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.

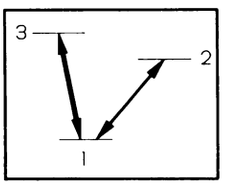
While encouraged by indications that such "glutamate antagonists" might totally prevent neurological symptoms in up to 80 percent of stroke cases, Dennis W. Choi of Stanford University calls these drugs "blunt axes" compared with even newer drugs that interfere more selectively with the neurotoxic cascade 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