

to balance the increased short-term risk—an extra 2 per 100 patients who will either attempt suicide or exhibit suicidality because of the use of an SSRI—and the potentially decreased long-term risk of suicidal thoughts and behavior attributable to depression, Dr. Ryan said.

Clinicians are left with the dilemma of what to do about the next depressed child to come into the office: Pick an SSRI alone, choose psychotherapy alone, or combine an SSRI with psychotherapy. “I think we’re going to have a rich debate on that,” he said.

When considering an SSRI in a pediatric patient, it’s important to inform the family of potential risks and benefits and follow the FDA’s monitoring suggestions. “I think also that we need to advocate for more studies. I think we’re all scared that we won’t get any more data on this question,” he said.

Mark Olfson, M.D., of Columbia University, New York, is not optimistic about the prospects for this type of research: “For the foreseeable future, I believe the pharmaceutical industry is going to view this whole area as radioactive and stay away from it.”

Future research should focus on which subgroups of patients are at higher risk and when in the course of treatment. One strategy would be to monitor depressed children closely for short periods of SSRI therapy, looking for somatic subjective

dysphoria, changes in attention, changes in impulsivity, or other indicators of suicidality, Dr. Olfson said.

Dr. Ryan said that he sees a need for longer-term studies.

The long-term effects of the treatment of depression have not been studied. It may be that effective drug therapy for depression may decrease the long-term risk of suicide, but there is no clear evidence yet, he said.

It’s also important to look at the bigger public health picture, Dr. Olfson said. “We need to be clear about the distinctions between suicidal ideation and the suicide attempts that were the subject of the randomized controlled trials analyses and actual suicide or serial suicide attempts that we encounter in practice.”

The rates of suicidal ideation and suicide attempts in a normal adolescent popula-

tion also need to be considered. According to the Centers for Disease Control and Prevention’s 2003 National Youth Risk Behavior Survey, 16.9% of normal adolescents in grades 9-12 had seriously considered attempting suicide in the previous 12 months and 8.5% had attempted suicide at least once in that time period, he noted.

“Those numbers stand in very sharp contrast to the comparatively small number of kids who show up in our emergency rooms and hospitals following actual suicide attempts,” Dr. Olfson said. “It’s my own belief—that, in fact, the recent increase in the use of these medications in kids has actually saved lives.” ■

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Genetic Defect May Raise Risk of Depression

A recently discovered genetic mutation that causes dysfunction in the synthesizing of serotonin might explain why some depressed patients are resistant to drug treatment, researchers say.

Xiaodong Zhang, M.D., and colleagues at Duke University, Durham, N.C., screened 87 adults with unipolar major depression, 60 adults with bipolar disorder, and 219 controls for a mutant allele known as 1463A in an enzyme that helps direct synthesis of serotonin known as human tryptophan hydroxylase 2 (hTPH2).

The gene mutation occurred in 10% of patients with major depression, compared with 1% of the controls. None of the individuals with bipolar disorder had the mutation (Neuron 2005;45:11-6).

Seven of the nine depression patients with the hTPH2 mutation had a family history of mental illness or drug and alcohol abuse, six had either attempted suicide or shown suicidal behavior, and four demonstrated generalized anxiety symptoms. In addition, seven of the patients with the mutation showed a lack of responsiveness to an SSRI, and the other two responded only to high doses.

Communication among neurons may stall if serotonin levels are low, as they often are in people with depression, anxiety, posttraumatic stress disorder, and even attention-deficit hyperactivity disorder. Additional larger studies are needed to confirm these findings and explore links between genetics and depression.

—Heidi Splete

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