

# DISEASE STATE MANAGEMENT™

*Managing Chronic Illness Across the Continuum*

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Alzheimer's management

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### Special Report: Alzheimer's management

## One-page Alzheimer's guidelines streamline care protocol

*One-page tool assures no need is overlooked*

Physicians receive so many guidelines these days that rather than becoming useful tools to improve patient care, they often collect dust. When the California Workgroup on Guidelines for Alzheimer's Disease Management, sponsored in part by the Alzheimer's Association of Los Angeles, set out to develop its "Guidelines for Alzheimer's Disease Management," it was determined that the document wouldn't suffer the same fate.

## Rising problem comes with rising costs

Alzheimer's disease costs an estimated \$1 billion annually — placing it right behind heart disease and cancer in straining the U.S. health care delivery system, according to the Alzheimer's Association in Chicago. Providing appropriate care for the more than 4 million Americans suffering from Alzheimer's poses difficult challenges for health care organizations. The average Alzheimer's patient survives an average of eight years and as many as 20 years with this multifaceted disease which leaves its victims with a unique set of social, medical, and psychological needs. The average lifetime cost of caring for an Alzheimer's patient is \$174,000, a staggering one considering that the Alzheimer's population in the United States is expected to reach 14 million by 2050.

In this special report, Disease State Management introduces the recently released Alzheimer's care guidelines developed by the California Workgroup on Guidelines for Alzheimer's Disease Management, sponsored in part by the Alzheimer's Association of Los Angeles, for use in the primary care setting. You will also find information on training your staff to work with Alzheimer's patients and their families, the 10 warning signs of early Alzheimer's, and a case study of an Alzheimer's management program developed by a large managed care organization. ■

"We knew from the beginning that we wanted to develop a one-page guideline that primary care physicians could keep close at hand," says **Debra L. Cherry**, PhD, associate executive director of the Alzheimer's Association of Los Angeles. "We realize that physicians don't have the resources to meet all the needs of the Alzheimer's patient. The tool suggests other members of the health care team and the community that are available to help the physician provide the care suggested on the guideline." (See guideline, inserted in this issue.)

"The thing that's very unique about this guideline is that it brings together in one place all the strategies for comprehensive Alzheimer's care," notes **Elizabeth Heck**, LCSW, physician education and outreach manager for the Alzheimer's Association of Los Angeles. "There are other Alzheimer's guidelines, including one specifically for psychologists, and one from the government on early recognition and assessment of memory loss. They complement this guideline. They fit inside the framework." (See p. 99 for a case study of an Alzheimer's program developed by a large managed care organization which includes the new guideline.)

The one-page guideline is organized into four sections. A booklet that clarifies each of the components within the four sections, including suggestions for which member of the health care team is best suited to provide the suggested care or evaluation, accompanies the one-page guideline. The sections are:

**I. Assessment.** The guideline recommends assessments of daily function, cognitive status, medical conditions, and behavioral problems. "Care managers, social workers, or nurses can perform much of the necessary assessment," notes Cherry. "As we work with managed care organizations and health systems to familiarize them with the new guideline, we emphasize that we expect physicians to work with other professionals to do any assessment or care that is not strictly medical."

**II. Treatment.** The guideline includes

recommendations for using the newest drugs available for management of cognitive decline and behavioral issues. (See recommendations on pharmacological management, inserted in this issue.) It also suggests appropriate activities and therapies to help maintain and enhance daily function. Referrals to community service agencies and support groups are also recommended.

"Alzheimer's must be addressed on three levels — biological, social, and psychological," notes Cherry. "Any interventions to support the patient and the family must also be on all three levels."

**III. Patient and caregiver education and support.** "This is clearly where professionals such as care managers play an explicit role," says Cherry. "However, it's up to care managers and developers of Alzheimer's programs to educate physicians on that role. Unless others explain the role of care managers and other support professionals, and consumers demand better care, physician behavior won't change. Care managers can be a tremendous support in making any guideline work."

**IV. Reporting requirements.** "Reporting laws vary from state to state. There are many considerations such as reporting elder abuse and reporting the necessity for driving restrictions," notes Heck. "Here again, care managers and other support staff can be invaluable in helping physicians keep up with reporting needs — providing the appropriate forms and making sure that the process is followed properly."

### *Putting them to use*

Of course, a guideline is only useful if it is used, note Cherry and Heck. The work group developed an elaborate consumer and provider education plan to disseminate the guideline and encourage providers to use them. The guideline was introduced at a statewide conference held in April. "We invited the medical directors of managed care organizations and community resource organizations around the state," says Cherry. The guideline was introduced to a national audience at the

## COMING IN FUTURE MONTHS

■ Who's in charge here? Finding the right professional to head your initiatives

■ Computer software provides for total population management

■ Grass roots: How to develop disease management in rural areas

■ The hows and whys of integrating complementary therapies into your pathways

■ Breathe easy: New approaches to cystic fibrosis management

Eighth Annual Alzheimer's Disease Education Conference in Long Beach, CA, in July.

"We have a two-pronged campaign planned — one for physicians and one for consumers. We want consumers to demand better care. We want them to say, 'Doctor, that's not enough. I know there are more treatment options and resources available to help me cope with this disease.' We hope to force doctors to work with partners, such as care managers and social workers, to meet their patients' needs," says Cherry.

"We want to target a wide range of people who come in contact with this disease," adds Heck. "We are also developing additional tools to make the process even easier. We're training physicians and other health care providers on how they can support the recommendations in the guideline. We're explaining how they are integral to making the process run and move smoothly. We are educating the care manager, the social worker, the nurse, on what their roles can be to help the process." **(If your staff come in contact with Alzheimer's patients and their families, disease-specific training is essential. See suggestions for developing an Alzheimer's training program on p. 100. Also, see Alzheimer's warning signs, p. 101.)**

For more information, contact the Alzheimer's Association of Los Angeles, 5900 Wilshire Blvd, Suite 1710, Los Angeles, CA 90036. Telephone: (323) 938-3379. Fax: (323) 938-1036. ■

## Creating single contact improves Alzheimer's care

*MCO finds too many cooks spoil the broth*

**A**lzheimer's patients have wide-ranging medical, social, and psychological needs, but when too many providers are involved with no single point of contact and coordination the result is less-than-optimum care. Kaiser Permanente recently piloted an Alzheimer's care project in six sites nationwide that shows great promise for eliminating barriers that often prevent Alzheimer's patients from receiving appropriate, holistic care that addresses those diverse needs.

"What typically happens is that people with dementia and their family members think that the only source of information and care is from the physician. They hesitate to make an appointment just to receive information about their condition,

and we've found that information is the greatest need for both Alzheimer's patients and their families," notes **Ingrid Venohr**, RN, PhD, director of senior programs for Kaiser Permanente Colorado Region in Denver and a senior researcher for the pilot program.

Kaiser Permanente set out to design a new system of care for Alzheimer's patients with a primary goal providing the information, resources, and support services necessary to prevent complications that lead to costs such as premature nursing home admissions. "An essential first step was to educate our physicians and their staff about Alzheimer's. We created a manual to educate physicians and their staffs about the components of appropriate Alzheimer's care. The manual lays out what is core content that Kaiser sites must cover with providers and what is optional material," notes Venohr.

The pilot programs had local variations, but each of the six sites developed models of Alzheimer's care that include the following core components:

- **member/caregiver education programs;**
- **provider education programs;**
- **caregiver support programs;**
- **formal links with community resources;**
- **single point of information contact for caregivers;**
- **mechanism for using volunteers and/or community health workers;**
- **mechanisms for identifying Alzheimer's patients.**

"The most important component of the program is that single point of contact. Too many times, the diverse needs of Alzheimer's patients go unmet because family members simply don't know who to contact," says Venohr. "The six sites each had a telephone number staffed by social workers or nurses trained to refer family members to case management and other resources. The number can also be used by community agencies to ask us to look at a member more carefully or address a specific problem that has been identified by the agency."

### *No one 'right' way*

Venohr says one of the strengths of the program is that it allows each site to implement the core components in the most effective way, based on local variances. "For example, the program requires each site to provide caregiver support but allows each site to provide that support in its

own way. In Colorado, we refer to existing caregiver support programs. In San Diego, they provide their own caregiver support programs," she says, adding that the Alzheimer's Association is an excellent source of caregiver support programs and education.

One of the six sites included a senior volunteer program to its Alzheimer's care program. "The site uses specially trained senior volunteers to call caregivers and ask them about their own health and whether they have any new needs," says Venohr. "The senior volunteers offer reassurance and support through weekly telephone calls and help us detect problems earlier."

"The bottom line is that physicians have limited time to spend with patients, and families aren't always comfortable turning to the physician for education and support services. We're used to the physician being in a hurry. We don't look for physicians to provide information or education," says Venohr.

"We have to improve our system of care to link Alzheimer's patients and their families earlier and more effectively with the education and support services that help them live longer, more comfortable lives in the community," she notes. "That means that insurance plans and health systems must be more proactive in linking patients with community-based services; and the key to making it work is providing a single point of contact — a number families can call to arrange all of the services and receive all of the education they need." ■

## Training improves Alzheimer's care

*Be sure you cover the basics*

If your staff works with Alzheimer's patients, even if those patients make up a small percentage of your patient population, you understand the necessity of Alzheimer's training. And, if it's been a while since your last Alzheimer's inservice, it's probably time for an update.

"The depth of your training depends on the specific purpose of your inservice," notes **Betsy Pegelow**, RN, MSN, director of Special Projects, Channeling Program, an Alzheimer's caregiver support program of the Miami Jewish Home and Hospital for the Aged. "But whether we are

training our dementia-specific case managers, caregivers, or support staff, there is some basic content that we always cover."

The following is some basic information that Pegelow suggests anyone working with Alzheimer's patients should receive — whether they are family members, housekeeping staff, nurses, social workers, or other professionals:

- **Characteristics of dementia.** "We cover not only the definition of dementia, theories for the causes of dementia, and diagnostic testing for dementia, but we also cover the impact of dementia on the caregiver and extended family," she explains. "We want our staff to understand not only the common problems they might encounter when working with the families of Alzheimer's patients, but how coping with those problems affects families."

- **Stages of disease.** "Alzheimer's is a progressive disease. Your professional staff — in particular — case managers, should understand how to stage the disease in order to help families plan and anticipate issues common to each stage," says Pegelow.

- **Drug therapy.** "There are drugs available to enhance memory and manage behavioral issues. Staff and caregivers should be updated regularly on the newest drug therapies," she adds.

- **Caregiver issues.** "Case managers, aides, and home health providers must partner with caregivers when working with Alzheimer's patients. Their relationship will be more with the caregiver than the patient."

- **Dementia-proofing the house.** "Living with an adult with dementia is very similar to living with a toddler," she notes. "Case managers, social workers, and home health staff should help caregivers evaluate safety issues in the home in order to limit the risk of accidents and injuries."

- **Techniques for behavior management.** "There are so many behavioral issues involved in Alzheimer's care," she notes. "There is agitation and the potential for injury. There is aggressive, abusive behavior." Pegelow teaches her staff and caregivers communication and distraction techniques to help manage behavior common to Alzheimer's. "Some techniques can be used with any frail, elderly population. However, redirection, distraction, and cueing are specific to dementia clients." **(Both the national office and your local chapter of the Alzheimer's Association have resources for training staff in these and other techniques for managing Alzheimer's patients. Also see editor's note at end of this article for**

## Watch for these 10 warning signs of Alzheimer's disease

According to the Alzheimer's Association in Chicago, here are the 10 early indicators of Alzheimer's disease:

**1. Recent memory loss.** It's normal to occasionally forget a colleague's name or telephone number and remember them later. Individuals with dementia may forget things more often and not remember them later.

**2. Difficulty performing familiar tasks.** Busy individuals can be so distracted that they may leave food cooking on the stove and only remember to serve it when the meal is nearly over. Individuals with Alzheimer's disease may prepare a meal, forget to serve it, but also forget that they prepared it.

**3. Problems with language.** It's normal to have occasional difficulty finding the right word. An individual with Alzheimer's may forget simple words or substitute inappropriate words, making his or her sentences incomprehensible.

**4. Disorientation of time and place.** It's normal to forget the day of the week or your destination for a brief moment. Individuals with Alzheimer's can become lost on their own streets, not knowing where they are, how they got there, or how to return home.

**5. Poor or decreased judgment.** Individuals can become so immersed in an activity that they temporarily forget important facts, such as

that they are supposed to be watching a young child. Individuals with Alzheimer's may forget entirely that the child is under their care. These individuals may also dress inappropriately, wearing several shirts or blouses on a warm day, or very little clothing in cold weather.

**6. Problems with abstract thinking.** Individuals with Alzheimer's may forget what the numbers in their checkbook are and what needs to be done with them.

**7. Misplacing personal items.** It's not uncommon to temporarily misplace a wallet or a set of keys. Individuals with Alzheimer's may put things in inappropriate places. For example, they may place an iron in the freezer, or a wrist watch in the sugar bowl.

**8. Changes in mood or behavior.** Everyone experiences occasional sadness. An individual with Alzheimer's may exhibit rapid mood swings. These individuals may move from calm to tears to anger for no apparent reason.

**9. Changes in personality.** Individuals often experience slight personality changes with age. An individual with Alzheimer's may change drastically, becoming extremely confused, suspicious, or fearful.

**10. Loss of initiative.** It's normal to tire of housework, business activities, or social obligations, but most people regain their initiative. Individuals with Alzheimer's may become very passive and require cues and prompting to become involved. ■

### other resource suggestions.)

• **Legal and financial issues.** "This is especially important for caregiver training," notes Pegelow. "The primary caregiver must have an emergency plan that clearly outlines what should happen if the caregiver becomes ill or injured." She adds that it's your staff's responsibility to explain the importance of such a plan and help the caregiver develop it. A case manager or social worker often fulfills this task.

• **Resources.** Of course, health care providers understand the value of information. Pegelow has a library of written materials and videos specific to dementia, and she refers to them regularly.

She has also taken all the handouts she's assembled through the years to fill a resource manual for her staff. The manual has plastic pages that staff members can pull out and copy

for families as needed. Many of the sheets discuss specific issues, such as coping with incontinence.

However, no inservice replaces the need for attending professional meetings, says Pegelow. "We send our staff to an annual meeting. We are fortunate enough to have a one-day workshop in our local area that provides updates on Alzheimer's and breakout sessions. It's very important to keep current, and nothing is as effective as a professional meeting," says Pegelow. "Consumers are very sophisticated. They have access to the latest developments via the Internet. Case managers have to be knowledgeable enough to answer caregivers' questions."

*[Editor's note: One Alzheimer's resource that Pegelow strongly recommends is now available through the Alzheimer's Association, Public Policy Division, in Washington, DC. Resources for Serving*

Caregivers in Culturally Diverse Communities: A Compendium of Products Developed through the HRSA-AOA Alzheimer's Demonstration Grant to States Project sells for \$12. It lists Alzheimer's-specific community resources with an emphasis on respite services and other caregiver support programs. It includes information on handbooks, manuals, pamphlets, videos, and other training materials. Pegelow notes that most local chapters of the Alzheimer's Association can also provide training for caregivers, staff, and aides. To order the compendium, contact the Alzheimer's Association, Public Policy Division, 1319 F St., N.W., Washington, DC 20004. Telephone: (202) 393-7737.

The national office of the Alzheimer's Association is

also an excellent resource. Contact the Alzheimer's Association, 919 N. Michigan Ave., Suite 1000, Chicago, IL 60611-1676. Telephone: (800)272-3900.

In addition, the National Chronic Care Consortium and the Alzheimer's Association recently completed a joint project called the Alzheimer's Disease Project. As part of that project, the organizations compiled and released a package that contains information on tools available to assess and treat patients with all stages of dementia, from early identification through the end-of-life in managed care settings. For more information, contact the National Chronic Care Consortium, 8100 26th Ave., S., Suite 120, Bloomington, MN 55425. Telephone: (612) 858-8999. ■

## Iron out a serious problem with your diabetic patients

*Don't ignore the risk of hemochromatosis*

**H**emochromatosis experts urge caregivers to consider whether iron disorders can be at the root of the problems their diabetic patients face. Often, the condition can go unrecognized, even though it's the most common potentially fatal disorder people in North America can inherit.

"Not too long ago, a physician might not expect to see more than one case of hemochromatosis in an entire career. Now we need to re-think that," says **Vincent Felitti**, MD, FACP, an internist in the department of preventive medicine at Kaiser-Permanente in San Diego.

### KEY POINTS

- Hemochromatosis occurs in approximately one in 250 Americans, making it much more common than most health care professionals realize.
- The iron-loading disorder can overload beta cells in the pancreas and restrict insulin production. If the iron-loading condition lasts long enough, it will destroy beta cell function, making diabetes irreversible.
- Iron experts recommend routine ferritin testing for all Type 2 diabetics, to determine if hemochromatosis is the underlying cause of their disease.

Hemochromatosis is a genetic metabolic disorder where an individual absorbs too much iron in the gastrointestinal tract, resulting in serious health problems including arthritis, cirrhosis, diabetes, impotence, heart failure, and death.

It's a disease frequently underdiagnosed, says **Mary Cogswell**, DrPH, an epidemiologist at the Centers for Disease Control and Prevention in Atlanta. But once it gets a foothold, diabetes can develop when iron accumulations cripple islet cells in the pancreas. Today, diabetes ranks fourth as a common comorbidity of hemochromatosis after arthritis, severe fatigue, and elevated concentration of liver enzymes. But if it can be recognized early enough in its development, the problems it causes can be reversed, says Felitti, who notes that depending on the age of the patient, hemochromatosis-induced diabetes may be diagnosed as Type 1 or Type 2.

### *Iron disorder often goes undetected*

Earlier this year in the *American Journal of Preventive Medicine*, Cogswell reported that doctors look for a traditional presentation of the disease, a triad of skin pigmentation, diabetes mellitus, and cirrhosis or liver disease. But the condition appears this way only in a minority of cases. Furthermore, Cogswell adds when those classic symptoms are present, the disease is already at the end stage and it's too late to try to reverse the diabetes.

Cogswell says statistics based on diagnostic data are probably underreported because hemochromatosis is rarely listed as the primary reason for a visit to the doctor when diabetes, arthritis, or other more symptomatic diseases are present.

The same holds true for death certificates, she

## An unhealthy bronze

Once known as “bronze diabetes” because of the darkened skin tones and hyperglycemia common among sufferers, hemochromatosis is much more common than most caregivers think.

Recent research shows it is present in about one in 250 Americans, mostly striking Caucasians of northern European descent. Among these populations, varying estimates of prevalence range from .2% to .5%, although it has been found in virtually every ethnic and racial group. In diabetics, the prevalence of hemochromatosis may be 1% or even higher, according to the Centers for Disease Control and Prevention in Atlanta. ■

says. For example, only 1.8 in a million deaths in 1992 were directly attributed to hemochromatosis, she says. The low death rate is perhaps partially attributable to effective treatment, she says, but more likely the disease has never been diagnosed in some patients at all. Doctors continue to treat patients as though they have diabetes alone, when in fact, the diabetes is secondary to a life-threatening iron disorder that could have been treated before it caused such complications.

Cogswell says studies show hemochromatosis is unlikely to be detected in patients with diabetes and liver diseases, unless doctors look for it specifically. And if conventional diabetic medications are started, the patient’s condition usually doesn’t respond to it.

The disease is like a “big bully” because it can bring such dire side effects, says **Eugene Weinberg**, PhD, professor emeritus of microbiology at Indiana University in Bloomington. But it is easily treated. And as it’s becoming more common, more clinicians are learning to recognize it more often in the United States, he says.

Felitti says he strongly advocates testing the general population for iron loading disorders at least once in a lifetime. The test should come early in life for those who have a family history of the disorder.

“At the very least,” he says, “All Type 2 diabetics should be tested as part of the standard work-up when blood sugars are found to be elevated enough to warrant a diagnosis of diabetes.”

A random transferrin saturation test is as simple as any other blood test and is both accurate and inexpensive, says Felitti. In fact, he says, the idea

of adding transferrin saturation and serum ferrin screenings to other types of blood panels has been considered by several health care organizations.

“Anyone with a serum iron saturation level over 50% is suspect for the disease, so a repeat test is warranted, with the patient fasting and abstaining from any vitamin or mineral supplements for at least 24 hours.

“If the serum iron saturation test is still over 50% and the ferritin level is elevated, I recommend proceeding directly to phlebotomy [the nearly universally successful therapy for hemochromatosis],” he says.

Cogswell notes that cutoff values should be lower for women than for men because their distribution of transferrin is lower than men’s.

Weinberg adds that men usually begin showing signs of hemochromatosis in their 20s or 30s, but women frequently show no signs until they reach menopause, when they no longer shed iron through normal menstruation.

But, he says, “It varies all over the map how much damage is done and when. It’s extraordinarily variable which organs are going to be affected.”

Cogswell stops short of recommending universal hemochromatosis screening, at least in terms of her role at the CDC, because she says there have not been enough detailed studies on the issue. However, “from a practical standpoint, it would make sense to screen,” she says.

She says the disease is “common in comparison with many genetic disorders” and it meets many of the criteria for population screening, but the statistics on its incidence need further verification with more studies. But she acknowledges “the potential for preventing hemochromatosis-associated illness and death through screening and treatment may be great.”

Prevalence of hemochromatosis in the general population is “borderline,” adds **Michael Engelgau**, MD, a medical epidemiologist at the CDC. However, he says, the prevalence of the disease in people with diabetes is “probably high enough to warrant special screening.”

### *Deterrents to testing*

The cost of an across-the-board screening of Type 2 diabetic patients, could be prohibitive, notes **Richard Dickey**, MD, president of the American Association of Clinical Endocrinology and a practicing endocrinologist in Hickory, NC.

“Medicare will not pay for it, precluding the

test in most patients, since it costs \$54 from my lab and they would have to pay for it themselves," Dickey says. He also says some labs include ferritin levels in some panels, thereby getting around that obstacle.

He also said that generalized testing could get the prices down to as little as \$20 per member of a large HMO or other large health care organization. But for individual patients seeing doctors in small practices, the price is not likely to drop.

Felitti also says hemochromatosis is hard to recognize, since patients frequently exhibit no symptoms. "There are people who have hemochromatosis that do not manifest it in any way except in death," Dickey says.

Felitti agrees, but encourages practitioners to look for hints of the disease. "An overloaded person can go for months of even years with no problem, and then suddenly flare up. It can be quite dramatic to see," he says.

The key is early diagnosis, says Felitti. "Complications are 100% preventable if it is caught early enough." Even later stage diagnoses are 99% reversible through phlebotomy, he says.

"I had an 82-year-old man in my office this morning who has had 120 pints of blood removed. His ferritin levels are now normal and he's feeling fine," says Felitti. A typical patient with hemochromatosis may require the gradual removal of as much as 80 pints of blood or more. If a patient is seriously overloaded with iron, phlebotomies could take place as often as twice a week, taking about a pint each time.

The goal is to return iron saturation to a normal level. Then maintenance phlebotomies at regular intervals will keep the patient stable and prevent iron buildup and the subsequent complications. Those diagnosed as a result of familial screening who present no symptoms may be deironed with the removal of only 10 or 15 pints of blood.

When the patient's ferritin levels have dropped below 1,000 ng/mL, treatment may be needed on a weekly or biweekly basis. Then, when ferritin levels are at 300 ng/mL for men and 200 ng/mL for women, treatment frequency drops to once or twice a month. At the maintenance level (25-75 ng/mL), drawing blood depends on the patient's condition. Phlebotomies are usually performed from once a month to quarterly.

Felitti also warns clinicians against expecting to see the typical darkened skin of "bronze diabetes," which is fairly uncommon. (See box, p. 103.) "But I did see a man at 7:15 this morning

who had remarkably dark skin, equally tan all over, even in the underarms. That was clearly bronze diabetes," Felitti says, who is a scientific advisor to the Iron Disorders Institute in Greenville, SC. "If you wait for bronze diabetes, you'll make only end-stage diagnoses in people who you are going to autopsy soon."

"Family practitioners are overwhelmingly unfamiliar with the disease. Even many hematologists have no familiarity with it at all," says Felitti.

He gives every patient who needs to be tested a printed letter of instruction explaining what tests they need. "We will even interpret the lab results at no charge because so many doctors are resistant to direction on this issue," he explains.

Dickey adds, "It's certainly not something we pick up as often as we should. Any patient with endocrine disorder or evidence of liver disease should be tested."

*[For more information, contact Eugene Weinberg at (812) 855-4842, Vincent Felitti at (858) 573-5454, Mary Cogswell at (770) 488-6053, and Richard Dickey at (828) 322-7338.] ■*

## Swedes say genetics can help tailor treatment

*Do benefits outweigh privacy implications?*

Members of a Swedish research team say physicians may one day use genetic tests to determine how well a drug will treat a patient's condition long before they write the first prescription to treat it.

### KEY POINTS

- In June, a Swedish team announced it has devised a genetic test to help doctors predict how hypertensive patients will respond to ACE inhibitor therapy.
- Observers say doctors need such tests so they can apply the findings of clinical trials to how they treat individual patients.
- Some ethicists say the benefits of the tests outweigh the risks of stigmatizing patients as difficult to treat.

Doctors say there is a great need to be able to preview how a patient will respond to a drug. And the benefits that could come from such tests far outweigh the risks to society, such as genetically stigmatizing some patients as difficult to treat.

At the recent Ninth European Meeting on Hypertension in Italy, the researchers from Uppsala University and Euron Medical AB announced they could identify a genetic marker in 31 of 102 patients, which they believed would indicate a good response to ACE inhibitors.

### **Results of the study**

Seventy-three percent of these patients had successful drug therapy, defined as a reduction of diastolic blood pressure by more than 10 mmHg or reaching a level below 90 mmHg. In the remaining patients who did not have this ACE inhibitor responder signature, 42% still had positive results.

Lead researcher **Hans Lithell**, MD, PhD, says his team is beginning with ACE inhibitors and hopes to be able to develop similar techniques for other classes of drugs like beta-blockers, diuretics, angiotensin II inhibitors, and calcium channel blockers.

"Today, doctors start treatment quite blindly," says Lithell, professor of geriatrics at Uppsala University. "Nobody knows any characteristics of which drug to start with."

In general, Lithell says, doctors know how to match up drugs and the conditions they treat. But on an individual basis, one patient may do well on a drug while another person with the same condition will not. Lithell says his team is working out a way to recognize genetic patterns — or polymorphisms — in patients that are related to favorable responses to particular types of drugs. "Our first study is with ACE inhibition," he says. "There is that relationship there."

Whether Lithell's study is a breakthrough or another step in the direction of a test is not certain, says **Jay N. Cohn**, MD, professor of medicine at the University of Minnesota in Minneapolis. But those steps need to be made. He says physicians must be able to apply the findings of large clinical trials to their individual patients in their own practices.

When large clinical drug trials become available, they show the trends of how patients responded to the treatment. "But everyone within the trial doesn't benefit," Cohn says. Doctors just can't get a copy of the published study and be

able to tease out how individuals did.

Genetic tests like Lithell's may be what doctors need, or perhaps the answer lies elsewhere, such as determining physiologic markers, Cohn says. Researchers may be able to look at the physical state of a blood vessel and be able to determine how it will respond to drugs. But the important thing, he stresses, is that researchers keep looking for the tests that will help doctors improve the care they give to patients. Working with genetic testing, however, leads to these questions:

**How should physicians counsel patients when test results return?**

**What will different interest groups such as insurers do with the information?**

"I don't think we should slow down the search for genetic markers for response because they will have social implications," Cohn adds. "Social issues have to be addressed as they develop."

"The general notion has been we're already going down this road," says **William Fassett**, PhD, MBA, a pharmacy ethicist and incoming dean of the school of pharmacy at the University of Washington in Seattle. Scientists are mapping the human genome. Doctors already have genetic tests that are markers for diseases like Tay-Sachs, he adds, so the need for counseling and the protection of privacy are not new concepts.

At one extreme, Fassett says, people may fear advances in genetics will lead to constant scrutiny. Each hair or flake of skin someone sloughs off and leaves behind could betray the privacy of the owner. But the other side of the story holds the promise of how doctors may be able to help patients.

"The need to be able to test drugs is so great that people will want that," Fassett says. "You're not going to stop the science."

The question to address is not how to control the science, Fassett explains, but how to use the information scientific research provides.

A good example is how Americans have been struggling with the use of personal credit reports and financial information. At any time, there are plenty of people who can get access to these personal records if they are willing to do some research and spend some money. Consumers can't do much about that, he says. But Congress can pass laws that protect an individual's rights by adding explanations to the report or note when it is being contested and why. Genetic testing may lead to similar measures for medical files.

Lithell notes his test isn't like the extreme that

Fassett describes — where tissue samples taken from patients are studied for all sorts of personal information. Rather, it's more like a blood test that looks for particular blood types, then discards the sample. The only trait the laboratory would be looking for would be the response to a particular drug. But even so, others say it will bring its own set of responsibilities.

"It's just what we are dealing with now," says **Bill Allen**, JD, assistant professor for the Program of Medical Ethics, Law and Humanities at the University of Florida College of Medicine in Gainesville.

Allen notes things can get a bit tangled when determining how the law protects patients' privacy of genetic information. In Florida, for example, genetic information is considered to be private, unless a patient gives consent for others to use it.

But insurers may be getting permission when new subscribers sign a general waiver that is often required to join a health plan. (Such a waiver often can act as a blanket permission statement to gain access to personal files.) It's a good idea to understand what members are permitting their insurers to see when they sign this statement, he says.

### *How protective are state laws?*

There is another wrinkle: Under the Employment Retirement Income Security Act (ERISA), state laws that protect individual genetic information may not apply to people who are self-insured or get their coverage through the large companies that insure their own employees and often use an insurer as a third-party administrator. Allen says when it comes to protecting the privacy of genetic information, "the state laws are not a huge significance."

There is protection under federal law, says **Philip Reilly**, MD, JD, president and CEO of the Eunice Kennedy Shriver Center in Waltham, MA, a research facility for developmental disabilities and mental retardation, and an editor of *The Gene Letter*. People are protected through the Health Insurance Portability and Accountability Act of 1996, he says, which keeps insurance companies from using genetic material as a basis for rejecting people who are switching health plans.

Lithell's test doesn't set off any alarms, he says, mostly because doctors need to have such tests to tailor care. He adds that he speaks with insurers all the time. They tell him they'll avoid using information as a basis for their underwriting because

the controversy "and political hot water" isn't worth the money they could save.

Federal legislators are also working on other bills this summer that contain provisions for keeping medical information private.

Allen notes that consumers should realize having such genetic tests could change the way insurance plans are structured. Companies may not use genetic information to keep people out of the plan but still could use it as a basis for coercion. Members who take the test and use the drugs that are indicated by the results may be rewarded with lower copayments.

Today, medical ethics needs to follow the relationship between doctor, patient, and insurer, Allen says. The trick is to come up with a system that gives the payer a legitimate voice without breaking down the relationship between doctor and patient. ■

## Depression can speed onset of Type 2 diabetes

*Risk factor for diabetes as well as other conditions*

Researchers have long known of the link between diabetes and depression, although no one is certain which comes first. They've also thought the depression meant that patients did not take good care of themselves and therefore had poor glycemic control.

But now a study from Washington University in St. Louis shows that the increases in cortisol relate to depression and that leads to hyperglycemia, for the first time linking the physiological effects of the

### KEY POINTS

- Depression can have a clinical effect on diabetic patients.
- Researchers at Washington University in St. Louis have found that depressed diabetics and even those with impaired glucose tolerance are more insulin-resistant.
- There are estimates that as many as 90% of all Type 2 diabetics have episodes of depression and 15% to 20% have major depressive disorders.

two disorders. Furthermore, depression — even in patients with pre-diabetes or impaired glucose tolerance — may promote insulin resistance and speed the onset of Type 2 diabetes, says lead author of the paper, **Patrick Lustman, PhD**. Lustman is a professor of medical psychology and director of the Office for the Study of Stress and Depression in Diabetes at Washington University School of Medicine.

Lustman presented his research at the 59th Scientific Sessions of the American Diabetes Association in San Diego in June. He estimates that 15% to 20% of all Type 2 diabetics suffer from major depressive disorders and perhaps as many as 90% of people with Type 2 diabetes have episodes of depression. “Depression is a risk factor for Type 2 diabetes,” he says, noting it may not get as much press as obesity.

Lustman and his colleagues are looking at the physical effects of depression at multiple levels from onset to the progression of the disease and its complications. In three studies, Lustman has found that successfully treating depression results in improved glycemic control — with patients reducing their HbA<sub>1c</sub> levels by .4 to 1.2%. “Nowhere else in medicine had there been as good a case made for treating an emotional problem and improving a patient’s medical condition,” Lustman says.

“Diabetes causes abnormalities in neurotransmitter function,” he continues. “Those abnormalities in dopamine and serotonin production have strong implications in depression.” He found that cognitive behavioral therapy, a form of psychotherapy designed for the treatment of depression, helped bring 85% of the diabetic patients in his study into remission.

Treatment was effective, but it is rarely permanent, as 80% of all depressed patients have recurrences and afflicted patients are rarely without symptoms for more than a year at a time.

In the cognitive behavioral therapy study, Lustman found that 92% of the patients treated averaged 4.8 episodes of recurrence of depression within a five-year follow-up period. He says further studies will provide more information about the effectiveness of cognitive behavioral therapy and maintenance anti-depressant medication.

In the paper presented at the ADA sessions, Lustman found that depressed diabetics experienced 31% more bodily pain, considered themselves 49% less vital than controls, and had lower scores on self-reported general health, mental health, and physical and social function.

Lustman also found that recurring depression was dependent on the severity of a patient’s medical condition and particularly the presence of neuropathy at the entry point.

“We have found that the status of a patient’s diabetes determines the course of the disease,” Lustman says. “It’s not really surprising since diabetes is a major stressor in itself. The disease is a roof that imposes itself over everything in his life. There are worries about complications. It’s hard to feel good when you’ve got an open sore on your foot that won’t heal.”

Mark Peyrot, PhD, of the Loyola College Center for Social and Community Research in Baltimore, found that diabetic patients at the highest risk of persistent depression were those who had more than two complications of the disease, were not treated with insulin, and who did not graduate from high school.

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Group Publisher: **Brenda Mooney**, (404) 262-5403, ([brenda.mooney@medec.com](mailto:brenda.mooney@medec.com)).

Executive Editor: **Park Morgan**, (404) 262-5460, ([park.morgan@medec.com](mailto:park.morgan@medec.com)).

Managing Editor: **Valerie Loner**, (404) 262-5536, ([valerie.loner@medec.com](mailto:valerie.loner@medec.com)).

Production Editor: **Nancy McCreary**.

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#### Editorial Questions

For questions or comments, call **Valerie Loner** at (404) 262-5536.



## Depression Rx

Researchers at Brown University recently found that a combination therapy of the anti-depressant drug Serzone and cognitive behavioral therapy seemed to have a synergistic effect: 85% of all depressed patients (nondiabetics) had significantly reduced or even eliminated depression after a 12-week course of treatment, compared to less than 50% success in patients taking either the drug or the therapy alone.

Lustman says the vast majority of diabetics with depression are not recognized by their physicians. "Probably two-thirds of the patients with depression are never diagnosed or treated," Lustman says. "Doctors need to ask patients about their state of mind and quality of life."

Even though doctors are pressed for time, Lustman says, they would likely find significant improvements in their patients' glycemic control if depression is treated pharmacologically and/or with psychotherapy. "If doctors would just rely on a couple of quick questions, we'd have much better results."

Unfortunately, in many primary care practices, patients who are diagnosed with depression are simply given anti-depressant medications without any emotional support or follow-up until the next semi-annual visit. A patient has a 25% chance of improving mentally and physically with treatment for depression, and that 25% is "no small prize in terms of quality of life," Lustman asserts.

He suggests asking patients these questions if they seem to be at risk of depression:

**1. Have you been feeling sad for more than two weeks?**

**2. Has your activity level changed?**

Even more effective, Lustman says, is the Beck Depression Inventory, a brief paper-and-pencil test in which the patient answers 21 questions. It measures cognitive and somatic symptoms that he says would point out about 70% of depressed diabetic patients.

Lustman's findings are similar to Peyrot's latest paper on Type 1 disease, published in the June issue of the *Journal of Health and Social Behavior*. In this study, Peyrot found that stress-related lapses in self-care resulted in poor glycemic control among the patients who can least afford it physiologically. Patients with Type 1 diabetes are more vulnerable than those with Type 2 to stress-related lapses in blood sugar maintenance, and

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failure to attend to these matters can have disastrous consequences.

In an earlier study, Peyrot found that 41.3% of all adult diabetics suffered from depression and 49.2% from anxiety, far higher than in the general population where estimated rates of depression and anxiety range between 10% and 20%.

Researchers at Kaiser-Permanente's Center for Health Research in Portland, OR, found the cost of treating depressed diabetic patients was 68% higher than all cost expenditures on nondepressed nondiabetic patients.

**Gregory A. Nichols, PhD**, a senior research assistant at Kaiser, says his organization has a data base of 35,000 diabetic patients treated since 1988, so there are ample opportunities to study issues like the links between depression and diabetes.

"We found people who are depressed are more likely to be taking insulin," Nichols says. "Also, the depressed group tended to be younger, were more likely to be female, had more comorbidities, and have a higher BMI [body mass index]."

[For more information, contact Patrick Lustman at (314) 362-2441 and Gregory Nichols at (503) 335-6733.] ■