Biomedical Update:

Respiratory symptoms: drug side effect

Doctors are familiar with the most common side effect of neuroleptic drugs: tardive dyskinesia (TD), or involuntary movements of the tongue, mouth, and limbs. But two doctors suggest that "respiratory dyskinesia"—a potentially life-threatening breathing disorder—also occurs in a surprising number of patients taking these drugs.

"Very few primary care physicians or subspecialists recognize and understand respiratory dyskinesia," Michael Rich and Steven Radwany say. "When reviewing tardive dyskinesia, textbooks and articles either fail to discuss this respiratory variant or dismiss it as rare. Unfortunately for those afflicted, respiratory dyskinesia is not rare."

Symptoms of respiratory dyskinesia include gasping, grunting, and labored breathing. Symptoms become worse when an individual is anxious or in pain, and disappear during sleep.

Rich and Radwany say studies suggest that as many as 16 percent of individuals with TD also suffer from respiratory dyskinesia. Although most cases are mild, they say, severe symptoms can cause cyanosis (lack of oxygen) or pneumonia. Based on the available research data, they estimate that more than 100,000 individuals in the U.S. may suffer from the disorder.

The researchers advise doctors to consider the possibility of respiratory dyskinesia in patients taking neuroleptic drugs who have tardive dyskinesia and experience difficulty breathing, and whose blood gas tests reveal respiratory alkalosis.

"Rabbit syndrome" reported

Israeli researchers report on another side effect of neuroleptic drugs, known as "rabbit syndrome:" rapid, rhythmic movements which mimic the chewing of a rabbit, often accompanied by a popping sound made by the lips. While rabbit syndrome resembles tardive dyskinesia, Miguel Schwartz et al. say that differential diagnosis is important because "rabbit syndrome improves with anticholinergic medication, while in tardive dyskinesia this medication often aggravates the movements."

Schwartz et al. note that rabbit syndrome usually occurs in middle-aged or elderly patients, and does not involve dyskinesia of the tongue. They add that the syndrome is often misdiagnosed as drug-induced parkinsonism.

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"Respiratory dyskinesia: an underrecognized phenomenon," Michael .W. Rich and Steven M. Radwany, *Chest*, Vol. 105, No. 6, June 1994. Address not listed.

—and—

"Rabbit syndrome and tardive dyskinesia: two complications of chronic neuroleptic treatment," Miguel Schwartz, Boaz Weller, Marius Erdreich, and Benjamin Sharf; *Journal of Clinical Psychiatry*, 56:5, May 1995, p. 212. Address not listed.

Urgent! Research Help Needed

An outstanding international team of researchers in genetics has asked the help of the Autism Research Institute in locating several families which have autistic children as first cousins. If your family, or a family you know, has three autistic first cousins, please write to ARRI with the details.

PKU diet: how low is low enough?

Infants in the United States are routinely tested for PKU (phenylketonuria), a disorder in which the body cannot properly metabolize the amino acid phenylalanine. Left untreated, PKU can cause autism, hyperactivity, seizures, and severe mental retardation.

PKU is treated with a diet low in phenylalanine. Generally, physicians try to keep blood levels of the amino acid to below five times normal. (In untreated PKU, levels can rise to 10 to 20 times normal.) But recent research suggests that current dietary standards aren't stringent enough.

Julie Ann Miller reports that significant problems are occurring in some children with PKU, including learning disabilities, minor neurological problems, and emotional problems. In addition, children with PKU tend to have lower IQs than their siblings.

Miller notes that research by Adele Diamond et al., who studied PKU-affected children between the ages of six months and seven years, showed that children with the highest phenylalanine levels performed poorly on five tests of brain function (all involving the prefrontal cortex). Further research on rats, also by Diamond et al., linked even moderately elevated levels of phenylalanine to cognitive problems.

Diamond believes children with PKU should adhere to stricter diets than currently recommended, and that better testing is needed to detect neurological dysfunction in PKU-affected individuals.

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"Strictest diet avoids subtle detriments of PKU," Julie Ann Miller, *BioScience*, Vol. 45, No. 4, April 1995, pp. 244-245.

Gene study points toward 15, 21

The Amish communities of America and the royal families of Europe have something in common: each group, because of generations of intermarriage, has a high rate of certain genetic diseases (including muscular dystrophy among the Amish, and porphyria and hemophilia among the royals). Now researcher Ann B. Goodman is using a similar group to study the genetics of both autism and schizophrenia.

Goodman is studying Eastern European (Ashkenazi) Jews, who for many generations intermarried very little with other groups. In any group with a restricted gene pool, certain genetic diseases are more common than in the general population; in the case of Ashkenazi Jews, these include the neurological disorders Tay Sachs and amyotrophic lateral sclerosis (ALS), and a blood disorder known as Gaucher's Disease. Goodman theorizes that the increased prevalence of such neurological and bleeding disorders among Ashkenazim might be related to the group's higher than average rate of schizophrenia (and apparently a higher than average rate of autism as well).

Goodman's study revealed that among Ashkenazi subjects, "rates of ALS and bleeding disorders were significantly increased among relatives of schizophrenic and autistic [subjects], compared to relatives of normal [subjects]." The risk of developing ALS increased 55-fold for relatives in families with autistic members, and 265-fold for relatives in families with schizophrenic members. Rates of leukemia, lymphoma and Hodgkins's disease were also elevated in families with autistic or schizophrenic relatives.

Goodman suggests that autism and schizophrenia might be "alternative manifestations" of an underlying genetic defect that could, in different individuals, cause blood disorders or motor neuron disorders such as Tay Sachs. In particular, she suggests that researchers should investigate chromosome 21 (site of the gene mutation that causes ALS) and chromosome 15 (site of the mutation that causes Tay Sachs). (Several reports have already linked some cases of autism to a defect on chromosome 15; see ARRI 8/3.)

Goodman cautions, however, that any genetic connections suggested by her research may be limited to the population she studied. She notes that data from a recent large-scale Utah study showed no increased incidence of ALS among families of autistic children.

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"A family history study of schizophrenia spectrum disorders suggests new candidate genes in schizophrenia and autism," Ann B. Goodman, *Psychiatric Quarterly*, Vol. 65, No. 4, Winter 1994. Address: Ann B. Goodman, Nathan S. Kline Institute for Psychiatric Research, Orangeburg, NY 10962.