

Stopgap measure could limit stroke damage

When a person suffering a stroke is rushed to a hospital, the problems are just starting. The oxygen deprivation caused by an obstructed blood flow to the brain slays an initial cluster of nerve cells, but perhaps twice as many nearby cells will die over the next day or two. "The later injury is actually what's important in stroke," says Maiken Nedergaard of New York Medical College in Valhalla.

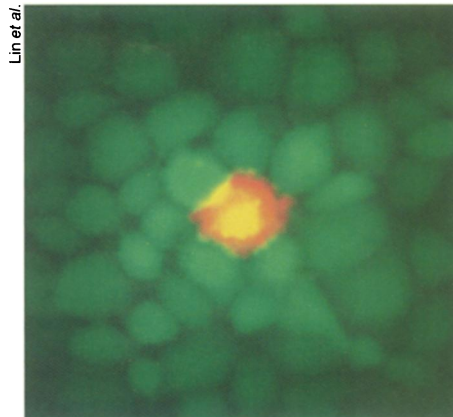
What's puzzling about this secondary damage is that the cells that die never suffer from a loss of blood flow. "They're not killed by a lack of oxygen," notes Nedergaard's colleague Jane H.-C. Lin.

Laboratory experiments now show that dying brain cells can induce the suicide of healthy neighboring cells, even ones deliberately made more resistant to cell death, report Lin, Nedergaard, Steven Goldman of Cornell University Medical Center in New York City, and their colleagues in the October *NATURE NEURO-*

SCIENCE. The command to die seems to propagate outward from the dying cells through cell-to-cell conduits called gap junctions, raising the hope that physicians may one day minimize stroke damage by blocking the junctions.

Almost wherever cells crowd together, gap junctions, formed by proteins called connexins, link the interiors of abutting cells. These tunnels allow certain molecules, such as calcium ions, to diffuse freely between cells. In the heart, for example, molecules flowing through gap junctions help synchronize the contractions of the organ.

Lin and her colleagues grew brain cells in the laboratory and then added the gene for a connexin. When the researchers forced the cells to the verge of death using oxygen deprivation or chemical treatment and then mixed them with untreated healthy cells, the dying cells somehow induced the suicide of healthy



Illustrating how gap junctions connect cells, a diffusible dye (green) spreads to other cells while a nondiffusible dye (red) remains in the initial cell (yellow).

cells connected to them by gap junctions. Even cells genetically engineered to resist apoptosis, the form of cell suicide observed by the scientists, fell prey to dying neighbors. Cells without the connexin gene didn't harm nearby cells, however.

The researchers also examined the astrocytes—one of the cell types that support the signal-processing neurons of the brain—of rodents subjected to a stroke-like event. They confirmed that the gap junctions among the astrocytes remained open during the event. Astrocytes have more than 30,000 gap junctions, making them a strong candidate to spread any apoptotic signal, says Nedergaard.

"When we think of apoptosis, we think of cells protecting their neighbors [by killing themselves]. This would be a different twist," notes Stuart A. Lipton of Brigham and Women's Hospital in Boston. He and his colleague Samantha L. Budd, in an accompanying commentary in *NATURE NEUROSCIENCE*, suggest that apoptosis "could be a 'contagious' process."

The nature of the death signal remains undetermined, although researchers raise calcium ions as a possibility. Ions flowing from dying cells to healthy neighbors could trigger apoptosis, they say.

Whatever the signal or signals, Nedergaard believes that by closing or blocking the gap junctions in astrocytes, physicians might one day lessen the secondary brain cell death caused by strokes. While several molecules that inhibit gap junctions have been identified, they don't specifically target the channels. "A big challenge for the future is to develop more efficient gap junction blockers," says Nedergaard.

Nevertheless, she and her colleagues are exploring the possibility of using one known gap junction blocker, halothane, on people who have suffered a stroke. Halothane is a widely used surgical anesthetic and has already shown some ability in animals to protect brain cells from stroke-like damage. —J. Travis

Orphanages improve image in child care

As an old blues song intones, "Motherless children have a hard time, when their mother is gone." For more than 50 years, child development research has expanded on that premise. Studies have concluded that psychological and behavioral problems frequently plague youngsters who grow up in institutional settings without a parent's love and guidance.

But new evidence out of war-weary Africa offers a counterpoint to this bleak outlook. Kids consigned to either of two orphanages early in their lives exhibited good emotional health and social adjustment as they neared adolescence, according to a report in the October *AMERICAN JOURNAL OF PSYCHIATRY*.

Moreover, children did best in an orphanage in which the entire staff helped to make decisions and in which children were encouraged to develop lasting relationships with staff members, contend psychiatrist Peter H. Wolff of Children's Hospital in Boston and Gebremeskel Fesseha, an educator and researcher living in Asmara, Eritrea.

"The findings challenge the conclusion that orphanages are breeding grounds of psychopathology and must be avoided at all costs," Wolff and Fesseha say.

Eritrea, located in eastern Africa, recently concluded a 30-year war with neighboring Ethiopia. The war created a large population of Eritrean children who have either no parents or a living parent who can't support them.

The researchers compared two Eritrean orphanages, one housing 450 children

in a city and the other accommodating 200 children in a rural area. About half the children had lived at the same orphanage for much of their lives; the rest had recently transferred from another orphanage. Children at both facilities attended nearby public schools. The orphanages employed one staff member for about every 17 youngsters.

The director and several workers at each orphanage completed questionnaires on institutional organization and child-care practices. The mental status of 40 children, ages 9 to 12, at each facility was established through staff members' reports of their behavior and the orphans' responses on memory and reasoning tests.

To probe for insecurities and fears about relationships with adults, the researchers had each child tell a story about a picture showing an Eritrean woman bending over a small boy.

Children in both orphanages exhibited good behavior and mental functioning, although those in the rural orphanage, which stressed consensus decisions by staff, did best. When shown the picture of a woman and child, many orphans reminisced about their war experiences and described orphanage life as a positive change.

These results support a 1996 survey, conducted by economist Richard B. McKenzie of the University of California, Irvine, which found good psychological health and job achievement in 1,600 adults raised in any of nine orphanages in the U.S. South or Midwest. —B. Bower