SCIENCE NEWS of the week

New Therapies Brighten Stroke Horizon

New insights into the complex language of nerve cells may soon give physicians their first useful emergency treatments for stroke, the third leading cause of death in the United States. The recent progress in stroke-drug development builds upon years of seemingly esoteric studies of the chemical messengers that transmit information within and between neuronal fibers.

With many of these molecular messenger systems now reasonably well deciphered, scientists have created experimental drugs that can block the destructive biochemical chatter typical of stroke-stressed neurons. Early clinical trials discussed this week at the Society for Neuroscience annual meeting in Phoenix, Ariz., indicate encouraging results with some drugs.

Despite a remarkably clear picture of what a stroke is (a blockage of blood flow in the brain, killing varying numbers of neurons) and what causes it (most commonly a blood clot lodging in an artery), clinicians remain frustrated by their inability to intervene before damage becomes widespread. Unlike research involving other neurodegenerative diseases such as Parkinson's and Alzheimer's — work that has spawned innovative experimental treatments despite a relatively poor understanding of the disorders' underlying mechanisms — stroke research has until very recently appeared stagnant, scientists say. A stroke's effects can range from minor, reversible loss of function in a few muscles to total paralysis or death.

"At present we have no generally accepted, specific [emergency] therapy for stroke," says Justin A. Zivin of the University of California, San Diego. However, he adds, research suggests some patients can expect "significant protections" against stroke-induced neuronal injury "within two years max." Zivin's optimism comes largely from scientists' improved understanding of the so-called second-messenger systems that mediate toxic reactions in oxygen-deprived neurons.

In recent years, for example, researchers have fingered a nerve-secreted chemical called glutamate as a major culprit in neuron death following stroke. When secreted in normal concentrations, glutamate provides a chemical phone link to neighboring nerve cells through its ability to bind to their outer membranes and then trigger waves of electrical impulses within those cells. But stroke-affected neurons squirt out the cellular equivalent of buckets of glutamate, providing an excitatory overdose that kills surrounding cells — probably by activating within them "second messengers" that invite fatal influxes of calcium ions. Moreover, many of these doomed neighboring cells undergo a similar, glutamate-purging reaction as they die, spurring the death of other nearby neurons.

Many tests in animals and a few trials in humans now suggest a new class of drug — glutamate-receptor blockers — can substantially reduce the number of neurons destined to topple in this domino effect, limiting or even preventing clinical symptoms such as paralysis. Oddly, one of the most promising of these drugs — for now bearing only the code name MK-801 — is a close chemical relative of the street drug PCP, which can induce schizophrenic symptoms in users. Dextromethorphan, another promising compound with a similar mode of action, is the active ingredient in a cough medicine.

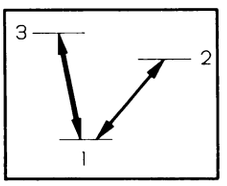
While encouraged by indications that such "glutamate antagonists" might totally prevent neurological symptoms in up to 80 percent of stroke cases, Dennis W. Choi of Stanford University calls these drugs "blunt axes" compared with even newer drugs that interfere more selectively with the neurotoxic cascade farther downstream. Rather than blocking reactions that have both good and bad effects, these experimental drugs block only the final, subtle reactions that trigger actual cell death, often by interfering with tiny phosphate groups that can transform mild-mannered second-messenger proteins into cell-killing toxins.

Recent tests of new compounds called lazaroids, for example, indicate they can block a cell-membrane-destroying reaction that escalates into a neuronal massacre in the hours after a stroke. Also promising are so-called gangliosides. These drugs hijack the biochemical shuttle that normally transports a potentially deadly enzyme to the nerve-cell membrane. Kept away from the membrane during the hours after a stroke, the enzyme remains harmless. Results from the first large clinical trial of a ganglioside, involving 502 European patients, show a significantly higher degree of neurologic improvement in the two weeks after a stroke in patients who received the drug within 12 hours, according to a report in the September STROKE.

Researchers also await results from two multicenter clinical trials in the United States looking at the value of tissue plasminogen activator (tPA) in stroke patients. Despite previous indications that the clot buster can be dangerous when administered more than a few hours after a stroke, several researchers now believe it could prove safe and immensely useful if given earlier.

Such a finding, they note, would necessitate a major change in emergency treatment standards, which today require diagnosis and immediate care only for patients suffering from a heart attack or trauma. Clinicians say proof that early intervention with tPA improves stroke outcome would probably trigger a massive public education campaign encouraging individuals to recognize stroke symptoms so they can call for immediate help from medics equipped with nerve-rescuing drugs. That would represent a major shift from today's "why hurry?" approach to stroke diagnosis, an approach based on the current lack of therapeutic interventions. — *R. Weiss*

Keeping a quantum kettle from boiling



The adage that a watched pot never boils may have some truth in it after all — at least in the quantum realm. A team of researchers has demonstrated that making frequent measurements of the state of a quantum system inhibits transitions from one state, or energy level, to another. In other words, the act of observing an atom to determine its state can interfere with quantum jumps between atomic energy levels.

"Our experiment demonstrates the effect clearly and simply," says Wayne M. Itano of the National Institute of Standards and Technology in Boulder, Colo. Itano and his colleagues describe their experiment in a paper recently submitted for publication. The research touches on a number of questions concerning the nature of quantum measurements.

The team used radio waves of a particular frequency to drive laser-cooled beryllium ions held in an electromagnetic trap from one energy level to another (from level 1 to level 2 in the diagram). While an ion was going through this quantum jump, the researchers sent in short pulses of light to determine the ion's state.

If the measurement happened to force the ion back into state 1, the light pulse could then shift the ion into energy level 3. The ion would immediately reemit that energy, and the researchers would see scattered light. If the ion were to end up in state 2, no transition to level 3 could occur, and the observers would see no scattered light.

According to quantum theory, the more frequently one tries to observe a system's

state as the system is going through a quantum jump, the more likely the system will show up in its initial state. Thus, observing the system's state should interfere with the transition that ought to take place between level 1 and level 2.

That's exactly what Itano and his colleagues found. They detected scattered light, indicating the ions tended to end up in state 1 despite the influence of the radio waves.

Such effects may play subtle but important roles in quantum measurements. "A lot of quantum mechanics and a lot of the things we observe in nature are under conditions where frequent measurements are being made," says physicist Richard J. Cook of the Frank J. Seiler Research Laboratory in Colorado Springs. For instance, looking at a particle means observing the photons of light scattered from the particle. "Every time a photon is scattered off and enters your eye, that's a measurement of the position of the particle," he says.

One intriguing possibility is that making appropriate measurements or observations quickly enough could slow or even stop the spontaneous decay of an unstable particle such as a radioactive isotope. But no one is certain whether such a scheme would ever be practical.

— I. Peterson

Panic attacks increase suicide attempts

Some psychiatric conditions, such as severe depression and schizophrenia, are known to increase a person's risk of suicide. But panic attacks and panic disorder, defined as frequently recurring panic attacks, are also linked to a strong and largely unappreciated risk of contemplating and attempting suicide, according to a new study.

Surprisingly, people with panic disorder have a higher rate of suicide attempts than do severely depressed individuals, report psychologist Myrna M. Weissman of Columbia University in New York City and her colleagues in the Nov. 2 NEW ENGLAND JOURNAL OF MEDICINE.

This finding is "quite remarkable" and marks panic disorder as a major new risk factor for suicide, writes psychiatrist Peter Reich of the Massachusetts Institute of Technology in Cambridge in an editorial in the same journal. Reich also notes that general practice physicians, who most commonly encounter panic disorder patients, can help prevent suicides by recognizing and treating symptoms of the disorder.

Panic disorder afflicts an estimated 1.5 percent of the U.S. population at some time in their lives. It involves repeated episodes of sudden, unpredictable, intense fear accompanied by symptoms such as heart palpitations, chest pain, faintness and the sense that one is about to die or go crazy. Less frequent panic attacks affect 3 to 4 percent of the population.

Weissman and her co-workers studied a random national sample of 18,011 adults taking part in a larger epidemiologic study of psychiatric disorders. Trained interviewers questioned each subject at home about psychiatric symptoms.

The 254 subjects with panic disorder and the 667 with panic attacks reported thinking about death, feeling as though they wanted to die, having thoughts of committing suicide or attempting suicide significantly more than did subjects with any other psychiatric disorder or with no disorder. One in five people with panic disorder had attempted suicide, compared with about one in eight with panic attacks, one in 16 with another psychiatric disorder and one in 100 with no disorder.

When the researchers statistically controlled for panic subjects who had another psychiatric disorder, such as severe depression or alcohol abuse, they still found substantially more suicidal thoughts and suicide attempts among the panic group. Nevertheless, the risk of suicide attempts proved greatest for panic disorder subjects who also abused alcohol or illicit drugs. People with less frequent panic attacks were more likely to report suicide attempts if they also were alcohol abusers or severely depressed.

The researchers have no data on the rate of completed suicides among panic subjects. However, Reich notes that about one in three people who kill themselves have made previous attempts. Furthermore, a recent study in which researchers followed hospitalized psychiatric patients with a primary diagnosis of panic disorder for 30 to 50 years revealed a significantly higher mortality rate — primarily due to suicide or heart disease — among these individuals than in a group of patients hospitalized for severe depression.

Subjects in the national sample with panic disorder were more likely than those with other psychiatric disorders to seek help for their emotional problems from general physicians or psychiatrists. Panic subjects were also more likely to use a hospital emergency ward, Weissman and her colleagues note. Because panic symptoms are often similar to those of medical illness, accurate diagnosis is imperative, the researchers assert. Drug and behavioral treatments often ease panic symptoms, they say, although there is no direct evidence that these efforts reduce suicide attempts.

— B. Bower

Marrow rebuilt with umbilical-cord blood

Testing an alternative to bone marrow transplants, researchers have reconstituted the marrow of a seriously ill boy using blood drawn painlessly from the umbilical cord of his newborn sister.

A newborn's blood contains stem cells, the parent cells of marrow and blood cells, says Arleen D. Auerbach of Rockefeller University in New York City, who describes the procedure with French and U.S. colleagues in the Oct. 26 NEW ENGLAND JOURNAL OF MEDICINE. Children and adults have stem cells only in the bone marrow.

Physicians could use a sibling's cord blood as a source of stem cells to treat leukemia, aplastic anemia or any other disease normally treated by marrow transplants, Auerbach says. However, the newborn's tissue must match the recipient's. Auerbach proposes setting up banks to store cord blood for patients with no compatible sibling donor.

The 5-year-old boy suffered from Fanconi's anemia, an inherited aplastic anemia that depleted his marrow. After his sister's birth, the researchers froze blood drawn from the cut umbilical cord still attached to the mother. They stored the blood for seven months, until the baby was old enough to provide marrow if the blood transplant failed.

Doctors then used drugs and radiation to destroy the remainder of the boy's marrow — a standard step in marrow transplants — and infused the thawed cord blood. Healthy stem cells replenished the marrow and changed his B+ blood type to his sister's O+. The boy now "leads a normal life," the researchers report.

A year after his September 1988 transplant, the team successfully performed the procedure on another pair of siblings, Auerbach told SCIENCE NEWS.

The new approach offers several advantages over marrow transplants, Auerbach says. Using cord blood allows the sick child to receive a transplant soon after the birth of a compatible sibling, whereas candidates for marrow transplants must wait until the donor is at least 6 months old. In addition, the cord blood donor avoids painful marrow extraction. The researchers say they do not know whether cord blood contains enough stem cells to treat an adult or large child. They also note a slight risk of the mother's immune cells mixing with the cord blood and attacking the transplant recipient.

David G. Nathan of Children's Hospital in Boston does not envision broad use of the procedure. "How many children are there," he asks, "who need a transplant and have a histocompatible sibling about to be delivered?"

— A. McKenzie