



birth, there were morphological changes in the ovary (including the presence of multi-oocyte follicles) that were associated with a 35% incidence of uterine tumors in animals at 18 months of age.

"These animals had premature reproductive senescence," said Newbold. "Their ovaries were malformed and not completely functional."

According to one report, the daily exposure of human infants to isoflavones in soy-based infant formulas is 6 to 11 times higher (based on body weight) than the dose that produces hormonal effects in adults consuming soy foods (Setchell et al. *Lancet*. 1997; 350:23-27). But for now, said Newbold, researchers don't know how animal findings about genistein translate to the human population. "I think we

have to be cautious," she added. "Humans are exposed to a number of estrogenic or endocrine-disrupting compounds and it makes sense to decrease those exposures as much as possible."

INDUSTRY RESPONSE

In the aftermath of the release of Swan's study of phthalates, the American Chemistry Council's Phthalate Esters Panel issued a statement asserting, "Initial analyses indicate that the [Swan] study has many weaknesses, suggesting that the study may not stand up under rigid scientific scrutiny. The authors themselves stated that the results need to be validated."

Meanwhile, a Web site sponsored by the Bisphenol A Global Industry Group of the American Plastics Council high-

lights a 2004 review by a panel of researchers convened by the Harvard Center for Risk Analysis—and funded by the American Plastics Council—in which the panel "found no consistent affirmative evidence of low-dose BPA effects for any endpoint."

Even so, a bill has been introduced in the California state legislature (AB 319) by Assembly member Wilma Chan (D, Oakland) that would ban the use of BPA and phthalates in toys and child-care products designed for infants and children younger than 3 years of age. Hearings on the bill are pending.

"The EPA [Environmental Protection Agency] is struggling with the idea of what levels are acceptable for each of these compounds," said Newbold. "Everybody is taking them seriously—but we need a lot more research." □

Mental Illness Takes Heavy Toll on Youth

Bridget M. Kuehn

A NEW SURVEY OF MENTAL illness in the United States indicates that mental illnesses tend to strike early in life and delays in treatment leave affected individuals vulnerable to debilitating symptoms during their most productive years.

Half of all individuals who have a mental illness during their lifetime report that the onset of disease occurred by age 14 years and three fourths by age 24 years, according to the National Institute of Mental Health (NIMH) National Comorbidity Survey Replication. The nationally representative, face-to-face household survey of more than 9000 individuals aged 18 years or older, conducted between February 2001 and April 2003, is a follow-up to the 1990 National Comorbidity Study. Four articles detailing the latest findings were published in the June issue of the *Archives of General Psychiatry*.

"[Mental illnesses] really are the chronic disorders of the young," said

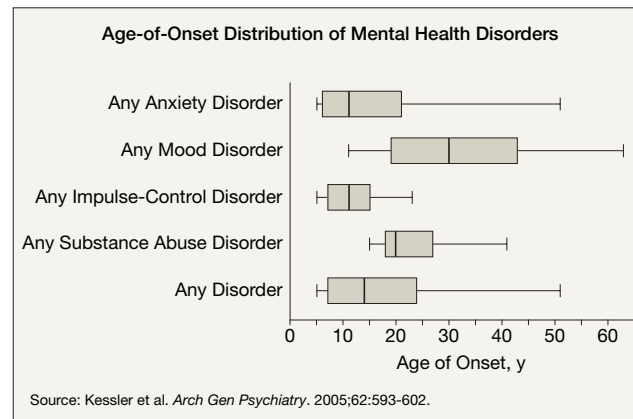
Thomas R. Insel, MD, director of the NIMH in Bethesda, Md.

The survey looked at the prevalence of common mental illnesses, such as mood and anxiety disorders, but did not measure other less common illnesses such as autism. It also did not include individuals who were homeless or institutionalized.

The study bolstered previous findings that mental illnesses are prevalent. It found that about half of all in-

dividuals in the United States will have a mental illness in their lifetime and about one fourth will have a mental illness in a given year (Kessler et al. *Arch Gen Psychiatry*. 2005;62:593-602, 617-627). However, Kathleen R. Merikangas, PhD, senior investigator at the NIMH, noted that most cases in a given year were mild and did not require professional intervention.

"It will be the task of the next decade to discriminate between those who



Data from the National Comorbidity Survey Replication reveal the early age of onset of many mental illnesses, particularly anxiety and impulse-control disorders. The boxes show the median and interquartile range for age of onset, and the whiskers indicate the 5th and 95th percentiles.



may progress to more severe forms of these disorders and those for whom these symptoms may resolve on their own," Merikangas said.

YOUTH HARD HIT

Those who did experience severe mental illness, about 6% in the previous 12 months, reported a mean of nearly 90 days during which they were unable to carry out normal daily activities because of mental illness or substance abuse problems. The findings show that all types of mental disorders can have a severe impact on an individual's life, said Merikangas, not only those mental illnesses that have traditionally been viewed as severe, such as schizophrenia, bipolar disorder, and drug dependence.

"We found people with anxiety disorders, such as social anxiety disorder and major depression, can be so disabled they cannot function in their major life role," she said.

While the majority of individuals with mental illnesses during their lifetime will eventually receive treatment, there may be long delays between disease onset and intervention. The survey showed delays ranging from 6 to 8 years for treatment for mood disorders and 9 to 23 years for anxiety disorders (Wang et al. *Arch Gen Psychiatry*. 2005;62:603-613).

Young people are the hardest hit by treatment delays. Early age of onset was associated with both failure to make initial treatment contact and with treatment delays, according to the survey. Ronald C. Kessler, PhD, professor of health care policy at Harvard Medical School in Boston, said young people who have an untreated mental illness may suffer debilitating symptoms during their most productive years, compromising educational attainment, and career and family building. Moreover, many may develop more severe illness or comorbidities such as substance abuse.

Although the impact on a person's life of serious mental disorders is comparable with that of serious somatic disorders, such as cardiovascular disease

and diabetes, the latter usually emerge later in life and may have less impact on society than early-onset mental disorders, Kessler said.

COMMON DISEASES

The most prevalent disorders reported over an individual's lifetime in the study were major depressive disorder (16.6%), alcohol abuse (13.3%), specific phobia (12.5%), and social phobia (12.1%). The most prevalent classes of disorders over the course of a year were anxiety disorders (18.1%), mood disorders (9.5%), impulse control disorders (8.9%), and substance abuse disorders (3.8%). Insel and Wayne S. Fenton, MD, deputy director of clinical affairs at the NIMH, said in a commentary accompanying the four articles that the relatively high rate of impulse control disorders over a 12-month period was surprising because many previous epidemiological studies have not examined this class of disorders. They also noted that the survey revealed that for a higher proportion of individuals with impulse control disorders, their condition was rated "serious" compared with individuals with anxiety or substance abuse disorders.

Consistent with previous findings, the survey also found high rates of comorbid mental disorders. Slightly less than half of individuals with a mental illness in a given year had more than one mental disorder; of those individuals, 22% had two conditions and 23% had three or more conditions.

Merikangas noted that individuals with depression or anxiety disorders often have comorbid substance abuse disorders, particularly those with the most severe illness. But these individuals may not get appropriate care for both conditions because there are few treatment programs that integrate treatment for substance abuse with treatment for comorbid mental disorders.

"Our findings highlight the importance of integrating services for people with comorbid mental and substance use disorders—treating the people rather than disorders," she said.

SUICIDE TRENDS

Despite growing numbers of patients receiving treatment, the number of individuals reporting suicidal thoughts, plans, gestures, or attempts during the previous year has remained steady since the last survey a decade ago. However, completed suicides decreased by 6% during the period. Kessler and his colleagues reported these results in a separate article in the May 25 issue of *JAMA* (Kessler et al. *JAMA*. 2005;293:2487-2495).

The lack of decrease in suicide attempts despite increased treatment efforts may indicate that such interventions are not occurring early enough to prevent attempts or that the treatments were ineffective, according to the researchers. Improving access to treatments and encouraging individuals who have suicidal thoughts to receive timely treatment may help, the researchers suggested. Better interventions also must be identified and implemented.

Those at highest risk of suicide-related behaviors were young people, women, individuals with low education, and individuals with unstable employment or relationships. The same highest-risk groups were found in the previous survey, suggesting greater efforts targeting these groups are necessary, according to the researchers.

Of the individuals who reported suicidal thoughts, plans, gestures, or attempts, at least 80% had one or more mental disorder in the previous year. Major depression was the most common disorder, affecting 37% to 51% of these individuals in the most recent survey; anxiety disorders comprised the most common class of disorders, affecting 52% to 81% of these individuals.

BETTER INTERVENTIONS

Steady gains in the number of individuals with mental illnesses receiving treatment have been recorded since the 1980s, when the Epidemiologic Catchment Area Study found that just 19% of respondents who had a mental illness received any treatment in the previous year. Since then, the 1990 National Comorbidity Survey found 25%



of respondents with a mental illness received treatment in the previous year and the most recent survey found 41% of individuals with a mental illness received treatment during the past year (Wang et al. *Arch Gen Psychiatry*. 2005; 62:629-640). And patients, particularly those with mood disorders, are now receiving treatment more quickly than in the past.

Philip S. Wang, MD, DrPH, assistant professor of health care policy at Harvard Medical School, attributed these advances to efforts by the NIMH and others to destigmatize mental illness and encourage individuals to seek care quickly. But he noted that there is still considerable work to be done: Only one third of individuals with mental illnesses in the past year who were treated received care that was classified as minimally adequate. Adequacy was defined by national standards for dose, intensity of treatment, duration of treatment, and the appropriateness of the selected treatment for the individual.

The growing acceptance of complementary and alternative medicine, despite unproven safety and effectiveness, accounts for some of the individuals receiving substandard care. One third of the individuals who were treated received a complimentary or alternative therapy, according to the survey. In addition, growing numbers of patients with mental illnesses are being treated in the primary care sector. According to the survey, patients who were treated by a mental health specialist were most likely to receive minimally adequate treatment. Those receiving primary care treatment were less likely to receive minimally adequate care.

But Wang was quick to point out that there are complex factors that may be outside the physician's control that can affect the quality of care in the primary care setting. For instance, individuals with mental illnesses seeing a primary care physician may present with such vague symptoms as difficulty sleeping, low energy, and various physical symptoms, while those consulting a mental health specialist are

more likely to present with changes in mood or higher levels of anxiety. In addition, said Wang, primary care physicians may also be treating the individual for various physical conditions. "A specialist focuses on mental health; they don't have as many competing demands," he noted.

Patients visiting primary care physicians may also be less committed than those seeing a specialist to receiving treatment for mental health and may prematurely end treatment. Richard K. Nakamura, PhD, deputy director of the NIMH, said that more fast-acting medications must be developed because individuals may stop treatment before the 6 to 8 weeks necessary for many currently available drugs to work.

Patients must be made aware that effective treatments are available and should take a more active role in seeking them out, Kessler said. Physicians also can improve adherence to therapy by talking to patients about adverse effects and monitoring them closely.

Collaborative management by primary care physicians and mental health

specialists has been demonstrated to improve adherence to antidepressant regimens in patients with depression (Katon et al. *JAMA*. 1995;273:1026-1031). But greater efforts must be made to find the most cost-effective ways to implement such models, Wang said.

Treating mental illness in children and adolescents also poses special challenges. "They are probably going to need an adult to recognize and . . . get them to treatment," Wang said.

There are also many unanswered questions about treating this population. "A lot of the people who have mild mental illnesses are young people who become severe over time," Kessler said. "Is good treatment with mild cases going to save us money over time? We just don't know."

The researchers called for more public sector involvement. "We urge policy makers to provide support for research that identifies the roots of these disorders and the most effective methods for prevention and intervention to reduce their burden on American youth," Merikangas said. □

Genetic Information: How Much Can Patients Handle?

Bridget M. Kuehn

GENOME-WIDE SCANS FOR disease-causing genes have been touted by some proponents as the future of medicine. But will the vast and potentially ambiguous data they provide be too much for patients and their physicians to handle?

To begin to answer this and other questions about how to translate genomics into clinical practice, the National Human Genome Research Institute is embarking on a pilot study. The effort, which is still in the planning stages, will involve enlisting healthy adult volunteers and sequencing a panel of 100 to 300 genes that have been as-

sociated with various disease phenotypes. Participants will also undergo a physical examination and a battery of tests. The collected information will be used to inform the individuals about potential genetic risk factors in their genome.

Leslie G. Biesecker, MD, a senior investigator at the National Human Genome Research Institute, said the study will have three components. One component will be developing the technology and tools necessary to scan and analyze individual genomes. The study will also examine how to best obtain participant consent and how these volunteers will respond to receiving large amounts of data about potential health