THE JOURNAL OF THE MINNESOTA MEDICAL ASSOCIATION

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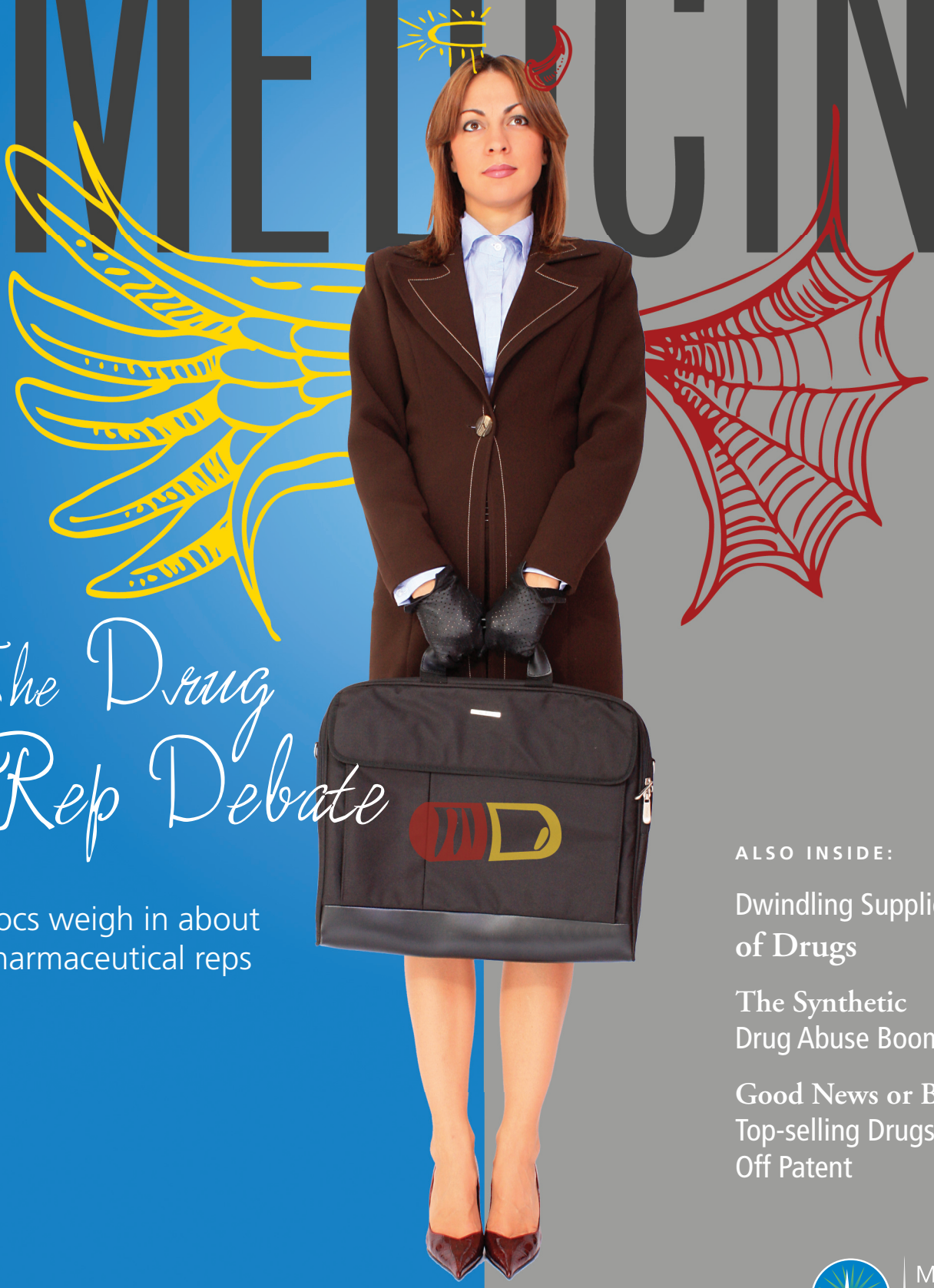

The Drug Rep Debate

Docs weigh in about pharmaceutical reps

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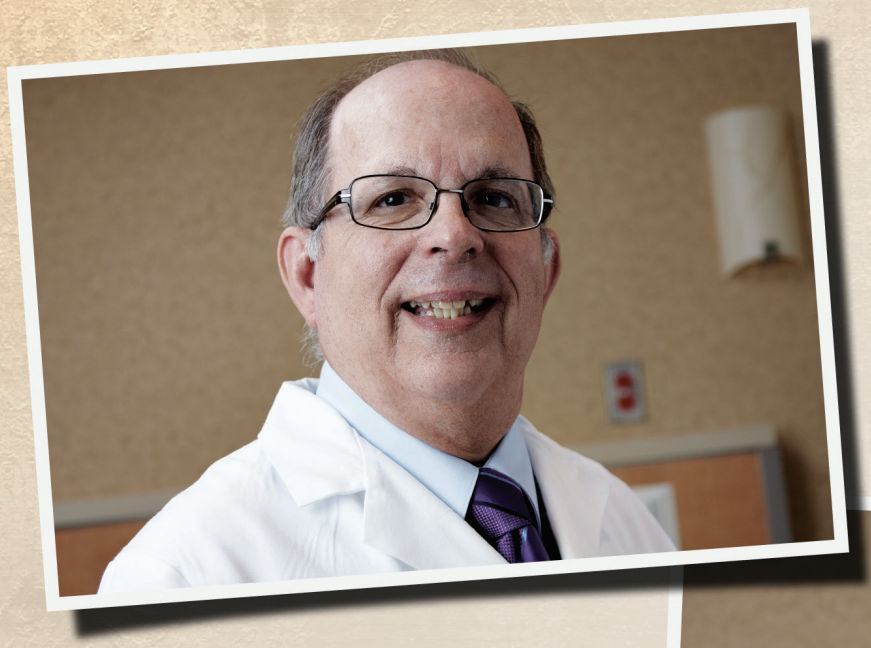
Dwindling Supplies of Drugs

The Synthetic Drug Abuse Boom

Good News or Bad? Top-selling Drugs Come Off Patent

Minnesota Medical Association

OCTOBER 2011 VOL. 94 ISSUE 10

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Minnesota Medical Association

Photo by Scott Walker

A Fouled-Up System

As a primary care internist, I don't cut, I don't deliver, and I don't catheterize. Although I do counsel patients on lifestyle and order nonmedical treatments such as physical therapy, many of my patients walk out of my office with a prescription. So you would think after all these years I would be an accomplished pill-pusher. But I'm not. Getting patients to take the right drugs is what I do poorest.

It should be simple, just like a recipe. Write out instructions and patients follow them. Yet study after study shows that the system breaks at every turn. Patients don't understand instructions, get their pills mixed up, or just don't take them. Pharmacists can't read prescriptions and can't reach providers. Hospitals have to make endless calls to verify medication lists on admitted patients, and, despite tireless efforts to get it right, discharged patients' medications get fouled up. There are a lot of players in the administration and use of medications, and getting everybody on the same page somehow doesn't seem to happen.

There are a lot of players in the administration and use of medications, and getting everybody on the same page somehow doesn't seem to happen.

As the "quarterback" in patient care, we primary care physicians should be able to get it right. But we see patients who have no idea what they're taking—"It's whatever it says there in my chart, doc" or "It's the blue ones." (Patients know colors, doctors know names.) We see patients who keep a medication list in their billfold, but it is a tattered, faded, folded piece of paper that was last modified four years ago. We get the puzzled inquiry from the pharmacy about the 50 mg atenolol that should be 25 mg. And we search 20 different pharmacy refill request fax forms for the right boxes to check.

If all these glitches were mere inconveniences, perhaps we could live with them. But mistakes can sicken or kill people. So how do we ensure patients are taking the right medications the right way every time? I dream of a perfect world with a master medication list, accessible to patient, doctor, pharmacy, and hospital, that registers changes instantaneously and warns everybody of dangerous drug interactions. The electronic health record (EHR) potentially could supply that list; but the EHR evolution is going the way of American capitalism, and at present, we have a supermarket farrago of systems being adopted by doctors, pharmacies, and hospitals. My clinic is currently installing an EHR on the platform used by the hospital we use. But if my patient has surgery at a hospital that uses a different EHR, that patient's information will flow back to me by the same inefficient, fallible routes it's traveled for years. And most pharmacies cannot yet communicate electronically with our EHR, so our fax machines will still be spitting out refill requests.

Perhaps someday there will be an electronic millennium, when all of the players in the medication melee will sit at a table, U.N.-like, and agree to communicate for the sake of patient safety. Yet even if that comes to pass, we won't have a solution for the human factor. Before he died earlier this year, my father-in-law was on about 10 medications. He was a meticulous retired dentist who prided himself on keeping track of the details of his life. But despite this and despite my wife's doting attention, he got his medications confused. When pill goes from bottle to mouth, no electronic gadget can help—if it's the wrong bottle.

I hope that I and the rest of the health care delivery system can get all this right some day. In the meantime, I'll keep writing prescriptions.

Charles R. Meyer, M.D., can be reached at cmeyer1@fairview.org

Reducing COPD Readmissions in Minnesota

In response to the cover story in the September issue ("Slowing the Revolving Door," p. 24), which highlights efforts in Minnesota to reduce the number of preventable hospital readmissions, we would like to call attention to the problem of chronic obstructive pulmonary disease (COPD) as a cause of readmissions and discuss what some Minnesota health systems are doing to reduce them.

In 2008, COPD became the third leading cause of death in the United States, overtaking stroke. An article published in the September 2011 issue of *The Lancet* reported that 25 percent of people 35 years of age and older are likely to develop COPD, making the overall risk for developing the disease greater than that for heart failure, breast cancer, and prostate cancer.

In March 2011, the Minnesota Hospital Association used 3M's Potentially Preventable Readmission software to run a data set at the request of the Minnesota COPD Coalition, a group of providers, payers, and others whose mission is to improve the health outcomes of patients with COPD, and discovered that the statewide readmission rate for patients with COPD was 12.53 percent, just behind the rates for patients with heart failure and pneumonia. The actual rate for COPD patients is probably much higher because the software only captured readmissions to the same hospital within 30 days.

With more research pointing to COPD as a major contributor to health care utilization, payers, systems, and public health organizations are now working to reduce COPD-related readmissions. Starting in 2012, the Centers for Medicare and Medicaid Services (CMS) will require all health plans that offer a Medicare Advantage product to conduct a performance improvement initiative to reduce hospital readmissions for all causes including COPD. In October of 2014, CMS will reduce payments to hospitals that have high readmission rates for COPD within 30 days of discharge.

Reducing COPD readmissions involves addressing a number of issues including:

1. Medication management. This involves prescribing the medication regimen best suited for the stage of the disease. The regimen should be manageable, and the patient should receive education on what their medications do and how and when to take them. Providers also should make sure patients are able to access these medications and refill them, if needed. In addition, they should reconcile the medications a patient was taking before their hospitalization with their new prescriptions to make sure they are appropriate and are consistent with the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines.

2. Discharge planning. Providers should create a discharge plan that addresses all of a patient's needs including follow-up appointments, medications, oxygen therapy, pulmonary rehabilitation, transportation, and support systems outside the hospital.

3. Transition planning. This involves making sure there is good communication and sharing of information among providers, home care agencies, and patients and their families when a patient moves from one care setting to another.

Some Minnesota hospitals are already making a concerted effort to address these and other concerns in order to prevent COPD readmissions. For example, hospitals, primary care clinics, and home health care providers in the Allina system are using the same computer charting system, which makes tracking changes in the condition of patients with COPD and managing their medications much easier. In addition, Allina is working on a model to predict which patients are most at risk for readmission. If providers can predict which patients have an elevated risk for readmission, they can implement an enhanced discharge plan. Allina is also participating in Reducing Avoidable Readmissions Effectively (RARE), a campaign to prevent 4,000 avoidable readmissions in Minnesota hospitals within 30 days of discharge between July 1, 2011, and December 31, 2012.

The Olmsted Medical Center is working with Roberto Benzo, M.D., of Mayo Clinic to enroll every patient who comes to the Olmsted Medical Center with a COPD exacerbation in a pulmonary rehab program. Each patient will learn home exercises and receive an exercise bicycle that can be set for different levels of resistance. Patients and their caregivers also will receive information about how to recognize an exacerbation early on and which medications to use when respiratory problems begin. The idea is that by providing better education about what to do at the onset of an exacerbation, increasing a patient's exercise capacity, and making sure they follow up for medication reconciliation, providers can improve a patient's quality of life and prevent readmissions for COPD.

In 2008, Sanford Health, formerly MeritCare, in Fargo undertook an initiative to standardize COPD care. The Inpatient COPD Care Program involved having a standardized COPD admitting order set; instituting a standardized respiratory therapy (RT) COPD medication protocol; deploying RT COPD specialists to oversee the program; and monitoring the use of evidence-based care, length-of-stay, 30-day readmission rates, and cost-of-care/reimbursement. Patient education, medication reconciliation, transition planning, and postdischarge follow-up were identified as critical to reducing readmissions. Sanford staff developed a tool

for their electronic medical record that allows the RT specialist to document a plan of care that may include providing inhaled medications at discharge, ordering pulmonary function tests, and prescribing pulmonary rehabilitation. The documented plan of care is made available to the patient's physician and other providers during transition planning. Since 2008, the 30-day readmission rate for any Medicare Severity Diagnosis Related Group (MS-DRG) among patients at Sanford's hospital dropped from a high of 28 percent to a current low of 6.25 percent; the most recent data show an 18-month average readmission rate of 13.4 percent for any MS-DRG. During that same period, the average 30-day readmission rate for COPD was 2.2 percent. Each week, the RT COPD specialists compile disease management notes for the primary care providers based on the 12-point quality recommendations from the American Medical Association that help the providers be proactive with patients.

The Minnesota COPD Coalition has been focusing on hospital readmissions for the past year. The coalition is a partner in RARE and sponsored a regional webinar highlighting successful programs in May 2011 (the webinar is archived at www.lungusa.org/associations/states/minnesota/events-programs/mn-copd-coalition/upcoming-copd-meeting/copd-discussion-group.html). The coalition also is working on defining quality for emergency care of patients with COPD and creating tools and resources that providers can use to ease transitions from one care setting to another and coordinate patient care. For more information about the Minnesota COPD Coalition, go to www.lungmn.org/copd or contact Jill Heins Nesvold at jill.heins@lungmn.org.

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Photo by Steve Wewerka

■ **Drug Supply**

Running Short

Dwindling supplies of some medications are affecting treatment regimens for many patients—with few long-term solutions on the horizon. | BY JEANNE METTNER

For Marjorie Swedberg, playing the waiting game is getting uncomfortably risky. After being diagnosed with fallopian tube cancer and undergoing a complete hysterectomy in February 2010, the 72-year-old Webster, Wisconsin, resident learned that the cancer had spread to her lung. After three different therapies proved ineffective in lowering the levels of the cancer marker CA125 in her blood, her doctors recommended that she try Doxil, a low-cost drug that has long been considered a mainstay therapy for ovarian cancer, multiple myeloma, sarcoma, and some breast cancers. Doxil brought Swedberg's CA125 levels down from 1,125 to 600 U/mL, moving her closer to a normal range, in just four months.

But by August of 2011, production challenges had created unexpected shortages of the drug, and its manufacturer, Johnson & Johnson warned that supplies would be only "intermittently available in the coming weeks." Within 10 days of the announcement, Minnesota Oncology in Minneapolis, where Swedberg received treatment, had gone through its supply of Doxil, ending treatment with the drug for Swedberg and others. Although Johnson & Johnson attributed the shortage to production delays, the reasons matter little to Swedberg, who continues to worry whether Doxil will be available. "I feel fine right now, but I wait and wonder how long it will be before they call and say that I can finally get the treatment that's working for me," she says.

Swedberg's case illustrates a disturbing trend: an increasing number of drugs are in short supply. In 2010, the FDA reported a shortage of 178 medications—triple the number that were in short supply in 2005. The causes are myriad—raw materials shortages, plant contaminations, inspection failures, drug company mergers, and glitches in manufacturer production capabilities.

But in the minds of many, the real problem revolves around profitability. "The profit margins on these drugs are very small, and because the pharmaceutical industry has become this globalized monster, there are fewer and fewer drug makers out there now," says Joseph Leach, M.D., a medical oncologist with Minnesota Oncology. "For some of these generic drugs, there is not only one company manufacturing them but literally only one plant in the entire world that makes the world supply; if they have a problem, there is no way to pick up the slack."

Marjorie Swedberg, who has had success with the drug Doxil for treating her cancer, has had to wait for a dose to become available.

Putting Lives on Hold

Patients in Minnesota and throughout the United States have felt the brunt of the diminished supply. Although providers have seen shortages of pain relievers, anesthetics, and heart medications, the majority of drugs that are currently in short supply are cancer therapies (see p. 10). At Children's Hospitals and Clinics of Minnesota, Minnesota Oncology, and a number of other oncology practices, shortages of cytarabine, a drug used to treat acute leukemia in children and adults, have sent providers scrambling for solutions. "Acute leukemia is a very aggressive cancer that can be curable but needs to be treated immediately," Leach says. "At one point last spring, we went day-to-day not knowing if we would have enough to give treatment at the hospital."

Although supplies eventually trickled in (suppliers say they are still experiencing shortages of cytarabine), Leach and his team began to discuss what they would do if they had to resort to "rationing." "Ultimately, the decision we came to was that we would administer the medication on a first-come, first-served basis," he says. "Ethically, we didn't feel that we could prevent a person from getting treatment if we had it on hand."

At Children's, the shortage of cytarabine affected patients on a three-drug regimen for acute leukemia that included intrathecal cytarabine. Because of the shortage, the drug was excluded from the regimen for a number of patients. "We have been able to get by so far, but we have had to make modifications for some of our patients," explains Bruce Bostrom, M.D., a pediatric hematologist and oncologist. "Whenever you have to change therapy, you don't know for sure what the outcome will be. Most malignancies are treated with a combination of drugs, so we think we will do O.K. by trying to substitute out or eliminate one of the drugs from the combination, but obviously we don't know for sure."

> "At one point last spring, we went day-to-day not knowing if we would have enough to give treatment at the hospital."
>
> —Joseph Leach, M.D.

Delaying Discoveries

In some cases, the paucity of certain medications is also affecting research. At Minnesota Oncology, patients enrolled in clinical trials for colon cancer often take an inexpensive drug called leucovorin as part of their treatment or as a prerequisite to study participation. After weeks of being without the drug, Leach, who directs Minnesota Oncology's research program, says the practice has had to "literally shut down" certain studies. "Not only is this shortage affecting people who are getting treatment right now; it's slowing down investigations for better treatments because it's throwing a monkey wrench into these research protocols," he says.

Similar problems are occurring with research trials involving cytarabine in pediatric patients. According to Bostrom, clinical trials of new treatments for acute leukemia in children typically require that patients first receive intrathecal cytarabine. Because cytarabine is not available, many patients have been disqualified from the clinical trials. "That obviously concerns us because advances over the last 50 years improved the cure rate of childhood acute lymphoblastic leukemia from under 10 percent to 80 or 85 percent today—thanks largely to clinical trials," he says. "If patients cannot be in a clinical trial, we will, of course, give them the best therapy available, but that's not going to contrib-

Cancer Drugs in Short Supply

The FDA recently notified hospitals and pharmacies of shortages (or potential shortages) of the following drugs:

Cytarabine • for acute myelogenous leukemia in children and adults

Doxil • for breast cancer, ovarian cancer, sarcoma, multiple myeloma

Leucovorin • for colon cancer

Fluorouracil (5FU) • for colon cancer

Cisplatin • for testicular cancer

A complete listing is available on the American Society of Health-Care Pharmacists website, www.ashp.org/DrugShortages/Current/.

ute to the knowledge base needed to improve the state of pediatric cancer treatment in the future."

A Short-term Solution

To U.S. Sen. Amy Klobuchar, the stories of drug shortages and their negative effect on patient care were a sign that something needed to be done as quickly as possible. "I see Minnesota as the canary in the coal mine when it comes to health care issues such as this," Klobuchar explains. "We tend to find out about problems in our state before they take hold nationally." Talking to hospital administrators, pharmaceutical groups, clinicians, and patients revealed many possible solutions to the problem of shortages, including reimportation of the drugs from countries where there are surpluses, which Klobuchar says is "not the law of the land" and would take time that some patients frankly don't have.

Klobuchar has proposed legislation that is based on fairly simple, short-term measures that helped the Food and Drug Administration (FDA) prevent supply shortages of 38 drugs in 2010. Known as the Preserving Access to Life-Saving Medication Act, the legislation requires prescription drug manufacturers to notify the FDA immediately when an incident occurs that could result in a drug shortage—such as a merger, a change in raw material supply, or the closing of or delayed production within a facility. In addition to allowing the FDA to coordinate efforts to prevent shortages from affecting patients—perhaps by helping to direct supplies to areas of need—the bill directs the FDA to notify the public about shortages and the actions the agency would take to address them. It also requires the FDA to include "prevalence of use" as a factor in determining whether a drug is medically necessary.

Introduced last February, the bill is currently in the hands of the Committee on Health, Education, Labor, and Pensions. It has the support of the Minnesota Hospital Association, the American Hospital Association, Fairview Health Services, the American Society of Clinical Oncologists, the Institute for Safe Medication Practices, the American Society of Health-System Pharmacists, and the American Society of Anesthesiologists.

"The legislation will be helpful because we don't know if there is going to be a drug shortage sometimes until literally a few days before there is no drug; but the larger problem is incredibly complex," Leach says. "This is not something that Congress can just legislate; you cannot force multinational companies to produce a drug for which there is little profit."

Meanwhile, Swedberg can only wait. If a shipment does not arrive soon, she says her oncologist plans to recommend a different treatment regimen. "I haven't asked my doctor if I can miss a month or so, but I imagine it can't be good to be putting things on hold," she says. "I don't want to lose progress in my battle with this cancer, but at this point, the only thing I really can do is remain optimistic." ■

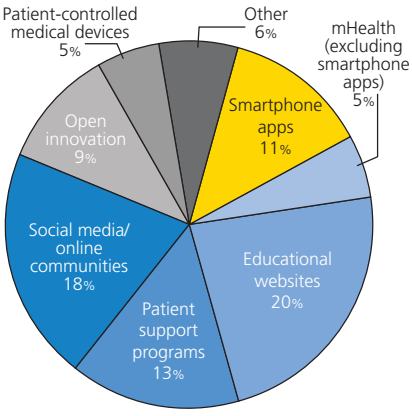
■ **Industry Trend**

There's an App for that (Drug)

As part of "Pharma 3.0," a pharmaceutical industry effort to encourage people to take the drugs they manufacture, drug companies have increased their investment in mobile technologies, particularly smart phone apps. In 2006, 11 percent of Pharma 3.0 initiatives were smart phone apps. In 2010, 41% were.

Some of the apps are aimed at patients; others at physicians. They do tasks ranging from helping patients manage medication schedules to providing physicians with an easy a way to contact a drug's manufacturer. Pfizer, for example, worked with Epocrates to include a feature that allows physicians to contact the company to ask questions or report adverse events.

2006-2009



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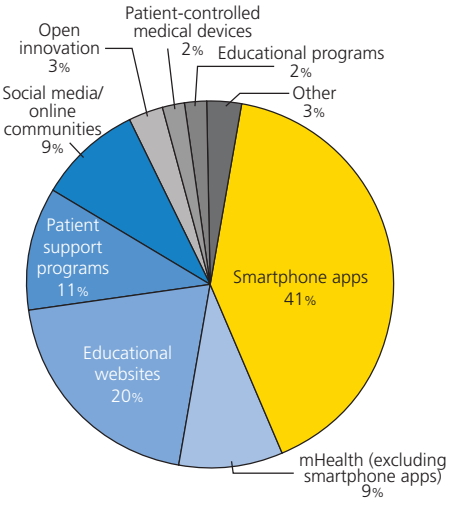


Source: "Progressions: Building Pharma 3.0," Ernst & Young's annual global pharmaceutical report, August 2011.

Photo courtesy of North Dakota State University

North Dakota has more than 70 telepharmacy sites. Here, a technician in Enderlin talks with a pharmacist in LaMoure, 50 miles away.

■ Telepharmacy

Rx for Rural Pharmacies

Small towns are finding creative ways to preserve access to pharmacy services.

BY KIM KISER

Diane Stusynski was working as a technician at the only pharmacy in Karlstad, Minnesota, in 2004 when she learned that her boss, the pharmacist, wanted to retire. The town's 850 residents, many of whom were elderly, depended on the store, and its closing would mean they would have to drive to Thief River Falls 35 miles away to have prescriptions filled—a trip that would be especially difficult during northwestern Minnesota's winters. "We needed to keep a pharmacy in town," she says. "The elderly population often can't get places. Sometimes they're lucky if they can get out of their homes or find people to pick things up for them."

At the time, other small towns were experimenting with telepharmacy, an approach in which a pharmacy technician such as Stusynski works under the supervision of a pharmacist in another community to fill prescriptions. In 2002, after the pharmacy closed in Sebeka, Minnesota, the town's clinic converted a room into a pharmacy and established computer, audio, and video connections with the outpatient pharmacy at the hospital in Wadena. (The Sebeka telepharmacy closed in 2010.)

Telepharmacy had also proved to be a way of maintaining pharmacy services in rural North Dakota. In 2001, that state became the first to allow the practice. Today, North Dakota has 73 telepharmacy sites, 51 of which are in retail stores.

After hearing about the success in North Dakota, the pharmacist in Karlstad approached officials at Thrifty White Pharmacy, a regional chain based in Maple Grove, Minnesota, that had several remote telepharmacy sites in North Dakota, about setting up a similar arrangement. Several months later, after receiving a variance from the Minnesota Board of Pharmacy's licensing rules, Thrifty White established a remote site in a grocery store in Karlstad.

The day after the old drug store closed, Stusynski reported to the new pharmacy, located in a corner of Supermarket Foods, where she has been filling prescriptions ever since.

The Way it Works

Now when a patient brings in a prescription, Stusynski scans it and sends an electronic copy to a pharmacist at Thrifty White's central facility in Fargo (the facility is licensed as a nonresidential pharmacy by the Minnesota Board of Pharmacy).

Stusynski then enters into Thrifty White's computer system the patient's name; the doctor's name; the name, strength, and quantity of the drug prescribed; directions for taking it; and information about whether it can be refilled. A claim is then sent to the patient's insurance company. After the pharmacist verifies the information entered by the tech, and if the claim is accepted, a label is printed out at the pharmacy in Karlstad. Stusynski then pulls the stock bottle of medication off the shelf, counts out the number of pills ordered, places them in a container, and attaches a portion of the label to the container.

Next, she sets the stock bottle and pill container in front of one of three cameras in the store and establishes a two-way audio/video connection with the pharmacist in Fargo. Under the eye of the camera, she shows the pharmacist the stock bottle and the pill container, removes the contents of the pill container, counts out the pills, then shows the pharmacist the label. The pharmacist compares what he or she sees with what's on the prescription and an image of the pill, and checks the National Drug Code directory to verify the product and manufacturer. Once the pharmacist determines that the prescription has been filled correctly and there are no potential drug interactions, Stusynski adheres the rest of the label to the container, seals it, and gives it to the patient.

The patient then goes to a corner of the store that has another two-way audio/video system to receive counseling from the pharmacist on how to use the medication, possible side effects, and what to do if he or she misses a dose. All the while, a security camera is monitoring the pharmacy area

and sending images back to Fargo.

Karlstad is one of 13 communities in rural Minnesota where this type of telepharmacy is in use, according to Cody Wiberg, Pharm.D., executive director of the Minnesota Board of Pharmacy. "These are towns that can't support a traditional pharmacy," he says.

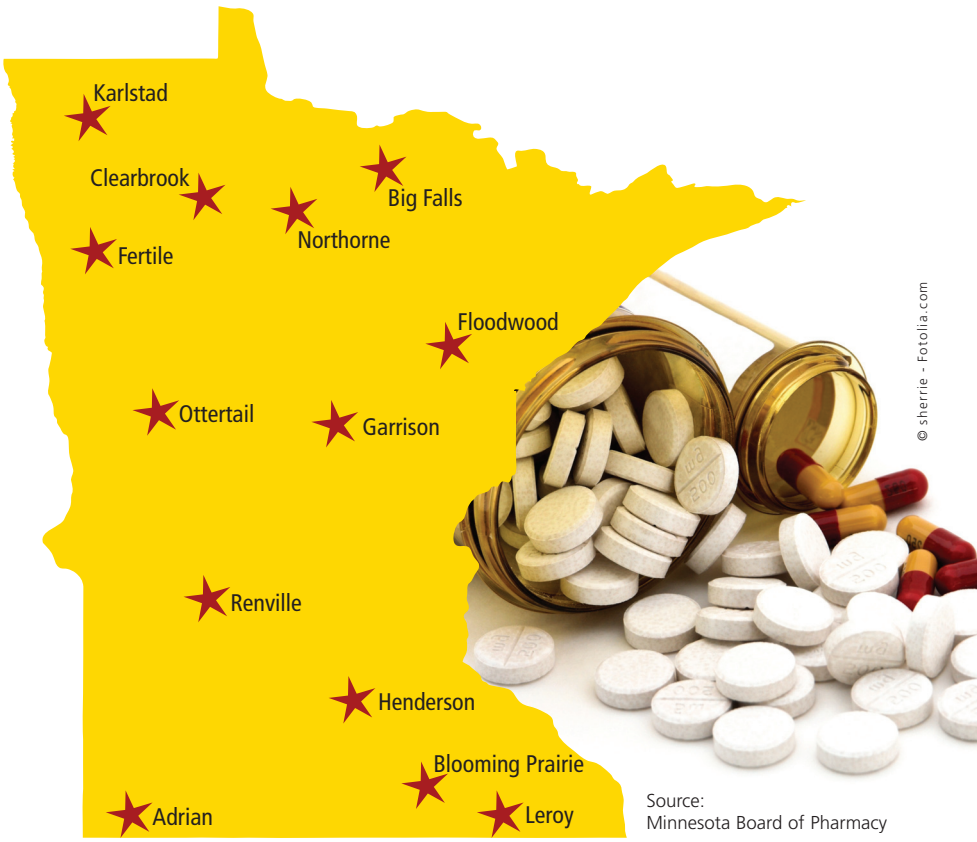
A Familiar Story

The fact that the average age of pharmacists in rural Minnesota is over 50 and that many, like Stusynski's former boss, are looking to retire is only part of the reason why telepharmacy is catching on. "It's really a combination of factors," Wiberg says.

For one thing, finding pharmacists to practice in or buy stores in rural communities has become as challenging as finding physicians to work in rural clinics. During the mid 2000s, Minnesota saw a significant shortage of pharmacists—a situation that is starting to change, according to Wiberg. "Salaries tripled between 1999 and 2009," he says. (According to the Minnesota Department of Employment and Economic Development, the mean salary for pharmacists in the state is more than $114,000.) To compete, pharmacies often had to offer signing bonuses. The ones that could do that were usually the larger chains with stores in metropolitan areas. "With the sort of salaries pharmacists coming out of school could make working for a chain and with the debt they're in—my oldest daughter graduated five years ago with $110,000 in school loans—there are a lot fewer young pharmacists who are willing to take a risk and buy a pharmacy in a town with 1,500 people," Wiberg says.

The other issue that discourages pharmacists from going into rural practice is reimbursement. "Gross margins have gone from 20 percent to 10 percent for prescriptions," he explains. Wiberg served as the state's Medicaid pharmacy program administrator from 1999 to 2005. He recalls reimbursement for pharmaceuticals being cut as part of a 2003 budget-balancing deal. Reimbursement had been based on the average wholesale price (AWP) of a drug minus 9 percent plus a $3.65 dis-

Minnesota Communities with Telepharmacies



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Source:
Minnesota Board of Pharmacy

The Hospital Connection

Since 2004, Minnesota hospitals that don't have pharmacist coverage 24/7 have begun connecting to pharmacies in larger hospitals for after-hours support. In most cases, a nurse at the rural facility faxes or electronically transmits the medication order to the hospital that does have full-time pharmacy coverage for review before the drugs are administered.

Cody Wiberg, Pharm.D., executive director of the Minnesota Board of Pharmacy, says one of the reasons for doing this is a Joint Commission best practice standard requiring a pharmacist to review an order before a drug is administered to a patient. "Some hospitals might be denied reimbursement if they were to lose Joint Commission accreditation," he says. "So they have a financial reason for doing this."

Wiberg says a number of large Minnesota-based systems including Allina, Mayo, and Fairview are providing after-hours pharmacy support to small hospitals. In addition, Catholic Health Initiatives in Fargo serves several hospitals in northwestern Minnesota through its ePharmacist Direct program, and Cardinal Health, an Ohio company, provides support to Virginia Regional Medical Center. Avera, based in Sioux Falls, South Dakota, is the most recent system to approach the Board about providing remote support.—K.K.

pensing fee. (Private insurers were paying AWP minus 13.5 percent plus a $2.50 dispensing fee at the time.) The state now pays AWP minus 15 percent plus the same dispensing fee. This year, however, lawmakers did vote to increase the dispensing fee by $1 for rural independent pharmacies—the first increase in reimbursement in more than a decade.

Consequently, "there's a real squeeze between expenses and reimbursements," Wiberg says. "The cost of drugs is going up and reimbursement is going down. In 1985, when I graduated from pharmacy school, you had to fill 70 to 75 prescriptions a day to make a profit. Now you have to fill a couple hundred to make a profit."

And that's where telepharmacy can make a difference, as the cost of running a remote site is lower than the cost of running a traditional pharmacy. According to Tim Weippert, executive vice president of pharmacy for Thrifty White, telepharmacy equipment costs between $15,000 and $20,000.

The error rate in remote telepharmacies is about the same as the rate in practices with a pharmacist on site.

Researchers have found that concern about whether care delivered via telepharmacy is as good as that provided by traditional community pharmacies is unfounded. A 45-month study by researchers at North Dakota State University found that the error rate in remote telepharmacies is slightly more than 1 percent, which is about the same as the rate in practices with a pharmacist on site. "It shows telepharmacy is as safe as traditional pharmacy," says Ann Rathke, telepharmacy coordinator for North Dakota State's College of Pharmacy, Nursing, and Allied Sciences and one of the authors of the study.

Since Stusynski began working at the telepharmacy in Karlstad, she has seen instances where errors have been prevented. "The checks and balances are stringent in Minnesota, and the quality assurance system we have in Fargo is so good that they're more likely to catch problems before prescriptions go out the door," she says.

This has proved to be an added bonus for the residents of Karlstad, who were concerned about losing their pharmacy not that long ago. "It's hard to find pharmacists to come to real rural areas unless there's a lake for them to fish on, and we don't have one," Stusynski says. "So this has been awesome for us." ■

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■ Medication Adherence

America's Other Drug Problem

A new campaign launched by the National Consumers League aims to get patients with chronic health problems to do what doctors often can't: take their medications. Called Script Your Future, the three-year U.S. Agency for Healthcare Research and Quality-funded effort is raising awareness about the importance of taking prescribed medicines, particularly for patients with diabetes, respiratory disease, and cardiovascular disease. It's also providing tools for patients. One is a service that will send a text message reminding patients to take their medicine.

Information about the campaign is online at www.scriptyourfuture.org.

Adding Up the Cost

- One in three Americans never fill their prescriptions.
- Three out of four do not always take their meds as directed.
- More than one-third of medication-related hospital admissions are related to poor adherence.
- The costs associated with not taking medications as prescribed is $300 billion in the United States.

Souce: National Consumers League

Photo courtesy University of Minnesota

Researcher Subhashree Rangarajan prepares samples for screening in the Institute for Therapeutics Discovery and Development.

■ **Drug Development**

Pharmaceutical Pipeline

The U makes a push to move drugs from the lab to the pharmacy. | BY TROUT LOWEN

The process of drug discovery and development is most often characterized as a pipeline that starts in the laboratory and ends with commercial production. What is less often talked about outside of the pharmaceutical industry is the decidedly uphill route that pipeline takes.

Thousands of compounds must be screened to find a few hundred that show promise. Of those, maybe five will make it to human clinical trials, and one will get to market. "It's an uphill battle," says Jay Schrankler, director of the Office for Technology Commercialization (OTC) at the University of Minnesota. The OTC assists university researchers in translating their discoveries into new products and services. Development of a commercially successful drug can take 10 years or more and cost around $1.8 billion.

Despite that steep trajectory, over the past five years university officials have been quietly assembling a network of industry scientists and academic researchers to advance the university's research along that pipeline, beginning in 2007 with the hiring Gunda Georg, Ph.D., and the creation of the Institute for Therapeutics Discovery and Development (ITDD). The ITDD has a number of missions: to enable drug discovery and development at the university, to expose students and Ph.D. researchers to industry best practices and project management techniques, and to earn revenue for the university by licensing promising new compounds to Big Pharma. "While we will never be able to market drugs, we will be able to help take these basic discoveries people make in the laboratory and bring them to the level where there is the potential to hand them over to industry," Georg, the ITDD's director, says.

Assembling the Experts

The university hired Georg away from the University of Kansas, where she ran an NIH-funded collaboration to develop experimental cancer drugs. Although impressed by her scientific achievements, university officials also were interested in Georg's experience in the commercial realm. She was co-founder of Proquest Pharmaceuticals and co-inventor of the anesthesia drug Luserda. She had also helped develop a male contraceptive that is now moving toward human trials.

George, who is also chair of the department of medicinal chemistry in the College of Pharmacy, hand-picked five of the directors of the ITDD's six core units. (The Pharmacology and Biomarkers unit is currently seeking a new director.) All are from industry.

Michael A. Walters, Ph.D., a former Pfizer chemist who heads the ITDD's Lead and Probe Discovery unit, says he and his colleagues from industry can offer researchers valuable insight into the drug development process. "Drug discovery and development requires knowledge of how industry does that process," he says. "It's not that we want to recreate a pharmaceutical company in academia, but we know how things are done in industry, and we can adopt some of their best practices." For example, the ITDD runs a large-scale lab on the St. Paul campus that operates under good manufacturing practices rules. It also does assay development, high-throughput screening, medicinal chemistry, and disease biomarker development, and it has the capacity to scale up production for clinical trials.

The ITDD is just one component of the university's focus on drug development. Others include the Center for Translational Medicine, the Biotechnology Resource Center, the Clinical and Translational Science Institute, and the OTC, which has added a number of

drug industry professionals to its staff including Reggie Bowerman, a former executive at MGI Pharma and Aventis.

A Nationwide Trend

Minnesota isn't the only university investing in drug development. A recent survey found approximately 80 small-molecule drug discovery centers located within U.S. universities or nonprofit centers, and that didn't include the ITDD, Walters notes.

A couple of factors are driving that trend. Pharmaceutical companies are cutting back on basic research, viewing it as too costly and too risky. And, increasingly, the National Institutes of Health, the biggest source of public grant funding for drug research, is expecting researchers to show how their work will translate into actual therapy. "So a lot of institutions are saying we need a drug discovery development unit like this, or we need to partner with one," Walters says.

> "The hope is that we bring new drugs to market for diseases where there was no good treatment before."
>
> —Gunda Georg, Ph.D.

And then there is the potential for a big payoff. Since 1999, the anti-HIV drug Ziagen, the most successful drug to be developed at the university, has generated close to $300 million, some of which has been used to fund the ITDD. But Ziagen's patents are expiring and the university stands to lose millions as a result. That's giving those driving the assembly of a commercialization pipeline a greater sense of urgency.

Although the chances of discovering the next Ziagen anytime soon are slim, the university continues to generate revenue by spinning off startup companies and concluding license agreements, and it's always on the lookout for marketable tools or medical devices that might result from researcher discoveries.

The university also hopes having the ITDD will help researchers land more federal grants. But that will require them to develop a new mindset about basic research, says Douglas Yee, M.D., director of the university's Masonic Cancer Center. "For many years, basic scientists worked on basic problems and didn't have that much interest in translation," he says. "I think in the past 10 or 15 years the idea that translation of their findings into something that changes human disease has become an important criterion." Federal funders such as the

National Cancer Institute also want to see multidisciplinary collaboration when recognizing comprehensive cancer centers. "We have to show we have outstanding science and that we work together," Yee says. To foster collaboration, the university has created formal units called "Corridors of Discovery" to bring people working in the same therapeutic areas together to share information and ideas. The corridors correlate to five general research areas: diabetes, infectious diseases, brain science, cancer, and cardiovascular disorders.

One of the most highly publicized products of these efforts so far is Minnelide, a new treatment for pancreatic cancer. Working in the lab, Ashok Saluja, Ph.D, vice chair of research in the department of surgery, identified several promising compounds that could destroy pancreatic cancer cells including triptolide, a plant substance used to treat arthritis in China. But he needed assistance to take the project farther. Pharmaceutical companies weren't interested, says Georg, because they couldn't patent an old natural remedy and, thus, had no incentive to develop a drug.

Triptolide also wasn't particularly water soluble, which made it difficult to administer. The ITDD stepped in to help. Georg and her research staff at the College of Pharmacy altered the chemical makeup of triptolide to produce a new more drug-like compound, Minnelide. The Center for Translational Medicine is now having Minnelide scaled up for a Phase 1 clinical trial that will probably begin later this year or in early 2012.

It's a team process, Georg says, with the ITDD acting like the coach or the captain. "I think we were sort of a catalyst," she explains. "Without us there would be no Minnelide."

Stewardship

One of the ITDD's other roles is as a repository of information on all the university's drug-related research. Two years ago, the ITDD surveyed the university to identify who was working on what drug-related research and at what stage of development it was at, Walters says. The idea was to identify which projects might benefit from collaboration or from additional funding.

As a result of that analysis, the ITDD now plans to focus more closely on diabetes research, an underrepresented area of drug discovery and development at the university. Last October, the university announced a 10-year partnership with Mayo Clinic aimed at curing diabetes. The ITDD expects to play a role in that effort. "The hope is that we bring new drugs to market for diseases where there was no good treatment before," Georg says.

In the long term, the university would like to have another Ziagen-sized commercial success, which could provide an endowment for the ITDD and its other drug-related research efforts. "That's certainly the hope," Georg says. "But are we going to succeed or not? We don't know." ■

■ **Medication Compliance**

Drug Test

A pilot program at Regions Hospital tests heart failure patients' ability to set up their meds. | BY KIM KISER

Mike Cannon's inspiration for creating a "medication boot camp" at Regions Hospital in St. Paul, where he is director of nursing for cardiovascular services, didn't come from the military. It came from his own parents' experience.

After a hospitalization for peripheral vascular disease, his father, who has since passed away, was sent home with about a dozen medications. Both the hospital staff and the family were convinced that Cannon's mother would be able to make sure her husband was taking them properly. "They appeared to me and the hospital staff to be pretty sharp; but what I found out pretty quickly was that they could not and did not set up their meds correctly at home," he says. "I thought, 'There's two people I know were fooling the system. I'll bet there are more out there.'"

With that in mind, Cannon came up with a plan to test whether patients with congestive heart failure who are being discharged from Regions understand their medication instructions. "It's not uncommon to send them home on 20 or more medications," he says. And not taking their medications or taking them incorrectly can cause problems that can land them back in the hospital—a situation all hospitals are trying to prevent.

In a pilot that began in September of 2010, patients with heart failure who were going home, rather than to a nursing home, met with a pharmacy technician the day before discharge. The tech gave them a seven-day four-times-a-day pill container along with several medication bottles, each of which contained a different-colored bead. The tech asked the patient (or the caregiver who would be setting up the meds) to follow the directions on the medication orders and place the correct bead in the correct hole in the pillbox. The person would have 15 minutes to complete the task. One mistake was considered failure.

Of the first 50 patients who were tested, 43 (86 percent) passed. Those who did not were referred to home health care, so a nurse could come in once a week to set up their medications. More important, the readmission rate for patients who went through boot camp was 14.6 percent; the rate for those who did not was 24 percent. After adjusting some parts of the process, Regions recently reinstituted the program.

Cannon says they plan to continue testing medication boot camp in hope of one day taking it beyond his department. "There are more people with heart failure in this country than any other diagnosis," he says. "It's a large population, and if you can make an impact on them, you can make a bigger impact on the whole issue of readmissions and general care." ■

Scenes from the 2011 Annual Meeting | Photography by Steve Wewerka

About 200 people attended the MMA's 158th Annual Meeting, which was held in September at the Duluth Entertainment Convention Center. The meeting was a time for physicians to meet, have fun, attend CME sessions, and discuss important health policy issues. More than 100 physicians served as delegates, helping to set the MMA's agenda for the coming year.

Rene Koronkowski, M.D., and Carolyn McClain, M.D., before the inaugural dinner.

MMA President Lyle Swenson, M.D., talks with a Duluth TV news reporter.

LEFT TO RIGHT: Wisconsin Medical Society President George Lange, M.D., David Agerter, M.D., Michael Heck, M.D., and Macaran Baird, M.D., meet in the lobby of the Duluth Entertainment Convention Center.

ABOVE: Former MMA President Kent Wilson, M.D., testifies before the House of Delegates.

RIGHT: Physicians convene the 158th MMA House of Delegates.

Newly elected Resident Fellow Section Chair Vikram Jadhav, M.D., Ph.D.

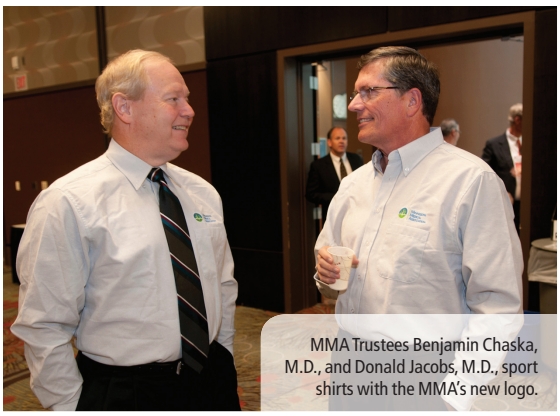
Fred Nobrega, M.D., executive director of the Zumbro Valley Medical Society, and Sally Trippel, M.D., talk in the vendor and sponsor area.

Ray Christensen, M.D., during a forum about the health care workforce shortage in rural Minnesota.

Maria Mendoza-Kundel, M.D., and Ana Fernandez-Pokorny, M.D., chat with Kevin Treacy, M.D.

Minnesota State Epidemiologist Ruth Lynfield, M.D., during a presentation about infectious diseases in Minnesota.

James Jordan, M.D., talks with Macaran Baird, M.D.



MMA Trustees Benjamin Chaska, M.D., and Donald Jacobs, M.D., sport shirts with the MMA's new logo.

Robert L. Veninga, Ph.D., professor emeritus in the University of Minnesota's School of Public Health, discusses physician well-being.

MMA staff member Mandy Rubenstein, Maya Babu, M.D., and Stephen Darrow, M.D., during the Resident and Fellow Section meeting.

Medical students Laura Gorsuch, Jessica van Lengerich, and Becky Stepan in the lobby of the Duluth Entertainment Convention Center.

Immediate Past-President Patricia Lindholm, M.D., talks to a news reporter about the annual meeting.

Lee Beecher, M.D., testifies before the MMA House of Delegates.

Louis Ling, M.D., John Abenstein, M.D., and Sandy Popham, M.D., serve on a reference committee.

Physicians Make Policy Recommendations

Minnesota physicians considered about 30 resolutions at the Annual Meeting. During their deliberations, the House of Delegates resolved that the MMA should:

- Oppose any amendment to the Minnesota Professional Firms Act that would further reduce physician autonomy (R105);
- Recommend that employers in Minnesota encourage exercise breaks, discounted membership to fitness centers, health coaching, and other efforts to increase physical activity among employees where appropriate (R202);
- Support legislation that requires anyone who administers vaccines to patients to enter the data into the Minnesota Immunization Information Connection registry (R206);
- Support efforts to prohibit the need to obtain prior authorization for medications that cost less than $25 (R207);
- Support legislation that would prohibit those younger than 18 years of age from using tanning beds (R209);
- Work with the Minnesota Department of Commerce to ensure that physicians are involved in the development of Minnesota's health insurance exchange and that the MMA study the issues relevant to physician practices associated with exchange implementation (R300);
- Support transparency in the Prepaid Medical Assistance Program and other state-supported medical plans to ensure efficient use of state dollars, quality care delivery, and access to care by patients (R301);
- Work with public and private payers to ensure at least one inhaled steroid and one short-acting beta adrenergic inhaler are included in their formularies with the lowest copay for that plan, and work with public and private payers to ensure coverage for at least one nebulizer and one asthma inhaler spacer and that any copays for those devices be at their lowest tier level (R306); and
- Work with the Minnesota Department of Health to evaluate the complexity and administrative burden of the health care home certification and recertification process and extend the time period between certification and recertification (R307).

Newly elected MMA Trustee Roy Yawn, M.D., listens to the debate at the MMA House of Delegates.

Not Adopted

Among the resolutions not adopted by the House of Delegates was one that called for the MMA to support annual screening for *Chlamydia* among all males and females 15 to 25 years of age with follow-up screening at the discretion of the physician (R201). The committee that considered the resolution said there were concerns about the cost-effectiveness of screening men and noted that the screening recommendation went beyond that suggested by the Centers for Disease Control and Prevention and the U.S. Preventive Services Task Force.

Look for the complete list of resolutions at mnmed.org or in the November issue of *Minnesota Medicine*.

Physicians Honor their Peers

Each year, the MMA honors physicians who have served medicine or their communities in extraordinary ways. The MMA presented the following awards at the annual meeting this year:

Distinguished Service Award

The MMA's highest award went to family physician **Anthony Jaspers, M.D.,** for his years of service to organized medicine. Jaspers graduated from the University of Minnesota Medical School in 1973 and completed his residency at Hennepin County Medical Center in 1976. He joined the Mankato Clinic in Lake Crystal, Minnesota, that same year and practiced there until 2009.

During his career, Jaspers held the top offices of the Blue Earth County Medical Society and served on the MMA Board of Trustees for 12 years. He also chaired the MMA Committee on Medical Practice and Planning and the MEDPAC Board. Jaspers served as vice speaker of the MMA House of Delegates from 1994 to 1995 and speaker from 1995 to 1997. He also has been an active member of the MMIC board.

Jaspers was elected an AMA alternate delegate in 1998 and served six years in that office. He was elected an AMA delegate in 2003 and is stepping down this year. He also has been active in the American Academy of Family Physicians and was chosen Minnesota Family Physician of the Year by the Minnesota Academy of Family Physicians in 1998.

Board Chair David Thorson, M.D., presents the Distinguished Service Award to Anthony Jaspers, M.D.

President's Award

Kenneth Crabb, M.D., an OB/GYN physician and founder of Advanced Specialty Care for Women in St. Paul, received the MMA president's award for leadership. Crabb is an adjunct professor at the University of Minnesota and past president of the East Metro Medical Society. Crabb has been active in the MMA for 31 years. During that time, he has served as a member of the MEDPAC Board, an AMA delegate, and a member the following MMA committees—Legislation; Medical Practice and Planning; Administration and Finance; and Nominating. He is a previous recipient of the MMA Community Service Award.

Community Service Award

Kenneth Ripp, M.D., a family physician at Raiter Clinic in Cloquet received the MMA's award for community service. After graduating from college, Ripp spent a year as a volunteer teacher in Kingston, Jamaica. In 1995, after medical school and residency in New York, he joined Raiter Clinic. His volunteer activities have included teaching English as a second language, acting as a medical liaison to the Hmong community, and encouraging youth participation in sports. Ripp helped create a Nordic ski program for youth in Cloquet and scours sales to buy skis for kids. The cross-country ski program has grown from six to 60 youngsters. In addition, he's coached youth soccer and helped found a year-round adult soccer league.

MMA Elects Officers

President

Lyle Swenson, M.D., an interventional cardiologist at East Metro Cardiology, St. Paul (see p. 28)

President-Elect

Dan Maddox, M.D., an internist and allergist at Mayo Clinic, Rochester

Secretary/Treasurer

David Westgard, M.D., a family physician and chief medical officer at Olmsted Medical Center, Rochester

Speaker of the House of Delegates

Mark Liebow, M.D., an internal medicine physician at Mayo Clinic, Rochester

Vice Speaker of the House

Robert Moravec, M.D., a family and emergency medicine physician at St. Joseph's Hospital in St. Paul

AMA Delegation

Paul Matson, M.D., an orthopedic surgeon with Orthopedic and Fracture Clinic in Mankato, was elected to the AMA Delegation. **Ray Christensen, M.D.,** a family physician at Gateway Family Health Clinic in Moose Lake, and **Sally Trippel, M.D.,** an internist at Mayo Clinic in Rochester, were re-elected to the delegation.

Steve Darrow, M.D., an internal medicine-pediatric nephrology fellow at the University of Minnesota, and **Will Nicholson, M.D.,** a family physician at St. John's Hospital in Maplewood, were elected alternate delegates. **John Abenstein, M.D.,** an anesthesiologist at Mayo Clinic, and **David Estrin, M.D.,** a pediatrician at South Lake Pediatrics in Plymouth, were re-elected as alternate delegates.

The MMA thanked **Blanton Bessinger, M.D.,** and **Anthony Jaspers, M.D.,** who are leaving the AMA Delegation, for their many years of service.

Ripp also has served as chief of Cloquet Community Memorial Hospital's Emergency Services and medical director of the city's ambulance service. He is medical director for quality at Raiter Clinic and president and medical director of quality for Integrity Health Network, which represents 25 independent clinics and 250 physicians.

MMA Immediate Past-President Patricia Lindholm, M.D., presents the Community Service Award to Kenneth Ripp, M.D.

MMA Board of Trustees

The following physicians were elected to the MMA Board of Trustees: **Macaran Baird, M.D.** (at-large), **Marilyn Peitso, M.D.** (North Central District), **Phillip Stoltenberg, M.D.** (Twin Cities District), and **Roy Yawn, M.D.** (Southeast District). Re-elected were **Beth Baker, M.D.** (Twin Cities District), **Michael Heck, M.D.** (Northeast District), **Donald Jacobs, M.D.** (Twin Cities District), and **Doug Wood, M.D.** (Southeast District).

Reinvigorating the MMA

Photo by Steve Wewerka

David Thorson, M.D.
MMA President

As I wrote in this column last year, the MMA Board of Trustees has been developing a strategic plan that will help the MMA respond to our changing times. Although our core purpose and mission are unchanged—to provide advocacy, information, education and leadership for Minnesota physicians and their patients—our long-term goals have been substantially modified.

Your voice is vital to helping us chart our course.

In developing our new goals, the board outlined a new vision for medicine in Minnesota, focusing on issues that matter most to you and to your patients. Our three- to five-year goals include:

1. Making Minnesota the healthiest state in the nation,
2. Making Minnesota the best place to practice medicine, and
3. Making the MMA the source for advancing physician professionalism in Minnesota.

To me, these goals are the very hallmarks of a strong medical association, and I am confident that they will position us to navigate the challenges we face regarding health care reform, cost pressures, clinical practice, and attitudes about joining organizations.

As we develop strategies for achieving these goals, we will need your help.

We recently sent out a survey asking for your opinion about the important issues outlined in the new MMA goals. I hope you responded. Your voice is vital to helping us chart our course for making Minnesota the healthiest state and the best place to practice.

Membership organizations like the MMA are experiencing tremendous change. We realize many factors influence the decision to join. To better understand what these are, we're attempting to learn more about members' and nonmembers' values and needs. We're asking members what they value most about membership and their reasons for joining, and we're asking nonmembers about the reasons that might lead them to become a member. We have started by talking with small groups of physicians, and we will continue to ask for your feedback during the coming months.

Going hand-in-hand with the new strategic plan is a new look for the MMA. We unveiled our new brand identity at the annual meeting, and you will be seeing our updated identity on all future MMA materials.

This is an exciting time for the MMA. I am proud of the work we have done to retool our strategy and implement a new, more modern brand identity. We see a future in which the MMA will play a significant role in the lives of Minnesotans and the physicians who provide their medical care. These steps will get us there.

Lyle Swenson, M.D., Inaugurated MMA President

MMA President Lyle Swenson, M.D., gives his inaugural address.

In his inaugural address, Lyle Swenson, M.D., said his goal for his year as MMA president is to fight the forces that drive physicians apart by supporting those principles of the profession that unify physicians. A specialist in interventional cardiology and cardiovascular diseases at East Metro Cardiology in St. Paul, Swenson noted that disagreements among specialty societies, the commercialization of health care, and the politicization of medicine threaten to drive physicians apart. He said he wants physicians to join together under the banner of the profession's core principles: to do no harm and to keep patients' health and well-being as the top priority.

During his speech at the annual meeting, Swenson reminded attendees of the origins of the medical profession. He talked about the contributions of the Greek physician Hippocrates, who established medicine's most enduring principles by calling on physicians to hold the health, well-being, and best interests of their patients above all else. And he noted that the prayer of Maimonides expressed a petition that is still relevant today: "Inspire me with love for my art and for thy creatures. Do not allow thirst for profit, nor ambition for renown, to interfere with my profession."

Swenson said that the current economic and political environment threatens to undermine the physician-patient relationship. "The conflict between economic survival and prosperity, on the one hand, and the best interest of our patients, on the other, is certainly not new; but our current conflict is unprecedented in its magnitude. How we as a profession respond to this conflict will have profound effects lasting many, many years," he said.

He ended by calling on physicians to renew their commitment to the profession so they "will be free to practice the science and the art of medicine with knowledge, integrity, empathy, and compassion for the benefit of their patients."

Lyle Swenson, M.D., at a Glance

Medical degree: University of Minnesota

Residency: Hennepin County Medical Center

Fellowship: Oregon Health Sciences University in Portland

Practice: Swenson practices at East Metro Cardiology in St. Paul and is a clinical assistant professor in the department of family medicine and community health at the University of Minnesota.

Swenson has served on the MMA committees on Legislation and Medical Practice and Planning and as vice speaker and speaker of the House of Delegates. He also has served as president of the Ramsey Medical Society. Swenson is a fellow of the American College of Cardiology and the Society for Cardiac Angiography and Intervention.

The Drug Rep Debate

By Howard Bell

Some miss them.

Some have moved on.

Docs weigh in on the value of pharmaceutical reps.

When Jon Hallberg, M.D., was medical director of the University of Minnesota's Primary Care Center in the early 2000s, managing the sample closet was a full-time job for a nurse. In 2004, the clinic went sample-free and drug rep-free, and Hallberg hasn't looked back. "Once you get rid of the samples and drug reps," he says, "you practice evidence-based prescribing. You don't get excited about new drugs that haven't been fully scrutinized and often aren't more effective than older drugs that cost much less. I don't miss the free lunches or the cakes shaped like Prozac. And I don't miss the information they provided, which is always one-sided." Instead, Hallberg uses UpToDate and the *Prescriber's Letter,* which he says is "fantastic," plus the *New England Journal of Medicine* and the *Journal of the American Medical Association* (*JAMA*) to learn how new drugs stack up against old ones.

Now medical director at Mill City Clinic in Minneapolis, where reps aren't allowed past the front desk, Hallberg says, "We've entered the golden age of generics, where we can prescribe so many great meds so cheaply. Cost is now part of the conversation between physicians and patients. I rarely put a patient on a new medication and only if there's a clear benefit to the patient."

Clinics and hospitals big and small throughout Minnesota have restricted drug company reps' access to physicians or completely banned them from their premises. It's a trend that gained momentum five years ago, after influential physicians writing in the January 25, 2006, issue of *JAMA* called on academic medical centers to set an example by no longer allowing their physicians to accept gifts, trinkets, vacations, tickets to shows and sporting events, or payment for speaking about a drug or device company's products. The concern was that such gifts influence prescribing.

As a result of hospitals and clinics tightening their rules about allowing drug reps through the door, physicians have had to find new ways to learn about the pharmaceuticals they prescribe. Some are happy with this change, others aren't. Here's how a few feel about the issue.

Moving On

Relying on Pharmacists

At Essentia Health in Duluth, "drug reps are pretty much totally out of the picture," says Kenneth Irons, M.D., a family physician who spearheaded Essentia's effort to purge its clinics of drug-related gifts and trinkets back in 2006. "I know a lot of reps in northeast Minnesota have lost their jobs in the last three years," he says.

There are a couple of exceptions to Essentia's no-rep, no-sample policy. Physicians can make a special request to get a sample of a particular drug. For example, some cardiologists request samples of Plavix, a medication used to prevent blood clots, which they will give to patients going home on weekends after a heart catheterization procedure to ensure that they have the medications they need until they can fill their prescription. Essentia doctors are allowed to attend dinners sponsored by drug companies on their own time, but Irons believes attendance at such events has drastically declined.

Essentia's electronic medical record (EMR) is linked to the *Medical Letter,* the *Pharmacist's Letter,* and UpToDate, along with a few peer-reviewed journals. "None of these accept grant money, donations, or advertising," Irons says.

In addition, Essentia's pharmacists research the safety, effectiveness, and cost of all drugs before they're added to the formulary. They also brief physicians on medical management issues, for example, for patients on warfarin. "Our staff pharmacists provide us good reviews on new drugs," Irons says.

Looking to Peers

At Olmsted Medical Center in Rochester, drug company reps used to be the ones to show nurses and physicians how to use technique-critical devices such as inhalers. So when Olmsted went rep-free five years ago, there was no one to take over that teaching role, according to Barbara Yawn, M.D., a family physician and director of research. That has since changed. Today, the allergy nurses, the allergist, and Yawn offer regular training sessions for the nurses, who then teach patients.

Reps are still allowed to give lunch talks at Olmsted, but Yawn says they're poorly attended because physicians are busy and many presenters "have no clinical experience and are unlikely to provide a balanced view." Instead, Yawn says, most of her colleagues rely on in-house CME sessions, along with "the usual journals of choice" and informal chats with other physicians to learn about new drugs. As for samples, most Olmsted docs don't long for the old days, although some psychiatrists wish they could still get samples.

Nearby at Mayo Clinic, hospitalist Christopher McCoy, M.D., says Mayo physicians get "excellent information" from clinical pharmacists, who answer questions about dosing, interactions, and appropriate uses. For information about newer meds, they sometimes rely on other Mayo physicians, who are experts on that particular drug. For example, McCoy's internal medicine hospitalist group recently invited a cardiologist to talk about dabigatran, a new anticoagulant. "I've never heard a Mayo physician lament no longer having the opportunity to meet with a drug rep," he says.

Nothing but Net

David Ross, M.D., a family physician at Affiliated Community Medical Centers in Willmar still relies on drug companies for information—but not the reps. "I Google a drug company website, where I read the factual drug information rather than the brochure propaganda," he says. He also likes the *Prescriber's Letter,* which he says tends to cover drugs germane to primary care and offers him the opportunity to earn CME credit. "It also provides alerts to the lines of reasoning drug reps may use for new drugs and comments on their validity," he adds.

The Internet has made Ross's withdrawal from drug reps easier. "In the age of computers, mobile devices, and applications, technology has placed a new spin on rural medicine," he says. "I'm a few keystrokes away from a wealth of information. Personally, I don't miss rep visits one bit. I got tired of the interruptions, the patronizing, the graphic distortion, and the donuts. And I agree with the studies that show that even minor gifts can influence prescribing habits."

Ross helped Affiliated change its policies and go sample-free and partially rep-free in 2007. No one-on-one visits are allowed in patient-care areas, but reps can still set up displays in non-patient-care areas, where physicians can seek them out instead of the other way around. He says physicians sometimes meet with drug reps by appointment. "We just don't want them popping up in the middle of the day to fill sample closets and interrupt patient care."

He says a few specialists still accept branded samples of drugs that have no generic alternative or where special patient instruction is needed. For example, Affiliated's neurologist requests injectable (branded) imitrex, which works more quickly than the oral generic version of the drug. He uses samples to show patients how easy it is to administer the injection in order to get them over their fear of doing them.

Turning to EMRs

Electronic medical record systems have made it possible to provide physicians with real-time, evidence-based drug information, according to Brian Rank, M.D., an oncologist and medical director of HealthPartners Medical Group. "A couple of clicks in the EMR gets us access to a number of resources including the *Medical Letter,* Micromedex, the Cochrane Library, UpToDate, and the Institute for Clinical Systems Improvement guidelines," he says. But physicians don't have to do all the searching themselves. HealthPartners' Pharmacy and Therapeutics Committee analyzes the clinical and cost-effectiveness of all drugs before they're added to the formulary. "We link our docs to the safest, most effective drugs, and that's typically a generic," Rank says. "Eighty-two percent of drugs we prescribe are generic."

Only a couple of the 150 clinical departments at HealthPartners still give samples to patients, according to Rank. Usually they do so to make sure the drug is effective and tolerated before it's prescribed, or if the drug requires prior authorization and the clinician believes the medication is needed immediately. He says drug and device reps can visit physicians only if a physician leader requests it, which rarely happens. "Physicians are way too busy, and there are far less biased sources of information readily available."

HealthPartners, Park Nicollet Health Services, Hennepin County Medical Center, Fairview Health Services, and Allina Hospitals and Clinics have all been learning from each other about best practices for interacting with drug and device companies, according to Rank. "We all have our own policies," he says. "But we're all headed in the same direction."

Do We Need *Firewalls?*

In 1993, Minnesota became the first state in the nation to ban gifts and payments from drug companies to physicians and other prescribers. Since then, a handful of states have followed suit with some sort of restriction on gifts.

Minnesota's gift ban does not apply to drug samples, items with a total combined retail value of less than $50 in a given year, consulting fees, paying reasonable amounts for expenses to physicians who present at conferences and meetings, and educational materials including textbooks.

In recent years, several attempts have been made to tighten up the law. In 2009, Sen. John Marty (DFL-Roseville) and Rep. Tina Liebling (DFL-Rochester) introduced legislation that would clarify what is considered a gift, who is a prescriber, how records are made public, and penalties for not reporting. It would not have prohibited practitioners from receiving free drug samples. The bill received hearings that year and was reintroduced in 2010. It has not gone beyond committee hearings.

Although it is not as extensive as Minnesota's gift ban, a provision in the 2010 Patient Protection and Affordable Care Act requires pharmaceutical companies and medical device manufacturers to report all direct payments or gifts made to physicians and teaching hospitals valued at more than $10 to the Department of Health and Human Services starting in January 2012. (Drug and device samples are exempt from this "sunshine provision.") The information will be made available on a searchable website starting September 30, 2013.

Not all support such attempts to erect firewalls between doctors and pharmaceutical and biomedical device industry reps. One of Minnesota's most vocal opponents is Eagan endocrinologist J. Michael Gonzalez-Campoy, M.D., Ph.D., FACE. Gonzalez-Campoy says physicians couldn't practice medicine without the drugs and technology provided by industry, "so casting them as the enemy is just plain wrong. We need to consider the working relationships between physicians and industry for what they are: incredibly beneficial to science."

Gonzalez-Campoy is so passionate about that belief that he's helped launch two groups to promote the benefits of industry-medicine partnerships: the national Association of Clinical Researchers and Educators (ACRE), which was established in 2009 in Boston, and the Minnesota Clinical Research Alliance, which was formed last June in Minneapolis. Both groups have the goal of influencing the public's and policy makers' thinking, which they say is decidedly anti-industry these days.

Gonzalez-Campoy believes attempts to limit physicians' access to industry reps is bad for medicine. "Physician education is advanced by marketing," he says. "Physicians need to have access to medical information of all kinds—including marketing materials." And he believes Minnesota's actions to separate medicine and industry have had a negative impact on the state's biomedical business climate. "The Minnesota economy has taken a tremendous hit because of all this. There has been a loss of sales jobs. Many biotech companies have gone under or chosen to move their business away from Minnesota. It's a big contributor to the economic downturn."

Gonzalez-Campoy does not believe he's alone in his thinking. "I think a large number of physicians feel the way we do," he says. "But most don't want to rock the boat."

Missing Them

Liaisons not Cheerleaders

Frank Rhame, M.D., an infectious disease specialist at Abbott Northwestern Hospital, reads journals and looks up drug information and consensus prescribing guidelines on UpToDate and Epocrates. But he doesn't like the way Epocrates sells his online search history to pharmaceutical companies. "I decided to subvert their little side business by repeatedly looking up birth control pills, just to confuse them."

Rhame, who's practiced infectious disease medicine since 1975, says he learned good information from drug reps if they were there to talk about drugs for infectious diseases. "I know that topic cold," he says, "so they can't shade things with me. But if they want to talk about drugs for hypertension or depression, then I needed protection from them."

As an HIV clinician, Rhame has always felt it's important for him to stay in touch with "medical science liaisons" from drug companies. Liaisons are usually M.D.s or pharmacy Ph.D.s who have a deeper knowledge than sales reps do. "Liaisons aren't former cheerleaders who've memorized five sentences from the label, which you can read yourself," he says. "Liaisons can talk about off-label uses and have high-level discussions about comparative research."

The FDA allows liaisons to meet with researchers in order to facilitate innovation. "The research information that liaisons give me," he says, "has already been presented somewhere else, like at resistance workshops, a metabolic side effect meeting, or a pharmacology meeting that I might not have attended and, therefore, might not see unless they talk with me.

"Some, shall we say, politically correct physicians might recoil from liaison meetings and dispute their benefit; but the fact is, infectious disease specialists benefit from talking with drug company folks with a high knowledge level. And if I benefit, then my patients benefit."

Limiting Face Time

Dermatologist Charles Crutchfield III, M.D., of Crutchfield Dermatology in Eagan, relies on conferences, specialty society sources, journals, and colleagues for drug information. "But," he says, "I still think pharmacy reps provide a valuable role in educating us about new meds, even given their bias." He says his clinic allows two to four visits per month and that he gives reps five minutes of face time. "It's very manageable."

Dermatologists have traditionally given out a lot of samples, especially to patients who need only a small amount of medicine or who have trouble paying for it. "They seem to keep me well-stocked," he says, "and the amount of time it takes to manage the cabinet is minimal."

Crutchfield says he doesn't miss the days when some reps had the audacity to ask if they could count on him to write the next five prescriptions for their medication. "Those really were the bad old days," he says.

Sorry to See Samples Go

Cardiologist Les Forgosh, M.D., misses the easy access he used to have to drug reps and the samples they provided. HealthEast acquired his clinic last January, so he and his colleagues at St. Paul Cardiology now must follow HealthEast's guidelines. "Yes, I know I can get the latest information from Medline, journals, and CME—and I use these," Forgosh says. "But that all takes time, and when it comes to getting the latest information about the newest drugs, reps are walking encyclopedias."

HealthEast allows each department to decide whether to meet with reps. As a group, the cardiologists decided not to, according to Forgosh. A physician can request a one-on-one meeting with a rep, but that rarely happens. Forgosh recently met with one for the first time in eight months.

"I'm a definite proponent of providing samples to patients, but I can't do that now," he says. "Samples are a good way to see if the patient tolerates a drug before they go out and buy it themselves, and samples provide a short-term supply until patients fill prescriptions."

Cardiologists often prescribe expensive medications, and samples help defray the costs for patients. Plus reps provide coupons. "With Plavix, you're talking about $180 per month. There are no generics, and it's one of only two drugs in its class, both of which are very pricey," he says. "Drugs for pulmonary hypertension can cost $1,000 per month. I know the coupons are online, but I have to search for them and that takes time. The reps just hand them to you."

Preferring Presentations

Harvey Frank, M.D., a family physician in Allina's clinic in Forest Lake, searches for drug information in UpToDate and Micromedex, which are embedded in Allina's employee intranet. But having practiced medicine for 34 years, during which drug company lunches and dinners were part of the routine, he admits that he misses those outings. "Often, the speaker at these was a local specialist talking about general topics, not a drug rep," Frank says. "But these went away along with the drug rep meetings. Historically, I've gotten my information from reps, articles, and conferences. Now I have to struggle to find what I need. Often, I don't learn about a new drug until well after it's released."

Frank also misses the quarterly presentations by Allina's Ph.D. pharmacists about new drugs and new uses for old drugs. Budget tightening put an end to those, he says. "I feel like primary care physicians are unfairly portrayed as being too quick to use branded meds because of drug rep presentations or samples. There's ample pressure from patients to stay away from high copays. Generally, we're all careful to prescribe generics whenever we can."

Devices are Different

Anesthesiologist Mark Eggen M.D., who practices at Allina's Unity and Mercy hospitals and admits to planning his route through the hospitals to avoid drug reps, says he still relies on reps from medical device companies for how-to information. "For new devices I use, such as ultrasounds for placing nerve blocks, the reps offer useful advice. Every hip and knee replacement I'm at, there's an orthopedic implant rep present in the OR and available if any questions arise."

Minnesota's gift ban law doesn't apply to device reps, according to Eggen, so it's common to see them outside the ORs where cardiac and orthopedic procedures are done.

That's changing, however. A sign recently posted outside the door to the physicians' lounge in Unity's surgery area says "Physicians only—vendors are prohibited from this area." In addition, Allina is changing its policy so that vendors will only be allowed in the surgical services area of its hospitals by appointment.

Maintaining avenues of communication can benefit both physicians and reps, according to Mayo's Christopher McCoy, M.D. "Especially for devices," he says, "it can be helpful for physicians and reps to meet face-to-face, so the reps can demonstrate how to use new devices and physicians can offer feedback on ways to improve them."

"You need a certain degree of engagement between clinicians and industry," HealthPartner's Brian Rank, M.D., says. "We do sometimes allow reps in the OR to assist with a new device, particularly when learning to use or researching a new device, which we recently did for percutaneous aortic valves at Regions Hospital." Rank says HealthPartners also has "entrepreneurial/inventor docs" who work with device industry researchers to invent or improve products, but not sales reps.

Who Should Teach Docs about Drugs?

In an article published in the *New England Journal of Medicine* in March, Jerry Avorn, M.D., of Harvard, pointed out that the United States has been debating the issue of who should teach doctors about drugs for 50 years, ever since Sen. Estes Kefauver (D-Tennessee) introduced legislation that sought, among other things, to place the burden of educating physicians on the federal government.

Opposed by the pharmaceutical industry and the American Medical Association, Kefauver's bill might have been defeated altogether had it not been for the thalidomide crisis in the early 1960s, which raised public consciousness about the potential dangers of pharmaceuticals as well as the public's general comfort with the idea of the government protecting their health. The resulting law wasn't quite what Kefauver envisioned, but it gave the Food and Drug Administration the authority to require pharmaceutical companies to provide evidence of efficacy and safety before a drug could be marketed. Since then, drug companies have been doing most of the educating about prescription drugs.

Academic Detailing

Some states, however, have tried an approach "invented" by Avorn himself. Hospitals and clinics have replaced visits from drug company reps with visits from physicians, nurses, and pharmacists who have been trained to provide doctors with independent drug reviews rather than sales pitches. Called "academic detailers," they provide information, much of which comes from Harvard's Independent Drug Information Service and Oregon Health & Science University's Drug Effectiveness Review Project.

The idea for academic detailing emerged 30 years ago when Avorn proposed using the pharmaceutical industry's marketing tactic of one-on-one visits with physicians to promote evidence-based prescribing. "Academic detailers even bring pizza for lunch," says Peter Wyckoff, director of the Minnesota Prescription Coalition, a group of consumers, providers, payers, and labor and professional organizations that has worked, so far unsuccessfully, with the Pew Charitable Trust Prescription Project to create an academic detailing program in Minnesota. "What changes is who's bringing lunch and how objective their information is." Academic detailers discuss the pros and cons of competing drugs and share a scope of knowledge that might be broader than the typical drug rep's.

Pennsylvania's academic detailing program is the nation's largest and oldest. It receives state funding because it is intended to reduce the amount the state spends on its Medicaid patients. A 2008 study by Harvard Medical School and the Pew Prescription Project showed that Pennsylvania doctors who participated in academic detailing visits for acid reflux medications saved $120 per doctor per month. Results of a multi-state randomized trial published in the *New England Journal of Medicine* in 1983 showed that academic detailing programs save $2 on drugs for every $1 it costs to run the program.

"Academic detailing saves money," Wyckoff says, "but it's not just about saving money by using generic drugs. We're talking about what's safest, cheapest, and most effective based on the best research available." For many chronic conditions, there's wide variation in prescribing patterns, according to Wyckoff. The research, he says, "shows there are best-in-class ways to treat most conditions. Academic detailing narrows the gap between evidence-based prescribing and actual prescribing that is often blamed on vigorous marketing of newer, more expensive drugs."

Supporters say academic detailing improves patient outcomes. But good data for that are lacking, according to Marjorie Powell, senior assistant general counsel for the Pharmaceutical Research and Manufacturers of America. "Some of these drug comparison studies don't even factor in the benefits some newer drugs offer," she says. For example, a newer drug might have fewer or less-severe side effects than its cheaper generic counterpart. Patients might not have to take a newer drug as often. And a newer drug might reduce or eliminate the need for frequent lab tests. "Everyone has their biases," Powell says. "Some academic detailers do little more than tell doctors, 'You don't need to use the newer drug.' The more money they can save a state in drug expenditures, the better they look, even if costs increase in other areas such as lab tests or more doctor visits."

As the cost of medications for chronic conditions has escalated, the number of state-sponsored academic detailing programs has grown, although slowly. Today, 17 such programs exist. Minnesota's Prescription Coalition submitted two bills to the Minne-

sota House and Senate in 2010 that would have established a detailing program in the state. They generated interest on both sides of the aisle in both chambers, according to Wyckoff, but not enough. "The mistake we made the first time around was in trying to do too much all at once," he explains. "We accidentally designed the nation's largest detailing program." Next time, he says, they'll start with a pilot program for one class of drugs in a limited geographic area. Minnesota's Department of Human Services would receive the money to administer the program and train detailers. Wyckoff estimates that a reasonably sized pilot would cost about $1 million per year.

Still Debating

Whether state-funded academic detailing programs will become a reality in Minnesota and elsewhere in the country and whether this approach is indeed the best way to help physicians make better decisions about prescription drugs remains to be seen. Indeed, for many, the answer to the question of who ought to be teaching physicians about new pharmaceuticals is still being sought.

Avorn wrote in his article that given current competing concerns about government intervention and industry involvement in medicine, the most likely answer today is some sort of public-nonprofit entity—one that is funded by government but run by a nongovernmental organization that has no ties to industry and that would generate the scientific content.

Avorn concluded, "Enlightened by our tumultuous experience with medications and drug communications over the past half-century, we are still working on a sustainable answer to this question that lies at the heart of medical practice." **MM**

Howard Bell is a freelance writer in Onalaska, Wisconsin.
Carmen Peota and Kim Kiser contributed to this article.

Don't Assume the Worst

What do you think when a patient comes to the ER seeking relief from chronic pain?

By Bradley S. Hernandez, M.D.

There are many aspects of my job as an emergency physician that I love. I love to care for the critically injured. I love knowing that when people have no one else to help, heal, or shelter them, they can come to my emergency department. Being part of the safety net for the community is an honor that I cherish and wear proudly, like a firefighter wears his badge. I also love having the opportunity to save a life occasionally, although I know that saving lives is really not what keeps me and other emergency physicians coming back for the next shift. What sustains us is our ability to reduce suffering, and we accomplish this in many ways. We do it by making a diagnosis that the patient's primary physician could not, by admitting an elderly parent who is too frail to stay at home, and by relieving the pain of the woman with the fractured wrist or the man with renal colic.

But there's a troubling paradox about our work: The very narcotics that we use to alleviate acute suffering can cause another kind of suffering. As a result, we face a very difficult population of patients—those who perpetually seek narcotics for their chronic pain.

I admit I would prefer to see almost anyone else. Bring me a non-English-speaking patient and I will readily dial the interpreter. Give me an elderly nursing home patient with dementia, and I will gladly review her medication list and do a thorough evaluation. Show me a patient who is angry because he feels he did not get good care and I am happy to defuse the tension by explaining what we did, why we did it, and where he should go from here.

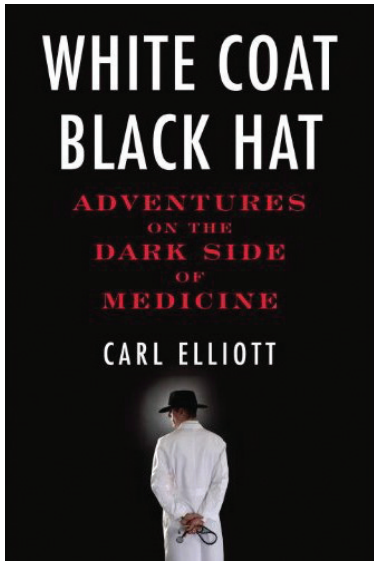
But the patient who comes to the emergency department seeking narcotics is my greatest challenge. Nothing makes me more anxious than seeing the name of a familiar patient yet again seeking treatment for chronic pain. And when I learn that this is her eighth visit in three months, I panic. Am I going to have to confront her? If I do, will she ask to see another provider? Will she complain to the patient representative? No provider wants to think he is being manipulated, so I am cautious, sometimes overly cautious.

But why is that? If the thing that puts a bounce in my step is relieving suffering, then shouldn't I have the most sympathy for the patient with the most pain? Unfortunately, it's not that simple. The medications used to treat pain can be sold illegally on the street. If I prescribe narcotics to a chemically dependent patient, I contribute to their addiction. Yet if I withhold medications from a patient with legitimate pain, I am cruel. Trying to understand a patient's true motivation in the 10 minutes I am allotted for a visit is daunting, if not impossible.

Much of my frustration stems from the fact that the patients who are seeking narcotics are a product of our own creation. At some point, we prescribed narcotic medications believing they were justified, and somewhere along the way, the patient's best interests got lost. Most do have some component of real disease, and we cannot forget that. These patients deserve our patience and attention, yet they also need our highest index of suspicion. What makes matters worse is at the end of the day we have no way of knowing whether we have relieved suffering or contributed to it. So what is a physician to do?

In the end, all you can do is give these patients the benefit of the doubt. If they tell you they are visiting from out of town and forgot their medicine, believe them. If they have a complicated history, listen to them. If they are angry, empathize with them. And if they admit to chemical dependency, ask them about it, listen to them, and offer resources that can help them. Doing so may relieve their suffering more than you know. **MM**

Bradley Hernandez is an emergency physician at Regions Hospital in St. Paul and an assistant professor of emergency medicine at the University of Minnesota Medical School.



White Coat, Black Hat: Adventures on the Dark Side of Medicine, Carl Elliott, Beacon Press, 2010

Shady Business

Ethicist Carl Elliott's latest book paints Big Pharma as medicine's worst bad guy but also implicates all sectors of health care in the seamy side of medicine.

BY CHARLES R. MEYER, M.D.

Who the bad guys in health care are today depends on who's doing the judging. Politicians seem to think it's doctors and hospitals who spend like lottery winners strolling Madison Avenue. Doctors and hospitals probably feel the same way about politicians, but clearly, insurance companies are high on their list, especially with their habit of practicing medicine from the board room. Some would even finger patients who feel entitled to their piece of the lush American medical mecca. But the ones who make everybody's list are the pharmaceutical companies, perceived as rich in dollars and poor in morals. Certainly "Big Pharma" is the main demon in bioethicist Carl Elliott's exposé *White Coat, Black Hat: Adventures on the Dark Side of Medicine*, in which he portrays them as mammoth businesses that stretch and warp ethical boundaries, frequently dragging physicians with them.

In chapters peppered with interviews with former pharmaceutical company employees, Elliott, a physician and faculty member in the University of Minnesota's Center for Bioethics, covers many of the well-publicized "sins" of the pharmaceutical industry—lavish wooing of physicians with dinners and trips, employment of "thought leaders" to provide glowing testimonials for their drugs, hiring medical "ghostwriters" to produce favorably spun research papers that list other authors, and sponsorship of private research to verify the benefits of their drugs. He devotes numerous pages to the case of Farouk Abuzzahab, M.D., a Minneapolis psychiatrist cited by the Minnesota Board of Medical Practice for endangering patients in private research projects performed through his office. Elliott's lead chapter, which was first published in *The New Yorker* in 2008, explores the strange world of professional subjects, dubbed guinea pigs, who participate in Phase I trials of new medications for substantial payments. Some of these people are college students looking for extra money, but many are down-on-their-luckers looking for any source of income. Each topic raises serious questions about the undue if not unholy influence of Big Pharma on the scientific practice of medicine.

Less publicized is the pharmaceutical industry's practice of "branding" diseases, which Elliott says occurs when drug companies have developed a drug for a disease that is uncommon or stigmatized. To expand the market, Elliott says, they "identify and promote a disease for the drug to treat." Branding originally targeted physicians, as when Merck in the 1960s sent a copy of the book *Recognizing the Depressed Patient* to physicians to convince them that depression, heretofore thought rare, was really quite common and needed treatment with their recently released drug, amitryptiline. Subsequently, drug companies have shifted their branding efforts to patients. "To brand a disease is to shape its public perception in order to make it more palatable to potential patients. This is usually done by telling people that the disease is taken seriously by doctors, that it is far more common than they ever realized, and that having it is nothing to be ashamed of. Bob Dole de-shamed erectile dysfunction, which led to sales of Viagra for Pfizer. Pharmacia redefined the yukky sounding "urge incontinence" as "overactive bladder," resulting in banner sales of Detrol.

According to Elliott, Big Pharma's appeal to patients has gone beyond direct-to-consumer advertising. They now search for and reach out to patient thought leaders, bloggers, and Tweeters. As one consultant describes these patient gurus, "You treat them almost the same way you'd treat a medical journalist. … They are your press." Drug companies also supply the funding for many patient support groups. Elliott opines that as the influence of physicians has waned in society, the power of

patients has increased: "If physicians are trying to sell you something, you can no longer assume they have your best interests at heart. Patients, on the other hand, are in a different position. At least on the surface, patients do not have any obvious financial interest in marketing a drug. Their authority comes from first-hand experience of an illness and its treatment."

Shady ethical behavior is at the core of most of the stories Elliott tells. And he doesn't spare his own profession. He describes multiple arrangements between drug companies and ethicists who serve on their advisory boards and review protocols for pay. Elliott questions whether paid ethics consultants can be truly objective. "Any ethical problem can be approached from many different perspectives, each of which will come with its own subtleties and nuances and compromises. It is entirely possible that puzzled executives may want to hire an ethicist to guide them through some perilous terrain. However, they might also simply want a congenial, like-minded ethicist to provide cover for what they plan to do anyway. And to the ethicist who is hired, this will not feel like a moral compromise. It will feel like working with an ally."

The sway of the pharmaceutical industry portrayed by Elliott is global if not cosmic. You leave this book wondering if anybody in medicine is free of the corrupting influence of Big Pharma.

White Coats, Black Hats is an expose and, as such, makes no pretense of even-handedness. We do need the pharmaceutical industry, but we clearly need to redefine its relationship with the medical profession. With sunshine laws requiring doctors to reveal their connections to industry, the ethical microscope is being focused, and hopefully we are moving toward a health care system without bad guys. **MM**

Charles Meyer is a practicing internist and editor in chief of *Minnesota Medicine*.

Going Over the Patent Cliff

What will it mean for physicians and patients as top-selling prescription drugs lose their patent protection?

By Jon C. Schommer, Ph.D.

Patents on a number of blockbuster drugs will expire in 2011 and 2012, costing the pharmaceutical industry an estimated $250 billion in sales over the next four years.[1] This long-anticipated "patent cliff" has haunted pharmaceutical companies for years but has been eagerly anticipated by generic manufacturers, consumers, and health plans. Once a drug loses its patent protection, a lower-priced generic version can quickly capture up to 90 percent of sales. For consumers, health plans, and others who pay for prescription drugs, the savings can be significant.

Some of the drugs set to lose patent protection in 2011 and 2012 are the cholesterol drug Lipitor, the antiplatelet medication Plavix, and the asthma drug Singulair (Table). Manufacturers will be able to sell these popular medications in generic form, making them more affordable. But what will this mean for future innovation in the pharmaceutical industry? Will it hinder the ability of drug companies to develop new and better products?

Industry Out of Control

The book *Pharmaplasia* by Michael Wokasch offers an interesting perspective on how we got to where we are today and what we might expect in the future. Wokasch asserts that the pharmaceutical industry's problems can be blamed on "pharmaplasia," rapid, uncontrolled growth of a pharmaceutical company that exceeds its capacity to be managed effectively, resulting in a series of unintended consequences.[2] He describes how advances in science and medicine, combined with dynamic health care

Table

Top Five Best-Selling Drugs Set to Lose Patent Protection in 2011 and 2012

Patent Expiring in 2011	Use	Manufacturer	2010 U.S. Sales (in millions)
Lipitor	Cholesterol	Pfizer	$5,329
Zyprexa	Antipsychotic	Eli Lily	$2,496
Levaquin	Antibiotic	Johnson & Johnson	$1,312
Concerta	ADHD/ADD	Johnson & Johnson	$ 929
Protonix	Antacid	Pfizer	$ 690
Patent Expiring in 2012			
Plavix	Antiplatelet	Bristol-Myers Squibb / Sanofi-Aventis	$6,154
Seroquel	Antipsychotic	AstraZeneca	$3,747
Singulair	Asthma	Merck	$3,224
Actos	Type 2 diabetes	Takeda	$3,351
Enbrel	Arthritis	Amgen	$3,304

Source: IBIS World

markets, created an increasingly complex environment for drug discovery, development, and marketing. That complexity, along with the industry's pursuit of revenue growth and profits, has driven decisions about which new drug products to develop.[2]

Having an extensive pipeline of commercially viable new products has been the foundation for long-term success in the pharmaceutical industry. Wokasch describes how a series of missteps in the past several decades has led to a high rate of failure in drug development efforts (for example, over-reliance on computer-assisted drug design and high throughput screening resulting in a hit-or-miss approach, mismanagement, dilution of scientific expertise, application of inferior research tools, inability to correctly interpret findings, unrealistic timelines, and clinical trial fraud). He explains that because of these missteps, many now companies have fewer products in the pipeline.[2]

Strategies to rebuild product pipelines through company mergers, patent extensions (reformulations and me-too products), or aggressive marketing schemes (illegal off-label promotion) have been, in my opinion, desperate and ineffective attempts to generate revenue and capture market share. As a result, the number of new molecular entities approved by the Food and Drug Administration fell from 53 in 1996 to just 18 in 2006.

Armed with new knowledge about the human genome, pharmaceutical companies recently have turned their attention to developing biologics.[3] The complexity of manufacturing these large-molecule proteins not only provides pharmaceutical companies the opportunity to seek intellectual property protection[4] but also supports these companies' arguments for charging very high prices for their biologic drugs (in the tens of thousands of dollars per month for some of these products as compared with hundreds of dollars per month for small-molecule pharmaceuticals).

What's Next?

It appears that the patent cliff has motivated the pharmaceutical industry to take a new high-risk/high-reward approach. As a result, it is likely that in the future prescribers will have to decide whether to use relatively inexpensive, generically available small-molecule drugs or very expensive, single-source, large-molecule biologics.

Several other factors are likely to influence prescribing decisions as well. They include:

1. The extent to which the delivery of health care will be managed;
2. Whether pricing pressures will continue to increase;
3. Whether traditional pharmaceutical industry marketing tactics will become obsolete;
4. Whether new products will have to meet market expectations for superiority over current options; and
5. The fact that evidence will have to be provided to support premium pricing.

That certain blockbuster drugs are becoming available as generics is welcome news for payers. However, the pharmaceutical industry already is reacting to the anticipated loss of revenue by changing its strategy. For that reason, health care providers who are able to translate evidence-based, comparative effectiveness information into patient-centered, individualized care are going to be more valuable than ever before. **MM**

Jon Schommer is a professor in the University of Minnesota College of Pharmacy.

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A Review of Multidrug-Resistant Enterobacteriaceae

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■ Enterobacteriaceae that are resistant to multiple drugs are a public health concern and present a challenge to health care providers in terms of prevention and control. This article describes the changing resistance mechanisms that allow bacteria to circumvent antibiotics and how multidrug-resistant bacterial infections can spread within hospitals, among health care facilities, and across national borders. It also discusses the challenges associated with identifying and treating these infections and what health care providers need to do to prevent their transmission.

In early 2009, a 50-year-old man with gastric cancer was admitted to a Minneapolis-St. Paul area intensive care unit (ICU) with severe dehydration and presumed *Clostridium difficile* infection. He spent a month in the hospital and was treated with several broad-spectrum antibiotics before being discharged to a local long-term acute care hospital. Midway through his hospitalization, a tracheal aspirate culture grew *Klebsiella pneumoniae* that was resistant to all cephalosporins and carbapenems. Polymerase chain reaction (PCR) testing by the Centers for Disease Control and Prevention (CDC) confirmed that the isolate carried the resistance gene for *K. pneumoniae* carbapenemase (KPC), bla_{KPC}. This was the first time this highly resistant bacterium was detected in Minnesota.

Choosing the right antibiotic for the right microbe is becoming increasingly difficult. Gram-negative organisms carrying multiple resistance genes that make them extremely drug-resistant have emerged; some are even pan-drug-resistant. The emergence of these highly resistant bacteria is rapidly changing the way health care providers and public health officials approach the treatment and control of bacterial infections, requiring us to invest heavily in the development of new antibiotics and to practice careful antimicrobial stewardship and infection control and prevention.

Brief History of ß-Lactamases

Among the many resistance mechanisms available to bacteria for circumventing antibiotics are the ß-lactamases, enzymes that target the ß-lactam ring found in penicillins, cephalosporins, monobactams, and carbapenems. They are naturally found in most Gram-negative bacteria (GNB).

Gram-negative resistance became a clinical concern soon after the introduction of ampicillin, the first semisynthetic penicillin shown to be active against GNB. In 1963, a strain of *Escherichia coli* discovered in Athens carried the first plasmid-encoded ß-lactamase, named TEM-1, which conferred resistance against ampicillin.[1] As different resistance mechanisms have evolved, plasmids and other mobile genetic elements have been instrumental in the horizontal transmission of resistance genes, with multiple genes conferring resistance to multiple antibiotics.

Plasmid-mediated ß-lactamases have spread worldwide. TEM-1 and another ß-lactamase, SHV-1, once were the most frequently occurring enzymes among the Enterobacteriaceae.[2] By the 1970s, resistant GNB had become the prominent nosocomial pathogen. Many of these organisms carried plasmids encoding multiple antibiotic-resistant genes in addition to ß-lactamases. Interestingly, TEM-1 and SHV-1 remained relatively unchanged for 20 years. However, in the early 1980s, several new antibiotics were introduced, including third-generation cephalosporins. By 1983, the first extended-spectrum ß-lactamase (ESBL) was found in strains of *Klebsiella* isolated in Germany. These mutants of SHV-1, designated SHV-2, inactivated the extended-spectrum cephalosporins.[3] As these enzymes mutated to make different classes of antibiotics inactive, the number of identified ß-lactamases has multiplied, and there are now hundreds.

The latest iteration of ß-lactamases is the carbapen-

emase. This enzyme inactivates carbapenem, a class of antibiotics indicated for the treatment of ESBL-producing bacteria. The most common carbapenemase is the KPC, which was first isolated in North Carolina in 1996.[4] *K. pneumoniae* carbapenemase has spread worldwide and has been responsible for a number of reported outbreaks of carbapenem-resistant Enterobacteriaceae (CRE). Hospitals in New York and New Jersey have been particularly affected. The most recent data collected by the CDC show that CRE caused by the KPC enzyme have been reported in 36 states.[5]

Another emerging carbapenemase is NDM-1, a metallo-ß-lactamase first isolated from a Swedish patient of Indian decent who had frequent hospitalizations in India.[6] Metallo-ß-lactamases differ from other ß-lactamases in that they require zinc for the active site instead of the amino acid serine. NDM-1 has been associated with receiving medical care in India and Pakistan, and is now the most common carbapenemase in the United Kingdom.[7] Metallo-ß-lactamases are not inactivated by monobactam antibiotics such as aztreonam, but isolates recovered in the United States carrying NDM-1 have expressed additional resistance to monobactams, presumably through a secondary resistance mechanism.[8]

Local to Global Transmission

The evolution of the ß-lactamases demonstrates that resistance mechanisms are in constant flux. Most concerning is how readily plasmid-mediated ß-lactamases are transferred between species of Enterobacteriaceae. Bacteria with mutations that confer resistance are expected to thrive when selective pressure caused by antibiotics occurs. Horizontal transmission of KPC between Enterobacteriaceae species within a single patient has been documented.[6,9,10] Surveillance cultures from documented cases have revealed that a different species of Enterobacteriaceae isolated from a different site harbored the same resistance gene as the original organism that infected the patient.

Beyond the transmissibility of genes via plasmids, the multidrug-resistant Enterobacteriaceae are readily spread within hospitals, between health care facilities, and across national borders. A surveillance study of multidrug-resistant GNB (defined as resistance to three or more different antibiotic classes) by D'Agata showed an increase from 0.5% to 17% of multidrug-resistant *K. pneumoniae* isolates in a U.S. tertiary care hospital between 1994 and 2001.[11] The Meropenem Yearly Susceptibility Test Information Collection (MYSTIC) Program reported 10.9% of *Klebsiella* spp. and 3.1% of *E. coli* isolates with ESBL from 15 U.S. medical centers in 2005.[12] MYSTIC data from 41 medical centers in 11 European countries in 2004 revealed 13.6% of *Klebsiella* spp. and 10.8% of *E. coli* isolates with ESBL.[13]

Klebsiella pneumoniae carbapenemase and other carbapenemases have not been disseminated to the extent that ESBLs have, but outbreaks have been documented worldwide. Particularly well-documented was a KPC outbreak in New York City hospitals, where 38% of *K. pneumoniae* isolates were KPC-positive. Isolates from 10 area hospitals were examined. Seventy-eight of 95 KPC-positive isolates belonged to the same ribotype, demonstrating likely transmission between facilities.[14,15] Reports of KPC outbreaks have come from several other countries as well. In 2009, a tertiary care hospital in Greece reported an outbreak of KPC-producing *K. pneumoniae* that began in May 2007. The majority of patients identified with KPC were housed in the ICU. During this outbreak, a total of 61 KPC-producing *K. pneumoniae* isolates were recovered from 23 patients. The hospital instituted outbreak control measures including adherence to strict hand hygiene practices and contact precautions. The outbreak culminated with closure of the ICU for decontamination in January 2008, after which only three additional patients with KPC-producing *K. pneumoniae* isolates were identified.[16]

Multidrug-resistant GNB also have been detected in Minnesota, and ESBL-producing organisms are already frequently seen in both inpatient and outpatient isolates. In February 2009, the first bla_{KPC} gene in a KPC isolate was confirmed by PCR by the Department of Health's Public Health Laboratory. The number of identified KPC isolates is not as high as that reported from the Northeast,[14] but isolates continue to be identified. It is not uncommon for these highly resistant isolates to be recovered from patients with a history of travel to or prior hospitalization in areas where KPCs are endemic. Even though the East Coast is considered the epicenter of KPC infections in the United States, outbreaks in health care facilities as close as Chicago have been documented.[17] Prompted by reports of outbreaks and the high case-fatality rates of patients with KPC-positive isolates, the Minnesota Department of Health began tracking CRE, specifically KPC, in early 2009. To date, the health department has tested more than 70 unique modified Hodge test-positive isolates for bla_{KPC}, of which 25 (36%) had the bla_{KPC} gene. Although the Department of Health has been alert to other carbapenemases such as NDM-1 and VIM, it currently tests only for bla_{KPC} by PCR. Only a handful of isolates from Minnesota have been sent to the CDC for bla_{NDM-1} or bla_{VIM} characterization by PCR. All have tested negative.

Long-term care facilities and long-term acute care hospitals play a major role in multidrug-resistant Enterobacteriaceae transmission. Residents of these facilities are frequently hospitalized for prolonged periods, during which they may be exposed to multidrug-resistant Enterobacteriaceae and often receive multiple courses of broad-spectrum antibiotics. These are ideal conditions for colonization with these organisms. A study looking at long-term care facilities documented a significant rise in infections caused by multidrug-resistant GNB over a two-year period, during which the prevalence surpassed that of methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant enterococcus.[18] Given their increasing presence, it is important that all health care facilities pay attention to infection prevention and control measures and communicate the history of colonization or recent infection with multidrug-resistant Enterobacteriaceae when patients are transferred between facilities. ↳

As we witness CRE flow in and out of hospitals with increasing prevalence, it is no surprise that we also see movement between countries. Medical tourism is a particularly concerning means by which patients are exposed to resistant bacteria. Travel to India and Pakistan has been linked to recent identification of the NDM-1 enzyme in Europe, the United States, and Canada.[7,8,19]

Treatment Limitations and Morbidity

With the plethora of antibiotics available, it is difficult to accept that certain infections are untreatable. The carbapenems (ertapenem, imipenem, meropenem, and doripenem) have typically been the last-line, broad-spectrum antibiotic of choice for resistant organisms. The emergence of CRE presents new challenges. Clinicians have been forced to use alternative antibiotics such as tigecycline and the polymixins (polymixin B or colistin) to treat infections caused by CRE. Tigecycline, which is FDA-approved for the treatment of complicated skin and skin structure infections, intra-abdominal infections, and certain types of community-acquired pneumonia, has been used off-label for the treatment of CRE infections. One concern with tigecycline is that poor serum levels are achieved, which may make it insufficient for treating certain infections. The polymixins, which were introduced decades ago, are nephrotoxic, which limits their use. Concerns about toxicity have eased as we have become more knowledgeable about the pharmacokinetics of polymixins.[20]

Unfortunately, new resistance mechanisms and antibiotic misuse are making CRE a major public health threat. An increased risk of mortality associated with CRE has been well-documented.[21-23] In locations where CRE are not endemic, empiric treatment typically does not include coverage for CRE. Thus, delays in diagnosis and inexperience with treatments for CRE can increase the likelihood of poor outcomes. Even in areas where CRE are common, mortality has increased. A case-control study of patients with invasive *K. pneumoniae* infections in a large tertiary care hospital in New York City showed an increased mortality rate (48% versus 20%) in patients with a carbapenem-resistant *K. pneumoniae* infection. This study also noted an average of 3.2 days between specimen collection and initiation of antibiotics with *in vitro* activity against the carbapenem-resistant *K. pneumoniae* isolate, compared with 0.8 days for control patients.[22]

Identification Challenges

The challenge of confronting multidrug-resistant Enterobacteriaceae is not only one of antibiotic resistance but also one of definitions and identification. Although we are familiar with the ß-lactamases, the nomenclature surrounding the hundreds of different enzymes that exist can be overwhelming. Multidrug-resistant Enterobacteriaceae constitute an entire family of bacteria. The ß-lactamases vary from chromosomally to plasmid-mediated, and can be induced or constitutively expressed; they also have a spectrum of antibiotic targets. It is not uncommon for highly resistant organisms to carry more than one ß-lactamase or other resistance mechanisms such as decreased porin production that enhance the resistance phenotype. Labeling such bacteria is difficult. Terms such as "multidrug-resistant," "KPC-producing," or "CRE" can be confusing and nonspecific.

The ability of laboratories to detect carbapenem resistance is limited, as many of the common screening methods have been shown to have poor sensitivity to KPC producers.[24,25] The modified Hodge test, an agar/antibiotic disk-based test, has been used as a confirmatory test with good sensitivity and specificity for detecting bla_{KPC} when compared with PCR testing.[24] The limitations of this test are that it is subject to reader interpretation and that it does not distinguish between different mechanisms of carbapenem resistance. Also, the test adds another step to the identification process, delaying the time until clinicians receive a final result, and requiring extra time and resources that some laboratories do not have.

Molecular testing such as PCR seems to be the ideal way to detect these enzymes, but PCR testing is often only available at reference laboratories. Even more promising is the development of microarray technology for the rapid identification of multiple-resistance genes from a single isolate, although the clinical utility of this technique needs to be assessed.[26,27]

Shifting Breakpoints

Microbiology laboratories in the United States follow guidelines issued by the Clinical and Laboratory Standards Institute (CLSI) for interpreting and reporting susceptibility data to clinicians. Susceptibility breakpoints for Enterobacteriaceae were revised in 2010 for cephalosporins (Table 1) and carbapenems (Table 2). Along with these changes came new recommendations for reporting resistance and conducting confirmatory tests for ß-lactamase production. Previously, laboratories were instructed to perform ESBL screening and confirmatory tests on appropriate isolates and, if positive, change the susceptibility results of penicillin, cephalosporins, and aztreonam from susceptible to resistant. The new recommendations lower the breakpoints for several cephalosporins, and the CLSI no longer recommends supplementary testing for ESBL. Instead, the CLSI recommends that laboratories report susceptibility results without applying resistance rules based on confirmatory test results. These changes were made in response to availability of additional data that conferred a better understanding of ß-lactamases and of pharmacokinetic and pharmacodynamic properties of cephalosporins.[28] The carbapenem breakpoints were also lowered and the CLSI no longer recommends performing a modified Hodge test for carbapenemase during routine testing. The changes for carbapenem breakpoints were made for similar reasons, in addition to reports showing deficiencies of common laboratory methods to detect carbapenem resistance using the previous breakpoints.[24,25]

The logistics involved in the CLSI changes further add to the complexity of dealing with multidrug-resistant Enterobacteriaceae. This is because the Food and Drug Administration must approve breakpoint recommendations on automated kits

Table 1

Revised Enterobacteriaceae Breakpoints (MIC in µg/mLl) for Cephalosporin Antibiotics, 2009-2011

Agent	2009			2011		
	Susceptible	Intermediate	Resistant	Susceptible	Intermediate	Resistant
Cefazolin	≤8	16	≥32	≤2	4	≥8
Cefotaxime	≤8	16-32	≥64	≤1	2	≥4
Ceftizoxime	≤8	16-32	≥64	≤1	2	≥4
Ceftriaxone	≤8	16-32	≥64	≤1	2	≥4
Ceftazidime	≤8	16	≥32	≤4	8	≥16

Source: Clinical and Laboratory Standards Institute. 2011. Performance standards for antimicrobial susceptibility testing.

Table 2

Revised Enterobacteriaceae Breakpoints (MIC in µg/mLl) for Carbapenem Antibiotics, 2009-2011

Agent	2009			2011		
	Susceptible	Intermediate	Resistant	Susceptible	Intermediate	Resistant
Doripenem	-	-	-	≤1	2	≥4
Ertapenem	≤2	4	≥8	≤0.25	0.5	≥1
Imipenem	≤4	8	≥16	≤1	2	≥4
Meropenem	≤4	8	≥16	≤1	2	≥4

Source: Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing.

and devices, and approval has not yet been granted. Laboratories are able to follow either recommendation to remain in good standing. A validation study using disk diffusion can help laboratories convert to the new CLSI breakpoints (see IDSA alert at www.idsociety.org/Content.aspx?id=17429).

During this transition period, there will be inconsistencies between laboratories regarding labeling of ESBLs and CREs. Different laboratory interpretations of minimum inhibitory concentration (MIC) values will lead to confusion among clinicians about when it is appropriate to use an extended spectrum cephalosporin, a carbapenem, or neither. Since these determinations are also linked to infection prevention and control practices, there may be discordant practices among clinicians. The hospital pharmacist also will need to be aware of these issues so that he or she can provide advice on the appropriate antibiotic choice. Improved interdepartmental communication within hospitals during this transition period is necessary.

Effective Prevention Measures

Amidst the failure of antibiotics and the confusion generated by resistant organisms, there has been some success in combating this growing problem. Using infection prevention and control strategies, hospitals have been able to prevent the spread of CREs. In one report, a New York hospital with endemic KPC-producing bacteria was able to significantly reduce the incidence of patients with carbapenem-resistant *K. pneumoniae* in the ICU through active surveillance with rectal swabs of all patients on admission and weekly throughout their ICU stay; contact precautions and cohorting of patients with positive cultures; and regular cleaning of environmental surfaces. In addition, members of the infection prevention service regularly participated in medical rounds and held meetings with the nursing staff to encourage adherence to contact precautions and other infection prevention measures. The decreased incidence of carbapenem-resistant *K. pneumoniae* was independent of the incidence of other resistant non-Enterobacteriaceae organisms.[29]

A similar scenario was reported in a Chicago-area long-term acute care hospital that demonstrated control of a KPC-producing *K. pneumoniae* outbreak. This facility's infection prevention program included patient decolonization, improved cleaning methods, active surveillance, and pre-emptive isolation with contact precautions.[17] In this case, active surveillance cultures were taken on admission and once a month to obtain point prevalence data. Admission surveillance cultures were taken from the rectum, nares, wounds, central vascular catheter insertion sites, and gastrostomy tube sites. Patients were placed in isolation if they were considered to be at high risk for carrying multidrug-resistant organisms until surveillance culture results returned. Within two months, their point prevalence data decreased from 21% to zero percent.

Conclusion

Multidrug-resistant Enterobacteriaceae are a growing concern. Controling the spread of these highly resistant bacteria requires

a multidisciplinary team approach that involves clinicians, laboratory staff, infection prevention specialists, and pharmacists. Seamless communication among these professionals within and between health care facilities is needed if we are to ensure that appropriate care is provided. In addition, facilities should have protocols in place for antimicrobial stewardship,[30] surveillance, and the prevention of transmission and control of infection with multidrug-resistant organisms. Information about identification and prevention and control measures can be found on the CDC and Minnesota Department of Health websites (www.cdc.gov and www.health.state.mn.us).[31,32]

Health care providers now need to work closely with one another if we are to ensure that we do not again face a time when we have no useful tools against bacterial infections. **MM**

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The Expanding Role of Minnesota Pharmacists in Primary Care

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Changes to pharmacy education have paralleled changes in the role pharmacists play in primary care. Today, pharmacists are often members of the health care team, providing medication management services to help patients control chronic illnesses and working to prevent adverse drug events by educating and guiding prescribers. This article describes the role of pharmacists today and what they are doing to improve outcomes related to patient care.

The Doctor of Pharmacy degree has been the sole professional degree conferred by pharmacy schools in the United States since 2001. Previously, pharmacy graduates earned a four-year bachelor's degree. Then, training emphasized the clinical issues associated with the dispensing of medications in community pharmacies or hospitals. In response to the growing complexity of medication use in the United States, pharmacy education requirements changed. Now, earning a degree requires four years of training following at least two years of undergraduate studies. Students also must do more than a year of field work. Doctor of Pharmacy students learn to assess a patient's drug-related needs; identify, resolve, and prevent drug-related problems; and ensure that the goals of therapy are achieved by developing a care plan and conducting follow-up evaluations at appropriate times. They also learn to work as part of interprofessional teams.

The University of Minnesota Academic Health Center's 1Health initiative, which was launched in 2010, offers one way for students from each of the health professions programs to learn to work together. Nearly 900 students from the College of Pharmacy, Medical School, Center for Allied Health, School of Dentistry, School of Nursing, School of Public Health, and College of Veterinary Medicine are involved in the first phase of 1Health. The goal is to teach them how to rely on each others' skills and talents in order to optimize patient care. (More about 1Health is available at www.ahc.umn.edu/1health/.)

The change in pharmacy education coincided with a significant expansion of the role of pharmacists in health care. Pharmacists now provide a variety of clinical services in a number of settings including primary care clinics. The scholarly work of faculty at the University of Minnesota College of Pharmacy, strong collaborations within the practice community, and an innovative health care environment have made Minnesota a leader in integrating pharmacists into primary care teams. This article describes the role pharmacists play and how their involvement has led to improvements in patient outcomes.

Playing a New Role

Today, more than 100 clinical pharmacists work in primary care clinics across Minnesota. Organizations in the Minneapolis/St. Paul metro area that have incorporated pharmacists into their clinic-based care models include Fairview Health Services, HealthPartners, Hennepin County Medical Center, and University of Minnesota Physicians. Park Nicollet Health Services and Allina Hospitals and Clinics are currently developing programs. Outside the metro area, Mayo Clinic, Essentia Health, and several small rural health systems have established clinical pharmacy programs in their outpatient clinics.[1]

Within these organizations, pharmacists work directly with patients. They also create and maintain medication-related information systems, implement medication use policies and procedures, lead quality-improvement initiatives focused on medication use, and provide medication education to physicians and other clinic staff.

As members of a primary care team, pharmacists conduct one-on-one visits with patients in order to evaluate their medications in relation to their medical conditions and treatment goals. Patients are frequently referred to a pharmacist by a primary care provider; systematic review of clinic records using predetermined criteria targeting patients at high risk for poor medication outcomes also can lead to a referral. Through collaborative practice agreements—formal protocol-based agree-

ments between a physician and a pharmacist—pharmacists in Minnesota can initiate therapy, alter doses, and order laboratory tests within predefined practice protocols.

One of the forces driving the trend of integrating pharmacists into primary care is the national emphasis on improving care for chronic diseases such as diabetes and heart diseases—diseases that if poorly controlled drive up health care costs. Recent data show that management goals for these diseases are not being met. As of 2009, only 33.9% of Medicaid patients with diabetes had achieved desirable HgbA1c levels.[2] The percentage of both Medicare and Medicaid beneficiaries with controlled hypertension is less than 60%. Similar results have been reported for cholesterol management.[2] According to MN Community Measurement, which publicly reports clinics' scores on a number of health measures, the overall percentage of patients with adequate control of diabetes, heart disease, and hypertension is far from desirable in Minnesota.[3] Controlling these conditions means that patients must make lifestyle changes and take medications. By providing medication management services, pharmacists can help ensure that patients make progress toward their goals.

Another role for pharmacists in primary care is helping to prevent adverse drug events. Adverse drug events have a significant impact on the cost of health care, as an estimated 700,000 emergency department visits and 120,000 hospitalizations in the United States each year are the result of ADEs and about $3.5 billion is spent annually to care for patients who have experienced ADEs. Among patients age 65 and older, 87% of hospitalizations are associated with their not taking prescription drugs properly. At least 40% of ADEs in the outpatient setting are considered preventable.[4,5] Pharmacists can work to reduce ADEs by educating physicians and other providers about medications and advising them while they are making prescribing decisions.

Improving Outcomes, Reducing Costs

Including pharmacists in interprofessional teams has been shown to improve outcomes for several chronic conditions. Carter et al. examined the effect of collaboration between physicians and pharmacists on hypertension management and found that this partnership resulted in patients achieving significantly better mean blood pressure control.[6] Similar outcomes have been seen in the management of diabetes, cardiovascular disease, and asthma.[7-9] A 2010 meta-analysis of 298 studies strongly supported the positive impact of clinical pharmacy services; specifically, measures such as medication adherence, patient knowledge, and quality of life were shown to have improved significantly.[10] Other studies evaluating pharmacist-led interventions in primary care show a significant reduction in overall hospital admissions. In a meta-analysis of patients in primary care, Royal et al. found an odds ratio of 0.64 for the reduction in hospital admissions when a pharmacist was involved in the primary care setting compared with when one was not.[11] A 2009 survey suggested that organizations that included pharmacists in the care management team saw improvements in quality of care/outcomes and patient and medical provider satisfaction.[12]

Health care payers have begun to recognize the benefit of pharmacists' contributions in medication management for chronic diseases. The Medicare Prescription Drug Improvement and Modernization Act of 2003 established medication management services as a core benefit of Medicare Part D.[13] In Minnesota, the state's Medical Assistance program, HealthPartners, and several self-insured employers have incorporated medication management services into their benefit packages.[14,15]

A 2003 study of Fairview Health Services pharmacists who work collaboratively with primary care providers found that 5,780 drug therapy problems were resolved for 2,524 patients. In addition, patients were more likely to achieve their therapeutic goals. At the beginning of the study, 74% of patients seen by clinical pharmacists were achieving their treatment goals; by the conclusion of the study, 89% were achieving them.[16] These improvements were attributed in part to the fact that Fairview clinical pharmacists have broad collaborative practice agreements that allow them to conduct comprehensive medication evaluations and work with primary care staff to revise treatment plans. A more recent cost-benefit analysis involving Blue Cross and Blue Shield of Minnesota beneficiaries found that medication management services reduced their annual per beneficiary costs from $11,965 to $8,197. The cost of medication management services averaged $92.50 per pharmacist encounter, resulting in $12 saved for every $1 in service costs.[17]

Acknowledging the benefits pharmacists can bring to a primary care team, the state of Minnesota has included pharmacists in its definition of a health care home. To be certified as a health care home, a clinic need only have a primary care provider and a care coordinator; however, specialists may be included in the team when appropriate, and pharmacists are included in the program's definition of "specialist." They are currently involved in about half of the state's 138 certified health care homes.[18,19]

Conclusion

Pharmacists perform a number of functions in health care. They can work jointly with physicians to manage chronic conditions, improve medication use systems, serve as a resource for drug information, and educate physicians and patients about medications. Studies have shown that including a pharmacist on the primary care team improves outcomes in patients with chronic conditions such as diabetes, hypertension, and asthma. Their involvement also reduces the incidence of adverse drug events and, thus, the cost of care. As health care leaders and payers better understand the contributions they make, it is likely that the number of pharmacists working collaboratively with primary care physicians will continue to grow in the future. **MM**

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Index of Advertisers

Illegal Drug Impersonators

The Synthetic Drug Abuse Boom

By Carol Falkowski

The Internet has opened the door to marketers of products that contain substances that when ingested mimic the effects of illegal drugs such as marijuana, cocaine, and LSD. This article traces the history of synthetic drugs, describes some of the newest substances on the market and their physiologic and psychological effects, and discusses efforts aimed at curbing their sale and use.

The latest development in recreational drug abuse is the aggressive, direct-to-consumer, web-based marketing of chemical substances that produce strong, psychoactive effects akin to those of illegal drugs such as marijuana, amphetamines, cocaine, LSD, MDMA, and other substances. The catch is that these substances are packaged as legitimate products such as bath salts, incense, plant food, or even research chemicals. For example, synthetic THC or "fake pot" (delta-9-tetrahydrocannabinol, the psychoactive ingredient in marijuana) is being sold as herbal incense.

Drug abusers learn about these substances by word of mouth and online. A growing number of people in Minnesota and across the United States are using them to get high and instead encounter negative effects. Case in point, young people at a party in Blaine, Minnesota, last March intentionally ingested what was purported to be a research chemical. Although the substance, which was purchased online, was labeled "not for human consumption," they took it anyway, expecting to feel euphoric. Instead, 11 young adults were hospitalized, and one 19-year-old man died.

This article describes this trend in drug abuse and discusses some of the newest synthetic drugs, how these substances work, the consequences associated with taking them, and what is being done to stop their sale and abuse.

It Started with Ecstasy

More than two decades ago, raves (dance parties) introduced America's young people to a variety of new party drugs, sometimes called "designer drugs" because they were variations on marijuana, amphetamines, cocaine, hallucinogens, and heroin. Instead of producing a single effect, they produced a combination of effects. One of the first such designer drugs was MDMA, also known as "ecstasy, " "X," or "e." It is an amphetamine-like stimulant that also produces mild hallucinogenic effects. MDMA (3, 4 methylenedioxymethamphetamine) sold for about $20 a pill, and its effects lasted for up to eight hours.

Raves were crowded, all-night dance parties with loud, highly percussive music. Initially, they were held in secret, remote locations with limited advance notice. Eventually, however, they became more mainstream, commercialized events that took place in large venues and featured noted disc jockeys.

Raves and the use of MDMA and similar designer drugs went hand in hand, as MDMA gave people the energy they needed to dance all night long. Among the physical effects of MDMA are increased motor activity, heightened tactile sensations, and increased alertness, heart rate, and blood pressure. The drug also can cause muscle tension, involuntary teeth clenching, muscle cramps, tremors, nausea, a faint feeling, chills, profuse sweating, and blurred vision. In high doses, MDMA can interfere with the body's ability to regulate tem-

perature, resulting in hyperthermia and possibly leading to liver, kidney, and cardiovascular failure.

In 1988, the U.S. Drug Enforcement Administration (DEA) designated MDMA a Schedule I drug (no approved medical use and high potential for abuse). Soon after, the hallucinogenic drug 2C-B (4-bromo-2, 5-dimethoxyphenethylamine), also known as "Nexus," began appearing in dance clubs in Miami, New York, and other major urban areas. Sold in head shops and sex shops, it produced MDMA-like effects and enhanced sexual pleasure in low doses; but larger amounts produced extreme, sometimes alarming LSD-like hallucinogenic effects, and pronounced delusions. In 1995, the DEA designated 2C-B a Schedule I drug.

Synthetic Drugs Sold Online

Since then, a number of other substances have come on the scene. By the late 1990s, with the growth of online retail marketing, rogue websites began selling designer drugs in disguise, that is, as products that are not manufactured for their stated purposes. Drug abusers learned that these substances could produce the same psychoactive effects as illegal drugs. They also became aware that it was unlikely that these new chemicals would be detected by routine urinalysis. (A number of labs can now detect their presence in urine; but these tests are not, as yet, part of a standard drug screen.) During the last decade, these drugs began to appear in the lockers of high school students and at college house parties. References to them began showing up in emergency room case studies and in poison control center reports. These substances represent a growing and significant threat to both public health and public safety. What follows are descriptions of the substances that have appeared in recent years.

■ Synthetic THC

According to the DEA, synthetic THC products first appeared in the United States in December of 2008. Synthetic THC is a man-made chemical concoction with properties similar to delta-9-tetrahydrocannabinol, the naturally occurring psychoactive ingredient found in plant marijuana. Synthetic THC is sprayed onto various herbal mixtures and sold as herbal incense on websites and in head shops and smoke shops. The most recognized product names are "K2"and "Spice." The cost is around $30 per gram. Like plant marijuana, synthetic THC products most often are smoked.

The effects of smoking synthetic THC are very different from those of smoking marijuana. Being under the influence of synthetic THC is typically not a laid-back, relaxing experience, and its adverse effects include anxiety, agitation, nausea, elevated blood pressure, tachycardia, seizures, and hallucinations.

The American Association of Poison Control Centers reported 2,874 calls regarding exposures to synthetic marijuana (THC homologs) in 2010, and 1,639 through April 20, 2011. In the Twin Cities, the Hennepin Regional Poison Center reported 89 synthetic cannabinoid calls in 2010 and 49 in the first quarter of 2011.

In March 2011, the DEA, using its emergency scheduling authority, temporarily designated five synthetic cannabinoids—JWH-018, JWH-073, JWH-200, CP-47,497, and cannabicyclohexanol—as Schedule I substances.

Nevertheless, online sales continue. Moreover, numerous reports from school counselors in the Twin Cities metro area document the escalating abuse of these mixtures by students. In several cases, the use of synthetic THC produced highly combative and aggressive behavior, vomiting, and seizures. One student, who was smoking up to 3 grams per day, experienced insomnia, delusions, and hair loss. In May 2011, two Twin Cities-area high school students were taken by ambulance from school to the hospital when they experienced vomiting and agitation after injesting "herbal incense" containing synthetic THC that was baked in cookies.

■ Research Chemicals

Chemical mixtures are being sold online as research drugs or research chemicals that are labeled "not intended for human consumption." Exactly what type of research these substances are used for is never specified. Nor is it always clear what these drugs are. Drug abusers may simply know that the chemicals can get them high. The young people in Blaine ingested a chemical compound known as 2C-E (2, 5-dimethoxy-4-ethylphenylethylamine) and were expecting to experience effects similar to those produced by MDMA or "ecstasy." Instead, they experienced profound hallucinations and became highly agitated and distressed. Later reports indicated that some thought they were ingesting 2C-I, a chemical cousin of 2C-E that allegedly has milder effects. Both are in the phenylethylamine class and share significant structural similarities with 2C-B, a Schedule I substance.

According to the DEA, oral doses of 2C-I ranging from 3 mg to 25 mg produce LSD-like hallucinations and visual distortions and MDMA-like empathy. Onset of action is 40 minutes, and duration of action is up to two hours. The delayed onset of action relative to other drugs can heighten the risk of accidental overdose.

Calls regarding 2C-I and related analogues reported to the Hennepin Regional Poison Center numbered four in 2009, seven in 2010, and 12 in the first quarter of 2011.

■ Bath Salts and Plant Food

A number of products being sold as bath salts and plant food were never intended for use in the bathtub or garden. They are chemical mixtures that have been manufactured to produce effects similar to those of drugs such as cocaine, methamphetamine, or MDMA. Their negative effects include chest pains, increased heart rate, elevated blood pressure, agitation, vomiting, dizziness, delusions, suicidal thoughts, severe psychotic episodes, the urge to wound oneself, and extreme paranoia. In some cases, profound paranoid delusions have persisted long after ingestion of the substance.

Mephedrone (4-methylmethcathinone or 4-MMC), a substance within the phenethylamine class that shares similarities with methcathinone, a Schedule I substance, has been found in

bath salts, as has methylenedioxypyrovalerone (MDPV), another substance in the phenethylamine class. MDPV is structurally related to cathinone, the active alkaloid found in the khat plant, and to methamphetamine and MDMA.

Bath salts are sold under many names including "Vanilla Sky," "Bliss," and "Ivory Wave." Mephedrone alone is also known as "Meow Meow," "M-CAT," "Bubbles," or "Mad Cow." It is snorted, smoked, taken orally with liquids, or injected. MDPV has been identified in "Energy 1" and is sold on United Kingdom-based websites.

The DEA's National Forensic Laboratory Information System (NFILS) reported local law enforcement encounters involving MDPV in 2009 and 2010 in Iowa, Kansas, Kentucky, Minnesota, North Dakota, Oklahoma, Texas, and Wisconsin. There were two incidents involving MDPV reported in NFLIS in 2009 and 161 in 2010.

The American Association of Poison Control Centers reported 303 calls regarding bath salts in 2010 and 3,470 through June 2011. Calls regarding bath salts reported to the Hennepin Regional Poison Center increased from six in 2010 to 26 in the first quarter of 2011.

In September of this year, the DEA published its intent to reschedule mephedrone, MDPV, and methylone—three stimulants frequently found in products marketed as bath salts or plant food—as Schedule 1 substances, making their sale and possession illegal. The change in scheduling will last for one year, during which time the government will determine whether it should permanently control these substances.

Stopping the Abuse

The Federal Controlled Substance Analogue Enforcement Act, which was passed in 1986, deemed the possession and sale of chemical analogues of otherwise illegal Schedule I substances to be illegal and prosecutable. To qualify as an analogue, a drug must be both chemically and pharmacologically similar to an illegal substance. In an effort to circumvent the law, manufacturers of these chemicals haved placed the warning on their packaging "not for human consumption."

The DEA has successfully conducted investigations that have resulted in the prosecution of online vendors of these products. Most notably, in 2004, they shut down five websites that were selling designer-drug analogues and were known to have thousands of customers. But just as the old vendors disappeared, new ones emerged.

Minnesota's version of the Federal Controlled Substance Analogue Enforcement Act, which took effect July 1, makes the sale and possession of controlled substance analogues of synthetic THC, methcathinone, and phenylethylamines (2C-I and 2C-E) punishable as a gross misdemeanor. Minnesota Sen. Amy Klobuchar is championing federal legislation that outlaws these three groups of substances as well.

Minnesota's new analogue law is a step toward preventing people from accessing and using these products. But the criteria and process for identifying a synthetic drug as an analogue in the first place is complicated, costly, and time-consuming, thus making it difficult to keep pace with the thousands of chemical formulations that can possibly produce mood-altering effects akin to those of scheduled substances.

Legal approaches are critical to curbing the sale and use of synthetic drugs. In addition, we can all engage in public dialogue about the dangers of these substances. Adolescents and young adults may not realize that ingesting them can be harmful or even fatal. Therefore, it's imperative that health professionals, parents, educators, and community leaders talk with them about the dangers of these products.

We are all still learning about these new substances. Odds are that the synthetic drug abuse business will expand and that the number of hospitalizations and deaths associated with these substances will increase before it starts to contract. In the meantime, we can all help by educating young people and each other. **MM**

Carol Falkowski is the drug abuse strategy officer at the Minnesota Department of Human Services and author of the book, *Dangerous Drugs: An Easy-to-Use Reference for Parents and Professionals.* She is also a member of the National Institute on Drug Abuse's Community Epidemiology Work Group and has written reports on current drug abuse trends twice a year since 1986.

Minnesota's Prescription Monitoring Program

How to Identify Patients Who May be Abusing Controlled Substances

By Barbara A. Carter and Cody Wiberg, Pharm.D., M.S., R.Ph.

■ The Minnesota Prescription Monitoring Program, which was launched by the Minnesota Board of Pharmacy last year, is collecting data on prescriptions of controlled substances. Reporting is required from in-state pharmacies and others including physicians who dispense medications as well as from out-of-state pharmacies that ship controlled substances to Minnesota residents. This article describes the program, how it works, and how it can benefit physicians.

The abuse and diversion of controlled substances is a significant and persistent problem in the United States. Current data from the Substance Abuse and Mental Health Services Administration show that approximately 7 million individuals ages 12 or older are nonmedical users of controlled prescription drugs (opioid pain relievers, tranquilizers, sedatives, or stimulants).[1] Although the number of nonmedical users has remained relatively unchanged over the past seven years, the number of drug-treatment admissions and controlled-substance-related deaths has increased significantly.[1]

In a July 2010 brief, the U.S. Centers for Diseases Control and Prevention (CDC) cited trend data showing that the number of unintentional drug overdose deaths increased five-fold from 1990 to 2006.[2] According to the report, in 2006, "overdose deaths were second only to motor vehicle crashes among leading causes of unintentional-injury death … in the United States," with opioid analgesics "involved in more overdose deaths than heroin and cocaine combined." In 2008, the number of emergency department visits involving the nonmedical use of prescription or over-the-counter drugs—about 1 million—was equal to those involving illicit substances.[2]

In 2007, in an effort to reduce the misuse of controlled substances and improve patient care, the Minnesota Legislature passed a law authorizing the Minnesota Board of Pharmacy to establish a program to help identify individuals who inappropriately obtain excessive amounts of controlled substances from multiple prescribers and pharmacies. Minnesota is now one of 34 states to monitor prescriptions of controlled substances.

The Minnesota Prescription Monitoring Program (PMP) collects data on prescriptions of all Schedule II to IV drugs and on certain prescriptions of federal Schedule V controlled substances that are designated as Schedule III substances in Minnesota (eg, codeine-containing cough syrups). Reporting is required from in-state pharmacies and other dispensers such as prescribers, hospitals, and clinics as well as from out-of-state pharmacies that ship controlled substances to Minnesota residents. The law allows prescribers, pharmacists, and other specified individuals to access the information in order to better treat patients and identify those who may be abusing prescription drugs.

As the legislation that established the PMP was being developed, some expressed concern about privacy, patients' rights, and the "chilling effect" that a registry might have on physicians' prescribing practices. In order to alleviate those concerns, the law placed limitations on the PMP and those who use it. For example:

- A PMP staff person who notices that an individual visited multiple prescribers and/or pharmacies in a 30-day period is not allowed to notify the prescribers and pharmacies. It is up to prescribers and pharmacists to identify patients whose behavior suggests prescription drug abuse and consult the PMP database to find out if that person is receiving controlled substances from multiple sources.
- Prescribers and pharmacists are not required to use the database to get information about a patient.
- Prescribers and pharmacists aren't required to report patients they suspect of drug abuse or withhold prescriptions from them.
- Pharmacists and prescribers are immune from criminal, civil, or administrative liability if they make a medical decision based on information provided by the database.
- Law enforcement officials can obtain data from the registry only if they obtain a search warrant from a judge.

Pharmacies and others began reporting the dispensing of controlled substances on January 4, 2010. During the first year, data on more than 6.6 million prescriptions were entered into the database. During the first six months of 2011, PMP data were used to identify 86 individuals who had seen 10 or more prescribers; one had seen 45 prescribers. Of those 86 people, 64 had received prescriptions from more than 10 different pharmacies; one had been to 47 pharmacies. Although this information by itself does not establish that these individuals are "doctor shoppers"—people who see more doctors and receive more medicine than necessary for their therapeutic needs, it certainly reflects behaviors that may indicate prescription drug abuse.

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Reporting to the PMP

Any physician who dispenses the substances described in the law (eg, a pain management specialist) will need to report to the PMP. Generally, dispensers are required to report daily. They are required to submit a "zero report" at least every seven days even if they have not dispensed a controlled substance in a given week.

Physicians who will be reporting to the PMP will need to register to do so. (This is a separate process from registering to access the database.) This can be done online. The steps are outlined in the Dispenser's Implementation Guide, which is available by selecting "Other Forms and Documents" on the PMP website (www.pmp.pharmacy.state.mn.us). The steps for reporting are also detailed in this guide. Reporting is done by uploading information (select "Uploader Website" from the options on the PMP site). The table lists the information that must be included.

Requesting a Patient Profile

Direct and secure access to the PMP database is available to any of the more than 25,000 Minnesota prescribers and pharmacists who are permitted by law to view controlled-substance prescription profiles of patients. Prescribers and pharmacists must apply for access to the database. (This is a separate process from registering to report dispensing of a controlled substance.) Access request forms can be downloaded from the PMP website (go to www.pmp.pharmacy.state.mn.us and select "Access Request Forms") or obtained by contacting the PMP office. The provider must not only fill out the form but also have it notarized and return it to the PMP office. Users can enter information directly into the online version of the form. However, information cannot be saved in the forms, and the forms must be printed out in order to be notarized. Once the PMP staff receive the form, they will verify the practitioner's credentials and employment and then email notification of approval and provide login instructions.

To request a profile of a patient, the prescriber will go to the PMP website and select "Login to the RxSentry PMP Database." There, he or she must submit, at minimum, the patient's name (full or partial) and date of birth. A report will be returned electronically. (A paper copy of the report is available upon request.) Users should be aware that the PMP does not warrant any patient profile to be accurate or complete, as it cannot guarantee that dispensers have accurately reported all of the controlled-substance prescriptions they have filled. First-time users are encouraged to go through the RxSentry Query and Reports Tutorial before submitting a query.

Prescribers may access the PMP database 24 hours a day, seven days a week. Prescribers or their employers may decide how often and when they will request patient profiles. Some may decide to do so for all patients. Others may do so only when they suspect potential abuse. The reports can be used to determine appropriate medical treatment such as referral to a pain-management specialist and to identify possible doctor-shopping. If a prescriber or pharmacist suspects a patient may be abusing a controlled substance, he or she can assist that person in finding help.

The patient profiles are private and, whether they are stored electronically or in print, must be given the same security considerations as other protected health information. Information about an individual cannot be used unless the prescriber or pharmacist is currently treating that person and is considering prescribing or dispensing a controlled substance for him or her. As of July 2011, more than 5,000 prescribers and pharmacists conducted more than 160,000 queries of the more than 7 million records stored in the secure database.

What's Ahead

In the coming months, the PMP staff will be working to increase awareness of the PMP and encourage prescribers and pharmacists to apply for PMP access and to provide guidance in the use of the database. Staff will continue to gather data to demonstrate the effect the PMP is having on reducing diversion, abuse, or inappropriate use of controlled substances in Minnesota. Also, the PMP staff will be working with others to develop a process for exchanging PMP information with other states in order to prevent cross-border diversion. Finally, the PMP office will continue to work with legislators to modify the law in order to make the program more useful.

The PMP is one way of addressing the problem of prescription drug abuse. Although the program will not change the circumstances that lead people to abuse prescription drugs, it can help clinicians and pharmacists distinguish between patients who may have unmet needs and those who are taking advantage of the health care system. **MM**

Table

Dispenser Reporting Requirements

- Name of the prescriber
- Prescriber's DEA number
- Name of the dispenser
- Dispenser's DEA number
- Prescription number
- Patient's name
- Patient's full address, including city, state, and ZIP code
- Patient's date of birth
- Date the prescription was written
- Date the prescription was filled
- Name and strength of the controlled substance (or NDC number)
- Quantity of controlled substance dispensed
- Number of days supply

Source: Minnesota Board of Pharmacy RxSentry Dispenser's Implementation Guide

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Collaborative Psychiatric Consultations

Guidance for Primary Care Providers Who Prescribe Psychotropic Medications for Children

By Mary Beth Reinke, Pharm.D., Glenace Edwall, Psy.D., Ph.D., Pat Nygaard, Ph.D., and John Zakelj

A 2010 Minnesota law required the Department of Human Services to develop a collaborative psychiatric consultation service for primary care practitioners and other health care professionals, with an initial focus on those who prescribe medications for children. Use of the service will be required for prescribers of certain psychotropic medications for children enrolled in fee-for-service Medical Assistance, the state's Medicaid program. This article discusses the impetus for the law, explains the new medication review requirements, and describes plans for the consultation service.

In 2009 and 2010, Minnesota lawmakers were looking for ways to improve services and save money. Two ideas relating to psychiatric services received considerable attention: providing rapid access to psychiatry services for adults and requiring providers who care for children needing certain psychiatric medications to consult with a psychiatric expert before prescribing them. A bill proposing those services did not pass in 2009, but a revised version was brought back in 2010. Whereas the scope of the original legislation was limited to requiring consultations when prescribing psychiatric medications for children in Medical Assistance (MA), the state's Medicaid program, the 2010 legislation was more broad in that it included provisions for voluntary consultations for both children and adults, as well as rapid access to direct psychiatric services for children and adults in certain situations.

During hearings on the 2010 bill, the Department of Human Services (DHS) presented data from the St. Cloud area showing that inpatient costs for children from school districts that participated in a project demonstrating the use of a collaborative consultation approach were less than those in districts that did not participate.[1] The approach used in that project included screening for mental health concerns in primary care settings, using evidence-based primary care management protocols for common psychiatric conditions in children, and providing access to child psychiatrists for case consultation.

In addition, the DHS presented data from the state of Washington that showed the cost of pediatric psychiatric consultations is more than offset by savings from reductions in inappropriate medication use.[2] The Minnesota Legislature also considered other evidence including findings from a 2008 report by the Minnesota Council of Health Plans, which analyzed claims data for 2.5 million Minnesotans enrolled in public and private health plans during 2005.[3] The report noted that:

- Nearly one in 10 children and adolescents ages 20 years and younger in Minnesota has a mental health diagnosis;
- Ninety-seven percent of children receiving antidepressants do not receive follow-up care recommended by the Food and Drug Administration (FDA);
- One of 15 people with a mental health diagnosis visited an emergency room or was hospitalized (the most expensive forms of care) at least once during the year; and
- More than 80% of the drugs used to treat mental illness in Minnesota are prescribed by family medicine, internal medicine, and OB/GYN physicians; only 20% are prescribed by psychiatrists.

Based on these and other findings, the Minnesota Legislature approved an ongoing appropriation of $1 million per year starting in 2011 to create a collaborative consultation service, with the cost expected to be fully offset by reduced inpatient and medication costs. Physicians would call the service in order to receive guidance and authorization for prescribing certain psychiatric medications for children enrolled in fee-for-service MA.

What the Law Requires

The 2010 Minnesota Legislature directed the DHS to undertake three concurrent and related activities:

- Appoint interdisciplinary workgroups to establish appropriate medication and psychotherapy protocols to guide the consultative process;[4]
- Issue a request for proposals for collaborative psychiatric consultation and related services (the legislation allows DHS officials to select the structure and funding method that would be most cost-effective; this may include direct provision of services by the state, a public-private partnership with a provider organi-

zation, or a grant or contract awarded to a provider organization);[5] and

- Identify situations for which a collaborative psychiatric consultation and prior authorization should be required before the initiation or continuation of psychiatric drug therapy in pediatric patients who have fee-for-service coverage in Medical Assistance.[6] In other words, before pediatric patients can be prescribed those drugs, their providers will need to use the new collaborative psychiatric consultation service.

The goals of the service are to 1) improve the quality of mental health treatment by encouraging the use of evidence-based treatments in addition to or in place of medication where appropriate, 2) increase access to care and the quality of that care by making more efficient use of both primary care and specialty mental health services, and 3) foster collaboration between primary care and behavioral health services.

The consultation service would be available to primary care providers, emergency department personnel, local crisis services staff, and mental health professionals. Cases involving children on fee-for-service MA would receive priority, followed by those involving children who have other forms of health insurance. Primary care providers will be able to bill MA for the time they spend obtaining a psychiatric consultation.[7]

Establishing the Medication Authorization Thresholds

From December 2010 through March 16, 2011, the DHS convened the Drug Thresholds Workgroup, which included specialists in child psychiatry, pediatrics, behavioral pediatrics, and family medicine, to establish thresholds for various drugs by age group, above which would require a psychiatric consult as part of the prior authorization process. The workgroup also discussed 1) off-label prescribing and whether there should be a diagnosis on the prescription claim; 2) use of multiple drugs or dose forms within a drug class; and 3) how to better ensure that monitoring occurs for medical issues such as metabolic risks associated with atypical antipsychotics. Using the American Academy of Child and Adolescent Psychiatry Practice Parameters, the FDA-approved uses and recommended doses for various age groups, and practitioners' clinical experience, they established dose thresholds for various age groups for atypical antipsychotics as well as for drugs used to treat attention deficit disorder and attention deficit hyperactivity disorder (Tables 1 and 2).

Table 1

Thresholds for Atypical Antipsychotics (mg/day)

Drug	≤5 years of age	6 to 12 years	13 to 17 years
Risperidone	0	3	6
Aripiprazole (Abilify)	0	10	20
Quetiapine (Seroquel and Seroquel XR)*	0	300 (6-9 years); 600 (≥10 years)	600
Olanzapine (Zyprexa)	0	0	10
Ziprasidone (Geodon)	0	80	120
Clozaril	0	0	600
Paliperidone (Invega)	0	3	6

*Additionally: low dose of ≤50mg/day

Table 2

Thresholds for Drugs Used for ADHD (mg/day)

Drug	< 3 years of age	3 to 5 years	6 to 9 years	10 to 12 years	13 to 17 years
Methylphenidate (Ritalin, Ritalin SR, Ritalin LA, Concerta)	0	40	80	108	108
Methylphenidate patches (Daytrana)	0	20	40	60	60
Dexmethylphenidate (Focalin, Focalin XR)	0	20	40	50	50
Mixed amphetamine (Adderall, Adderall XR)	0	20	40	60	60
Dextroamphetamine (Dextrostat)	0	20	40	60	60
Lixdexamfetamine (Vyvanse)	0	50	70	70	70
Atomoxetine (Strattera)	0	0	100	100	100
Clonidine (Clonidine, Kapvay)	0	0.2	0.4	0.4	0.4
Guanfacine (Guanfacine, Intuniv)	0	2	4	4	4

For newer antipsychotics such as Fanapt, Saphris, and Latuda as well as for those that have yet to be developed, the workgroup recommended following the FDA guidelines regarding use in children and for treating certain conditions. Other uses and doses would require a psychiatric consult. The rationale for the consult is that existing atypical antipsychotics should be considered first-line therapy because they have a proven track record. The FDA-approved adult threshold could be considered the dose limit for the 13- to 17-year-old age group after trying existing atypical antipsychotics without benefit.

Additionally, duplicate therapy with two or more atypical antipsychotics for more than 60 days and with three or more mood stabilizers for more than 30 days will require a consultation.

Developing the Service

The DHS established the Children's Psychiatric Consultation Protocols Workgroup in January 2011 to guide the design and development of the service. The group includes representatives from the Minnesota Psychiatric Society, Min-

nesota Society of Child and Adolescent Psychiatry, American Academy of Pediatrics-Minnesota Chapter, Minnesota Academy of Family Physicians, Minnesota Chapter-National Association of Pediatric Nurse Practitioners, American Psychiatric Nurses Association-Minnesota Chapter, Minnesota Psychological Association, Minnesota Chapter-National Association of Social Workers, other mental health provider and advocacy groups, and consumer and parent groups. A subgroup was convened to develop a method for triaging calls to ensure rapid response to mandatory medication reviews and critical psychiatric concerns.

Separate subgroups were convened to design protocols for the psychiatric consultations based on current research and practice standards to assist primary care physicians in determining what steps to take to ensure patient safety, how to screen for specific disorders, and when to refer to a mental health professional for assessment or treatment. Thus far, protocols have been developed for depression, anxiety, trauma, disruptive behavior, ADHD, bipolar disorders, eating disorders, and substance abuse.[8] Additional protocols will be developed for autism and psychotic disorders.

Selecting a Vendor

On June 6, 2011, DHS issued a request for proposals for a provider to administer the collaborative psychiatric consultation service. The provider will not only be expected to provide the consultation services, but also will be required to coordinate this new service with health care homes and other services offered by health plans such as HealthPartners and PrimeWest. It also will need to conduct a variety of outreach and training activities to inform primary care providers and others about the new service. Department of Human Services officials are expected to select a vendor later this month. Once a provider is chosen, the new authorization requirements will be phased in for children in the fee-for-service MA program.

How the Service Will Work

Many of the details regarding this new service will be worked out after a vendor is selected. The way it is expected to work is that the vendor will operate a call center that will be available statewide Monday through Friday from 7 a.m. to 7 p.m. A triage professional, most likely a licensed social worker, will answer calls and determine the most appropriate response to each request. Requests for medication authorization and/or collaborative psychiatric consultation will be routed to on-call psychiatrists who have qualifications specific to the request. For example, all requests relating to children's psychiatric medications will be handled by board-certified child and adolescent psychiatrists. The protocols developed by the Children's Psychiatric Consultation Protocols Workgroup will be used to guide the consultations.

Based on September 2010 fee-for-services claims, an estimated 16% (n=480) of children with MA fee-for-service coverage would exceed atypical antipsychotic thresholds and 5% (n=391) would exceed stimulant and atomoxetine drug thresholds during the first month. In order to not overwhelm the service, implementation will progress gradually.

Initially, 90% of the services will be provided for patients younger than 21 years of age. Consultations for both ADHD drugs and atypical antipsychotics initially will be mandatory for children under 5 years of age. Voluntary consultations for children and adults are expected to make up a larger share of the caseload in the future as prescription patterns for children are expected to change, thus reducing the need for mandatory consultations and freeing up resources for voluntary consultations.

Department of Human Services officials will track the cost of the consultation services provided and monitor the effect of the program on emergency room utilization, inpatient psychiatric hospitalizations, use of psychotropic medications, use of residential and day treatment, partial hospitalizations, use of outpatient therapies and rehabilitation services, and use of other health care services. In addition to tracking costs and utilization, they will measure whether access to and quality of treatment improves as a result of better collaboration between primary care and behavioral health providers.

Conclusion

Minnesota's collaborative psychiatric consultation service is being developed to assist physicians who prescribe psychotropic medications for children covered by the state's MA program. It is expected that this service will lead to better outcomes for young patients with mental health concerns and lower health care costs for the state. **MM**

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Drug-Nutrient Interactions

A Case and Clinical Guide

By Gregory A. Plotnikoff, M.D., M.T.S., FACP

Advances in pharmacokinetics and pharmacodynamics require new competencies related to pharmaceutical prescribing. First, both physicians and pharmacists need to recognize the potential negative impact of nutrients and dietary supplements on the absorption, metabolism, and utilization of prescription drugs. Second, physicians, even more than pharmacists, need to recognize the potential negative effects of pharmaceuticals on the absorption, metabolism, and utilization of nutrients. This article discusses common drug-nutrient interactions and presents a case that illustrates how unrecognized nutrient disruption may negatively affect a patient's health and potentially result in unnecessary prescribing of medications. In presenting the case, we also provide a conceptual framework for assessing and treating this patient and a summary of current knowledge regarding drug-nutrient interactions.

In recent years, we have become increasingly aware of the potential negative effects of nutrients on the absorption, metabolism, and utilization of prescription medications. Classic examples described in the medical literature include the effect of calcium on thyroid medications,[1] iron on levodopa or methyldopa,[2] and iron and zinc on tetracyclines and quinolones.[3-5] In addition, both grapefruit juice[6] and St. John's wort[7] have been shown to affect the functioning of the gastrointestinal cytochrome P450 enzyme CYP3A4 (Tables 1, 2). The potential for compromised efficacy or enhanced toxicity is of particular concern for patients taking medications with narrow therapeutic margins such as digoxin, lithium, phenytoin, and theophylline or for those taking drugs such as coumadin and cyclosporine, which require careful monitoring.

Until now, this concern has been excessively one-dimensional, focusing on the effect of nutrients on medications. However, knowledge of the opposite effect—drug-induced nutrient deficiencies—may be as or even more important. For example, recent articles have reported on the adverse effects of proton pump inhibitors on key nutrients such as B12, calcium, magnesium, and iron.[8,9]

Many commonly used pharmaceuticals can adversely affect nutrient status (Table 3) and precipitate development of new symptoms such as anxiety, depression, fatigue, fibromyalgia, or insomnia. Yet few articles in the medical literature summarize what is known about mechanism-based and idiosyncratic adverse drug reactions.[10,11] This article attempts to raise awareness of the growing body of knowledge about the interaction between pharmaceuticals and nutrients and show how it might be used in clinical practice. It presents the case a patient who was seen in our clinic after his psychiatrist wanted to add a costly drug to his regimen to treat his ongoing depression and describes the testing that was done to determine whether his symptoms may have been caused by nutritional deficiencies. It also describes our approach to treatment.

Is Abilify Needed?

Mr. T is a 49-year-old white male who presented with significant fatigue as well as depression and insomnia that have severely affected his quality of life and capacity to work. His past history is remarkable for GERD, for which he has taken a proton pump inhibitor for seven years; worsening depression that has required trials of both SSRI and SNRI medications in increasing doses; borderline diabetes requiring exercise and weight loss; and hypertension requiring a thiazide diuretic. He has difficulty maintaining a normal potassium level despite supplemental prescription dosing. Mr. T recently started taking zolpidem (Ambien) and has noticed some improvement in his sleep. He reports drinking 4 to 6 ounces of alcohol per week and eating a diet high in processed foods that are rich in saturated fat. Despite his best efforts, he has failed to lose weight. He takes no supplements other than the prescribed potassium and has had to give up exercise because of his symptoms. His psychiatrist, concerned about the refractory depression, has recommended that he take aripiprazole (Abilify). Mr. T is concerned about both the cost of the drug ($450 per month) and its extensive toxicity profile. He came to our clinic asking whether this medication was necessary and what else he could do to control his depression.

The addition of aripiprazole to Mr. T's regimen represents one medically appropriate approach to treating his symptoms. There is another one, however. Before writing another prescrip-

Table 1

Nutrient-Induced Drug Deficiencies

Medication/Class	Confounding Nutrient
Bisphosphonates	Zinc
Levodopa, methyldopa	Iron
Levothyroxine	Calcium
Penicillamine	Copper, vitamin B6, zinc
Quinolone antibiotics	Iron, zinc
Tetracycline antibiotics	Iron, zinc

Table 2

Common Nutrients' Effect on Prescription Drugs

Grapefruit* increases bioavailability for
- Buspirone
- Calcium channel blockers
- Carbamazepine
- Cyclosporin
- Ethinylestradiol
- Saquinavir
- Sildenafil
- Sirolimus and tacrolimus
- Simvastatin

St. John's wort decreases the bioavailability of**
- Calcium channel blockers
- Coumadin
- Cyclosporine
- Digoxin
- Irinotecan
- Oral contraceptives
- Protease inhibitors
- Simvastatin
- Tacrolimus
- Theophylline

*The magnitude of the inhibition effect is dose-dependent.
**Effect can remain strong for weeks after stopping ingestion.

tion, we might consider whether Mr. T has nutritional deficiencies that may be causing or exacerbating his symptoms or affecting the way his medications are working. Clinical indications for medical assessment of altered nutritional status include significant changes in affect, energy, memory, pain, sleep, or strength—symptoms that affect Mr. T.

To begin with, we considered whether Mr. T was making enough serotonin for his SSRI to work. If he was not making sufficient serotonin, he could not make melatonin, which is necessary for sleep. Could his need for a hypnotic agent and increased dosing of his SSRI suggest significant disruption of neurotransmitter production? And might any of his symptoms be attributed to adverse drug-nutrient interactions?

Two of Mr. T's prescription medications had the potential to block his ability to properly digest and absorb the key amino acids (phenylalanine, tyrosine, tryptophan, methionine, cysteine), minerals (copper, zinc), and B vitamins necessary for neurotransmitter production. Proton pump inhibitors are extremely effective at blocking acid production and shifting the mean gastric pH toward the alkaline end of the scale. As we have learned from bariatric surgery patients and years of animal studies, increased gastric pH may inhibit digestion of proteins and absorption of crucial micronutrients including iron and vitamin B12.[12] In addition, thiazide diuretics can deplete the body of magnesium, potassium, and zinc.[13,14] Concerning in Mr. T's case was his significant need for potassium dosing and borderline hypokalemia.

Table 3

Adverse Effects of Common Medications on Nutrient Status

Medication Class (examples)	Potential Nutrient Deficiency
Antacids (PPIs, H2 blockers)	B12, iron, folic acid, amino acids, calcium, phosphorous, copper, zinc
Antibiotics (augmentin, vanco)	Vitamins C, K, and all B vitamins
Antibiotics (TCN)	Calcium, magnesium, zinc, B6, B12
Antibiotics (cephalosporins)	Vitamin K
Antidepressants (TCA)	Vitamin B2, coenzyme Q10
Antiseizure agents	Vitamin D, calcium, folic acid, B12, biotin (phenytoin, carbamazepine, primidone)
Antipsychotic agents	Vitamin B2, coenzyme Q10 Vitamin B6 (valproic acid only)
Antiviral (protease inhibitors)	Vitamin D
Aspirin	Vitamins C, K, panthothenate, folic acid
Beta-blockers	Coenzyme Q10
Bile acid sequestrants	Vitamins A, D, E, K, B2, B3, B9, B12 (cholecystyramine, colestipol)
Corticosteroids	Vitamin D, potassium, selenium, zinc
Diuretics (loop)	Magnesium, potassium, zinc, B1, B6
Diuretics (thiazide)	Magnesium, potassium, sodium, zinc
Diuretics (K+ sparing)	Folic acid, magnesium, potassium, sodium, zinc
Estrogens	Vitamin B6, folic acid
NSAIDs (Ibuprofen, naproxen, sulindac)	Folic acid
NSAIDs (idomethacin, indocin)	Vitamin C, folic acid
Statins	Coenzyme Q10
Sulfonylureas	Coenzyme Q10
Metformin	Vitamin B12
Methotrexate	Folate
Theophylline	Vitamin B6
Warfarin	Vitamin K

Sources: Felípez L, Sentongo TA. Drug-induced nutrient deficiencies. Pediatr Clin N Am. 2009;56:1211-24; Lord RS, Bralley A, Nelson-Dooley C. Interactions of Drugs, Nutritional Supplements and Dietary Components in Laboratory Evaluations for Integrative and Functional Medicine. Lord RS, Bralley JA (eds.) Duluth, Georgia. Metametrix Institute, 2008; Mason P. Important drug-nutrient interactions. Proc Nutr Soc. 2010;69:551-7.

This is a sign of functionally insufficient magnesium.

We also considered whether his diet and alcohol consumption were exacerbating any potential adverse drug-nutrient interactions. Surgery, malabsorption syndromes, and consuming a diet high in processed foods or very low in calories or an insufficiently planned vegetarian diet can place a person at risk for poor nutri-

tional status. Because Mr. T ate a typical American diet, that is, one that is heavy on processed foods that are high in saturated fat, and consumed alcohol, he was at increased risk for both low vitamin B6 and low magnesium.

We ordered standard laboratory tests specific to our concerns. Those included tests for homocysteine (to assess B6, B9, B12 function), fasting B6, fasting B12, serum or urine amino acid profile, magnesium, and potassium.

Mr. T's homocysteine level returned markedly elevated at 14.3 ng/mL (<9 µmol/L) with a normal glomerular filtration rate (GFR) of >60. His B12 was cautiously low-normal at 320 (200 to 1,000 pg/mL), which, when combined with the markedly elevated homocysteine, is an indication for a methylmalonic acid test for functional B12 deficiency. His B6 was barely measurable at 2 µg/L (6 to 50 µg/L), and his serum magnesium was low at 1.8 mg/dL (1.8 to 2.6 mg/dL). Urine amino acid testing demonstrated hypoaminoaciduria including low tryptophan, cysteine, methionine, and taurine.

In this case, the combination of low tryptophan and B6 likely blocked the patient's capacity to make serotonin, as serotonin is derived from tryptophan in the presence of B6 as pyridoxal-5-phosphate (P5P). Melatonin, the neurotransmitter so important for sleep, and which plays a role in metabolic syndrome, weight control, type 2 diabetes, and insulin resistance,[15] mood,[16] and antioxidant activity,[17] is two biochemical steps removed from serotonin. B vitamins, methionine, cysteine, and magnesium are required for the transformation of serotonin to melatonin.

Additionally, the low taurine may have been clinically significant. In brain cells, taurine is required for retention of calcium, magnesium, and potassium. Low levels of taurine, an inhibitory neurotransmitter, mean less neuroprotection against glutamate-induced excitatory states.[18] Taurine is also an antioxidant; and low taurine is associated with excess oxidative damage and aldehyde production in inflammatory states.

Mr. T's low vitamin B6 was also clinically important. Nearly 60 enzymes in amino acid metabolism require vitamin B6 as P5P, so multiple pathways may be affected. These include the pathways for the production of serotonin from tryptophan and taurine from cysteine. Additionally, magnesium (as Mg-ATP) is a crucial cofactor in more than 300 enzymatic reactions including those for protein, carbohydrate, and fatty acid metabolism as well as those for the activation of vitamin B6. The combination of Mr. T's low magnesium, low B6, and low amino acids highlights the cumulative or synergistic risks that come with interactions of pharmaceuticals and diet.

In treating Mr. T, we recommended supplementation with vitamin B6 (a total of 50 mg/day), a multivitamin with B vitamins and minerals, magnesium glycinate 600 mg/day, and a broad amino acid supplement. While on this regimen and undergoing other interventions including cognitive behavioral therapy and exercise, Mr. T did improve clinically.

Conclusion

What was responsible for Mr. T's improvement? In the absence of controlled trials, we cannot state that treating documented nutrient deficiencies accounted for his clinical improvement. However, the growing evidence about drug-induced nutrient deficiencies and our expanding understanding of the effect of various nutrients on biochemical processes provides a rationale for our treatment of Mr. T and for testing for nutrient deficiencies in other patients who present with similar symptoms and medical histories.

The case of Mr. T illustrates the potential value of the expanded differential and laboratory testing used in the emerging discipline of interventional nutrition. In the future, physicians likely will not only need to know when and how to prescribe pharmaceuticals but also when and how not to prescribe them. To this end, gaining knowledge of the potential drug-nutrient interactions is a crucial first step. **MM**

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A *Waste* of Time

A prescription for citalopram reveals much about what's askew in health care.

| BY JON VAN LOON, M.D.

The patient first came to me several years ago newly abstinent from methamphetamines and committed to a sober and productive life. She had maintained sobriety through hard work and had developed a mature sense of responsibility related to her job. She recently had received a promotion and finally qualified for her employer's health plan.

When she proudly marched into a local pharmacy to use her well-earned health care coverage to refill the medications that had, in no small part, played a significant role in her transformation into a responsible and productive citizen, she was told that the insurer would not pay for 80 mg of citalopram (three years earlier, an increase in her citalopram dose had facilitated the discontinuation of quetiapine, a considerably more expensive medication).

Of course, this refusal prompted my office to submit a prior authorization request, which took about 20 minutes of my nurse's time. The prior authorization request was denied. That necessitated an appeal, which involved another 20 minutes or so of nursing time. Within a few days, we were notified that the appeal had been denied. The company provided an address and fax number where we could submit our secondary appeal.

After taking a few days to cool down, I opened the patient's chart, reviewed her entire course of care, and drafted a letter that concisely summarized the rationale for prescribing citalopram above 60 mg. This process took about 30 minutes of my time plus time for a transcriptionist to prepare the letter. I wasn't surprised to learn that my nurse then spent two more hours on this secondary appeal because the fax number initially provided was wrong. We still haven't heard back from the insurer regarding the secondary appeal.

Physicians are routinely blamed for wasting health care dollars. Of course, the people leading the charge insist that the only way to control health care costs is through management of resources by the insurance industry. I am disgusted by the blatant disrespect many insurers show for our patients' health and well-being, their time, and the time and resources of our clinics and practices.

The scenario I describe is not unique to my practice, that patient, or that day. It is repeated over and over throughout our state—and it needs to stop. **MM**

Jon Van Loon is a psychiatrist in Rochester and former president of the Minnesota Psychiatric Society.

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