New treatments for macular degeneration

Age-related macular degeneration, a progressive scarring of the retina, is the leading cause of impaired vision and blindness among the elderly. In a severe form, called wet macular degeneration, an overgrowth of blood vessels causes scar tissue to form as blood and other fluids leak inside the eye. Up to 200,000 people in the United States are diagnosed with this form of the disease each year, and most eventually become legally blind.

Current treatment of wet macular degeneration is limited to lasers, which can destroy the blood vessels before further scarring occurs. Often, however, surgeons cannot pinpoint the leaking blood vessels accurately enough to attack them safely with a laser beam.

Now, three other treatments are showing promise—surgery to reposition the retina, low-level radiation to stanch blood flow, and photochemical dyes that assail the offending blood vessels. The research was unveiled in Los Angeles this week at a seminar hosted by Research to Prevent Blindness, a New York–based nonprofit group that sponsors eye research in the United States.

The three-pronged attack on wet macular degeneration has a single goal, notes Harold F. Spalter, an ophthalmologist at Columbia University College of Physicians and Surgeons—"to selectively kill off the abnormal blood vessels."

Vision loss results when scarring strikes the macula, the central part of the retina near the back of the eye. The center of the macula contains densely packed, light-sensitive cells that enable people to read words, recognize faces, and discern other fine details.

Researchers at the Johns Hopkins Medical Institutions in Baltimore have performed 17 retinal repositioning operations on people with scarring precariously close to the center of the macula. Standard laser surgery would worsen vision in such cases by destroying the light-sensitive cells. Instead, doctors cut through the outer wall of the eye to gain access to the retina, which they can then detach and reposition without cutting.

The technique enables surgeons to maneuver the center of the macula away from the leaking blood vessels and place it next to healthier eye tissue. They then use a laser to demolish the offending tissue without damaging the central macula, says Eugene de Juan, the ophthalmologist who presented the findings.

Of seven patients who had retinal repositioning at least 6 months ago, four now have improved vision. One went from legally blind to 20/25 vision in one eye, de Juan says. "The real challenge is to make the procedure more predictable and prevent complications," he adds.

To stop the blood vessel proliferation that leads to macular degeneration, ophthalmologist Dennis M. Marcus of the Medical College of Georgia in Augusta is looking into radiation treatment. In people with cancer, radiation is commonly used to cut off blood supply to a tumor by inhibiting the growth of its blood vessel cells.

In 1993, a study of radiation treatment for 19 macular degeneration patients in Northern Ireland gave hints of success. Since then, more than 500 people have been treated worldwide. In some cases, the disease was stabilized, but most of the studies lacked a control group for comparison, Marcus says, and some of the studies found no benefit from the treatment.

Marcus and his colleagues are currently treating 100 macular degeneration patients who aren't candidates for laser therapy. Half receive radiation; the others get a sham treatment. Neither patients nor researchers know, for now, who is getting which treatment.

In a year, the researchers expect to learn what effect the radiation had on the disease. So far, no harmful side effects have been noted.

"At the doses used, the retina is relatively radiation-resistant. We hope the blood vessels are susceptible at these doses," says Marcus. The same doses have been used previously in successful treatments. Six other research institutions have applied to join the study.

The third new treatment comes from researchers at Harvard Medical School in Boston. They inject photosensitive chemicals into the bloodstream of people with macular degeneration and use lasers to stimulate those chemicals in the eye. When activated, the substances halt the proliferation of blood vessels, says ophthalmologist Joan W. Miller.

If blood vessels begin to grow again, repeat doses seem to close them off without any side effects, Miller says. Encouraged by these preliminary studies, 22 research centers in North America and Europe are starting to treat and evaluate 540 patients. *—N. Seppa*

Brain region takes a hack at navigation

A good taxicab driver listens to a passenger's request and, often before hitting the gas pedal, mentally delineates the best route to the desired destination. In the teeming neural metropolis of the brain, the road to navigational recall of this kind passes through a critical checkpoint known as the right hippocampus, a new study finds.

In familiar real-world settings, where many paths may lead to a particular destination, the right hippocampus integrates memories of spatial information so that individuals can get from point A to point B, contend neuroscientist Eleanor A. Maguire of the Institute of Neurology in London and her coworkers.

"A network of brain regions may support the construction of a mental map of space, but only the right hippocampus is specifically involved in relating the elements of a route together into a framework for navigation," Maguire holds.

The researchers examined the brains of 11 London taxi drivers, all men between 38 and 52 years old. Participants' tenure as licensed London cabbies, a status attained through strict testing, ranged from 3 to 26 years. A positron emission tomography (PET) scanner measured changes in cerebral blood flow, an indirect sign of rises or drops in neural activity.

Blood flow in the right hippocampus, which is located near the center of the brain, increased sharply when the taxi drivers described the shortest legal route between assigned starting and destination points in London, Maguire's group reports in the Sept. 15 JOURNAL OF NEUROSCIENCE.

That jump in activity failed to occur when drivers recalled and described world-famous landmarks that they had never visited, such as the Statue of Liberty. Hippocampal activity also remained unchanged as drivers recounted the plots of familiar, famous movies, a task that invokes memory for a sequence of events similar to the recall of routes.

Both the route and landmark memory tasks also activated interconnected regions toward the back of the brain. These areas may respond to relevant features of physical space and surroundings, the researchers propose. The right hippocampus helps this flexible but undiscriminating "topographic representation system" to compose a plan for navigating through complex environments, they theorize.

The movie recall test stimulated activity in the left frontal lobe of the taxi drivers' brains, indicating that it did not tap into the neural system devoted to memory for spatial layout and landmarks.

"It's been known for some time that the hippocampus is involved in spatial cognition in nonhuman animals," remarks neuroscientist Patricia E. Sharp of Yale University. "But Maguire's work is exciting because it's the first to suggest that the hippocampus is important for human route planning."

The brain's memory system for physical space may have ancient evolutionary roots, rendering it largely independent of the frontal regions, which have assumed prominence in humans, Maguire's group suggests. *—B. Bower*