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July 2, 2010

Newspaper of the
American
Psychiatric
Association

PSYCHIATRIC NEWS

inside

PERIODICALS:
TIME-SENSITIVE MATERIALS

Credit: David Hathcox

Outgoing APA President Alan Schatzberg, M.D., presents a check for $6,100 to Martha McCarty, director of family services for the New Orleans Mission, at the Opening Session of APA's 2010 annual meeting in New Orleans in May. The funds came from APA members who responded to a donation program sponsored by APA prior to the meeting. The mission assists homeless individuals by providing meals, clothing, shelter, and literacy and job-skills training. For more annual meeting photos, see page 6.

White House Wants More Heed Paid To Community-Care Mandate

Eleven years after the Supreme Court's landmark *Olmstead* ruling that seriously mentally ill individuals have a right to be treated in community settings, the Obama administration launches a new effort to boost compliance.

BY RICH DALY

This month's 20th anniversary of the Americans With Disabilities Act (ADA) comes with a renewed focus by the Obama administration on encouraging state compliance with the Supreme Court's landmark ADA-related decision regarding people with serious illnesses, including mental illness.

July 26 will mark two decades since President George H.W. Bush signed the sweeping federal protections for people with disabilities into law. That law took on increased significance for people with mental illness when, nine years after it was signed, the Supreme Court handed down its decision in *Olmstead v. L.C.*, which declared that "unjustified institutional isolation of persons with disabilities is a form of discrimination" under the ADA. The decision obligates states to serve those individuals in the most "integrated" setting possible that allows them to still receive the treatment they need.

The ruling was widely hailed as an imperative to move people with serious

please see ***Community Care*** *on page 26*

Small Practices Win Delay In I.D. Theft Regulations

A delay in the requirement that physicians undertake measures to prevent the theft of their patients' identities comes as physician groups file suit and Congress considers exempting them from the requirement.

BY RICH DALY

Small and independent physicians' practices won't have to implement federally mandated identity theft protection measures for their patients' information until the end of the year, at the earliest.

The decision by federal regulators in May to delay implementation of a requirement that physicians' practices develop policies and procedures to safeguard their patients' identity-related information came as several physician groups filed a legal challenge to the requirement and as Congress was considering a targeted exemption from it for physicians.

Known as the "red-flags rule" because it aims to limit "possible risks to account holders or customers or to the safety and soundness of the institution or customers," the Federal Trade Commission (FTC) regulation requires businesses offering credit to develop and regularly update a written policy for finding, preventing, and resolving identity theft.

But physicians' advocates have argued that physicians are not creditors like banks and lenders, which the regulation is intended to target, and that the rule should not apply to them.

The AMA "is pleased that [the FTC] has announced today they are delaying the compliance deadline for the red-flags rule until the end of this year," said Cecil Wilson, M.D., then AMA president-elect, in a written statement. "We call on the FTC to exempt physicians from the rule completely."

Regulators have delayed the application of the controversial regulations to physicians several times already, including scrapping the most recent compliance deadline of June 1.

The FTC said in a May 28 statement that the latest delay came at the request of several members of Congress, who are pushing legislation to exempt small businesses, including medical practices, with 20 or fewer employees from the requirements.

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Innovative Minority MH Efforts Awarded at Foundation Gala

Some $80,000 was raised at the event, which was held at the Grand Oaks Mansion near the Port of New Orleans.

BY MARK MORAN

Five agencies working to advance minority mental health care were honored by the American Psychiatric Foundation at its annual benefit, held in May at APA's 2010 annual meeting in New Orleans.

The Awards for Advancing Minority Mental Health honor the commitments and efforts undertaken by psychiatrists and mental health professionals who have organized programs that provide for the mental health needs of minorities.

The ceremony was held at Grand Oaks Mansion, near the Port of New Orleans. The mansion is restored inside a domed replica of 19th-century splendor: brick walkways, moss-draped oaks, and wooden bridges crossing meandering streams. The dome above simulates a starlit night.

These are the five award-winning programs:

Credit: David Hathcox

American Psychiatric Foundation President Richard Harding, M.D., announces the winners of the Awards for Advancing Minority Mental Health.

• **Hermano Pedro D.C. Multicultural Day Shelter of Catholic Charities** in Washington, D.C., received an award for its efforts to empower underserved low-income and homeless people who are affected by mental illness and substance abuse. The shelter offers a full range of social services including case management, counseling, education, and referral services through a bilingual staff and a group of psychiatry residents from the District of Columbia's Department of Mental Health. Approximately 200 people come to the shelter daily.

• **Merced Lao Family Community Inc.** in Merced, Calif., received an award for its Southeast Asian Consumer Advocacy Program (SEACAP), which provides culturally centered mental health services that include a combination of traditional cultural practices and Western methods of care. A wide range of services is offered by SEACAP including individual and group therapy and rehabilitation, treatment, case management, family intervention, and peer support.

• **The Center for Latino Mental Health** in Chicago received an award for its work to increase understanding of and access to culturally competent mental health services through its three main components: research, community service, and education. The center spurs research on the diagnosis, treatment, and prevention of mental disorders among

please see ***Awards*** *on page 26*

APA Voting Moving to Online Only

Is Your Correct E-Mail Address on File?

APA's national elections are transitioning to an all-electronic process with a fast, easy, and secure means to vote online. Online voter participation has steadily increased, reaching a rate of 50 percent in APA's last election, and shows promise of continued growth. Beginning with the 2011 election, all eligible voting members with a valid e-mail address on file will receive only an electronic ballot.

To ensure that you get your ballot, please update your contact information in Members Corner on APA's Web site at <https://myaccount.psych.org/MembershipProfileUpdate/tabid/163/Default.aspx>. E-mails sent directly from APA will include a link to personalized electronic ballots, voting instructions, and candidate information.

Voting members without a valid e-mail address on file will still be sent a paper ballot for the 2011 election. APA members with questions or comments may e-mail them to election@psych.org.

APA RESOURCES

- ***Psychiatric News* Web Site:** pn.psychiatryonline.org
- **APA and the APA Answer Center:** (888) 35-PSYCH in the U.S. and Canada; in other countries: (703) 907-3700. The Answer Center is open Monday through Friday, 8:30 a.m. to 6 p.m. Eastern time. All APA departments and staff may be reached through the Answer Center. Fax: (703) 907-1085 E-Mail: apa@psych.org
- **APA Web Site:** www.psych.org
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Reaching Out to the Next Generation

CAROL A. BERNSTEIN, M.D.

As some of you may know, my career in psychiatry has been in the education and training of the next generation of psychiatrists. We must continue to nurture the next generation of clinical and scientific leaders to ensure the continued viability of our Association. Why is this particularly significant now? For the first time in U.S. history, there are four generations in the workplace in the United States: The World War II generation (born 1925-1945), the baby boomers (1946-1964), the generation Xers (1965-1981), and the millennials (1982-2000).

The gen Xers and the millennials are our field's future leaders, educators, researchers, and clinicians. The communication and technological changes they have experienced have already radically altered the way in which they live their lives. They are the most racially and ethnically diverse in our nation's history. The oldest millennials are approaching age 30 and represent most of our medical students and residents. Generation X is moving into its peak family-raising years. They are looking for a less hectic lifestyle and are passionate about their wish for work-life balance.

In part because of my lifelong involvement with our younger colleagues, and in part because I have been concerned about the fall-off in APA membership, particularly among our early-career psychiatrists (ECPs), I decided to hold a series of "town halls" throughout my president-elect term to gain a better understanding of some of the vital issues that are of concern to the next generation.

I held four of these events: one in New York at APA's 2009 Institute on Psychiatric Services, one in Boston at the meeting of the Association of American Medical Colleges, one in Washington, D.C., at the fall meeting of the APA Assembly, and one in May at APA's annual meeting in New Orleans.

Several clear themes emerged at these sessions. Networking and mentoring at both the local and national levels were consistently highlighted as major needs. Lack of dissemination of information about APA in ways that effectively reach our members continues to be problematic, and the Web site has been extremely difficult to navigate. APA needs to be a source of readily available information on a multitude of topics, and these must be easily accessible to members. Although surveys have routinely been done by the Office of Membership, the Assembly Committee of Members-in-Training is developing a survey specifically for ECPs to try to get a better understanding of why this particular group seems to be leaving the organization after training.

My perspective is that we have not done a very good job of outreach. We need to connect our national and academic leaders to local leaders and clinicians. Just as we have had silos in our academic medical centers, we have had silos in our organization. Although there are wonderful ways to use technology, most of us are so overwhelmed with information that it is difficult to absorb every message that reaches our computers, our I-Phones, and our Blackberries, to say nothing of our mailboxes, electronic and otherwise.

Every APA member who is actively involved in the Association has a responsibility to reach out to younger colleagues—in their hospitals, their clinics, their specialty associations, and in their private offices. Invite someone for coffee, breakfast, or lunch. These connections do not need to require major time, effort, or expense. If each of us reaches out, we can have a significant impact.

I plan to help APA establish a national mentoring framework to facilitate this type of interaction. For example, local leadership can offer to do grand rounds at academic medical centers to describe the role of APA in educating legislators and the general public about the issues facing psychiatric patients and to facilitate engagement of our academic leadership. National leaders can work locally to mentor and advise the next generation. A few "pot luck" dinners around the country in some of our major cities (Boston, New York, Philadelphia, Washington, D.C., Atlanta, Chicago, Houston, Dallas, San Francisco, Los Angeles, Denver, Miami) could engage 10 or 20 ECPs and graduating residents at little or no expense to the person holding them. Inviting key academic and clinical leaders to such dinners would also be useful.

I welcome your suggestions and further thoughts about how best to implement a nationwide mentoring program. Please contact me at cbernstein@psych.org. ■

Apply for Fellowship

September 1 is the application deadline for members who want to be recognized with fellowship status in APA. The eligibility criteria to become an APA fellow are five years as a general member, board certification, and two letters of recommendation from APA fellows or distinguished fellows.

Three key benefits of fellowship are use of the FAPA designation on all professional documentation; recognition at the Convocation of Distinguished Fellows at the APA annual meeting, which next year will be in Honolulu, Hawaii; and a lapel pin and an embossed certificate indicating that the member is an APA fellow. Being an APA fellow is an honorary designation and does not increase membership dues.

More information and an application are posted at <www.psych.org/Resources/Membership/FellowsDistinguishedFellows.aspx>. Information about fellowship status is also available from Membership Department staff at (888) 357-7924. ■

A Job Well Done

BY JAMES H. SCULLY JR., M.D.

As many of you may have read in the April 16 issue, Dr. Jim Krajeski announced that he was resigning as editor in chief of *Psychiatric News* effective at the end of APA's 2010 annual meeting in New Orleans. The Board of Trustees has appointed former APA President Carolyn Robinowitz, M.D., as interim editor until a new editor is appointed.

The first step of the search process is now under way—in March, outgoing APA President Alan Schatzberg, M.D., appointed a work group to determine the future directions of *Psychiatric News*. I expect that in addition to continuing to produce a print version, *Psychiatric News* will launch an e-mail newsletter and enhance its Web site. But more about that in a future issue. Right now I'd like to say a few words about the work that Jim has done for *Psychiatric News* and for APA over the years.

Jim took over as editor in chief of *Psychiatric News* in 1998. At that time, many thought that *Psychiatric News* should be APA's "house organ," that is, a publication that would mainly report on and reflect the Association's positions. Jim had a greater vision. We needed a newspaper that would reshape coverage of APA news—that would help members better understand how the Association's efforts directly benefited them and their patients—as well as keep readers current with cutting-edge clinical and research news and policy-related issues that affect the profession and practice of psychiatry. To do so responsibly and credibly, he believed, necessitated objective reporting and comprehensive coverage of controversial issues internal and external to APA.

Jim's focus has always been on you, our members. When Jim assumed the position of editor in chief, he began by surveying members about their informational needs and expectations and then translated those findings into reshaping the newspaper. And to ensure that *Psychiatric News* continued to respond to members' needs, he conducted surveys on a regular basis and fine-tuned the paper's content to keep it relevant to members.

In addition, Jim brought many innovative changes to *Psychiatric News*. Among them were redesigning the newspaper to transform it into a publication as attractive as any large, profitable commercial publication; increasing the total amount of editorial content and devoting more of it to research and clinical news, as members had requested in the readership surveys; making the newspaper reader friendly by adding section heads identified by color and article summaries to introduce each article so that busy readers could decide quickly what they wanted to read; and increasing the use of charts, photographs, art, and other items of visual interest.

But the changes Jim made to the newspaper went beyond cosmetics. His goal was to be inclusive of all APA members and the many constituencies they represent. Also, he ensured that members had a chance to have their voice heard, even when—or perhaps especially when—they disagreed with APA. One indicator of the strength of an organization, he believed, is the extent to which it embraces a diversity of opinion.

Members have often told me how much they like and appreciate *Psychiatric News*, and Board members have heard similar comments about the efforts of Jim and his staff.

Jim's dedication to APA began long before he was appointed editor in chief of *Psychiatric News*. He chaired the Committee on Gay, Lesbian, and Bisexual Issues from 1983 to 1989 and APA's Commission on AIDS from 1990 to 1991. He also served as an Assembly representative for the Caucus of Lesbian, Gay, and Bisexual Psychiatrists (1983 to 1998) and as a member of the Ad Hoc Committee of the Board of Trustees on AIDS (1987-88), Assembly Executive Committee and Assembly Committee on Planning (1988-89), Joint Commission on Government Relations (1991-94), Joint Commission on Public Affairs (1996-98), and Task Force on Strategic Planning (1997-98). Moreover, he was instrumental in the work that led to removing the diagnosis of ego-dystonic homosexuality from *DSM* in 1986.

For many years, Jim, a resident of Corte Madera, Calif., was in private practice and also served as the regional medical advisor to the Social Security Administration Disability Program for Region 9, San Francisco. He was active in the Northern California Psychiatric Society as well as the California and San Francisco medical societies.

Among the many awards he has received are the 2006 Area 6 Warren Williams Award, the 2000 Presidents' Distinguished Service Award from the Northern California Psychiatric Society, the 1998 James Paulsen Award of the Association of Gay and Lesbian Psychiatrists, and the 1992 Regional Commissioner's Citation of the Social Security Administration for outstanding medical and program guidance for the SSA Disability Program.

Jim's connection to *Psychiatric News* isn't ending yet, however. He is a member of the work group that is looking at the future of *Psychiatric News* and will pass on its recommendations to the Board of Trustees later this year. And in recognition of his appreciation of electronic technology—he telecommuted from California with the *Psychiatric News* staff using a variety of electronic means—the Board of Trustees presented him with an apt thank-you gift at its meeting in May: an Apple I-Pad. I'm told that an "app" will soon be in development for this popular device so that *Psychiatric News* will look good and can be read easily almost anywhere.

Jim has set the bar high for the next editor in chief. He knew that *Psychiatric News* had to be more than a house organ to best serve APA members. He took that position because of his commitment to APA—our members, our profession, and our patients—and because of his own extraordinary integrity. His combined skills as an editor, a diplomat, and a dedicated leader have been a remarkable gift to us all.

Well done. ■

Credit: David Hathcox

James Krajeski, M.D., holds the Apple I-Pad presented to him by outgoing APA President Alan Schatzberg, M.D., at the Board of Trustees meeting in May in New Orleans. The I-Pad was a gift from the APA Board to thank Krajeski for his 12 years of service as editor in chief of *Psychiatric News.*

Credit: Mark Moran

Brown Takes Top Honors

James Ingraham, M.D., Natalie Lester, M.D., and **Todd Peters, M.D.,** residents in the psychiatry program at Brown University, were the winners of this year's MindGames competition at APA's 2010 annual meeting in May in New Orleans. The director of the program at Brown (not pictured) is Jane Eisen, M.D.

The three trainees bested residents from Boston University and Virginia Tech-Carilion School of Medicine in a "Jeopardy"-like quiz game testing residents' knowledge of psychiatric diagnosis, neuropsychiatry, genetics, psychopharmacology, and psychodynamic psychotherapy, as well as general medical knowledge.

The game, now in its fourth year, was hosted by Glen Gabbard, M.D. Serving as judges in the competition were past APA President Michelle Riba, M.D., Charles Nemeroff, M.D., and Richard Balon, M.D.

Residents from Boston University were Rohit Chandra, M.D., Ana Ivkovic, M.D., and Mark Oldham, M.D. The training director there is Janet Osterman, M.D. The team from Virginia Tech-Carilion included Nina Khachiyants, M.D., Nitin Khadilkar, M.D., and Ronny Paul Meunier, M.D. The training director is Ben Borja, M.D.

The three teams were finalists in a competition that began earlier this year when residency teams of three members each from the United States and Canada took a time-limited online examination consisting of multiple-choice questions. The questions followed the ABPN Part I content outline.

The three top-scoring teams with the fastest posted time received a $4,000 grant from APA to send their teams to the final round of MindGames at the annual meeting. The process will begin again in 2011, and next year's finalists, who will compete at the 2011 annual meeting in Honolulu, Hawaii, will be announced in March 2011 at the annual meeting of the American Association of Directors of Psychiatric Residency Training.

More information is posted at <www.psych.org/mindgame>.

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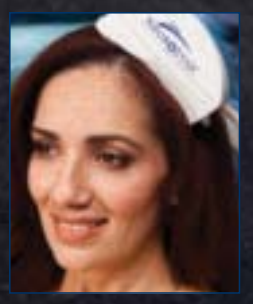

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APA'S 2010 ANNUAL MEETING: BIG IDEAS IN THE BIG EASY

Photos by David Hathcox

Few cities make hospitality as much a part of their culture as New Orleans, and about 11,000 psychiatrists and other annual meeting attendees were able to bask in that welcome at APA's annual meeting in May. While world-renowned culinary traditions and the French Quarter's unique architecture and ambience drew big crowds to the Big Easy, the meeting's real bounty was found in the comprehensive scientific program that covered every major area in clinical practice and cutting-edge research, and was spiced up with a few esoteric offerings as well.

Meeting goers also were able to register for next year's annual meeting, and upon learning that it will be held in Honolulu, Hawaii, more than 200 people took advantage of the opportunity and received a lei as a thank-you gift. Learn more about that meeting at <http://psych.hawaiiconvention.com/us>.


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1 APPI staff member Jan Roque demonstrates PsychiatryOnline.org at the APPI bookstore. This online service is a powerful Web-based portal that features the *DSM-IV-TR* library and provides access to APA journals and psychiatric texts published by APPI. 2 Annual meeting attendees peruse books and multimedia items at the APPI bookstore. 3 APA's changing of the guard—at least presidentially speaking—took place at the Board of Trustees meeting. Outgoing APA president Alan Schatzberg, M.D., handed over the gavel to APA's new president, Carol Bernstein, M.D., after placing the ceremonial presidential medallion around her neck. 4 A Dixieland band begins the Opening Session with an energetic rendition of "When the Saints Go Marching In." 5 Women who have served as president of APA gather for a photo before the Opening Session. From left are Nada Stotland, M.D. (2008-2009), Michelle Riba, M.D. (2004-2005), Marcia Goin, M.D. (2003-2004), Carol Nadelson, M.D. (1985-1986), Elissa Benedek, M.D. (1990-1991), and Carolyn Robinowitz, M.D. (2007-2008). Missing is Mary Jane England, M.D. (1995-1996). 6 Newly inducted APA fellows, distinguished fellows, life fellows, and distinguished life fellows take "The Pledge of Distinguished Fellowship." 7 Actress and author Carrie Fisher presents the William C. Menninger Memorial Lecture at APA's Convocation of Distinguished Fellows. 8 Sylke Vothknecht, M.D., and Ben Blansjaar, M.D., share the annual meeting experience with their daughter, Isabella. It's never too soon to extol the feelings of personal fulfillment of being a psychiatrist with others.

Safety Strategies Reduce Risk of Patient Attacks

Psychiatry can be a dangerous profession, and several events in recent years have shown that no clinician is invulnerable.

BY AARON LEVIN

Patients assault psychiatrists four times more frequently than physicians in general, a statistic that members of the profession ought to keep in mind every day, said Robert Simon, M.D., at APA's 2010 annual meeting in New Orleans in May.

Simon and Kenneth Tardiff, M.D., M.P.H., were named the winners of the 2010 Manfred S. Guttmacher Award, presented for co-editing the *Textbook of Violence Assessment and Management*, published by American Psychiatric Publishing Inc.

"We have to recognize that every health care professional is a potential target of the rare, but ever-present, risk of patient violence," said Simon in his portion of the lecture.

Simon asked how many in the audience had ever been assaulted by a patient. About one-third raised a hand, a close approximation of past surveys showing that 40 percent of psychiatrists have been attacked during their careers. That is the result of having an annual rate of 68 nonfatal violent crimes per 1,000 psychiatrists compared with about 16 per 1,000 physicians overall.

Safety measures should be an integral part of clinical practice, said Simon, a clinical professor of psychiatry and director of the Program in Law and Psychiatry at Georgetown University School of Medicine.

The deaths in recent years of two mental health clinicians provided cautionary insights into patient violence. Psychiatrist Wayne Fenton, M.D., was beaten to death in 2006 by a patient whom he saw alone in his office on a weekend. Having an escape route from the room and the presence of a third party who could be summoned by a silent alarm might prevent such outcomes, said Simon.

He also noted the murder of Katherine Faughey, Ph.D., killed by a patient of an office suitemate in 2008. The killer had not even seen the other clinician for 17 years, but nursed a murderous grudge during that time and took it out on Faughey, whom he had never previously met.

"Wherever there is a patient, there is the potential for violence," said Simon. "You are not invulnerable."

Patient violence can occur anywhere, he said. The emergency room is the riskiest place. Patients are unscreened, there is no therapeutic alliance established, patients may have used toxic substances, and guns and knives may be in their back pockets. However, the emergency room is also best equipped and trained to handle potential violence. The worst place is probably the home office, where there is no secretary or security guard to call.

Patient violence can take many forms in addition to physical attacks. The Internet provides a starting point for many who wish ill for their therapists. Web searches, forums, chat rooms, and social networking sites all provide ways to find a doctor. Google provides not only street maps but also pictures of residences on those streets. Information about one's personal life and family members is readily available, too. False accusations abound on the Internet.

Google yourself? "I'm afraid of what I'm going to find," said Simon.

please see ***Attacks*** *on page 15*

Credit: Ellen Dallager Photography

Robert Simon, M.D. (left), and Kenneth Tardiff, M.D., M.P.H., receive the 2010 Manfred S. Guttmacher Award for co-editing the *Textbook of Violence Assessment and Management,* published by American Psychiatric Publishing Inc.

Gabbard: To Teach Is to 'Witness Something Transcendent'

Teaching is like throwing a pebble in the water; it creates an endless array of concentric circles that can extend the teacher's influence well beyond his or her lifetime.

BY MARK MORAN

It's all about remembering and being remembered.

That's how renowned psychoanalyst and educator Glen Gabbard, M.D., summarized the motivations behind a teaching career that has made him beloved of students and mentees and one of the most sought-after lecturers in psychiatry.

He presented the lecture "Why I Teach" at APA's 2010 annual meeting in May in New Orleans, where he received the APA/NIMH Vestermark Award. He is the Brown Foundation Professor of Psychoanalysis and director of the Baylor Psychiatry Clinic at Baylor College of Medicine.

With characteristic facility, Gabbard wove personal reflections, neuroscientific findings, psychoanalytic insights, and a sprinkling of humor into a narrative describing the teaching profession as an interpersonal transaction in which the teacher is internalized by the student and the teacher, in turn, learns from and internalizes the learner.

He emphasized as well that the human interaction that is at the heart of teaching is also inherent in psychotherapy and needs to be preserved as a part of the psychiatric identity. And so the preservation of psychotherapy forms an urgent motive for passing those skills along to tomorrow's psychiatrists.

"We are trying to preserve a dying art," Gabbard said of the teachers of psychiatric psychotherapy. "I sometimes encounter residents who say, 'We don't really need to learn psychotherapy as psychiatrists anymore because psychologists and social workers do psychotherapy.' Or they'll say, 'I'm really more interested in genetics, neuroscience, or psychopharmacology.' And even though the [Residency Review Committee] mandates psychotherapy training, it doesn't mean that people will read the texts, go to class, or make appointments with supervisors."

Credit: David Hathcox

Glen Gabbard, M.D. (right), is presented the APA/NIMH Vestermark Award by Frederick Guggenheim, M.D. Gabbard observed that psychotherapy remains integral to all aspects of psychiatric practice.

An analysis of data from the National Ambulatory Medical Care Survey, presented at last year's annual meeting, showed that the percentage of visits to a psychiatrist involving psychotherapy declined from 44.4 percent in 1996-1997 to 28.9 percent in 2004-2005.

But Gabbard said that even the so-called 15-minute "med check" draws on the alliance-building skills of psychotherapeutic learning. "When residents tell me they don't really need psychotherapy training to be a psychiatrist, I tell them, 'Lot's of luck.' The way I see it, there is no area of psychiatry that can be divorced from the use of psychotherapeutic skills."

Therapeutic Alliance Stil Matters

He cited the landmark NIMH Collaborative Depression Research Study showing that in a comparison of two forms of psychotherapy, imipramine with clinical management, and placebo, the therapeutic alliance accounted for more of the variance in outcome than any of the treatments themselves.

"The therapeutic alliance is at the heart of what we do as psychiatrists," Gabbard said.

Beneath the economic or practical reasons residents may give for turning away from psychotherapy is likely to be a fear of the kind of mutual internalization that is at the heart of therapy (and of teaching).

"I think a lot of trainees are terrified to look inward and see what's there," he said. "They would rather think of themselves as a healthy doctor treating a sick person. But we have a common humanity that allows us to see ourselves in even the most disturbed patient. By turning inward, we know the patient in a way that other people don't. We discover truths that aren't available in a brain scan. . . . You can't see the self in a brain scan; you have to see the self by sounding it out with your own human instrument. . . . I teach to preserve the idea that we don't just treat disorders—we treat a person."

Wanting to Be Remembered

From long experience in the practice of psychoanalysis, Gabbard said he has learned that one of patients' greatest fears is the fear of not being remembered. It is a fear to which anyone should be able to relate.

"It is not only our patients who wish to be remembered. They are simply reminding us of a universal—we all want to be remembered. Life is brief and mysterious, and we do not want to think of ourselves as merely a flash of light between two periods of darkness. I think this is one of the reasons I teach."

please see ***Gabbard*** *on facing page*

Overcoming Patient's Stigma When It's Directed at You

Stigma directed toward psychiatrists by their patients can impede an evaluation unless clinicians confront the problem and take steps to manage it.

BY AARON LEVIN

Some people would prefer hearing they've been diagnosed with cancer than having to undergo a psychiatric evaluation, James Griffith, M.D., told listeners at an APA annual meeting session in New Orleans in May.

The mere fact that they will be having a psychiatric consultation may be seen as bad news by some patients, especially if they already harbor negative views of the profession and its practitioners.

"Psychiatrists are not only bothersome for some patients, but a stigma to be avoided at all costs," said Griffith, a professor of psychiatry and neurology at George Washington University School of Medicine.

If the patient has not requested the consultation, the psychiatrist may be resented as a stranger with whom there is no reason to build a therapeutic alliance. For some, just the presence of the psychiatrist confers a mark of shame and lowers the patient's self-esteem, said Griffith.

Some patients may even hold religious beliefs that psychiatrists are evil emissaries of Satan, complicating the clinician's task, he said.

Those negative views stigmatize psychiatrists as much as prejudices against people with mental illness do in the outside world.

Credit: David Hathcox

James Griffith, M.D., says that psychiatrists can be stigmatized by patients, but they "can also learn to treat people who stigmatize psychiatrists despite their views and bring those skills into other areas of our practice."

In some ways, however, stigma simplifies life.

"You only need to know one thing about a person and then you know everything" or at least think you do, said Griffith. Stigma allows an observer to make quick, decisive judgments about a person's social identity with little mental effort. Of course, that leaves out a lot of other things about the stigmatized individual.

The origins of stigma lie not in ignorance or psychopathology but in Darwinian biology, said Griffith. Sociobiological systems involved in peer affiliation, social hierarchy, kin recognition, and social exchange operate through the dorsal anterior cingulate gyrus. That part of the brain detects information conflicts and prompts the prefrontal cortex to resolve them with reference to some quickly identifiable but potentially stigmatizing mark—race, gender, age, clothing, and so on.

Stigma processes operate automatically, outside volitional control, and within tenths of a second, he said. They take precedence over more conscious reasoning, which may take seconds to minutes. They activate the amygdala, stimulate a threat/aversion response, and deactivate empathy. These processes increase the dominance of social identity relative to personal identity.

These are normal sociobiological processes, but psychopathology may amplify a stigma's intensity.

The psychiatrist's difficult job is to reverse that pattern, often under professionally stressful conditions, in a brief first encounter that lacks a therapeutic alliance, while already being stigmatized by the patient.

"What happens in the first session is critical," said Griffith. The interviewer

please see ***Stigma*** *on page 27*

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References: 1. Reisberg B, Doody R, Stöffler A, Schmitt F, Ferris S, Möbius HJ, for the Memantine Study Group. Memantine in moderate-to-severe Alzheimer's disease. *N Engl J Med.* 2003;348:1333-1341. **2.** Tariot PN, Farlow MR, Grossberg GT, Graham SM, McDonald S, Gergel I, for the Memantine Study Group. Memantine treatment in patients with moderate to severe Alzheimer disease already receiving donepezil: a randomized controlled trial. *JAMA.* 2004;291:317-324. **3.** Cummings JL, Schneider E, Tariot PN, Graham SM, for the Memantine MEM-MD-02 Study Group. Behavioral effects of memantine in Alzheimer disease patients receiving donepezil treatment. *Neurology.* 2006;67:57-63. **4.** Data on file. Forest Laboratories, Inc. **5.** NAMENDA® (memantine HCl) Prescribing Information. Forest Pharmaceuticals, Inc., St Louis, Mo. **6.** Wimo A, Winblad B, Stöffler A, Wirth Y, Möbius HJ. Resource utilisation and cost analysis of memantine in patients with moderate to severe Alzheimer's disease. *Pharmacoeconomics.* 2003;21:327-340. **7.** Winblad B, Poritis N. Memantine in severe dementia: results of the ³M-BEST Study (Benefit and efficacy in severely demented patients during treatment with memantine). *Int J Geriatr Psychiatry.* 1999;14:135-146.

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PRECAUTIONS
Information for Patients and Caregivers: Caregivers should be instructed in the recommended administration (twice per day for doses above 5 mg) and dose escalation (minimum interval of one week between dose increases).

Neurological Conditions
Seizures: Namenda has not been systematically evaluated in patients with a seizure disorder. In clinical trials of Namenda, seizures occurred in 0.2% of patients treated with Namenda and 0.5% of patients treated with placebo.

Genitourinary Conditions
Conditions that raise urine pH may decrease the urinary elimination of memantine resulting in increased plasma levels of memantine.

Special Populations
Hepatic Impairment
Namenda undergoes partial hepatic metabolism, with about 48% of administered dose excreted in urine as unchanged drug or as the sum of parent drug and the N-glucuronide conjugate (74%). No dosage adjustment is needed in patients with mild or moderate hepatic impairment. Namenda should be administered with caution to patients with severe hepatic impairment.

Renal Impairment
No dosage adjustment is needed in patients with mild or moderate renal impairment. A dosage reduction is recommended in patients with severe renal impairment (see CLINICAL PHARMACOLOGY and DOSAGE AND ADMINISTRATION in Full Prescribing Information).

Drug-Drug Interactions
N-methyl-D-aspartate (NMDA) antagonists: The combined use of Namenda with other NMDA antagonists (amantadine, ketamine, and dextromethorphan) has not been systematically evaluated and such use should be approached with caution.

Effects of Namenda on substrates of microsomal enzymes: In vitro studies conducted with marker substrates of CYP450 enzymes (CYP1A2, -2A6, -2C9, -2D6, -2E1, -3A4) showed minimal inhibition of these enzymes by memantine. In addition, *in vitro* studies indicate that at concentrations exceeding those associated with efficacy, memantine does not induce the cytochrome P450 isoenzymes CYP1A2, CYP2C9, CYP2E1, and CYP3A4/5. No pharmacokinetic interactions with drugs metabolized by these enzymes are expected.

Effects of inhibitors and/or substrates of microsomal enzymes on Namenda: Memantine is predominantly renally eliminated, and drugs that are substrates and/or inhibitors of the CYP450 system are not expected to alter the metabolism of memantine.

Acetylcholinesterase (AChE) inhibitors: Coadministration of Namenda with the AChE inhibitor donepezil HCl did not affect the pharmacokinetics of either compound. In a 24-week controlled clinical study in patients with moderate to severe Alzheimer's disease, the adverse event profile observed with a combination of memantine and donepezil was similar to that of donepezil alone.

Drugs eliminated via renal mechanisms: Because memantine is eliminated in part by tubular secretion, coadministration of drugs that use the same renal cationic system including hydrochlorothiazide (HCTZ), triamterene (TA), metformin, cimetidine, ranitidine, quinidine, and nicotine, could potentially result in altered plasma levels of both agents. However, coadministration of Namenda and HCTZ/TA did not affect the bioavailability of either memantine or TA, and the bioavailability of HCTZ decreased by 20%. In addition, coadministration of memantine with the antihyperglycemic drug Glucovance® (glyburide and metformin HCl) did not affect the pharmacokinetics of memantine, metformin, and glyburide. Furthermore, memantine did not modify the serum glucose lowering effect of Glucovance®.

Drugs that make the urine alkaline: The clearance of memantine was reduced by about 80% under alkaline urine conditions at pH 8. Therefore, alterations of urine pH towards the alkaline condition may lead to an accumulation of the drug with a possible increase in adverse effects. Urine pH is altered by diet, drugs (e.g. carbonic anhydrase inhibitors, sodium bicarbonate), and clinical state of the patient (e.g. renal tubular acidosis or severe infections of the urinary tract). Hence, memantine should be used with caution under these conditions.

Carcinogenesis, Mutagenesis and Impairment of Fertility
There was no evidence of carcinogenicity in a 113-week oral study in mice at doses up to 40 mg/kg/day (10 times the maximum recommended human dose [MRHD] on a mg/m² basis). There was also no evidence of carcinogenicity in rats orally dosed at up to 40 mg/kg/day for 71 weeks followed by 20 mg/kg/day (20 and 10 times the MRHD on a mg/m² basis, respectively) through 128 weeks.

Memantine produced no evidence of genotoxic potential when evaluated in the *in vitro S. typhimurium* or *E. coli* reverse mutation assay, an *in vitro* chromosomal aberration test in human lymphocytes, an *in vivo* cytogenetics assay for chromosome damage in rats, and the *in vivo* mouse micronucleus assay. The results were equivocal in an *in vitro* gene mutation assay using Chinese hamster V79 cells.

No impairment of fertility or reproductive performance was seen in rats administered up to 18 mg/kg/day (9 times the MRHD on a mg/m² basis) orally from 14 days prior to mating through gestation and lactation in females, or for 60 days prior to mating in males.

Pregnancy
Pregnancy Category B: Memantine given orally to pregnant rats and pregnant rabbits during the period of organogenesis was not teratogenic up to the highest doses tested (18 mg/kg/day in rats and 30 mg/kg/day in rabbits, which are 9 and 30 times, respectively, the maximum recommended human dose [MRHD] on a mg/m² basis).

Slight maternal toxicity, decreased pup weights and an increased incidence of non-ossified cervical vertebrae were seen at an oral dose of 18 mg/kg/day in a study in which rats were given oral memantine beginning pre-mating and continuing through the postpartum period. Slight maternal toxicity and decreased pup weights were also seen at this dose in a study in which rats were treated from day 15 of gestation through the post-partum period. The no-effect dose for these effects was 6 mg/kg, which is 3 times the MRHD on a mg/m² basis.

There are no adequate and well-controlled studies of memantine in pregnant women. Memantine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers
It is not known whether memantine is excreted in human breast milk. Because many drugs are excreted in human milk, caution should be exercised when memantine is administered to a nursing mother.

Pediatric Use
There are no adequate and well-controlled trials documenting the safety and efficacy of memantine in any illness occurring in children.

ADVERSE REACTIONS
The experience described in this section derives from studies in patients with Alzheimer's disease and vascular dementia.

Adverse Events Leading to Discontinuation: In placebo-controlled trials in which dementia patients received doses of Namenda up to 20 mg/day, the likelihood of discontinuation because of an adverse event was the same in the Namenda group as in the placebo group. No individual adverse event was associated with the discontinuation of treatment in 1% or more of Namenda-treated patients and at a rate greater than placebo.

Adverse Events Reported in Controlled Trials: The reported adverse events in Namenda (memantine hydrochloride) trials reflect experience gained under closely monitored conditions in a highly selected patient population. In actual practice or in other clinical trials, these frequency estimates may not apply, as the conditions of use, reporting behavior and the types of patients treated may differ. Table 1 lists treatment-emergent signs and symptoms that were reported in at least 2% of patients in placebo-controlled dementia trials and for which the rate of occurrence was greater for patients treated with Namenda than for those treated with placebo. No adverse event occurred at a frequency of at least 5% and twice the placebo rate.

Table 1: Adverse Events Reported in Controlled Clinical Trials in at Least 2% of Patients Receiving Namenda and at a Higher Frequency than Placebo-treated Patients

Body System Adverse Event	Placebo (N = 922) %	Namenda (N = 940) %
Body as a Whole		
Fatigue	1	2
Pain	1	3
Cardiovascular System		
Hypertension	2	4
Central and Peripheral Nervous System		
Dizziness	5	7
Headache	3	6
Gastrointestinal System		
Constipation	3	5
Vomiting	2	3
Musculoskeletal System		
Back pain	2	3
Psychiatric Disorders		
Confusion	5	6
Somnolence	2	3
Hallucination	2	3
Respiratory System		
Coughing	3	4
Dyspnea	1	2

Other adverse events occurring with an incidence of at least 2% in Namenda-treated patients but at a greater or equal rate on placebo were agitation, fall, inflicted injury, urinary incontinence, diarrhea, bronchitis, insomnia, urinary tract infection, influenza-like symptoms, abnormal gait, depression, upper respiratory tract infection, anxiety, peripheral edema, nausea, anorexia, and arthralgia.

The overall profile of adverse events and the incidence rates for individual adverse events in the subpopulation of patients with moderate to severe Alzheimer's disease were not different from the profile and incidence rates described above for the overall dementia population.

Vital Sign Changes: Namenda and placebo groups were compared with respect to (1) mean change from baseline in vital signs (pulse, systolic blood pressure, diastolic blood pressure and weight) and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. There were no clinically important changes in vital signs in patients treated with Namenda. A comparison of supine and standing vital sign measures for Namenda and placebo in elderly normal subjects indicated that Namenda treatment is not associated with orthostatic changes.

Laboratory Changes: Namenda and placebo groups were compared with respect to (1) mean change from baseline in various serum chemistry, hematology, and urinalysis variables and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses revealed no clinically important changes in laboratory test parameters associated with Namenda treatment.

ECG Changes: Namenda and placebo groups were compared with respect to (1) mean change from baseline in various ECG parameters and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses revealed no clinically important changes in ECG parameters associated with Namenda treatment.

Other Adverse Events Observed During Clinical Trials
Namenda has been administered to approximately 1350 patients with dementia, of whom more than 1200 received the maximum recommended dose of 20 mg/day. Patients received Namenda treatment for periods of up to 884 days, with 862 patients receiving at least 24 weeks of treatment and 387 patients receiving 48 weeks or more of treatment.

Treatment emergent signs and symptoms that occurred during 8 controlled clinical trials and 4 open-label trials were recorded as adverse events by the clinical investigators using terminology of their own choosing. To provide an overall estimate of the proportion of individuals having similar types of events, the events were grouped into a smaller number of standardized categories using WHO terminology, and event frequencies were calculated across all studies.

All adverse events occurring in at least two patients are included, except for those already listed in Table 1, WHO terms too general to be informative, minor symptoms or events unlikely to be drug-caused, e.g., because they are common in the study population. Events are classified by body system and listed using the following definitions: frequent adverse events - those occurring in at least 1/100 patients; infrequent adverse events - those occurring in 1/100 to 1/1000 patients. These adverse events are not necessarily related to Namenda treatment and in most cases were observed at a similar frequency in placebo-treated patients in the controlled studies.

Body as a Whole: *Frequent:* syncope. *Infrequent:* hypothermia, allergic reaction.

Cardiovascular System: *Frequent:* cardiac failure. *Infrequent:* angina pectoris, bradycardia, myocardial infarction, thrombophlebitis, atrial fibrillation, hypotension, cardiac arrest, postural hypotension, pulmonary embolism, pulmonary edema.

Central and Peripheral Nervous System: *Frequent:* transient ischemic attack, cerebrovascular accident, vertigo, ataxia, hypokinesia. *Infrequent:* paresthesia, convulsions, extrapyramidal disorder, hypertonia, tremor, aphasia, hypoesthesia, abnormal coordination, hemiplegia, hyperkinesia, involuntary muscle contractions, stupor, cerebral hemorrhage, neuralgia, ptosis, neuropathy.

Gastrointestinal System: *Infrequent:* gastroenteritis, diverticulitis, gastrointestinal hemorrhage, melena, esophageal ulceration.

Hemic and Lymphatic Disorders: *Frequent:* anemia. *Infrequent:* leukopenia.

Metabolic and Nutritional Disorders: *Frequent:* increased alkaline phosphatase, decreased weight. *Infrequent:* dehydration, hyponatremia, aggravated diabetes mellitus.

Psychiatric Disorders: *Frequent:* aggressive reaction. *Infrequent:* delusion, personality disorder, emotional lability, nervousness, sleep disorder, libido increased, psychosis, amnesia, apathy, paranoic reaction, thinking abnormal, crying abnormal, appetite increased, paronia, delirium, depersonalization, necrosis, suicide attempt.

Respiratory System: *Frequent:* pneumonia. *Infrequent:* apnea, asthma, hemoptysis.

Skin and Appendages: *Frequent:* rash. *Infrequent:* skin ulceration, pruritus, cellulitis, eczema, dermatitis, erythematous rash, alopecia, urticaria.

Special Senses: *Frequent:* cataract, conjunctivitis. *Infrequent:* macula lutea degeneration, decreased visual acuity, decreased hearing, tinnitus, blepharitis, blurred vision, corneal opacity, glaucoma, conjunctival hemorrhage, eye pain, retinal hemorrhage, xerophthalmia, diplopia, abnormal lacrimation, myopia, retina detachment.

Urinary System: *Frequent:* frequent micturition. *Infrequent:* dysuria, hematuria, urinary retention.

Events Reported Subsequent to the Marketing of Namenda, both US and Ex-US
Although no causal relationship to memantine treatment has been found, the following adverse events have been reported to be temporally associated with memantine treatment and are not described elsewhere in labeling: aspiration pneumonia, asthenia, atrioventricular block, bone fracture, carpal tunnel syndrome, cerebral infarction, chest pain, cholelithiasis, claudication, colitis, deep venous thrombosis, depressed level of consciousness (including loss of consciousness and rare reports of coma), dyskinesia, dysphagia, encephalopathy, gastritis, gastroesophageal reflux, grand mal convulsions, intracranial hemorrhage, hepatitis (including increased ALT and AST and hepatic failure), hyperglycemia, hyperlipidemia, hypoglycemia, ileus, increased INR, impotence, lethargy, malaise, myoclonus, neuroleptic malignant syndrome, acute pancreatitis, Parkinsonism, acute renal failure (including increased creatinine and renal insufficiency), prolonged QT interval, restlessness, sepsis, Stevens-Johnson syndrome, suicidal ideation, sudden death, supraventricular tachycardia, tachycardia, tardive dyskinesia, thrombocytopenia, and hallucinations (both visual and auditory).

ANIMAL TOXICOLOGY
Memantine induced neuronal lesions (vacuolation and necrosis) in the multipolar and pyramidal cells in cortical layers III and IV of the posterior cingulate and retrosplenial neocortices in rats similar to those which are known to occur in rodents administered other NMDA receptor antagonists. Lesions were seen after a single dose of memantine, in a study in which rats were given daily oral doses of memantine for 14 days, the no-effect dose for neuronal necrosis was 6 times the maximum recommended human dose on a mg/m² basis. The potential for induction of central neuronal vacuolation and necrosis by NMDA receptor antagonists in humans is unknown.

DRUG ABUSE AND DEPENDENCE
Controlled Substance Class: Memantine HCl is not a controlled substance.

Physical and Psychological Dependence: Memantine HCl is a low to moderate affinity uncompetitive NMDA antagonist that did not produce any evidence of drug-seeking behavior or withdrawal symptoms upon discontinuation in 2,504 patients who participated in clinical trials at therapeutic doses. Post marketing data, outside the U.S., retrospectively collected, has provided no evidence of drug abuse or dependence.

OVERDOSAGE
Signs and symptoms associated with memantine overdosage in clinical trials and from worldwide marketing experience include agitation, confusion, ECG changes, loss of consciousness, psychosis, restlessness, slowed movement, somnolence, stupor, unsteady gait, visual hallucinations, vertigo, vomiting, and weakness. The largest known ingestion of memantine worldwide was 2.0 grams in a patient who took memantine in conjunction with unspecified antidiabetic medications. The patient experienced coma, diplopia, and agitation, but subsequently recovered.

Because strategies for the management of overdose are continually evolving, it is advisable to contact a poison control center to determine the latest recommendations for the management of an overdose of any drug. As in any cases of overdose, general supportive measures should be utilized, and treatment should be symptomatic. Elimination of memantine can be enhanced by acidification of urine.

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Daunting Challenges Don't Dim Former First Lady's Mission

Within Our Reach **stresses recent improvements in diagnosis, treatment, and recovery for the vast majority of people with mental illness and expresses hope that policymakers, clinicians, and patients will embrace the range of options available.**

BY RICH DALY

The day that former First Lady Rosalynn Carter unerstood that a person may appear physically healthy and yet suffer from hidden psychiatric illness or mental wounds came nearly 60 years ago.

She was driving the babysitter home with her 2-year-old son in the car when they were struck from behind by another vehicle, which flipped her car over. Although she, her son, and the babysitter were not physically injured, the psychological impact of the accident deeply affected her long afterwards.

"After my own terrifying experience, whenever I saw the headline of an article about an accident, my heart raced," she wrote in her new book, *Within Our Reach: Ending the Mental Health Crisis*. "I became sweaty and shook all over, and it was a very long time before I could make myself drive past the place where my accident occurred."

The story is one of many personal accounts in her book about her own experiences and those of people who have recovered from serious mental illness to illustrate the impact of both psychological trauma and mental illness.

"My hope is that this book will dispel the myths and misconceptions about mental illness," Carter said at a book signing at the Library of Congress in Washington, D.C., in May

The personal stories also illustrate the daunting stigma that still lingers about mental illness. Indeed, the societal stigma surrounding mental illness not only has hampered funding efforts and access to care but also has kept many from seeking treatment for their psychiatric conditions.

"I wrote this book so we would get over the stigma and get on with what we need to do," Carter emphasized.

Credit: Rich Daly

Former First Lady Rosalynn Carter describes some of the personal stories that motivated her lasting interest and leadership in mental health care during a discussion about her new book.

But the book is also about her hope that policymakers, clinicians, and people with mental illness will take advantage of the many effective treatments and approaches to psychiatric illness that have emerged in recent decades.

Recovery Goal Becomes Prominent

"The goal of recovery is the single biggest advance [in mental health] in the last 30 years," she said.

Carter has been a national leader and advocate for improved mental health since her husband, former President Jimmy Carter, was a candidate for president in the 1970s. In her book she repeatedly stresses the importance of people not only seeking mental health treatment when they need it but also taking "a key role in their treatment and recovery." Her book is rife with examples of individuals overcoming incredible mental health challenges through the care of family members and clinicians, but also through their own perseverance and hope that they could recover.

It's a lesson in the power of hope that other leaders in the mental health field have learned as well. Carter described a meeting with Thomas Insel, M.D., director of the National Institute of Mental Health, in which he lamented that science had not discovered drugs that would permanently cure mental illness. At the same time, however, he and other leaders have begun embracing the recovery philosophy, which maintains that most people with mental illness can live happy and productive lives if they receive the help they need.

"We're learning from the consumer advocates that recovery works," Carter added.

Many Challenges Yet to Be Met

Unfortunatley the hope provided by available and emerging treatments and patient support systems is challenged by the daunting number of people who need mental health care and are unable to afford it or sometimes even find it. Carter confronts the range of such challenges, including an underfunded public-health system, insurance discrimination, and private care that many simply cannot afford.

Financial obstacles are not actually the main problem, according to Carter. Rather, she noted, the problem is that the nearly $120 billion spent each year on direct mental health care is so inefficiently spent that it often does not benefit the people with mental illness for whom the money was intended in the first place. Recounting a conversation she had with Ronald Mandersheid, Ph.D., a sociologist and researcher—and one of many mental health experts she interviewed for the book—Carter concluded that "our real problem is not a lack of enough money."

"He explained that because our services and funding sources are so fragmented, so uncoordinated, so complicated, we fall short of realizing all of the benefits we might expect from such a huge investment in mental health," she said.

Carter praised passage of the federal insurance parity law in 2008 and hailed the wider availability of health insurance under the health care reform law passed this year, but even those two measures will leave treatment gaps, she pointed out. She identified peer-support networks, community residential facilities, and vocational training for people with mental illness as critical needs that will require sources of funding other than those provided under health reform.

Acknowledging that more work remains to be done, Carter emphasized that the two recent federal initiatives—and the way in which regulators implement them—could vastly improve the recovery prospects for many people with mental illness.

"If we can get [strong regulations] done, it can change the way we get mental health care done," Carter said.

More information on Carter's book and advocacy work is posted on the Carter Center Web site at <www.cartercenter.org/homepage.html>. ■

Gabbard

continued from facing page

He recounted the kinds of experiences that are familiar to any passionate educator and that confirm the adage that the teacher lives on in the student: Residents, mentees, and supervisees have acknowledged over the years, in word and deed, the impact he has made on their training and their lives and on the lives of the patients they treat.

"When you teach, you throw a pebble into the water that ripples and will create an endless array of concentric circles in such a way that you never know where your influence ends," Gabbard said. "My passion for teaching is very much linked to the immortality motive—maybe I can pass something on to those I teach that will make a difference in their lives."

As it happens, the enduring value of interpersonal connections—of the influence of teachers on students and of psychotherapists on patients—is borne out in what neuroscience has demonstrated about how neural networks are formed and sustained, Gabbard said.

"Neural network theory has greatly increased our understanding of internalization," Gabbard said. "Neural networks begin with the firing of neurons in repetitive patterns, and experience creates certain connections between neurons. We take people inside of us as we pass through life. . .and a set of representations are laid down in the synapses.

"We internalize the way people in our lives have related to us. As we take in the memories of our interactions with others, we wire our cortex with these memories. Those who are significant leaders in our lives become part of us.

"We learn through our mentors, supervisors, and teachers. They inhabit us; they help us get through the day. They may be dead in some cases, but they are not gone."

So, too, altruism appears to be "hard wired." Gabbard cited the discovery of "mirror neurons" that appear to be activated both when an animal acts and when the animal observes the same action in another—hence allowing one animal to understand the mind and motivations of another.

"Mirror neurons help us empathize with our fellow creatures on the planet," he said. "The mirror system allows for the direct and immediate understanding of the inner world of another person, and it is the manifestation of one of the most noble features of homo sapiens."

Gabbard drew attention to a 2006 study by researchers at Duke University that used functional magnetic resonance imaging to analyze brain function while subjects performed either altruistic or selfish acts. "Altruism appears to generate brain activity in areas associated with selfish pleasures such as eating and sex," Gabbard said. "Helping others has a self-interest that is undeniable."

And so it would seem there is more than pretty sentiment to the idea that to give is to receive.

"Each time we enter a classroom, begin a supervision, or mentor a protégé, we are witness to something transcendent," Gabbard said. "We internalize and we are internalized; we teach and we learn. We give to others while enriching our own lives. We remember and are remembered. We become a part of our students and they become a part of us. We are wired together forever, and in the ebb and flow of conversation about ourselves, our patients, and our field, we make a small contribution to the world, and we both part the wiser for it. For everything we take, we leave something behind.

"And we never forget." ■

Key Cases Occupy Intersection Of Psychiatry and Law

Court rulings to clarify when capital punishment may be invoked have raised more questions—such as how to define mental retardation in capital cases and whether competence for execution requires an appreciation of death.

BY MARK MORAN

To kill or not to kill.

That's the question that has engaged the United States Supreme Court in at least two recent cases in which psychiatric testimony and expertise have been central.

The decisions handed down by the Court reflect its profound ambivalence about capital punishment—an ambivalence that is mirrored in the public at large, where 34 states allow capital punishment but where lower courts have continuously striven to refine the circumstances under which convicts can be executed.

"Mostly right, but on the wrong track" is how Richard Bonnie, LL.B., director of the Institute of Law, Psychiatry, and Public Policy at the University of Virginia, described the Court's recent decisions—right when the justices have upheld the validity of psychiatric expertise, but wrong because the Court has continued to support the use of an ultimate punishment for which there has developed no rational means of determining who does and doesn't deserve it.

"In my judgment, the death penalty project has been a complete failure" in terms of its use to exact retribution and serve as a deterrent, Bonnie said at APA's annual meeting in May in New Orleans at the symposium "The Supreme Court and Psychiatry in the 21st Century."

Bonnie was the discussant for a panel presentation by experts in psychiatry and the law about four recent Court decisions in which psychiatric testimony was prominent in or central to the case. Two of those were capital cases—*Atkins v. Virginia* (2002), discussed by past APA President Paul Appelbaum, M.D., and *Panetti v. Quarterman* (2007), discussed by Howard Zonana, M.D., a professor of psychiatry and director of the psychiatry and law program at Yale University.

> **"The most prominent determinant for who receives the death penalty is the person's race."**

Credit: David Hathcox

Richard Bonnie, LL.B., discusses recent Supreme Court cases involving psychiatric expertise and testimony.

A third case, *Indiana v. Edwards* (2008), presented by Debra Pinals, M.D., of the University of Massachusetts, involved the standard for competency to represent oneself in a trial (see article below). And a fourth case, *Clarke v. Arizona* (2006), discussed by Steven Hoge, M.D., appears to be an anomalous and somewhat puzzling decision in which the Court upheld Arizona's use of the insanity defense, while also upholding the state's very narrow standard for when psychiatric expertise may be admissible.

Death Penalty Operates Arbitrarily

Of the capital cases, Bonnie said the judicial system has tried without success to rationally and fairly distinguish those who merit death from those who do not. But in practice, the death penalty operates arbitrarily—like a "roulette wheel," he said—with odds tilted against those of color and lower socioeconomic class.

"The most prominent determinant for who receives the death penalty is the person's race," he said.

In *Panetti v. Quaterman*, the Supreme Court ruled that criminal defendants sentenced to death may not be executed if they do not understand the reason for their imminent execution. In 1992, Scott Panetti killed his mother-in-law and father-in-law; three years later, he was tried in a Texas state court for capital murder.

Though floridly psychotic, with a long psychiatric history, he was found by a lower court to be competent for execution on the basis of a 1986 Supreme Court decision, *Ford v. Wainwright*, which stated that a defendant could be executed providing that he or she was aware of the state's rationale for the execution. The Supreme Court agreed to hear Panetti's appeal.

The ruling was overturned. "The Supreme Court said that the *Ford* standard was too restrictive," Zonana said. "According to the Court's ruling [in *Panetti*], a defendant's awareness of the State's rationale for execution is not the same as a rational understanding of it."

Noting that the concept of "rational" has been debated for centuries, Zonana added that the Court was careful to distinguish "irrationality" in its reasoning from psychopathy or lack of conscience or remorse about a deed. Rather, incompetence for execution depends on gross delusions stemming from serious mental illness, which,

please see ***Key Cases*** *on page 27*

When Are Defendants Too Ill To Represent Themselves?

The Supreme Court said that incompetence to represent oneself requires severe mental illness, but beyond that did not establish a clear standard for what is required to demonstrate that incompetence.

BY MARK MORAN

The competence of criminal defendants to represent themselves in a trial, rather than have an attorney represent them, is separate from competence to stand trial. That was the ruling in the 2008 United States Supreme Court case, *Edwards v. Indiana*.

Thus competence to represent oneself could require a psychiatric evaluation separate from the evaluation of competence to stand trial.

But in a presentation about that case during a symposium at the APA annual meeting in May, psychiatry and law expert Debra Pinals, M.D., said that a problem relating to that decision is that the Court did not spell out precise criteria for determining competence to represent oneself at trial.

"The Court was willing to say that incompetence for self-representation required [the presence of] severe mental illness, but beyond that, [it] did not agree or put out any clear standard as to what the specific competence would entail," Pinals said. "Justice Stephen Breyer [who wrote the majority opinion] stated that the judge at the trial-court level would be the one who would need to make the determination of competence for self-representation based, in a way, on fairness and dignity of the proceedings."

Credit: David Hathcox

Debra Pinals, M.D., says that the 2008 *Edwards v. Indiana* case established a new type of mental competence for self-representation, but it is unknown to what extent psychiatrists will be called upon to assess that competence.

Pinals is director of forensic psychiatry education and an associate professor in the law and psychiatry program at the University of Massachusetts Medical School. She is also assistant commissioner of forensic services for the Massachusetts Department of Mental Health.

In 1999, Ahmad Edwards tried to steal a pair of shoes from a department store. When approached by a security guard, he drew a shotgun and fired at the guard and wounded a bystander. One of the charges against him was attempted murder.

After three hearings to determine his competency to stand trial, Edwards was found at times to be incompetent and was sent to a hospital where he was restored to competence. Finally, six years after the original offense, he went to trial asking to represent himself. The judge in the case, citing Edwards' history of mental illness, denied the request and appointed counsel to represent him. Edwards was convicted on some of the charges.

Edwards appealed the denial of the request to represent himself to a state appeals court, and after yet another denial, to the Indiana Supreme Court and finally to the U.S. Supreme Court.

The U.S. Supreme Court held in its ruling in the *Edwards* case that states are not forbidden from appointing counsel to represent a defendant who is competent to stand trial but who suffers from mental illness that is severe enough to render him or her incompetent for self-representation.

Pinals said that this ruling from the Supreme Court establishes a new type of trial-related competence. Not fully known, however, is the extent to which psychiatrists and mental health professionals will be tapped to do assessments of a defendant's competence for self-representation. "And without a clear standard or guideline, it is difficult to know how to carry out these assessments," she said.

"However, because the courts will need to look at the issue of whether a severe mental illness may compromise a defendant's ability to represent himself, it is likely that these assessments will require psychiatric or other mental health professional evaluation.

"Psychiatrists have been asked in some cases to assess defendants' competence to proceed [without an attorney], and have done so with little guidance as to what the standard should be to define this competence," Pinals said. "We recognize that the competence would likely involve things other than the requirements for competence to stand trial, possibly including assessing defendants' understanding of law and legal proceedings [and] their ability to sustain attention, strategize, and plan a defense."

She added that when a psychiatric evaluator is conducting a court-ordered evaluation of competence to stand trial, there is no automatic requirement to assess competence for self-representation as well. However, when defendants state in the context of an evaluation of competence to stand trial that they want to represent themselves, the evaluation might at that point include further exploration of the defendant's reasoning and could "provide the court with functional assessment data that a judge might consider in an analysis of competence to represent oneself," Pinals said. ■

BIPOLAR I MAINTENANCE TREATMENT

GEODON + LITHIUM OR VALPROATE PROVEN SUPERIOR TO LITHIUM OR VALPROATE ALONE IN PREVENTING RELAPSE

GEODON® (ziprasidone HCl) Capsules

GEODON is indicated for acute treatment as monotherapy of manic or mixed episodes associated with bipolar I disorder and for maintenance treatment of bipolar I disorder as an adjunct to lithium or valproate. For full symptoms and diagnostic criteria, see the *DSM-IV-TR*® (2000).

IMPORTANT SAFETY INFORMATION

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death compared to placebo. GEODON is not approved for the treatment of patients with dementia-related psychosis.

GEODON is contraindicated in patients with a known history of QT prolongation, recent acute myocardial infarction, or uncompensated heart failure, and should not be used with certain other QT-prolonging drugs. GEODON has a greater capacity to prolong the QT_c interval than several antipsychotics. In some drugs, QT prolongation has been associated with torsade de pointes, a potentially fatal arrhythmia. In many cases this would lead to the conclusion that other drugs should be tried first. Hypokalemia may increase the risk of QT prolongation and arrhythmia.

As with all antipsychotic medications, a rare and potentially fatal condition known as neuroleptic malignant syndrome (NMS) has been reported with GEODON. NMS can cause hyperpyrexia, muscle rigidity, diaphoresis, tachycardia, irregular pulse or blood pressure, cardiac dysrhythmia, and altered mental status. If signs and symptoms appear, immediate discontinuation, treatment, and monitoring are recommended.

Prescribing should be consistent with the need to minimize tardive dyskinesia (TD), a potentially irreversible dose- and duration-dependent syndrome. If signs and symptoms appear, discontinuation should be considered since TD may remit partially or completely.

Hyperglycemia-related adverse events, sometimes serious, have been reported in patients treated with atypical antipsychotics. There have been few reports of hyperglycemia or diabetes in patients treated with GEODON, and it is not known if GEODON is associated with these events. Patients treated with an atypical antipsychotic should be monitored for symptoms of hyperglycemia.

Precautions include the risk of rash, orthostatic hypotension, and seizures.

The most common adverse events associated with GEODON in bipolar mania were somnolence, extrapyramidal symptoms, dizziness, akathisia, and abnormal vision.

The most common adverse events (≥5%) associated with GEODON in the bipolar maintenance study were tremor and insomnia.

Please see brief summary of prescribing information on adjacent page.

For more information, please visit www.pfizerpro.com/GEODON

GEODON® (ziprasidone HCl) Capsules

GEODON® (ziprasidone mesylate) injection for intramuscular use

BRIEF SUMMARY: See package insert for full prescribing information.

INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS—Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Analyses of seventeen placebo-controlled trials (modal duration of 10 weeks), largely in patients taking atypical antipsychotic drugs, revealed a risk of death in drug-treated patients of between 1.6 to 1.7 times the risk of death in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature. Observational studies suggest that, similar to atypical antipsychotic drugs, treatment with conventional antipsychotic drugs may increase mortality. The extent to which the findings of increased mortality in observational studies may be attributed to the antipsychotic drug as opposed to some characteristic(s) of the patients is not clear. GEODON (ziprasidone) is not approved for the treatment of patients with Dementia-Related Psychosis (see WARNINGS).

INDICATIONS

GEODON is indicated for the treatment of schizophrenia, as monotherapy for the acute treatment of bipolar manic or mixed episodes, and as an adjunct to lithium or valproate for the maintenance treatment of bipolar disorder. GEODON intramuscular is indicated for acute agitation in schizophrenic patients.

DOSAGE AND ADMINISTRATION

Schizophrenia GEODON Capsules should be administered at an initial daily dose of 20 mg twice daily with food. In some patients, daily dosage may subsequently be adjusted on the basis of individual clinical status up to 80 mg twice daily. Dosage adjustments, if indicated, should generally occur at intervals of not less than 2 days, as steady-state is achieved within 1 to 3 days. In order to ensure use of the lowest effective dose, patients should ordinarily be observed for improvement for several weeks before upward dosage adjustment. Efficacy in schizophrenia was demonstrated in a dose range of 20 mg to 100 mg twice daily in short-term, placebo-controlled clinical trials. There were trends toward dose response within the range of 20 mg to 80 mg twice daily, but results were not consistent. An increase to a dose greater than 80 mg twice daily is not generally recommended. The safety of doses above 100 mg twice daily has not been systematically evaluated in clinical trials. *Maintenance Treatment*—While there is no body of evidence available to answer the question of how long a patient treated with ziprasidone should remain on it, a maintenance study in patients who had been symptomatically stable and then randomized to continue ziprasidone or switch to placebo demonstrated a delay in time to relapse for patients receiving GEODON. No additional benefit was demonstrated for doses above 20 mg twice daily. Patients should be periodically reassessed to determine the need for maintenance treatment. **Bipolar I Disorder** *Acute Treatment of Manic or Mixed Episodes*—Dose Selection: Oral ziprasidone should be administered at an initial daily dose of 40 mg twice daily with food. The dose may then be increased to 60 mg or 80 mg twice daily on the second day of treatment and subsequently adjusted on the basis of tolerance and efficacy within the range 40 mg to 80 mg twice daily. In the flexible-dose clinical trials, the mean daily dose administered was approximately 120 mg. *Maintenance Treatment* (as an adjunct to lithium or valproate)—Continue treatment at the same dose on which the patient was initially stabilized, within the range of 40 mg to 80 mg twice daily with food. Patients should be periodically reassessed to determine the need for maintenance treatment. **Acute Treatment of Agitation in Schizophrenia** *Intramuscular Dosing*—The recommended dose is 10 mg to 20 mg administered as required up to a maximum dose of 40 mg per day. Doses of 10 mg may be administered every two hours; doses of 20 mg may be administered every four hours up to a maximum of 40 mg/day. Intramuscular administration of ziprasidone for more than three consecutive days has not been studied. If long-term therapy is indicated, oral ziprasidone hydrochloride capsules should replace the intramuscular administration as soon as possible. Since there is no experience regarding the safety of administering ziprasidone intramuscular to schizophrenic patients already taking oral ziprasidone, the practice of co-administration is not recommended. Ziprasidone intramuscular is intended for intramuscular use only and should not be administered intravenously. Intramuscular Preparation for Administration GEODON for Injection (ziprasidone mesylate) should only be administered by intramuscular injection and should not be administered intravenously. Single-dose vials require reconstitution prior to administration. Add 1.2 mL of Sterile Water for Injection to the vial and shake vigorously until all the drug is dissolved. Each mL of reconstituted solution contains 20 mg ziprasidone. To administer a 10 mg dose, draw up 0.5 mL of the reconstituted solution. To administer a 20 mg dose, draw up 1.0 mL of the reconstituted solution. Any unused portion should be discarded. Since no preservative or bacteriostatic agent is present in this product, aseptic technique must be used in preparation of the final solution. This medicinal product must not be mixed with other medicinal products or solvents other than Sterile Water for Injection. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. **Dosing in Special Populations** *Oral:* Dosage adjustments are generally not required on the basis of age, gender, race, or renal or hepatic impairment. GEODON is not approved for use in children or adolescents. *Intramuscular:* Ziprasidone intramuscular has not been systematically evaluated in elderly patients or in patients with hepatic or renal impairment. As the cyclodextrin excipient is cleared by renal filtration, ziprasidone intramuscular should be administered with caution to patients with impaired renal function. Dosing adjustments are not required on the basis of gender or race.

CONTRAINDICATIONS

QT Prolongation Because of ziprasidone's dose-related prolongation of the QT interval and the known association of fatal arrhythmias with QT prolongation by some other drugs, ziprasidone is contraindicated in patients with a known history of QT prolongation (including congenital long QT syndrome), with recent acute myocardial infarction, or with uncompensated heart failure (see **WARNINGS**). Pharmacokinetic/pharmacodynamic studies between ziprasidone and other drugs that prolong the QT interval have not been performed. An additive effect of ziprasidone and other drugs that prolong the QT interval cannot be excluded. Therefore, ziprasidone should not be given with dofetilide, sotalol, quinidine, other Class Ia and III anti-arrhythmics, mesoridazine, thioridazine, chlorpromazine, droperidol, pimozide, sparfloxacin, gatifloxacin, moxifloxacin, halofantrine, mefloquine, pentamidine, arsenic trioxide, levomethadyl acetate, dolasetron mesylate, probucol or tacrolimus. Ziprasidone is also contraindicated with other drugs that have demonstrated QT prolongation as one of their pharmacodynamic effects and have this effect described in the full prescribing information as a contraindication or a boxed or bolded warning [see **WARNINGS**]. Ziprasidone is contraindicated in individuals with a known hypersensitivity to the product.

WARNINGS

Increased Mortality in Elderly Patients with Dementia-Related Psychosis: Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. GEODON is not approved for the treatment of dementia-related psychosis (see BOXED WARNING).

QT Prolongation and Risk of Sudden Death Ziprasidone use should be avoided in combination with other drugs that are known to prolong the QT_c interval. Additionally, clinicians should be alert to the identification of other drugs that have been consistently observed to prolong the QT_c interval. Such drugs should not be prescribed with ziprasidone. Ziprasidone should also be avoided in patients with congenital long QT syndrome and in patients with a history of cardiac arrhythmias (see **CONTRAINDICATIONS**).

QT Prolongation in Clinical Trials A study directly comparing the QT/QT_c prolonging effect of oral ziprasidone with several other drugs effective in the treatment of schizophrenia was conducted in patient volunteers. The mean increase in QT_c from baseline for ziprasidone ranged from approximately 9 to 14 msec greater than for four of the comparator drugs (risperidone, olanzapine, quetiapine, and haloperidol), but was approximately 14 msec less than the prolongation observed for thioridazine. In this study, the effect of ziprasidone on QT_c length was not augmented by the presence of a metabolic inhibitor (ketoconazole 200 mg twice daily). In placebo-controlled trials, oral ziprasidone increased the QT_c interval compared to placebo by approximately 10 msec at the highest recommended daily dose of 160 mg. In clinical trials the electrocardiograms of 2/2988 (0.06%) patients who received GEODON and 1/440 (0.23%) patients who received placebo revealed QT_c intervals exceeding the potentially clinically relevant threshold of 500 msec. In the ziprasidone-treated patients, neither case suggested a role of ziprasidone. **QT Prolongation and Torsade De Pointes** Some drugs that prolong the QT/QT_c interval have been associated with the occurrence of torsade de pointes and with sudden unexplained death. The relationship of QT prolongation to torsade de pointes is clearest for larger increases (20 msec and greater) but it is possible that smaller QT/QT_c prolongations may also increase risk, or increase it in susceptible individuals. Although torsade de pointes has not been observed in association with the use of ziprasidone in premarketing studies and experience is too limited to rule out an increased risk, there have been rare post-marketing reports (in the presence of multiple confounding factors) (see **ADVERSE REACTIONS**). A study evaluating the QT/QT_c prolonging effect of intramuscular ziprasidone, with intramuscular haloperidol as a control, was conducted in patient volunteers. In the trial, ECGs were obtained at the time of maximum plasma concentration following two injections of ziprasidone (20 mg then 30 mg) or haloperidol (7.5 mg then 10 mg) given four hours apart. Note that a 30 mg dose of intramuscular ziprasidone is 50% higher than the recommended therapeutic dose. The mean change in QT_c from baseline was calculated for each drug, using a sample-based correction that removes the effect of heart rate on the QT interval. The mean increase in QT_c from baseline for ziprasidone was 4.6 msec following the first injection and 12.8 msec following the second injection. The mean increase in QT_c from baseline for haloperidol was 6.0 msec following the first injection and 14.7 msec following the second injection. In this study, no patients had a QT_c interval exceeding 500 msec. As with other antipsychotic drugs and placebo, sudden unexplained deaths have been reported in patients taking ziprasidone at recommended doses. The premarketing experience for ziprasidone did not reveal an excess risk of mortality for ziprasidone compared to other antipsychotic drugs or placebo, but the extent of exposure was limited, especially for the drugs used as active controls and placebo. Nevertheless, ziprasidone's larger prolongation of QT_c length compared to several other antipsychotic drugs raises the possibility that the risk of sudden death may be greater for ziprasidone than for other available drugs for treating schizophrenia. This possibility needs to be considered in deciding among alternative drug products. Certain circumstances may increase the risk of the occurrence of torsade de pointes and/or sudden death in association with the use of drugs that prolong the QT_c interval, including (1) bradycardia; (2) hypokalemia or hypomagnesemia; (3) concomitant use of other drugs that prolong the QT_c interval; and (4) presence of congenital prolongation of the QT interval. **Electrolyte Disturbances May Increase The Risk of QT Prolongation** It is recommended that patients being considered for ziprasidone treatment who are at risk for significant electrolyte disturbances, hypokalemia in particular, have baseline serum potassium and magnesium measurements. Hypokalemia (and/or hypomagnesemia) may increase the risk of QT prolongation and arrhythmia. Hypokalemia may result from diuretic therapy, diarrhea, and other causes. Patients with low serum potassium and/or magnesium should be repleted with those electrolytes before proceeding with treatment. It is essential to periodically monitor serum electrolytes in patients for whom diuretic therapy is introduced during ziprasidone treatment. Persistently prolonged QT_c intervals may also increase the risk of further prolongation and arrhythmia, but it is not clear that routine screening ECG measures are effective in detecting such patients. Rather, ziprasidone should be avoided in patients with histories of significant cardiovascular illness, e.g., QT prolongation, recent acute myocardial infarction, uncompensated heart failure, or cardiac arrhythmia. Ziprasidone should be discontinued in patients who are found to have persistent QT_c measurements >500 msec. **Neuroleptic Malignant Syndrome (NMS)** A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with administration of antipsychotic drugs. The management of NMS should include: (1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy; (2) intensive symptomatic treatment and medical monitoring; and (3) treatment of any concomitant serious medical problems for which specific treatments are available. If a patient requires antipsychotic drug treatment after recovery from NMS, the potential reintroduction of drug therapy should be carefully considered. The patient should be carefully monitored, since recurrences of NMS have been reported. **Tardive Dyskinesia** A syndrome of potentially irreversible, involuntary, dyskinetic movements may develop in patients undergoing treatment with antipsychotic drugs. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible to rely upon prevalence estimates to predict, at the inception of antipsychotic treatment, which patients are likely to develop the syndrome. If signs and symptoms of tardive dyskinesia appear in a patient on ziprasidone, drug discontinuation should be considered. **Hyperglycemia and Diabetes Mellitus** Hyperglycemia-related adverse events, sometimes serious, have been reported in patients treated with atypical anti-psychotics. There have been few reports of hyperglycemia or diabetes in patients treated with GEODON, and it is not known if GEODON is associated with these events. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia.

PRECAUTIONS

Leukopenia, Neutropenia, and Agranulocytosis In clinical trial and postmarketing experience, events of leukopenia/neutropenia and agranulocytosis (including fatal cases) have been reported temporally related to antipsychotic agents. Possible risk factors for leukopenia/neutropenia include pre-existing low white blood cell count (WBC) and history of drug induced leukopenia/neutropenia. Patients with a pre-existing low WBC or a history of drug induced leukopenia/neutropenia should have their complete blood count (CBC) monitored frequently during the first few months of therapy and should discontinue GEODON at the first sign of decline in WBC in the absence of other causative factors. Patients with neutropenia should be carefully monitored for fever or other symptoms or signs of infection and treated promptly if such symptoms or signs occur. Patients with severe neutropenia (absolute neutrophil count <1000/mm3) should discontinue GEODON and have their WBC followed until recovery. **Rash** In premarketing trials with ziprasidone, about 5% of patients developed rash and/or urticaria, with discontinuation of treatment in about one-sixth of these cases. The occurrence of rash was related to dose of ziprasidone, although the finding might also be explained by the longer exposure time in the higher dose patients. Several patients with rash had signs and symptoms of associated systemic illness, e.g., elevated WBCs. Most patients improved promptly with adjunctive treatment with antihistamines or steroids and/or upon discontinuation of ziprasidone, and all patients experiencing these reactions were reported to recover completely. Upon appearance of rash for which an alternative etiology cannot be identified, ziprasidone should be discontinued. **Orthostatic Hypotension** Ziprasidone may induce orthostatic hypotension associated with dizziness, tachycardia, and, in some patients, syncope, especially during the initial dose-titration period, probably reflecting its α_1-adrenergic antagonist properties. Syncope was reported in 0.6% of the patients treated with ziprasidone. Ziprasidone should be used with particular caution in patients with known cardiovascular disease (history of myocardial infarction or ischemic heart disease, heart failure or conduction abnormalities), cerebrovascular disease, or conditions which would predispose patients to hypotension (dehydration, hypovolemia, and treatment with antihypertensive medications). **Seizures** In clinical trials, seizures occurred in 0.4% of patients treated with ziprasidone. There were confounding factors that may have contributed to the occurrence of seizures in many of these cases. As with other antipsychotic drugs, ziprasidone should be used cautiously in patients with a history of seizures or with conditions that potentially lower the seizure threshold, e.g., Alzheimer's dementia. Conditions that lower the seizure threshold may be more prevalent in a population of 65 years or older. **Dysphagia** Esophageal dysmotility and aspiration have been associated with antipsychotic drug use. Aspiration pneumonia is a common cause of morbidity and mortality in elderly patients, in particular those with advanced Alzheimer's dementia, and ziprasidone and other antipsychotic drugs should be used cautiously in patients at risk for aspiration pneumonia (see **BOXED WARNING** and **Increased Mortality in Elderly Patients with Dementia-Related Psychosis in WARNINGS**). **Hyperprolactinemia** As with other drugs that antagonize dopamine D2 receptors, ziprasidone elevates prolactin levels in humans. Tissue culture experiments indicate that approximately one-third of human breast cancers are prolactin-dependent *in vitro*, a factor of potential importance if the prescription of these drugs is

contemplated in a patient with previously detected breast cancer. Neither clinical studies nor epidemiologic studies conducted to date have shown an association between chronic administration of this class of drugs and tumorigenesis in humans; the available evidence is considered too limited to be conclusive at this time. **Potential for Cognitive and Motor Impairment** Somnolence was a commonly reported adverse reaction in patients treated with ziprasidone. In the 4- and 6-week placebo-controlled trials, somnolence was reported in 14% of patients on ziprasidone compared to 7% of placebo patients. Somnolence led to discontinuation in 0.3% of patients in short-term clinical trials. Since ziprasidone has the potential to impair judgment, thinking, or motor skills, patients should be cautioned about performing activities requiring mental alertness, such as operating a motor vehicle (including automobiles) or operating hazardous machinery until they are reasonably certain that ziprasidone therapy does not affect them adversely. **Priapism** One case of priapism was reported in the premarketing database. **Body Temperature Regulation** Although not reported with ziprasidone in premarketing trials, disruption of the body's ability to reduce core body temperature has been attributed to antipsychotic agents. **Suicide** The possibility of a suicide attempt is inherent in psychotic illness and close supervision of high-risk patients should accompany drug therapy. Prescriptions for ziprasidone should be written for the smallest quantity of capsules consistent with good patient management in order to reduce overdose risk. **Patients With Concomitant Illnesses** Clinical experience with ziprasidone in patients with certain concomitant systemic illnesses is limited. Ziprasidone has not been evaluated or used to any appreciable extent in patients with a recent history of myocardial infarction or unstable heart disease. Patients with these diagnoses were excluded from premarketing clinical studies. Because of the risk of QT_c prolongation and orthostatic hypotension with ziprasidone, caution should be observed in cardiac patients (see **QT Prolongation and Risk of Sudden Death** in **WARNINGS** and **Orthostatic Hypotension in PRECAUTIONS**). **Information for Patients** To assure safe and effective use of GEODON, the information and instructions provided in the patient information should be discussed with patients. **Laboratory Tests** Patients being considered for ziprasidone treatment who are at risk of significant electrolyte disturbances should have baseline serum potassium and magnesium measurements. Low serum potassium and magnesium should be replaced before proceeding with treatment. Patients who are started on diuretics during Ziprasidone therapy need periodic monitoring of serum potassium and magnesium. Discontinue ziprasidone in patients who are found to have persistent QT_c measurements >500 msec (see **WARNINGS**).

DRUG INTERACTIONS

(1) Ziprasidone should not be used with any drug that prolongs the QT interval. (2) Given the primary CNS effects of ziprasidone, caution should be used when it is taken in combination with other centrally acting drugs. (3) Because of its potential for inducing hypotension, ziprasidone may enhance the effects of certain antihypertensive agents. (4) Ziprasidone may antagonize the effects of levodopa and dopamine agonists. **Effect of Other Drugs on Ziprasidone** *Carbamazepine*, 200 mg bid for 21 days, resulted in a decrease of approximately 35% in the AUC of ziprasidone. Ketoconazole, a potent inhibitor of CYP3A4, 400 mg qd for 5 days, increased the AUC and Cmax of ziprasidone by about 35-40%. *Cimetidine*, 800 mg qd for 2 days, did not affect ziprasidone pharmacokinetics. Co-administration of 30 mL of Maalox® did not affect ziprasidone pharmacokinetics. Population pharmacokinetic analysis of schizophrenic patients enrolled in controlled clinical trials has not revealed evidence of any clinically significant pharmacokinetic interactions with benztropine, propranolol, or lorazepam. **Effect of Ziprasidone on Other Drugs** *In vitro* studies revealed little potential for ziprasidone to interfere with the metabolism of drugs cleared primarily by CYP1A2, CYP2C9, CYP2C19, CYP2D6 and CYP3A4, and little potential for drug interactions with ziprasidone due to displacement. Ziprasidone 40 mg bid administered concomitantly with *lithium* 450 mg bid for 7 days did not affect the steady-state level or renal clearance of lithium. *In vivo* studies have revealed no effect of ziprasidone on the pharmacokinetics of estrogen or progesterone components. Ziprasidone 20 mg bid did not affect the pharmacokinetics of concomitantly administered *oral contraceptives*, ethinyl estradiol (0.03 mg) and levonorgestrel (0.15 mg). Consistent with *in vitro* results, a study in normal healthy volunteers showed that ziprasidone did not alter the metabolism of *dextromethorphan*, a CYP2D6 model substrate, to its major metabolite, dextrorphan. There was no statistically significant change in the urinary dextromethorphan/dextrorphan ratio.

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility Lifetime carcinogenicity studies were conducted with ziprasidone in Long Evans rats and CD-1 mice. In male mice, there was no increase in incidence of tumors relative to controls. In female mice, there were dose-related increases in the incidences of pituitary gland adenoma and carcinoma, and mammary gland adenocarcinoma at all doses tested. Increases in serum prolactin were observed in a 1-month dietary study in female, but not male, mice. Ziprasidone had no effect on serum prolactin in rats in a 5-week dietary study at the doses that were used in the carcinogenicity study. The relevance for human risk of the findings of prolactin-mediated endocrine tumors in rodents is unknown (see **Hyperprolactinemia** in **PRECAUTIONS**). *Mutagenesis:* There was a reproducible mutagenic response in the Ames assay in one strain of *S. typhimurium* in the absence of metabolic activation. Positive results were obtained in both the *in vitro* mammalian cell gene mutation assay and the *in vitro* chromosomal aberration assay in human lymphocytes. *Impairment of Fertility:* Ziprasidone increase time to copulation in Sprague-Dawley rats in two fertility and early embryonic development studies at doses of 10 to 160 mg/kg/day (0.5 to 8 times the MRHD of 200 mg/day on a mg/m2 basis). Fertility rate was reduced at 160 mg/kg/day (8 times the MRHD on a mg/m2 basis). There was no effect on fertility at 40 mg/kg/day (2 times the MRHD on a mg/m2 basis). The fertility of female rats was reduced.

USE IN SPECIFIC POPULATIONS

Pregnancy *Pregnancy Category C:* There are no adequate and well-controlled studies in pregnant women. Ziprasidone should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. **Labor and Delivery** The effect of ziprasidone on labor and delivery in humans is unknown. **Nursing Mothers** It is not known whether ziprasidone or its metabolites are excreted in human milk. It is recommended that women receiving ziprasidone should not breastfeed. **Pediatric Use** The safety and effectiveness of ziprasidone in pediatric patients have not been established. **Geriatric Use** Of the total number of subjects in clinical studies of ziprasidone, 2.4 percent were 65 and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects. Nevertheless, the presence of multiple factors that might increase the pharmacodynamic response to ziprasidone, or cause poorer tolerance or orthostasis, should lead to consideration of a lower starting dose, slower titration, and careful monitoring during the initial dosing period for some elderly patients.

ADVERSE REACTIONS

Adverse Findings Observed in Short-term, Placebo-Controlled Trials The following findings are based on the short-term placebo-controlled premarketing trials for schizophrenia (a pool of two 6-week, and two 4-week fixed-dose trials) and bipolar mania (a pool of two 3-week flexible-dose trials) in which GEODON was administered in doses ranging from 10 to 200 mg/day. **Adverse Events Associated With Discontinuation** *Schizophrenia:* Approximately 4.1% (29/702) of ziprasidone-treated patients in short-term, placebo-controlled studies discontinued treatment due to an adverse reaction, compared with about 2.2% (6/273) on placebo. The most common reaction associated with dropout was rash, including 7 dropouts for rash among ziprasidone patients (1%) compared to no placebo patients (see **PRECAUTIONS**). *Bipolar Mania:* Approximately 6.5% (18/279) of ziprasidone-treated patients in short-term, placebo-controlled studies discontinued treatment due to an adverse reaction, compared with about 3.7% (5/136) on placebo. The most common reactions associated with dropout in the ziprasidone-treated patients were akathisia, anxiety, depression, dizziness, dystonia, rash and vomiting, with 2 dropouts for each of these reactions among ziprasidone patients (1%) compared to one placebo patient each for dystonia and rash (1%) and no placebo patients for the remaining adverse events. **Adverse Events at an Incidence of ≥5% and at Least Twice the Rate of Placebo** The most commonly observed adverse events associated with GEODON in schizophrenia trials were somnolence (14%) and respiratory tract infection (8%). The most commonly observed adverse events associated with the use of GEODON in bipolar mania trials were somnolence (31%), extrapyramidal symptoms (31%), dizziness (16%), akathisia (10%), abnormal vision (6%), asthenia (6%), and vomiting (5%). The following list enumerates the treatment-emergent adverse events that occurred during acute therapy, including only those events that occurred in 2% of GEODON patients and at a greater incidence than in placebo. Schizophrenia: *Body as a Whole*—asthenia, accidental injury, chest pain. *Cardiovascular*—tachycardia. *Digestive*—nausea, constipation, dyspepsia, diarrhea, dry mouth, anorexia. *Nervous*—extrapyramidal symptoms, somnolence, akathisia, dizziness. *Respiratory*—respiratory tract infection, rhinitis, cough increased. *Skin and Appendages*—rash, fungal dermatitis. *Special Senses*—abnormal vision. Bipolar Mania: *Body as a Whole*—headache, asthenia, accidental injury. *Cardiovascular*—hypertension. *Digestive*—nausea, diarrhea, dry mouth, vomiting, increased salivation, tongue edema, dysphagia. *Musculoskeletal*—myalgia. *Nervous*—somnolence, extrapyramidal symptoms, dizziness, akathisia, anxiety, hypesthesia, speech disorder. *Respiratory*—pharyngitis, dyspnea. *Skin and Appendages*—fungal dermatitis. *Special Senses*—abnormal vision. **Dose Dependency** An analysis for dose response in the schizophrenia 4-study pool revealed an apparent relation of adverse reaction to dose for the following reactions: asthenia, postural hypotension, anorexia, dry mouth, increased salivation, arthralgia, anxiety, dizziness, dystonia, hypertonia, somnolence, tremor, rhinitis, rash, and abnormal vision. **Extrapyramidal Symptoms (EPS)** The incidence of reported EPS for ziprasidone patients in the short-term, placebo-controlled schizophrenia trials was 14% vs. 8% for placebo. Objectively collected data from those trials on the Simpson-Angus Rating Scale (for EPS) and the Barnes Akathisia Scale (for akathisia) did not generally show a difference between ziprasidone and placebo. **Dystonia** Symptoms of dystonia, prolonged abnormal contractions of muscle groups, may occur in susceptible individuals during the first few days of treatment. While these symptoms can occur at low doses, they occur more frequently and with greater severity with high potency and at higher doses of first generation antipsychotic drugs. Elevated risk of acute dystonia is observed in males and younger age groups. **Vital Sign Changes** Ziprasidone is associated with orthostatic hypotension (see **PRECAUTIONS**). **Weight Gain** In short-term schizophrenia trials, the proportions of patients meeting a weight gain criterion of ≥7% of body weight were compared, revealing a statistically significantly greater incidence of weight gain for ziprasidone (10%) compared to placebo (4%). A median weight gain of 0.5 kg was observed in ziprasidone patients compared to no median weight change in placebo patients. Weight gain was reported as an adverse event in 0.4% of both ziprasidone and placebo patients. During long-term therapy with ziprasidone, a categorization of patients at baseline on the basis of body mass index (BMI) revealed the greatest mean weight gain and highest incidence of clinically significant weight gain (>7% of body weight) in patients with low BMI (<23) compared to normal (23-27) or overweight patients (>27). There was a mean weight gain of 1.4 kg for those patients with a "low" baseline BMI, no mean change for patients with a "normal" BMI, and a 1.3 kg mean weight loss for patients who entered the program with a "high" BMI. **ECG Changes** Ziprasidone is associated with an increase in the QT_c interval (see **WARNINGS**). In the schizophrenia trials, ziprasidone was associated with a mean increase in heart rate of 1.4 beats per minute compared to a 0.2 beats per minute decrease among placebo patients. **Other Adverse Events Observed During the Premarketing Evaluation of Ziprasidone in Schizophrenia** Frequent adverse events are those occurring in at least 1/100 patients; infrequent adverse events are those occurring in 1/100 to 1/1000 patients; rare adverse events are those occurring in fewer than 1/1000 patients. *Body as a Whole*—Frequent: abdominal pain, flu syndrome, fever, accidental fall, face edema, chills, photosensitivity reaction, flank pain, hypothermia, motor vehicle accident. *Cardiovascular System*—Frequent: tachycardia, hypertension, postural hypotension. Infrequent: bradycardia, angina pectoris, atrial fibrillation. Rare: first degree AV block, bundle branch block, phlebitis, pulmonary embolus, cardiomegaly, cerebral infarct, cerebrovascular accident, deep thrombophlebitis, myocarditis, thrombophlebitis. *Digestive System*—Frequent: anorexia, vomiting. Infrequent rectal hemorrhage, dysphagia, tongue edema. Rare: gum hemorrhage, jaundice, fecal impaction, gamma glutamyl trans-peptidase increased, hematemesis, cholestatic jaundice, hepatitis, hepatomegaly, leukoplakia of mouth, fatty liver deposit, melena. *Endocrine*—Rare: hypothyroidism, hyperthyroidism, thyroiditis. *Hemic and Lymphatic System*—Infrequent: anemia, ecchymosis, leukocytosis, leukopenia, eosinophilia, lymphadenopathy. Rare: thrombocytopenia, hypochromic anemia, lymphocytosis, monocytosis, basophilia, lymphedema, polycythemia, thrombocythemia. *Metabolic and Nutritional Disorders*—Infrequent: thirst, transaminase increased, peripheral edema, hyperglycemia, creatine phosphokinase increased, alkaline phosphatase increased, hypercholesteremia, dehydration, lactic dehydrogenase increased, albuminuria, hypokalemia. Rare: BUN increased, creatinine increased, hyperlipemia, hypocholesteremia, hyperkalemia, hypochloremia, hypoglycemia, hyponatremia, hypoproteinemia, glucose tolerance decreased, gout, hyperchloremia, hyperuricemia, hypocalcemia, hypoglycemic reaction, hypomagnesemia, ketosis, respiratory alkalosis. *Musculoskeletal System*—Frequent: myalgia. Infrequent: tenosynovitis. Rare: myopathy. *Nervous System*—Frequent: agitation, extrapyramidal syndrome, tremor, dystonia, hypertonia, dyskinesia, hostility, twitching, paresthesia, confusion, vertigo, hypokinesia, hyperkinesia, abnormal gait, oculogyric crisis, hypesthesia, ataxia, amnesia, cogwheel rigidity, delirium, hypotonia, akinesia, dysarthria, withdrawal syndrome, buccoglossal syndrome, choreoathetosis, diplopia, incoordination, neuropathy. Infrequent: paralysis. Rare: myoclonus, nystagmus, torticollis, circumoral paresthesia, opisthotonos, reflexes increased, trismus. *Respiratory System*—Frequent: dyspnea Infrequent pneumonia, epistaxis. Rare: hemoptysis, laryngismus. *Skin and Appendages*—Infrequent: maculopapular rash, urticaria, alopecia, eczema, exfoliative dermatitis, contact dermatitis, vesiculobullous rash. *Special Senses*—Frequent: fungal dermatitis. Infrequent: conjunctivitis, dry eyes, tinnitus, blepharitis, cataract, photophobia. Rare: eye hemorrhage, visual field defect, keratitis, keratoconjunctivitis. *Urogenital System*—Infrequent: impotence, abnormal ejaculation, amenorrhea, hematuria, menorrhagia, female lactation, polyuria, urinary retention, metrorrhagia, male sexual dysfunction, anorgasmia, glycosuria. Rare: gynecomastia, vaginal hemorrhage, nocturia, oliguria, female sexual dysfunction, uterine hemorrhage. **Adverse Findings Observed in Trials of Intramuscular Ziprasidone** In these studies, the most commonly observed adverse reactions associated with the use of intramuscular ziprasidone (≥5%) and observed at a rate on intramuscular ziprasidone (in the higher dose groups) at least twice that of the lowest intramuscular ziprasidone group were headache (13%), nausea (12%), and somnolence (20%). **Adverse Events at an Incidence of ≥1% in Short-Term Fixed-Dose Intramuscular Trials** The following list enumerates the treatment-emergent adverse events that occurred in ≥1% of patients during acute therapy with intramuscular ziprasidone: *Body as a Whole*—headache, injection site pain, asthenia, abdominal pain, flu syndrome, back pain. *Cardiovascular*—postural hypotension, hypertension, bradycardia, vasodilation. *Digestive*—nausea, rectal hemorrhage, diarrhea, vomiting, dyspepsia, anorexia, constipation, tooth disorder, dry mouth. *Nervous*—dizziness, anxiety, insomnia, somnolence, akathisia, agitation, extrapyramidal syndrome, hypertonia, cogwheel rigidity, paresthesia, personality disorder, psychosis, speech disorder. *Respiratory*—rhinitis. *Skin and Appendages*—furunculosis, sweating. *Urogenital*—dysmenorrhea, priapism. **Other Events Observed During Post-marketing Use** Adverse reaction reports not listed above that have been received since market introduction include rare occurrences of the following—*Cardiac Disorders:* Tachycardia, torsade de pointes (in the presence of multiple confounding factors), (see **WARNINGS**); *Digestive System Disorders:* Swollen Tongue; *Reproductive System and Breast Disorders:* Galactorrhea, priapism; *Nervous System Disorders:* Facial Droop, neuroleptic malignant syndrome, serotonin syndrome (alone or in combination with serotonergic medicinal products), tardive dyskinesia; *Psychiatric Disorders:* Insomnia, mania/hypomania; *Skin and subcutaneous Tissue Disorders:* Allergic reaction (such as allergic dermatitis, angioedema, orofacial edema, urticaria), rash; *Urogenital System Disorders:* Enuresis, urinary incontinence; *Vascular Disorders:* Postural hypotension, syncope.

DRUG ABUSE AND DEPENDENCE

Controlled Substance Class Ziprasidone is not a controlled substance.

OVERDOSAGE

In premarketing trials in over 5400 patients, accidental or intentional overdosage of oral ziprasidone was documented in 10 patients. All patients survived without sequelae. In the patient taking the largest confirmed amount (3240 mg), the only symptoms reported were minimal sedation, slurring of speech, and transitory hypertension (200/95).

Delay in Medicare Fee Cut Caught in Dispute Over Cost

Physicians express disappointment as lawmakers, driven by election-year politics and a national mood hostile to more debt and spending, scale back a proposed five-year delay in planned cuts to Medicare physician fees.

BY RICH DALY

In a dizzying series of back-and-forth actions that began months ago, the House of Representatives and the Senate have both passed legislation to delay the scheduled 21 percent cut to Medicare physician reimbursements, but at press time, no final agreement had been reached regarding the delay's length of time.

On May 28, the House passed a 19-month delay in the physician reimbursement cuts, but on June 18, the Senate passed only a six-month delay. The Senate also passed a 2.2 percent increase instead of the 21 percent cut. Now the ball is back in the House's court.

After the Senate vote, the Centers for Medicare and Medicaid Services (CMS) announced that it would begin processing June claims with the 21 percent cut. This lower rate had gone into effect on June 1, but CMS had granted a delay to give Congress additional time to act. The grace period expired on June 17.

Prior to the latest round of activity, Congress had dropped plans to pass a five-year delay. Proponents of the five-year delay hoped that it would provide sufficient time to work out a permanent overhaul of the much-criticized payment system.

The legislation is running into opposition from Republicans concerned about deficit spending. Their stand drew the ire of President Obama, who derided Republicans as "willing to walk away from the needs of our doctors and our seniors" in comments during his June 12 weekly radio address. The scaled-back time frame of the payment freeze was described by congressional staff as a concession to growing concerns about how to pay for a longer freeze. Putting a six-month freeze on the 21 percent cut required by Medicare's automatic payment formula and adding a 2.2 percent increase to physician payments is projected by the Congressional Budget Office (CBO) to cost $6.5 billion, compared with $23 billion for a 19-month delay and an $88.5 billion cost for a five-year freeze.

The effort by many in the medical field to avoid the cut has become entangled in an increasingly fiscally conservative atmosphere in Congress. Fiscally conservative and politically vulnerable Democrats have pressured their leadership to limit federal spending that is not offset by taxes or cuts elsewhere in the budget. Such so-called offsets are required for nonemergency spending under Congress's "pay-as-you-go" rule. No offsets have been offered for the physician payment freeze.

The AMA, which is leading the lobbying effort on the Medicare payment rate issue, along with other physician organizations, continues to call for a permanent repeal of the funding formula used by Medicare. The formula, called the sustainable growth rate (SGR), requires the payment cuts as a way to offset other spending growth in Medicare.

Temporary delays in Medicare payment cuts "just treat the symptoms and not the disease," said then AMA President J. James Rohack, M.D., in a press conference call in early June.

The cornerstone of the AMA's call for immediate replacement of the SGR stems from the growing cost of waiting to do so. The AMA says that replacement now would cost about $250 billion but repealing it in five years, for example, would cost more than $500 billion, citing an analysis by the CBO.

"More delays will only grow the problem," Rohack said.

That's also the message of a multimillion-dollar national ad campaign launched by the AMA in June designed to pressure Congress into devising a permanent replacement system this year (*Psychiatric News*, June 4).

The campaign emphasizes that physicians are souring on Medicare because of ongoing uncertainty about what they will be paid, according to Rohack. That uncertainty stems from the increasing frequency with which Congress has used short-term fixes to head off major payment cuts in recent years. Additionally, Medicare officials have used emergency action to forestall some scheduled cuts because they technically went into effect before Congress could enact a postponement.

The impact of the frequently looming payment cuts has led to nearly 1 in 5 physicians limiting the number of Medicare patients they see, according to an online AMA survey of more than 9,000 physicians who care for Medicare patients. Perhaps most ominously, nearly 60 percent of them considered opting out of Medicare under this year's threat of a 21 percent cut.

The continuing refusal of congressional leaders to act on revising the payment formula comes despite the strong backing that the AMA and other physician groups gave to the federal health care reform legislation enacted earlier this year. Physician advocates hoped that this support would push Congress to act this year on a permanent replacement to the Medicare payment formula.

Asked by a reporter if he regretted that the AMA provided that support now that a permanent payment overhaul has failed to materialize, Rohack said he did not, because many of the changes included in the law were needed to improve the overall health care payment and delivery system.

Instead, Rohack questioned the CBO's estimates of the cost of replacing the payment formula, which he said ignores the savings in hospital costs resulting from better-treated patients.

Information on the AMA campaign is posted at <www.ama-assn.org/ama/pub/advocacy/current-topics-advocacy/practice-management/medicare-physician-payment-reform-regulatory-relief/fix-medicare-now.shtml>. ■

Some States Buck Trend to Cut Mental Health Care Funding

The mental health parity mandate may expand in California, even as other states delay expanding mental health services or slash mental health care spending to close large budget gaps.

BY RICH DALY

California is moving toward broadening the state's mental health insurance parity requirements. Such an expansion in protection for people with mental illness would buck a more prevalent trend in which states are cutting mental health care spending as a way to help offset growing recession-driven budget woes.

The California Assembly passed an expansion of the state's mental health parity law (AB 1600) on June 1 requiring most health insurance plans to provide coverage for all *DSM* mental illness diagnoses (including substance abuse) and "medically necessary" treatment for those illnesses. The bill would expand the current coverage requirement from undefined "severe mental illnesses" to any diagnosis in *DSM-IV* and subsequent editions of the diagnostic manual.

The state Senate has not yet taken up the measure.

The measure goes beyond the federal health care overhaul law, which requires parity insurance coverage only in plans that already offer coverage for psychiatric conditions.

The bill, sponsored by State Assembly Member Jim Beall Jr. (D)—the 2009 recipient of APA's Jacob K. Javits Public Service Award—would apply to insurance policies issued after January 1, 2011, and includes some exceptions for public-employee plans.

The full chamber is not expected to pass the bill this year due to its ongoing scramble to address the state's looming $19 billion budget deficit, according to Marc Graff, M.D., president of the California Psychiatric Association.

Wisconsin Improves MH Coverage

Another state that recently moved to expand coverage for people with mental illness was Wisconsin, where state officials eliminated all dollar-amount and service limitations for mental health and substance abuse treatment in the Medicaid program's BadgerCare Plus Benchmark Plan. The move was designed to mandate equality in coverage for mental illness treatment and other types of medical care.

The change—retroactive to January 1—is expected to benefit the 14,496 children and pregnant or postpartum women enrolled in Wisconsin's Medicaid program. It also brings the state into compliance with the 2008 federal parity law, which requires Medicaid managed care organizations that offer mental health coverage to do so at parity with other types of medical care.

Minnesota Creates Task Force

In another Midwestern state, however, mental health care services could expand. The Minnesota legislature created the Chemical and Mental Health Services Transformation Task Force, which will suggest ways in which lawmakers can act to improve the continuum of services needed for people with mental illnesses, including substance abuse and traumatic brain injury.

The task force, which will be composed of legislators, state mental health officials, and mental health advocates, is to recommend changes in service-delivery models, ways to eliminate gaps in and barriers to accessing quality care, and plans to ensure that individuals with complex mental health needs receive the appropriate level of care. The task force's recommendations are due to the legislature by December 15.

The task force was one of several created by the Minnesota legislature in the recent session as election year pressures led members to defer funding expansions for care sought by mental health and other patient-care advocates.

Care Reductions Coming in Missouri

Among the states cutting mental health spending due to budget constraints is Missouri. The state's $23.3 billion Fiscal 2011 budget reduced spending by $500 million overall, including $1.4 million in cuts to federally qualified community mental health centers and elimination of state funding for rural health clinics.

Missouri mental health care advocates said the cuts for the fiscal year beginning July 1 eliminate publicly funded care for about 2,200 Missourians with severe mental illness.

The California parity bill can be accessed at <www.assembly.ca.gov/defaulttext.asp> by searching on the bill number, AB 1600. ■

Psychiatry Meeting In Asheville, N.C.

The Southern Psychiatric Association and the Tennessee Psychiatric Association are holding their annual meeting from September 29 to October 3 at the Grove Park Inn in Asheville, N.C. The meeting theme is "Psychiatry on the Verge of *DSM-5*."

Further information and a registration form are posted at <www.sopsych.org>. Additional information is available from Susan Proctor at sproctor@sheppardpratt.org or (410) 938-3403. ■

More Psychiatry Residents Getting Enriched Neurology Education

Psychiatry residents often feel that their knowledge of neurology is inadequate as their residency progresses. So some programs have launched innovative solutions.

BY AARON LEVIN

What do psychiatry residents want?

More neurology, according to surveys by the National Institute of Mental Health, and that's what several innovative programs around the United States are giving them.

At the 2010 APA annual meeting in New Orleans in May, residents and training directors from several universities reported on creative ways to provide that training.

The speakers noted that psychiatry residents often grow less confident about their knowledge of neurology as their residency progresses.

Formerly at the University of Wisconsin, psychiatry residents took two months of neurology in their first year, then saw nothing in that field until board exams loomed on the horizon in the last year of residency, said Art Walaszek, M.D., residency training director, vice chair for education, and an associate professor of psychiatry at Wisconsin.

Walaszek and chief resident Claudia Reardon, M.D., surveyed 172 other psychiatric residency programs and found that about 75 percent of the 57 responding programs offered didactic neurology instruction specifically for psychiatrists in training, concentrating on epilepsy, stroke, dementia, headache, and electroencephalography.

Most of the learning came in lecture form, but some programs also offered neuroradiology rounds and neuroanatomy lab sessions. Training came mostly in the first and last years of residency.

Only 55 percent of trainees surveyed, however, said they felt the neurology experiences were adequate.

"Psychiatry and neurology could be better integrated into grand rounds and in didactic instruction throughout the curriculum," said Reardon.

University of Michigan residents have gone a step further, said chief resident M. Justin Coffey, M.D.

"Residency programs do a good job of teaching neurology to tests but not for patient diagnosis or care," said Coffey.

Psychiatry residents at Michigan developed their own eight-week summer grand rounds, taught by neurology residents. The one-hour lectures covered clinical neuroradiology, abnormal movements, stroke and its symptoms, neuropsychiatry and dementia, epilepsy and nonepileptic seizures, pain, sleep and sleep disorders, and catatonia.

'We Made It Fun'

The most significant aspect of the Michigan program was not its content but its faculty.

"We wanted good teachers but not research experts," said Coffey. "Having the neurology residents teach helped allay the fears of being taught by the big names in the [neurology] department."

The neurology residents enjoyed teaching, and the psychiatry residents found peer education an efficient and effective way to learn the fundamentals of clinical neurology.

"We made it easy, we made it useful, and we made it fun," said Coffey.

The next step is to integrate this learning process into the year-round curriculum. In the future, the Michigan team hopes to combine peer teaching with peer learning by inviting social-work and nursing students and psychology post-docs to join the psychiatry residents in the audience.

Psychiatry Takes Back the Brain

At the University of Massachusetts Medical School, the war cry in this campaign is "It's time for psychiatry to take back the brain."

This approach might alleviate some of the stigma against psychiatry within the medical profession to the extent that it is produced by the perception that working in psychiatry means "not doing science," suggested University of Massachusetts psychiatry training director Sheldon Benjamin, M.D.

His department has worked up a range of required and elective training segments, plus a biological psychiatry seminar for third- and fourth-year residents.

At the program's core are month-long rotations in adult inpatient neurology (or pediatric neurology for child psychiatry residents), neurology inpatient consultation, and neuropsychiatry.

Residents can also attend an elective neuropsychiatry seminar open to all residents.

"The objective is not to do neurology but to be able to order, interpret, and use results from neuropsychological testing, structural imaging, EEGs, and evoked potentials," said Benjamin, who is a neurologist as well as a psychiatrist.

The department also offers a six-year combined neuropsychiatry program that includes a year of medical internship, two years each of psychiatry and neurology, and a final year of neuropsychiatry.

> **"When psychiatrists help the neurologists take care of their difficult patients, we make friends forever."**

All this interaction benefits both the residents and their patients, said Benjamin.

"Now psychiatry residents see neurology residents as colleagues," he said. "Co-teaching helps break down barriers between the two fields. When psychiatrists help the neurologists take care of their difficult patients, we make friends forever."

Finally, waiting until residency to address the gap between the two fields may not be the only way of bridging it, said several speakers.

They noted that collaborations might usefully begin in medical school classrooms, or even in the premedical curriculum, to begin instilling the ever-growing interaction between neurology and psychiatry, they said. ■

What a Psychiatrist Should Know About Clinical Neuroscience

"Taking ownership of the brain" is the mantra of the Psychiatry Department at the University of Massachusetts, which has developed a curriculum that teaches neuroscience from several perspectives.

Neuropsychiatric Science	Psychiatric Neuroscience
• Neuropsychiatric evaluation	• Genetics
• Neurological/medical causes of psychiatric symptoms and syndromes	• Molecular basis of neuronal transmission/communication
• Developmental/genetic syndromes with behavioral/psychiatric presentations	• Behavioral neuroanatomy
• Neurodegenerative disorders	• Developmental neuroscience
	• Cognitive neuroscience
	• Social neuroscience

Source: Sheldon Benjamin, M.D., University of Massachusetts Medical School

Attacks

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Cyberstalking takes cybersnooping one step further.

"Take it seriously," said Simon. "Never arrange to meet anyone harassing you."

A restraining order won't necessarily stop such behavior, but it will provide some recourse if violated.

If threats start to escalate, the psychiatrist should verbally engage the patient, actively respond to threat behaviors, try to summon help, and have an escape route planned.

In a clinical setting, a psychiatrist may not have much time to assess whether a patient is likely to resort to violence in the short term, said Tardiff, a professor of psychiatry and public health and an attending psychiatrist at the Payne Whitney Clinic of the New York Hospital-Cornell Medical Center.

> **"You're not compiling a rating scale. You're making a global medical decision by framing an opinion and weighing all the factors."**

A history of violence is the prime risk factor for future acts.

"Treat a history of violence like any other symptom," said Tardiff. "The gateway questions should be: Have you ever gotten into a fight? When? What were you thinking? How badly were you or the other person injured?"

Beyond that, the psychiatrist should probe for specific plans for violence, access to the victim, and available means, he said. "For example, move to get a gun out of the house, not just hide it, then get the patient into treatment."

Look, too, for a history of child abuse or other intrafamilial violence, brain trauma, and impulsive behavior, like dangerous driving, suicide attempts, or gambling, he said.

"You're not compiling a rating scale," said Tardiff. "You're making a global medical decision by framing an opinion and weighing all the factors."

Psychiatric disorders have variable connections to violent behavior, he said. Here are some examples:

- Violence is rare among people with depression unless it is accompanied by psychosis or delusions of guilt.
- In intermittent explosive disorder, violence is often related to stress, the patient seems calm between episodes, and the patient expresses remorse after the blowup.
- In antisocial personality disorder, the patient typically does not express postviolence regret and leads a chaotic life—lying, cheating, and stealing.
- With borderline personality disorder, violence is often related to rejection or perceived rejection by others.
- Violence is rare among people with paranoid personalities, but it may be extreme when it does happen. Prediction is difficult, so monitoring to detect change in ideation may have to serve.
- People with schizophrenia can become violent for reasons other than as a symptom of their psychosis. A patient with akathisia may bump into someone while walking around the day room, and the incident escalates into a fight, or violence may be "goal-directed," intended to influence others or get what the patient wants.
- Finally, substance abuse serves as an added layer of risk under any circumstances. Alcohol reduces inhibition and impairs cognition. ■

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Gender a Key Consideration In Substance Abuse Treatment

Although men still outnumber women with regard to the prevalence of alcohol and substance use disorders, women-specific concerns are gaining more attention in research.

BY JUN YAN

Women with substance use disorders (SUDs) do not have the same risk factors, comorbidities, disease course, and treatment response as male patients, and addiction psychiatrists should be mindful of the gender differences. This was the message conveyed by experts at a symposium at APA's 2010 annual meeting in New Orleans in May.

The symposium was part of a track supported by the National Institute on Drug Abuse (NIDA) at the meeting.

Women are traditionally considered to have a much lower prevalence of SUDs than men, but the epidemiology is changing. In 2004, 7.7 million women in the United States were estimated to have alcohol or substance use disorders, according to Kathleen Brady, M.D., a professor of psychiatry and associate dean for clinical research at the Medical University of South Carolina. Alcohol dependence is two to three times more common in men, but the gender gap is smaller for illicit drug dependence at 5.6 percent for women versus 9.2 percent for men. "When it comes to prescription drug misuse or abuse, men and women are about equal," Brady said.

Among the gender differences are the risk factors for substance abuse. Having a significant other with heavy drinking or drug use problems and having a history of childhood abuse or family violence are very strongly associated with an increased likelihood of substance abuse in women, much more so than in men, according to Brady. The role of childhood trauma appears to be a key risk factor in many women with SUDs.

In addition, Brady cited an abundance of data demonstrating some gender differences in comorbidities: Women with SUDs are more likely to have depressive and anxiety disorders, while men with SUDs are more likely to have attention-deficit/hyperactivity disorder and concurrent alcohol use.

In terms of disease trajectory, telescoping refers to the phenomenon that women appear to progress faster than men from first alcohol and substance use to abuse and to dependence and treatment seeking, Brady said. "In alcohol dependence, we know there are physiological bases that may be underpinning some of the telescoping [effects]," she said. For example, alcohol on average has higher circulating blood levels in women than in men because women tend to be smaller in size, have a lower proportion of body water, and less alcohol dehydrogenase activity. Thus, women are more likely to become intoxicated than men on the same amount of drinking.

Sex Hormones Influence Craving, Relapse

The physiological differences between men and women may help predict treatment response and the risk of relapse as mediated by stress- and cue-induced drug cravings, according to Rajita Sinha, Ph.D., a professor of psychiatry at Yale University School of Medicine.

"Cocaine dependence—and we've shown this also in alcohol—is associated with an enhanced sensitivity to stress- and cue-induced craving, but responses are different by sex and modulated by sex hormones," she said. In laboratory studies, she found that stress-induced craving is significantly associated with time to relapse in both men and women, but cue-induced craving is associated with time to relapse in women but not in men. In addition, women's brain and biochemical responses to stress appear to differ from men's.

In a pilot study, blood levels of estradiol and progesterone, which fluctuate with a woman's menstrual cycle, appear to influence stress- and cue-induced cravings to cocaine. Women with a high level of estradiol had stronger craving than men, while women with a moderate or high level of progesterone had weaker craving than both men and high-estradiol women.

If these findings are confirmed, treatments that target the stress- and cue-induced craving can be expected to prevent relapse, especially in women.

Women's Group Therapy Shows Promise

Shelly Greenfield, M.D., M.P.H., presented results from stage 1 of the Women's Recovery Group Study funded by NIDA. In this study, adult women with any substance dependence other than nicotine were randomized to either women-only group therapy (n=16) or mixed-gender group therapy (n=17; seven women and 10 men).

Greenfield is the chief academic officer and director of clinical and health services research and education in the Division on Alcohol and Drug Abuse at McLean Hospital and an associate professor of psychiatry at Harvard Medical School.

Both groups received 12 once-weekly therapy sessions, led by female therapists, and were followed for up to six months. Subjects in the mixed-gender group received manual-based behavioral treatment for substance abuse that did not focus on gender-specific issues. In contrast, the women-only group discussed issues and techniques that are related to substance abuse as well as women's concerns, including the effect of drugs and alcohol on women's health; how to manage mood, anxiety, and eating problems without using substances; violence, abuse, and how to get help for them; and how to cope with stress.

Both groups improved significantly from baseline in the 12-week treatment phase, Greenfield reported. However, those in the women-only group maintained their improvement to a greater extent than the women in the mixed-gender group. The patients in the women-only group also reported a higher level of satisfaction with treatment. In addition, women with more severe psychiatric illness and low self-efficacy, as measured by standardized psychological tools, appeared to achieve greater substance use reduction in the women-only group than in the mixed-gender group.

"Certain women with substance use disorders may prefer single-gender [therapy] settings," said Greenfield. There is research evidence to suggest that the single-gender versus mixed-gender format may influence group process and dynamics, including gender stereotype and cohesion. Based on her study, she noted that "within a single first session, in the all-women context, the amount of fairly sensitive and private information women are able to share with each other early on . . . is rather remarkable." ■

Aspirin Regimen May Help Counter Schizophrenia Symptoms

Some people take aspirin for pain, others to prevent a heart attack. But how about taking it to banish hallucinations? The notion is not as outlandish as it may seem at first glance.

BY JOAN AREHART-TREICHEL

Aspirin beat a placebo as an adjunctive medication for schizophrenia in an intriguing new study.

William Carpenter Jr., M.D., a professor of psychiatry and pharmacology at the University of Maryland and editor in chief of *Schizophrenia Bulletin*, calls the finding "exciting."

"The question of infectious, immune, and/or inflammatory pathophysiology in schizophrenia is old, but interest has increased recently," Carpenter explained to *Psychiatric News*. "This is especially relevant to therapeutic discovery where novel targets and mechanisms are needed to supplement six decades of dopamine antagonists as antipsychotic drugs. . . . Replication [of this study] is essential, but if successful, a new treatment approach is introduced, and a new window for therapeutic discovery is opened."

The study was headed by Wijnand Laan, Ph.D., an assistant professor at the University Medical Center Utrecht in the Netherlands, and was reported in the May *Journal of Clinical Psychiatry*. The goal was to see whether adding aspirin to antipsychotic medications could reduce symptoms in individuals with schizophrenia.

The study sample consisted of 70 subjects with a *DSM-IV-TR* diagnosis of schizophrenia spectrum disorder. Half were randomly allocated to a test group and the others to a placebo group. Positive and Negative Syndrome Scale (PANSS) scores for the two groups were comparable. The only differences between the two groups was that the duration of illness was slightly shorter and the proportion of those treated with clozapine slightly higher in the placebo group.

All subjects continued to receive their usual antipsychotic medications during the three-month study period, but the test group also received 1,000 mg of aspirin daily, while the placebo group received an identical-appearing placebo daily.

During a three-month follow-up period, the PANSS was again used to evaluate the subjects for schizophrenia symptoms. Before and after the study, subjects were also given cognitive tests. Results from baseline and the follow-up period were compared.

Positive PANSS scores and total PANSS scores for both groups declined, the researchers found, but more so in the aspirin group; the differences were statistically significant. For the positive PANSS score, the difference was 1.57 points, and for the total PANSS score, the difference was 4.86 points, differences that the researchers described as "of medium size."

Negative PANSS scores for both groups also declined, and again especially in the aspirin group, but these differences were small and not statistically significant. No effect of aspirin on cognitive function could be detected.

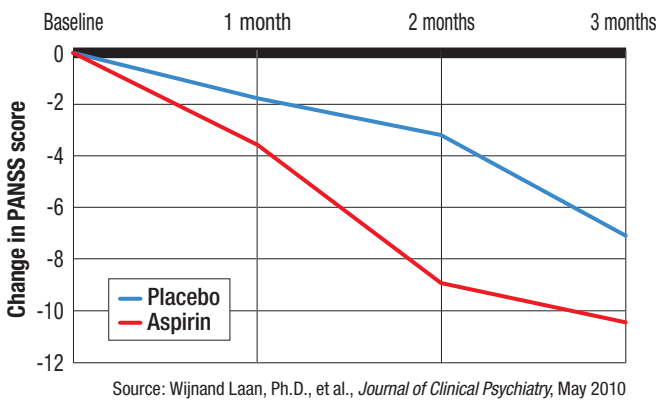
If aspirin may be able to reduce schizophrenia symptoms, how might it do so? By correcting an imbalance in the production of pro-inflammatory and anti-inflammatory cytokines by helper T cells, the researchers proposed. Other researchers have implicated such an imbalance in schizophrenia.

Thus, "given the considerable effect

please see ***Aspirin*** *on page 26*

Can an Aspirin a Day Keep Schizophrenia Away?

In a study with 70 subjects with schizophrenia, all subjects received their usual antipsychotic medications, but in addition half received aspirin daily, and half received a placebo pill. PANSS scores for both the placebo group and the aspirin group declined over the three-month study period, but more so for the latter.



Source: Wijnand Laan, Ph.D., et al., *Journal of Clinical Psychiatry*, May 2010

Genes Will Someday Help Select Depression Treatment

Researchers find a variable treatment response to citalopram based on polymorphisms in the corticotropin-releasing-factor system.

BY MARK MORAN

Individualized treatment, based on analysis of individual patient genetic polymorphisms, is the future for the treatment of depression.

So said Charles Nemeroff, M.D., Ph.D., at APA's 2010 annual meeting in May in New Orleans. He presented recent data on genetic polymorphisms in components of the serotonin, dopamine, and norepinephrine transmitter systems as well as the cortocotropin-releasing-factor (CRF) system that have been found to be associated with variable treatment response to different classes of medication.

The findings promise to enable clinicians to match treatments to genetic subtypes. "We hope in the near future to be where infectious disease and oncology are in [terms of] individualized treatment," Nemeroff said. "We should be able to see patients, study them in terms of their genomics, characterizing them biologically, then match them to a particular treatment regimen.

"That's what we do in oncology, and there is no reason why we can't do it in psychiatry," he said. "Ten or 20 years from now, we will be sending our patients to the laboratory to characterize them in terms of genetic polymorphisms and/or to an imaging laboratory. Then based on those findings, and on the clinical presentation of the patient, we will be able to do what we can't do right now, which is to answer the question—of all the treatments that are effective for depression, what is the best one for this particular patient?"

Nemeroff is the Leonard M. Miller professor and chair of psychiatry at the University of Miami Miller School of Medicine. Nemeroff's remarks were part of a three-hour symposium that included presentations on augmentation and combination strategies in the treatment of depression by Linda Carpenter, M.D., and management of comorbid depression and substance abuse by Ihsan Salloum, M.D., M.P.H.

> **"We hope in the near future to be where infectious disease and oncology are in [terms of] individualized treatment."**

Michael Thase, M.D., discussed methodological issues in antidepressant studies that have led to flawed reports in the popular media suggesting that antidepressant medications do not work for most patients (see article below).

Reviewing the function of serotonin in depression, Nemeroff explained that neuroimaging has shown that some, though not all, patients with depression have a reduction in binding of the serotonin transporter in the mid-brain raphe neurons. "I would suggest to you that these patients are likely the SSRI responders."

He added that different polymorphisms of the serotonin transporter (5-HTT) gene render individuals more or less susceptible to depression: patients with a short arm of the transporter gene express fewer serotonin transporters. He cited a now-famous report by Avshalom Caspi, Ph.D., that found that individuals with the short allele were highly susceptible to depression in the face of early childhood trauma, while those with the long allele experienced a protective effect.

(That study, "Influence of Life Stress on Depression: Moderation by a Polymorphism in the 5-HTT Gene," appeared in the July 18, 2003, *Science*.)

Similar findings exist for dopamine, and Nemeroff described postmortem studies in suicide victims showing a reduction in dopamine transporters in the amygdala and a compensatory increase in postsynaptic D_2/D_3 receptors. Moreover, while studies of normal volunteers aged 18 to 55 show an age-related reduction in dopamine transporters, depressed patients exhibit a lower density of transporters across the age range than do healthy comparison subjects.

Nemeroff also presented data from two of his studies finding variable treatment response to antidepressants based on polymorphisms in the norepinephrine transporter gene and in genes regulating the corticotropin-releasing-factor system.

The latter study, "Association of Polymorphisms in Genes Regulating the Corticotropin-Releasing Factor System With Antidepressant Treatment Response," was published in the April *Archives of General Psychiatry*. The study analyzed the association of genetic variants in 10 genes that regulate the CRF and arginine vasopressin systems with treatment response to citalopram using data from the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study.

It found that one single-nucleotide polymorphism in the CRF system showed a significant association with both remission and reduction in depressive symptoms in response to citalopram.

And a September 2004 report in the *American Journal of Psychiatry* showed a variable response to milnacipran—an agent now approved for the treatment of fibromyalgia and, in some countries in Europe, for depression—based on polymorphisms in the norepinephrine transporter gene.

In that study, 96 Japanese patients with major depressive disorder were treated with milnacipran, 50mg/day to 100 mg/day, for six weeks. The presence of one specific polymorphism of the NET gene was associated with a superior antidepressant response, whereas another polymorphism was associated with a slower onset of therapeutic response.

"This is where the future of psychiatry is going," Nemeroff said. "The task before us is very large because each of these subtypes of depression is biologically distinct and will have different predictors of treatment response. But there is no doubt that what we will be able to do is end this interminable trial-and-error method that all of us are stuck with treating depressed patients."

"Prediction of Antidepressant Response to Milnacipran by Norepinephrine Transporter Gene Polymorphisms" is posted at <http://ajp.psychiatryonline.org/cgi/content/full/161/9/1575>. "Association of Polymorphisms in Genes Regulating the Corticotropin-Releasing Factor System With Antidepressant Treatment Response" is posted at <http://archpsyc.ama-assn.org/cgi/content/full/67/4/369>. ■

Does Placebo Effect Mask True Efficacy of Antidepressants?

Placebo effects have grown steadily in modern studies of antidepressants, owing mainly to the nature of patients who enter randomized clinical trials and changes in study design, leaving a small zone in which to demonstrate a drug effect.

BY MARK MORAN

Modern randomized, controlled studies of antidepressants demonstrate increasing effects of placebo because of patient selection and study design—a fact that has obscured the real value of antidepressants in the treatment of millions of people.

So said Michael Thase, M.D., at APA's 2010 annual meeting in New Orleans in May. Thase, a professor of psychiatry at the University of Pennsylvania School of Medicine, spoke at the session "Unmet Needs in Antidepressant Therapy."

Thase addressed a theme picked up by the popular media recently that antidepressants don't work, or don't work any better than placebo—as exemplified in the January 29 article in *Newsweek*, "The Depressing News About Antidepressants."

That conclusion is based on some recent research, including a meta-analysis in the January 6 *Journal of the American Medical Association (JAMA)* showing that the magnitude of benefit of antidepressant medication compared with placebo increases with severity of depression and may be "minimal or nonexistent, on average, in patients with mild or moderate symptoms." The study was titled "Antidepressant Drug Effects and Depression Severity: A Patient-Level Meta-Analysis" (*Psychiatric News*, February 5).

But Thase said the conclusion drawn in the popular media—that the effects of antidepressants generally are "trivial"—is a distortion of the meaning of a placebo effect. And he noted that the *JAMA* study also found that for patients with more severe depression, the benefit of medications over placebo is substantial—a fact that he said comes as no surprise to psychiatrists.

"The decision not to treat someone in clinical practice is not the same as receiving eight weekly visits in a placebo-controlled trial under double-blind conditions," Thase said. "Physicians cannot use placebo in their clinical practice—it's unethical. Their options are watchful waiting, which is not equivalent to a placebo effect; prescribing something; or seeing the patient for psychotherapy."

> **"The effects are not trivial in a condition that affects 14 million people at any given time."**

He noted that even psychotherapy has an analogue to the placebo effect, and studies of psychotherapy efficacy often cannot reliably separate out treatment effects from nonspecific effects.

Moreover, the value of antidepressants in treating the most severely ill patients gets lost in studies that include large numbers of mildly depressed individuals who are more likely to respond to placebo, he said.

"The effects are not trivial in a condition that affects 14 million people at any given time," he said. "A 10 percent advantage, if applied to the whole population, would mean that 1.4 million people were being helped. A large effect for 10 percent of people looks like a small effect when it's spread out across the remaining 90 percent of placebo responders and nonresponders."

Thase showed data demonstrating that placebo effects have grown in studies over the years, owing largely to the nature of people who enter randomized, controlled trials and changes in study design. He noted that participants in contemporary studies are liable to be either the easiest to treat or the hardest to treat—those who respond to anything, including placebo, or to little or nothing. "That leaves a very small zone in which to show an effect," he said.

"We may never find newer antidepressants if we don't fix this problem of the metastasizing placebo effect rate in modern studies," he said.

"Antidepressant Drug Effects and Patient Severity: A Patient Level Meta-Analysis," is posted at <http://jama.ama-assn.org/cgi/content/short/303/1/47>. ■

Some With Psychosis Decide Social Life Not Worth It

If people with schizophrenia function poorly in social settings, it may be because they have developed negative beliefs about social functioning, perhaps to protect themselves from rejection.

BY JOAN AREHART-TREICHEL

"Get a life!" people sometimes quip.

"Well, that's not easy to do if you've got schizophrenia," an individual with this illness might respond.

But it might still be possible. The reason? Negative beliefs about a social life seem to be the major reason why individuals with schizophrenia don't have a social life, a new study has found. And if that is the case, then changing those beliefs might help them "get a life."

> **"We propose that the patients' asocial beliefs trump their need for social acceptance."**

The study was conducted by Paul Grant, Ph.D., a research assistant professor of psychology in psychiatry at the University of Pennsylvania, and Aaron Beck, M.D., University Professor Emeritus of Psychiatry at the University of Pennsylvania. Beck is also considered "the father of cognitive therapy." Results were published in the May 15 *Psychiatry Research*.

People with schizophrenia tend to isolate themselves from others, yet at the same time they say that they would like to have friends, get a job, and perhaps have a family. What is the explanation for this discrepancy? Could it be negative beliefs and expectations rather than the illness itself? Grant and Beck conducted a study to find out.

The study sample included 123 adults with an average age of 39 who had been diagnosed with schizophrenia or schizoaffective disorder. Various scales were used to evaluate subjects on social functioning, neurocognition, emotion perception, positive symptoms, negative symptoms, depression, anxiety, and negative beliefs about social functioning.

Negative beliefs about a social life were determined with 15 statements from the Revised Social Anhedonia Scale. Several of the statements, for example, were "People are usually better off if they stay aloof from emotional involvement with others," "Making new friends isn't worth the effort it takes," and "Having close friends is not as important as most people say." For each statement, subjects answered yes or no. Subjects' responses were summed into a total score of 0-15, with higher scores indicating more negative beliefs about a social life.

The researchers then used correlational analysis to see whether there were any orderly, predictable relationships between subjects' social functioning scores and their scores on the other measures. None could be found between their social functioning scores and their neurocognition, emotion perception, positive symptoms, and anxiety scores. But such a link could be found between their social functioning scores and their negative symptoms, depression, and scores indicating negative beliefs about the value of a social life.

And most striking, high scores on negative beliefs about a social life were associated with poor social functioning scores.

The researchers then determined the relative contribution to social functioning of neurocognition, emotion perception, negative symptoms, depression, and negative beliefs about social function. They found that neurocognition and emotion perception contributed a negligible amount—a finding that surprised them—but they also found that negative symptoms and depression accounted for somewhat more, and that negative beliefs about a social life accounted for the largest contribution to social functioning.

Finally, they conducted a longitudinal analysis of 13 of the subjects to see whether negative beliefs about social functioning at baseline significantly predicted social withdrawal a year later, or whether social withdrawal at baseline predicted negative beliefs about social function a year later. The former was the case.

Putting all these results together, it looks as if negative beliefs about a social life may be a major reason why people with schizophrenia don't relish social interactions, the researchers concluded. "We propose that the patients' asocial beliefs trump their need for social acceptance," they wrote.

And, if that is the case, would certain interventions help individuals with schizophrenia change such beliefs and thus improve their social lives? The researchers think that they might.

For example, "encouraging the patient to engage in social contact can expose the dysfunctional beliefs, which can then be the target for cognitive restructuring. Various behavioral techniques such as social-skills training and assertiveness training can facilitate social engagement and demonstrate to the patient the positive consequences of social engagement. . . . Modifying beliefs that maintain depression, which is also linked to poor social functioning, can further motivate the patient to socialize productively."

The study was funded by the Foundation for Cognitive Therapy and Research, NARSAD, and the Heinz Foundation.

An abstract of "Asocial Beliefs as Predictors of Asocial Behavior in Schizophrenia" is posted at <www.sciencedirect.com/science/journal/01651781> under the May 15 issue. ■

Diabetes Regimen Adherence Better In Those With Schizophrenia

The finding on patients with comborbid psychosis and diabetes points to better outcomes as they increase the frequency of their contact with clinicians and repeatedly hear messages about medication adherence.

BY MARK MORAN

People with schizophrenia and diabetes are more adherent to oral hypoglycemia medication regimens than people who do not have schizophrenia, according to an analysis of Department of Veterans Affairs health system data.

This finding, reported in the March *Schizophrenia Bulletin*, may surprise clinicians used to hearing about the generally poor quality of medical care received by people with schizophrenia. But one psychiatrist who has been a leader in advocating for better general medical care for psychiatric patients says the study results appear to be consistent with previous research suggesting that serious mental illness is often associated with more doctor visits, typically with mental health clinicians who are likely to emphasize adherence to all prescribed medications.

"The overall message is that more visits create the potential for better adherence and better outcomes, and patients with severe mental illness who are being treated tend to have a lot of contact with the health care system," said John Newcomer, M.D., a professor of psychiatry at Washington University School of Medicine in St. Louis, who reviewed the report for *Psychiatric News*.

In the study, researchers at the University of Maryland, University of Michigan, and VA Capital Healthcare Network compared adherence to oral hypoglycemia medications for diabetes among 11,454 patients with schizophrenia and 10,560 patients with diabetes who did not have schizophrenia.

They used data from the VA's National Patient Care Database and National Psychosis Registry. Adherence to medication was calculated as a "medication possession ratio (MPR)," derived by summing the total days' supply of medication dispensed from VA outpatient pharmacies, beginning with the date of the first prescription for an oral hypoglycemic in 2002 and dividing it by the number of days' supply required for continuous treatment during outpatient days over a 12-month period.

Nonadherence was defined as having an MPR of less than 80 percent of needed hypoglycemic medications.

They found that poor adherence was less prevalent among diabetes patients with schizophrenia (43 percent) than among those without schizophrenia (52 percent).

Lead author Julie Kreyenbuhl, M.D., and colleagues noted that individuals with schizophrenia showed better adherence despite having higher rates of risk factors that were shown to be independently associated with nonadherence. These factors, which were controlled for in statistical analysis, included black race, homelessness, depression, and substance use disorders.

"However, several characteristics shown to promote medication adherence also occurred more frequently in diabetes patients with schizophrenia," they said. "These patients had significantly greater contact with the health care system overall, having had significantly more hospitalizations and a greater number of outpatient visits for diabetes-, non-diabetes medical-, and psychiatric-related reasons in the prior year."

Newcomer told *Psychiatric News* that the study is not the first to demonstrate the association between frequency of contacts with the health care system and quality of care or health outcome, though the message tends to be obscured by the overall finding of generally poor medical care received by patients with serious mental illness.

He noted that a landmark 11-year follow-up study of mortality in patients with schizophrenia that appeared in the August 22, 2009, *Lancet* found that the antipsychotic clozapine was associated with lower mortality than other medications—a finding that Newcomer said has been widely interpreted as supporting the deregulation of clozapine. Unrecognized in the interpretation of results, he said, is the likelihood that patients on clozapine had better outcomes because of the greater frequency of contact with the health care system that is required for use of this antipsychotic.

Newcomer added that he believes psychiatry has tended to do a better job of monitoring compliance with medications than other specialties have. "Some of our patients are in and out of the clinic every month, and patients in psychiatric clinics tend to hear the message all the time—'take your meds, take your meds.' "

> **"The overall message is that more visits create the potential for better adherence and better outcomes. . . ."**

"Does Adherence to Medications for Type 2 Diabetes Differ Between Individuals With vs Without Schizophrenia" is posted at <http://schizophreniabulletin.oxfordjournals.org/cgi/content/full/36/2/428>. An abstract of "11-Year Follow-up of Mortality in Patients With Schizophrenia: A Population-Based Cohort Study" is posted at <www.thelancet.com/journals/lancet/article/PIIS0140-6736(09)60742-X/abstract>. ■

Treat your patients with the demonstrated efficacy of LEXAPRO[1-5]

In adolescents aged 12 to 17 with Major Depressive Disorder (MDD)[1]

In adults with MDD and Generalized Anxiety Disorder (GAD)[1]

Lexapro® escitalopram oxalate

WARNING: SUICIDALITY AND ANTIDEPRESSANT DRUGS

Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders. Anyone considering the use of Lexapro or any other antidepressant in a child, adolescent or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. Lexapro is not approved for use in pediatric patients less than 12 years of age.

Please see additional Important Safety Information on following pages.

There is no generic available for LEXAPRO

- Significantly improved MDD symptoms in adolescents[2]

Lexapro (escitalopram oxalate) is indicated for the acute and maintenance treatment of major depressive disorder (MDD) in adults and adolescents aged 12-17 years. Lexapro is also indicated for the acute treatment of generalized anxiety disorder (GAD) in adults.

*LEXAPRO is indicated as an integral part of a total treatment program for MDD. Drug treatment may not be indicated for all adolescents with this syndrome.

IMPORTANT SAFETY INFORMATION (continued)

Contraindications

- Lexapro is contraindicated in patients taking monoamine oxidase inhibitors (MAOIs). There have been reports of serious, sometimes fatal, reactions with some cases resembling neuroleptic malignant syndrome (NMS) and serotonin syndrome. Features may include hyperthermia, rigidity, myoclonus, autonomic instability with possible rapid fluctuations of vital signs, and mental status changes that include extreme agitation progressing to delirium and coma. These reactions have also been reported in patients who have recently discontinued SSRI treatment and have been started on an MAOI. Serotonin syndrome was reported for two patients who were concomitantly receiving linezolid, an antibiotic which has MAOI activity. Lexapro should not be used in combination with an MAOI or within 14 days of discontinuing an MAOI. MAOIs should not be initiated within 14 days of discontinuing Lexapro.
- Lexapro is contraindicated in patients taking pimozide or with hypersensitivity to escitalopram or citalopram.

Warnings and Precautions

- All patients treated with antidepressants should be monitored appropriately and observed closely for clinical worsening, suicidality and unusual changes in behavior, especially within the first few months of treatment or when changing the dose. Consideration should be given to changing the therapeutic regimen, including discontinuing medication, in patients whose depression is persistently worse, who are experiencing emergent suicidality or symptoms that might be precursors to worsening depression or suicidality, especially if these symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms. Families and caregivers of patients treated with antidepressants should be alerted about the need to monitor patients daily for the emergence of agitation, irritability, unusual changes in behavior, or the emergence of suicidality, and report such symptoms immediately. Prescriptions for Lexapro should be written for the smallest quantity of tablets, consistent with good patient management, in order to reduce the risk of overdose.

- Significantly higher rates of response and remission vs placebo in MDD and GAD in adults[4,5]

- A major depressive episode may be the initial presentation of bipolar disorder. In patients at risk for bipolar disorder, treating such an episode with an antidepressant alone may increase the likelihood of precipitating a mixed/manic episode. Prior to initiating treatment with an antidepressant, patients should be adequately screened to determine if they are at risk for bipolar disorder. Lexapro should be used cautiously in patients with a history of mania or seizure disorder. Lexapro is not approved for use in treating bipolar depression.
- The concomitant use of Lexapro with other SSRIs, SNRIs, triptans, tryptophan, antipsychotics or other dopamine antagonists is not recommended due to potential development of life-threatening serotonin syndrome or neuroleptic malignant syndrome (NMS)-like reactions. Reactions have been reported with SNRIs and SSRIs alone, including Lexapro, but particularly with drugs that impair metabolism of serotonin (including MAOIs). Management of these events should include immediate discontinuation of Lexapro and the concomitant agent and continued monitoring.
- Patients should be monitored for adverse reactions when discontinuing treatment with Lexapro. During marketing of Lexapro and other SSRIs and SNRIs, there have been spontaneous reports of adverse events occurring upon discontinuation, including dysphoric mood, irritability, agitation, dizziness, sensory disturbances (e.g., paresthesias), anxiety, confusion, headache, lethargy, emotional lability, insomnia and hypomania. A gradual dose reduction rather than abrupt cessation is recommended whenever possible.
- SSRIs and SNRIs have been associated with clinically significant hyponatremia. Elderly patients and patients taking diuretics or who are otherwise volume-depleted appear to be at a greater risk. Discontinuation of Lexapro should be considered in patients with symptomatic hyponatremia and appropriate medical intervention should be instituted.

Please see Boxed Warning on first page and additional Important Safety Information on next page.

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Visit the LEXAPRO website at www.lexapro.com

LEXAPRO: Proven efficacy in MDD in adolescents aged 12 to 17, and in MDD and GAD in adults[1-5]

Warnings and Precautions (continued)

- SSRIs (including Lexapro) and SNRIs may increase the risk of bleeding. Patients should be cautioned that concomitant use of aspirin, NSAIDs, warfarin or other anticoagulants may add to the risk.
- Patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that Lexapro does not affect their ability to engage in such activities.
- Lexapro should be used with caution in patients with severe renal impairment or with diseases or conditions that alter metabolism or hemodynamic responses. In subjects with hepatic impairment, clearance of racemic citalopram was decreased and plasma concentrations were increased. The recommended dose of Lexapro in hepatically impaired patients is 10 mg/day.
- For pregnant or nursing mothers, Lexapro should be used only if the potential benefit justifies the potential risk to the fetus or child.

Adverse Reactions

- In clinical trials of MDD, the most common adverse reactions in adults treated with Lexapro (approximately 5% or greater and at least twice the incidence of placebo) were nausea (15% vs 7%), insomnia (9% vs 4%), ejaculation disorder (9% vs <1%), fatigue (5% vs 2%), somnolence (6% vs 2%), and increased sweating (5% vs 2%). In pediatric patients, the overall profile of adverse reactions was similar to that seen in adults; however, the following additional adverse reactions were reported at an incidence of at least 2% for Lexapro and greater than placebo: back pain, urinary tract infection, vomiting, and nasal congestion.
- In clinical trials of GAD, the most common adverse reactions in adults treated with Lexapro (approximately 5% or greater and at least twice the incidence of placebo) were nausea (18% vs 8%), ejaculation disorder (14% vs 2%), insomnia (12% vs 6%), fatigue (8% vs 2%), decreased libido (7% vs 2%) and anorgasmia (6% vs <1%).

Please see accompanying brief summary of Prescribing Information for LEXAPRO, including Boxed Warning.

References: 1. LEXAPRO [package insert]. St. Louis, Mo: Forest Pharmaceuticals, Inc.; 2009. **2.** Emslie GJ, Ventura D, Korotzer A, Tourkodimitris S. Escitalopram in the treatment of adolescent depression: a randomized placebo-controlled multisite trial. *J Am Acad Child Adolesc Psychiatry*. 2009;48:721-729. **3.** Burke WJ, Gergel I, Bose A. Fixed-dose trial of the single isomer SSRI escitalopram in depressed outpatients. *J Clin Psychiatry*. 2002;63:331-336. **4.** Davidson JRT, Bose A, Korotzer A, Zheng H. Escitalopram in the treatment of generalized anxiety disorder: double-blind, placebo controlled, flexible dose study. *Depress Anxiety*. 2004;19:234-240. **5.** Wade A, Lemming OM, Hedegaard KB. Escitalopram 10 mg/day is effective and well tolerated in a placebo-controlled study in depression in primary care. *Int Clin Psychopharmacol*. 2002;17:95-102.

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WARNINGS: SUICIDALITY AND ANTIDEPRESSANT DRUGS

Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders. Anyone considering the use of Lexapro or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. Lexapro is not approved for use in pediatric patients less than 12 years of age. *[See Warnings and Precautions: Clinical Worsening and Suicide Risk, Patient Counseling Information: Information for Patients, and Used in Specific Populations: Pediatric Use].*

INDICATIONS AND USAGE: Major Depressive Disorder-Lexapro (escitalopram) is indicated for the acute and maintenance treatment of major depressive disorder in adults and in adolescents 12 to 17 years of age [*see Clinical Studies*]. A major depressive episode (DSM-IV) implies a prominent and relatively persistent (nearly every day for at least 2 weeks) depressed or dysphoric mood that usually interferes with daily functioning, and includes at least five of the following nine symptoms: depressed mood, loss of interest in usual activities, significant change in weight and/or appetite, insomnia or hypersomnia, psychomotor agitation or retardation, increased fatigue, feelings of guilt or worthlessness, slowed thinking or impaired concentration, a suicide attempt or suicidal ideation. **Generalized Anxiety Disorder**-Lexapro is indicated for the acute treatment of Generalized Anxiety Disorder (GAD) in adults [*see Clinical Studies*]. Generalized Anxiety Disorder (DSM-IV) is characterized by excessive anxiety and worry (apprehensive expectation) that is persistent for at least 6 months and which the person finds difficult to control. It must be associated with at least 3 of the following symptoms: restlessness or feeling keyed up or on edge, being easily fatigued, difficulty concentrating or mind going blank, irritability, muscle tension, and sleep disturbance.

CONTRAINDICATIONS: Monoamine oxidase inhibitors (MAOIs)-Concomitant use in patients taking monoamine oxidase inhibitors (MAOIs) is contraindicated [*see Warnings and Precautions*]. **Pimozide**-Concomitant use in patients taking pimozide is contraindicated [*see Drug Interactions*]. **Hypersensitivity to escitalopram or citalopram**-Lexapro is contraindicated in patients with a hypersensitivity to escitalopram or citalopram or any of the inactive ingredients in Lexapro.

WARNINGS AND PRECAUTIONS: Clinical Worsening and Suicide Risk-Patients with major depressive disorder (MDD), both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality) or unusual changes in behavior, whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. Suicide is a known risk of depression and certain other psychiatric disorders, and these disorders themselves are the strongest predictors of suicide. There has been a long-standing concern, however, that antidepressants may have a role in inducing worsening of depression and the emergence of suicidality in certain patients during the early phases of treatment. Pooled analyses of short-term placebo-controlled trials of antidepressant drugs (SSRIs and others) showed that these drugs increase the risk of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults (ages 18-24) with major depressive disorder (MDD) and other psychiatric disorders. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction with antidepressants compared to placebo in adults aged 65 and older. The pooled analyses of placebo-controlled trials in children and adolescents with MDD, obsessive compulsive disorder (OCD), or other psychiatric disorders included a total of 24 short-term trials of 9 antidepressant drugs in over 4400 patients. The pooled analyses of placebo-controlled trials in adults with MDD or other psychiatric disorders included a total of 295 short-term trials (median duration of 2 months) of 11 antidepressant drugs in over 77,000 patients. There was considerable variation in risk of suicidality among drugs, but a tendency toward an increase in the younger patients for almost all drugs studied. There were differences in absolute risk of suicidality across the different indications, with the highest incidence in MDD. The risk differences (drug vs. placebo), however, were relatively stable within age strata and across indications. These risk differences (drug-placebo difference in the number of cases of suicidality per 1000 patients treated) are provided in Table 1.

TABLE 1

Age Range	Drug-Placebo Difference in Number of Cases of Suicidality per 1000 Patients Treated
	Increases Compared to Placebo
<18	14 additional cases
18-24	5 additional cases
	Decreases Compared to Placebo
25-64	1 fewer case
≥65	6 fewer cases

No suicides occurred in any of the pediatric trials. There were suicides in the adult trials, but the number was not sufficient to reach any conclusion about drug effect on suicide. It is unknown whether the suicidality risk extends to longer-term use, i.e., beyond several months. However, there is substantial evidence from placebo-controlled maintenance trials in adults with depression that the use of antidepressants can delay the recurrence of depression. All patients being treated with antidepressants for any indication should be monitored appropriately and observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases. The following symptoms, anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, and mania, have been reported in adult and pediatric patients being treated with antidepressants for major depressive disorder as well as for other indications, both psychiatric and nonpsychiatric. Although a causal link between the emergence of such symptoms and either the worsening of depression and/or the emergence of suicidal impulses has not been established, there is concern that such symptoms may represent precursors to emerging suicidality. Consideration should be given to changing the therapeutic regimen, including possibly discontinuing the medication, in patients whose depression is persistently worse, or who are experiencing emergent suicidality or symptoms that might be precursors to worsening depression or suicidality, especially if these symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms. If the decision has been made to discontinue treatment, medication should be tapered, as rapidly as is feasible, but with recognition that abrupt discontinuation can be associated with certain symptoms [*see Dosage and Administration*]. Families and caregivers of patients being treated with antidepressants for major depressive disorder or other indications, both psychiatric and nonpsychiatric, should be alerted about the need to monitor patients for the emergence of agitation, irritability, unusual changes in behavior, and the other symptoms described above, as well as the emergence of suicidality, and to report such symptoms immediately to health care providers. Such monitoring should include daily observation by families and caregivers [*see also Patient Counseling Information*]. Prescriptions for Lexapro should be written for the smallest quantity of tablets consistent with good patient management, in order to reduce the risk of overdose. **Screening Patients for Bipolar Disorder**-A major depressive episode may be the initial presentation of bipolar disorder. It is generally believed (though not established in controlled trials) that treating such an episode with an antidepressant alone may increase the likelihood of precipitation of a mixed/manic episode in patients at risk for bipolar disorder. Whether any of the symptoms described above represent such a conversion is unknown. However, prior to initiating treatment with an antidepressant, patients with depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression. It should be noted that Lexapro is not approved for use in treating bipolar depression. **Serotonin Syndrome or Neuroleptic Malignant Syndrome (NMS)-like Reactions**-The development of a potentially life-threatening serotonin syndrome or Neuroleptic Malignant Syndrome (NMS)-like reactions have been reported with SNRIs and SSRIs alone, including Lexapro treatment, but particularly with concomitant use of serotonergic drugs (including triptans) with drugs which impair metabolism of serotonin (including MAOIs), or with antipsychotics or other dopamine antagonists. Serotonin syndrome symptoms may include mental status changes (e.g., agitation, hallucinations, coma), autonomic instability (e.g., tachycardia, labile blood pressure, hyperthermia), neuromuscular aberrations (e.g., hyperreflexia, incoordination) and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea). Serotonin syndrome, in its most severe form can resemble neuroleptic malignant syndrome, which includes hyperthermia, muscle rigidity, autonomic instability with possible rapid fluctuation of vital signs, and mental status changes. Patients should be monitored for the emergence of serotonin syndrome or NMS-like signs and symptoms. The concomitant use of Lexapro with MAOIs intended to treat depression is contraindicated. If concomitant treatment of Lexapro with a 5-hydroxytryptamine receptor agonist (triptan) is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases. The concomitant use of Lexapro with serotonin precursors (such as tryptophan) is not recommended. Treatment with Lexapro and any concomitant serotonergic or antidopaminergic agents, including antipsychotics, should be discontinued immediately if the above events occur and supportive symptomatic treatment should be initiated. **Discontinuation of Treatment with Lexapro**-During marketing of Lexapro and other SSRIs and SNRIs (serotonin and norepinephrine reuptake inhibitors), there have been spontaneous reports of adverse events occurring upon discontinuation of these drugs, particularly when abrupt, including the following: dysphoric mood, irritability, agitation, dizziness, sensory disturbances (e.g., paresthesias such as electric shock sensations), anxiety, confusion, headache, lethargy, emotional lability, insomnia, and hypomania. While these events are generally self-limiting, there have been reports of serious discontinuation symptoms. Patients should be monitored for these symptoms when discontinuing treatment with Lexapro. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the physician may continue decreasing the dose but at a more gradual rate [*see Dosage and Administration*]. **Seizures**-Although anticonvulsant effects of racemic citalopram have been observed in animal studies, Lexapro has not been systematically evaluated in patients with a seizure disorder. These patients were excluded from clinical studies during the product's premarketing testing. In clinical trials of Lexapro, cases of convulsion have been reported in association with Lexapro treatment. Like other drugs effective in the treatment of major depressive disorder, Lexapro should be introduced with care in patients with a history of seizure disorder. **Activation of Mania/Hypomania**-In placebo-controlled trials of Lexapro in major depressive disorder, activation of mania/hypomania was reported in one (0.1%) of 715 patients treated with Lexapro and in none of the 592 patients treated with placebo. One additional case of hypomania has been reported in association with Lexapro treatment. Activation of mania/hypomania has also been reported in a small proportion of patients with major affective disorders treated with racemic citalopram and other marketed drugs effective in the treatment of major depressive disorder. As with all drugs effective in the treatment of major depressive disorder, Lexapro should be used cautiously in patients with a history of mania. **Hyponatremia**-Hyponatremia may occur as a result of treatment with SSRIs and SNRIs, including Lexapro. In many cases, this hyponatremia appears to be the result of the syndrome of inappropriate antidiuretic hormone secretion (SIADH), and was reversible when Lexapro was discontinued. Cases with serum sodium lower than 110 mmol/L have been reported. Elderly patients may be at greater risk of developing hyponatremia with SSRIs and SNRIs. Also, patients taking diuretics or who are otherwise volume depleted may be at greater risk [*see Geriatric Use*]. Discontinuation of Lexapro should be considered in patients with symptomatic hyponatremia and appropriate medical intervention should be instituted. Signs and symptoms of hyponatremia include headache, difficulty concentrating, memory impairment, confusion, weakness, and unsteadiness, which may lead to falls. Signs and symptoms associated with more severe and/or acute cases have included hallucination, syncope, seizure, coma, respiratory arrest, and death. **Abnormal Bleeding**-SSRIs and SNRIs, including Lexapro, may increase the risk of bleeding events. Concomitant use of aspirin, nonsteroidal anti-inflammatory drugs, warfarin, and other anticoagulants may add to the risk. Case reports and epidemiological studies (case-control and cohort design) have demonstrated an association between use of drugs that interfere with serotonin reuptake and the occurrence of gastrointestinal bleeding. Bleeding events related to SSRIs and SNRIs use have ranged from ecchymoses, hematomas, epistaxis, and petechiae to life-threatening hemorrhages. Patients should be cautioned about the risk of bleeding associated with the concomitant use of Lexapro and NSAIDs, aspirin, or other drugs that affect coagulation. **Interference with Cognitive and Motor Performance**-In a study in normal volunteers, Lexapro 10 mg/day did not produce impairment of intellectual function or psychomotor performance. Because any psychoactive drug may impair judgment, thinking, or motor skills, however, patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that Lexapro therapy does not affect their ability to engage in such activities. **Use in Patients with Concomitant Illness**-Clinical experience with Lexapro in patients with certain concomitant systemic illnesses is limited. Caution is advisable in using Lexapro in patients with diseases or conditions that produce altered metabolism or hemodynamic responses. Lexapro has not been systematically evaluated in patients with a recent history of myocardial infarction or unstable heart disease. Patients with these diagnoses were generally excluded from clinical studies during the product's premarketing testing. In subjects with hepatic impairment, clearance of racemic citalopram was decreased and plasma concentrations were increased. The recommended dose of Lexapro in hepatically impaired patients is 10 mg/day [*see Dosage and Administration*]. Because escitalopram is extensively metabolized, excretion of unchanged drug in urine is a minor route of elimination. Until adequate numbers of patients with severe renal impairment have been evaluated during chronic treatment with Lexapro, however, it should be used with caution in such patients [*see Dosage and Administration*]. **Potential for Interaction with Monoamine Oxidase Inhibitors**-In patients receiving serotonin reuptake inhibitor drugs in combination with a monoamine oxidase inhibitor (MAOI), there have been reports of serious, sometimes

fatal, reactions including hyperthermia, rigidity, myoclonus, autonomic instability with possible rapid fluctuations of vital signs, and mental status changes that include extreme agitation progressing to delirium and coma. These reactions have also been reported in patients who have recently discontinued SSRI treatment and have been started on an MAOI. Some cases presented with features resembling neuroleptic malignant syndrome. Furthermore, limited animal data on the effects of combined use of SSRIs and MAOIs suggest that these drugs may act synergistically to elevate blood pressure and evoke behavioral excitation. Therefore, it is recommended that Lexapro should not be used in combination with an MAOI, or within 14 days of discontinuing treatment with an MAOI. Similarly, at least 14 days should be allowed after stopping Lexapro before starting an MAOI. Serotonin syndrome has been reported in two patients who were concomitantly receiving linezolid, an antibiotic which is a reversible non-selective MAOI.

ADVERSE REACTIONS: Clinical Trials Experience-Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice. **Clinical Trial Data Sources; Pediatrics (6 -17 years)**-Adverse events were collected in 576 pediatric patients (286 Lexapro, 290 placebo) with major depressive disorder in double-blind placebo-controlled studies. Safety and effectiveness of Lexapro in pediatric patients less than 12 years of age has not been established. **Adults**-Adverse events information for Lexapro was collected from 715 patients with major depressive disorder who were exposed to escitalopram and from 592 patients who were exposed to placebo in double-blind, placebo-controlled trials. An additional 284 patients with major depressive disorder were newly exposed to escitalopram in open-label trials. The adverse event information for Lexapro in patients with GAD was collected from 429 patients exposed to escitalopram and from 427 patients exposed to placebo in double-blind, placebo-controlled trials. Adverse events during exposure were obtained primarily by general inquiry and recorded by clinical investigators using terminology of their own choosing. Consequently, it is not possible to provide a meaningful estimate of the proportion of individuals experiencing adverse events without first grouping similar types of events into a smaller number of standardized event categories. In the tables and tabulations that follow, standard World Health Organization (WHO) terminology has been used to classify reported adverse events. The stated frequencies of adverse reactions represent the proportion of individuals who experienced, at least once, a treatment-emergent adverse event of the type listed. An event was considered treatment-emergent if it occurred for the first time or worsened while receiving therapy following baseline evaluation. **Adverse Events Associated with Discontinuation of Treatment; Major Depressive Disorder; Pediatrics (6 -17 years)**-Adverse events were associated with discontinuation of 3.5% of 286 patients receiving Lexapro and 1% of 290 patients receiving placebo. The most common adverse event (incidence at least 1% for Lexapro and greater than placebo) associated with discontinuation was insomnia (1% Lexapro, 0% placebo). **Adults**-Among the 715 depressed patients who received Lexapro in placebo-controlled trials, 6% discontinued treatment due to an adverse event, as compared to 2% of 592 patients receiving placebo. In two fixed-dose studies, the rate of discontinuation for adverse events in patients receiving 10 mg/day Lexapro was not significantly different from the rate of discontinuation for adverse events in patients receiving placebo. The rate of discontinuation for adverse events in patients assigned to a fixed dose of 20 mg/day Lexapro was 10%, which was significantly different from the rate of discontinuation for adverse events in patients receiving 10 mg/day Lexapro (4%) and placebo (3%). Adverse events that were associated with the discontinuation of at least 1% of patients treated with Lexapro, and for which the rate was at least twice that of placebo, were nausea (2%) and ejaculation disorder (2% of male patients). **Generalized Anxiety Disorder; Adults**-Among the 429 GAD patients who received Lexapro 10-20 mg/day in placebo-controlled trials, 8% discontinued treatment due to an adverse event, as compared to 4% of 427 patients receiving placebo. Adverse events that were associated with the discontinuation of at least 1% of patients treated with Lexapro, and for which the rate was at least twice the placebo rate, were nausea (2%), insomnia (1%), and fatigue (1%). **Incidence of Adverse Reactions in Placebo-Controlled Clinical Trials; Major Depressive Disorder; Pediatrics (6 -17 years)**-The overall profile of adverse reactions in pediatric patients was generally similar to that seen in adult studies, as shown in Table 2. However, the following adverse reactions (excluding those which appear in Table 2 and those for which the coded terms were uninformative or misleading) were reported at an incidence of at least 2% for Lexapro and greater than placebo: back pain, urinary tract infection, vomiting, and nasal congestion. **Adults**-The most commonly observed adverse reactions in Lexapro patients (incidence of approximately 5% or greater and approximately twice the incidence in placebo patients) were insomnia, ejaculation disorder (primarily ejaculatory delay), nausea, sweating increased, fatigue, and somnolence. Table 2 enumerates the incidence, rounded to the nearest percent, of treatment-emergent adverse events that occurred among 715 depressed patients who received Lexapro at doses ranging from 10 to 20 mg/day in placebo-controlled trials. Events included are those occurring in 2% or more of patients treated with Lexapro and for which the incidence in patients treated with Lexapro was greater than the incidence in placebo-treated patients.

TABLE 2
Treatment-Emergent Adverse Reactions Observed with a Frequency of ≥ 2% and Greater Than Placebo for Major Depressive Disorder

Adverse Reaction	Lexapro (N=715)	Placebo (N=592)
Autonomic Nervous System Disorders		
Dry Mouth	6%	5%
Sweating Increased	5%	2%
Central & Peripheral Nervous System Disorders		
Dizziness	5%	3%
Gastrointestinal Disorders		
Nausea	15%	7%
Diarrhea	8%	5%
Constipation	3%	1%
Indigestion	3%	1%
Abdominal Pain	2%	1%
General		
Influenza-like Symptoms	5%	4%
Fatigue	5%	2%
Psychiatric Disorders		
Insomnia	9%	4%
Somnolence	6%	2%
Appetite Decreased	3%	1%
Libido Decreased	3%	1%
Respiratory System Disorders		
Rhinitis	5%	4%
Sinusitis	3%	2%
Urogenital		
Ejaculation Disorder[1,2]	9%	<1%
Impotence[2]	3%	<1%
Anorgasmia[3]	2%	<1%

[1]Primarily ejaculatory delay.
[2]Denominator used was for males only (N=225 Lexapro; N=188 placebo).
[3]Denominator used was for females only (N=490 Lexapro; N=404 placebo).

Generalized Anxiety Disorder; Adults-The most commonly observed adverse reactions in Lexapro patients (incidence of approximately 5% or greater and approximately twice the incidence in placebo patients) were nausea, ejaculation disorder (primarily ejaculatory delay), insomnia, fatigue, decreased libido, and anorgasmia. Table 3 enumerates the incidence, rounded to the nearest percent of treatment-emergent adverse events that occurred among 429 GAD patients who received Lexapro 10 to 20 mg/day in placebo-controlled trials. Events included are those occurring in 2% or more of patients treated with Lexapro and for which the incidence in patients treated with Lexapro was greater than the incidence in placebo-treated patients.

TABLE 3
Treatment-Emergent Adverse Reactions Observed with a Frequency of ≥ 2% and Greater Than Placebo for Generalized Anxiety Disorder

Adverse Reactions	Lexapro (N=429)	Placebo (N=427)
Autonomic Nervous System Disorders		
Dry Mouth	9%	5%
Sweating Increased	4%	1%
Central & Peripheral Nervous System Disorders		
Headache	24%	17%
Paresthesia	2%	1%
Gastrointestinal Disorders		
Nausea	18%	8%
Diarrhea	8%	6%
Constipation	5%	4%
Indigestion	3%	2%
Vomiting	3%	1%
Abdominal Pain	2%	1%
Flatulence	2%	1%
Toothache	2%	0%
General		
Fatigue	8%	2%
Influenza-like Symptoms	5%	4%
Musculoskeletal System Disorder		
Neck/Shoulder Pain	3%	1%
Psychiatric Disorders		
Somnolence	13%	7%
Insomnia	12%	6%
Libido Decreased	7%	2%
Dreaming Abnormal	3%	2%
Appetite Decreased	3%	1%
Lethargy	3%	1%
Respiratory System Disorders		
Yawning	2%	1%
Urogenital		
Ejaculation Disorder[1,2]	14%	2%
Anorgasmia[3]	6%	<1%
Menstrual Disorder	2%	1%

[1]Primarily ejaculatory delay.
[2]Denominator used was for males only (N=182 Lexapro; N=195 placebo).
[3]Denominator used was for females only (N=247 Lexapro; N=232 placebo).

Dose Dependency of Adverse Reactions-The potential dose dependency of common adverse reactions (defined as an incidence rate of ≥5% in either the 10 mg or 20 mg Lexapro groups) was examined on the basis of the combined incidence of adverse events in two fixed-dose trials. The overall incidence rates of adverse events in 10 mg Lexapro-treated patients (66%) was similar to that of the placebo-treated patients (61%), while the incidence rate in 20 mg/day Lexapro-treated patients was greater (86%). Table 4 shows common adverse reactions that occurred in the 20 mg/day Lexapro group with an incidence that was approximately twice that of the 10 mg/day Lexapro group and approximately twice that of the placebo group.

TABLE 4
Incidence of Common Adverse Reactions in Patients with Major Depressive Disorder

Adverse Reaction	Placebo (N=311)	10 mg/day Lexapro (N=310)	20 mg/day Lexapro (N=125)
Insomnia	4%	7%	14%
Diarrhea	5%	6%	14%
Dry Mouth	3%	4%	9%
Somnolence	1%	4%	9%
Dizziness	2%	4%	7%
Sweating Increased	<1%	3%	8%
Constipation	1%	3%	6%
Fatigue	2%	2%	6%
Indigestion	1%	2%	6%

Male and Female Sexual Dysfunction with SSRIs-Although changes in sexual desire, sexual performance, and sexual satisfaction often occur as manifestations of a psychiatric disorder, they may also be a consequence of pharmacologic treatment. In particular, some evidence suggests that SSRIs can cause such untoward sexual experiences. Reliable estimates of the incidence and severity of untoward experiences involving sexual desire, performance, and satisfaction are difficult to obtain, however, in part because patients and physicians may be reluctant to discuss them. Accordingly, estimates of the incidence of untoward sexual experience and performance cited in product labeling are likely to underestimate their actual incidence.

TABLE 5
Incidence of Sexual Side Effects in Placebo-Controlled Clinical Trials

Adverse Event	Lexapro	Placebo
	In Males Only	
	(N=407)	(N=383)
Ejaculation Disorder (primarily ejaculatory delay)	12%	1%
Libido Decreased	6%	2%
Impotence	2%	<1%
	In Females Only	
	(N=737)	(N=636)
Libido Decreased	3%	1%
Anorgasmia	3%	<1%

There are no adequately designed studies examining sexual dysfunction with escitalopram treatment. Priapism has been reported with all SSRIs. While it is difficult to know the precise risk of sexual dysfunction associated with the use of SSRIs, physicians should routinely inquire about such possible side effects. **Vital Sign Changes**-Lexapro and placebo groups were compared with respect to (1) mean change from baseline in vital signs (pulse, systolic blood pressure, and diastolic blood pressure) and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses did not reveal any clinically important changes in vital signs associated with Lexapro treatment. In addition, a comparison of supine and standing vital sign measures in subjects receiving Lexapro indicated that Lexapro treatment is not associated with orthostatic changes. **Weight Changes**-Patients treated with Lexapro in controlled trials did not differ from placebo-treated patients with regard to clinically important change in body weight. **Laboratory Changes**-Lexapro and placebo groups were compared with respect to (1) mean change from baseline in various serum chemistry, hematology, and urinalysis variables, and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses revealed no clinically important changes in laboratory test parameters associated with Lexapro treatment. **ECG Changes**-Electrocardiograms from Lexapro (N=625), racemic citalopram (N=351), and placebo (N=527) groups were compared with respect to (1) mean change from baseline in various ECG parameters and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses revealed (1) a decrease in heart rate of 2.2 bpm for Lexapro and 2.7 bpm for racemic citalopram, compared to an increase of 0.3 bpm for placebo and (2) an increase in QTc interval of 3.9 msec for Lexapro and 3.7 msec for racemic citalopram, compared to 0.5 msec for placebo. Neither Lexapro nor racemic citalopram were associated with the development of clinically significant ECG abnormalities. **Other Reactions Observed During the Premarketing Evaluation of Lexapro**-Following is a list of treatment-emergent adverse events, as defined in the introduction to the ADVERSE REACTIONS section, reported by the 1428 patients treated with Lexapro for periods of up to one year in double-blind or open-label clinical trials during its premarketing evaluation. The listing does not include those events already listed in Tables 2 & 3, those events for which a drug cause was remote and at a rate less than 1% or lower than placebo, those events which were so general as to be uninformative, and those events reported only once which did not have a substantial probability of being acutely life threatening. Events are categorized by body system. Events of major clinical importance are described in the Warnings and Precautions section. Cardiovascular - hypertension, palpitation. Central and Peripheral Nervous System Disorders - light-headed feeling, migraine. Gastrointestinal Disorders - abdominal cramp, heartburn, gastroenteritis. General - allergy, chest pain, fever, hot flushes, pain in limb. Metabolic and Nutritional Disorders - increased weight. Musculoskeletal System Disorders - arthralgia, myalgia jaw stiffness. Psychiatric Disorders - appetite increased, concentration impaired, irritability. Reproductive Disorders/Female - menstrual cramps, menstrual disorder. Respiratory System Disorders - bronchitis, coughing, nasal congestion, sinus congestion, sinus headache. Skin and Appendages Disorders - rash. Special Senses - vision blurred, tinnitus. Urinary System Disorders - urinary frequency, urinary tract infection. **Post-Marketing Experience; Adverse Reactions Reported Subsequent to the Marketing of Escitalopram**-The following additional adverse reactions have been identified from spontaneous reports of escitalopram received worldwide. These adverse reactions have been chosen for inclusion because of a combination of seriousness, frequency of reporting, or potential causal connection to escitalopram and have not been listed elsewhere in labeling. However, because these adverse reactions were reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. These events include: Blood and Lymphatic System Disorders: anemia, agranulocytis, aplastic anemia, hemolytic anemia, idiopathic thrombocytopenia purpura, leukopenia, thrombocytopenia. Cardiac Disorders: atrial fibrillation, bradycardia, cardiac failure, myocardial infarction, tachycardia, torsade de pointes, ventricular arrhythmia, ventricular tachycardia. Ear and Labyrinth Disorders: vertigo Endocrine Disorders: diabetes mellitus, hyperprolactinemia, SIADH. Eye Disorders: diplopia, glaucoma, mydriasis, visual disturbance. Gastrointestinal Disorders: dysphagia, gastrointestinal hemorrhage, gastroesophageal reflux, pancreatitis, rectal hemorrhage. General Disorders and Administration Site Conditions: abnormal gait, asthenia, edema, fall, feeling abnormal, malaise. Hepatobiliary Disorders: fulminant hepatitis, hepatic failure, hepatic necrosis, hepatitis. Immune System Disorders: allergic reaction, anaphylaxis. Investigations: bilirubin increased, decreased weight, electrocardiogram QT prolongation, hepatic enzymes increased, hypercholesterolemia, INR increased, prothrombin decreased. Metabolism and Nutrition Disorders: hyperglycemia, hypoglycemia, hypokalemia, hyponatremia. Musculoskeletal and Connective Tissue Disorders: muscle cramp, muscle stiffness, muscle weakness, rhabdomyolysis. Nervous System Disorders: akathisia, amnesia, ataxia, choreoathetosis, cerebrovascular accident, dysarthria, dyskinesia, dystonia, extrapyramidal disorders, grand mal seizures (or convulsions), hypoaesthesia, myoclonus, nystagmus, Parkinsonism, restless legs, seizures, syncope, tardive dyskinesia, tremor. Pregnancy, Puerperium and Perinatal Conditions: spontaneous abortion. Psychiatric Disorders: acute psychosis, aggression, agitation, anger, anxiety, apathy, completed suicide, confusion, depersonalization, depression aggravated, delirium, delusion, disorientation, feeling unreal, hallucinations (visual and auditory), mood swings, nervousness, nightmare, panic reaction, paranoia, restlessness, self-harm or thoughts of self-harm, suicide attempt, suicidal ideation, suicidal tendency. Renal and Urinary Disorders: acute renal failure, dysuria, urinary retention. Reproductive System and Breast Disorders: menorrhagia, priapism. Respiratory, Thoracic and Mediastinal Disorders: dyspnea, epistaxis, pulmonary embolism, pulmonary hypertension of the newborn. Skin and Subcutaneous Tissue Disorders: alopecia, angioedema, dermatitis, ecchymosis, erythema multiforme, photosensitivity reaction, Stevens Johnson Syndrome, toxic epidermal necrolysis, urticaria. Vascular Disorders: deep vein thrombosis, flushing, hypertensive crisis, hypotension, orthostatic hypotension, phlebitis, thrombosis.

DRUG INTERACTIONS: Serotonergic Drugs-Based on the mechanism of action of SNRIs and SSRIs including Lexapro, and the potential for serotonin syndrome, caution is advised when Lexapro is coadministered with other drugs that may affect the serotonergic neurotransmitter systems, such as triptans, linezolid (an antibiotic which is a reversible non-selective MAOI), lithium, tramadol, or St. John's Wort [*see Warnings and Precautions*]. The concomitant use of Lexapro with other SSRIs, SNRIs or tryptophan is not recommended. **Triptans**-There have been rare postmarketing reports of serotonin syndrome with use of an SSRI and a triptan. If concomitant treatment of Lexapro with a triptan is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases [*see Warnings and Precautions*]. **CNS Drugs**- Given the primary CNS effects of escitalopram, caution should be used when it is taken in combination with other centrally acting drugs. **Alcohol**-Although Lexapro did not potentiate the cognitive and motor effects of alcohol in a clinical trial, as with other psychotropic medications, the use of alcohol by patients taking Lexapro is not recommended. **Monoamine Oxidase Inhibitors (MAOIs)**-[*see Contraindications and Warnings and Precautions*]. **Drugs That Interfere With Hemostasis (NSAIDs, Aspirin, Warfarin, etc.)**-Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies of the case-control and cohort design that have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding have also shown that concurrent use of an NSAID or aspirin may potentiate the risk of bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when SSRIs and SNRIs are coadministered with warfarin. Patients receiving warfarin therapy should be carefully monitored when Lexapro is initiated or discontinued. **Cimetidine**-In subjects who had received 21 days of 40 mg/day racemic citalopram, combined administration of 400 mg/day cimetidine for 8 days resulted in an increase in citalopram AUC and C_{max} of 43% and 39%, respectively. The clinical significance of these findings is unknown. **Digoxin**-In subjects who had received 21 days of 40 mg/day racemic citalopram, combined administration of citalopram and digoxin (single dose of 1 mg) did not significantly affect the pharmacokinetics of either citalopram or digoxin. **Lithium**-Coadministration of racemic citalopram (40 mg/day for 10 days) and lithium (30 mmol/day for 5 days) had no significant effect on the pharmacokinetics of citalopram or lithium. Nevertheless, plasma lithium levels should be monitored with appropriate adjustment to the lithium dose in accordance with standard clinical practice. Because lithium may enhance the serotonergic effects of escitalopram, caution should be exercised when Lexapro and lithium are coadministered. **Pimozide and Celexa**-In a controlled study, a single dose of pimozide 2 mg co-administered with racemic citalopram 40 mg given once daily for 11 days was associated with a mean increase in QTc values of approximately 10 msec compared to pimozide given alone. Racemic citalopram did not alter the mean AUC or C_{max} of pimozide. The mechanism of this pharmacodynamic interaction is not known. **Sumatriptan**-There have been rare postmarketing reports describing patients with weakness, hyperreflexia, and incoordination following the use of an SSRI and sumatriptan. If concomitant treatment with sumatriptan and an SSRI (e.g., fluoxetine, fluvoxamine, paroxetine, sertraline, citalopram, escitalopram) is clinically warranted, appropriate observation of the patient is advised. **Theophylline**-Combined administration of racemic citalopram (40 mg/day for 21 days) and the CYP1A2 substrate theophylline (single dose of 300 mg) did not affect the pharmacokinetics of theophylline. The effect of theophylline on the pharmacokinetics of citalopram was not evaluated. **Warfarin**-Administration of 40 mg/day racemic citalopram for 21 days did not affect the pharmacokinetics of warfarin, a CYP3A4 substrate. Prothrombin time was increased by 5%, the clinical significance of which is unknown. **Carbamazepine**-Combined administration of racemic citalopram (40 mg/day for 14 days) and carbamazepine (titrated to 400 mg/day for 35 days) did not significantly affect the pharmacokinetics of carbamazepine, a CYP3A4 substrate. Although trough citalopram plasma levels were unaffected, given the enzyme-inducing properties of carbamazepine, the possibility that carbamazepine might increase the clearance of escitalopram should be considered if the two drugs are coadministered. **Triazolam**-Combined administration of racemic citalopram (titrated to 40 mg/day for 28 days) and the CYP3A4 substrate triazolam (single dose of 0.25 mg) did not significantly affect the pharmacokinetics of either citalopram or triazolam. **Ketoconazole**-Combined administration of racemic citalopram (40 mg) and ketoconazole (200 mg), a potent CYP3A4 inhibitor, decreased the C_{max} and AUC of ketoconazole by 21% and 10%, respectively, and did not significantly affect the pharmacokinetics of citalopram. **Ritonavir**-Combined administration of a single dose of ritonavir (600 mg), both a CYP3A4 substrate and a potent inhibitor of CYP3A4, and escitalopram (20 mg) did not affect the pharmacokinetics of either ritonavir or escitalopram. **CYP3A4 and -2C19 Inhibitors**-*In vitro* studies indicated that CYP3A4 and -2C19 are the primary enzymes involved in the metabolism of escitalopram. However, coadministration of escitalopram (20 mg) and ritonavir (600 mg), a potent inhibitor of CYP3A4, did not significantly affect the pharmacokinetics of escitalopram. Because escitalopram is metabolized by multiple enzyme systems, inhibition of a single enzyme may not appreciably decrease escitalopram clearance. **Drugs Metabolized by Cytochrome P4502D6**-*In vitro* studies did not reveal an inhibitory effect of escitalopram on CYP2D6. In addition, steady state levels of racemic citalopram were not significantly different in poor metabolizers and extensive CYP2D6 metabolizers after multiple-dose administration of citalopram, suggesting that coadministration, with escitalopram, of a drug that inhibits CYP2D6, is unlikely to have clinically significant effects on escitalopram metabolism. However, there are limited *in vivo* data suggesting a modest CYP2D6 inhibitory effect for escitalopram, i.e., coadministration of escitalopram (20 mg/day for 21 days) with the tricyclic antidepressant desipramine (single dose of 50 mg), a substrate for CYP2D6, resulted in a 40% increase in C_{max} and a 100% increase in AUC of desipramine. The clinical significance of this finding is unknown. Nevertheless, caution is indicated in the coadministration of escitalopram and drugs metabolized by CYP2D6. **Metoprolol**-Administration of 20 mg/day Lexapro for 21 days in healthy volunteers resulted in a 50% increase in C_{max} and 82% increase in AUC of the beta-adrenergic blocker metoprolol (given in a single dose of 100 mg). Increased metoprolol plasma levels have been associated with decreased cardioselectivity. Coadministration of Lexapro and metoprolol had no clinically significant effects on blood pressure or heart rate. **Electroconvulsive Therapy (ECT)**-There are no clinical studies of the combined use of ECT and escitalopram.

USE IN SPECIFIC POPULATIONS: Pregnancy; Pregnancy Category C-In a rat embryo/fetal development study, oral administration of escitalopram (56, 112, or 150 mg/kg/day) to pregnant animals during the period of organogenesis resulted in decreased fetal body weight and associated delays in ossification at the two higher doses (approximately ≥ 56 times the maximum recommended human dose [MRHD] of 20 mg/day on a body surface area [mg/m^2] basis). Maternal toxicity (clinical signs and decreased body weight gain and food consumption), mild at 56 mg/kg/day, was present at all dose levels. The developmental no-effect dose of 56 mg/kg/day is approximately 28 times the MRHD on a mg/m^2 basis. No teratogenicity was observed at any of the doses tested (as high as 75 times the MRHD on a mg/m^2 basis). When female rats were treated with escitalopram (6, 12, 24, or 48 mg/kg/day) during pregnancy and through weaning, slightly increased offspring mortality and growth retardation were noted at 48 mg/kg/day which is approximately 24 times the MRHD on a mg/m^2 basis. Slight maternal toxicity (clinical signs and decreased body weight gain and food consumption) was seen at this dose. Slightly increased offspring mortality was also seen at 24 mg/kg/day. The no-effect dose was 12 mg/kg/day which is approximately 6 times the MRHD on a mg/m^2 basis. In animal reproduction studies, racemic citalopram has been shown to have adverse effects on embryo/fetal and postnatal development, including teratogenic effects, when administered at doses greater than human therapeutic doses. In two rat embryo/fetal development studies, oral administration of racemic citalopram (32, 56, or 112 mg/kg/day) to pregnant animals during the period of organogenesis resulted in decreased embryo/fetal growth and survival and an increased incidence of fetal abnormalities (including cardiovascular and skeletal defects) at the high dose. This dose was also associated with maternal toxicity (clinical signs, decreased body weight gain). The developmental no-effect dose was 56 mg/kg/day. In a rabbit study, no adverse effects on embryo/fetal development were observed at doses of racemic citalopram of up to 16 mg/kg/day. Thus, teratogenic effects of racemic citalopram were observed at a maternally toxic dose in the rat and were not observed in the rabbit. When female rats were treated with racemic citalopram (4.8, 12.8, or 32 mg/kg/day) from late gestation through weaning, increased offspring mortality during the first 4 days after birth and persistent offspring growth retardation were observed at the highest dose. The no-effect dose was 12.8 mg/kg/day. Similar effects on offspring mortality and growth were seen when dams were treated throughout gestation and early lactation at doses ≥ 24 mg/kg/day. A no-effect dose was not determined in that study. There are no adequate and well-controlled studies in pregnant women; therefore, escitalopram should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Pregnancy-Nonteratogenic Effects-Neonates exposed to Lexapro and other SSRIs or SNRIs, late in the third trimester, have developed complications requiring prolonged hospitalization, respiratory support, and tube feeding. Such complications can arise immediately upon delivery. Reported clinical findings have included respiratory distress, cyanosis, apnea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycemia, hypotonia, hypertonia, hyperreflexia, tremor, jitteriness, irritability, and constant crying. These features are consistent with either a direct toxic effect of SSRIs and SNRIs or, possibly, a drug discontinuation syndrome. It should be noted that, in some cases, the clinical picture is consistent with serotonin syndrome [*see Warnings and Precautions*]. Infants exposed to SSRIs in late pregnancy may have an increased risk for persistent pulmonary hypertension of the newborn (PPHN). PPHN occurs in 1-2 per 1000 live births in the general population and is associated with substantial neonatal morbidity and mortality. In a retrospective, case-control study of 377 women whose infants were born with PPHN and 836 women whose infants were born healthy, the risk for developing PPHN was approximately six-fold higher for infants exposed to SSRIs after the 20th week of gestation compared to infants who had not been exposed to antidepressants during pregnancy. There is currently no corroborative evidence regarding the risk for PPHN following exposure to SSRIs in pregnancy; this is the first study that has investigated the potential risk. The study did not include enough cases with exposure to individual SSRIs to determine if all SSRIs posed similar levels of PPHN risk. When treating a pregnant woman with Lexapro during the third trimester, the physician should carefully consider both the potential risks and benefits of treatment [*see Dosage and Administration*]. Physicians should note that in a prospective longitudinal study of 201 women with a history of major depression who were euthymic at the beginning of pregnancy, women who discontinued antidepressant medication during pregnancy were more likely to experience a relapse of major depression than women who continued antidepressant medication. **Labor and Delivery**-The effect of Lexapro on labor and delivery in humans is unknown. **Nursing Mothers**-Escitalopram is excreted in human breast milk. Limited data from women taking 10-20 mg escitalopram showed that exclusively breast-fed infants receive approximately 3.9% of the maternal weight-adjusted dose of escitalopram and 1.7% of the maternal weight-adjusted dose of desmethylcitalopram. There were two reports of infants experiencing excessive somnolence, decreased feeding, and weight loss in association with breastfeeding from a racemic citalopram-treated mother; in one case, the infant was reported to recover completely upon discontinuation of racemic citalopram by its mother and, in the second case, no follow-up information was available. Caution should be exercised and breastfeeding infants should be observed for adverse reactions when Lexapro is administered to a nursing woman. **Pediatric Use**-Safety and effectiveness of Lexapro has not been established in pediatric patients (less than 12 years of age) with Major Depressive Disorder. Safety and effectiveness of Lexapro has been established in adolescents (12 to 17 years of age) for the treatment of major depressive disorder [*see Clinical Studies*]. Although maintenance efficacy in adolescent patients with Major Depressive Disorder has not been systematically evaluated, maintenance efficacy can be extrapolated from adult data along with comparisons of escitalopram pharmacokinetic parameters in adults and adolescent patients. Safety and effectiveness of Lexapro has not been established in pediatric patients less than 18 years of age with Generalized Anxiety Disorder. **Geriatric Use**-Approximately 6% of the 1144 patients receiving escitalopram in controlled trials of Lexapro in major depressive disorder and GAD were 60 years of age or older; elderly patients in these trials received daily doses of Lexapro between 10 and 20 mg. The number of elderly patients in these trials was insufficient to adequately assess for possible differential efficacy and safety measures on the basis of age. Nevertheless, greater sensitivity of some elderly individuals to effects of Lexapro cannot be ruled out. SSRIs and SNRIs, including Lexapro, have been associated with cases of clinically significant hyponatremia in elderly patients, who may be at greater risk for this adverse event [see *Hyponatremia*]. In two pharmacokinetic studies, escitalopram half-life was increased by approximately 50% in elderly subjects as compared to young subjects and C_{max} was unchanged [*see Clinical Pharmacology*]. 10 mg/day is the recommended dose for elderly patients [*see Dosage and Administration*]. Of 4422 patients in clinical studies of racemic citalopram, 1357 were 60 and over, 1034 were 65 and over, and 457 were 75 and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but again, greater sensitivity of some elderly individuals cannot be ruled out.

DRUG ABUSE AND DEPENDENCE: Abuse and Dependence; Physical and Psychological Dependence-Animal studies suggest that the abuse liability of racemic citalopram is low. Lexapro has not been systematically studied in humans for its potential for abuse, tolerance, or physical dependence. The premarketing clinical experience with Lexapro did not reveal any drug-seeking behavior. However, these observations were not systematic and it is not possible to predict on the basis of this limited experience the extent to which a CNS-active drug will be misused, diverted, and/or abused once marketed. Consequently, physicians should carefully evaluate Lexapro patients for history of drug abuse and follow such patients closely, observing them for signs of misuse or abuse (e.g., development of tolerance, incrementations of dose, drug-seeking behavior).

OVERDOSAGE: Human Experience-In clinical trials of escitalopram, there were reports of escitalopram overdose, including overdoses of up to 600 mg, with no associated fatalities. During the postmarketing evaluation of escitalopram, Lexapro overdoses involving overdoses of over 1000 mg have been reported. As with other SSRIs, a fatal outcome in a patient who has taken an overdose of escitalopram has been rarely reported. Symptoms most often accompanying escitalopram overdose, alone or in combination with other drugs and/or alcohol, included convulsions, coma, dizziness, hypotension, insomnia, nausea, vomiting, sinus tachycardia, somnolence, and ECG changes (including QT prolongation and very rare cases of torsade de pointes). Acute renal failure has been very rarely reported accompanying overdose. **Management of Overdose**-Establish and maintain an airway to ensure adequate ventilation and oxygenation. Gastric evacuation by lavage and use of activated charcoal should be considered. Careful observation and cardiac and vital sign monitoring are recommended, along with general symptomatic and supportive care. Due to the large volume of distribution of escitalopram, forced diuresis, dialysis, hemoperfusion, and exchange transfusion are unlikely to be of benefit. There are no specific antidotes for Lexapro. In managing overdosage, consider the possibility of multiple-drug involvement. The physician should consider contacting a poison control center for additional information on the treatment of any overdose.

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Obsessive Tanning Resembles Addictive Behavior

Young people with a passion for indoor tanning may have some psychiatric issues that need attention—anxiety, depression, or addiction tendencies, for example.

BY JOAN AREHART-TREICHEL

Oh, to be young, sleek, supple, sexy, and tanned! Well, maybe not the last one of these.

The American Academy of Dermatology has issued a warning on the Internet about indoor tanning, pointing out that it has been linked with skin cancer, including the most deadly form, melanoma.

Moreover, a number of college students who pursue indoor tanning may be addicted to it, a study published in the April *Archives of General Dermatology* suggests.

Credit: Vidmantas Goldbergas/istockphoto

The study was conducted by Catherine Mosher, Ph.D., a postdoctoral researcher at Memorial Sloan-Kettering Cancer Center in New York City, and Sharon Danoff-Burg, Ph.D., an associate professor of psychology at the State University of New York at Albany.

The researchers recruited 421 students at a large state university in the northeastern United States to take part in their study. Subjects anonymously completed a questionnaire reporting their demographic information and whether they had ever tanned indoors. The researchers also had them fill out the Beck Anxiety Inventory and the Beck Depression Inventory to assess symptoms of anxiety and depression, the Core Alcohol and Drug Survey to measure substance use, and two questionnaires to determine whether they appeared to be addicted to indoor tanning.

One of the questionnaires, called the CAGE questionnaire, had been adapted from one used to screen for alcoholism. One of the questions was, "Do you try to cut down on the time you spend in tanning beds or booths, but find yourself still tanning?" The other questionnaire had been adapted from *DSM-IV-TR* criteria for substance-related disorders. Two of the questions it asked were, "How many days a week do you spend in tanning beds or booths?" and "Do you think you need to spend more and more time in tanning beds or booths to maintain your perfect tan?"

Of the 421 subjects, 237 had used indoor tanning facilities. Data were assessed for 229 subjects after eight of them were omitted from subsequent analyses because of missing information.

Of these 229 subjects, 70 (31 percent) met CAGE criteria for addiction to indoor tanning, and 90 (39 percent) met addiction-to-tanning criteria adapted from *DSM-IV-TR* criteria for substance-related disorders.

"The proportion of respondents who were classified as addicted to indoor tanning on the two measures surprised me," Mosher told *Psychiatric News*.

Furthermore, 42 percent of the 50 indoor tanners who appeared to be addicted to the process according to both criteria reported use of two or more substances (excluding alcohol) during the prior month, compared with 17 percent of subjects who tanned indoors and who appeared not to be addicted to tanning. In addition, only 16 percent of those who had never tanned indoors reported use of two or more substances other than alcohol. Other studies have also found a link between indoor tanning and substance use. "Tanning and drug use may be reinforced by peer-group norms," the researchers suggested.

Finally, those 50 indoor tanners who seemed to be addicted to that activity according to both CAGE and *DSM-IV* criteria had twice as many anxiety and depressive symptoms as did other indoor tanners and those who had never tanned indoors. "Anxiety and depression are often comorbid with substance dependence, and the present findings suggest that affective disturbance may also be comorbid with dependence on indoor tanning," the researchers observed.

"This thought-provoking study highlights the integral connection between skin and psyche," Eva Ritvo, M.D., a Miami psychiatrist with a special interest in the health aspects of tanning, told *Psychiatric News*. "The study revealed a high incidence of possible mental health issues, such as anxiety disorders and substance abuse, in students who frequently use indoor tanning. This finding emphasizes the fact that more sophisticated methods of diagnosis and treatment must be considered to alter the use of tanning beds. Underlying or associated mental health issues must also be addressed to successfully reduce this high-risk behavior."

Some earlier studies have also "demonstrated the addiction potential of tanning," Caroline Koblenzer, M.D., a clinical professor of dermatology at the University of Pennsylvania, pointed out in an interview with *Psychiatric News*. "That tanning has addiction potential is certainly understandable, since UV light on the skin affects the opioid pathways."

In other words, UV light from tanning may lead to addiction by activating the opioid receptors that are known to be present in skin, Robin Hornung, M.D., an Everett, Wash., dermatologist, proposed in the April *Expert Review of Dermatology*. In fact, a small pilot study reported in the April 2006 *Journal of the American Academy of Dermatology* supports this hypothesis. It found that the opioid antagonist natrexone induced withdrawal symptoms, such as nausea and jitteriness, in frequent tanners but not in infrequent ones.

The study was funded by the National Cancer Institute.

An abstract of "Addiction to Indoor Tanning" is posted at <http://archderm.ama-assn.org/cgi/content/short/146/4/412>. ■

Bilingualism Brings Benefits To Asian-American Children's MH

Being able to speak two languages seems to reduce negative internalizing and externalizing behaviors in Asian-American children. In contrast, not being able to speak English appears to promote such problems.

BY JOAN AREHART-TREICHEL

Bilingualism can benefit children not only academically, but psychologically, research has shown.

Now it looks as if being bilingual can reduce internalizing and externalizing behaviors as well, at least in Asian-American children, a new study suggests.

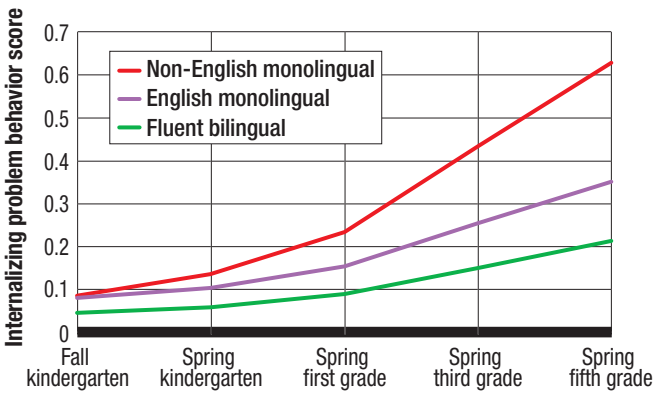
The study was conducted by Wen-Jui Han, Ph.D., an associate professor at the Columbia University School of Social Work, and Chien-Chung Huang, Ph.D., an associate professor at the Rutgers University School of Social Work. Their results are published in the May *American Journal of Public Health*.

A nationally representative sample of 21,260 children who entered kindergarten in 1998-1999 were enrolled in the Early Childhood Longitudinal Study. The children's developmental trajectories were followed through the eighth grade. For instance, data about the children's internalizing problems (the apparent presence of anxiety, loneliness, low self-esteem, and sadness) and externalizing behaviors (the frequency of arguing, fighting, getting angry, acting impulsively, and disturbing ongoing activities) were gathered from their teachers during the follow-up years. Also, the language or languages that the youngsters spoke when they entered kindergarten were documented.

Han and Huang decided to tap information collected about a subset of subjects in this study—12,580—for their own investigation. Of these youngsters, 11,060 were American-born, non-Hispanic whites, and 1,520 had family roots in Asia. Of the 11,060 youngsters, 10,850 spoke English only, and 210 were bilingual, mostly in European languages such as French, German, or Italian. Of the 1,520 with Asian ancestry, 910 were bilingual, 380 spoke only English, and 230 spoke only a foreign language. Those who were bilingual or who spoke only a foreign language spoke Chinese, Filipino, Japanese, Korean, or a Southeast-Asian language.

Is Bilingualism a Bulwark Against Anxiety and Depression?

By the fifth grade, Asian-American children who were bilingual had the fewest internalizing problems, those who spoke only English had somewhat more, and those who spoke only a foreign language had the most.



Source: Wen-Jui Han, Ph.D., and Chien-Chung Huang, Ph.D., *American Journal of Public Health*, May 2010

Han and Huang investigated whether there were any links between being bilingual in kindergarten and later internalizing problems and externalizing behaviors, while considering several possibly confounding variables such as country of origin, socioeconomic status, size of family, school type and standards, and academic performance.

They found that such links did exist. Although all the children had a similar level of internalizing and externalizing problems at kindergarten entry, those who were bilingual had slower growth rates in

please see ***Bilingualism*** *on page 27*

COMPILED BY JUN YAN

This is part 1 of a two-part special edition of Med Check featuring new research posters presented at APA's 2010 annual meeting in New Orleans in May.

New research poster presentations are usually preliminary in nature and often involve results that have not been peer reviewed for publication. In addition, reports may involve the use of medications for indications that the Food and Drug Administration has not approved, and they are predominantly funded by product manufacturers.

Depression

• A brief behavioral intervention targeting insomnia in patients with major depressive disorder improved not only sleep but also depressive symptoms.

Norio Watanabe, M.D., Ph.D., of the Nagoya City University in Japan and colleagues randomly assigned 37 adult patients who had depression with mood symptoms and insomnia to either treatment as usual (n=17) or a brief behavioral therapy focused on insomnia (n=20). The behavioral intervention was given in one-hour individual sessions weekly for four weeks. Blinded raters rated patients' clinical outcomes at four and eight weeks.

At eight weeks, patients who received the behavioral therapy had significantly lower scores on the Insomnia Severity Index and higher sleep efficiency than patients under usual care ($p<0.05$ for both comparisons). Behavioral therapy–treated patients also had significantly lower Hamilton Rating Scale for Depression (HAM-D) total scores and HAM-D scores after excluding sleep-related questions ($p<0.05$ for both comparisons).

• In a phase 3, randomized, double-blind, controlled clinical trial of ***vilazodone***, the investigational antidepressant was compared with placebo in 481 adult patients with a diagnosis of major depressive disorder. After eight weeks of treatment, vilazodone-treated patients (n=231) had a mean reduction of 13.9 points in Montgomery-Asberg Depression Rating Scale (MADRS) total score, the primary outcome. Placebo-treated patients had a mean reduction of 10.8 points. The difference was statistically significant ($p=0.009$). The rate of response, defined as at least 50 percent reduction in MADRS score from baseline, was 44 percent in the vilazodone group and 30 percent in the placebo group ($p=0.002$). The rates of remission, defined as a MADRS score of less than 10, were 27 percent and 20 percent, respectively, which was not statistically significant. The most common vilazodone-associated adverse events were diarrhea, nausea, headache, dry mouth, dizziness, and insomnia.

Vilazodone is being developed by Clinical Data Inc., and the study was funded by the company. The drug is both a selective serotonin reuptake inhibitor and a partial agonist of the serotonin $5HT_{1A}$ receptor. A new drug application for vilazodone was submitted to the Food and Drug Administration (FDA) in May.

• A randomized, double-blind, placebo-controlled clinical trial was conducted in Europe to study the efficacy of ***levomilnacipran*** to treat patients with major depressive disorder. Enrolled patients were titrated up to 75 mg to 100 mg of levomilnacipran (or equivalent placebo) during the first two weeks and then continued for another eight weeks. At the end of 10 weeks, the reductions in MADRS and HAM-D scores from baseline were statistically significantly higher in the levomilnacipran group (n=276) than the placebo group. The mean reduction in actual scores was not presented. The levomilnacipran group also had statistically significantly greater reduction in functional impairment, as measured by the Sheehan Disability Scale score, than the placebo group. The most common adverse events associated with levomilnacipran were nausea, headache, dizziness, and excessive sweating.

The study was funded by Forest Laboratories and Pierre-Fabre Medicament, which are studying the drug in phase 3 clinical trials. Levomilnacipran is an enantiomer of milnacipran, a drug approved in the United States to treat fibromyalgia, and selectively inhibits norepinephrine and serotonin reuptake.

• Partam Manalai, M.D., of the Mood and Anxiety Program in the University of Maryland Psychiatry Department and colleagues identified an association between allergy related to seasonal pollen exposure and depressive mood symptoms during the peak pollen season.

Among the 100 recruited study participants with a prior diagnosis of either major depressive disorder or bipolar disorder, approximately half had positive allergen-specific immunoglobulin E (IgE) in blood samples, indicating an allergic reaction to airborne pollen. Their allergy symptoms were measured with the Allergy Symptom Severity Assessment (ASSA) scale, and their mood symptoms were assessed using the questionnaire Structured Interview Guide for the Hamilton Depression Rating Scale, Seasonal Affective Disorders Version (SIGH-SAD).

After controlling for various confounding factors with multiple regression analysis, the researchers found that the participants' score change in the typical depression portion of the SIGH-SAD was statistically associated with worse ASSA score ($p=0.008$), and the change in the atypical depression portion of the SIGH-SAD was associated with IgE positivity ($p=0.033$). "The relationship between. . . [the] allergen-specific IgE and changes in mood supports a biological. . .mediation of the association between allergy and depression," the authors wrote.

Bipolar Disorder

• In a randomized, placebo-controlled trial, ***asenapine*** outperformed placebo as an adjunctive therapy to mood stabilizers in patients with bipolar I disorder. Adult patients in a current manic or mixed episode who had been on lithium and valproate for at least two weeks were randomly assigned to receive either asenapine or placebo as an add-on treatment. Changes in Young Mania Rating Scale (YMRS) scores from baseline showed a statistically significant reduction in the asenapine group (n=155) compared with the placebo group (n=163) at week 3 and week 12.

The 116 patients who completed the 12-week study phase continued on their treatment in a blinded manner for another 40 weeks while being maintained on the mood stabilizers. Patients on asenapine (n=41) and on placebo (n=36) did not differ significantly in YMRS score at the end of the 40-week extension.

Asenapine is currently approved for acute treatment of mania or mixed episode and for schizophrenia. The study was supported by Schering-Plough, now part of Merck.

• The proportion of patients discharged from hospitals with a diagnosis of bipolar disorder increased, on average, by 10 percent per year, while the average length of hospital stay decreased from 14 days to 6.4 days between 1979 and 2006, according to a large epidemiological study.

Natalya Weber, M.D., M.P.H., of the Department of Epidemiology in the Division of Preventive Medicine at the Walter Reed Army Institute of Research analyzed hospital-discharge records of patients aged 13 to 64 using data from the National Hospital Discharge Survey (NHDS). The NHDS is a nationally representative survey of hospital records collected by the Centers for Disease Control and Prevention and contains up to seven *ICD-9* diagnoses.

Compared with discharged patients without bipolar disorder, the types of nonpsychiatric comorbidities significantly more common in bipolar patients included diseases of sebaceous glands, extrapyramidal disease and abnormal-movement disorders, poisoning by psychotropic agents, dermatophytosis, open wound of elbow, forearm, or wrist, acquired hypothyroidism, psoriasis and similar disorders, and contact dermatitis and other eczema. Although many of these comorbidities have well-known links to bipolar disorder or its treatment, some "warrant additional investigation to determine any commonality" in etiology, the authors said. The study was funded by the Stanley Medical Research Institute.

Electroconvulsive Therapy

• John Olsen, M.D., and colleagues at the University of Utah School of Medicine conducted a retrospective review of the records of 1,002 patients who received a first series of electroconvulsive therapy (ECT) treatments in the decade from 1999 to 2009 and analyzed the reported somatic side effects in adolescent and adult patients. About three-fourths of the patients (n=744) had a diagnosis of depression, and one-fourth (n=239) had bipolar disorder. The incidences of headache, nausea, and myalgia within one to seven days after ECT were 39.9 percent, 15.6 percent, and 13.3 percent of the patients, respectively. These side effects showed a diminishing trend after the first ECT session in subsequent treatments. Patients aged 60 or older appeared to have lower rates of these somatic side effects than did patients younger than 60. ■

Verbal Abuse Can Seriously Harm Far More Than Self-Esteem

Just as physical or sexual abuse appears to be capable of damaging youngsters' brains and making them vulnerable to psychiatric illness later in life, the same seems to be the case for verbal abuse.

BY JOAN AREHART-TREICHEL

The nasty things that their peers say to them can not only hurt adolescents emotionally, but may also damage their brains and set the stage for psychiatric illness later, a new study suggests.

The study was headed by Martin Teicher, M.D., Ph.D., director of the Developmental Biopsychiatry Research Program at McLean Hospital in Belmont, Mass. The report was tentatively scheduled for publication July 1 on the *American Journal of Psychiatry's AJP in Advance* Web site.

Teicher and his colleagues selected 707 late teens or young adults (aged 18 to 25) to participate in their study. None of the subjects reported having experienced domestic violence, sexual abuse, parental physical abuse, parental verbal abuse, or physical bullying by peers during childhood. So the researchers could examine peer verbal abuse independently of these other adverse experiences.

Teicher and his colleagues administered the Verbal Abuse Questionnaire, which contains 15 items and addresses various types of verbal abuse such as criticizing, belittling, blaming, insulting, demeaning, or ridiculing, to determine how many of their subjects had experienced peer verbal abuse during childhood or adolescence.

Nine percent had, they found. Furthermore, the bulk of peer verbal abuse transpired during the middle-school years, which generally includes youngsters aged 11 to 14. Males tended to have experienced verbal abuse from male peers, and females from female peers.

Teicher and his colleagues also had their subjects fill out several questionnaires—the Kellner Symptom Questionnaire, the Limbic Symptom Checklist-33, and the Dissociative Experiences Scale—to assess the participants' current psychological health. Then they looked to see whether there were links between having experienced peer verbal abuse during

please see ***Verbal Abuse*** *on page 27*

Regulations

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The exemption legislation (HR 3763), sponsored by Rep. John Adler (D-N.J.), would exclude medical practitioners and others from the rule. That bill passed the House with no dissenting votes in October 2009 and was referred to the Senate, where it has yet to advance.

Since then, the AMA and two other physician groups—the American Osteopathic Association and the Medical Society of the District of Columbia—joined forces to file suit in May to block the application of the regulation to physicians. The American Bar Association won an exemption for attorneys after it filed a similar suit last year.

"Regulators have delayed the application of the controversial regulations to physicians several times already."

The AMA suit challenges the FTC's interpretation of the 2003 law (PL 108-159) that created the red-flags rule—an interpretation that categorizes physicians as "creditors" because they usually don't receive full payment at the time they provide care. The AMA argues that the realities of an insurance-based health care system are among the reasons physicians do not demand payment in full at the time of treatment.

"In many cases, a physician is not entitled to bill patients immediately upon providing services under contracts with health insurance carriers," stated the AMA lawsuit

Physician groups opposing the regulations also note that the 1996 federal health privacy law commonly referred to as HIPAA and other regulations already safeguard patient data.

"Pursuant to this statutory [HIPAA] mandate, [the Department of Health and Human Services] has promulgated regulations creating a web of physical, administrative, and technical security requirements that physicians and other health care providers must follow to safeguard the security and integrity of their patient records," stated the lawsuit.

The FTC also acknowledges in its online guidance for physicians on the regulations that there is a lower risk of identity theft at small physician practices, where many patients may be known to the staff. In such situations the FTC is unlikely to bring enforcement lawsuits, according to the commission's Web site. However, both the FTC and state enforcement agencies would retain authority under the regulations to bring lawsuits against solo practitioners and small practices.

Supporters of the FTC effort to include physicians in the identity-theft requirements, such as the American Health Information Management Association, maintain, however, that Medicare, Medicaid, and insurance fraud often is facilitated by the theft of patients' identities from physician records. And the red-flags rule could be a key factor in reducing fraud and abuse in the health care system.

Credit: Office of Rep. John Adler (D-N.J.)

Rep. John Adler (D-N.J.) sponsored legislation to exempt physicians and others from a pending customer privacy regulation. The bill, he said, is needed to "help protect small businesses from overreaching federal regulations during these tough economic times."

The AMA lawsuit is posted at <www.ama-assn.org/ama1/pub/upload/mm/395/red-flags-lawsuit.pdf>. ■

Awards

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the Latino/Latina population, offers a Latino Mental Health concentration within its master's in clinical counseling program, and offers educational opportunities for mental health professionals and students to share research and best practices surrounding the Latino/Latina population.

• **Comunidades Latinas Unidas en Servicio (CLUES)** in Minneapolis, Minn., received an award for its mental health services that holistically address the unmet mental health needs of Minnesota's Latino population through direct services and through efforts to increase access to culturally competent care by training bilingual, bicultural mental health providers.

• **Native American Community Academy** in Albuquerque, N.M., received an award for its Student Support Services program and its efforts to provide comprehensive, culturally sensitive, school-based mental health and supportive services for students and their families at no charge. Some of the services offered are crisis intervention, individual and family counseling, group therapy, and community outreach.

Each organization was presented with a plaque and $5,000 for its work in and commitment to advancing minority mental health. The awards are made possible through an unrestricted educational grant from Otsuka America Pharmaceutical Inc.

"We are proud to present these awards to these mental health professionals and organizations that continue their strong commitment to reducing mental health disparities for racial and ethnic minorities," said Richard Harding, M.D., American Psychiatric Foundation president and a past APA president. "I congratulate all the recipients of the Awards for Advancing Minority Mental Health and, as a psychiatrist, commend all their efforts to educate and raise awareness of the mental health needs and services available. With education, we are well on our way to a national movement to rid the stigma associated with mental illness."

The gala raised nearly $80,000, according to Lindsey McClenathan, the foundation's development officer. More than 200 people were in attendance. The funds will be used to support the foundation's work in advancing public understanding of mental illnesses and their treatment.

Information about the foundation is posted at <www.psychfoundation.org>. Donations can be made at <https://myaccount.psych.org/APACustomizations/OneClickDonation/tabid/154/Default.aspx>. ■

Community Care

continued from page 1

mental illness who were able to function with proper treatment out of institutional settings and into group homes or other community-based facilities where they could receive needed treatment.

Now, the Obama administration is moving to encourage more states to comply with *Olmstead* by removing barriers to community living for people with serious mental illness and giving them more control over their lives.

"Since the passage of the ADA and the *Olmstead* decision, progress has been made to improve community living opportunities for people with disabilities," said Cindy Mann, director of the federal Center for Medicaid and State Operations, in a May 20 letter to state Medicaid directors. "However, the demand for community services continues to grow, and many individuals in need of these services struggle without them."

Mental health advocates said increased focus on *Olmstead* implementation is needed because the already uneven compliance among states has been threatened by growing recession-related budget deficits that have made mental health budgets targets of steep cuts.

The federal effort to encourage *Olmstead* compliance most recently included updates sent to state Medicaid directors on how they can use provisions of the new federal health care overhaul law to better implement the *Olmstead* requirements.

Specifically, the new law authorizes federal officials to offer technical assistance to states to help them meet their obligations under the ADA.

In addition, the administration launched the Community Living Initiative—a partnership between the departments of Housing and Urban Development and Health and Human Services to help fulfill the critical housing element of the shift to noninstitutional living. Since April, the partnership has made $40 million in grants available to the states to provide about 5,300 housing vouchers for people with serious mental illness already living in the community and for those transitioning out of institutional care.

Upcoming *Olmstead*-related policies include a new requirement starting on October 1 that Medicaid's Certified Nursing Facilities ask residents directly if they are "interested in learning about the possibility of returning to the community." If a resident indicates that he or she is interested, the nursing facility makes a referral to "community integration agencies," such as their state Medicaid agency.

Similarly in support of the Obama administration's *Olmstead* push, the Department of Justice (DoJ) announced in May that it has filed briefs in three separate cases in Florida, Illinois, and New Jersey related to enforcement of the *Olmstead* decision. The DoJ filings support two private lawsuits in Florida and New Jersey, as well as a proposed statewide class-action settlement in Illinois, all aimed at getting states to offer community-based care for institutionalized residents.

Information on the administration's* Olmstead *initiatives is posted at <www.disability.gov/clickTrack/confirm/13450598?external=false&parentFolderId=7214&linkId=360650>. ■

clinical & research news

Aspirin

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of aspirin over three months, the refractory character of symptoms while on antipsychotics alone, and the safety of aspirin, this drug might become a useful addition to regular treatment," the scientists concluded.

The findings also raise the question of whether aspirin as a stand-alone treatment might benefit schizophrenia patients. Unfortunately, this question cannot be easily answered, the researchers wrote, "since it would be unethical to randomly assign patients with schizophrenia spectrum disorders to placebo alone."

The study was funded by the Stanley Medical Research Institute.

An abstract of "Adjuvant Aspirin Therapy Reduces Symptoms of Schizophrenia Spectrum Disorders: Results From a Randomized, Double-Blind, Placebo-Controlled Trial" is posted at <http://article.psychiatrist.com/dao_1-login.asp?ID=10006874&RSID=52441098641642>. ■

APA Needs Your Help

APA needs its members who have billing experience with general evaluation and management codes (99XXX series codes) to participate in a survey designed to evaluate the time, complexity, and intensity of work required to perform a procedure, relative to other procedures used for comparison. APA members interested in participating in the survey should call the Office of Healthcare Systems and Financing at (888) 357-7924, ext. 8593, or e-mail Becky Yowell at byowell@psych.org.

Verbal Abuse

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childhood or adolescence and current psychological problems.

The researchers found that the more exposure to peer verbal abuse subjects reported, the more likely they were to be experiencing anxiety, depression, anger-hostility, dissociation, or drug use at the time of the study. Peer verbal abuse during the middle-school years was found to be especially noxious in this regard.

Finally, the researchers obtained neuroimaging scans of a subset of their sample—63 young adults who had been exposed to varying degrees of peer verbal abuse. They wanted to see if they could find a significant link between subjects' exposure to peer verbal abuse during childhood or adolescence and damage to the corpus callosum.

They looked for damage in the corpus callosum because it connects the left and right hemispheres of the brain, it contains nerves that carry nearly all the neural traffic to and from the cerebral cortex, and types of maltreatment other than verbal abuse had already been linked with corpus callosum damage. In other words, the researchers believed that if they could document corpus callosum damage in subjects who had experienced peer verbal abuse, it might explain why these subjects subsequently experienced psychological problems such as anxiety, depression, anger-hostility, dissociation, or drug use.

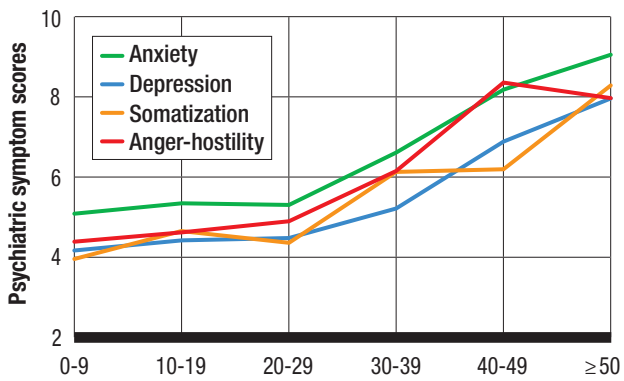
Indeed they did find evidence of corpus callosum damage in their verbal-abuse subjects. So it looks as if peer verbal abuse can lead to damage in the corpus callosum, and corpus callosum damage in turn can increase the risk that young people will experience psychological problems.

The study was funded by the National Institutes of Health, NARSAD, and donations from the Simches and Rosenberg families.

"Hurtful Words: Exposure to Peer Verbal Aggression Is Associated With Elevated Psychiatric Symptom Scores and Corpus Callosum Abnormalities" is posted at <http://ajp.psychiatryonline.org> under "AJP in Advance." ■

Peer Verbal Abuse Can Leave a Pernicious Legacy

Young adults rated the amount of peer verbal abuse they had received during childhood or adolescence and their current psychiatric symptoms. A dose-dependent relationship between subjects' peer verbal abuse scores and their psychiatric symptom scores was found. The greater the verbal abuse, the greater the symptoms.



Source: Martin Teicher, M.D., Ph.D., et al., *American Journal of Psychiatry,* in press

Bilingualism

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such problems subsequently and a lower level of such problems by the fifth grade than did children who spoke English only.

So it looks as if being bilingual can reduce internalizing and externalizing problems in Asian-American children, Han and Huang concluded, and they proposed several explanations. "In addition to having no problems with English in the school environment, bilingual children receive extra benefits from the cultural resources in their families and ethnic communities. The ability to understand two cultures intimately is also likely to help children appreciate diversity and get along with peers and teachers," they said.

The study also demonstrated that those children who spoke a foreign language and not English experienced even more internalizing and externalizing behaviors by the fifth grade than did English-only-speaking children. Han told *Psychiatric News* that he was surprised by this outcome. He had expected that not being fluent in English might hurt children's social and emotional well-being, but not to the extent that their study found.

The findings have practical implications, the researchers pointed out in their paper. "Parents should be encouraged to speak their native language with their children, [and] schools should be encouraged to nurture bilingualism, not just English. . . ." But parents and schools should also make sure that children reared in a foreign language become fluent in English so that they can function well academically and not suffer psychologically because of their difficulty in communicating in English.

The study was funded by the Foundation for Child Development PK-3 Initiative and the Taiwan University Social Policy Research Center.

An abstract of "The Forgotten Treasure: Bilingualism and Asian Children's Emotional and Behavioral Health" is posted at <http://ajph.aphapublications.org/cgi/content/abstract/100/5/831>. ■

Nominations Invited

APA's Council on Adult Psychiatry invites nominations for the 2011 Jack Weinberg Memorial Award for excellence in the field of geriatric psychiatry.

The award, established in 1983, recognizes a psychiatrist who has demonstrated special leadership or has done outstanding work in clinical practice, training, or research in geriatric psychiatry.

Candidates must be psychiatrists who are nominated by an APA member. Nominations must include a letter describing the accomplishments of the nominee, two additional letters of endorsement by APA members, and a current curriculum vitae including bibliography. The selected individual will receive a plaque at the APA Convocation and $500.

The deadline for nominations is August 13. Nomination materials should be mailed to American Psychiatric Association, QIPS, Attn: Urysha Moseley, 1000 Wilson Boulevard, Suite 1825, Arlington, Va. 22209.

More information is available from Moseley at umoseley@psych.org. ■

Stigma

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must decide early what stigmatizing process is at work in the patient's mind.

What is the patient's group of identity? How does the group perceive threats to its identity and interests? How does the group monitor outsiders? But those are just the first considerations.

"The prime objective is to establish relatedness to the patient as a person, not a category," he said.

Griffith's strategy is to use "negative goodness," that is, not attacking the group with which the patient identifies, while assuring him or her that the psychiatrist is not going to act harmfully.

That reassurance opens the door to better communication. When psychological arousal is high, sociobiological barriers rise, and lowering arousal lowers the barriers, he said. "Then stigma shifts further into the background of the patient's awareness."

There are compelling reasons why a clinician must forge ahead with a patient's evaluation even when confronted with patients who hate or fear psychiatrists, said Griffith. Among these reasons are the potential risk of violence or suicide and other people's fears about the person's behavior.

A sociobiological understanding of stigma does more than lead to a better evaluation of a few difficult patients, said Griffith. "We can also learn to treat people who stigmatize psychiatrists despite their views and bring those skills into other areas of our practice." ■

Key Cases

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quoting Justice Anthony Kennedy, "may put an awareness of the link between crime and punishment in a context so far removed from reality that punishment can serve no proper purpose."

But Zonana said the ruling and other similar cases before the Supreme Court have served to raise further difficult questions: Does someone need to understand death to be executed? And what is the difference between a factual and a rational understanding of the reason for execution?

Moreover, the issue of treating someone to restore competence for execution raises its own ethical problems for psychiatrists and other physicians. Zonana noted that the AMA, with help from APA, approved a policy in 1995 stating that physicians should not treat someone solely for the purpose of restoring the person to competence for execution and that to participate in an execution is unethical.

It's an issue that has surfaced in North Carolina, where the medical board had decreed—on the basis of the AMA policy—that physicians who participate in executions could lose their licenses, a decree that resulted in a virtual moratorium on executions in the state. The state Supreme Court then ruled that the medical board had exceeded its prerogative in impeding state law.

"So this subject is an ongoing struggle with enormous issues for people on both sides of the question," Zonana said.

In *Atkins v. Virginia*, the Court ruled 6-3 that the use of capital punishment for defendants with mental retardation (MR) violates the Eighth Amendment's ban on cruel and unusual punishment, overturning the Court's earlier support of the same in the 1989 *Penry v. Lynaugh* decision.

Daryl Atkins and a codefendant in 1996 kidnapped a serviceman, forced him at gunpoint to withdraw money from an ATM, then drove to a secluded spot and shot him to death. A psychologist testifying for the defense said that Atkins was mentally retarded, but the jury sentenced him to death.

"The Supreme Court agreed to hear the appeal of Atkins and agreed to consider again whether mental retardation was an absolute bar to execution, 13 years after *Penry*," Appelbaum said. "And indeed the Court this time held that executions of persons with mental retardation did violate the Eighth Amendment's proscriptions against cruel and unusual punishment."

So what had changed?

Principally what had changed, according to the Court's ruling, was the "evolving standard of decency": since *Penry*, 18 states ruled against use of execution for people with mental retardation. And the Court argued that in the case of mental retardation, execution does not contribute to the goals of either retribution or deterrence.

But Appelbaum added that the Court's decision, seemly straightforward, left many practical matters unresolved. These include how to define MR, how to assess MR, and what procedures should be allowed when attempting to make a determination of MR, including who should make it.

Appelbaum noted that some authorities speak of a numerical "bright line—the *DSM-IV,* for instance, defines MR as an IQ of 70 or below. But the American Association of Intellectual and Developmental Disabilities does not cite such a numerical cutoff.

"States differ in how they define MR," he continued. "A bottom line on these differences is that a defendant may be eligible for the death penalty in one state, but not in another. We have a patchwork quilt of rules that have flowed out of *Atkins*, a case that was intended to create uniform proscription."

Echoing Bonnie, Appelbaum said the Court's decision reflects society's ambivalence about the death penalty. "We are reluctant and unwilling to surrender the death penalty, but we nonetheless surround it with so many obstacles to its use that it can only rarely be applied." ■

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This is an advertisement for an immediate opening for a Senior Physician- Psychiatrist- SES position located at prisons throughout the state.

ANNUAL SALARY RANGE: $183,000.22–188,000.02

QUALIFICATIONS:
Licensure as a Physician (FL Statue 458) or Licensure as an Osteopathic Physician (FL Statue 459) with specialty training in psychiatry and two years of post-licensure professional experience; or a current public psychiatry certificate issued by the Florida Board of Medical Examiners (FL Statue 458.3165). Certification by a recognized board in a medical specialty area can substitute for the required experience.

JOB DESCRIPTION:
This is work providing diagnoses, treatments, and helping to prevent diseases and injuries that commonly occur in the general population. Some positions in this occupation may be responsible for coordinating work and supervising employees.

COMPREHENSIVE STATE OF FLORIDA BENEFITS INCLUDE:
Varied Retirement Plans offered, Excellent Health Care/Supplemental Insurance, Annual and Sick Leave Accrual and Paid Holidays.

For further information visit ***www.fldocjobs.com*** or contact:
Jennifer Dudley
(850) 410-4615
dudley.jennifer@mail.dc.state.fl.us

TO APPLY VISIT: www.peoplefirst.myflorida.com

IOM International Organization for Migration
OIM Organisation Internationale pour les Migrations
OIM Organización Internacional para las Migraciones

PSYCHIATRIST (Bangkok, Thailand) – P3 level

The International Organization for Migration (IOM) in Thailand is looking for a Psychiatrist who will evaluate patients referred by panel physicians or others, for possible psychiatric conditions, including major and minor psychiatry, mental deficiencies and brain damage and substance abuse problems, provide opinion on diagnosis and classification and a comprehensive report on behalf of the Resettlement Health Assessment Programmes.

Qualifications and Core Competencies: University degree in Medicine with specialization in psychiatry. Five years work experience as a psychiatrist; working experience in general medicine practice as well as background in inter-cultural or ethno-medicine an advantage. Working experience with international organizations, non-governmental or governmental institutions/ organization with a multi-cultural setting and understanding of local conditions and refugees' needs an advantage. Excellent writing, communication and negotiation skills; ability to write reports concisely. Strong analytical skills. Good basic knowledge of neurology and child psychiatry. Demonstrated gender awareness and gender sensitivity. Personal commitment, drive for results, flexibility and efficiency. High level of integrity, sensitivity to confidentiality, cultural and social issues. Ability to work effectively and harmoniously with colleagues from varied cultures and professional backgrounds; team-work oriented with capacity to work independently. Good level of computer literacy. Ability and willingness to work in difficult conditions with frequent travel. Fluency in the English language is essential.

Salary: IOM offers an attractive salary package based on the United Nations System at P3 level.

Full terms of reference are available at the IOM website: www.iom.int. Deadline for submitting applications is 31 July 2010. Candidates should submit their applications at http://www.iom.int/jahia/Jahia/pid/165. The successful candidate will be requested to start as soon as possible.

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Issue	Deadline (Friday, 2 p.m. E.T.)
August 6	July 23
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Top Docs has immediate positions available for Adult and Child Psychiatrists throughout the US. Long and short term positions available including locum tenens and permanent positions. Please call **Top Docs** ***TODAY*** @ 866-867-3621. www.topdocs.net.

FCS

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Over 400 permanent searches nationwide.
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ARIZONA

Unit Director

Aurora Behavioral Health System, a 90 bed JC Accredited, Psychiatric Hospital located in Glendale, Arizona is seeking a BE/BC Psychiatrist to join our team. This position offers clinical opportunities to join our medical staff comprised of private physicians. Our facility offers high quality mental health and chemical dependency programs for adults and adolescents. We are located in the Phoenix area and are only minutes away from professional sports venues, winter snow skiing, and renowned dining and shopping opportunities. Clinical hospital experience in Psychiatry is preferred.

For consideration, please send your C.V. and letter of interest to Sally Fangman at: **Aurora Behavioral Health Systems, 6015 W. Peoria Avenue, Glendale, AZ 85302, or call 623-344-4403.**

ARKANSAS

FAYETTEVILLE- General or Child Psychiatrists. Staff position. Inpatient & partial programs. Fulltime or part-time with highly competitive salary, benefits & bonus. **Student loan assistance.** Contact Joy Lankswert, In-house recruiter @ 866-227-5415 or email joy.lankswert@uhsinc.com.

CALIFORNIA

Mental Health — Care and Treatment with Respect and Dignity — Patton State Hospital — Patton, CA

CALIFORNIA
BC/BE STAFF PSYCHIATRIST

Patton State Hospital is recruiting board certified/eligible psychiatrists. Patton is a Joint Commission accredited, 1500 bed, adult forensic psychiatric hospital, with an extremely interesting and challenging patient population. The hospital is nestled below Arrowhead and the San Bernardino Mountains, 65 miles east of Los Angeles; an hour's drive to beaches, Palm Springs, or mountain lakes and skiing. Salary with Board Certification starts at **$18,622 and goes to $21,311 monthly.** Salary for Board Eligible starts at **$18,146 and goes to $20,711 monthly.** In addition, Patton offers excellent benefits (health, dental, and vision; license renewal; malpractice insurance; tax-deferred compensation; paid annual leave and 12 holidays (plus one personal holiday), as well as seven days per fiscal year of Continuing Medical Education leave). Voluntary on call duty is compensated on an hourly basis over and above base salary. We provide civil service security and retirement plans (including safety retirement). For confidential consideration, send CV to George Christison, M.D., (A) Medical Director, 3102 East Highland Avenue, Patton, California 92369, (909) 425-7326 or Fax (909) 425-6635.

Adventist Health — Central Valley Network

PRIVATE PRACTICE OPPORTUNITY-CENTRAL CALIFORNIA

Adventist Health Hospitals seek full time general psychiatrist for private practice. Offer includes practice establishment assistance, two year income guarantee, sign on bonus, five weeks paid time off, stipend for CME, and relocation reimbursement. Only California licensed BC/BE need apply.
- **Email CV to Physician Services: larkinme@ah.org or Tel: (559) 585-5275.**

BE/BC Psychiatrists for CA locations $160-185/hr. Up to $44k/month 8-12hr/day 40hr/wk. Wknds avail. On call $42/hr.

BAY AREA DOCTORS, INC
Tel:(707)694-6890/(707)226-2426/(707)694-3805
Fax:(415)814-5764
bayareadoctors@gmail.com.

Full Time contract psychiatrists needed at Napa & Coalinga State Hospitals, CA. No weekends or calls. Pays $180/hr+ malpractice. Call 661-274-9674. Fax CV to 800-758-7013. E-mail hahacorp@gmail.com. Work with recruiters.

COLORADO

Metro West Denver
JEFFERSON CENTER FOR MENTAL HEALTH
Solutions Now Program

Part time and full time opportunities for adult psychiatrist(s) in an outpatient program serving clients from insurance health plans. Advantages of clinical practice without the administrative hassles. Guaranteed payment, flexible hours, days and locations, we provide billing and front office support, you provide the care.

MD or DO degree, satisfactory completion of ACGME-accredited residency training program in General Psychiatry (adult psychiatrists), unrestricted Colorado medical license and DEA certificate; ABPN Board-certification preferred.

For more information: danielf@jcmh.org
Submit resumes to: Careers@JCMH.org
OR Fax to: 303-32-5018.

CONNECTICUT

Staff Psychiatrists and Principal Psychiatrists

The Department of Mental Health & Addiction Services has challenging opportunities for Staff Psychiatrists and Principal Psychiatrists to work with multi-disciplinary staff to provide a variety of behavioral health care services for adult individuals in collaboration with other State and community agencies.

Email Robert.Paolitto@po.state.ct.us or call Robert Paolitto (860) 262-6745. For more information log on to www.ct.gov/dmhas/employmentopportunities.

DMHAS is an **Affirmative Action/Equal Opportunity Employer**. Members of protected classes and/or individuals in recovery are encouraged to apply.

INPATIENT ADULT PSYCHIATRIST-*CENTRAL CT*

FT/PT opportunity for BC/BE adult psychiatrist in 16-bed inpatient service with a community hospital offering a comprehensive mental health continuum. Enjoy working with an established team bringing a multidisciplinary approach to patient care. Crisis Center located in emergency department. This position offers a competitive salary and benefits and adaptable hours for the right individual. Call 1:5.

The practice is located in a family-oriented city located approximately two hours from NYC and Boston and 20 minutes to the capitol city of Hartford. Enjoy the charm of four seasons with a choice of attractive communities with Connecticut's best rated schools, shopping, award-winning restaurants, and regional theatre and easy access to skiing and the coast.

For more information about this opportunity, please contact Carolyn Doughtie of Physician Recruitment at 800.892.3846 or fax/email your CV to 860.585.3133. EOE

Email address: cdoughti@bristolhospital.org.

N. STONINGTON-Fulltime or part-time employment or contract weekend coverage. Inpatient rehab and partial programs. Salaried employment or independent contractor compensation. Contact Joy Lankswert, In-house recruiter @ 866-227-5415 or email joy.lankswert@uhsinc.com.

DELAWARE

DOVER: General or Child Psychiatrist. Inpatient/partial programs for adolescents & adults. Highly competitive salary, benefits & incentive plans. Contact Joy Lankswert In-house recruiter @ 866-227-5415; OR email joy.lankswert@uhsinc.com.

FLORIDA

PSYCHIATRIST; FULL TIME, FL LICENSE REQUIRED; Aventura, FL; private practice located equidistant between Miami and Ft. Lauderdale; children/adolescent/adult/geriatric pts; email CV to aventuraoffices@bellsouth.net or FAX to Dusty: 305-935-1717.

LifeStream, an accredited community health center in Central Florida is seeking **Psychiatrists, ARNP and Physician's Assistants** to provide comprehensive psychiatric care to children and/or adults. The position delivers psychiatric healthcare services to individuals in the inpatient and/or outpatient facilities and determines the most appropriate level of care required. This position is responsible for the psychiatric evaluation, treatment, emergency intervention and psychopharmacological treatment of clients of LifeStream Behavioral Center. Must have a clear understanding of the characteristics and problems of individuals with severe and persistent mental illnesses. **Apply online at www.lsbc.net.**

DAYTONA - MELBOURNE - ORLANDO - OCALA-
Psychiatrists needed for rapidly expanding Nursing Home Service. Great support. No call. Average Salary 210K + benefits. Part-time available. Some travel required. Must have FL Medicare & FL Medicaid individual provider #s. No Restrictions (H1B Candidates Considered). Call our Clinical Coordinator, Linda at 866-936-5250.

Florida
Psychiatrist needed FT, Tampa, Fl. for outpatient med. management, some therapy - great staff, pts., benefits. See website: Http://DrBonnieSaks.com FAX resume to 813-354-9436 or email BRS331@gmail.com

Addiction Psychiatrist- Board Certified with added qualifications in addiction and/or ASAM/ABAM Certification. **Assistant Medical Director Position** for PRN of Florida, the Florida Impaired HealthCare Practitioners Program. Salary commensurate with experience. Excellent benefits package. PRN is affiliated with the Florida Medical Assocation. Send CV and letter of interest to PRN, P.O. Box 1020, Fernandina Beach, FL 32035.

PSYCHIATRIST
DELRAY BEACH, FLORIDA

South County Mental Health Center offers an exciting opportunity for a full time psychiatrist.

South County Mental Health Center is an outpatient community based mental health center located in beautiful southeast Florida. We offer a competitive salary and excellent benefits package.

CV/Resume may be faxed to:
(561)637-1005 or submitted to:
Human Resources
Email: SCMHCHR@scmhcinc.org.

GEORGIA

Well-established multi-disciplinary mental health practice in Northwest Atlanta suburb seeking general **adult psychiatrist**. Wide referral base from physicians, schools, and therapists. Secretarial/billing services available. **See www.cherokeecounseling.com**. Contact shelly.hutchinson@gmail.com or 770-924-1818 X303.

Georgia Regional Hospital in Atlanta, a 300-bed Joint Commission accredited State Psychiatric Facility, is currently seeking Board Certified or Board Eligible Psychiatrists to work in our inpatient Mental Health units and inpatient Forensic units **(Forensic experience preferred)**. In addition to a competitive and negotiable salary, we offer a generous benefits package. Selected applicants may be eligible for up to $100,000 in educational loan reimbursements.

Please email your resume in Microsoft Word format to:
DHR_GRHAtlanta_HR@dhr.state.ga.us with Psychiatrist in the subject line.

ATLANTA: Medical Director & Staff Positions - Inpatient, residential, or partial day programs. Child/Adol, Adult, Addiction, and Geriatric services depending on location. Contact Joy Lankswert, In-house recruiter @ 866-227-5415 or email joy.lankswert@uhsinc.com.

Medical College of Georgia
Augusta, GA
Growing Department Seeks New Faculty in Adult, Child and Adolescent, Neuroscience and Public Psychiatry Programs

The Medical College of Georgia (MCG) Department of Psychiatry and Health Behavior is recruiting MD and PhD faculty in adult, consultation/liaison, forensic, child and adolescent and public psychiatry. Both clinician-educator and research intensive positions are available, including a dedicated research neuroscientist position in psychotic disorders. The department, which is growing and financially stable, has strong training programs in general, child and adolescent, and forensic psychiatry, an internship program in health psychology, and competitively funded clinical and preclinical research. Our new public psychiatry partnership with the Georgia Department of Behavioral Health and Developmental Disabilities to manage and provide clinical care to the regional state hospital (located only five miles from the medical school campus), expands our faculty recruitment, educational and clinical research opportunities. MCG's strong research infrastructure includes core laboratories, statistical consultation and core genetics facilities. Extensive research training program for junior faculty includes a master's program in clinical translational, internal grant programs with generous career development awards.

Augusta, home of Masters Golf Tournament, is a charming Southern city with low cost of living (particularly housing), and is close to Georgia/Carolina mountains and Georgia/Florida coast. The position has excellent salary and benefits. Academic appointment depends on qualifications. MCG is an equal employment, equal access and equal educational opportunity and affirmative action institution. It is the policy of the University to recruit, hire, train, promote and educate persons without regard to age, disability, gender, national origin, race, religion, sexual orientation or veteran status.

See http://www.mcg.edu/som/psychiatry/ for more information. Contact: Donald Manning, MD, Director of Public Psychiatry, dmanning@mcg.edu or (706) 721-6719.

Atlanta Psych Consultants, an established multidisciplinary private practice strategically located in Atlanta, has an immediate need for an Adult or Child Psychiatrist to affiliate with 2 psychiatrists and 5 psychologists. Full service practice is located in class 'A' medical building near 3 major hospitals. Collegial atmosphere with great potential for a clinical practice through medication management for current patients, referral sharing and joint marketing.

Please email CV to consula@bellsouth.net or call Kim Oppenheimer, Ph.D. at 404-847-9560.

Georgia Psychiatric Position

Medical Resources, LLC, a nationwide staffing agency is currently assisting our clients located in Georgia in their search for a BE/BC psychiatrist. Highlights are:

- Multiple openings for permanent and locum positions in coastal South Georgia region.
- Attractive compensation package.
- Telepsychiatry capacity.
- C&A patients as well as adults.

For further information on the GA positions or other states contact:
Paul Sparks
Medical Resources, LLC
Phone: 877-297-4084
Fax: 248-649-4112

ILLINOIS

Part-time Psychiatrist to provide group therapy to Chicago North Side Psychiatric Rehabilitation Day Program. Hours are Monday through Thursday 9:00 a.m. until 11:00 a.m. Also have a p.m. groups at scattered sites. We are a friendly and highly professional environment. Call: 847-778-4280. Fax: 773-777-7416 or e-mail abcincorp@sbcglobal.net.

Adolescent/Adult Psychiatrist

Large outpatient practice looking to add additional Psychiatrist to work in our Crystal Lake office. Flexiblehours and ability to work with great team of therapists and physicians in highly respected practice. **Email CV to Paula Comm, Practice Administrator at pmc@prapsych.com.**

IOWA

Psychiatrist Needed. Medical Degree, State of Iowa Medical License, DEA certification, BE/BC Psychiatry. Send resumes to Jerry Truemper, Mercy Medical Center - Cedar Rapids, 701 10th Street SE, Cedar Rapids, Iowa 52403. EOE.

KENTUCKY

LOUISVILLE /RADCLIFF: Staff Psychiatrist - General & Specialty Inpatient & Day Programs including work with military personnel. Fulltime or part-time positions, Mon-Fri schedule. Contact: Joy Lankswert In-house recruiter @ 866-227-5415 or email joy.lankswert@uhsinc.com.

MAINE

Adult inpatient psychiatrist. Mid Coast Hospital is an independent, non-profit community hospital located in beautiful coastal Maine one of Maine's most desirable regions. We are searching for an inpatient psychiatrist for our 12-bed unit. Our team uses a multi-disciplinary approach to treat both voluntary and involuntary patients. This is a full-time position for a BC/BE psychiatrist. Must have or be willing to obtain certification for ECT and a waiver for suboxone management. Share on-call responsibilities with eight other physicians. 40-hour week. Generous benefits, excellent work environment. Please send letter of introduction with CV to: mmackellar@midcoasthealth.com.

MARYLAND

Potomac Psychiatry seeks part-time outpatient psychiatrist. Expertise treating eating disorders, substance abuse, desired.

Send C.V. to:
terry.vinston@potomacpsychiatry.com.

Inpatient, Special Unit for Deaf Patients. Springfield Hospital Center is seeking a BC/BE **general psychiatrist** for the state of Maryland's special inpatient psychiatric unit for deaf patients. ASL interpreters are available 24/7. Salary is negotiable, within MHA guidelines. For other descriptive information, please see our accompanying ad for a general psychiatrist. Please send CV to **Jonathan Book, M.D., Clinical Director, SHC, 6655 Sykesville Road, Sykesville, MD 21784. For questions, call (410)970-7006 or e-mail JBook@dhmh.state.md.us.** EOE

Springfield Hospital Center is seeking Board-certified or Board-eligible **general psychiatrists** for our 350-bed MHA adult inpatient facility. Salary is negotiable, within MHA guidelines. Our rural, tobacco-free campus is 22 miles west of Baltimore, convenient to the Chesapeake Bay, Washington, and a variety of cultural, historic, sports, and recreational venues. Benefits include 27 paid days off in the first year, subsidized health insurance, free parking, a generous retirement program, and a truly pleasant workplace. A Medical Services physician is always on campus to attend to patients' somatic needs. Staff psychiatrists are not expected to work after hours, but some choose to supplement their salary by providing evening and weekend/holiday coverage under contract. In addition, we offer after-hours coverage contracts to psychiatrists who are not full-time staff members. Please send CV to **Jonathan Book, M.D., Clinical Director, SHC, 6655 Sykesville Road, Sykesville, MD 21784. For questions, call (410)970-7006 or e-mail JBook@dhmh.state.md.us.** EOE.

MASSACHUSETTS

WORCESTER, Child Psychiatry - ½ time position at UMass Medical School/UMass Memorial Medical Center providing a mix of Inpatient Child Psychiatry Consultation-Liaison and Outpatient Child Psychiatry. The Outpatient component involves oversight of a multidisciplinary team that is located at Community HealthLink, part of the UMass Memorial Health Care system. CHL is a multi-service, non-profit organization committed to promoting, maintaining and restoring the dignity, well-being and mental health of individuals and families in Central Massachusetts. The child psychiatrist works with a dedicated multidisciplinary team and provides evaluation and treatment services to persons with a range of psychiatric and substance abuse disorders. Our Department of Psychiatry has a large clinical faculty with clinical, teaching and academic opportunities at a wide variety of inpatient and outpatient programs. We have faculty development programs, commitment to our care, training and research missions, and a great living and learning environment in Central Massachusetts. Join a vibrant and growing Division of Child and Adolescent Psychiatry. Must be BE/BC in Child Psychiatry with experience in Child Psych C/L.

If you want to know more about job opportunities or the department in general, please email. Please send CV and letter of interest to: psychiatryrecruitment@umassmemorial.org or fax to 508-856-5990. Or, please call Cara Sanford at 508-856-3079. We are an AA/EOE employer. No recruiting agencies please. Thank you.

Staff Psychiatrist
Hallmark Health System, Inc.

Full- or part-time psychiatrist sought for expanding outpatient mental health clinic in a community hospital system located seven miles north of Boston. This position may be combined with other opportunities within Behavioral Health Services. Tufts faculty appointment is available. We offer a competitive salary and benefits package along with a friendly atmosphere and flexible schedule.

Interested candidates should apply online at **www.hallmarkhealth.org** or send resume to lmargossian@hallmarkhealth.org; phone: 781-306-6583. EOE.

Tufts Health Plan is seeking a half-time board certified psychiatrist to function as a Medical Director, perform utilization review and work with staff on complex cases at our Watertown facility.

Send a letter of interest and CV to: Paul Fulton, Ed.D., Director of Mental Health, Tufts Health Plan, 705 Mt. Auburn St., Watertown, MA 02472-1508. Email: Paul_Fulton@Tufts-health.com. Phone: 617-972-1070.

BOSTON - Central & Suburb locations - Westwood, Brookline, Pembroke, Attleboro, Lowell. Medical Director & Staff Positions—General and Child.. Inpatient & Partial. Salary, benefits & incentive plans. **NO CALL**. Contact Joy Lankswert, In-house recruiter @ 866-227-5415; OR email joy.lankswert@uhsinc.com.

Attending Psychiatrist-UMass Department of Psychiatry seeks a half to full-time attending psychiatrist for its adult mental health unit at the university medical center. A strong focus on teaching residents and medical students. Moderate case load, multidisciplinary treatment team, and superb treatment program. The position involves academic appointment to the medical school and opportunities for involvement in the academic activities of the department based on interests.

Our Department of Psychiatry has a large clinical faculty with clinical, teaching and academic opportunities at a wide variety of inpatient and outpatient programs. We have faculty development programs, commitment to our care, training and research missions, and a great living and learning environment in Central Massachusetts.

If you want to know more about job opportunities or the department in general, please email psychiatryrecruitment@umassmemorial.org or fax to 508-856-5990. Or, please call Cara Sanford at 508-856-3079.

We are an AA/EOE employer. No recruiting agencies please. Thank you.

CAMBRIDGE: Adult Psychiatry

Weekend Moonlighting Psychiatrist Positions available at Cambridge Health Alliance: Lucrative and flexible opportunities available for attending psychiatrists to provide weekend/holiday coverage of inpatient units at our Whidden Memorial Hospital campus.

Cambridge Health Alliance is an Equal Employment Opportunity employer, and women and minority candidates are strongly encouraged to apply.

CV & letter to: Susan Lewis, Department of Psychiatry, 1493 Cambridge Street, Cambridge, MA; Fax: 617-665-1204. **Email preferred:** SLewis@challiance.org.

Starr Psychiatric Center seeks a 20-40 hr psychiatrist for dynamic established psychiatric practice On Boston's South Shore. Medical model, multi-disciplinary staff. Stimulating environment, good pay. Clinic has a reputation for successful care, where others have failed. Email davidzstarr@juno.com or call 508.580.2211.

MICHIGAN

Southeast Michigan - Mercy Memorial Hospital seeking BC/ BE General Adult Psychiatrist; employed full time; inpatient & outpatient; 16-bed adult unit; work with 4 other doctors & 12 therapists; major depression/anxiety/bipolar/psychosis/mania; inpatient call is 1:3; competitive comp & hospital benefits.

Contact: Dennis Burns, Physician Recruiter
dennis.burns@mercymemorial.org

Opportunity for attending psychiatrist in the U.P. of Michigan. Mostly outpatient work with some inpatient responsibility on 20-bed, adult psychiatric unit. Excellent salary and benefits. For more information contact: Mark Blakeney, Voice: 972-420-7473, Fax: 972-420-8233; email: mark.blakeney@horizonhealth.com EOE.

An Easy Income of $200k (Or More) - No long workdays necessary to make a great income in Saginaw. Adult and C/A psychiatric services. Very close to Bay City on Lake Huron. Only an hour and a half to Detroit and Ann Arbor. Please call **Terry B. Good at 1-804-684-5661**, Fax #: 804-684-5663; Email: terry.good@horizonhealth.com.

MINNESOTA

Clinical Psychiatrist

Sophisticated, innovative healthcare system offers new and exciting career opportunities. Generous salary and benefit package. 651-431-3724 or trace.kinley@state.mn.us

MISSISSIPPI

North Central Mississippi, just one hour south of **Memphis, TN.** Attending Psychiatrist position available for 15-bed Adult and 22-bed Geriatric inpatient units, in addition to a 23-bed Chemical Dependency Program. Excellent salary and benefits. For more information contact: Mark Blakeney, Voice: 972-420-7473, Fax: 972-420-8233; email: mark.blakeney@horizonhealth.com EOE.

Forrest County General Hospital d/b/a South Mississippi Psychiatric Group seeks BC/BE Psychiatrist to evaluate patients with mental, emotional, or behavioral disorders; diagnose disorders, including nature and extent, and determine the appropriate course of treatment for the patient; and prescribe medication when necessary, at South Mississippi Psychiatric Group, 1 Lincoln Parkway Suite 202 Hattiesburg MS 39402; Pine Grove Behavioral Health, 2255 Broadway Drive Hattiesburg MS 39402; and Forrest General Hospital, HWY 49, Hattiesburg MS 39401. Applicant must be able to obtain a Mississippi Medical License. Send resumes to Celtie Wade, South Mississippi Psychiatric Group, 1 Lincoln Parkway Suite 202, Hattiesburg MS 39402.

MISSOURI

Enjoy a 4-day Workweek!

Medical Arts Clinic, part of BJC Medical Group, is seeking a psychiatrist to join our team in Farmington, Missouri. This collaborative practice has a strong outpatient component with some coverage of a 10-bed geriatric psychiatry unit. Setting provides tremendous work/life balance with a four-day workweek and shared call of 1:2. You will also enjoy competitive compensation and excellent benefits including malpractice coverage. Contact Selena Dickherber at 800-678-7858 x63755 or selenad@bjcmgphysicians.org. ID#134947PY.

Medical Director - Base Salary $220k to $230k - Can easily make well over base with Very Generous Bonus Plan - Close to Springfield - Extremely lucrative opportunity. Can be inpatient and nursing homes or inpatient and outpatient work. Unit is a 10-bed geropsychiatric program; outpatient adult &/or geriatric. Strong hospital support for behavioral health with plans for expansion. Please **call Terry B. Good at 1-804-684-5661**, Fax #: 804-684-5663; Email: terry.good@horizonhealth.com.

KANSAS CITY: Medical Director & Staff Physicians. Inpatient & Partial programs. Adult & Geriatric. Salary, benefits & incentive plan. Contact: Joy Lankswert In-house recruiter @ 866-227-5415 or email joy.lankswert@uhsinc.com.

MONTANA

Horizon Health invites you to consider an exciting practice opportunity for two NEW distinct **Adult** and **Geriatric** Inpatient Psychiatric Units, comprised of 26 total beds in Helena, MT. Nestled beneath the foothills of the Montana Rockies, **Helena**, the Capital of Montana, is alive with history and culture. This charming and beautiful Victorian city of 70,000 people provides a diverse attraction with many street festivals, theater, museums, symphonies, fairs and rodeos. There is truly something for everyone here! Excellent practice opportunity with great income ($200K+) and unparalleled quality of life! For more information contact: Mark Blakeney, Voice: 972-420-7473, Fax: 972-420-8233; email: mark.blakeney@horizonhealth.com EOE.

NEW JERSEY

CHILD & ADOLESCENT PSYCHIATRIST
WESTFIELD, CEDAR KNOLLS, RIDGEWOOD & PRINCETON

Excellent opportunity for Child/Adolescent Psychiatrist to join our Center in one of our four locations. We are a successful private fee for service comprehensive child, adolescent and adult therapy Center with locations in Westfield, Princeton, Cedar Knolls and Ridgewood, New Jersey. Candidate will be part of a multi-disciplinary team and will provide psychiatric evaluation, medication management and, if desired, psychotherapy. He/She will also clinically oversee treatment at the Center. Salary and benefit package is generous and includes medical/dental insurance, retirement plan, professional liability coverage and substantial continuing education and vacation. Supportive collegial atmosphere. Candidate must be board certified or board eligible in child/adolescent psychiatry. E-mail cv to abbazn@aol.com.

Westampton Township - Just East of Philadelphia. Geriatric or General Psychiatrist - predominant caseload geriatric w/ some adult. Competitive compensation and benefits. Minimal call - no w/end on site. Joy Lankswert, In-house recruiter @ 866-227-5415 or email joy.lankswert@uhsinc.com.

NEW YORK CITY & AREA

The Institute for Family Health is seeking a part- time psychiatrist to provide care to diverse populations, including those with intellectual and other developmental disabilities, in our Kingston, New York office. The schedule is very flexible. The Institute for Family Health is a nationally recognized organization dedicated to serving the needs of the underserved throughout New York's Hudson Valley region and New York City.

Please visit our website to learn more about our organization and the wonderful work we do here. **www.institute2000.org.** Please fax CVs to 845-255-3753 or email directly to mduffy@institute2000.org.

Child and Adolescent Psychiatrist
P/T - 10-15 hours per week (evenings and/or weekends) in a Child and Family Mental Health Center in Brooklyn. Excellent compensation. No call. Fax resume to (718) 553-6769, or email to clinicaldirector@nypcc.org.

NEW YORK STATE

Rockland Psychiatric Center, a 470 bed state hospital that takes referrals from Manhattan and the 4 counties to the north, has an opening for an inpatient psychiatrist. RPC has a staff of 70 psychiatrists in our network between the hospital and clinics, so there are opportunities for advancement or movement to other locations once in the system.

RPC is located 30 minutes north of Manhattan, in the beautiful Hudson Valley. The hospital is affiliated with NYU, offers CME, regular hours, on-call is voluntary and for extra pay.

Send CV to Mary Barber, MD
Clinical Director
rpmeb01@omh.state.ny.us.

Horizon Health seeks **Medical Director** and **Associate Medical Director** for 20-Bed Inpatient Acute Psychiatric Service in Scenic Southern Tier Finger Lakes area of New York State . The Inpatient unit treats over 1000 clients per year and is part of 283 Bed Acute Care Hospital and Comprehensive Health Care Organization. Enjoy a variety of coverage responsibilities including consults, outpatient contract coverage rotation, and call with other members of a highly collaborative team of psychiatrists. Competitive salary and benefits package included. Successful candidate must be Board eligible or Boarded in Psychiatry. For more information contact: Mark Blakeney, Voice: 972-420-7473, Fax: 972-420-8233; email: mark.blakeney@horizonhealth.com EOE.

Psychiatrists-Inpatient/Consultation Liaison/ Emergency Department Psychiatrists, P/T & F/T B/E, B/C to work with 6 other Psychiatrists in a community Hospital. Excellent benefits and desirable location with opportunity for private-practice. Contact: BSposato@hunthosp.org or fax to B. Sposato @ 631-351-2064. EOE.

Hudson Valley Mental Health, Inc.,
PSYCHIATRIST/NURSE PRACTITIONER
Full/Part Time Hours

HVMH, a provider of outpatient adult mental health services in Dutchess County, New York is seeking applicants for full-time/part-time Psychiatrist & Nurse Practitioner positions in our outpatient clinics. NYS license and BC/BE in psychiatry; Nurse Practitioner license. Monday-Friday, no weekends, no "on-call". Send CV and cover letter to Medical Director, Hudson Valley Mental Health, Inc. 230 North Road, Poughkeepsie, NY 12601. Fax: 845-790-2199; email richardmil@dcdmh.org or call 486-2781 for additional information.

STAFF PSYCHIATRIST

The Lewis County Community Mental Health Center, a county-operated NYS Office of Mental Health certified outpatient clinic in Northern New York has an opening for a full-time or half-time Staff Psychiatrist to work under the direction of our Medical Director providing services to both children and adults. No evening or weekend call. Responsible to provide initial psychiatric evaluations (60 minutes) and ongoing medication management treatment (30 minutes). Patient population includes approximately 55% adult, 10% geriatric, 15% child, and 20% adolescent. Candidate must hold a valid license to practice medicine in New York State; AND be board eligible or certified in psychiatry. Excellent benefits, with NYS retirement. Competitive salary. J1 Visa Waivers considered. LCCMHC is an approved National Health Service Corps site which allows qualified employees to apply for student loan repayment.

Send letter of interest and vita to: William F. Kenny, M.D., F.A.P.A., Medical Director, LCCMHC, 7550 S. State Street, Lowville, NY 13367 or at wkenny@lewiscountyny.org. **Phone:** (315) 376-5450. **Website:** www.lewismh.org.

ClearView Center Inc. is looking for a part time (4-5hrs/week) Psychiatrist with an interest working in Community Psychiatry. Flexible hours, evenings possible, no call, no weekends. Responsibilities include: providing initial psychiatric evaluations, and medication reviews. Qualifications: Current license to practice medicine in NYS, with Board certification or Board eligible in Psychiatry. Send resumes to Human Resources: 500 Central Ave., Albany, NY 12206. P(518)435-9931; F(518)435-9937. E- hr1@clearviewcenter.com. **www.clearviewcenter.com.**

The Albany Medical Center Faculty Practice Group is currently recruiting for two psychiatric faculty positions to join the Department of Psychiatry: one **child psychiatrist** and one **general psychiatrist**. Responsibilities include patient care, didactic and clinical instruction for residents and medical students. Participation in clinical research is encouraged. Albany is located within easy driving distance of Boston and New York City. It offers excellent schools and diverse recreational and cultural opportunities.

Send CV to: Jana Mastandrea, Physician Recruitment Coordinator, Albany Medical Center, MC 47, 47 New Scotland Ave, Albany, NY 12208; email mastanj@mail.amc.edu, (518) 262-1333, Fax (518) 262-6996.

Western New York-Chautauqua Region: Jamestown Psychiatric PC is seeking a Psychiatrist to join our rapidly growing Adult and Child Psychiatric team. Competitive salary and flexible growth opportunities are offered. We will offer a starting bonus to eligible candidates. Loan repayment, J1 or H1 assistance available. Please contact Mrs. Linda Jones, office manager @ lj@psychwebmd.com or Phone 716-483-2603. Fax CV and qualifications to 716-483-2828.

NORTH CAROLINA

LUCRATIVE POSITION, GREAT LOCATION- Adult inpatient and outpatient work right near Raleigh. Offering very attractive package: salary with benefits and bonus plan or practice opportunity. Contact **Terry B. Good at 1-804-684-5661**, Fax #: 804-684-5663; terry.good@horizonhealth.com.

THE GUILFORD CENTER
PSYCHIATRIST
Greensboro/High Point, NC

The Guilford Center has an immediate opening for Adult Psychiatrists. Our Psychiatrists provide high quality clinical services to consumers of all diagnostic categories. Services include psychiatric and medical evaluations. Flexible scheduling and no required on call or weekend coverage! Must have N.C. medical license prior to hire, prefer board certified. We offer an excellent benefit package with salary negotiable depending on experience.

Interested individuals must apply at www.co.guilford.nc.us. For additional information contact Denise Cox at DCox@GuilfordCenter.com. (EOE)

Adult Staff Psychiatrist
Emergency Room Psychiatrist
Charlotte, NC

Carolinas HealthCare System has unique opportunities for Adult Staff Psychiatrists at its Behavioral Health Center. The center is part of a 874- bed regional teaching facility nestled in the heart of Charlotte. Join an outstanding team of psychiatrists in a very collegial working environment.
Adult Staff Position - Inpatient and outpatient.
Emergency Room Psychiatry Position - Work in the facility's in-house emergency department. Rotating shifts.
Excellent benefits package which includes:
- **Two weeks CME**
- **Paid vacation**
- **Short and long-term disability**
- **401K, 457B and pension plan**

Opportunity for extra income by seeing private patients or by taking shifts in the ER
Interested applicants should email their CV to Elaine Haskell at: elaine.haskell@carolinashealthcare.org **or call 800-847-5084 for more information.**

EOE/AA

OHIO

PSYCHIATRIST NEEDED IN DAYTON!
Full or Part-Time

The candidate would function as a member of a treatment team to deliver direct patient care in an adult and child outpatient mental health clinic in a community behavioral health setting.
Qualifications required are below:
- Graduate of an accredited psychiatric training program.
- Professional licensure by the State of Ohio Medical Board.
- Board eligible or Board certified in adult and/or child psychiatry.

Full benefits package available! As an EEO/AA employer, we recognize and appreciate the benefits of diversity in the workplace.

Please email CV to: mmhouser@shp-dayton.org or view our website at http://www.sbhihelp.org.

OKLAHOMA

Psychiatrist (BE) or (BC)
Announcement #2010-07
DMHSAS/Oklahoma Forensic Center (OFC)-Vinita, OK
Salary Range: $184,000-$215,500

Minimum Qualifications: Must be licensed to practice medicine by the State of Oklahoma and be Board Eligible or Board Certified.
Benefits include: Insurance, Retirement, Vacation, Holiday & Sick Leave. Must be able to pass drug screen and OSBI background check. Reasonable accommodations to individuals with disabilities may be provided upon request. To apply contact Human Resources at 918-713-5549. OFC is an EOE.

OREGON

BC/BE Psychiatrists
Oregon State Hospital (OSH)
Salem, Oregon

Oregon Department of Human Services (DHS), OSH is looking for Oregon BC/BE Psychiatrists. OSH offers FT, PT and flexible opportunities in our general adult, geriatric, and forensic programs. A generous and comprehensive benefit and PERS retirement package is included, as well as a new hospital in 2011 which will incorporate state-of-the-art architecture, treatment space and technology. Salary is very competitive and includes psychiatric differential, certification pay and opportunities for additional on-call work.

Dr. Mark Diamond, CMO, invites you to call and/or send your CV to us today! Phone: (503) 945-2887; email: lila.m.lokey@state.or.us; fax: (503) 945-9910; mail: Human Resources, 2600 Center Street NE, Salem, OR 97301-2682. Please visit our website at www.oregon.gov/DHS/mentalhealth/osh. The State of Oregon is an Equal Opportunity Employer.

PENNSYLVANIA

PSYCHIATRIST
Full-time or part-time BE/BC adult or child psychiatrist for private outpatient clinic located 45 minutes north of downtown Pittsburgh in designated Health Physician Shortage Area (HPSA). Duties include psychiatric evaluations and medication management. 37 ½ -hour work week M-F 8:30A.M. to 4:30P.M. with no on-call. $170,000-$190,000 with excellent compensation package including health care, retirement, paid time off, malpractice insurance, and CME. Will participate in moving expenses. EOE.

Submit Vita by e-mail to hr@fccac.org or mail to Executive Director, Family Counseling Center of Armstrong County, 300 South Jefferson Street, Kittanning PA 16201 **www.fccac.org.**

DIRECTOR,
Child Psychiatry Division

The Department of Psychiatry at The Penn State Hershey Medical Center and College of Medicine is currently recruiting a board-certified child psychiatrist to provide leadership to growing division of child psychiatry. This position will also hold the University Chair in Child Psychiatry, an endowed position, at Penn State University. The Director's responsibilities will include the development of an expanding clinical program and quality improvement initiatives. Teaching of residents, child fellows and medical students will be essential facets of the position, as well as scholarly pursuits in a specific area of expertise.

With our clinical partner, Pennsylvania Psychiatric Institute, the Department staffs a 16 bed child and adolescent inpatient unit, a child and adolescent partial hospitalization program and outpatient services at two locations. Our faculty have research interests in eating disorders, PTSD, anxiety, mood disorders, and substantial research funding in the areas of sleep, imaging and autism. Our current child/adolescent psychiatry faculty numbers 12, and we have 6 fellows in training.

The successful candidate should have strong clinical skills and an established record of scholarly achievement. An established program of research and a history of extramural grant funding are highly desirable. The successful candidate will also have evidence of effective leadership and a demonstrated ability to promote an environment that fosters productive collaboration with colleagues in psychiatry and other disciplines.

Candidates with interest and skills in this area should send a curriculum vitae and cover letter to:
Alan J. Gelenberg, MD
Professor and Interim Chair
Penn State Hershey Medical Center
Department of Psychiatry, H073
P.O. Box 850, Hershey, PA 17033
Phone: 717.531.8516
Fax: 717.531.6491
agelenberg@hmc.psu.edu

Penn State Hershey Medical Center is committed to affirmative action, equal opportunity and the diversity of its workforce.

Psychiatrists:

Currently we have exciting full- and part-time positions in a rapidly expanding department. Opportunities include responsibilities in and outside our five-hospital health system. There are immediate openings for child/adolescent, adult and addictions psychiatrists.

There are also practice options in a traditional psychotherapy model. Psychiatric Hospitalist positions are available for weekday and weekend rounding and Crisis. Excellent salaries, no on-call nor rounding responsibilities ever and exceptional benefits package offered. Send CV to Kevin Caputo, M.D., Vice President and Chairman, Department of Psychiatry, Crozer-Keystone Health System, One Medical Center Blvd., Upland, PA 19013 or contact the department manager, Kathy Waring at 610-619-7413.

PITTSBURGH SOUTH HILLS-Office space available. Remarkable practice opportunity for BE/BC psychiatrist. Affiliate with our premier community hospital. Outpatient and inpatient work. Call 412-429-1646/fax 412-531-1617/email burstpsych@aol.com.

EASY DRIVE TO PHILADELPHIA, BALTIMORE, AND WASHINGTON, DC -Seeking a Psychiatrist for inpatient work in an impressive med/surg hospital in eastern PA. Can be primarily adult or gero or a mix of both. Offering salary/benefits, relo pkg, and bonus plan. Please call **Terry B. Good at 1-804-684-5661**, Fax #: 804-684-5663; Email: terry.good@horizonhealth.com.

Meadowbrook, PA - Philadelphia Suburb Associate Medical Director on geropsychiatric unit in the Holy Redeemer Hospital. Great location-close to Philly. Please call for details: **Terry B. Good at 1-804-684-5661**, Fax #: 804-684-5663; Email: terry.good@horizonhealth.com.

PHILADELPHIA and suburbs- Child Psychiatrists for Inpatient, RTC and/or Partial Programs. **CLARION-just east of Pittsburgh.** Child OR General Psychiatrist for inpatient & partial programs. **SHIPPENSBURG:** General Psychiatrist with interest in Dual Diagnoses. **STATE COLLEGE:** Child OR General Psychiatrist for inpatient & partial programs. Some outpatient also an option. Fulltime positions. Salary & benefits. **Student loan assistance at Clarion**. Contact Joy Lankswert @ 866-227-5415; OR email joy.lankswert@uhsinc.com.

SOUTH CAROLINA

Income Potential $280k to $350+
Medical Director -New Geropsych Unit
Very lucrative position (salaried with benefits or practice opportunity for those who prefer independence) in northeast SC-a small town with a BIG opportunity. An easy drive to Florence, SC and Fayetteville, NC; 2 hours from Columbia, Myrtle Beach, Charlotte and Raleigh. Please **call Terry B. Good at 1-804-684-5661**, Fax #: 804-684-5663; Email: terry.good@horizonhealth.com.

Psychiatrists needed in Greenwood, SC, a beautiful city located in the northwestern part of SC nestled amidst many gorgeous lakes and rolling hills. Recreational activities include golf, tennis, watersports, hunting, cultural performances and more. Greenwood has been recognized as a Top 50 "Best Towns in America". Western Carolina Psychiatric Associates is a Self Regional Healthcare-owned practice in close proximity to the medical center. This practice includes three general psychiatrists and three psychiatric LISWs. Western Carolina Psychiatric Associates is seeking BE/BC general psychiatrists for inpatient/outpatient work. The call schedule is one in five. Weekend call is back-up to a resident or fellow. The option for primary weekend call with additional reimbursement is also available. Psychiatrists will be hospital employees with full benefits including 403B, medical insurance, paid time off, CME days and reimbursement, and malpractice insurance. Self Regional was named of the world's top 20 "Great Workplaces" by the Gallup organization for three years in a row starting in 2008.

Contact: Tori Roatch
Physician Services Representative
800-859-0599, ext. 4254
or by email at tlroatch@selfregional.org.
Also visit us on our website at
www.selfregional.org.

AIKEN: Staff Psychiatrist - Predominant caseload in Partial Day - some inpatient & C/L (Adult with some adolescent if interested). Salaried Position with benefits and bonus - good call. Contact: Joy Lankswert In-house recruiter @ 866-227-5415 or email joy.lankswert@uhsinc.com.

TENNESSEE

Board-certified/eligible psychiatrists needed for a large Psychiatry Service at Mountain Home VAMC in Johnson City, Tennessee. Inpatient/outpatient psychiatrist on a 24 bed teaching unit staffed by two psychiatrists, 1 NP, 1 PA, and residents rotating from ETSU College of Medicine. Must be board certified in psychiatry or board eligible if within 2 years of residency completion. Join staff of 30 prescribers, including 18 psychiatrists at ETSU-affiliated residency training program with medical students, adult and med-psych residencies. Clinical appointment potential and some teaching expected. Research a plus. On-call (full time positions only) is backup to residents and shared amongst staff psychiatrists.

NO STATE INCOME TAX, LOW COST OF LIVING, BEAUTIFUL MOUNTAINOUS REGION, LOTS OF PARKS, GOLF COURSES, LAKES, NATIONAL FOREST.

Inquiries: Tana Johnson, (423) 926-1171, ext. 7184, or Tana.Johnson@va.gov and George.Brown@va.gov. Applications and/or CVs to: James H. Quillen VA Medical Center P.O. Box 4000 (05), Mountain Home, TN 37684 or Fax: (423) 979-3443 or Email: mtnhomehrmservice@va.gov
Equal Opportunity Employer

TEXAS

Texas A&M College of Medicine and Scott & White Healthcare
Growing Department Seeks Faculty in Adult and inChild & Adolescent Psychiatry

The Texas A&M and Scott & White Department of Psychiatry in Temple is recruiting faculty in adult and in child & adolescent psychiatry. The Department is growing and has healthy training programs in general and child & adolescent.

Texas A&M is ranked as a top university worldwide, with strong clinical and basic research and excellent biomedical research infrastructure. The Department has competitive federal funding with active imaging and stem cell research and the resources to support academic work. A&M offers an extensive research training program for junior faculty, and Scott & White, one of the nation's largest and most respected health care systems, offers a strong career development program in medical management. Joint appointment with the Central Texas VA is available where advantageous to career development.

Scott & White is a fully integrated health system and is the largest multi-specialty practice in Texas, and the sixth largest group practice in the nation. Scott & White employs more than 1,100 providers, physicians and research scientists who care for patients covering 25,000 square miles across Central Texas. Scott & White owns, is partnered with, or manages 9 hospitals across Central Texas. Scott & White primary facility is a 636-bed Level I Trauma acute care facility in Temple, along with an additional 50-bed Long Term Acute Care Hospital in Texas, another 150-bed acute care hospital in Temple, a 76-bed acute care facility in Round Rock (greater Austin area), and a network of 50 primary and specialty clinics throughout the region.

Salaries are competitive, with excellent benefits and an incentive plan. Temple has a warm climate and strong schools and is close to Austin. There are many area locations for boating, fishing, skiing, golf, and hiking.

Academic appointment depends on qualifications. Women and minorities are encouraged to apply. **Contact Karmen Smotek, RN, BSN, Physician Recruiter, klsmotek@swmail.sw.org.**

AMARILLO - Hospitalist - Salaried Employment & benefits offered. Adult general psych and dual programs. Contact: Courtney Williams, In-house recruiter @ 866-227-5415 or email courtney.williams@uhsinc.com.

McALLEN: Private Practice Opportunity. Inpatient & Outpatient. General Psychiatrist.
WEST TEXAS San Angelo: Child or General Psychiatrist. Salaried Employment or Private Practice. **Student Loan assistance in San Angelo.** Contact: Joy Lankswert, In-house recruiter @ 866-227-5415 or email joy.lankswert@uhsinc.com.

Salaried Opportunities for Adult Psychiatrists - San Antonio, TX

Vericare (www.vericare.com) is the leader in providing mental health services to residents of long term care. We have immediate, salaried positions for Adult or Geriatric Psychiatrists in San Antonio. We offer flexible scheduling, 100% paid malpractice, administrative support, no on call/weekend requirement and a complete benefits package. Board Certified preferred. **Call Sanel Lekic at 800-257-8715 x1166 or email your resume/inquiry to slekic@vericare.com.**

UTAH

PSYCHIATRIST

Ski Park City and Snowbird, attend Sundance film festival, and work in nearby Provo! On-Call is optional. **Utah State Hospital** seeks psychiatrists for adult inpatient unit. JCAHO/MEDICAID/CMS accredited. Electronic chart and pharmacy. New buildings on a 300-acre campus at the base of the mountains. Collegial environment. Salary negotiable, with full benefits.

Send CV to: Richard Spencer, MD, Clinical Director, PO Box 270, Provo, UT 84603, (801) 344-4201, rspencer@utah.gov. EOE.

VERMONT

We are looking for a ***Medical Director and Inpatient Clinical Psychiatrist*** to join our Psychiatric Services Department here at Rutland Regional Medical Center. This is a hospital employed position in a 19 bed inpatient unit. Includes 80% general, 20% Geriatric, pediatric consults only and no forensics. Oversee physicians and staff in Outpatient facility which opened October 2008. Call 1 in 5 with strong Crisis Team doing intake in the Emergency Dept. Benefits include Malpractice, Health, Dental, and Disability insurances, Pension Plan, 403B with match, CME account, and relocation. Educational loan repayment money available. It's a chance to do what you love...in a setting you'll adore!

Rebecca Banco, CMSR
Physician Recruiter
Rutland Regional Medical Center
160 Allen Street
Rutland, Vermont 05701
bbanco@rrmc.org
802-747-3844

VIRGINIA

Inpatient and Outpatient Psychiatric Opportunities

Norfolk Community Services Board is a community-based behavioral health care organization located in Norfolk, Virginia. We are seeking **full-time inpatient psychiatrists** for our adult and geropsychiatric teams. Board Certification in Psychiatry is required. Norfolk CSB enjoys partnerships with Eastern Virginia Medical School, area universities, and local mental health and health care systems. There are opportunities for medical student/resident teaching and research. Academic appointment as EVMS Community Faculty is available.

We are also recruiting **full and part time psychiatrists** for positions within our continuum of outpatient services, including our Adult Outpatient Clinic. BC/BE.

Our excellent employee benefits package includes 13 paid holidays, generous leave, paid malpractice insurance, life insurance, health and dental insurance, and a professional development allowance. Salary is commensurate with experience.

Applicants must possess or be eligible to obtain a full, unrestricted Virginia medical license. Apply to Norfolk Community Services Board, 225 West Olney Road, Norfolk, Virginia 23510-1523, or call (757) 823-1693 if you require special assistance.

On-line application at www.norfolkcsb.org.
EOE M/F/D/V
Background check required.

WASHINGTON

Summit Research Network (Seattle) LLC is seeking a licensed, board certified Psychiatrist to work with adult and pediatric/adolescent populations in clinical research trials. Must be comfortable working in a team environment as a Sub Investigator and Principal Investigator in primarily psychiatric pharmaceutical research at our site in Seattle, WA.This position is part time with the potential to increase to full time. Summit offers competitive salary based on experience/credentials with an excellent benefit package. Please send inquiries and CV to: Shannon Kinzebach, Summit Research Network, 901 Boren Ave Ste 1800; Seattle, WA 98104 or via email: shannonk@summitnetwork.com.

WEST VIRGINIA

Shenandoah Valley-Recruiting 3rd psychiatrist for behavioral health department in multi- disciplinary community health center **90 minutes from Washington/Baltimore**. Experience/training in addictionology and/or child/adolescent psychiatry a plus. Salaried position w/incentive compensation, standard benefits. Approved site for Federal Loan Repayment.

Contact Tina Burns 304 596 2610, ext 1066; tburns@svms.net FAX 304 263 0984. Visit our website **www.svms.net!**

PSYCHIATRIST-West Virginia University School of Medicine, The Department of Behavioral Medicine and Psychiatry, has ongoing opportunities and faculty positions for full-time, part-time or per diem **BE/BC Adult and Child Psychiatrists** in various locations throughout the state of West Virginia, including its primary clinical, educational and research location in Morgantown, WV, as well as William R. Sharpe Jr. Hospital, a 150-bed, JCAHO-accredited, state psychiatric hospital in Weston, WV.Responsibilities include patient care and teaching, with opportunities for research. Positions will remain open until filled. **Contact Susan Clayton at sclayton@hsc.wvu.edu. WVU is an AA/EO employer.**

WISCONSIN

Psychiatrist

Clement J. Zablocki VA Medical Center, Milwaukee, Wisconsin, is an academic tertiary care facility closely affiliated with the Medical College of Wisconsin. We are seeking a BC/BE psychiatrist to work in our outpatient mental health clinic.

Mental Health outpatient care involves treating a wide range of patients with mental health issues in a setting with a strong multi-disciplinary orientation and collaborative approach to care. There are opportunities to participate in the clinical training and education of medical students, residents and fellows in the clinic. The successful candidate should possess strong clinical and interpersonal skills. Faculty appointment with the Medical College of Wisconsin is available, with appropriate credentials. **Must be a U.S. Citizen to be considered.**

Inquiries may be directed to: Gunnar Larson, M.D. 888-469-6614, x 41270, gunnar.larson@va.gov.

Submit cover letter and CV to:
Clement J. Zablocki VA Medical Center
Attn: Prudy Kitterman, Physician Recruiter
5000 W. National Ave., Milwaukee, WI 53295
Fax: (414) 382-5378 prudy.kitterman@va.gov
EOE/Random Drug Screen.
http://www.usajobs.org.

Wisconsin - Integrated healthcare organization that has been selected as a "Top 100 Hospital" for the fifth consecutive year seeks a dynamic Psychiatrist for primarily outpatient responsibilities. Enjoy an industry leading salary and benefits package including paid time off, CME with stipend, relocation and more. Enjoy neighborhoods filled with diverse and friendly people, a riverfront downtown filled with the arts, restaurants, and history, numerous parks and trails and easy access to Milwaukee and a host of cultural amenities.

Contact Marie Haines, **Alpha Medical Group** at 800.504.3411 or mhaines@alphamg.org. Additional opportunities at www.alphamg.org.

WYOMING

CASPER & CHEYENNE: Psychiatrist for inpatient & outpatient services. Highly competitive salary, benefits, & bonus plan. Student loan assistance negotiable. Contact Joy Lankswert, In-house recruiter @ 866-227-5415 or email joy.lankswert@uhsinc.com.

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Fellowships

EAST TENNESSEE STATE UNIVERSITY
JAMES H. QUILLEN COLLEGE OF MEDICINE
Department of Psychiatry
and Behavioral Sciences

THE SOTERION
NEUROPSYCHIATRIC and MOLECULAR IMAGING
RESEARCH (POST DOCTORAL) FELLOWSHIP

The Research Fellow will carry out a number of multimodal imaging studies, with an emphasis on EEG and PET. Studies include antibody removal of Alzheimer's disease plaques, and investigational PET scans of these plaques. Research includes other dementias, neuropathic pain and EEG biofeedback. Opportunities for additional clinical research and training are available. The Fellowship will be for two years, with the salary based on that of a PGY-V. Position contingent upon outside funding. The position will be classifed as an Administrative Post Doctoral Fellow.

Apply to the position at https://jobs.etsu.edu/applicants/Central?quickFind=51015. Applicants should have two letters of reference sent directly to Norman C. Moore, MD, Professor of Psychiatry, East Tennessee State University, Box 70567, Johnson City, TN 37614. Inquiries can be made by telephone to 423-439-2235 or by email to lovedayc@etsu.edu. AA/EOE.

Practice for Sale

Central Ohio Psychiatric Practice for Sale

All cash collections psychiatric practice in beautiful office near Easton. Practice has solid and stable revenues with nice margin to owner. Many opportunities for growth. Practice would be perfect for acquisition by an existing group or physician looking to start their own office.

For more details please send an email to marketerpractice@yahoo.com or (614) 457-8613.

Office Space Available

N. Bethesda, MD. Available Full or Part Time immediately. Fully furnished spacious, sunny, luxury office and waiting room in mental health suite. This office, located in a prestigious office building with concierge, has large windows and offers a beautiful view. Easy access to White Flint Mall + Metro. Call (301) 881-0433 OR email jbgoodman1@aol.com.

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PsychiatryOnline.com is a powerful website that features *DSM-IV-TR*® and *The American Journal of Psychiatry* as the cornerstones of an unsurpassed collection of psychiatric references, including books, journals, and self-assessment tools. Much more than simply books and journals presented online, **PsychiatryOnline.com** features sophisticated searching and indexing tools that enable you to quickly target all the information you need.

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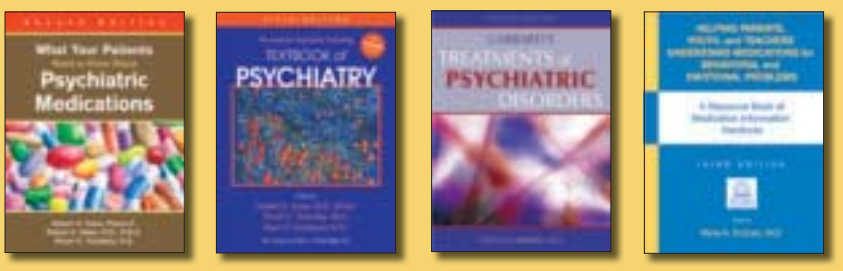

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BRIEF SUMMARY. See package insert for full Prescribing Information. For further product information and current package insert, please visit www.wyeth.com or call our medical communications department toll-free at 1-800-934-5556.

WARNING: Suicidality and Antidepressant Drugs

Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of Major Depressive Disorder (MDD) and other psychiatric disorders. Anyone considering the use of Pristiq or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. Pristiq is not approved for use in pediatric patients [*see Warnings and Precautions (5.1), Use in Specific Populations (8.4), and Patient Counseling Information (17.1 in the full prescribing information)*].

INDICATIONS AND USAGE: Pristiq, a selective serotonin and norepinephrine reuptake inhibitor (SNRI), is indicated for the treatment of major depressive disorder (MDD).

CONTRAINDICATIONS: Hypersensitivity-Hypersensitivity to desvenlafaxine succinate, venlafaxine hydrochloride or to any excipients in the Pristiq formulation. **Monoamine Oxidase Inhibitors-**Pristiq must not be used concomitantly in patients taking monoamine oxidase inhibitors (MAOIs) or in patients who have taken MAOIs within the preceding 14 days due to the risk of serious, sometimes fatal, drug interactions with SNRI or SSRI treatment or with other serotonergic drugs. Based on the half-life of desvenlafaxine, at least 7 days should be allowed after stopping Pristiq before starting an MAOI [*see Dosage and Administration (2.5) in the full prescribing information*].

WARNINGS AND PRECAUTIONS: Clinical Worsening and Suicide Risk-Patients with major depressive disorder (MDD), both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality) or unusual changes in behavior, whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. Suicide is a known risk of depression and certain other psychiatric disorders, and these disorders themselves are the strongest predictors of suicide. There has been a long-standing concern, however, that antidepressants may have a role in inducing worsening of depression and the emergence of suicidality in certain patients during the early phases of treatment. Pooled analyses of short-term placebo-controlled studies of antidepressant drugs (SSRIs and others) showed that these drugs increase the risk of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults (ages 18-24) with major depressive disorder (MDD) and other psychiatric disorders. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction with antidepressants compared to placebo in adults aged 65 and older. The pooled analyses of placebo-controlled studies in children and adolescents with MDD, obsessive-compulsive disorder (OCD), or other psychiatric disorders included a total of 24 short-term studies of 9 antidepressant drugs in over 4,400 patients. The pooled analyses of placebo-controlled studies in adults with MDD or other psychiatric disorders included a total of 295 short-term studies (median duration of 2 months) of 11 antidepressant drugs in over 77,000 patients. There was considerable variation in risk of suicidality among drugs, but a tendency toward an increase in the younger patients for almost all drugs studied. There were differences in absolute risk of suicidality across the different indications, with the highest incidence in MDD. The risk differences (drug vs. placebo), however, were relatively stable within age strata and across indications. These risk differences (drug-placebo difference in the number of cases of suicidality per 1000 patients treated) are provided in Table 1 of the full prescribing information. No suicides occurred in any of the pediatric studies. There were suicides in the adult studies, but the number was not sufficient to reach any conclusion about drug effect on suicide. It is unknown whether the suicidality risk extends to longer-term use, ie, beyond several months. However, there is substantial evidence from placebo-controlled maintenance studies in adults with depression that the use of antidepressants can delay the recurrence of depression. **All patients being treated with antidepressants for any indication should be monitored appropriately and observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases.** The following symptoms, anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, and mania, have been reported in adult and pediatric patients being treated with antidepressants for major depressive disorder as well as for other indications, both psychiatric and nonpsychiatric. Although a causal link between the emergence of such symptoms and either the worsening of depression and/or the emergence of suicidal impulses has not been established, there is concern that such symptoms may represent precursors to emerging suicidality. Consideration should be given to changing the therapeutic regimen, including possibly discontinuing the medication, in patients whose depression is persistently worse, or who are experiencing emergent suicidality or symptoms that might be precursors to worsening depression or suicidality, especially if these symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms. If the decision has been made to discontinue treatment, medication should be tapered, as rapidly as is feasible, but with recognition that abrupt discontinuation can be associated with certain symptoms [*see Warnings and Precautions (5.9) and Dosage and Administration (2.3) in the full prescribing information for a description of the risks of discontinuation of Pristiq*]. Families and caregivers of patients being treated with antidepressants for major depressive disorder or other indications, both psychiatric and nonpsychiatric, should be alerted about the need to monitor patients for the emergence of agitation, irritability, unusual changes in behavior, and the other symptoms described above, as well as the emergence of suicidality, and to report such symptoms immediately to health care providers. Such monitoring should include daily observation by families and caregivers. Prescriptions for Pristiq should be written for the smallest quantity of tablets consistent with good patient management, in order to reduce the risk of overdose. Screening patients for bipolar disorder- A major depressive episode may be the initial presentation of bipolar disorder. It is generally believed (though not established in controlled studies) that treating such an episode with an antidepressant alone may increase the likelihood of precipitation of a mixed/manic episode in patients at risk for bipolar disorder. Whether any of the symptoms described above represent such a conversion is unknown. However, prior to initiating treatment with an antidepressant, patients with depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression. It should be noted that Pristiq is not approved for use in treating bipolar depression. **Serotonin Syndrome or Neuroleptic Malignant Syndrome (NMS)-like Reactions-** The development of a potentially life-threatening serotonin syndrome or Neuroleptic Malignant Syndrome (NMS)-like reactions have been reported with SNRIs and SSRIs alone, including Pristiq treatment, but particularly with concomitant use of serotonergic drugs (including triptans), with drugs that impair metabolism of serotonin (including MAOIs), or with antipsychotics or other dopamine antagonists. Serotonin syndrome symptoms may include mental status changes (eg, agitation, hallucinations, coma), autonomic instability (eg, tachycardia, labile blood pressure, hyperthermia), neuromuscular aberrations (eg, hyperreflexia, incoordination) and/or gastrointestinal symptoms (eg, nausea, vomiting, diarrhea). Serotonin syndrome in its most severe form can resemble neuroleptic malignant syndrome, which includes hyperthermia, muscle rigidity, autonomic instability with possible rapid fluctuation of vital signs, and mental status changes. Patients should be monitored for the emergence of serotonin syndrome or NMS-like signs and symptoms. The concomitant use of Pristiq with MAOIs intended to treat depression is contraindicated [*see Contraindications (4.2)*]. If concomitant treatment of Pristiq with a 5-hydroxytryptamine receptor agonist (triptan) is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases. The concomitant use of Pristiq with serotonin precursors (such as tryptophan) is not recommended. Treatment with Pristiq and any concomitant serotonergic or antidopaminergic agents, including antipsychotics, should be discontinued immediately if the above events occur, and supportive symptomatic treatment should be initiated. **Elevated Blood Pressure-** Patients receiving Pristiq should have regular monitoring of blood pressure since dose-dependent increases were observed in clinical studies. Pre-existing hypertension should be controlled before initiating treatment with Pristiq. Caution should be exercised in treating patients with pre-existing hypertension or other underlying conditions that might be compromised by increases in blood pressure. Cases of elevated blood pressure requiring immediate treatment have been reported with Pristiq. Sustained hypertension- Sustained blood pressure increases could have adverse consequences. For patients who experience a sustained increase in blood pressure while receiving Pristiq, either dose reduction or discontinuation should be considered [*see Adverse Reactions (6.1)*]. Treatment with Pristiq in controlled studies was associated with sustained hypertension, defined as treatment-emergent supine diastolic blood pressure (SDBP) ≥90 mm Hg and ≥10 mm Hg above baseline for 3 consecutive on-therapy visits. In clinical studies, regarding the proportion of patients with sustained hypertension, the following rates were observed: placebo (0.5%), Pristiq 50 mg (1.3%), Pristiq 100 mg (0.7%), Pristiq 200 mg (1.1%), and Pristiq 400 mg (2.3%). Analyses of patients in Pristiq controlled studies who met criteria for sustained hypertension revealed a dose-dependent increase in the proportion of patients who developed sustained hypertension. **Abnormal Bleeding-**SSRIs and SNRIs can increase the risk of bleeding events. Concomitant use of aspirin, other drugs that affect platelet function, nonsteroidal anti-inflammatory drugs, warfarin, and other anticoagulants can add to this risk. Bleeding events related to SSRIs and SNRIs have ranged from ecchymosis, hematoma, epistaxis, and petechiae to life-threatening hemorrhages. Patients should be cautioned about the risk of bleeding associated with the concomitant use of Pristiq and NSAIDs, aspirin, or other drugs that affect coagulation or bleeding. **Narrow-angle Glaucoma-**Mydriasis has been reported in association with Pristiq; therefore, patients with raised intraocular pressure or those at risk of acute narrow-angle glaucoma (angle-closure glaucoma) should be monitored. **Activation of Mania/Hypomania-**During all MDD and VMS (vasomotor symptoms) phase 2 and phase 3 studies, mania was reported for approximately 0.1% of patients treated with Pristiq. Activation of mania/hypomania has also been reported in a small proportion of patients with major affective disorder who were treated with other marketed antidepressants. As with all antidepressants, Pristiq should be used cautiously in patients with a history or family history of mania or hypomania. **Cardiovascular/Cerebrovascular Disease-**Caution is advised in administering Pristiq to patients with cardiovascular, cerebrovascular, or lipid metabolism disorders [*see Adverse Reactions (6.1)*]. Increases in blood pressure and heart rate were observed in clinical studies with Pristiq. Pristiq has not been evaluated systematically in patients with a recent history of myocardial infarction, unstable heart disease, uncontrolled hypertension, or cerebrovascular disease. Patients with these diagnoses, except for cerebrovascular disease, were excluded from clinical studies. **Serum Cholesterol and Triglyceride Elevation-**Dose-related elevations in fasting serum total cholesterol, LDL (low-density lipoprotein) cholesterol, and triglycerides were observed in the controlled studies. Measurement of serum lipids should be considered during treatment with Pristiq [*see Adverse Reactions (6.1)*]. **Discontinuation of Treatment with Pristiq-** Discontinuation symptoms have been systematically and prospectively evaluated in patients treated with Pristiq during clinical studies in major depressive disorder. Abrupt discontinuation or dose reduction has been associated with the appearance of new symptoms that include dizziness, nausea, headache, irritability, insomnia, diarrhea, anxiety, fatigue, abnormal dreams, and hyperhidrosis. In general, discontinuation events occurred more frequently with longer duration of therapy. During marketing of SNRIs (Serotonin and Norepinephrine Reuptake Inhibitors) and SSRIs (Selective Serotonin Reuptake Inhibitors), there have been spontaneous reports of adverse events occurring upon discontinuation of these drugs, particularly when abrupt, including the following: dysphoric mood, irritability, agitation, dizziness, sensory disturbances (eg, paresthesia, such as electric shock sensations), anxiety, confusion, headache, lethargy, emotional lability, insomnia, hypomania, tinnitus, and seizures. While these events are generally self-limiting, there have been reports of serious discontinuation symptoms. Patients should be monitored for these symptoms when discontinuing treatment with Pristiq. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the physician may continue decreasing the dose, but at a more gradual rate [*see Dosage and Administration (2.4) and Adverse Reactions (6.1) in full prescribing information*]. **Renal Impairment-**In patients with moderate or severe renal impairment or end-stage renal disease (ESRD) the clearance of Pristiq was decreased, thus prolonging the elimination half-life of the drug. As a result, there were potentially clinically significant increases in exposures to Pristiq [*see Clinical Pharmacology (12.6) in full prescribing information*]. Dosage adjustment (50 mg every other day) is necessary in patients with severe renal impairment or ESRD. The doses should not be escalated in patients with moderate or severe renal impairment or ESRD [*see Dosage and Administration (2.2) in full prescribing information*]. **Seizure-**Cases of seizure have been reported in premarketing clinical studies with Pristiq. Pristiq should be prescribed with caution in patients with a seizure disorder. **Hyponatremia-** Hyponatremia can occur as a result of treatment with SSRIs and SNRIs, including Pristiq. In many cases, this hyponatremia appears to be the result of the syndrome of inappropriate antidiuretic hormone secretion (SIADH). Elderly patients can be at greater risk of developing hyponatremia with SSRIs and SNRIs. Also, patients taking diuretics or who are otherwise volume depleted can be at greater risk [*see Use in Specific Populations (8.5) and Clinical Pharmacology (12.6) in full prescribing information*]. Discontinuation of Pristiq should be considered in patients with symptomatic hyponatremia and appropriate medical intervention should be instituted. **Coadministration of Drugs Containing Desvenlafaxine and Venlafaxine-** Desvenlafaxine is the major active metabolite of venlafaxine. Products containing desvenlafaxine and products containing venlafaxine should not be used concomitantly with Pristiq. **Interstitial Lung Disease and Eosinophilic Pneumonia-** Interstitial lung disease and eosinophilic pneumonia associated with venlafaxine (the parent drug of Pristiq) therapy have been rarely reported. The possibility of these adverse events should be considered in patients treated with Pristiq who present with progressive dyspnea, cough, or chest discomfort. Such patients should undergo a prompt medical evaluation, and discontinuation of Pristiq should be considered.

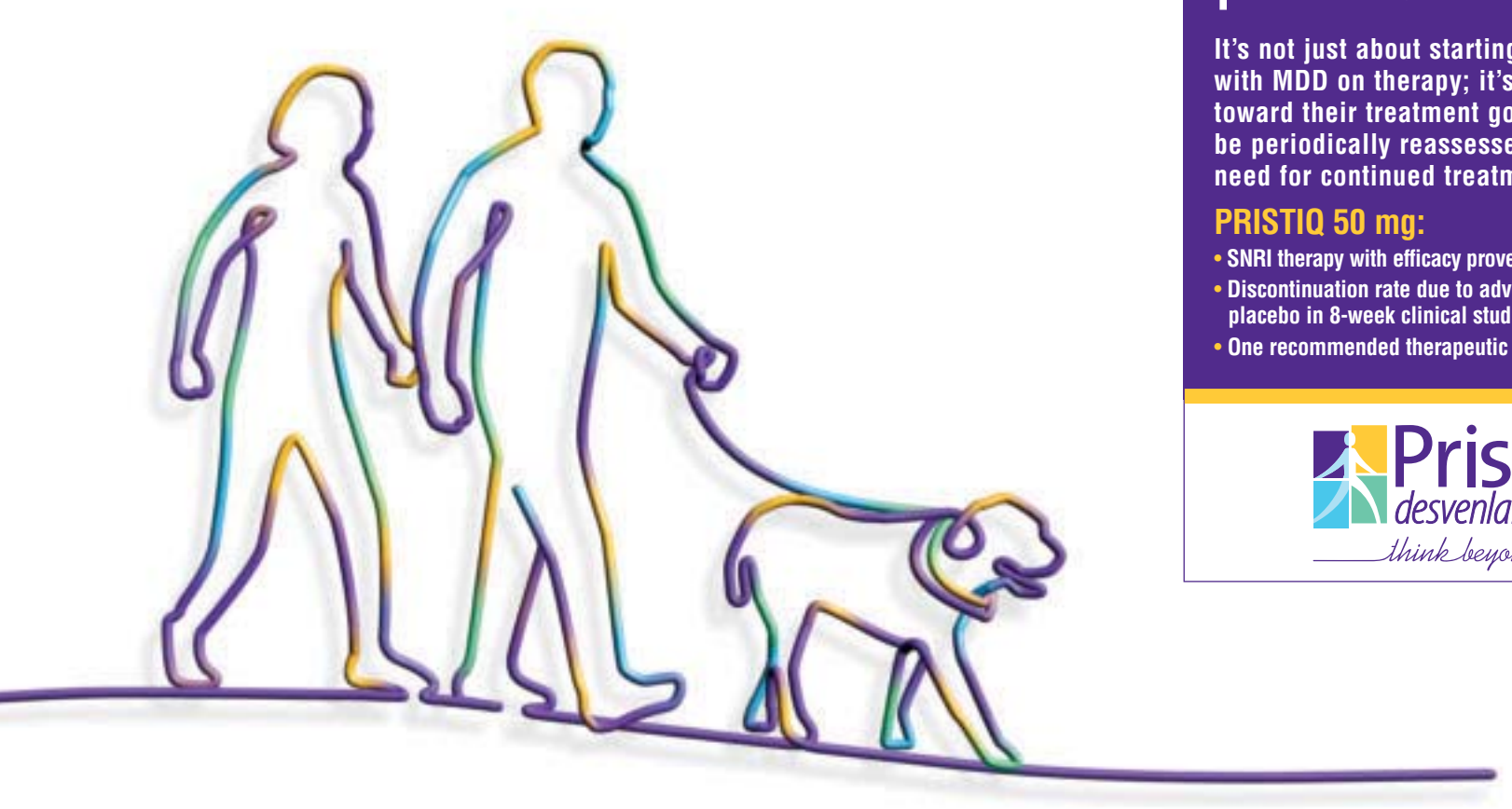
ADVERSE REACTIONS: Clinical Studies Experience: The most commonly observed adverse reactions in Pristiq-treated MDD patients in short-term fixed-dose studies (incidence ≥5% and at least twice the rate of placebo in the 50- or 100-mg dose groups) were nausea, dizziness, insomnia, hyperhidrosis, constipation, somnolence, decreased appetite, anxiety, and specific male sexual function disorders. Adverse reactions reported as reasons for discontinuation of treatment- The most common adverse reactions leading to discontinuation in at least 2% of the Pristiq-treated patients in the short-term studies, up to 8 weeks, were nausea (4%); dizziness, headache and vomiting (2% each); in the long-term study, up to 9 months, the most common was vomiting (2%). Common adverse reactions in placebo-controlled MDD studies- Table 3 in full PI shows the incidence of common adverse reactions that occurred in ≥2% of Pristiq-treated MDD patients at any dose in the 8-week, placebo-controlled, fixed-dose, premarketing clinical studies. In general, the adverse reactions were most frequent in the first week of treatment. Cardiac disorders: Palpitations, Tachycardia, Blood pressure increased; Gastrointestinal disorders: Nausea, Dry mouth, Diarrhea, Constipation, Vomiting; General disorders and administration site conditions: Fatigue, Chills, Feeling jittery, Asthenia; Metabolism and nutrition disorders: Decreased appetite, weight decreased; Nervous system disorders: Dizziness, Somnolence, Headache, Tremor, Paraesthesia, Disturbance in attention; Psychiatric Disorders: Insomnia, Anxiety, Nervousness, Irritability, Abnormal dreams; Renal and urinary disorders: Urinary hesitation; Respiratory, thoracic, and mediastinal disorders: Yawning; Skin and subcutaneous tissue disorders: Hyperhidrosis, Rash; Special Senses: Vision blurred; Mydriasis, Tinnitus, Dysgeusia; Vascular Disorders: Hot flush. Sexual function adverse reactions-Table 4 shows the incidence of sexual function adverse reactions that occurred in ≥2% of Pristiq-treated MDD patients in any fixed-dose group (8-week, placebo-controlled, fixed and flexible-dose, premarketing clinical studies). Men Only: Anorgasmia, Libido decreased, Orgasm abnormal, Ejaculation delayed, Erectile dysfunction, Ejaculation disorder, Ejaculation failure, Sexual dysfunction; Women Only: Anorgasmia; Other adverse reactions observed in premarketing clinical studies: Other infrequent adverse reactions occurring at an incidence of <2% in MDD patients treated with Pristiq were: *Immune system disorders* – Hypersensitivity. *Investigations* – Weight increased, liver function test abnormal, blood prolactin increased. *Nervous system disorders* – Convulsion, syncope, extrapyramidal disorder. *Musculoskeletal and connective tissue disorders* – Musculoskeletal stiffness. *Psychiatric disorders* – Depersonalization, hypomania. *Respiratory, thoracic and mediastinal disorders* – Epistaxis. *Vascular disorders* – Orthostatic hypotension. In clinical studies, there were uncommon reports of ischemic cardiac adverse events, including myocardial ischemia, myocardial infarction, and coronary occlusion requiring revascularization; these patients had multiple underlying cardiac risk factors. More patients experienced these events during Pristiq treatment as compared to placebo [*see Warnings and Precautions (5.7)*]. Discontinuation events-Adverse events reported in association with abrupt discontinuation, dose reduction or tapering of treatment in MDD clinical studies at a rate of ≥5% include dizziness, nausea, headache, irritability, insomnia, diarrhea, anxiety, abnormal dreams, fatigue, and hyperhidrosis. In general, discontinuation events occurred more frequently with longer duration of therapy [*see Dosage and Administration (2.4) and Warnings and Precautions (5.9) in full prescribing information*]. Laboratory, ECG and vital sign changes observed in MDD clinical studies-The following changes were observed in placebo-controlled, short-term, premarketing MDD studies with Pristiq. *Lipids*-Elevations in fasting serum total cholesterol, LDL (low-density lipoprotein) cholesterol, and triglycerides occurred in the controlled studies. Some of these abnormalities were considered potentially clinically significant [*see Warnings and Precautions (5.8)*]. *Proteinuria*-Proteinuria, greater than or equal to trace, was observed in the fixed-dose controlled studies (see Table 6 in full prescribing information). This proteinuria was not associated with increases in BUN or creatinine and was generally transient. *ECG changes*-Electrocardiograms were obtained from 1,492 Pristiq-treated patients with major depressive disorder and 984 placebo-treated patients in clinical studies lasting up to 8 weeks. No clinically relevant differences were observed between Pristiq-treated and placebo-treated patients for QT, QTc, PR, and QRS intervals. In a thorough QTc study with prospectively determined criteria, desvenlafaxine did not cause QT prolongation. No difference was observed between placebo and desvenlafaxine treatments for the QRS interval. *Vital sign changes*-Table 7 summarizes the changes that were observed in placebo-controlled, short-term, premarketing studies with Pristiq in patients with MDD (doses 50 to 400 mg). Relative to placebo, Pristiq was associated with mean increase of up to 2.1 mm Hg in systolic blood pressure, 2.3 mm Hg in diastolic blood pressure, and 4.1 bpm with supine pulse. At the final on-therapy assessment in the 6-month, double-blind, placebo-controlled phase of a long-term study in patients who had responded to Pristiq during the initial 12-week, open-label phase, there was no statistical difference in mean weight gain between Pristiq- and placebo-treated patients. *Orthostatic hypotension*- In the short-term, placebo-controlled clinical studies with doses of 50-400 mg, systolic orthostatic hypotension (decrease ≥30 mm Hg from supine to standing position) occurred more frequently in patients ≥65 years of age receiving Pristiq (8.0%, 7/87) versus placebo (2.5%, 1/40), compared to patients <65 years of age receiving Pristiq (0.9%, 18/1,937) versus placebo (0.7%, 8/1,218). **Adverse Reactions Identified During Post-Approval Use-** The following adverse reaction has been identified during post-approval use of Pristiq. Because post-approval reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure: *Skin and subcutaneous tissue disorders* – Angioedema. **DRUG INTERACTIONS: Central Nervous System (CNS)-Active Agents-**The risk of using Pristiq in combination with other CNS-active drugs has not been systematically evaluated. Consequently, caution is advised when Pristiq is taken in combination with other CNS-active drugs [*see Warnings and Precautions (5.13)*]. **Monoamine Oxidase Inhibitors (MAOIs)-** Adverse reactions, some of which were serious, have been reported in patients who have recently been discontinued from a monoamine oxidase inhibitor (MAOI) and started on antidepressants with pharmacological properties similar to Pristiq (SNRIs or SSRIs), or who have recently had SNRI or SSRI therapy discontinued prior to initiation of an MAOI [*see Contraindications (4.2)*]. **Serotonergic Drugs-** Based on the mechanism of action of Pristiq and the potential for serotonin syndrome, caution is advised when Pristiq is coadministered with other drugs that may affect the serotonergic neurotransmitter systems [*see Warnings and Precautions (5.2)*]. **Drugs that Interfere with Hemostasis (eg, NSAIDs, Aspirin, and Warfarin)-** Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies of case-control and cohort design have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. These studies have also shown that concurrent use of an NSAID or aspirin may potentiate this risk of bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when SSRIs and SNRIs are coadministered with warfarin. Patients receiving warfarin therapy should be carefully monitored when Pristiq is initiated or discontinued. **Ethanol-** A clinical study has shown that desvenlafaxine does not increase the impairment of mental and motor skills caused by ethanol. However, as with all CNS-active drugs, patients should be advised to avoid alcohol consumption while taking Pristiq. **Potential for Other Drugs to Affect Desvenlafaxine-**Inhibitors of CYP3A4 (ketoconazole)- CYP3A4 is a minor pathway for the metabolism of Pristiq. Concomitant use of Pristiq with potent inhibitors of CYP3A4 may result in higher concentrations of Pristiq. Inhibitors of other CYP enzymes- Based on *in vitro* data, drugs that inhibit CYP isozymes 1A1, 1A2, 2A6, 2D6, 2C8, 2C9, 2C19, and 2E1 are not expected to have significant impact on the pharmacokinetic profile of Pristiq. **Potential for Desvenlafaxine to Affect Other Drugs-** Drugs metabolized by CYP2D6 (desipramine)- *In vitro* studies showed minimal inhibitory effect of desvenlafaxine on CYP2D6. Clinical studies have shown that desvenlafaxine does not have a clinically relevant effect on CYP2D6 metabolism at the dose of 100 mg daily. Concomitant use of desvenlafaxine with a drug metabolized by CYP2D6 can result in higher concentrations of that drug. Drugs metabolized by CYP3A4 (midazolam)- *In vitro*, desvenlafaxine does not inhibit or induce the CYP3A4 isozyme. Concomitant use of Pristiq with a drug metabolized by CYP3A4 can result in lower exposures to that drug. Drugs metabolized by CYP1A2, 2A6, 2C8, 2C9 and 2C19- *In vitro*, desvenlafaxine does not inhibit CYP1A2, 2A6, 2C8, 2C9, and 2C19 isozymes and would not be expected to affect the pharmacokinetics of drugs that are metabolized by these CYP isozymes. **P-glycoprotein Transporter-** *In vitro*, desvenlafaxine is not a substrate or an inhibitor for the P-glycoprotein transporter. The pharmacokinetics of Pristiq are unlikely to be affected by drugs that inhibit the P-glycoprotein transporter, and desvenlafaxine is not likely to affect the pharmacokinetics of drugs that are substrates of the P-glycoprotein transporter. **Electroconvulsive Therapy-** There are no clinical data establishing the risks and/or benefits of electroconvulsive therapy combined with Pristiq treatment. **USE IN SPECIFIC POPULATIONS: Pregnancy-** Patients should be advised to notify their physician if they become pregnant or intend to become pregnant during therapy. Teratogenic effects– Pregnancy Category C- There are no adequate and well-controlled studies of Pristiq in pregnant women. Therefore, Pristiq should be used during pregnancy only if the potential benefits justify the potential risks. Non-teratogenic effects- Neonates exposed to SNRIs (Serotonin and Norepinephrine Reuptake Inhibitors), or SSRIs (Selective Serotonin Reuptake Inhibitors), late in the third trimester have developed complications requiring prolonged hospitalization, respiratory support, and tube feeding. Such complications can arise immediately upon delivery. Reported clinical findings have included respiratory distress, cyanosis, apnea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycemia, hypotonia, hypertonia, hyperreflexia, tremor, jitteriness, irritability, and constant crying. These features are consistent with either a direct toxic effect of SSRIs and SNRIs or, possibly, a drug discontinuation syndrome. It should be noted that, in some cases, the clinical picture is consistent with serotonin syndrome [*see Warnings and Precautions (5.2)*]. When treating a pregnant woman with Pristiq during the third trimester, the physician should carefully consider the potential risks and benefits of treatment [*see Dosage and Administration (2.2)*]. **Labor and Delivery-** The effect of Pristiq on labor and delivery in humans is unknown. Pristiq should be used during labor and delivery only if the potential benefits justify the potential risks. **Nursing Mothers-** Desvenlafaxine (O-desmethylvenlafaxine) is excreted in human milk. Because of the potential for serious adverse reactions in nursing infants from Pristiq, a decision should be made whether or not to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. Only administer Pristiq to breastfeeding women if the expected benefits outweigh any possible risk. **Pediatric Use-** Safety and effectiveness in the pediatric population have not been established [*see Box Warning and Warnings and Precautions (5.1)*]. Anyone considering the use of Pristiq in a child or adolescent must balance the potential risks with the clinical need. **Geriatric Use-** Of the 3,292 patients in clinical studies with Pristiq, 5% were 65 years of age or older. No overall differences in safety or efficacy were observed between these patients and younger patients; however, in the short-term, placebo-controlled studies, there was a higher incidence of systolic orthostatic hypotension in patients ≥65 years of age compared to patients <65 years of age treated with Pristiq [*see Adverse Reactions (6)*]. For elderly patients, possible reduced renal clearance of desvenlafaxine should be considered when determining dose [*see Dosage and Administration (2.2) and Clinical Pharmacology (12.6)*]. If Pristiq is poorly tolerated, every other day dosing can be considered. SSRIs and SNRIs, including Pristiq, have been associated with cases of clinically significant hyponatremia in elderly patients, who may be at greater risk for this adverse event [*see Warnings and Precautions (5.12)*]. Greater sensitivity of some older individuals cannot be ruled out. **Renal Impairment-** In subjects with renal impairment the clearance of Pristiq was decreased. In subjects with severe renal impairment (24-hr CrCl < 30 mL/min) and end-stage renal disease, elimination half-lives were significantly prolonged, increasing exposures to Pristiq; therefore, dosage adjustment is recommended in these patients [*see Dosage and Administration (2.2) and Clinical Pharmacology (12.6) in the full prescribing information*]. **Hepatic Impairment-** The mean $t_{1/2}$ changed from approximately 10 hours in healthy subjects and subjects with mild hepatic impairment to 13 and 14 hours in moderate and severe hepatic impairment, respectively. The recommended dose in patients with hepatic impairment is 50 mg/day. Dose escalation above 100 mg/day is not recommended [*see Clinical Pharmacology (12.6)*].

OVERDOSAGE: Human Experience with Overdosage- There is limited clinical experience with desvenlafaxine succinate overdosage in humans. In premarketing clinical studies, no cases of fatal acute overdose of desvenlafaxine were reported. The adverse reactions reported within 5 days of an overdose >600 mg that were possibly related to Pristiq included headache, vomiting, agitation, dizziness, nausea, constipation, diarrhea, dry mouth, paresthesia, and tachycardia. Desvenlafaxine (Pristiq) is the major active metabolite of venlafaxine. Overdose experience reported with venlafaxine (the parent drug of Pristiq) is presented below; the identical information can be found in the *Overdosage* section of the venlafaxine package insert. In postmarketing experience, overdose with venlafaxine (the parent drug of Pristiq) has occurred predominantly in combination with alcohol and/or other drugs. The most commonly reported events in overdosage include tachycardia, changes in level of consciousness (ranging from somnolence to coma), mydriasis, seizures, and vomiting. Electrocardiogram changes (eg, prolongation of QT interval, bundle branch block, QRS prolongation), sinus and ventricular tachycardia, bradycardia, hypotension, rhabdomyolysis, vertigo, liver necrosis, serotonin syndrome, and death have been reported. Published retrospective studies report that venlafaxine overdosage may be associated with an increased risk of fatal outcomes compared to that observed with SSRI antidepressant products, but lower than that for tricyclic antidepressants. Epidemiological studies have shown that venlafaxine-treated patients have a higher pre-existing burden of suicide risk factors than SSRI-treated patients. The extent to which the finding of an increased risk of fatal outcomes can be attributed to the toxicity of venlafaxine in overdosage, as opposed to some characteristic(s) of venlafaxine-treated patients, is not clear. Prescriptions for Pristiq should be written for the smallest quantity of tablets consistent with good patient management, in order to reduce the risk of overdose. **Management of Overdosage-** Treatment should consist of those general measures employed in the management of overdosage with any SSRI/SNRI. Ensure an adequate airway, oxygenation, and ventilation. Monitor cardiac rhythm and vital signs. General supportive and symptomatic measures are also recommended. Gastric lavage with a large-bore orogastric tube with appropriate airway protection, if needed, may be indicated if performed soon after ingestion or in symptomatic patients. Activated charcoal should be administered. Induction of emesis is not recommended. Because of the moderate volume of distribution of this drug, forced diuresis, dialysis, hemoperfusion, and exchange transfusion are unlikely to be of benefit. No specific antidotes for desvenlafaxine are known. In managing an overdose, consider the possibility of multiple drug involvement. The physician should consider contacting a poison control center for additional information on the treatment of any overdose. Telephone numbers for certified poison control centers are listed in the Physicians Desk Reference (PDR®).

This brief summary is based on Pristiq Prescribing Information W10529C009, revised September 2009.

FOR MAJOR DEPRESSIVE DISORDER

Help your patients



on a path forward with proven SNRI therapy

It's not just about starting your adult patients with MDD on therapy; it's about helping them toward their treatment goals. Patients should be periodically reassessed to determine the need for continued treatment.[1]

PRISTIQ 50 mg:

- **SNRI therapy with efficacy proven in 8-week clinical studies**
- **Discontinuation rate due to adverse events comparable to placebo in 8-week clinical studies**
- **One recommended therapeutic dose from the start[1]**

Pristiq® desvenlafaxine 50 mg

think beyond start™

Important Treatment Considerations for PRISTIQ

PRISTIQ is indicated for the treatment of major depressive disorder in adults.

WARNING: SUICIDALITY AND ANTIDEPRESSANT DRUGS

Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of Major Depressive Disorder (MDD) and other psychiatric disorders. Anyone considering the use of PRISTIQ or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. PRISTIQ is not approved for use in pediatric patients.

Contraindications

- PRISTIQ is contraindicated in patients with a known hypersensitivity to PRISTIQ or venlafaxine.
- PRISTIQ must not be used concomitantly with an MAOI or within 14 days of stopping an MAOI. Allow 7 days after stopping PRISTIQ before starting an MAOI.

Warnings and Precautions

- **All patients treated with antidepressants should be monitored appropriately and observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the first few months of treatment and when changing the dose.** Consider changing the therapeutic regimen, including possibly discontinuing the medication, in patients whose depression is persistently worse or includes symptoms of anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia, hypomania, mania, or suicidality that are severe, abrupt in onset, or were not part of the patient's presenting symptoms. **Families and caregivers of patients being treated with antidepressants should be alerted about the need to monitor patients.**
- Development of a potentially life-threatening serotonin syndrome or Neuroleptic Malignant Syndrome-like reactions have been reported with SNRIs and SSRIs alone, including PRISTIQ treatment, but particularly with concomitant use of serotonergic drugs, including triptans, with drugs that impair the metabolism of serotonin (including MAOIs), or with antipsychotics or other dopamine antagonists. If concomitant use with a triptan is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases. Concomitant use of PRISTIQ with serotonin precursors is not recommended.
- Patients receiving PRISTIQ should have regular monitoring of blood pressure since increases in blood pressure were observed in clinical studies. Pre-existing hypertension should be controlled before starting PRISTIQ. Caution should be exercised in treating patients with pre-existing hypertension or other underlying conditions that might be compromised by increases in blood pressure. Cases of elevated blood pressure requiring immediate treatment have been reported. For patients who experience a sustained increase in blood pressure, either dose reduction or discontinuation should be considered.
- SSRIs and SNRIs, including PRISTIQ, may increase the risk of bleeding events. Concomitant use of aspirin, NSAIDs, warfarin, and other anticoagulants may add to this risk.
- Mydriasis has been reported in association with PRISTIQ; therefore, patients with raised intraocular pressure or those at risk of acute narrow-angle glaucoma (angle-closure glaucoma) should be monitored.
- PRISTIQ is not approved for use in bipolar depression. Prior to initiating treatment with an antidepressant, patients should be adequately screened to determine the risk of bipolar disorder.
- As with all antidepressants, PRISTIQ should be used cautiously in patients with a history or family history of mania or hypomania, or with a history of seizure disorder.
- Caution is advised in administering PRISTIQ to patients with cardiovascular, cerebrovascular, or lipid metabolism disorders. Increases in blood pressure and small increases in heart rate were observed in clinical studies with PRISTIQ. PRISTIQ has not been evaluated systematically in patients with a recent history of myocardial infarction, unstable heart disease, uncontrolled hypertension, or cerebrovascular disease.
- Dose-related elevations in fasting serum total cholesterol, LDL (low density lipoprotein) cholesterol, and triglycerides were observed in clinical studies. Measurement of serum lipids should be considered during PRISTIQ treatment.
- On discontinuation, adverse events, some of which may be serious, have been reported with PRISTIQ and other SSRIs and SNRIs. Abrupt discontinuation of PRISTIQ has been associated with the appearance of new symptoms. Patients should be monitored for symptoms when discontinuing treatment. A gradual reduction in dose rather than abrupt cessation is recommended whenever possible.
- The recommended dose in patients with severe renal impairment or end-stage renal disease (ESRD) is 50 mg every other day. The dose should not be escalated in patients with moderate or severe renal impairment or ESRD.
- Products containing desvenlafaxine and products containing venlafaxine should not be used concomitantly with PRISTIQ.
- Hyponatremia may occur as a result of treatment with SSRIs and SNRIs, including PRISTIQ. Discontinuation of PRISTIQ should be considered in patients with symptomatic hyponatremia.
- Interstitial lung disease and eosinophilic pneumonia associated with venlafaxine (the parent drug of PRISTIQ) therapy have been rarely reported.

Adverse Reactions

- The most commonly observed adverse reactions in patients taking PRISTIQ vs placebo for MDD in short-term fixed-dose premarketing studies (incidence ≥5% and ≥2x the rate of placebo in the 50-mg dose group) were nausea (22% vs 10%), dizziness (13% vs 5%), hyperhidrosis (10% vs 4%), constipation (9% vs 4%), and decreased appetite (5% vs 2%).

Reference: 1. Pristiq® (desvenlafaxine) Prescribing Information, Wyeth Pharmaceuticals Inc.

Please see brief summary of Prescribing Information on adjacent page.

For more information on PRISTIQ, please visit **www.PristiqHCP.com**.

Pristiq®
EXTENDED-RELEASE TABLETS

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