tion, had argued that Doppler radar does not have enough useful range to fill in between sites, which are planned to be about 400 kilometers apart. Experience so far, at least according to the Silver Spring NWS group's statistics, suggests that such fears are unfounded, however. Considering warnings out of Norman, none of the measures of warning skill—detection, false alarms, or lead times —changed significantly with increasing distance from the radar, right out to 240 kilometers.

That is not to say that NEXRAD is omniscient; it has its blind spots. One is distant heavy weather that in effect hides behind weather that is closer in. Radar reflections may actually arrive from the distant storm, but NEXRAD—or any other radar—cannot say whether they were emitted recently and came from close by or were sent earlier and are just arriving from a great distance. On 6 August, such range-folding initially hid from the Sterling NEXRAD, which was 200 kilometers away, the severe storms that eventually generated 17 tornadoes near Petersburg, Virginia. Four persons died and 200 were injured when a tornado sliced through a Wal-Mart store without warning.

During congressional hearings last spring on the NWS modernization, such inevitable shortcomings prompted Robert Ryan, WRC-TV meteorologist in Washington, D.C., and president of the American Meteorological Society, to voice a word of caution. Ryan noted that weather forecasting will always have its limitations, no matter how spectacular the advances. NEXRAD will never catch every severe thunderstorm or tornado. Heavy snowstorms will still surprise forecasters and the public. And improved hurricane forecasts will continue to be hard to come by. "Our future challenge...may be as much educating the public as to our scientific limitations," he said, "as it is detailing our present accomplishments."

**–Richard A. Kerr**

GENETIC DISEASES

# Copper Clues Clarify Metabolic Puzzle

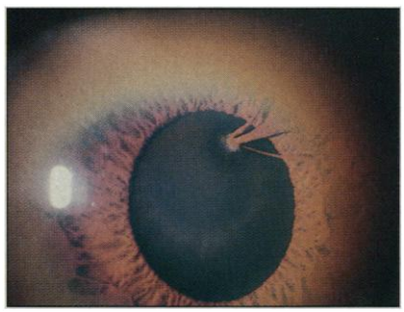
When researchers told a recent psychiatric genetics meeting in New Orleans* that they had identified a gene for a disease that destroys the liver, the announcement wasn't really out of place. The illness is Wilson's disease, a disorder that can mimic symptoms of schizophrenia and other neurological disorders and place misdiagnosed patients in psychiatric wards. It can also kill people, if untreated, and identifying the gene means there is now a prospect of a genetic test that would lead to treatment with drugs before any symptoms even appeared.

Striking 30 in every million people, Wilson's disease is a rare, inherited illness that stems from an abnormal buildup of copper in many organs. The buildup causes brain damage, and in the liver, where the buildup is most dramatic, copper toxicity ravages the organ and, without a transplant, causes death by early adolescence.

Researchers have long wondered why Wilson's patients are unable to get rid of excess copper, and in New Orleans, psychiatric geneticist T. Conrad Gilliam of Columbia University may have provided an answer. He reported that a team he led had found mutations that may account for the problems in copper transport. Gilliam cautions, however, that the gene may be susceptible to so many mutations that those wishing to develop a reliable genetic screening test could face a formidable challenge. The discovery's most immediate benefit may be to basic research, helping to clear up the biological mystery of copper transport. "Learning about these defects will tell us how the body moves copper from one part of the body to another molecularly," says geneticist George Brewer of the University of Michigan Medical Center, who has also been pursuing the gene.

The search for the Wilson's disease gene began in earnest in 1985, when genetic linkage studies of families prone to the disease placed the gene on chromosome 13. To home in further, Gilliam's group this year developed a physical map of nine "microsatellite" markers, short repetitive sequences of DNA, that spanned the region. By examining the DNA of 115 Wilson's disease families, Gilliam's group could determine which markers were inherited most frequently by those with the illness. That data indicated the gene was associated with two markers on a stretch of chromosome 13 less than 200,000 base pairs long.

But the scientists couldn't get any closer without a candidate gene. Then, in January, three other groups independently reported in *Nature Genetics* on a gene involved in another rare, fatal, copper-related illness: Menkes disease. Menkes' patients suffer from copper "starvation" in which all the copper-dependent enzymes in the body shut down, leading to progressive brain damage and vascular defects. Dietary copper in these patients apparently cannot travel out of intestinal cells and into the bloodstream. That appears to be the fault of mutations in the gene, which normally codes for a protein that looks like it transports copper across cell membranes.



**Eye of copper.** The ring on the upper half of the iris is a sign of Wilson's disease, indicating copper has passed from liver to brain.

It seemed clear to Gilliam and others that Wilson's disease might result from a defect in a simliar transport protein, so his group began looking in the suspect region on chromosome 13 for stretches of DNA that might match the Menkes gene. At the same time, Gilliam mentioned this effort to Rudolph Tanzi, a neurologist at Massachusetts General Hospital who, as part of his work on Alzheimer's disease, was screening genes that appeared to code for metal-binding proteins. And Tanzi, it turned out, had located one such gene—right on chromosome 13.

After talking with Gilliam, Tanzi quickly compared his candidate gene to the gene for Menkes disease and found the encoded amino acids were 76% identical. Next, Gilliam and his colleagues showed that Tanzi's gene indeed lay in the suspect region on chromosome 13. Moreover, the investigators found that the RNA produced by the gene is expressed most vigorously in the liver. And finally, Gilliam, Tanzi and their colleagues returned to the genetic data from the Wilson's families, looking for mutations in the gene that could affect the function of what is apparently another copper-transport protein. So far, the researchers have found four mutations that show up only in Wilson's patients and not in unaffected relatives.

But they also learned these mutations account for much less that 50% of their cases. That indicates that Wilson's disease, like cystic fibrosis, is caused by a large variety of mutations in a single gene, many of them rare. "Wilson's disease is going to be even worse [than cystic fibrosis]. Carrier detection is going to be really difficult," said Gilliam. But even if the identification of the gene for Wilson's disease doesn't turn into a clinical blessing, teasing out the gene's workings, along with those of the Menkes gene, should help clear up some mysteries behind the body's molecular metalworks.

**–John Travis**



* *1993 World Congress on Psychiatric Genetics, New Orleans.*