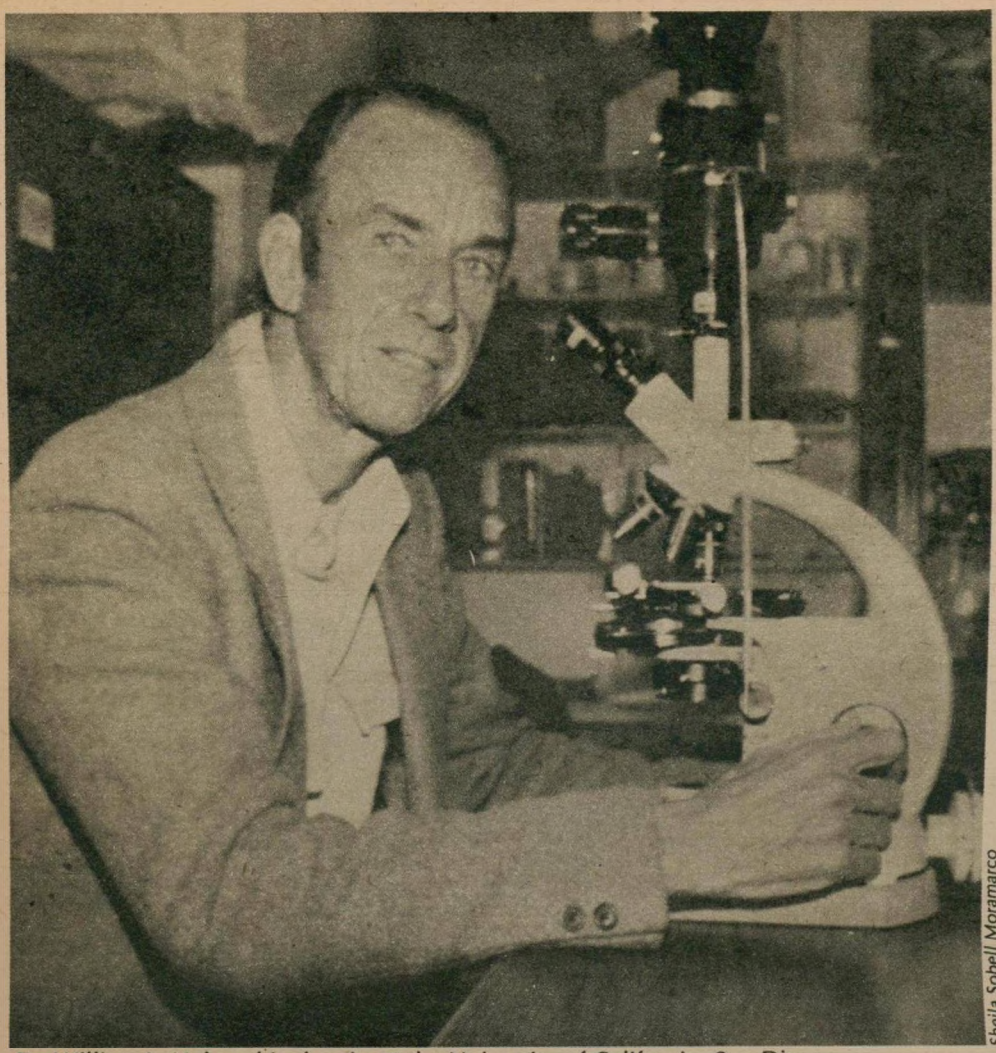

Sheila Sobell Moramarco

Dr. William L. Nyhan, biochemist at the University of California, San Diego, has developed major advances in the treatment of inherited disorders.

For many who have genetic disease, there is only suffering, but scientific sleuths are making breakthroughs

WHEN IT TAKES A MIRACLE

by Sheila Sobell Moramarco

The Joseph family of Northern California endures an almost unheard-of tragedy. Over the past century, more than 100 members in 11 generations have been struck down by a fatal, inherited disease peculiar to the Josephs.

In 1975, family member Rosemary Silva wrote a desperate letter to the National Genetics Foundation in New York asking for help. The case was referred to Dr. William L. Nyhan—world-renowned genetic sleuth, biochemist, chairman of pediatrics at the University of California at San Diego (UCSD) School of Medicine, and operator of one of the world's most important research and treatment facilities for genetic disorders.

Until Nyhan and Dr. Roger Rosenberg—chairman of the department of neurology at the University of Texas Southwestern Medical School at Dallas—unraveled the Josephs' complex genealogy, no one in the family un-

One disorder, resulting in coma and death when certain foods are eaten, can now be treated

Sheila Sobell Moramarco

Nyhan checks patient Ebtihal Aboaziza, who is kept alive by a special formula fed via tube into the baby's nose.

an afflicted infant can tolerate and still develop normally. The good news is that, properly maintained, children like Ebtihal can expect to lead normal lives without impaired brain function."

Victims of other inherited diseases are not always as fortunate. Researchers have made progress in prolonging the lives of children with the Lesch-Nyhan syndrome—an illness Nyhan discovered along with Dr. Michael Lesch, chief of the cardiology department at Northwestern University Medical School in Illinois. In addition, Nyhan and a colleague, Bohdan Bakay, a research biochemist at UCSD, pioneered tests to identify women carriers and detect the syndrome in the uterus. But there is as yet no cure for the disease nor any way to halt its appalling symptoms.

For Lesch-Nyhan families, the only hope is genetic counseling. Once female carriers of the disease are identified, parents who know their baby will be afflicted can decide whether or not to carry the pregnancy to term.

Physicians hope that knowledge gained through genetic sleuthing may eventually shed some light on sudden infant death syndrome (crib death). "We suspect that a lot of inexplicable deaths of young children may be due to inborn metabolic errors that could be detected in fetuses," says Dr. Lawrence Sweetman, associate professor of pediatrics at UCSD.

But few hospitals in the country are equipped with staffs trained in the sophisticated detection and management of genetic abnormalities. That is why afflicted families flock to San Diego. "This way," says Herman Weiner, who uprooted his family from New York three years ago, "if anything new comes up, we'll be right here."

Ann Gore of New Jersey had the same idea. In 1968, her baby daughter Loren was close to death. Despite frequent hospitalization for vomiting, acid in the urine, respiratory infections and seizures, Loren's condition went undiagnosed until, at 14 months, she was referred to Dr. Nyhan. By then, her physical and intellectual development were completely arrested.

"Loren looked and acted like a 3-month-old infant," Nyhan recalls. Within a few months, he had stabilized her condition and pinpointed its cause—a metabolic disorder called methylalonic acidemia.

Loren is now 14 years old. In her first 14 months of life, she had to be hospitalized almost continuously. In the last five years, she has not had to be admitted at all. Despite an incredible first year during which all maturation came to a standstill, thanks to a genetic sleuth in San Diego she survived and has overcome many handicaps to lead a nearly normal life. Though she receives special help with academic subjects, she is mainstreamed for other activities.

"Loren was in extremely critical condition when Dr. Nyhan got her," reports a grateful Ann Gore. "He gave her back her life and a chance to be the talented, well-adjusted and happy young person she is." P

To help locate a genetic-disease treatment center in your area, write or call: The National Genetics Foundation, Dept. P, 555 W. 57th St., Room 1240, New York, N.Y. 10019 (212) 586-5800.

derstood the cause or pattern of the blight that was devastating them. After months of work, the investigators determined that the disease is hereditary.

The prognosis, however, is harsh. There is as yet no way to detect the disease in fetuses or diagnose its victims before symptoms appear (which can occur any time between ages 16 and 45, when many already have had children). And no treatment. The only way to eliminate the disease is for all offspring of an affected parent to remain childless.

Such diseases do not yield their secrets easily. Fortunately, the type peculiar to a single family is extremely unusual. But genetically transmitted disorders in general are not: Scientists have already identified 30,000—"approximately 1300 new syndromes since 1966," according to Dr. Rosenberg.

Dr. Nyhan's patients include a boy of 17 who looks like an underdeveloped 11-year-old. He sits propped up in a wheelchair, his hands buried under mounds of pillows to protect him from a compulsion to mutilate himself. His speech is garbled, and periodically he screams obscenities. He is a victim of the Lesch-Nyhan syndrome, caused by an inherited, defective enzyme. There is no known cure.

At San Diego's University Hospital, Ebtihal Aboaziza, 9 months old, is fed a customized, artificial formula through a tube inserted in her nose. She has lived on this hospital ward almost since birth and is not expected to return home until after her first birthday. She, too, is the victim of an inherited malfunctioning enzyme. It affects her body's ability to convert protein into energy. Her disease, propionic acidemia, killed the Aboazizas' first child in 1974 when he was 6 weeks old. But there is hope for Ebtihal—a new treatment, thanks to the work of Dr. Nyhan.

Dr. Nyhan's role in unraveling genetic conundrums began in 1960 with a baby named Eric at Johns Hopkins University School of Medicine. It was an unusual case. Eric had undergone surgery at another hospital for pyloric stenosis, a condition resulting in a narrowing of the digestive tract. Unless corrected surgically, the disorder brings digestion to a halt, backing up the food and causing severe vomiting. Despite the operation, however, symptoms persisted until the infant, weakened from vomiting and dehydration, lapsed into a coma. In that condition, Eric arrived at Johns Hopkins. Nyhan—at the time a 35-year-old associate professor of pediatrics—was called in to consult.

"The fact that surgery hadn't corrected Eric's condition told us that the disorder probably didn't fit into our knowledge of established diseases," Nyhan explains. "An analysis of Eric's blood and urine revealed an elevated level of glycine, one of the amino acids in the blood, leading us to suspect that he very possibly had an intolerance to protein." But protein is complex. The question was: What part of protein?

Nyhan went sleuthing. He isolated each of the amino acids that comprise protein and, one by one, fed them to Eric, mapping the infant's biochemical reaction. Within a few weeks, he had the answer. Eric was suffering from propionic acidemia—the first case ever diagnosed.

Victims of this disorder cannot metabolize food properly. For them, eating foods containing certain amino acids produces a toxic reaction. Untreated, they become dehydrated, severely retarded and eventually comatose. Death is likely.

Nyhan eventually discovered that the disease could be controlled through a meticulously monitored diet therapy. Unfortunately, this treatment was developed too late to help Eric, but the baby's case has become the prototype for successful management of a host of similar metabolic defects—including that of Ebtihal Aboaziza.

"Feeding children with these types of disorders is tricky," Nyhan observes. "If a baby doesn't have a certain amount of protein, he can't survive. The catch is determining the exact minimal amount

continued

Lesch-Nyhan