Antipsychotic drug doses climb over time

Psychiatrists who prescribe antipsychotic medication for severely mentally ill individuals living in board-and-care facilities, halfway houses and other private housing arrangements tend to administer progressively larger doses of the drugs over time, according to a report in the June AMERICAN JOURNAL OF PUBLIC HEALTH.

This practice, uncovered in a study of 243 formerly hospitalized mental patients interviewed in 1973 and again in 1985, may stem primarily from a lack of community mental health services, which encourages an over-reliance on antipsychotic drugs by clinicians, asserts psychologist Steven P. Segal of the University of California, Berkeley. Segal conducted the survey with psychologist David Cohen of the University of Montreal and psychiatrist Stephen R. Marder of the University of California, Los Angeles.

One in three people contacted in 1985 by the researchers reported moderate to severe restlessness, body rigidity or spasms of the mouth and facial muscles. Antipsychotic drugs can cause these symptoms, which sometimes lead to a serious movement disorder known as tardive dyskinesia (TD). Segal's team did not assess the number of TD cases in the sample.

However, the findings challenge the notion that increasing concern over TD during the 1980s led to more conservative long-term prescriptions for antipsychotic drugs (also called neuroleptics), the scientists contend.

No other studies have examined prescription practices for mentally ill people living in "sheltered-care facilities," Segal says. Essentially a private system of residential care, the living arrangements that comprise sheltered care in the United States now house between 300,000 and 400,000 mentally ill adults. Prescriptions may be handled either by a physician working for a particular residence or by an individual's private physician or psychiatrist.

Segal's group conducted interviews in 1973 with 393 former psychiatric patients living in sheltered-care facilities located throughout California. In 1985, the investigators reinterviewed 243 surviving participants and verified the dosages of all prescribed medications. Most of those in the survey suffered from schizophrenia, a severe disruption of thought and emotion that strikes about one in 100 people.

Slightly more than three-quarters of the sample received neuroleptics in both 1973 and 1985. Of that number, nearly half experienced an increase in the prescribed neuroleptic dose over 12 years, and almost 10 percent ended up taking extreme doses, the researchers maintain.

"I was surprised at some of those doses," Segal remarks. "They're very high."

The average daily dose of antipsychotic medication increased markedly from 1973 to 1985, particularly among the 22 people receiving long-acting injections, rather than short-acting pills, at follow-up.

At the same time, Segal sees room for optimism in the finding that nearly 40 percent of persons given neuroleptics in 1973 received a lower dose 12 years later and displayed no significant drop in psychological functioning. And study participants age 56 to 65 received an average of half the neuroleptic dose prescribed for younger adults, following guidelines established for treating the older mentally ill.

Nonpsychiatric physicians took a more cautious approach to prescribing neuroleptics, perhaps because they were less familiar with the drugs, Segal notes. Patients with muscular rigidity or twitching often received additional drugs to help ease their irregular movements.

Sheltered-care facilities usually maintained links to local mental health programs that provided former patients with job training and other services, but funding cuts undermined those organizations during the 1980s, Segal contends.

He hopes to conduct a 20-year follow-up of the California sample in 1993.

– B. Bower

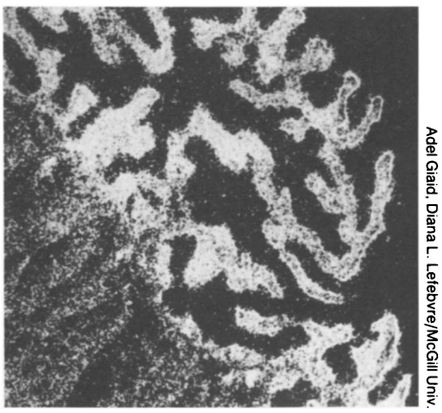
Explanation for premature and delayed labor

Untimely spurts of the hormone oxytocin may be to blame for premature labor, according to a study of pregnant rats. Similarly, delayed release of the hormone may postpone labor beyond the healthiest time to deliver, the study suggests.

These findings could lead to the development of drugs to prevent premature labor by blocking the action of oxytocin in the uterus. Prematurity is a major cause of death among newborns, because early uterine contractions often expel a fetus before its lungs and other vital organs have matured. Similarly, a delay in labor can cause suffocation as the fetus outgrows the placenta's oxygen-bearing capabilities. Delayed labor can also endanger the mother, causing complications such as vaginal ruptures because of the child's larger size.

For years, obstetricians have administered oxytocin to stimulate labor in women whose pregnancies extended beyond the normal 40 weeks. In most cases, shots of the hormone quickly bring on intense contractions, followed by birth. But physicians have remained stumped over oxytocin's normal function during childbirth, because women who enter labor spontaneously do not have significantly higher blood concentrations of the hormone than pregnant women who aren't in labor. Moreover, animal tests have shown that injections of antibodies that block oxytocin in the blood do not delay the onset of labor.

The new study – led by neuroendocrinologist Hans H. Zingg of the Royal Victoria Hospital at McGill University in Montreal – resolves this paradox. In the June 12 SCIENCE, Zingg and his colleagues report that a gene in the uterus of pregnant rats that codes for the production of oxytocin becomes steadily more active during pregnancy, peaking just before labor at more than 150 times its normal level of expression. In contrast, the gene's activity in the hypothalamus – the brain region previously believed responsible for making oxytocin – rose less than threefold, they found.



Adel Giaid, Diana L. Lefebvre/McGill Univ.

The oxytocin gene's activity shows up as dark spots in rat uterine tissue.

Zingg's group concludes that the hypothalamus is relatively unimportant in regulating the oxytocin levels that prompt labor. Instead, they assert, unknown factors spur the uterus itself to make oxytocin, which then causes the organ to contract. Errors in this process may cause premature or delayed labor, they suggest.

Zingg says the production of oxytocin by the uterus explains the lack of elevated oxytocin concentrations in the blood of pregnant women. Similarly, he says, oxytocin-blocking antibodies would not delay labor, because such comparatively large antibodies cannot leave the blood and enter the uterus.

Bryan F. Mitchell, an obstetrician at the University of Alberta in Edmonton, says he and his colleagues have found evidence to support this conclusion in human placental tissue. They discovered that women who enter labor spontaneously have much higher placental concentrations of oxytocin messenger RNA – which directs the production of the hormone – than women whose babies are delivered by cesarean section before labor begins.

– C. Ezzell