-treated patient who developed serum calcitonin >50 ng/L had an elevated pre-treatment serum calcitonin of 10.7 ng/L that increased to 30.7 ng/L at Week 12 and 53.5 ng/L at the end of the 6-month trial. Follow-up serum calcitonin was 22.3 ng/L more than 2.5 years after the last dose of Victoza®. The largest increase in serum calcitonin in a comparator-treated patient was seen with glimepiride in a patient whose serum calcitonin increased from 19.3 ng/L at baseline to 44.8 ng/L at Week 65 and 38.1 ng/L at Week 104. Among patients who began with serum calcitonin <20 ng/L, calcitonin elevations to >20 ng/L occurred in 0.7% of Victoza®-treated patients, 0.3% of placebo-treated patients, and 0.5% of active-comparator-treated patients, with an incidence of 1.1% among patients treated with 1.8 mg/day of Victoza®. The clinical significance of these findings is unknown. Counsel patients regarding the risk for MTC and the symptoms of thyroid tumors (e.g. a mass in the neck, dysphagia, dyspnea or persistent hoarseness). It is unknown whether monitoring with serum calcitonin or thyroid ultrasound will mitigate the potential risk of MTC, and such monitoring may increase the risk of unnecessary procedures, due to low test specificity for serum calcitonin and a high background incidence of thyroid disease. Patients with thyroid nodules noted on physical examination or neck imaging obtained for other reasons should be referred to an endocrinologist for further evaluation. Although routine monitoring of serum calcitonin is of uncertain value in patients treated with Victoza®, if serum calcitonin is measured and found to be elevated, the patient should be referred to an endocrinologist for further evaluation. **Pancreatitis: Based on spontaneous postmarketing reports, acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis, has been observed in patients treated with Victoza®. After initiation of Victoza®, observe patients carefully for signs and symptoms of pancreatitis (including persistent severe abdominal pain, sometimes radiating to the back and which may or may not be accompanied by vomiting). If pancreatitis is suspected, Victoza® should promptly be discontinued and appropriate management should be initiated. If pancreatitis is confirmed, Victoza® should not be restarted. Consider antidiabetic therapies other than Victoza® in patients with a history of pancreatitis.** In clinical trials of Victoza®, there have been 13 cases of pancreatitis among Victoza®-treated patients and 1 case in a comparator (glimepiride) treated patient (2.7 vs. 0.5 cases per 1000 patient-years). Nine of the 13 cases with Victoza® were reported as acute pancreatitis and four were reported as chronic pancreatitis. In one case in a Victoza®-treated patient, pancreatitis, with necrosis, was observed and led to death; however clinical causality could not be established. Some patients had other risk factors for pancreatitis, such as a history of cholelithiasis or alcohol abuse. **Use with Medications Known to Cause Hypoglycemia:** Patients receiving Victoza® in combination with an insulin secretagogue (e.g., sulfonylurea) or insulin may have an increased risk of hypoglycemia. The risk of hypoglycemia may be lowered by a reduction in the dose of sulfonylurea (or other concomitantly administered insulin secretagogues) or insulin **Renal Impairment:** Victoza® has not been found to be directly nephrotoxic in animal studies or clinical trials. There have been postmarketing reports of acute renal failure and worsening of chronic renal failure, which may sometimes require hemodialysis in Victoza®-treated patients. Some of these events were reported in patients without known underlying renal disease. A majority of the reported events occurred in patients who had experienced nausea, vomiting, diarrhea, or dehydration. Some of the reported events occurred in patients receiving one or more medications known to affect renal function or hydration status. Altered renal function has been reversed in many of the reported cases with supportive treatment and discontinuation of potentially causative agents, including Victoza®. Use caution when initiating or escalating doses of Victoza® in patients with renal impairment. **Hypersensitivity Reactions:** There have been postmarketing reports of serious hypersensitivity reactions (e.g., anaphylactic reactions and angioedema) in patients treated with Victoza®. If a hypersensitivity reaction occurs, the patient should discontinue Victoza® and other suspect medications and promptly seek medical advice. Angioedema has also been reported with other GLP-1 receptor agonists. Use caution in a patient with a history of angioedema with another GLP-1 receptor agonist because it is unknown whether such patients will be predisposed to angioedema with Victoza®. **Macrovascular Outcomes:** There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with Victoza® or any other antidiabetic drug.

ADVERSE REACTIONS: Clinical Trials Experience: Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. The safety of Victoza® has been evaluated in 8 clinical trials: A double-blind 52-week monotherapy trial compared Victoza® 1.2 mg daily, Victoza® 1.8 mg daily, and glimepiride 8 mg daily; A double-blind 26 week add-on to metformin trial compared Victoza® 0.6 mg once-daily, Victoza® 1.2 mg once-daily, Victoza® 1.8 mg once-daily, placebo, and glimepiride 4 mg once-daily; A double-blind 26 week add-on to glimepiride trial compared Victoza® 0.6 mg daily, Victoza® 1.2 mg once-daily, Victoza® 1.8 mg once-daily, placebo, and rosiglitazone 4 mg once-daily; A 26 week add-on to metformin + glimepiride trial, compared double-blind Victoza® 1.8 mg once-daily, double-blind placebo, and open-label insulin glargine once-daily; A double-blind 26-week add-on to metformin + rosiglitazone trial compared Victoza® 1.2 mg once-daily, Victoza® 1.8 mg once-daily and placebo; An open-label 26-week add-on to metformin and/or sulfonylurea trial compared Victoza® 1.8 mg once-daily and exenatide 10 mcg twice-daily; An open-label 26-week add-on to metformin trial compared Victoza® 1.2 mg once-daily, Victoza® 1.8 mg once-daily, and sitagliptin 100 mg once-daily; An open-label 26-week trial compared insulin detemir as add-on to Victoza® 1.8 mg + metformin to continued treatment with Victoza® + metformin alone. *Withdrawals:* The incidence of withdrawal due to adverse events was 7.8% for Victoza®-treated patients and 3.4% for comparator-treated patients in the five double-blind controlled trials of 26 weeks duration or longer. This difference was driven by withdrawals due to gastrointestinal adverse reactions, which occurred in 5.0% of Victoza®-treated patients and 0.5% of comparator-treated patients. In these five trials, the most common adverse reactions leading to withdrawal for Victoza®-treated patients were nausea (2.8% versus 0% for comparator) and vomiting (1.5% versus 0.1% for comparator). Withdrawal due to gastrointestinal adverse events mainly occurred during the first 2-3 months of the trials. *Common adverse reactions:* Tables 1, 2, 3 and 4 summarize common adverse reactions (hypoglycemia is discussed separately) reported in seven of the eight controlled trials of 26 weeks duration or longer. Most of these adverse reactions were gastrointestinal in nature. In the five double-blind clinical trials of 26 weeks duration or longer, gastrointestinal adverse reactions were reported in 41% of Victoza®-treated patients and were dose-related. Gastrointestinal adverse reactions occurred in 17% of comparator-treated patients. Common adverse reactions that occurred at a higher incidence among Victoza®-treated patients included nausea, vomiting, diarrhea, dyspepsia and constipation. In the five double-blind and three open-label clinical trials of 26 weeks duration or longer, the percentage of patients who reported nausea declined over time. In the five double-blind trials approximately 13% of Victoza®-treated patients and 2% of comparator-treated patients reported nausea during the first 2 weeks of treatment. In the 26-week open-label trial comparing Victoza® to exenatide, both in combination with metformin and/or sulfonylurea, gastrointestinal adverse reactions were reported at a similar incidence in the Victoza® and exenatide treatment groups (Table 3). In the 26-week open-label trial comparing Victoza® 1.2 mg, Victoza® 1.8 mg and sitagliptin 100 mg, all in combination with metformin, gastrointestinal adverse reactions were reported at a higher incidence with Victoza® than sitagliptin (Table 4). In the remaining 26-week trial, all patients received Victoza® 1.8 mg + metformin during a 12-week run-in period. During the run-in period, 167 patients (17% of enrolled total) withdrew from the trial: 76 (46% of withdrawals) of these patients doing so because of gastrointestinal adverse reactions and 15 (9% of withdrawals) doing so due to other adverse events. Only those patients who completed the run-in period with inadequate glycemic control were randomized to 26 weeks of add-on therapy with insulin detemir or continued, unchanged treatment with Victoza® 1.8 mg + metformin. During this randomized 26-week period, diarrhea was the only adverse reaction reported in ≥5% of patients treated with Victoza® 1.8 mg + metformin + insulin detemir (11.7%) and greater than in patients treated with Victoza® 1.8 mg and metformin alone (6.9%).

Table 1: Adverse reactions reported in ≥5% of Victoza®-treated patients in a 52-week monotherapy trial

	All Victoza® N = 497	Glimepiride N = 248
Adverse Reaction	(%)	(%)
Nausea	28.4	8.5
Diarrhea	17.1	8.9
Vomiting	10.9	3.6
Constipation	9.9	4.8
Headache	9.1	9.3

Table 2: Adverse reactions reported in ≥5% of Victoza®-treated patients and occurring more frequently with Victoza® compared to placebo: 26-week combination therapy trials

Add-on to Metformin Trial			
	All Victoza® + Metformin N = 724	Placebo + Metformin N = 121	Glimepiride + Metformin N = 242
Adverse Reaction	(%)	(%)	(%)
Nausea	15.2	4.1	3.3
Diarrhea	10.9	4.1	3.7
Headache	9.0	6.6	9.5
Vomiting	6.5	0.8	0.4
Add-on to Glimepiride Trial			
	All Victoza® + Glimepiride N = 695	Placebo + Glimepiride N = 114	Rosiglitazone + Glimepiride N = 231
Adverse Reaction	(%)	(%)	(%)
Nausea	7.5	1.8	2.6
Diarrhea	7.2	1.8	2.2
Constipation	5.3	0.9	1.7
Dyspepsia	5.2	0.9	2.6
Add-on to Metformin + Glimepiride			
	Victoza® 1.8 + Metformin + Glimepiride N = 230	Placebo + Metformin + Glimepiride N = 114	Glargine + Metformin + Glimepiride N = 232
Adverse Reaction	(%)	(%)	(%)
Nausea	13.9	3.5	1.3
Diarrhea	10.0	5.3	1.3
Headache	9.6	7.9	5.6
Dyspepsia	6.5	0.9	1.7
Vomiting	6.5	3.5	0.4
Add-on to Metformin + Rosiglitazone			
	All Victoza® + Metformin + Rosiglitazone N = 355	Placebo + Metformin + Rosiglitazone N = 175	
Adverse Reaction	(%)	(%)	
Nausea	34.6	8.6	
Diarrhea	14.1	6.3	
Vomiting	12.4	2.9	
Headache	8.2	4.6	
Constipation	5.1	1.1	

Table 3: Adverse Reactions reported in ≥5% of Victoza®-treated patients in a 26-Week Open-Label Trial versus Exenatide

	Victoza® 1.8 mg once daily + metformin and/or sulfonylurea N = 235	**Exenatide 10 mcg twice daily + metformin and/or sulfonylurea** N = 232
Adverse Reaction	(%)	(%)
Nausea	25.5	28.0
Diarrhea	12.3	12.1
Headache	8.9	10.3
Dyspepsia	8.9	4.7
Vomiting	6.0	9.9
Constipation	5.1	2.6

Table 4: Adverse Reactions in ≥5% of Victoza®-treated patients in a 26-Week Open-Label Trial versus Sitagliptin

	All Victoza® + metformin N = 439	**Sitagliptin 100 mg/day + metformin** N = 219
Adverse Reaction	(%)	(%)
Nausea	23.9	4.6
Headache	10.3	10.0
Diarrhea	9.3	4.6
Vomiting	8.7	4.1

Immunogenicity: Consistent with the potentially immunogenic properties of protein and peptide pharmaceuticals, patients treated with Victoza® may develop anti-liraglutide antibodies. Approximately 50-70% of Victoza®-treated patients in the five double-blind clinical trials of 26 weeks duration or longer were tested for the presence of anti-liraglutide antibodies at the end of treatment. Low titers (concentrations not requiring dilution of serum) of anti-liraglutide antibodies were detected in 8.6% of these Victoza®-treated patients. Sampling was not performed uniformly across all patients in the clinical trials, and this may have resulted in an underestimate of the actual percentage of patients who developed antibodies. Cross-reacting anti-liraglutide antibodies to native glucagon-like peptide-1 (GLP-1) occurred in 6.9% of the Victoza®-treated patients in the double-blind 52-week monotherapy trial and in 4.8% of the Victoza®-treated patients in the double-blind 26-week add-on combination therapy trials. These cross-reacting antibodies were not tested for neutralizing effect against native GLP-1, and thus the potential for clinically significant neutralization of native GLP-1 was not assessed. Antibodies that had a neutralizing effect on liraglutide in an *in vitro* assay occurred in 2.3% of the Victoza®-treated patients in the double-blind 52-week monotherapy trial and in 1.0% of the Victoza®-treated patients in the double-blind 26-week add-on combination therapy trials. Among Victoza®-treated patients who developed anti-liraglutide antibodies, the most common category of adverse events was that of infections, which occurred among 40% of these patients compared to 36%, 34% and 35% of antibody-negative Victoza®-treated, placebo-treated and active-control-treated patients, respectively. The specific infections which occurred with greater frequency among Victoza®-treated antibody-positive patients were primarily nonserious upper respiratory tract infections, which occurred among 11% of Victoza®-treated antibody-positive patients; and among 7%, 7% and 5% of antibody-negative Victoza®-treated, placebo-treated and active-control-treated patients, respectively. Among Victoza®-treated antibody-negative patients, the most common category of adverse events was that of gastrointestinal events, which occurred in 43%, 18% and 19% of antibody-negative Victoza®-treated, placebo-treated and active-control-treated patients, respectively. Antibody formation was not associated with reduced efficacy of Victoza® when comparing mean HbA_{1c} of all antibody-positive and all antibody-negative patients. However, the 3 patients with the highest titers of anti-liraglutide antibodies had no reduction in HbA_{1c} with Victoza® treatment. In the five double-blind clinical trials of Victoza®, events from a composite of adverse events potentially related to immunogenicity (e.g. urticaria, angioedema) occurred among 0.8% of Victoza®-treated patients and among 0.4% of comparator-treated patients. Urticaria accounted for approximately one-half of the events in this composite for Victoza®-treated patients. Patients who developed anti-liraglutide antibodies were not more likely to develop events from the immunogenicity events composite than were patients who did not develop anti-liraglutide antibodies. *Injection site reactions:* Injection site reactions (e.g., injection site rash, erythema) were reported in approximately 2% of Victoza®-treated patients in the five double-blind clinical trials of at least 26 weeks duration. Less than 0.2% of Victoza®-treated patients discontinued due to injection site reactions. *Papillary thyroid carcinoma:* In clinical trials of Victoza®, there were 7 reported cases of papillary thyroid carcinoma in patients treated with Victoza® and 1 case in a comparator-treated patient (1.5 vs. 0.5 cases per 1000 patient-years). Most of these papillary thyroid carcinomas were <1 cm in greatest diameter and were diagnosed in surgical pathology specimens after thyroidectomy prompted by findings on protocol-specified screening with serum calcitonin or thyroid ultrasound. *Hypoglycemia* :In the eight clinical trials of at least 26 weeks duration, hypoglycemia requiring the assistance of another person for treatment occurred in 11 Victoza®-treated patients (2.3 cases per 1000 patient-years) and in two exenatide-treated patients. Of these 11 Victoza®-treated patients, six patients were concomitantly using metformin and a sulfonylurea, one was concomitantly using a sulfonylurea, two were concomitantly using metformin (blood glucose values were 65 and 94 mg/dL) and two were using Victoza® as monotherapy (one of these patients was undergoing an intravenous glucose tolerance test and the other was receiving insulin as treatment during a hospital stay). For these two patients on Victoza® monotherapy, the insulin treatment was the likely explanation for the hypoglycemia. In the 26-week open-label trial comparing Victoza® to sitagliptin, the incidence of hypoglycemic events defined as symptoms accompanied by a fingerstick glucose <56 mg/dL was comparable among the treatment groups (approximately 5%).

Table 5: Incidence (%) and Rate (episodes/patient year) of Hypoglycemia in the 52-Week Monotherapy Trial and in the 26-Week Combination Therapy Trials

	Victoza® Treatment	**Active Comparator**	**Placebo Comparator**
Monotherapy	**Victoza®** (N = 497)	**Glimepiride** (N = 248)	**None**
Patient not able to self-treat	0	0	—
Patient able to self-treat	9.7 (0.24)	25.0 (1.66)	—
Not classified	1.2 (0.03)	2.4 (0.04)	—
Add-on to Metformin	**Victoza® + Metformin** (N = 724)	**Glimepiride + Metformin** (N = 242)	**Placebo + Metformin** (N = 121)
Patient not able to self-treat	0.1 (0.001)	0	0
Patient able to self-treat	3.6 (0.05)	22.3 (0.87)	2.5 (0.06)
Add-on to Victoza® + Metformin	**Insulin detemir + Victoza® + Metformin** (N = 163)	**Continued Victoza® + Metformin alone** (N = 158*)	**None**
Patient not able to self-treat	0	0	—
Patient able to self-treat	9.2 (0.29)	1.3 (0.03)	—
Add-on to Glimepiride	**Victoza® + Glimepiride** (N = 695)	**Rosiglitazone + Glimepiride** (N = 231)	**Placebo + Glimepiride** (N = 114)
Patient not able to self-treat	0.1 (0.003)	0	0
Patient able to self-treat	7.5 (0.38)	4.3 (0.12)	2.6 (0.17)
Not classified	0.9 (0.05)	0.9 (0.02)	0
Add-on to Metformin + Rosiglitazone	**Victoza® + Metformin + Rosiglitazone** (N = 355)	**None**	**Placebo + Metformin + Rosiglitazone** (N = 175)
Patient not able to self-treat	0	—	0
Patient able to self-treat	7.9 (0.49)	—	4.6 (0.15)
Not classified	0.6 (0.01)	—	1.1 (0.03)
Add-on to Metformin + Glimepiride	**Victoza® + Metformin + Glimepiride** (N = 230)	**Insulin glargine + Metformin + Glimepiride** (N = 232)	**Placebo + Metformin + Glimepiride** (N = 114)
Patient not able to self-treat	2.2 (0.06)	0	0
Patient able to self-treat	27.4 (1.16)	28.9 (1.29)	16.7 (0.95)
Not classified	0	1.7 (0.04)	0

*One patient is an outlier and was excluded due to 25 hypoglycemic episodes that the patient was able to self-treat. This patient had a history of frequent hypoglycemia prior to the study.

In a pooled analysis of clinical trials, the incidence rate (per 1,000 patient-years) for malignant neoplasms (based on investigator-reported events, medical history, pathology reports, and surgical reports from both blinded and open-label study periods) was 10.9 for Victoza®, 6.3 for placebo, and 7.2 for active comparator. After excluding papillary thyroid carcinoma events *[see Adverse Reactions]*, no particular cancer cell type predominated. Seven malignant neoplasm events were reported beyond 1 year of exposure to study medication, six events among Victoza®-treated patients (4 colon, 1 prostate and 1 nasopharyngeal), no events with placebo and one event with active comparator (colon). Causality has not been established. **Laboratory Tests:** In the five clinical trials of at least 26 weeks duration, mildly elevated serum bilirubin concentrations (elevations to no more than twice the upper limit of the reference range) occurred in 4.0% of Victoza®-treated patients, 2.1% of placebo-treated patients and 3.5% of active-comparator-treated patients. This finding was not accompanied by abnormalities in other liver tests. The significance of this isolated finding is unknown. **Vital signs:** Victoza® did not have adverse effects on blood pressure. Mean increases from baseline in heart rate of 2 to 3 beats per minute have been observed with Victoza® compared to placebo. The long-term clinical effects of the increase in pulse rate have not been established. **Post-Marketing Experience:** The following additional adverse reactions have been reported during post-approval use of Victoza®. Because these events are reported voluntarily from a population of uncertain size, it is generally not possible to reliably estimate their frequency or establish a causal relationship to drug exposure: Dehydration resulting from nausea, vomiting and diarrhea; Increased serum creatinine, acute renal failure or worsening of chronic renal failure, sometimes requiring hemodialysis; Angioedema and anaphylactic reactions; Allergic reactions: rash and pruritus; Acute pancreatitis, hemorrhagic and necrotizing pancreatitis sometimes resulting in death.

OVERDOSAGE: Overdoses have been reported in clinical trials and post-marketing use of Victoza®. Effects have included severe nausea and severe vomiting. In the event of overdosage, appropriate supportive treatment should be initiated according to the patient's clinical signs and symptoms.

More detailed information is available upon request.

For information about Victoza® contact: Novo Nordisk Inc., 800 Scudders Mill Road, Plainsboro, NJ 08536, 1–877-484-2869

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Manufactured by: Novo Nordisk A/S, DK-2880 Bagsvaerd, Denmark

Victoza® is covered by US Patent Nos. 6,268,343, 6,458,924, 7,235,627, 8,114,833 and other patents pending.
Victoza® Pen is covered by US Patent Nos. 6,004,297, RE 43,834, RE 41,956 and other patents pending.

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Opioid prescribing primer

Doctors urged to become knowledgeable about risks

BY CARMEN PEOTA

If there was a take-away message from a February educational session at the University of Minnesota's McNamara Center, it was that physicians need to know a great deal before they ever prescribe long-acting and extended-release opioids.

PHOTO BY JULIANA MILHOFER

Physicians and other health care professionals took part in the seminar on minimizing the risks associated with prescribing opioids.

That message was delivered by Gavin Bart, M.D., Ph.D., and Charlie Reznikoff, M.D., both addiction medicine specialists at Hennepin County Medical Center. The two were asked by the Minnesota Medical Association to present curriculum on mitigating risks related to these drugs, which are often prescribed for pain.

Reznikoff told audience members to base decisions about prescribing opioids on evidence and indications. He also emphasized the importance of getting to know patients in order to weigh potential benefits against potential risks, including addiction and abuse. To illustrate the challenge of doing that, he asked the audience to picture a 25-year-old military veteran who has PTSD and is an amputee and complains of pain. The patient would have a compelling indication for treatment, he said, but also would be in the highest risk category for substance abuse.

Bart addressed technical issues, including the differences between specific formulations and brands. He said physicians must do their homework long before they prescribe or counsel patients. They need to know about disposal, limitations of usage and that dose equivalency tables are problematic. They also need to know about the indications and potential interactions.

Both presenters said doctors need to be forthright when talking to patients about the risk of mixing alcohol and opioids. Reznikoff said patients need to be told that mixing any amount of alcohol and opioids is dangerous. And Bart said the best approach is to bluntly state, "If you misuse this drug, it could lead to death."

A video of the session is available online at www.mnmed.org (click on Events, then Education, then CME Webinars). Physicians who view the webinar and complete the evaluation are eligible for CME credit.

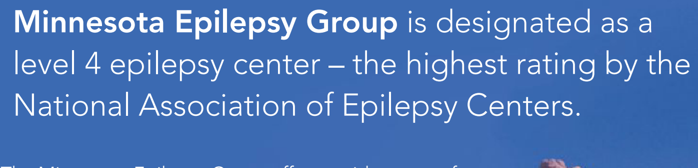
FDA approves new opioid formulation

The Food and Drug Administration's February approval of Zohydro sparked a rash of criticism from experts across the country. The drug is the first extended-release hydrocodone product to be approved that does not contain acetaminophen.

A coalition of 40 groups called on the FDA to revoke the decision, pointing out that the drug was so potent a single dose could kill a child. Critics also noted that the drug is prone to abuse because it is crushable.

Zohydro's maker, Zogenix, claims its product meets the needs of patients at risk of liver damage if they take acetaminophen or who aren't helped by combination pain drugs.

In a statement, company president Stephen Farr, Ph.D., said Zogenix would provide education on safe use to physicians, patients and pharmacies and that the company was developing a noncrushable formulation.



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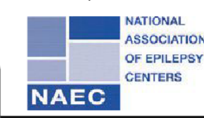

PHOTO COURTESY OF LEXI REED HOLTUM

Lexi Reed Holtum and her fiancé Steve Rummler, who died of a heroin overdose in 2011. As vice president of the Steve Rummler Hope Foundation, Reed Holtum has been pushing a bill to increase access to naloxone. The legislation will be known as "Steve's Law" if it passes.

Reversing tragedy

Proposed legislation will increase access to an antidote to opioid overdose.

BY JEANNE METTNER

When Sen. Chris Eaton of Brooklyn Center lost her 23-year-old daughter Ariel Eaton-Willson to a heroin overdose in 2007, it was heart-wrenching and painful. It was also preventable. Eaton-Willson was in a Burger King parking lot in Brooklyn Center with another person when the overdose occurred; but instead of calling 911 right away, her companion spent 20 to 30 minutes purging the car of drug paraphernalia and other incriminating evidence. Hearing the commotion, the restaurant manager summoned a nearby police officer, who called paramedics. At the scene, the paramedics administered naloxone (Narcan), a drug that, in seconds, can reverse the effects of an opiate or opioid overdose. But it was too late, and Eaton-Willson was pronounced dead a short time later.

In February, Eaton, along with Rep. Dan Schoen, introduced a bill that she hopes will prevent others from enduring the same loss. Known as "911 Good Samaritan + Naloxone," the proposed legislation has two components: It provides immunity to those who call 911 in good faith to prevent an overdose death, and it authorizes law enforcement officers, emergency medical responders and staff from community health and social service programs to administer naloxone if they encounter someone experiencing an opioid or opiate overdose. Currently in Minnesota, naloxone can only be administered by medical professionals and paramedics.

During a press conference last December, Eaton called the bill "a simple solution to a terrible problem," noting that she was unaware that her daughter was using heroin.

In 2012, Hennepin and Ramsey counties reported 129 deaths due to opiate overdoses—a 40 percent increase from 2010. The estimated number of emergency department visits attributed to heroin nearly tripled in the past several years—from 1,189 in 2004 to 3,493 in 2011. The jump in ED admissions for "unspecified opiates/opioids" has been even more staggering—162 admissions were reported in 2004 compared with 1,619 in 2011.

The 911 Good Samaritan + Naloxone bill has support from multiple organizations and agencies, including the Minnesota Board of Pharmacy, Minnesota Department of Human Services, Minnesota Society of Addiction Medicine, Minnesota Department of Health and Minnesota Medical Association. Thus far, it has encountered no formal opposition. If it becomes law, Minnesota will join 17 other states and the District of Columbia in having some form of naloxone legislation in place.

Quick, safe, life-saving

An opioid antagonist, naloxone binds to opioid receptors in the central nervous system, blocking the action of an opioid. When administered to someone who is overdosing from an opioid or opiate, it can reverse the effects of the drug, often improving respiration in just seconds. "The good news is that it very quickly reverses the effects of overdose, which is life-saving and necessary," says Cody Wiberg, executive director of the Minnesota Board of Pharmacy. He explains that naloxone also will cause symptoms of physical withdrawal, such as agitation, trembling, nausea, sweating and mood changes in persons who are addicted to opioids. "While these things are not pleasant," he says, "the alternative is death from respiratory depression."

Naloxone can be injected or inhaled. When injected, it works almost immedi-

> "The good news is that [naloxone] very quickly reverses the effects of overdose, which is life-saving and necessary."
> – CODY WIBERG, EXECUTIVE DIRECTOR, MINNESOTA BOARD OF PHARMACY

ately. The intranasal formula, which is not being used in Minnesota, takes effect in minutes rather than seconds.

Research has shown that administering naloxone saves lives. A team from Boston Medical Center, Boston University Schools of Medicine and Public Health, and the Massachusetts Department of Public Health compared deaths in 19 communities before and after they distributed naloxone to potential "overdose bystanders" (eg, social service staff, families and friends of opioid users, and opioid users at risk of overdose) and taught them when and how to administer it. In an article published in the *British Medical Journal* in February 2013, they reported a 46 percent reduction in opioid overdose deaths after distributing the drug. Another article in the February 2012 *Morbidity and Mortality Weekly Report* reported findings from a survey of the 50 community-based opioid overdose prevention programs known to distribute naloxone in the United States. Since 1996, when the first naloxone program began, about 53,000 people have been trained to administer naloxone, which led to 10,171 overdose reversals.

"These reports point to the fact if someone is overdosing from an opiate, this is the antidote," says Gavin Bart, M.D., director of the Division of Addiction Medicine at Hennepin County Medical Center. "It does it quickly; it does it safely. It does not have street value, it's not a sought-after drug, no one can get intoxicated off it. It doesn't cause any kind of organ damage. And it works really well."

"Steve's Law"

The 911 Good Samaritan + Naloxone legislation (SF 1900 and HF 2307) was introduced on February 25. Lexi Reed Holtum, vice president of the Steve Rummler Hope Foundation, which has been helping advance the bill, expects it to be approved in both legislative bodies. (At presstime, it was still alive in both the House and Senate.) If it is, it will be known as "Steve's Law," named after her fiancé, Steve Rummler, who died in July 2011 after taking heroin for the first time.

Although Rummler was alone when his body was found, others were believed to have been with him when he overdosed. "We can and must give first responders and citizens the tools they need to save a life," says Reed Holtum. "We would have preferred that 911 was called and he was alive than to see someone in jail after his death—as would every single person who's lost a loved one to this epidemic." **MM**

Jeanne Mettner is a frequent contributor to *Minnesota Medicine*.

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Rocky Mountain reality

Minnesota can learn from **Colorado's experience with medical marijuana.** INTERVIEW BY KIM KISER

Jan Kief, M.D., became immersed in the debate over whether to legalize recreational marijuana in 2012, the year she was president-elect of the Colorado Medical Society. That year, voters approved Amendment 64, a constitutional amendment allowing anyone over 21 years of age to grow and possess up to an ounce of cannabis. More than a decade earlier, the state legalized the drug for medical purposes.

Kief, an internal medicine physician, now speaks to others around the country about Colorado's experience with medical marijuana. She shared some of the lessons learned as well as her thoughts about the consequences of legalizing marijuana for recreational use.

Why did you get so involved in this?

I was a chemist before I became a physician. I did my residency in internal medicine and emergency medicine. I worked in a big trauma center in Denver and saw lots of people coming in overdosed. I'm also a mother of five, and when I learned about the irreparable damage marijuana can do to the brains of adolescents, I became upset about what was happening in Colorado. I knew medical marijuana was being abused, and once I started immersing myself in the science I said, "I can't ignore this."

You say medical marijuana was being abused. In what way?

It's been clearly shown that in medical marijuana states, it's getting diverted to children. Seventy-four percent of teens in the Denver area who are in treatment said they used someone else's medical marijuana on average 50 times. At one of the universities in Denver, because the legal age for medical marijuana is 18, it was almost considered a rite of passage during your first week of school to get a medical marijuana referral. You didn't have to register with the state; you just needed a physician's written referral.

And were many physicians giving these referrals?

A dozen physicians were writing more than half of the referrals. Most physicians said "No, I won't touch this." But there was no guidance on how to deal with it, and our major malpractice carrier told physicians that if they did recommend it, they'd be on their own in terms of protection against claims.

Jan Kief, M.D.

Were there concerns about the way the law was written?

It has some real big problems. It allows personal in-home cultivation and allows people to cultivate six plants. But if it isn't enough to cover your pain, your caregiver can get approval for more. Some people were cultivating over 100 plants in their homes. The other issue is the caregiver model. In Colorado, a caregiver can oversee five patients and can petition to oversee more. Patients are supposed to have a bona fide relationship with their physician, but people were being bussed in to Denver from rural areas to get referrals.

Were there unintended consequences as a result of medical marijuana being legalized?

From 2000 to 2012, we saw hospital cannabis admissions more than double. It's part of the potency thing. One of the biggest issues with marijuana now is that it's so potent. In the 1960s, the level of THC, the psychoactive component, was maybe 2 percent. It's now more than 10 times that. And in some of the medical strains we were seeing, it was 48 percent. In an ounce of marijuana concentrate, it was 84 percent. Also, auto fatalities involving drivers who tested positive for marijuana rose by 112 percent,

and drugged driving, where people tested positive for marijuana, tripled between 2009 and 2012.

Given the experience with medical marijuana, what were your thoughts when the state legalized recreational marijuana?

It was very frustrating. The advocacy group for legalization has big plans. They have infiltrated legislatures and influenced organizations at all levels. They want to see it legal in 10 more states by 2017. Physicians didn't take any sort of stand early enough.

The governor appointed a task force in 2013 to make recommendations regarding implementation of Amendment 64. I was not on that, but it was pretty amazing to look at some of the people who were. Some big proponents of legalizing marijuana were on it. Every meeting I attended, they almost didn't want to hear about the science.

What was the sentiment among the medical community?

We had 300 physicians on board with legalization. Their concern was people being in jail because they possessed small amounts. The statistics show that among sentenced people in state jurisdictions in 2008, 18 percent were sentenced for drug offenses but only 0.2 percent for possession. The rest were for trafficking. Those medical professionals and the public hung their hats on that issue. They weren't going with the science.

Does the medical marijuana industry in Colorado still exist?

Yes. Some people still want to get referrals because it's less expensive (the standard sales tax applies to medical marijuana; recreational marijuana is subject to sales tax plus special state sales and excise taxes and, in some communities, local sales and excise taxes); they can possess up to two ounces rather than just one, and they only have to be 18. Recreational marijuana is legal for those over 21.

What can the 15 states that are currently considering legislation to legalize medical marijuana learn from Colorado's experience?

If you're going to do this, you have to have good regulations. You don't want home cultivation. Instead, you should have highly regulated dispensaries. We tried to get it where dispensaries are owned by the state like some states and municipalities do with liquor stores. It's the best way to regulate a substance that can be abused and help ensure the quality and standardization of the product. You also want the caregiver to care for only one person and to make sure the physician really has a relationship with the patient.

Also, you need to have a baseline list of conditions that a referral can be written for. If there are too many or if the definition is too loose, it's a problem. In Colorado, 94 percent of the more than 150,000 referrals made were for chronic or severe pain. Only 2 percent were for cancer, 1 percent for HIV and 1 percent for glaucoma. People would say "I have pain" and get a referral. You need to make the conditions very legitimate and really make it about compassionate care.

Is there a better approach than legalizing medical marijuana for helping patients get the benefits?

There's an organization called Project SAM—Smart Approaches to Marijuana—that's calling for rapid expansion of research into cannabis-based medicines. Marinol is one example. It has been available in the United States for chemotherapy-related nausea for several years. Sativex is in the FDA's final stages of approval for cancer pain, and Epidiolex, which is useful in children with seizures, is available through the FDA or the manufacturer for investigational use.

What can physicians do?

That's a good question. I think we need to be very open to the science. People look to us for informed opinions and we're not as informed as we need to be. Physicians, teachers, parents, journalists, politicians, the faith community all need to come together to promote research, promote accurate information, promote access to medications. We need to keep this from becoming another Big Tobacco. **MM**

Kim Kiser is senior editor of *Minnesota Medicine.*

Taking a stand

What **physicians** are saying about legalizing marijuana

Physicians do not think alike when it comes to marijuana. But they are thinking. *Minnesota Medicine* recently invited readers to share their thoughts. We asked three questions: Should marijuana be legalized for medical purposes in Minnesota? Should it be legalized across the board as it is in Colorado and Washington? And would you consider recommending it to your patients if it were legal?

About 40 individuals took the time to respond. Three-fourths were against legalizing medical marijuana. A handful favored legalizing it for both medical and recreational purposes. Some were in favor of legalizing it for one purpose but not the other.

We found the reasons why physicians think the way they do to be particularly interesting. Certainly, there are compelling arguments on all sides.

Not all of the physicians who responded shared their names. As one anonymous writer stated, "I am personally afraid of speaking out on this matter, yet consider myself quite knowledgeable about it. Fear relates to silence!" We hope that by sharing some of the comments we received, we'll encourage those who have hesitated to speak out to join the conversation.—*The editors*

On legalizing marijuana for medical purposes

It is suitable for some patients who cannot tolerate or whose symptoms are not adequately treated with conventional medications. For example, nausea and anorexia from pain medication can be reduced; some neurological conditions, such as painful spasms from multiple sclerosis, also improve with marijuana.

SARA LANGER, M.D.

We already have "medical marijuana" in two forms: dronabinol and nabilone. Their usage should be expanded for many other problems: chronic pain, neuropathic pain, migraine, chronic headache, etc. Smokable marijuana should not be legalized for medical purposes.

WILLIAM G. DICKS, M.D.

It's less dangerous than many/most of our drugs and is occasionally helpful. It's stupid to forbid it based on the old hysterical concept of its "addictiveness."

BARRY BERSHOW, M.D.

There are legal alternatives for the diseases that marijuana could help. It's a gateway drug. I don't believe it should be used.

TERESA JENSEN, M.D.

I don't know how to prescribe it, and I don't think it has been proven to have great benefits. It will become a drug of abuse that will need to be followed on the Prescription Monitoring Program, like Vicodin and Percocet.

TERESE SHEARER, M.D.

Marijuana's medical benefits have not been rigorously established. The Legislature and advocates are getting out ahead of the medical community. Something of this magnitude shouldn't be rushed through the legislative session because once the door is open, it would be very difficult to close. We need to examine not just the personal

claims of advocates, but we need to examine it from a community health standpoint. Do we know what the effects might be? The current issues with narcotics are difficult enough.
TIMOTHY EBEL, M.D.

If society wants to legalize marijuana, fine; but leave the medical profession out of it. It is a social issue, not a medical one. There is no medical indication to prescribe marijuana. If there were, THC should be available in a quality-controlled and dose-controlled pill.
BRUCE YOUNG, M.D.

It is not a drug with exact dosages, safety and efficiency studies and a uniform delivery system.
GEORGE REALMUTO, M.D.

It should be legal, but with oversight and clear boundaries.
LISA MATTSON, M.D.

I do not believe there is adequate evidence to prescribe marijuana for psychiatric and medical disorders. As a physician, I do not want to prescribe (or utilize my medical license to authorize) a substance that has not be rigorously studied.
KATHRYN LOMBARDO, M.D.

Why not focus on changing legislation to allow more study?
ELISABETH BILDEN, M.D.

Marijuana is a potent and effective drug for certain conditions. As an internist, I see very sick people day in and day out. Many chronic illnesses including cancer, advanced vascular, autoimmune, bowel and inflammatory illnesses leave patients with chronic nausea and vomiting and weight loss. For some patients, traditional anti-emetics including Zofran are ineffective, while marijuana works. We routinely prescribe many drugs with dramatically worse risk.
R. LUBKA, M.D.

What some **physician organizations** are saying about medical marijuana

In Minnesota

Minnesota Medical Association

The Minnesota Medical Association will not support legislation intended to involve physicians in certifying, authorizing or otherwise directing patients in the use of medical marijuana outside of clinical trials until it is approved for use by the Food and Drug Administration and is no longer classified as a Schedule I drug by the Drug Enforcement Administration.

Minnesota Psychiatric Society

The Minnesota Psychiatric Society is concerned that legitimizing the medical/psychiatric use of marijuana gives the public—especially children and teens who are most vulnerable to its neuropsychological effects—the impression that it is safe. The society recognizes there may be valid arguments for decriminalizing the recreational use of marijuana; however, it believes psychiatric patients, who are often extremely vulnerable, will not benefit from this effort.

Across the nation

American Medical Association

The American Medical Association (AMA) opposes marijuana legalization. It does call for further studies of marijuana and related cannabinoids in patients who have serious conditions for which evidence suggests possible efficacy. The AMA also urges that marijuana's status as a federal Schedule I controlled substance be reviewed with the goal of facilitating clinical research and development of cannabinoid-based medicines and alternate delivery methods.

American Society of Addiction Medicine

The American Society of Addiction Medicine asserts that cannabis, cannabis-based products, and cannabis delivery devices should be subject to the same standards as other prescription medications and medical devices, and that these products should not be distributed or otherwise provided to patients unless they have received approval from the FDA. The society also rejects smoking as a means of drug delivery and recommends that its members and other physician organizations reject responsibility for providing access to cannabis and cannabis-based products until they receive approval from the FDA.

American Academy of Pediatrics

The American Academy of Pediatrics opposes the legalization of marijuana and supports rigorous scientific research regarding the use of cannabinoids for the relief of symptoms not currently ameliorated by existing legal drug formulations.

Physician organizations on medical marijuana
(continued from previous page)

American Academy of Child and Adolescent Psychiatry

The American Academy of Child and Adolescent Psychiatry opposes medical marijuana dispensing to adolescents but urges more scientific evaluation and a risk-benefit analysis by interdisciplinary experts to determine whether there is any medical indication for marijuana dispensing given the potential harm to adolescents.

American Academy of Family Physicians

The American Academy of Family Physicians opposes the use of marijuana except under medical supervision and control for specific medical indications.

American Osteopathic Association

In 2011, the American Osteopathic Association's House of Delegates passed a resolution calling on the National Institutes of Health to fund well-designed clinical trials to investigate marijuana's medicinal properties.

American College of Physicians

The American College of Physicians supports programs and funding for rigorous scientific evaluation of the potential therapeutic benefits of medical marijuana and supports increased research for conditions where the efficacy of marijuana has been established to determine optimal dosage and route of delivery. The ACP also urges an evidence-based review of marijuana's status as a Schedule I controlled substance to determine whether it should be reclassified.

American Psychiatric Association

The American Psychiatric Association maintains there is no current scientific evidence that marijuana is in any way beneficial for the treatment of any psychiatric disorder. In contrast, current evidence supports, at minimum, a strong association between cannabis use with the onset of psychiatric disorders. Further research on the use of cannabis-derived substances as medicine should be encouraged and facilitated by the federal government. The adverse effects of marijuana, including, but not limited to, the likelihood of addiction, must be simultaneously studied. Policy and practice surrounding cannabis-derived substances should not be altered until sufficient clinical evidence supports such changes and cannabis-derived substances are approved by the FDA.

More problems and issues will surface. We will be forced, as physicians, to police this activity, and I do not want to be in that position. There is no good science behind the argument for legalizing this.

DALE E. LOEFFLER, D.O.

There are no medical indications that cannot be successfully treated with already approved medication. There's no consistency in dosing, and administration is through smoking. There's no FDA oversight/regulation and a significant lack of evidence for help and significant evidence for harm.

DAN SWARTZ, M.D.

I say yes, but not according to the present bill, only if it were very limited. By "limited" I mean dispensed at three sites—Duluth, U of Minnesota and Mayo—and prescribed by only a handful of physicians. I would not include chronic pain patients in the system. I would also ask the Legislature include chronic opiate therapy in the same limited system if they chose to include chronic pain patients.

DAVID DETERT, M.D.

On making it legal across the board

I favor decriminalizing marijuana, as that would diminish the collateral damage caused by the illegal drug trade.

SARA LANGER, M.D.

From a merely practical standpoint, given its widespread use and lack of significant health effects (debatable), too much treasure is squandered on enforcement and on incarceration. Basically, many innocent lives have been destroyed by over-zealous enforcers. The "war on drugs" is a total failure, foisted on us by, of all things, the right wing and libertarians who want to get the government off our backs. It allows sleazy crooks to get very rich. If it is legalized fully, it must be highly controlled.

WILLIAM DICKS, M.D.

Legalize it and regulate it like tobacco and alcohol. I am not convinced that most "medical" marijuana gets used for medical

purposes. In Los Angeles, for example, there are more medical marijuana dispensaries than coffee shops. The problem of prescription drug diversion is so big. Let's not add this substance to the mix. Let's just regulate and tax what is a commonly used product.
DAVID MOSEMAN, M.D., M.P.H.

It will cause as much or more harm as tobacco and alcohol in terms of death, destruction, crime, illness, lost productivity, etc., if legalized.
ROBERT FOOTE, M.D.

It's less dangerous than alcohol.
BARRY BERSHOW, M.D.

It has similar effects as alcohol as a depressant, and it is addictive. It will just add to the general malaise in society.
TERESE SHEARER, M.D.

It is going to take some time for Colorado and Washington to know how this is going to play out in terms of social and community costs. How are these states going to deal with impaired driving? How are they going to keep college kids or others from selling pot to high schoolers? How should physicians account for risks of medication interactions with their pot-smoking patients? How are Colorado and Washington going to avoid becoming a nexus in the drug trade? How does legalized marijuana affect the workforce in those states? Do you want a "stoned" mechanic to fix your brakes? The full implications are yet to be determined. Why do we want Minnesota to plunge down the waterfall with these two states?
TIMOTHY EBEL, M.D.

It would lead to increased use in teens because teens would come to think of it as acceptable and less risky.
GEORGE REALMUTO, M.D.

Prohibition only ruins people's lives, with no upside. And besides, there is a black market that we want to see go away.
R. LUBKA, M.D.

It's a gateway drug, especially for adolescents.
JEREMY SPRINGER, M.D.

I am concerned about addiction, cognitive decline affecting educational and occupational objectives of individuals and society, and inconsistency with current anti-smoking campaigns.
DAN SWARTZ, M.D.

On one hand, we are trying to dissuade people from using tobacco, and then we legitimize marijuana, which doesn't seem logical. Yet prohibition does not work. What I would really like to see is people being held responsible for their use medically, economically and socially.
DAVID DETERT, M.D.

On recommending it for your patients

I would only use the present forms of THC or cannabidiol. The term "medical marijuana" needs clarification. It should be understood that there's a dichotomy between smoking "medical pot" and using pure THC and/or cannabidiol. I do not want my patients smoking pot. Getting high is recreation, not medicine.
WILLIAM DICKS, M.D.

I wouldn't. I have seen too much drug diversion and am not convinced that there is a medical need.
DAVID MOSEMAN, M.D., M.P.H.

There is no evidence it is any better than other drugs for the diseases that I treat.
ROBERT FOOTE, M.D.

I don't have any patients who have used it or have told me that it has benefits for them. I work in urgent care. It would be inappropriate for me to prescribe it.
TERESE SHEARER, M.D.

I would prescribe it if I had good indications—the same way I prescribe narcotics, H_2 blockers, birth control, etc.
LISA MATTSON, M.D.

I am not in the type of practice where marijuana would be indicated, and I will not plan to prescribe this drug. Still I support additional research to evaluate its effectiveness and to determine the appropriate medical indication(s) for which marijuana might be used. It should then be tested and approved through the FDA.
ELIZABETH BILDEN, M.D.

For some patients and some diagnoses, the choice to prescribe is obvious!
R. LUBKA, M.D.

I am not going [to prescribe] something I do not support or believe in.
DALE E. LOEFFLER, D.O.

Medicine OR Menace?

What we know about **medical marijuana**

BY HOWARD BELL

At Gillette Children's Specialty Healthcare in St. Paul, pediatric pain and palliative care specialist Scott Schwantes, M.D., was recently talking with the mother of one of his patients—an 8-year-old boy with cerebral palsy, epilepsy, spasticity, dystonia, dysautonomia, irritability and pain. "I fed my son marijuana brownies and it really helped his dystonia," the mom said. "Am I crazy for doing this?"

Schwantes and his partners have heard other parents say the same thing. Although he says he cannot tell families to try this approach, he says some studies show marijuana can help relieve symptoms such as those exhibited by the boy. "Anecdotally, in our patient population, marijuana has been helpful," he says.

It's also illegal. Physicians can't prescribe it even in states where medical marijuana is legal because it's a Schedule I drug deemed to have no medical value. That also means no federal funds are available to study its potential benefits and clear the air for physicians who feel stuck in the middle as more patients turn to marijuana, mostly in desperation, when conventional drugs don't work or aren't tolerated. "Most people who smoke it for medical reasons do so because they don't have an alternative that works well," says J. Michael Bostwick, M.D., a Mayo Clinic psychiatrist and medical marijuana expert who has written on the subject.

Medical marijuana timeline

Over the last 5,000 years, medical marijuana has been embraced, then demonized, only to be embraced again.

2800 B.C. First reported use of medical marijuana in China.

1500 B.C. Earliest written references to medical marijuana in Chinese Pharmacopeia.

1542 British doctors begin using marijuana as an analgesic, anti-spasmodic and anti-emetic.

1854 Marijuana added to the U.S. Pharmacopeia. Physicians routinely prescribe marijuana cigarettes and extracts to treat anorexia, headaches, insomnia and sexual dysfunction.

Early 1900s Medical use of marijuana begins to decline because of increasing availability of synthetic pharmaceuticals, potency variability and unreliable supply sources.

1936 The film *Reefer Madness* depicts marijuana smokers as addicted maniacs and killers.

Forty-eight states have laws that regulate marijuana.

1937 Marijuana Tax Act causes further decline in prescribing medical marijuana. The American Medical Association opposes the Marijuana Tax Act, fearing it would limit research on its benefits for treating a variety of conditions.

1942 Marijuana removed from the U.S. Pharmacopeia, eliminating its last vestige of legitimacy as a therapeutic drug.

1964 The principal psychoactive ingredient in cannabis, THC, is identified and synthesized.

1970 Congress makes marijuana a Schedule I drug, a class reserved for street drugs with abuse potential and "no currently accepted medical use."

1976 A man with glaucoma becomes the first American to receive government-supplied marijuana for a medical disorder.

1978 New Mexico passes the first state law recognizing the medical value of marijuana.

The federal government's Compassionate Use Program begins supplying free marijuana to seriously ill patients who might benefit from it.

1980 National Cancer Institute tests dronabinol (Marinol), a synthetic THC, on cancer patients.

1985 Food and Drug administration approves dronabinol.

1988 Researchers discover a THC protein receptor located on human nerve cells—cannabinoid receptor 1 (CB1). Soon after, the same researchers discover a cannabinoid receptor 2 (CB2) on white blood cells and immune tissue. The search for cannabinoid-based pharmaceuticals begins.

1991 In an anonymous survey by the American Society of Clinical Oncology, 53 percent of respondents say marijuana should be available by prescription.

The federal government suspends the Compassionate Use Program because it undercuts Bush administration policy against use of illegal drugs.

1992 Israeli researchers discover the brain's first endogenous cannabinoid and call it anandomide, from the Sanskrit word *ananda* meaning eternal bliss or supreme joy.

1996 California becomes first state to legalize medical marijuana.

1997 *New England Journal of Medicine* publishes editorial calling for marijuana to be reclassified a Schedule II drug to acknowledge it has some medical use.

1999 Institute of Medicine publishes its first meta-analysis on the medical effects of marijuana.

Dronabinol reclassified as a Schedule III drug to increase availability to patients.

Canada begins funding research on medical uses for marijuana.

2003 Institute of Medicine publishes its second meta-analysis listing several medical conditions for which marijuana appears to have benefit.

2004 Drug Enforcement Administration instructs the Department of Health and Human Services to review marijuana for possible rescheduling.

2008 American College of Physicians calls for making marijuana a Schedule II drug, the same classification as opioid narcotics, and supports use of nonsmoked forms of medical marijuana.

2014 20 states plus the District of Columbia have legalized medical use of marijuana, which remains a Schedule I drug "with no currently accepted medical use."

Sources: Bostwick JM, Blurred boundaries: the therapeutics and politics of medical marijuana, Mayo Clinic Proceedings, February 2012, 172-186; Robson PJ, Therapeutic potential of cannabinoid medicines, Drug Test Analysis, 2014, 6, 24-30; ProCon.org

The human cannabinoid system

In 1988, researchers discovered that the human body produces its own cannabinoids that attach to cannabinoid receptor sites throughout the body. The "endocannabinoid system" (ECS) affects nearly every physiologic function in the body by regulating neurotransmission between synapses.

The cannabinoids in marijuana exert their effects on the body and brain by attaching to these cannabinoid receptor sites. THC, a cannabinoid found in marijuana that produces the high users experience, attaches to cannabinoid receptor 1 (CB1), which is found mostly on cells in the brain, spinal cord and gut. CB1 helps regulate movement, pleasure, learning, memory, processing, attention and appetite. Recreational marijuana smokers may get the munchies when THC attaches to the CB1 receptors that govern food intake, according to J. Michael Bostwick, M.D., a Mayo Clinic psychiatrist and medical marijuana expert.

Another cannabinoid in marijuana called cannabidiol (CBD) attaches to cannabinoid receptor 2 (CB2), which is also found in the brain, but mostly on cells in the gut and on white blood cells. CB2 helps regulate digestion, inflammation and immune response, as well as cardiovascular, reproductive and endocrine function.

The ECS's widespread influence explains why marijuana has been used for thousands of years to treat many conditions, Bostwick says. "And it's why discovery of the ECS has ignited interest in cannabis-based medicines and prompted high hopes for developing many new drugs that will eliminate the need for or interest in using smoked cannabis."

Researchers have found CBD switches off the malignant effects of the virus that causes Kaposi's sarcoma and regulates movement of white blood cells important in immune defenses. CBD also has anti-seizure effects and reduces anxiety and psychotic symptoms, prompting some to speculate that it could someday be used to treat psychotic disorders.

THC relieves pain, relaxes muscles, prevents nausea, stimulates appetite, reduces intraocular pressure, acts as a bronchodilator and inhibits the growth and spread of lung cancer. CBD does the same for breast cancer. Both have anti-inflammatory effects.

Most of this research is still at the molecular stage or being done in animals. It may lead to the development of cannabinoid pharmaceuticals to treat ileus, inflammatory bowel disease, neuropathic pain, tumor growth and metastasis, hypertension, anxiety, psychosis and immune dysfunction. "We need to figure out how synthetic cannabinoids can modify the function of the ECS with potential implications for helpful treatments in a plethora of diseases," Bostwick says.

To prevent the cognitive clouding and memory impairment marijuana causes, researchers are trying to create cannabinoid drugs that attach only to CB2 receptors, which are nearly absent from the brain and therefore don't cause these cognitive side-effects. Another line of research is developing drugs that attach to CB1 receptors, but only those outside of the brain.

Nobody knew about the ECS in 1970 when the federal government banned medical research on marijuana by making it a Schedule I drug. "It's sad and frustrating that there are so many barriers to translating what we've learned about the endocannabinoid system into beneficial pharmaceuticals," Bostwick says.—H.B.

Smoking your medicine

Smoking is the primary way medical marijuana is used in the states where it's legal, although state dispensaries also sell marijuana-infused baked goods and other edibles. Thus far, 20 states and the District of Columbia have legalized medical marijuana use in some way.

Physicians in those states can recommend that their patients enroll in their state's medical cannabis program. To qualify, a patient must have an approved condition for which conventional treatments either didn't work or caused intolerable side effects.

A growing body of evidence from lab studies and human clinical trials shows that smoked marijuana can reduce symptoms in a wide range of conditions including severe chronic pain, peripheral neuropathy, intractable nausea and vomiting, MS spasticity, cancer, epilepsy, severe anorexia, PTSD, glaucoma, hepatitis C infection (and undergoing antiviral treatment), HIV/AIDS, rheumatoid arthritis, ALS, Crohn's disease, cervical dystonia, inclusion body myositis, spinal cord damage with intractable spasticity, Parkinson disease and Huntington disease.

Its most commonly accepted—and studied—use is for relieving nausea and improving appetite. Robson's review of the therapeutic potential of cannabinoid medicines published in *Drug Test Analysis* earlier this year cited a number of clinical studies done in the 1970s and '80s that showed THC and cannabidiol could alleviate both nausea and vomiting through different pharmacological mechanisms. Thomas Flynn, M.D., an oncologist with Minnesota Oncology in Minneapolis, says some of his younger chemotherapy patients have told him "smoking marijuana is especially helpful for nausea when standard anti-emetics weren't fully effective."

Cannabis is also used to reduce pain in people with multiple sclerosis when other treatments are ineffective or not tolerated. Robson noted that clinical trials in the United Kingdom showed that four weeks of treatment with either synthetic THC (dronabinol or nabilone) or a marijuana extract called nabiximols (Sativex) signifi-

cantly lowered pain scores as compared with placebo. They also reduced spasticity and improved sleep. A double-blind trial using Sativex for intractable central neuropathic MS pain was so convincing that the results were the primary basis for approving Sativex in the United Kingdom in 2010. (It is not yet approved in the United States.)

For treating PTSD, the evidence is thinner and more anecdotal, but many states include it on their list of authorized conditions. In New Mexico, which created its medical cannabis program in 2007, 42 percent of the enrolled patients smoke marijuana to relieve PTSD symptoms. "We've known for years that many PTSD patients smoke marijuana to help them cope with symptoms," says Steven Jenison, M.D., a medical cannabis expert who directed the program from 2007 to 2009. "Now there's compelling evidence that supports their experience."

Clinical and lab studies suggest that cannabinoids may reduce PTSD symptoms by attaching to cannabinoid receptors in the amygdala, the part of the brain that controls fear conditioning, memory storage and retrieval, arousal, mood, sleep, anxiety and depression. A team of investigators from Germany, the United States and the United Kingdom reported in *Drug Test Analysis* in 2012 that marijuana works better than antidepressants for alleviating some symptoms. Last month, the Department of Health and Human Services signed off on a study of marijuana to treat PTSD symptoms in veterans. Researchers from the University of Arizona will evaluate the effects of five different potencies of smoked or vaporized marijuana in 50 veterans, assuming they receive clearance from the DEA.

A thicker stack of studies shows marijuana's potential for treating epilepsy. Certain cannabinoids in marijuana reduce seizure intensity and frequency in some types of epilepsy. "We've known for years that cannabinoids help prevent seizures in research animals," says Ilo Leppik, M.D., a neurologist who directs the University of Minnesota's Epilepsy Research and Education Program. "In neuroscience, animal research often translates well to humans."

Some of Leppik's patients have told him they sometimes smoke marijuana and it seems to reduce seizure frequency and intensity. "They ask me what I think. I tell them I can't recommend it. We know there's a cannabinoid receptor in the brain associated with seizures. But we need to study the potential of specific cannabinoids, not whole marijuana."

The U.K. drug company that created Sativex is doing just that—testing what it calls Epidiolex, a highly purified liquid cannabidiol extracted from

marijuana plants, to treat pediatric epilepsy syndromes. Unlike THC, cannabidiol doesn't have psychoactive effects. Robson's review found that in animal studies, several cannabinoids, especially cannabidiol, have shown significant anti-convulsant properties. The company expects to begin Phase 2 clinical studies of Epidiolex in the latter half of 2014.

Several studies show THC and cannabidiol have anti-inflammatory effects, which may explain why some medical marijuana smokers say it relieves symptoms of inflammatory bowel disease. In the lab, cannabinoids show promise for treating several gastrointestinal conditions. As Mayo Clinic gastroenterologist Michael Camilleri, M.D., wrote in his 2008 review in *Gut*: "Cannabinoids may benefit patients with irritable bowel syndrome by inhibiting intestinal motility and secretions by docking onto cannabinoid receptors in the gut and acting as a physiological brake." He qualified that statement by saying "Further clinical trials are required to assess the potential impact on disease."

Cannabinoids may reverse hepatic fibrosis and have anti-tumor effects in the liver as well. Animal studies show cannabinoids shrink tumors and slow metastasis in colon, liver and pancreatic cancer. "They have been reported to have remarkable growth-inhibiting effects on pancreatic cancer cells," Camilleri wrote.

Marijuana's anti-inflammatory effects also may explain why many medical marijuana smokers use it for arthritis pain. In a randomized double-blind trial of 58 rheumatoid arthritis patients comparing Sativex to placebo, most had significant improvements in pain, movement and quality of sleep after only five weeks of treatment. That same study, which was published in *Rheumatology* in 2006, showed that in many patients the THC and cannabidiol in Sativex actually slowed rheumatoid arthritis progression, based on a standard measure of rheumatoid arthritis disease activity.

Not ready for prime time?

The American Medical Association (AMA), Institute of Medicine and American College of Physicians agree that specific cannabinoids show potential. But that doesn't mean they support smoking whole marijuana, which many view as an imprecise "shotgun" way to treat anything because it contains 400 different chemicals.

Leppik says smoking marijuana has so many downsides that even if Minnesota legalizes medical marijuana he'd tell his patients not to smoke it. "They're still going to have seizures, and they'd need to stay high all the time in order to maintain a steady dose. Smoking itself is harmful, and in epilepsy it's important to minimize side-effects from whatever drugs they're taking because side-effects can aggravate the condition." Leppik says he is irritated with the recent flurry of media stories about marijuana as a miracle cure for seizures. "They do a great disservice because they create false hope."

"Most people who smoke marijuana for medical reasons do so because they don't have an alternative that works well."

– J. MICHAEL BOSTWICK, M.D.

Another concern is that whole marijuana might increase the risk for earlier and more intense emergence of psychoses, including schizophrenia, especially in susceptible adolescents and young adults. A 2011 meta-analysis by Kuepper published in *BMJ* looked at the results from three dozen studies of young people in Sweden, New Zealand and the Netherlands and found a strong link between regular marijuana use and later development of schizophrenia and other psychoses in those predisposed to the conditions. "Marijuana doesn't cause schizophrenia," Bostwick says. "But in those predisposed to it, it may cause schizophrenia to appear earlier and perhaps be harder to treat."

Exactly why isn't known. But Bostwick says some studies have noted an association between schizophrenia and excessive amounts of an endocannabinoid called anandamide in cerebrospinal fluid. Marijuana may further deregulate an already deregulated endocannabinoid system.

A Swedish longitudinal study of 50,000 people reported in *BMJ* in 2002 showed that over a 27-year period, the more marijuana people used in adolescence, the more likely they were to develop schizophrenia. Those who had used cannabis more than 50 times were six times more likely to develop schizophrenia. Several studies published in the past year have shown connections between marijuana use and psychiatric disorders. One by Griffin-Lendering in *Addiction* showed an increase in psychosis among adolescents using marijuana. Another by Kuepper in *PLoS* showed marijuana increasing dopamine in users (increased dopamine is a risk factor for psychosis).

Although many believe the psychosis concern has been overstated, psychiatrists remain concerned. Charles Schulz, M.D., head of the University of Minnesota's psychiatry department, says he's talked with

a number of colleagues around the state who are worried about the possible link. Minnesota's Psychiatric Society and the American Psychiatric Association both oppose using marijuana to treat psychiatric conditions. "There are no scientifically controlled studies that clearly demonstrate marijuana has any therapeutic effects for any psychiatric condition," says Carrie Borchardt, M.D., the society's president and a child and adolescent psychiatrist at Children's Hospitals and Clinics of Minnesota. "Claims that marijuana improves anxiety and depression are anecdotal," she says, noting that many studies show marijuana can actually worsen anxiety and depression.

Borchardt also points to several studies connecting regular marijuana use in adolescence with a long-term drop in overall intelligence, memory impairment and an increased rate of dropping out of school. "Legitimizing the medical use of marijuana gives children and teens who are especially vulnerable to its effects the impression that it's safe." She says one study found teens who used marijuana to be at a six-fold increased risk for developing schizophrenia. "These are people who did not have signs of the disorder earlier—and after they develop it, there's no undoing it."

Gavin Bart, M.D., Ph.D., an internist and addiction medicine specialist at Hennepin County Medical Center who directs their Addiction Medicine Program, recently traveled on a U.S. Embassy-sponsored public health mission to Papua New Guinea, where marijuana grows wild and is freely available. "At the country's only psychiatric hospital," Bart says, "the No. 1 reason for admission is marijuana-induced psychosis. It may have to do with a genetic predisposition combined with dose. But if it's all dose-related, that's a problem for using marijuana medically."

Marijuana's effects differ greatly among individuals. Where it may make one person happy, it may make another sad. Where one person feels relaxed after smoking it, another may feel anxious. Sometimes, it causes all of these in the same person at different times, and its use often makes normal everyday functioning difficult. The American Psychiatric Association's DSM-5 includes a diagnosis of "cannabis use disorder," characterized by an inability to fulfill work, school or family responsibilities.

As for addiction, contrary to the 1936 film *Reefer Madness*, women don't cry for it and men don't die for it. Physical addiction is rare; psychological addiction is more common. Bart says the 2013 National Household Survey on Drug Use and Health shows that among regular marijuana users, one in 11 met the criteria for being addicted to it during that year, compared with one in 21 alcohol users and one in eight prescription opioid users. "During the second half of 2013," he says, "16 percent of all admissions to Twin Cities-area addiction treatment programs were for marijuana addiction."

More study needed

For all of those reasons and more, Bart believes it's too early for marijuana to enter the House of Medicine. "We need clinical trials that compare marijuana to approved

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June 5-7, 2014

NPHTI Pediatric Clinical Hypnosis
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Synthetic cannabinoids

Minnesota physicians can prescribe two pills that contain pure THC, the cannabinoid in marijuana that creates the high recreational users seek and is also medically useful. Dronabinol (Marinol) and nabilone (Cesamet) were approved by the FDA in 1985 for preventing chemotherapy-induced nausea and severe weight loss caused by HIV/AIDS. Both are on most hospital formularies.

Thomas Flynn, M.D., an oncologist with Minnesota Oncology in Minneapolis, says he and other oncologists he knows sometimes prescribe dronabinol for cancer-related nausea and anorexia. "It works," he says, "but usually not as well as the highly effective 5HT3 antagonists like ondansetron, granisetron and palenosetron."

Dronabinol (Marinol) also has more side effects, including a high or feeling of dysphoria that elderly patients in particular don't like. For those reasons, dronabinol and nabilone have never been first-choice treatments. "We only use them if the 5HT3 drugs aren't working or aren't tolerated," he says.

Nabilone (Cesamet) is sometimes also used for cancer pain. Flynn says he and his colleagues don't use it because they have more effective drugs to control pain. A 2014 report by Robson on the therapeutic potential of cannabinoid medicines published in *Drug Test Analysis* showed nabilone sometimes relieves cancer pain to a degree equivalent to codeine, but that it causes sedation and cognitive clouding in most patients.

Pediatric pain and palliative care specialist Scott Schwantes, M.D., has prescribed dronabinol for his end-of-life patients at St. Paul's Gillette Children's Specialty Healthcare to reduce neuropathic pain, anxiety, nausea and spasticity. "It was moderately effective sometimes," he says. But he agrees that better drugs are available.

Nabiximols (Sativex), a third synthetic cannabinoid, is not yet approved in the United States but has been approved in 22 countries including Canada to treat spasticity caused by multiple sclerosis, as well as cancer pain and neuropathic pain. It's currently in Phase 3 clinical trials in this country for treating persistent pain that can't be controlled with other medications.

Sativex is an oral spray containing one part THC and one part cannabidiol (CBD), another compound in marijuana that shows therapeutic promise. Unlike THC, CBD does not cause euphoria, dysphoria, cognitive clouding or sedation. It also reduces anxiety, which pure THC can cause.

Sometimes called "liquid medical marijuana," nabiximols is an extract made from marijuana plants. The U.K. drug company that makes Sativex grows the plants in its own greenhouses (something that is not allowed in the United States). The drug is absorbed rapidly through the mucosa, offering the same rapid-onset advantage as smoked marijuana but without the side effects or the risk for addiction.

Nabiximols, dronabinol and nabilone are examples of how compounds in marijuana can be turned into therapeutic drugs, according to J. Michael Bostwick, M.D., a Mayo Clinic psychiatrist and medical marijuana expert. "You get a quality-controlled standardized potency without having to inhale a smoke containing hundreds of compounds," he says. "And there's little evidence of abuse or addiction because these cannabinoid preparations aren't much fun to take."—H.B.

medications, not to a placebo," he says. "And then we need standardized quality, purity and doses. What's a physician supposed to tell a patient? Here, take this joint and smoke it? How much? How fast? How long before you exhale?" He adds that the people dispensing it in states where medical marijuana is legal don't even have training in medicine or pharmacology. In addition, no one in those states is tracking adverse effects. "Before we let marijuana in the door," Bart says, "we need to learn the same things we learn about every other drug before it gets approved and used—and we shouldn't be placing physicians in the awkward position of gatekeeper for something that has legislatively been deemed 'medicine.' It's too soon to call marijuana a medicine."

But all medicines have risks, Bostwick points out. Many routinely prescribed drugs cause a long list of adverse effects including mental clouding, memory impairment and mood changes—effects that sometimes are so adverse that patients turn to marijuana instead. States that have legalized medical marijuana have decided that whatever the risks may be, the benefits outweigh them for patients with serious chronic conditions who couldn't be helped with conventional treatments. Meanwhile, Bostwick says, "the [federal] government is essentially blocking research on the medical benefits of cannabinoids, which could yield an armada of pharmaceuticals to treat many conditions."

One way to encourage research is to reschedule marijuana. "I think everyone agrees smoking marijuana isn't good for patients," Schwantes says. "But if compounds in marijuana help our patients, then we owe it to our patients to study them." The AMA, the American College of Physicians and the editorial boards of a number of peer-reviewed medical journals have called for changing marijuana to a Schedule II drug so the NIH will fund randomized controlled trials. Until this happens, Leppik says, "the medical marijuana discussion will be based on very little sci-

ence and mostly on anecdotes, politics and sob stories."

New Mexico's Jenison agrees that rescheduling marijuana is an important first step, but he says it's not likely to happen in the foreseeable future. Meanwhile, he says, the public is growing impatient. "Patients who benefit from medical cannabis find uncompelling the argument that they should wait for rigorous clinical trials when they know that their government has not only failed to support this promising area of research but has actively obstructed it. Twenty states now protect patients who benefit from medical cannabis from criminal liability. Until better cannabinoid drugs are available by prescription, I consider this a fair and just compromise." **MM**

Howard Bell is a medical writer and frequent contributor to *Minnesota Medicine*.

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J. Michael Bostwick, M.D., a professor of psychiatry at the Mayo Clinic College of Medicine, provided an overview on medical marijuana for the March 4 policy forum in Eagan.

MMA not supportive of medical marijuana legislation

After 15 years without a policy on the controversial topic of medical marijuana, the MMA now has a position that calls for more research to be conducted before it would consider supporting legislation to make the drug available to patients.

Since the late 1990s, the MMA has taken a nonposition on the issue. Even when the 2009 Legislature voted to approve the use of medical marijuana (only to be vetoed by then Gov. Tim Pawlenty), MMA leadership remained neutral.

However, this year, legislation has gained momentum partly because of the growing number of families with heart-wrenching stories of children suffering from seizures who could benefit from legalizing the substance.

"Although we've discussed this in the past, we have not passed a policy that would guide us on legislative action," says Robert Meiches, M.D., MMA CEO. "We decided that with the pending legislation at the Capitol, it's time again to hear from members and discuss the pros and cons of taking a position."

The pros and cons came through several avenues: a March 4 policy forum in Eagan; an email survey to all members on March 7; a discussion by the MMA's public health committee on March 11; and then a formal vote by the board of trustees on March 15. Each time, the majority voted not to support the current legislation.

"We don't have the evidence and the science to really say where it works well and where it doesn't, and we don't have a way of knowing at this point in time what the availability of the drug is and the product that's being used," Board Chair Dave Thorson, M.D., told Minnesota Public Radio after the board's decision.

No. 1 topic

Medical marijuana has certainly been a hot topic this spring (see Viewpoint on page 34).

The March 7 email survey generated the largest response from members in MMA history. Nearly 900 physician members weighed in on the topic with 46 percent asking the MMA to oppose legalizing medical marijuana. Thirty-three percent wanted the MMA to support it, 9 percent said the MMA should not take a position and 10 percent said they didn't know. The results of this large survey mirrored the sentiments of participants at the March 4 forum.

The press has closely monitored each step the MMA has taken on the issue, featuring stories on each metro-area television network, multiple articles in the dailies and numerous updates on the radio.

The MMA's position is based on the fact that there is a lack of research on the drug in the United States. As part of its policy, the MMA's board voted to call "for further adequate and well-controlled studies of marijuana and related cannabinoids in patients who have serious conditions for which preclinical, anecdotal, or controlled evidence suggests possible efficacy and the application of such results to the understanding and treatment of disease."

In addition, the MMA "urges that marijuana's status as a federal Schedule I controlled substance be reviewed with the goal of facilitating the conduct of clinical and public health research and development of cannabinoid-based medicines, and alternate delivery methods."

Until marijuana is FDA-approved and is no longer classified in Schedule I by the Drug Enforcement Administration, the MMA's leaders say they cannot support legislation intended to involve physicians in certifying, authorizing or directing people toward medicinal marijuana outside of scientific clinical trials.

As this issue went to press, the Legislature continued the debate the topic. It had passed through only one committee and appeared to be stalled for the session.

ALL PHOTOS BY KATHRYN FORSS

Day at the Capitol 2014

Dozens of physicians, medical students and residents descended on the state Capitol in St. Paul on March 13 as part of the MMA's annual Day at the Capitol.

The MMA's legislative team briefed participants on top priorities for the session. Then, physicians, students and residents met with their representatives and senators to discuss health care issues.

Sen. Julie Rosen (R-Fairmont) spoke to the group on a range of topics including the advanced practice registered nurses' push for independent practice, prohibiting minors from using tanning devices and medical marijuana.

❶ Rep. Tom Huntley (DFL-Duluth) spoke with medical students before the event.

❷ Medical student Nathan Beerling went over proposed legislation with Rep. Ernie Leidiger (R-Mayer).

❸ Lisa Mattson, M.D., and Lisa Erickson, M.D., conversed with Rep. Sarah Anderson (R-Plymouth) outside the House chambers.

❹ Sen. Julie Rosen (R-Fairmont) reviewed several health care bills with the group.

❺ Sen. John Marty (DFL-Roseville) meets with Mac Baird, M.D., and Laurel Ries, M.D.

❻ Day at the Capitol attendees were briefed on a number of health care bills currently working through the Legislature.

LEGISLATIVE UPDATE

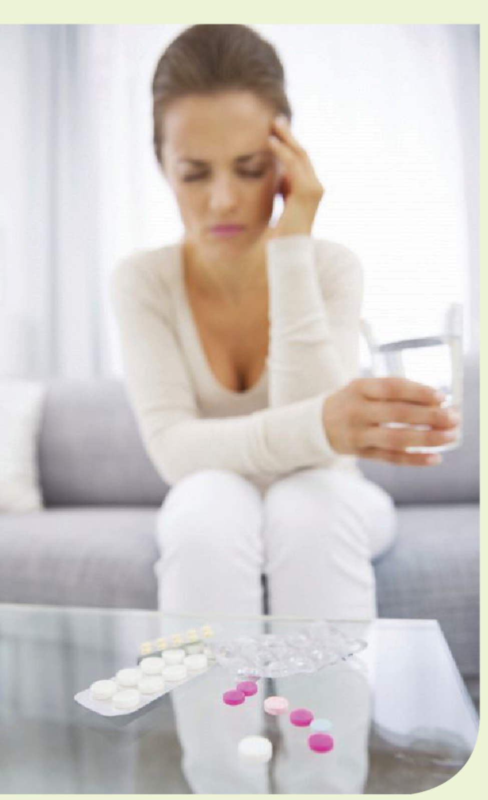
TOP MMA PRIORITIES

Where things stand midway through the session

PRIORITY: Physician-led team-based care

The MMA supports a collaborative practice framework among physicians and other health care providers. Advanced Practice Registered Nurses (APRNs) are pushing for more independence (for example, allowing them prescribing authority). Collaboration is crucial to ensure that patients receive the best care possible by the right practitioner. We support physician-led team-based care.

Status: This legislation continues to move through House and Senate committees and will be laid over for possible inclusion in an omnibus bill later in the session.



PRIORITY: Battling prescription opioid misuse

The MMA supports strengthening the Minnesota Prescription Monitoring Program so that alerts are sent to prescribers on patients who may be "doctor shopping." The MMA also supports "911 Good Samaritan + Naloxone" legislation that is designed to reduce the number of opioid overdose deaths by providing immunity to those who call 911 in good faith to save a life and increasing public access to the antidote naloxone. The law would allow first responders to carry naloxone and make the drug available through community-based agencies that work with intravenous drug users.

Status: The naloxone portion of the bill is moving forward. However, some law enforcement officials have questioned the 911 Good Samaritan part.

PRIORITY: Regulating e-cigarettes

The MMA supports prohibiting the use of e-cigarettes in public indoor spaces such as workplaces and bars by expanding the Freedom to Breathe Act. The MMA is also looking at additional regulations for retailers such as requiring tobacco sellers to obtain a license to sell e-cigarettes and place the product behind their counters. Requiring ingredient disclosure on the product's packaging is another option being considered.

Status: This legislation is moving through House and Senate committees. The Senate bill contains one key provision that the House bill does not—adding e-cigarettes to the state's Freedom to Breath indoor air quality laws. The House bill contained the same language upon introduction, but it was stripped in the face of opposition from e-cigarette retailers. The House bill does, however, include a provision that would ban the use of e-cigarettes in all state-owned buildings.

PRIORITY: Prohibiting use of tanning beds by minors

The MMA supports legislation to prohibit the use of indoor tanning devices by minors, require a warning notice be provided to each consumer, update posted warning signs and create a licensing fee for tanning facilities to pay for enforcement.

Status: This appears to be moving quite quickly and was scheduled for a House vote in March. The bill received support from the tanning industry, which has historically opposed the bill.

PRIORITY: Restoring the newborn screening program

The MMA is urging the Legislature to restore the state's newborn screening program to its prior nation-leading status by removing the arbitrary retention periods for test samples and data established in 2012.

Status: The bill continues to move through both House and Senate committees.

PRIORITY: Cost and quality data for hospitals and clinics

The MMA supports eliminating Provider Peer Grouping (PPG) and focusing more attention on the all-payer claims database (APCD) as the tool for creating public comparisons of the cost and quality of care provided by hospitals and clinics.

Status: Legislation to indefinitely suspend PPG and designate new uses for the state's APCD continues to move quickly through committees.

PRIORITY: Expediting the provider tax phase-out

In 2011, legislators voted for the phase-out and eventual repeal of the provider tax (December 31, 2019). The 2 percent tax has driven up the cost of health care and falls more heavily on sick and low-income Minnesotans. The MMA will continue to lobby to ensure the repeal and will oppose any efforts to use the Health Care Access Fund, which is funded by the tax, for any new purposes.

Status: The MMA has heard rumblings that some legislators might try to use these funds for other projects, but nothing concrete has progressed.

PRIORITY: Aligning clinical data sharing

The MMA supports legislation that would bring the Minnesota Health Records Act into alignment with HIPAA, the existing federal standards governing the sharing of health information. Enhanced information sharing is crucial to the functioning of accountable care organizations, health care homes and total cost of care arrangements. Appropriately shared clinical data will increase the quality of patient care and decrease costs.

Status: It is not likely that this bill will get a hearing.

News briefs

MMA board member Doug Wood, M.D., (left) and MMA President Cindy Firkins Smith, M.D., met with Rep. Collin Peterson (DFL-Seventh District) in early March to discuss SGR.

MMA leaders meet with Minnesota Congress members

While attending the AMA's National Advocacy Conference in early March, several MMA members met with Minnesota's Congressional representatives to push for the repeal of the Medicare Sustainable Growth Rate formula.

MMA President Cindy Firkins-Smith, M.D., MMA board member Doug Wood, M.D., AMA board member Maya Babu, M.D, and MMA CEO Robert Meiches, M.D., met with Rep. Betty McCollum (DFL-Fourth District) and a representative for Sen. Amy Klobuchar. The following day, Smith, Wood and Meiches met with Sen. Al Franken, Rep. Collin Peterson (DFL-Seventh District), a representative from Rep. Tim Walz' (DFL-First District) office and a representative for Rep. Erik Paulsen (R-Third District).

U of M report: health care homes deliver quality, lower costs

A recent University of Minnesota study shows that the MMA-backed health care home concept, which emphasizes preventive and coordinated care, is transforming primary care in Minnesota.

Researchers from the U of M's School of Public Health have found that health care home-style clinics reduced Medicaid costs and outperformed other clinics on quality measures during a three-year period. Furthermore, researchers found that health care home clinics outperformed non-health care home clinics during 2010 to 2012 on measures of care related to cancer screening, asthma, diabetes, vascular care and depression.

In addition, health care homes are providing access to care for Medicaid enrollees with more severe conditions and from disadvantaged populations.

According to a report from the Minnesota Department of Health and the Minnesota Department of Human Services, 43 percent of all primary care clinics in Minnesota are now certified as health care homes. These clinics serve nearly 3.3 million Minnesotans.

The MMA urged the inclusion of health care homes in the 2008 health care reform bill. In fact, the MMA included the concept in its 2005 Physicians Plan for a Healthy Minnesota.

"It's great to see the solid results by the U of M study," says Janet Silversmith, MMA director of health policy. "It proves that we can improve the patient experience and improve quality while lowering costs."

MMA leadership nomination process continues

The nomination process for the MMA's 2014-15 leadership continues through April 25.

The following needs to be filled: the president-elect position, three board of trustees positions, and two AMA delegate and two alternate delegate positions. One of the trustees must be from the North Central Trustees district; the other two can be from anywhere in the state.

In order to keep a representative balance on the board, the nominating committee will seek nominees from non-primary care specialties and large groups.

The nominating committee will meet in early May and recommend a slate of candidates for each position in July. The MMA's first member-wide electronic election will occur in mid-July and close 30 days later. Results will be announced at the 2014 Annual Meeting in Brainerd in September.

Contact Shari Nelson (at snelson@mnmed.org) with questions or to submit your nominations by April 25.

MMA launches contest to promote Choosing Wisely

On April 1, the MMA launched a video contest. The idea is for members to create short videos to promote the Choosing Wisely campaign to a physician audience.

Members are asked to submit videos, five minutes or shorter, by July 1. Winners will be chosen by the MMA's Choosing Wisely Task Force. The top three will receive $100, $200 or $300 gift cards. In addition, MMA members will be able to vote for their favorite video. The winner of this People's Choice award will receive $100.

For more details on the contest, go to www.mnmed.org/ChoosingWisely.

Annual Meeting new and improved in 2014

A new, updated MMA Annual Meeting will replace the suspended House of Delegates this year. The MMA is planning a completely revamped event for Friday and Saturday, September 19 and 20, at Madden's on Gull Lake in Brainerd.

It will feature national speakers; a gubernatorial debate; CME programs that are relevant to practicing physicians; activities for young physicians, students, residents and fellows; policy discussions and a meeting of the new Policy Council.

Mark your calendar and watch for more details. It's an event you won't want to miss.

For more information, visit www.mnmed.org/AbouttheMMA/AnnualMeeting.

Duluth student receives medical award

Fourth-year medical student Mark Bergstrand received the MMA Foundation's 2013 Medical Student Leadership Award. Bergstrand, a student at the University of Minnesota Medical School, Duluth campus, was nominated by Ruth Westra, D.O., M.P.H., chair of the department of family medicine and community health Duluth, and Ray Christensen, M.D., associate dean for rural health.

Bergstrand, chair of the MMA's Medical Student Section, comes from a family of physicians. He and his wife, Maria, will both graduate from the University of Minnesota Medical School in 2014. His sister is also enrolled at the University of Minnesota Medical School, Duluth campus. Their father, Paul Bergstrand, M.D., is a family physician in Alexandria. The family was featured in "A family tradition" in the January 2014 edition of *Minnesota Medicine.*

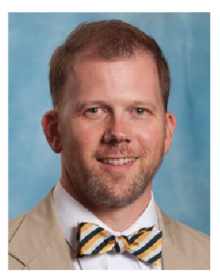
The Medical Student Leadership Award has been presented annually by the MMA Foundation since 2003.

Barbara Daiker

Terry Ruane

Mandy Rubenstein

Kathleen Baumbach



Brian Strub

Teresa Knoedler

MMA in action

Barbara Daiker, MMA manager of quality, presented "Reaching the Triple Aim: How to measure what is important to your practice" at the Minnesota Medical Group Management Association's winter conference in Minneapolis in early March. The conference was also attended by **Terry Ruane**, MMA director of membership, marketing and communications, and MMA managers of physician outreach **Mandy Rubenstein**, **Kathleen Baumbach** and **Brian Strub**.

Teresa Knoedler, MMA policy counsel, attended the March meeting of the Minnesota Board of Medical Practice.

Robert Meiches, M.D., MMA president, **Dave Renner**, MMA director of state and federal legislation, **Juan Bowen**, M.D., president of the Zumbro Valley Medical Society (ZVMS) and **John Shonyo,** ZVMS executive director, met with Mayo Clinic leadership in late February.

In early March, Meiches, **Dave Thorson**, M.D., MMA board chair, Daiker and **Janet Silversmith**, MMA director of health policy, met with AMA leadership and Minnesota Community Measurement to discuss a pre-diabetes measure.

In mid-February, the MMA and Twin Cities Medical Society (TCMS) co-hosted a lunch-and-learn on "What we know and what to tell patients about e-cigarettes" at the University of Minnesota Medical School, Twin Cities campus. Staff attending included **Juliana Milhofer**, MMA policy analyst, **Evelyn Clark**, MMA manager of grassroots and political engagement, Strub, Baumbach and the TCMS's **Nancy Bauer**.

In late February, Rubenstein and Baumbach met with Steve Gerberding and Terry Tone, clinic administrators at Affiliated Community Medical Centers in Willmar.

In separate meetings, Rubenstein met with Mary Hondl, clinic administrator at Regional Diagnostic Radiology in Sartell, and William Worzala, clinic administrator at St. Cloud Orthopedics in Sartell. She and Patrick Zook, M.D., president of the Stearns Benton Medical Society, attended a seminar at St. Cloud Hospital to learn about funding options for the Central Minnesota Circle of Health. They also met with Central Minnesota Circle of Health to discuss the launch of their medication safety campaign for 2014-2015.

VIEWPOINT

March madness

PHOTO BY STEVE WEWERKA

Dave Thorson, M.D.
MMA Board Chair

No matter where you turned in March, you found someone eager to discuss medical marijuana.

During the first week of March alone, I felt I spent more time talking to the media than practicing medicine. The *Minneapolis Star Tribune, St. Paul Pioneer Press*, nearly all of the local television stations, Minnesota Public Radio and the Associated Press all wanted to talk about medical marijuana and what the physicians of Minnesota thought about it. And interest came from beyond the state's borders. Our views on legalizing marijuana garnered attention in newspapers from Alaska to South Carolina and all points in-between.

Lawmakers wanted to talk about it, too, sometimes in lieu of other health care matters. Our legislative team often would begin meetings discussing one of the MMA's priorities only to get sidetracked with a question on what we thought of therapeutic cannabis.

If only there was this much interest in the MMA's priority issues. Medical marijuana, as sexy a topic it may be, is not one of our top priorities at the Legislature this year. We are also taking on other issues such as promoting team-based care and resisting independent practice by advanced practice registered nurses, prohibiting the use of tanning devices by minors, regulating e-cigarettes and battling prescription opioid misuse. These issues will directly affect our practices, yet they aren't receiving a pittance of the coverage focused on medical marijuana.

Up until our board voted on a policy in mid-March (see page 28), we didn't have an official opinion on medical marijuana. The MMA first discussed the subject in the late 1990s. We decided at that time not to take a position. We maintained that nonposition until this year. With pending legislation, we felt we needed to revisit it—thus the impetus for the March 4 policy forum. Although it turned out to be a spirited debate, with both sides making valid arguments, we decided to take an extra step to gather more opinions.

So, three days after the forum we sent out a survey to all of our active members. The responses flooded in, more than 200 in the first 15 minutes. The survey elicited an 11 percent response rate (nearly 900 respondents). A normal, acceptable response rate is around 2 percent, so receiving more than five times that really drives home the fact that the media and politicians were not the only ones intrigued by the issue. Doctors were, too.

The MMA strives to focus on the issues that most directly affect its members and their practices. That's why our legislative and policy team deliberates over this extensively—to make sure we are working most efficiently on behalf of the profession. We want to make an impact. And we do. It just becomes more challenging to work on the issues that affect your practices when contentious issues such as medical marijuana threaten to pull us off course.

If only there was this much interest in the MMA's priority issues. Medical marijuana, as sexy a topic it may be, is not one of our top priorities at the Legislature this year.

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WE NEED TO RESCHEDULE CANNABIS

A sane solution to an irrational standoff

BY J. MICHAEL BOSTWICK, M.D.

As state after state legalizes medical marijuana, the United States is moving back to the future. Prior to the enactment of the Controlled Substances Act (CSA) in 1970, multiple formulations of cannabis-based medications were used as standard treatments for many of the same indications for which medical marijuana is now touted to be beneficial. For more than a century, cannabis was listed on the U.S. Pharmacopeia; but with the advent of the CSA, it was branded a Schedule I drug, a designation indicating that it had no medical value and a high risk of abuse.[1,2]

The Schedule I designation spat in the face of 5,000 years of cannabis use in folk medicine throughout the world. And while folk medicine *per se* doesn't meet federal standards of what constitutes legitimate (meaning Food and Drug Administration-approved) medication, neither does the science justify the demonization of cannabis. In 1970, the chemical structure of delta-9-tetrahydrocannabinol (THC), the principal active ingredient in medical marijuana, had been elucidated for only six years. That was the extent of our knowledge about the properties of cannabis. We did not yet understand the ubiquitous nature of the modulatory endocannabinoid system, as it wasn't until 1988 that the CB1 receptor would be cloned, and the early 1990s before the CB2 receptor would be discovered and the extent of the endocannabinoid system appreciated.[1,3]

Indeed, the last several decades of scientific discoveries suggest that marijuana is anything but a product devoid of medical value. Even as current federal bureaucracy stymies efficient development of cannabis-based pharmaceuticals, researchers posit therapeutic targets for cannabinoids ranging from gastrointestinal disorders and cancers to autoimmune dysfunctions and neurological derangements.[3-6]

Analyzing our anxiety

Admittedly, the medical marijuana product that's currently available challenges our ideas about what constitutes a legitimate medication. First, it is a raw plant containing at least 60 distinct cannabinoids among nearly 500 discrete chemical compounds, the vast majority of which are uncharacterized, let alone studied.[7,8] Moreover, the concentrations of THC and cannabidiol (CBD), marijuana's two known active ingredients, are essentially idiosyncratic, depending on the strain.[9,10] Amateur Luther Burbanks-*qua*-drug dealers have bred strains containing up to 30 percent THC and minimal CBD in order to intensify the high the user feels.[11] (The presence of CBD would otherwise dampen the effects of THC.) Cultivators have also developed strains such as Charlotte's Web, which minimizes the amount of THC and maximizes CBD and is purported to be effective against treatment-resistant epilepsy in children. Thus, marijuana buyers have little guarantee of what they are purchasing, whether the drug comes from a dealer or a state-authorized distributor.

Convoluted bureaucracy stymies study

Unlike any other medication, medical marijuana is typically smoked, invoking intense concern in a profession sensitized to the health consequences of exposure to tobacco smoke. Moreover, users decide for themselves how much is the right amount, titrating their inhalation to their symptoms, thereby challenging a system premised on the prescriber—usually a physician—decreeing the amount and frequency of dosing based on approved standards derived from a series of FDA-ordained trials designed to establish that the benefits of a proposed medication outweigh its risks. All of this occurs against the reality that cannabis is the most popular illicit drug in the United States.[12]

On its website, the National Institute of Drug Abuse (NIDA) contends disingenuously that research-grade cannabis is readily available for legitimate research.[13] The definition of what NIDA considers "legitimate" notwithstanding, the process for gaining research approval is cumbersome at best, more byzantine than Byzantium at worst—a complexity that is the direct result of cannabis' Schedule I status. For starters, to do clinical research using cannabis, a would-be investigator must gain the approval of not one but two federal agencies: the Drug Enforcement Administration (DEA) for issuance of a license and the FDA for approval of a protocol authorizing use as an Investigational New Drug. The researcher would then have to petition a third agency, NIDA, for the right to use the only federally acceptable research-grade botanical cannabis, a strain from the 1970s grown to order on a farm under the auspices of the University of Mississippi.

The petition could then only go forward when one of two other agencies has authorized the planned research. The three-stage NIH process would include not only peer-review but also subsequent review by both the NIH National Advisory Council and NIDA's director "who makes the final decision on the merit of an application … based on peer review, public health significance, and institution priorities." The other route involves a Department of Health and Human Services review that would deem whether or not the proposal has scientific

validity. Only after endorsement by at least four agencies with multiple independent reviews—any one of which could jettison the proposal—could research proceed.[14]

This entire process is laid out on NIDA's website, which makes no bones about its primary and overarching commitment to pursuing "the science of drug abuse and addiction."[13] In a list of the types of cannabis research it funds as part of its mandate, only one of nine items alludes to "potential therapeutic uses of THC and other cannabinoids in treatment of pain, HIV and addiction."[13] All the others relate to the study of some aspect of addiction, whether it be the effects of marijuana use on the developing brain, patterns of use in adolescents, screening for abuse, treating abuse or exploring the public health implications of medical marijuana-related legislation.[13]

Although one brief paragraph acknowledges potential applications of CBD in schizophrenia treatment, the website mainly supports the case for why medical marijuana is not legitimately medical and paints a grim picture of THC "artificially disrupting function of natural cannabinoids."[13] Couple all of this with the reality that there is little financial incentive for pharmaceutical companies to launch multimillion-dollar studies on a ubiquitous plant rather than a proprietary agent—if it were even legal to do so—and it becomes clear that a would-be investigator would have to make (ahem) a federal case to get a study launched.[13]

Legal yet illegal

The states that have legalized medical marijuana have essentially gone rogue in defiance of federal constraints. As Seamon explains, both federal and state governments have implemented laws to regulate marijuana use. In the United States, when federal and state laws are in disagreement, the federal statute trumps the state statute.[8] With the federal government having declared cannabis illegal, no matter what protocols and safeguards individual states implement to govern the practices of the physicians they license, practitioners who prescribe medical marijuana violate federal law and run the risk of losing their DEA license or facing criminal prosecution.[2] Federal facilities such as those run by the Veterans Administration do not permit medical marijuana use, and state proposals to make hospitals that receive federal funding into medical marijuana dispensaries are fraught with risk for the hospitals.

Although a federal appeals court did rule in 2000 that forbidding physicians from recommending medical marijuana violated their right to free speech,[15] the federal courts have otherwise "not directly addressed the conflict between the CSA and state medical marijuana laws."[8] With states proceeding as if their laws are legitimate and the federal government erratically enforcing its own statutes outlawing cannabis use for any purpose, patients and health care providers are left with no clear guidance.[8]

A way out of the debacle

With the federal government essentially disregarding decades of bench research begging for clinical application and with states ignoring their obligations to the orderly rule of law, there is no readily apparent way out of the current medical marijuana debacle. Even though as recently as June 2011 the DEA refused to reschedule marijuana, reiterating its decades-long position that scientific or medical evidence is lacking to justify such a move,[2] the only logical exit is a rescheduling of cannabis to Schedule II. If this were to happen, precedent would *not* be set. Heroin, an opiate, is on Schedule I; opiates routinely used in medical treatment of pain and arguably more dangerous than medical marijuana are Schedule II and III. Methamphetamine is Schedule I, while amphetamines—a mainstay of ADHD treatment—are Schedule II. Indeed, precedent would not even be set by having legal cannabinoid-based substances. Dronabinol (Marinol), oral synthetic THC, and nabilone (Cesamet), an oral synthetic THC analog, have been FDA-approved since 1985 and are used for treating cancer pain and anorexia induced by chronic illness.[1]

By rescheduling cannabis, the past and the future could be reconciled. Schedule II status would facilitate development of additional cannabinoid-derived medications with novel formulations and delivery strategies to improve efficacy and minimize side effects. Research could go forward with the goal of deriving cannabis-based pharmaceuticals that would in all likelihood render medical marijuana in its current crude, smoked-form obsolete. **MM**

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REFERENCES

1. Bostwick JM. Blurred boundaries: the therapeutics and politics of medical marijuana. Mayo Clin Proc. 2012;87(2):172-86.

2. Marcoux RM, Larrat EP, Vogenberg FR. Medical marijuana and related legal aspects. PT. 2013;38(10):612-9.

3. Baker D, Pryce G, Giovannoni G, Thompson AJ. The therapeutic potential of cannabis. Lancet Neurol. 2003;2(5):291-8.

4. Carter GT, Ugalde V. Medical marijuana: emerging applications for the management of neurologic disorders. Phys Med Rehabil Clin. N Am. 2004;15(4):943-54.

5. Grant I, Atkinson JH, Gouaux B, Wilsey B. Medical marijuana: clearing away the smoke. Open Neurol J. 2012;6:18-25.

6. Piomelli D, Giuffrida A, Calignano A, Rodriguez de Fonseca F. The endocannabinoid system as a target for therapeutic drugs. Trends in Pharmacol Sci. 2000;21(6):218-24.

7. DuPont RL. The Selfish Brain: Learning from Addiction. Center City, MN; Hazelden; 2000.

8. Seamon MJ. The legal status of medical marijuana. Ann Pharmacother. 2006;40(12):2211-5.

9. Bostwick JM, Reisfield GM, DuPont RL. Clinical decisions. Medicinal use of marijuana. N Engl J Med. 2013;368(9):866-8.

10. Pavlopoulos S, Thakur GA, Nikas SP, Makriyannis A. Cannabinoid receptors as therapeutic targets. Current Pharmaceutical Design 2006;12:1751-1769.

11. Grotenhermen F. Cannabinoids. Curr Drug Targets CNS Neurol Disord. 2005;4(5):507-30.

12. Cerda M, Wall M, Keyes KM, Galea S, Hasin D. Medical marijuana laws in 50 states: investigating the relationship between state legalization of medical marijuana and marijuana use, abuse, and dependence. Drug and Alcohol Dependence. 2012;120(1-3):22-7.

13. National Institute on Drug Abuse. Available at: www.drugabuse.gov/marijuana-research-nida. Accessed March 1, 2014.

14. Ferro S. Why it's so hard for scientists to study medical marijuana. Popular Science. April 18, 2013. Available at: www.popsci.com/science/article/2013-04/why-its-so-hard-scientists-study-pot. Accessed March 1, 2014.

15. Summary of class action challenging lawfulness of the federal government's policy to punish physicians who "recommend" marijuana to patients. Available at: https://www.wamm.org/conant-v-mccaffrey.pdf

WHY WE NEED TO LEGALIZE MEDICAL MARIJUANA

One more potential therapy

BY JACOB MIRMAN, M.D.

I am a primary care internist. I am a not a politician, a law enforcement officer or a medical policy expert. Yet I feel I have a valid view that should be considered in the debate over whether to legalize medical marijuana. Although the bill being considered by the Minnesota Legislature this year may need to be adjusted to satisfy all concerns, I hope it eventually passes. Here's why.

Patients come to me because they need help. I agree to see them and do my best to help them. I get paid for it. The buck stops with me. If I send a patient to a specialist and he or she is unable to help, the patient comes back to me and their medical care is again my responsibility. This is the contract I work under.

When standard approaches do not help the patient, my responsibility as their physician does not end. I have to become creative and look outside of standard practices. I have to continue learning and looking for new methodologies. In our integrative medicine clinic, we have done that and added a number of modalities including homeopathy, acupuncture, supplements, herbs and low-level laser therapy, all of which are done by qualified specialists. This enables us to help many more patients than we could with conventional approaches alone. Yet some people are still not helped. So we have to continue looking.

I see marijuana as one more potential complementary therapy. We can help a vast majority of our patients with other methods, but for some, marijuana may be the only thing that works. Those patients will come to you and say: "Doctor, I don't know how to put it, but I have to smoke pot to feel better. My specialists have already tried everything else and nothing works." Then they add, "I know it's illegal, so don't put this in the notes, please."

I've had two such cases. One was a patient with end-stage breast cancer and the other a patient with severe MS. I couldn't help either of them with the modalities we have, nor could their specialists. These patients found their own way to get relief, albeit an illegal one. In cases such as these, the law does not make sense. It interferes with my contract with the patient, and it forces me to do something that I feel is unethical (suggest they stop the sole effective therapy) or potentially illegal (suggest they break the law in order to obtain relief).

Some patients don't know marijuana might be an effective therapy. I, on the other hand, know about it but can't suggest it. The law prevents me from treating those patients the best way I know how. You may argue that marijuana can be misused. It can. But so can amphetamines, opioids, benzodiazepines, Tylenol and every other drug we prescribe or patients buy over the counter. Would you deny a patient Tylenol for their headache because some people use it to commit suicide? Sure, it's an extreme example, but misuse of drugs happens every day.

Prescribing is always a matter of judgment. If we physicians feel a patient may be suicidal, we should be careful about suggesting they take Tylenol. Similarly, if I suspected a patient was asking for marijuana for reasons other than what they claimed, I wouldn't recommend it. But if in my judgment the benefits outweighed the risks in a particular case, I would want to be able to recommend this treatment—just as I would any other medication.

A few more people will misuse marijuana if it becomes legal and, therefore, more available. Sorry, but this is not my responsibility. My contract is only with my patient.

If law enforcement wants to create more fail-safes for keeping it out of the hands of those who may want it for nonmedical purposes, I'll be happy. Driving under the influence is illegal, and I'll tell my patient not to do that, just as I do when I prescribe other mind-altering drugs.

Those who oppose legalization of medical marijuana cite a number of reasons for their argument: not enough research on the effects of smoke inhalation, the side effects, the abuse potential, the theoretical concern about the multitude of alkaloids in the whole plant that we don't know much about, etc., etc., etc. None of their concerns strike me as any more worrisome than those associated with other treatments we use all the time. Many of our treatments have side effects and the potential for abuse. We deal with those issues, and not by making the treatments illegal.

The law needs to be changed so doctors can do what they do best. **MM**

Jacob Mirman is a primary care internist and classical homeopath. He is medical director of Life Medical, an integrative medicine clinic in St. Louis Park.

WHY WE NEED TO BE CAUTIOUS ABOUT MEDICAL MARIJUANA

Reefer sadness

BY CAROL FALKOWSKI

Marijuana smoke is blanketing the United States. Medical marijuana dispensaries outnumber coffee shops in some communities. And no matter where you go, there's no escaping the debate over whether the drug should be legalized for medical or recreational purposes.

Thus far, 20 states and the District of Columbia have passed laws allowing medical use of marijuana. An additional 15, including Minnesota, are considering medical marijuana legislation. Voters in Colorado and Washington recently legalized recreational marijuana use, and Oregon and Alaska may also have full legalization measures on the ballot soon.

Faced with the daily barrage of marijuana chatter, I find myself rehashing the most salient issues, listening to multiple perspectives and wondering what the key tipping points will be in this historic, escalating conversation.

Growing use, addiction

More people than ever are using marijuana. According to the 2012 National Survey on Drug Use and Health, more than 111 million people in the United States age 12 and older have used marijuana at least once in their lifetime, and 31.5 million have done so in the past year. In 2012, an estimated 18.8 million people (7.3 percent of the population) used marijuana in the past month, compared with 14.6 million (6.2 percent) in 2003.[1]

Although most people who use the drug will not develop an addiction to it, marijuana is addictive. It is estimated that 9 percent of people who use marijuana will become dependent on it.[2] That number goes up when you talk about those who begin using it at a young age. About one in six who start using marijuana in their teens and 25 to 50 percent of daily users do become addicted.[3,4] The earlier the age of onset of use, the more likely the development of addiction.

Roughly 18 percent of people age 12 and older who entered drug abuse treatment programs in this country in 2009 reported marijuana as their primary drug of abuse.[5] Among those age 14 years of age and younger, 61 percent indicated marijuana was their primary drug of abuse.[5]

Adolescents most affected

Marijuana use among adolescents is increasing, according to the 2013 Monitoring the Future Study, a national study that tracks substance abuse among high school students in the United States. In 2013, 12.7 percent of 8th graders reported using marijuana in the past year, compared with 11.4 percent in 2012. Among 10th graders, 29.8 percent reported marijuana use in the past year, compared with 28 percent in 2012.[6] And 22.7 percent of 12th graders reported marijuana use in past month, 36.4 percent in the past year, and 45 percent at least once in their lifetime.

The survey also found that more kids now use marijuana than smoke cigarettes. Among 12th graders, 16 percent reported smoking cigarettes in the past month, compared with 22.7 percent who said they used marijuana.[6]

Marijuana was reported as "fairly easy" or "very easy" to get by 81.4 percent of 12th graders and by 39.1 percent of 8th graders. Moreover, of the marijuana-using 12th graders in states that allow medical marijuana, one-third reported obtaining it through someone who was authorized to get medical marijuana. Six percent had their own marijuana authorization. It appears as if medical marijuana is another access channel for teens.[6]

Moreover, the perceived risk of using marijuana is declining among students at all grade levels. From 2005 to 2013, the percentage of students who report being at "great risk" as a result of regular marijuana use has fallen from 74 percent to 61 percent among 8th graders, from 66 percent to 47 percent among 10th graders and from 58 percent to 40 percent among 12th graders. Repeated analysis of these data has demonstrated that when the perception of risk falls, marijuana use rises.[7]

Some proponents of legalizing medical marijuana argue that it would be kept out of the hands of youths because access to it would be regulated in the same way access to alcohol is. Yet in spite of the drinking age being 21, 68.2 percent of high school seniors say they have tried alcohol at least once.[6] Clearly, efforts to regulate alcohol access aren't as effective as they should be.

Science has shown that marijuana use has pronounced effects on the developing brains of adolescents. This is of particular significance inasmuch as the areas of the brain most affected by marijuana (cognition, memory and learning) are the same areas of the brain required to help them successfully transition to adulthood.

A recent longitudinal study found that regular marijuana use starting during the teen years and continuing into adulthood was associated with a drop in IQ.[8] Researchers administered IQ tests to more than 1,000 individuals at age 13

and assessed their patterns of cannabis use at several points as they aged. Subjects were again tested for IQ at age 38, and the two scores were compared. Those who used cannabis heavily in their teens and continued through adulthood showed a significant drop in IQ—an average of eight points for those who met criteria for cannabis dependence. Those who started using marijuana regularly or heavily after age 18 showed minor declines, and those who never used marijuana showed no declines.

Modest medicinal effects

The last major comprehensive review of the scientific literature related to marijuana was the Institute of Medicine report, *Marijuana and Medicine: Assessing the Science Base*, which was first published in 1999 and updated in 2003.[9] It reviewed the potential health benefits and risks of marijuana and its constituent cannabinoids, assessed findings and included testimony from experts in multiple disciplines. The report concluded that further research on cannabinoid drugs and safe delivery systems was warranted. Wrote co-principal investigator John Benson Jr., M.D., dean and professor of medicine emeritus at the Oregon Health Sciences University School of Medicine: "Marijuana's medical effects are generally modest, and for most symptoms there are more effective medicines already available on the market."[10]

In 1999, dronabinol (Marinol) and nabilone (Cesamet) were the only FDA-approved, marijuana-based medications. Today, nabiximols (Sativex), a chemically pure mixture of plant-derived THC and cannabidiol that is formulated as a mouth spray, is approved for the relief of cancer-associated pain and spasticity and neuropathic pain in multiple sclerosis in the United Kingdom, Canada and other countries. It is currently in Phase 3 clinical trials for cancer pain in the United States.

The National Institute on Drug Abuse summarizes the medicinal argument as follows: "Many have called for the legalization of marijuana to treat conditions including pain and nausea caused by HIV/AIDS, cancer and other conditions, but clinical evidence has not shown that the therapeutic benefits of the marijuana plant outweigh its health risks. To be considered a legitimate medicine by the FDA, a substance must have well-defined and measurable ingredients that are consistent from one unit (such as a pill or injection) to the next. As the marijuana plant contains hundreds of chemical compounds that may have different effects and that vary from plant to plant, and because the plant is typically smoked, its use as a medicine is difficult to evaluate."[11]

Reasons for recommendations

In the 20 states in which medical marijuana is dispensed, there are variations in state law and dispensary specifications. Yet according to a summary by the White House Office of National Drug Control Policy, most people who receive marijuana as medicine—in states that allow it—do not suffer from chronic, life-threatening diseases.[12] Ninety-four percent of medical marijuana dispensary users in Colorado reported getting marijuana for severe pain. Only 3 percent received it for cancer and 1 percent for HIV/AIDS.[13] Yet it is this very argument—to reduce the pain and suffering of the very ill with these conditions—that is often advanced to get medical marijuana legislation passed in the first place. Once distraught but now grateful parents tell policymakers they had tried everything for their severely ill children with no success, until they administered marijuana. Personal accounts of others describe marijuana's remarkable effectiveness in relieving their symptoms of certain medical conditions. I have no reason not to believe them. Whether they tried the already available prescription drugs containing marijuana constituents is often unclear.

I am a staunch defender of the rigorous process of drug approval in this country that exists to help ensure that drugs marketed are safe and effective. During my tenure on the Food and Drug Administration's Drug Abuse Advisory Committee, we reviewed the scientific evidence on newly developed drugs and made recommendations regarding their safety, efficacy, abuse potential, approval and labeling. In spite of the limitations of that process and the extra steps one must take in order to conduct research with a Schedule I drug, which marijuana is, I believe that our country's over-the-counter and prescription medications are safer because of it.

The economic cost

Many people assume that if the government simply collects enough tax revenue from marijuana sales it will offset the societal costs of marijuana abuse. Based on our experience with alcohol, I believe nothing could be further from the truth. The Minnesota Department of Health estimates the annual costs associated with alcohol use in the state to be $5 billion—an amount 17 times greater than that collected in tax revenues from alcohol sales ($296 million).[14] The same pattern holds true nationally.

Clearly, the costs that stem from alcohol, our most widely used addictive and legal substance, are not offset by the amount collected in taxes from its sale. Alcohol is not a budget-neutral item. There is no reason to believe things would be much different with marijuana.

And so?

Despite these arguments, more people than ever support legalizing marijuana. In fact, according to the latest Gallup poll, 58 percent of Americans said they are in favor of it. This compares with only 12 percent when this poll was first administered in 1969.[15]

As I ponder the inevitable expanded use that would stem from legalizing marijuana for medical or recreational purposes, I fear the prospect of more broadly exposing young people to yet another addictive substance with known, sometimes long-term damaging effects. It seems inconsistent with protecting and promoting public health. I'm also curious as to why the government hasn't fast-tracked research on cannabinoid constituents and their development as medications, just as it fast-tracked AIDS research in the 1990s

in light of the widespread professional and public outcry to do so.

Because the issues associated with marijuana are complicated and the implications far-reaching, voters and lawmakers need to proceed with caution. **MM**

Carol Falkowski is the former director of the Minnesota state drug and alcohol abuse agency, and former director of research communications at Hazelden. She is part of a 20-member nationwide drug abuse epidemiology network of the National Institute on Drug Abuse and author of the book *Dangerous Drugs: An Easy-to-Use Reference for Parents and Professionals.*

REFERENCES

1. Substance Abuse and Mental Health Services Administration. Results from the 2012 National Survey on Drug Use and Health: Summary of National Findings, NSDUH Series H-46, HHS Publication No. (SMA) 13-4795. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2013. Available at: www.samhsa.gov/data/NSDUH/2012SummNatFindDetTables/Index.aspx. Accessed March 12, 2014.

2. Anthony J, Warner LA, Kessler RC. Comparative epidemiology of dependence on tobacco, alcohol, controlled substances, and inhalants: basic findings from the National Comorbidity Survey. Exp Clin Psychopharmacol. 1994; 2(3):244-68.

3. Hall W, Degenhardt L. Adverse health effects of non-medical cannabis use. Lancet. 2009;374(9698):1383-91.

4. Hall W. The adverse health effects of cannabis use: what are they, and what are their implications for policy? Int J Drug Policy. 2009;20(6):458-66.

5. Department of Health and Human Services. Substance Abuse and Mental Health Services Administration. Office of Applied Studies. Treatment Episode Data Set (TEDS) 1997-2007. National Admissions to Substance Abuse Treatment Services. Office of Applied Studies, DASIS Series: S-45, DHHS Publication No. SMA 09–4360, Rockville, MD, 2009. Available at: www.samhsa.gov/data/DASIS/TEDS2k7AWeb/TEDS2k7AWeb.pdf. Accessed March 12, 2014.

6. Johnston LD, O'Malley PM, Bachman JG, Miech RA, Schulenberg JE. Monitoring the Future: National Results on Drug Use, 2013 Overview. Available at: www.monitoringthefuture.org//pubs/monographs/mtf-overview2013.pdf. Accessed March 12, 2014.

7. Falkowski CL. Dangerous Drugs: An Easy-to-Use Reference for Parents and Professionals. Hazelden Publishing, 2000 and 2003 (2nd edition).

8. Meier MH, Caspi A, Ambler A, et al. Persistent cannabis users show neuropsychological decline from childhood to midlife. Proc Natl Acad Sci USA. 2012;109(40):E2657-64. Available at: www.ncbi.nlm.nih.gov/pmc/articles/PMC3479587/. Accessed March 12, 2014.

9. Joy JE, Watson SJ Jr., Benson JA Jr. (eds). Marijuana and Medicine: Assessing the Science Base. Washington, DC: National Academy Press, Division of Neuroscience and Behavioral Health, Institute of Medicine, 1999. Available at: www.nap.edu/openbook.php?record_id=6376. Accessed March 12, 2014.

10. Marijuana's Components Have Potential as Medicine: Clinical Trials, Drug Development Should Proceed. News from the National Academies. March 17, 1999. Available at: www8.nationalacademies.org/onpinews/newsitem.aspx?RecordID=6376. Accessed March 12, 2014.

11. National Institute on Drug Abuse. Drug Facts: Marijuana. January 2014. Available at: www.drugabuse.gov/publications/drugfacts/marijuana. Accessed March 12, 2014.

12. White House Office of National Drug Control Policy. Medical Marijuana Information. Available at: www.whitehouse.gov/sites/default/files/ondcp/issues-content/medical_marijuana_information_packet.pdf. Accessed March 12, 2014.

13. Colorado Department of Health. Medical Marijuana Statistics. Available at: www.colorado.gov/cs/Satellite/CDPHE-CHEIS/CBON/1251593017044. Accessed March 12, 2014.

14. Minnesota Department of Health. The Human and Economic Cost of Alcohol in Minnesota. March 2011. Available at: www.health.state.mn.us/cdrr/alcohol/alcpdf/HumanandEconomicCostofAlcoholUseinMinnesota.pdf. Accessed March 12, 2014.

15. Swift A. For First Time, Americans Favor Legalizing Marijuana: support surged 10 percentage points in past year, to 58%. Gallup Politics. October 22, 2013. Available at: www.gallup.com/poll/165539/first-time-americans-favor-legalizing-marijuana.aspx. Accessed March 12, 2014.

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WHY THE MEDICAL COMMUNITY NEEDS TO BE EDUCATED

Medical marijuana—are we ready?

BY CHARLES REZNIKOFF, M.D.

Medical marijuana is being pushed on the medical community by popular demand, as all 20 of the states (plus the District of Columbia) that allow its use have approved it through constitutional amendments or legislative action. This is unusual in the world of medicine. I worry that in our haste to make marijuana available in Minnesota as a potential therapy, we are bypassing the normal avenues by which new medications are approved and endorsed. Doctors, I believe, are not ready to take on the responsibility of recommending marijuana. And worse, the medical references and guidelines we normally turn to for information are absent.

To better understand how others in the medical community feel about Minnesota's proposed medical marijuana legislation, I conducted an email survey of physicians in the psychiatry and internal medicine departments at Hennepin County Medicine Center, where I work as an addiction medicine specialist. I asked three yes-or-no questions and invited comments. (I assured respondents that their answers would remain anonymous.) Within seven days, I received 117 responses (approximately 50 percent of those who received the email answered the questions) and 45 comments.

The questions and answers

The first question I asked was: "Are you familiar with the specifics of Minnesota's medical marijuana bill (ie, how the marijuana would be grown, distributed, prescribed and regulated)?" Only four of 117 respondents answered this question affirmatively. I answered no. In fact, before writing this article, I opposed the bill without understanding its content. I assumed that it would be analogous to those passed in other states. (California's medical marijuana law was written very loosely such that the production and distribution of the drug is poorly regulated; Colorado's has much more tightly controlled production of marijuana. In both states, the indications for medical marijuana use are broad to the point of being nonspecific.) At the time of this writing, Minnesota's bill was undergoing revision in various legislative committees. The revision process is yet another barrier to physicians understanding the proposed law.

The second question was: "Are you prepared to weigh the risks and benefits of marijuana use with your patients, if they wished to seek medical marijuana?" Thirteen respondents said "yes" and the remaining 114 answered "no." This is consistent with my experience as one who teaches medical students and residents about marijuana use. Nearly 40 percent of adults have used marijuana,[1] yet most doctors cannot explain its health risks and benefits. It is not necessary for all doctors to understand all diseases and their treatments, of course. Many important treatments (chemotherapy for cancer, antiretrovirals for HIV, for example) are prescribed only by a group of trained subspecialists. Medical marijuana could follow this model, if a subset of doctors developed a medical marijuana practice. However, I worry that this will attract unprofessional or untrained prescribers.

Many primary care doctors worry that their practices will be overrun with requests for the drug. And they are correct to worry: The indications for medical marijuana include some that are typically treated in the primary care setting.

I am concerned about the lack of resources available to help doctors learn about marijuana. There is no standardized curriculum for medical marijuana prescribing and to my knowledge, there is no established community standard. The states in which medical marijuana is legal do not provide resources or funding to educate or regulate marijuana providers. The authors of the laws in those states either assume we already know how to prescribe marijuana or that we will figure it out on our own. This lack of education poses a serious problem for the safe use of medical marijuana.

The third question was: "Do you support Minnesota passing a medical marijuana law as you currently understand it?" Fifty-eight respondents said "no," 32 said "yes," and 26 refused to answer the question. If my survey is any indication, the percentage of doctors opposing medical marijuana is greater than that of the general public.[2] Although the first two questions may have biased doctors in answering the third question (by pointing out their ignorance about Minnesota's medical marijuana legislation), 91 of 117 respondents still felt comfortable answering the question. Many who said they disapproved of the law explicitly stated in their comments that they did so because they lacked knowledge. The four respondents who said they understood the bill also said they supported it. Seven of 13 who said they felt knowledgeable about marijuana supported the bill. I applaud the 26 respondents who abstained from answering on the basis of their ignorance. I personally have opposed having medical marijuana in Minnesota all along; after learning more about the bill under consideration, I realized that my initial opinion was not informed but instead based on my own biases.

Subverting the process

Public health officials indicate that the perceived risk of using marijuana has fallen and that the social acceptability of marijuana has risen, resulting in increased experimentation by adolescents.[3] This is not without risk for harm: Marijuana use affects adolescents' neurocognitive development, mental health and ability to drive safely. The rebranding of marijuana as a medicine may be causing this change in social perception. More worrisome, the pathway taken to legalizing medical marijuana in states may change how the public views treating disease, maintaining health and approving new medicines. The question at stake is not solely about the value of marijuana as a medicine but about the process by which all medicines are introduced to the public.

I believe marijuana is not a good medicine, but neither is it a terrible poison. Yet I oppose medical marijuana strongly on the grounds that it subverts our normal processes of medicine in a way that will have repercussions going forward. I believe that medical marijuana will corrode the doctor-patient relationship. My survey shows that many in the medical community are largely uneducated about the risks and benefits of marijuana, and the indications for which it might be appropriate under the law. Doctors have been passive both about educating themselves and participating in the medical marijuana debate. I suggest most of us will conclude the answer to the question of whether we're ready for medical marijuana in Minnesota is: Not yet. **MM**

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REFERENCES

1. Saad L. In U.S., 38% Have Tried Marijuana, Little Changed Since '80s. Available at: http://www.gallup.com/poll/163835/tried-marijuana-little-changed-80s.aspx. Accessed March 19, 2014.

2. Brooks J. Minnesota Poll: Majority support legalization of medical marijuana. Available at: http://www.startribune.com/politics/statelocal/245910931.html. Accessed March 19, 2014.

3. Monitoring the Future: A continuting study of American youth. Available at: www.monitoringthefuture.org. Accessed March 19, 2014.

Comments from the survey

On our lack of knowledge

"Although I think medical marijuana can be a benefit to some patients and should be available in Minnesota, I do not know enough about the specifics of the law, and especially about who would be able to prescribe it, to say I support or do not support passing the law."

"We have no education (from medical school through residency) on when or how to prescribe medical marijuana. If studies are out there showing efficacy for specific diseases, then that would be enlightening."

"I expect we would get a lot of questions from our patients. I don't feel prepared enough."

On relieving suffering

"I support it, I guess, as long as it is restricted to certain indications and patient populations."

"If I had a terminal cancer with pain that did not respond to standard therapies, I would want the option to use it."

"There are clear benefits for chronic pain management, severe nausea, in cachectic patients as an appetite stimulant, in end-stage HIV patients and in cancer patients with pain."

"Using marijuana to ease pain and anxiety seems less harmful than benzodiazepines or opioids."

Practical considerations

"I predict 25 percent of my patients (anyone who thinks they have PTSD) will ask me for it and I will have to decline. I will just say it is not a part of my practice because they can't argue with that. … I have seen so many patients where I feel marijuana triggered or worsened their symptoms."

"I am concerned about the interface of police and medical marijuana; for example, if a patient legally prescribed medical marijuana is arrested for disorderly conduct or reckless driving and is found to have marijuana in their system, what is the responsibility/liability of the medical community?"

"Will marijuana be covered by insurance? Seems like it should be if marijuana is an effective treatment."

"I would hope that providers could opt out of prescribing medical marijuana."

On the experience of other states

"I just moved back from Colorado last year after practicing there for several years and having been exposed to the legality there. I am all for passing the law here. Some people do benefit from it (even if it's just perceived benefit), especially chemo patients."

"My own feeling about this is jaded by the experience of my niece and nephew in California. Both had medical marijuana cards issued in high school. My nephew had a sports injury with knee pain. My niece had headaches, diagnosed as migraines, but only missed about one or two days of school a year…. There was clearly a little recreational diversion at times, including at a family wedding in Minnesota."

"It seems like many of the medical laws are abused, so I would favor just legalizing it like Colorado or Washington, or decriminalizing (pay a fine like parking ticket) it in preference to medical marijuana."

"I am from Montana originally, and my observation of how Montana fared when it legalized medical marijuana is that it was basically a disaster. Most doctors did not feel comfortable prescribing, and those who did held day-long clinics in hotel meeting rooms and handed out a 'green card' every five minutes. Hundreds of people per day received prescriptions—mostly 20 and 30 year old ski bums and snowboarders with 'back pain.'"

"I used to live in San Francisco, where many people I knew got 'pot cards' for migraines or back pain or other nonspecific ailments."

Medical marijuana—coming soon to a medicine cabinet near you?

Where the nation stands in terms of legalizing medical cannabis.

BY JULIANA MILHOFER, J.D.

The opinions on medical marijuana are as diverse as the legislative battles that have ensued over allowing for its use have been divisive. For physicians, the debate can be particularly nuanced. Those who oppose its use cite research showing the negative effects of smoking marijuana on the lungs, brain, heart and immune system.[1] Others note the lack of research on how marijuana can provide medical benefit and the fact that the studies that have been done are not controlled clinical trials to assess its effectiveness and safety. Yet others are concerned that medical marijuana may be a "gateway" drug that could lead to use of other illicit drugs such as cocaine and heroin. On the other side are those whose patients suffer from severe pain or seizures and don't find relief from conventional remedies, or who are at the end of life and seek relief from their discomfort. Physicians who treat those patients argue that allowing them to use medical marijuana is the compassionate thing to do.

The fact that we already have drugs derived from the cannabis plant has prompted some to ask whether medical marijuana needs to be legalized. Dronabinol (Marinol), a synthetic tetrahydrocannabinol (more commonly known as THC),[2] was approved by the U.S. Food and Drug Administration (FDA) in 1985 to treat nausea and vomiting in patients undergoing chemotherapy.[3] In 1992, the FDA gave approval for its use in treating loss of appetite for persons with AIDS. Nabilone (Cesamet), a synthetic analog of THC,[2] was approved in 1985 as an antiemetic but did not actually become available until 2006.

Despite the lingering debate and despite the fact that the U.S. Drug Enforcement Administration (DEA) still categorizes marijuana as a Schedule I drug, meaning it has "no currently accepted medical use and a high potential for abuse,"[4] state legislatures across the country have moved ahead and passed laws related to medical and recreational marijuana use. This article briefly describes where the country stands in terms of legalizing medical marijuana. It also outlines legislation that is being considered in Minnesota.

Is the country turning green?

Currently, 20 states plus the District of Columbia have legalized medical marijuana. Two states, Colorado and Washington, have also legalized marijuana for recreational use. Fifteen others including Minnesota are considering whether they should make medical marijuana legal.[5]

Of the states that have legalized medical marijuana, most of their laws address: 1) whether home cultivation is allowed; 2) the role of caregivers (eg, how many patients they can assist at a time and whether they themselves can cultivate plants); 3) how much marijuana or how many plants a patient can possess; 4) whether dispensaries are allowed within the state; 5) what conditions would qualify a patient for medical marijuana use; 6) whether patients are issued identification cards; and 7) whether the state will recognize patients possessing out-of-state identification cards.[6]

Here's a look at what some of those states have done.

California

On November 5, 1996, California became the first state to legalize medical marijuana.[7] The law allowed for physicians to "recommend" medical marijuana use for certain patients; for development of a "medical marijuana identification card" for those patients; and for creation of an online registry and verification system.

Many have argued that California's law is too broad. When it passed in 1996, physicians were permitted to recommend medical marijuana not only for serious medical issues such as cancer, anorexia, AIDS, chronic pain, spasticity, glaucoma, arthritis and migraines,[7] but also "for any other illness for which marijuana provides relief"[8] such as depression and anxiety. Other states have learned from California's experience and have made the list of qualifying conditions for medical marijuana more limited.

Arizona
In 1996, Arizona passed a ballot initiative allowing physicians to write a "prescription" for marijuana.[9] That initiative was subsequently invalidated because of marijuana's Schedule I designation. (The federal government prohibits "prescription" of Schedule I drugs.) In 2010, the state went on to pass a law creating a program in which physicians can "recommend" medical marijuana or "refer" patients to state-approved dispensaries.

Colorado and Washington
Colorado and Washington are the only two states that have legalized both the medical and recreational use of marijuana.

In November 1998, when Washington voters legalized medical marijuana, they removed the state-level criminal penalties attached to its use, possession and cultivation by patients who had valid documentation from their physician.[10]

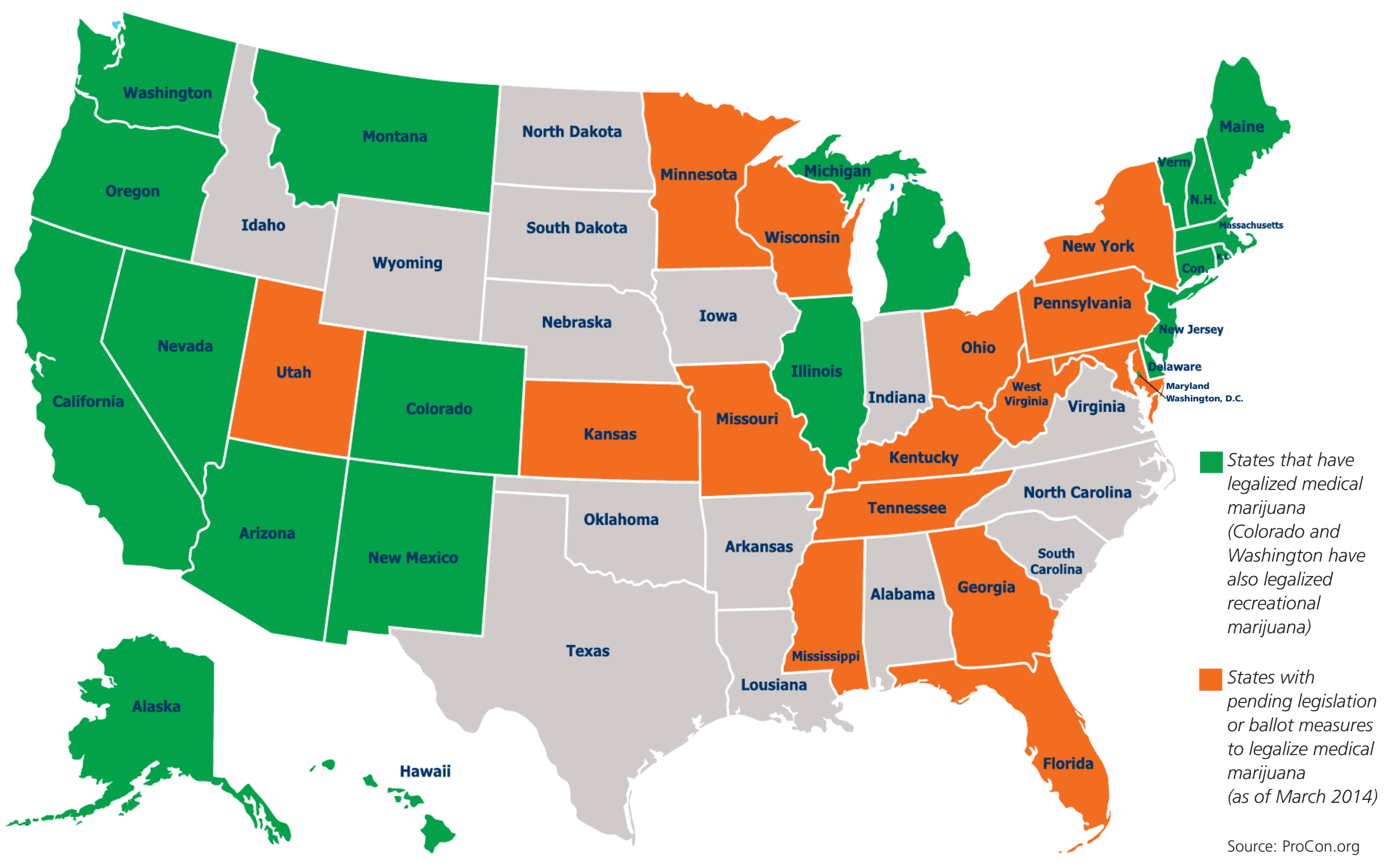
In Colorado, voters legalized medical marijuana in November 2000 through a constitutional amendment that authorized the possession, cultivation and use of medical marijuana by patients and their caregivers.[11] In 2010, Colorado saw the passage of its second medical marijuana law, which created a dual-licensing scheme to regulate medical marijuana businesses at the state and local level.[11]

In November 2012, voters in both states legalized the production, sale and use of recreational marijuana.

New York
In January 2014, the governor of New York issued a directive that would allow 20 hospitals in the state to dispense medical marijuana to patients who have been certified by a doctor as having certain conditions including cancer, glaucoma, and others listed by the health department or who are in a "life-threatening or sense-threatening situation."[12,13] Unlike the other states that have legalized medical marijuana, New York is creating a limited research program. Through this program, New York's health department would establish guidelines and make decisions as to which hospitals can participate in the program.[14] Those hospitals would then be charged with deciding which patients would qualify for medical marijuana use. New York's Health Commissioner has noted that the research done in these hospitals would be used to help evaluate the effectiveness of marijuana as a treatment.[15] Unlike other states that rely on dispensaries for marijuana, the hospitals participating in New York's program will receive marijuana directly from the federal government.[15]

New York's proposed research program is already being criticized. Some argue that limiting the research to federally sourced marijuana is restrictive and not sufficient. Whether New York's program will be successful, and whether New York voters will

States with medical marijuana laws or pending legislation



Source: ProCon.org

push for the legalization of medical marijuana remains to be seen.

Maryland

Maryland allows medical marijuana to be used as a legal defense in drug-possession cases.[9] In May of 2013, Maryland's governor signed a law creating a hospital-based medical marijuana research program. Under this law, marijuana would only be provided through teaching hospitals, and these hospitals would have the option of having a program for patients. The research program is not scheduled to begin until at least 2015.[6]

Medical marijuana in Minnesota

In Minnesota, legislation that would have allowed for the limited use of medical marijuana by qualified patients was passed in 2009, only to be vetoed by Gov. Tim Pawlenty. In 2013, legislation was again introduced to allow medical marijuana to become an option for certain patients.

The legislation attempts to address some of the problems other states have encountered since legalizing medical marijuana. For example, one of the biggest criticisms of California's law is that it was vague in terms of conditions that qualified a patient to receive medical marijuana.

Minnesota's legislation defines a "qualifying patient" as one "who has been diagnosed by a practitioner as having a debilitating medical condition."[16,17] The list of such conditions is extensive and includes cancer, glaucoma, HIV/AIDS, hepatitis C, post-traumatic stress disorder, and a chronic or debilitating disease/medical condition or its treatment that produces wasting syndrome, severe nausea and seizures.[16,17] Minnesota's legislation allows for additional conditions to be approved by the Commissioner of Health. It also creates a patient registry. Patients would be required to register and pay a fee to be included in it. Patients would receive a registry card that would verify their status as a qualifying patient. The Minnesota Department of Health would be charged with licensing and regulating dispensaries.

The role of physicians is also outlined in the legislation. Practitioners would be required to perform a full physical examination of the patient and fully assess the patient's medical history and current medical condition. Documentation of this, along with a diagnosis, would be included in a written certification that would be signed and dated by the physician. The legislation would allow patients and their caregivers to possess up to 2.5 ounces of marijuana and authorize certain patients to cultivate up to six marijuana plants.

Advocates for the medical marijuana legislation hoped Minnesota lawmakers would approve the legislation this year. But that is not likely to happen. The challenge has been coming up with language that addresses the concerns of both supporters and opponents. In late March, Gov. Mark Dayton asked lawmakers to grant $2.2 million for clinical research into the drug's efficacy for some seizure disorders at Mayo Clinic. The governor also called for a larger study of the benefits, costs and risks associated with medical marijuana.

Conclusion

The legalization of medical marijuana will continue to dominate conversations at the Capitol, in doctors' offices and among the public. Which side of the debate Minnesota will land on remains to be seen, but one thing is certain: both physicians and patients are paying attention. MM

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REFERENCES

1. U.S. Drug Enforcement Administration. Exposing the Myth of Smoked Medical Marijuana- Marijuana: The Facts. Available at: http://csmbio.csm.jmu.edu/biology/renfromh/bio366/maryjane/dea.pdf. Accessed March 4, 2014.

2. U.S. Department of Justice. Pharmaceutical products already exist—they are called Marinol & Cesamet, Available at: www.justice.gov/dea/divisions/sea/in_focus/marinol-cessmet.pdf. Accessed March 3, 2014.

3. ProCon.org. What is Marinol? Available at: http://medicalmarijuana.procon.org/view.answers.php?questionID=000089. Accessed March 4, 2014.

4. U.S. Drug Enforcement Administration. Drug Schedules. Available at: www.justice.gov/dea/druginfo/ds.shtml. Accessed March 4, 2014.

5. ProCon.org. 15 States with Pending Legislation to Legalize Medical Marijuana http://medicalmarijuana.procon.org/view.resource.php?resourceID=002481

6. Marijuana Policy Project. Key Aspects of State and D.C. Medical Marijuana Laws. Available at: www.mpp.org/assets/pdfs/library/Medical-Marijuana-Grid.pdf. Accessed March 4, 2014.

7. California Department of Public Health. Medical Marijuana Program Frequently Asked Questions. Available at: www.cdph.ca.gov/programs/MMP/Pages/MMPFAQ.aspx#1. Accessed March 4, 2014.

8. Bostwick MJ. Blurred boundaries: the therapeutics and politics of medical marijuana. Mayo Clin Proc. 2012; 87(2): 172-86. Available at: www.mayoclinicproceedings.org/article/S0025-6196%2811%2900021-8/fulltext#sec9. Accessed March 4, 2014.

9. National Conference of State Legislatures. State Medical Marijuana Laws. Available at: www.ncsl.org/research/health/state-medical-marijuana-laws.aspx Accessed March 4, 2014.

10. NORML. Washington Medical Marijuana. Available at: http://norml.org/legal/item/washington-medical-marijuana?category_id=835 . Accessed March 4, 2014.

11. Sensible Colorado. History of Colorado's Medical Marijuana Laws. Available at: http://sensiblecolorado.org/history-of-co-medical-marijuana-laws/ Accessed March 4, 2014.

12. Adler M. New York's Medical Marijuana Experiment Begins with Caution. NPR. January 19, 2014. Available at: www.npr.org/2014/01/19/263904664/new-yorks-medical-marijuana-experiment-begins-with-caution. Accessed March 4, 2014.

13. CBS News. Gov. Cuomo Outlines Details of Medical Marijuana Plan. January 8, 2014. Available at: http://newyork.cbslocal.com/2014/01/08/gov-cuomo-expected-to-outline-details-of-medical-marijuana-plan/. Accessed March 4, 2014.

14. Sgueglia K, Botelho G. New York governor announces plan for medical marijuana at hospitals. CNN Health. January 9, 2014. Available at: www.cnn.com/2014/01/08/health/new-york-state-medical-marijuana/. Accessed March 4, 2014.

15. Associated Press. NY medical marijuana program expected to be running within a year, health commish says. Available at: www.syracuse.com/news/index.ssf/2014/02/ny_medical_marijuana_program_expected_to_be_running_within_a_year_health_commish.html. Accessed March 4, 2014.

16. House File 1818. Minnesota, 88th Legislature, House File 1818, Available at: www.revisor.mn.gov/bills/bill.php?f=HF1818&y=2013&ssn=0&b=house. Acessed March 21, 2014.

17. Senate File 1641. Minnesota, 88th Legislature, Senate File 1641, Available at: www.revisor.mn.gov/bills/bill.php?f=SF1641&y=2013&ssn=0&b=senate. Acessed March 21, 2014.

A Protocol for Addressing Acute Pain and Prescribing Opioids

BY HOWARD EPSTEIN, M.D., CARMEN HANSEN, B.S.N., AND DAVID THORSON, M.D.

Physicians across the country are re-examining their role in the prescription opioid abuse problem. In response to growing public awareness about the dangers of opioids, the Minnesota Medical Association formed a Prescription Opioid Management Advisory Task Force. As part of its work, the task force partnered with the Institute for Clinical Systems Improvement (ICSI) to develop a protocol for prescribing opioids for acute pain. This article describes the development of the new ICSI Acute Pain Assessment and Appropriate Opioid Prescribing Protocol and highlights key aspects of the protocol, which emphasizes shared decision-making and careful, conservative prescribing.

Many were shocked to learn of the recent heroin overdose death of actor Philip Seymour Hoffman, who after 20 years of sobriety again started abusing drugs. Another noteworthy actor, Heath Ledger, died in a similar incident six years earlier. According to the New York City medical examiner's office, Ledger died "as the result of acute intoxication by the combined effects of oxycodone, hydrocodone, diazepam, temazepam, alprazolam and doxylamine."[1]

The tragic reality is that for every Hoffman or Ledger, there are thousands of others, as the medical and recreational use of opioids has exploded over the last decade. Between 2001 and 2012, the number of prescriptions for opioids in the United States rose 33%, from 181.7 million to 240.9 million, and total sales of opioids rose 110%, from $3.97 billion to $8.34 billion.[2] Americans, who comprise 5% of the world's population, now consume 80% of the world's opioid supply.[3]

Although most people take prescription medications responsibly, an estimated 52 million (20% of those ages 12 years and older) have used prescription drugs for nonmedical reasons at least once in their lifetime.[4] Every day, 2,500 youths (ages 12 to 17 years) abuse a prescription pain reliever for the first time. The problem is evident in U.S. emergency rooms, where the number of cases related to nonheroin opioid abuse increased from 299,498 in 2004 to 885,348 in 2011.[2] It is also evident in addiction treatment facilities. Minnesota's own Hazelden saw the portion of patients treated for painkiller or heroin addiction rise from 15% in 2001 to 41% in 2011.[2]

Dilemma for Physicians

Physicians often find themselves feeling conflicted about opioids. They have both a desire and an ethical responsibility to relieve suffering. They know many patients' acute pain episodes can be appropriately managed with opioid therapy. However, they also know prescriptions for opioids written by well-meaning physicians like themselves have started many patients down the road to drug dependence. How does that happen?

Part of the problem is that physicians have relied on a thin evidence base regarding the use of opioids for pain. The literature supporting chronic opioid therapy for noncancer pain is very weak. In fact, some of the most vocal proponents now admit that their justification for prescribing opioids for this population was a small case series report suggesting that the use of opioids in this situation was safe and carried an addiction risk of <1%.[5]

From this, expert panels and specialty groups developed guidelines and position statements encouraging providers to take an aggressive stance and prescribe opioids for all pain. The Joint Commission promoted pain as the "fifth vital sign" in response to what was viewed as inadequate pain management in the past. As a result, in the last 20 years, we've seen a fourfold increase in opioid prescriptions in the United States.[4] And we underestimated the risks of opioids including abuse, misuse, addiction, diversion and unintentional overdose.

Health Community Takes Action

Late in 2012, in response to growing public awareness about the dangers of opioids, the Minnesota Medical Association (MMA) formed a group to assess what physicians could do about the problem in Minnesota. The Prescription Opioid Management Advisory Task Force began its work by identifying these four objectives:

1. Raise awareness among Minnesota physicians about the nature and extent of the problems associated with prescription opioid addiction, abuse and diversion
2. Examine specific strategies for improving physician management of opioid prescribing (eg, education, use of the Minnesota Prescription Monitoring Program, controlled-substance contracts)
3. Facilitate MMA participation in multidisciplinary, communitywide conversations/coalitions aimed at addressing prescription opioid addiction, abuse and diversion
4. Identify and disseminate resources and tools to physicians for opioid prescribing best practices.

To help achieve these objectives, the task force partnered with the Institute for Clinical Systems Improvement (ICSI), which produces evidence-based clinical guidelines and protocols. ICSI brought together a workgroup, whose members had expertise in pain management, addiction management, primary care, specialty care, emergency medicine, pharmacy, physical therapy, dentistry and hospital medicine (Table 1). Several MMA task force members were among them. The workgroup reviewed clinical evidence, best practices from specialty societies, the work of local and national experts, guidelines from other states and ICSI's own Chronic Pain Guideline.

Acknowledging that the process of assessing pain and appropriately prescribing opioids is complex, workgroup members decided they needed to identify certain values and drivers to guide their efforts. They took the following considerations into account during each step in the process:

- Patient safety. The group considered that opioids have known side effects and that those effects may be particularly adverse in patients with specific comorbid conditions. The workgroup also considered the potential for misuse, addiction and diversion. The group held that safe prescribing requires careful assessment of patient risk and history of opioid use from available sources including patient self-reports, medical records and a prescription-monitoring program.
- The need for supportive pain management. The group considered that patients expect their physician to help them determine the best course of treatment to manage their acute pain.
- Community safety and population health. The group acknowledged that easy access to opioids in the home and elsewhere may contribute to inappropriate use, addiction and related crime.
- Prevention of inappropriate or overuse of opioids. The group wanted the protocol to offer clinical guidance for the appropriate use of opioid and nonopioid therapies.
- Informed patients and shared decision-making. Members felt patients needed to be included in decision-making about opioid use and that they needed information about the risks and benefits of opioid use. The group felt this would support culture change over time and help reset patients' expectations of physicians and about opioid prescriptions.

After multiple revisions, a public comment period and final review by ICSI's Committee for Evidence Based Practice, the new Acute Pain Assessment and Opioid Prescribing Protocol was formally approved and published on the ICSI website in January 2014. It is available at www.icsi.org (search "acute pain protocol").

TABLE 1

Members of the Protocol Development Work Group

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Howard Epstein, M.D., FHM, ICSI
Justin Hora, Pharm.D., Allina Medical Clinic
Chris Johnson, M.D., Emergency Physicians, PA
Susan Van Pelt, M.D., Emergency Physicians, PA
Faris Keeling, M.D., Essentia Health
Anne Kokayeff, M.D., Fairview Health Services
Bret Haake, M.D., HealthPartners Medical Group and Regions Hospital
Mary Pat Noonan, Ph.D., ABPP, HealthPartners Medical Group
Charles Reznikoff, M.D., Hennepin County Medical Center
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Anne Trujillo, R.N., C.N.P., MAPS Medical Pain Clinic
Michael Hooten, M.D., Mayo Clinic
Erin Krebs, M.D., M.P.H., Minneapolis VA Health System
John Wainio, D.D.S., Minnesota Dental Association
Brian Nelson, M.D., Physicians Neck and Back Clinic
Paul Biewen, M.D., Twin Cities Orthopedics

The Protocol

The new protocol, summarized in Table 2, guides physicians through the following steps:

Target population

Patients must be adult (18 years of age and older) outpatients who do not have cancer but who have 1) acute or subacute pain, 2) chronic pain but are experiencing unrelated acute pain or 3) an acute exacerbation of chronic pain.

It is not intended to be used with patients who have active cancer and/or are receiving palliative or hospice care. Nor is it intended for patients with nontraumatic dental pain. Those patients should be referred to a dental provider and should never be prescribed opioids, as they may mask an abscess and thus increase the potential for adverse outcomes.

Assess the Patient's Pain

Physicians are to begin with a brief assessment of pain and administer emergent use of opioids if the situation dictates (ie, the patient is experiencing overwhelming pain). A more thorough assessment of pain that covers its etiology and nature should be done in most cases. The assessment should include a review of appropriate diagnostics and the patient's medication history including past and current opioid use. The physician should consider querying a prescription monitoring program.

Evaluate Treatment Options and Risks

The physician should explore treatment options and work with the patient to create a plan to manage pain and optimize function. The goal is to use appropriate therapies and use pain medications conservatively.

Common conditions that are almost never indicated for opioids include but are not limited to fibromyalgia, headache, uncomplicated neck and back pain or musculoskeletal pain, and pain—such as sore throat pain—that is related to a self-limiting illness.

TABLE 2

Acute Pain Assessment and Appropriate Opioid Prescribing Protocol Summary

If after a doing a thorough assessment to determine the etiology, type and anticipated duration of a patient's acute pain, carefully assessing the possible risks (ABCDPQRS) and evaluating all other possible therapies, you determine that opioids will offer significant treatment value, take into consideration these recommendations before prescribing them:

- Avoid prescribing more than a three-day supply (or 20 pills) of low-dose, short-acting opioids, unless circumstances clearly warrant additional opioid therapy (Tramadol is an atypical opioid and should be managed appropriately)
- Never prescribe long-acting/extended-release preparations for acute pain
- Maximize appropriate nonopioid therapies
- Review side effects with your patient
- Review safe driving, work, storage and disposal concerns with your patient
- Use shared decision-making with your patient; the patient must be educated about opioid risks and benefits to make an informed decision
- Use additional caution when prescribing opioids for the elderly and other patients with known risks for complications
- Ensure some method of follow up with the patient's primary care provider within three to five days to re-evaluate pain and response to treatment

Source: ICSI Acute Pain Assessment and Appropriate Opioid Prescribing Protocol

Chronic pain patients who are using opioids and who present with acute pain will need to be managed according to their pain management plan and/or in collaboration with the prescribing provider. Additional information about managing the chronic pain patient can be found in the ICSI Assessment and Management of Chronic Pain Guideline (www.icsi.org/_asset/bw798b/ChronicPain.pdf).

Risks and benefits should always be carefully explored when considering treatment of pain. There is no way to calculate the absolute risk of misuse, abuse, addiction or overdose in any individual patient. However, knowing about a factor such as a history of drug abuse can help a physician make a general assessment of relative risks/benefits. And factors such as the patient's condition should be considered when determining potential benefit.

The mnemonic "ABCDPQRS" provides an easy way for clinicians to remember what to cover when assessing opioid risk:

- **Alcohol use.** Assessing the patient for alcohol use is essential, as no amount of alcohol is safe for a patient on opioids. For patients with a positive screen for misuse of drugs or alcohol, the Screening, Brief Intervention, and Referral to Treatment (SBIRT) model is recommended. Use of SBIRT has been shown to reduce alcohol consumption and alcohol-related harm.[6]
- **Benzodiazepines and similar drugs.** Benzodiazepines can cause over-sedation in combination with opioids.[7]
- **Clearance and metabolism of the drug.** Many opioids require renal clearance of active metabolites. Be aware that potential renal or hepatic impairment will accentuate the side effects of opioids.[8]
- **Delirium, dementia and risk of falls.** Opioids will further compromise patients with these concerns. Opioids should be prescribed judiciously in the elderly because of these risks.[9]
- **Psychiatric comorbidities.** Many mental health disorders are correlated with increased opioid misuse, opioid-related accidents and accidental opioid overdose death. Physicians should take a thorough personal and family history to learn about any psychiatric conditions a patient may have and any substance abuse and sexual abuse in order to iden-

tify individuals who may need closer assessment and monitoring.[10]

- **Query the Minnesota Prescription Monitoring Program.** This statewide database can provide a better picture of a patient's history with certain prescriptions.
- **Respiratory insufficiency and sleep apnea.** Patients with hypoxia, hypercapnea and other conditions or medications that affect their ability to breathe will be at increased risk of respiratory insufficiency and respiratory arrest if they use opioids.
- **Safe driving, work, storage and disposal.** Opioids are a controlled substance. Patients need to be counseled about the dangers of driving or working while taking these drugs and reminded to safely store and dispose of them to prevent diversion.[11]

Consider the Side Effects

Physicians and patients alike need to be aware that numerous biochemical and physiologic changes can occur in patients taking opioids. Opioids change the chemistry of the brain and its response to pain. Following opioid exposure, homeostatic adaptations within the central nervous system may contribute to the development of tolerance, cause increased neuropathic pain, lead to the release of excitatory neuropeptides that cause peripheral nociceptive stimulation and result in opioid-induced hyperalgesia, defined as a state of nociceptive sensitization caused by exposure to opioids. This increased sensitization to painful stimuli may clinically manifest as apparent opioid tolerance, worsening pain or abnormal pain symptoms such as allodynia.[12-16]

Among the other numerous side effects associated with opioids are:

- Constipation, anorexia, bloating, nausea/vomiting and abdominal cramping[17]
- Respiratory concerns including decreased central drive, suppressed gag reflex, reduced frequency of respirations, altered breathing rhythm, inhibition of brain stem arousal centers, and blunted response to hypoxia and hypercapnia[18]

What Physicians Can Do about the Opioid Abuse Problem

- Become familiar with the ICSI prescribing protocol and use the risk assessment mnemonic in your practice.
- Have the latest information on opioids and other therapies that may better support patients through the acute phase of an injury.
- Use tools such as the Opioid Prescription Patient Agreement and Scripting Support for Saying No to a Patient in appropriate circumstances.
- Discuss with colleagues how to help a patient in pain.
- Encourage your organization to develop policies on appropriate opioid administration for acute pain, including prescription limitations that support the clinician and promote patient and community safety.
- Collaborate with dental organizations, specialty groups and patient groups within your community to create a standardized approach to pain management and opioid prescribing.

- An increased percentage of sleep time spent in light sleep and a decreased percentage of time spent in deep sleep[19]
- Bladder effects including decreased detrusor muscle tone and force of contraction, decreased sensation of fullness and urge to void, and inhibition of voiding reflex[20]
- Immune system changes including diminished cellular immune responses, natural-killer cell activity, cytokine expression and phagocytic activity[20]
- Endocrine system changes including inhibition of adrenocorticotropic hormone ACTH and cortisol secretion, causing a decreased glucocorticoid response; inhibition of LH- and gonadotropin-releasing hormone secretion, resulting in lower steroid hormone levels; inhibition of estradiol and testosterone secretion, resulting in hypogonadism, menstrual irregularities, sexual dysfunction, infertility and osteoporosis; inhibition of insulin secretion, leading to hyperglycemia and worsening diabetes.[21]

Shared Decision-Making

The patient and his or her physician should engage in a thoughtful discussion about the benefits and risks of all treatment options. This discussion should be coupled with education about pain management, the side effects of opioids and potential adverse effects of treatment. Decisions should support patient safety while improving function and be made collaboratively.

Prescribe Conservatively

If after thorough assessment, evaluation and exploration of all other options for pain management, the physician and patient together agree that opioids are needed for the patient's acute pain, the physician should prescribe no more than three days (or 20 pills) of low-dose, short-acting opioids. Patients with acute tissue damage and inflammation should experience a decrease in pain during this period. If not, their primary care physician or treating physician should re-evaluate them for ongoing or unrecognized issues. Use of a controlled-substance contract sends a message about the patient's responsibility in opting to use an opioid medication (a sample is included in the protocol).

Conclusion

Physicians alone cannot solve our society's opioid abuse problem. But as prescribers of these highly addictive drugs, they can do a lot to help prevent their inappropriate use, misuse and other untoward effects. They can first become more knowledgeable about the indications for and against prescribing opioids. In addition, they need to carefully assess the risks and benefits of these drugs for each patient before prescribing them. Finally, physicians need to involve the patient in the decision about whether to take these drugs and make sure

they prescribe the lowest effective dose for the shortest duration needed to manage acute pain. This protocol is one attempt to ensure that physicians are doing what they can to prevent abuse and harm while ensuring proper treatment of pain. MM

Howard Epstein is chief health systems officer and Carmen Hansen is a project manager at the Institute for Clinical Systems Improvement. Dave Thorson is a family physician with Entira Family Clinics and chair of the MMA board of trustees.

REFERENCES

1. CNN. Ledger's death caused by accidental overdose. Available at: www.cnn.com/2008/SHOWBIZ/Movies/02/06/heath.ledger/. Accessed February 28, 2014.

2. The soaring cost of the opioid economy. NY Times. June 22, 2013. Available at: www.nytimes.com/interactive/2013/06/23/sunday-review/the-soaring-cost-of-the-opioid-economy.html. Accessed February 28, 2014.

3. Meier B. Profiting from pain. NY Times. June 22, 2013. Available at: www.nytimes.com/2013/06/23/sunday-review/profiting-from-pain.html?action=click&module=Search®ion=searchResults%230&version=&url=http%3A%2F%2Fquery.nytimes.com%2Fsearch%2Fsitesearch%2F%23%2Fprofiting%2Bfrom%2Bpain%2F. Accessed February 28, 2014.

4. U.S. Department of Health and Human Services. Prescription drugs: abuse and addiction. National Institute on Drug Abuse. NIH Publication Number 11-4881. October 2011.

5. Portenoy RK, Foley KM. Chronic use of opioid analgesics in non-malignant pain: report of 38 cases. Pain. 1986; 25(2):171-86.

6. SAMHSA. Screening, Brief Intervention, and Referral to Treatment (SBIRT). Available at: www.samhsa.gov/prevention/sbirt/. Accessed February 28, 2014.

7. Bohnert AS, Valenstein M, Bair MJ, et al. Association between opioid prescribing patterns and opioid overdose-related deaths. JAMA 2011;305(13):1315-21.

8. Johnson SJ. Opioid safety in patients with renal or hepatic dysfunction. 2007. Available at: www.pain-topics.org.

9. Manchikanti L, Abdi S, Atluri S, et al. American Society of Interventional Pain Physicians guidelines for responsible opioid prescribing in chronic non-cancer pain: part I – evidence assessment. Pain Physician. 2012;15:S1-65.

10. Lépine JP, Briley M. The epidemiology of pain in depression. Hum Psychopharmacol. 2004;19:S3-7.

11. Centers for Disease Control and Prevention. Vital signs: overdoses of prescription opioid pain relievers and other drugs among women–United States, 1999-2010. MMWR Morb Mortal Wkly Rep. 2013;62(26):537-42.

12. Christie MJ. Cellular neuroadaptations to chronic opioids: tolerance, withdrawal and addiction. Br J Pharmacol. 2008;154(2):384-96.

13. Trescot AM, Datta S, Lee M, Hansen H. Opioid pharmacology. Pain Physician. 2008;11:S133-53.

14. Chou R, Fanciullo GJ, Fine PG, et al. Opioids for chronic noncancer pain: prediction and identification of aberrant drug-related behaviors: a review of the evidence for an American pain society and American academy of pain medicine clinical practice guideline. J Pain. 2009;10(2):131-46.

15. Lee M, Silverman S, Hansen H, et al. A comprehensive review of opioid-induced hyperalgesia. Pain Physician. 2011;14(2):145-61.

16. Angst MS, Clark JD. Opioid-induced hyperalgesia: a qualitative systematic review. Anesthesiology. 2006;104(3):570-87.

17. Kurz A, Sessler DI. Opioid-induced bowel dysfunction: pathophysiology and potential new therapies. Drugs. 2003;63(7):649-71.

18. Koo CY, Eikermann M. Respiratory effects of opioids in perioperative medicine. Open Anesth J. 2011;5:23-24.

19. Dimsdale JE, Norman D, DeJardin D, Wallace MS. The effect of opioids on sleep architecture. J Clin Sleep Med. 2007;3:33-36.

20. Benyamin R, Trescot AM, Datta S, et al. Opioid complications and side effects. Pain Physician. 2008;11:s105-20.

21. Vuong C, Van Uum SHM, O'Dell LE, et al. The effects of opioids and opioid analogs on animal and human endocrine systems. Endocrine Reviews. 2010;31:98-132.

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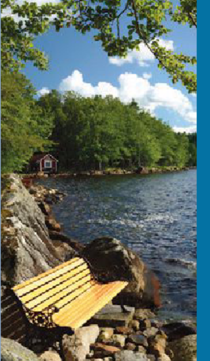

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Forcing a pause

Finding gratitude on our life's journey is an intentional act.

BY PIERRE TAWFIK

As I stood in the office of my preceptor during my family medicine rotation, a nurse interrupted our discussion and handed Dr. Murray a note. "Dr. Murray, I think you should see this," she said.

"Where is he? Bring him right in," Dr. Murray said, his face growing serious.

We walked into the exam room and found a short man dressed in jeans and a long-sleeved shirt and vest staring out the window. Mr. Johnson did not move when we entered. He appeared to connect with something else, something more important. He breathed and sighed, still looking away from us. Then he made his way to the chair, his eyes on the floor.

When he looked up he said, "She was so alive the day before. We went up to our cabin and she was perky as hell, so full of life. And the bright sunny weather and the fall trees and the lake shining that day were beautiful. It was all perfect."

He stopped and exhaled, his voice shaky but steady enough to show that he was familiar with grief. "Then I woke up at night. She was moving down the stairs. I said 'honey,' and she just leaned on the stair rail quietly struggling to walk down. I ran to her. Her whole body was tense. All she could say through her gritted teeth was 'I…Just…Can't…Breathe.'"

Mrs. Johnson died that night. There was no explanation as to why.

Mr. Johnson and his wife married when they were 17. As he described his wife, you could tell that he had loved her passionately. Time had flown by, he said.

"That night we went to bed. I got up to go to the bathroom and my movement woke her. She seemed worried about me and asked if everything was OK. I said yes. Then she said 'I love you, goodnight.'" Mr. Johnson reenacted his wife's words and tone as if he was trying to engrave them in his mind. "So I said 'I love you, too.'" He paused. "She was so hard-headed. She would not stop smoking, and I again had just gotten on her to stop. She was tough, but God, I loved that woman."

Although he was broken by his loss, Mr. Johnson had lived a life worth living. After 30 years of marriage, he was still as in love with his wife as the day they met. He had taken every opportunity to let her know how much she meant to him. They had responsibilities, financial troubles, four kids and many grandchildren. Yet somehow they had paused their fast-paced life to appreciate those around them, especially each other. One cannot love a person for 30 years, with all their nuisance habits and tendencies, without cherishing them.

After I stepped out of that room, I sent a text message to my fiancée telling her she was incredible. I plan on making it a habit. I want to cherish those who share my journey with me.

I had seen slow-paced death before, but Mr. Johnson's account of sudden loss reminded me of my own mortality. In medicine, we think we are invincible and sprint toward goals without feeling contented. We plan for the coming rotation, residency and subspecialty. Yet if we only run from goal to goal, we risk neither enjoying the journey nor the people we meet along the way.

A growing body of research shows that being grateful is associated with increased happiness. Being grateful for our journey and for those around us is an intentional act. It requires us to spend time thinking about our blessings: How many people wish they had a medical career but do not? How many people desire a sense of purpose in life and cannot find it? We physicians and future physicians, no matter our specialty, have that—the ability to touch lives in ways that no one else can.

Mr. Johnson reminded me that I can choose to focus on the goal or the path. In 30 years, I may well experience a loss of a similar magnitude. I can't prevent that from happening. But I can choose how contented I will be on my journey. **MM**

Pierre Tawfik is a third-year medical student at the University of Minnesota.

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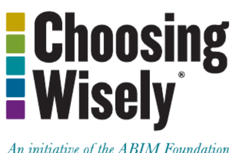

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