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History paints a colorful portrait of the American Indians who live today in the Gila River Indian Community. Their ancestors were among the first people to set foot in the Americas 30,000 years ago. They have lived in the Sonoran Desert near the Gila River in what is now southern Arizona for at least 2,000 years.

Called the Pima Indians by exploring Spaniards who first encountered them in the 1600s, these early Americans called themselves "O'Odham," the River people, and those with whom they intermarried, "Tohono O'Odham," the Desert people.

Archaeological finds suggest that the Pima Indians descended from the Hohokam, "those who have gone," a prehistoric people who originated in Mexico. Strong runners, the Pima Indians were also master weavers and farmers who could make the desert bloom. Once trusted scouts for the U.S. Cavalry, the Pima Indians are pathfinders for health, helping scientists from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), a part of the National Institutes of Health (NIH), learn the secrets of diabetes, obesity, and their complications.

Migrating from Mexico, the people settled the land up to where the Gila River and the Salt River meet, in what is now Arizona. They established a sophisticated system of irrigation that made the desert fruitful with wheat,

beans, squash and cotton. The women of the community made exquisite baskets so intricately woven that they were watertight.

They were also a generous people. They sheltered the Pee Posh (or Maricopa Indians) who fled attack by hostile tribes, and who also became part of the Gila River community. Anyone who followed the Gila river, the main southern route to the Pacific, encountered these peaceful and productive traders who gave hospitality to travellers for hundreds of years. "Bread is to eat, not to sell. Take what you want," they told Kit Carson in 1846.

Today, the Pima Indians of the Gila River Indian Community are still an agricultural people, nurturing orchards of orange trees, pistachios and olives. They are still giving, too. Eleven thousand strong, the

members of the Gila River Indian Reservation have participated in 30 years of research that will help people avoid diabetes, have healthier eyes, hearts, and kidneys, and to understand how and why people gain weight and what can be done to prevent it.

"The Pima Indians are giving a great gift to the world by continuing to volunteer for research studies. Their generosity contributes to better health for all people, and we are all in their debt," says Dr. Peter Bennett, Chief of the Phoenix Epidemiology and Clinical Research Branch of the NIDDK.

The Pima Indians' help is so important to the ability of doctors to understand and treat diabetes, obesity, and kidney disease because of the uniqueness of the community. There are few like it in the world.

Young Pima Indians often marry other Pimas. Many Pima families have lived in the Gila River Indian Community for generations. Because of this, scientists can search for root causes of disease through several generations of many families. The length of NIDDK's study and the number of families involved allows scientists an invaluable perspective on how the disease progresses. The more generations studied, the deeper and better the understanding of how diabetes affects people, and the greater the opportunity to develop drug or genetic therapy, or lifestyle changes that will slow or prevent the coming of disease.



NIH offices in Phoenix, Arizona

The research takes so long, says NIH scientist Dr. Bill Knowler, because diseases like obesity and diabetes are so hard to understand. There seem to be several different causes, and the complex interaction between the genes a person inherits and the lifestyle a person chooses can make it hard to find treatments and cure. Scientists are trying to find a path through this maze.

Thirty years of research show that exercising and eating lower fat, fiber-rich foods can at least delay diabetes. "If you delay it long enough," adds Dr. Knowler, "It's almost as good as preventing it."

This cooperative search between the Pima Indians and the NIH began in 1963 when the NIDDK (then called the National Institute of Arthritis, Diabetes and Digestive and Kidney Diseases), made a survey of rheumatoid arthritis among the Pimas and the Blackfeet of Montana. They discovered an extremely high rate of diabetes among the Pima Indians. Two years later, the Institute, the Indian Health Service, and the Pima community set out to find some answers to this mystery. They hoped to shed light on an even broader question: Why do Native Americans, Hispanics and other non-white peoples have up to ten times the rate of diabetes as Caucasians?

Three decades' collective efforts by scientists and volunteers have laid the foundation for eventually curing or preventing diabetes and its complications. The work begun in 1965 has yielded a definition of diabetes that is now used worldwide, and set out diagnostic criteria used by doctors from Sacaton, Arizona to Sicily to identify and treat diabetes and to anticipate how it is likely to develop.



Doctors can best treat a disease when they understand what causes it and how it progresses. By studying Pima volunteers for many years, NIH doctors learned that unhealthy weight is a strong predictor of diabetes. Eighty percent of people with diabetes are overweight. They also discovered that high levels of insulin in the blood, or hyperinsulinemia, is another strong risk factor.

Studying this clue, researchers working with patients found that high levels of insulin were linked to insulin resistance. Normally, the pancreas releases insulin to regulate the amount of sugar or glucose in

the blood. People who have non-insulin-dependent or Type II diabetes (hereafter referred to simply as "diabetes") produce insulin, but their bodies don't respond to it effectively. NIH researchers have made it clear that people with insulin resistance are those most likely to get diabetes.

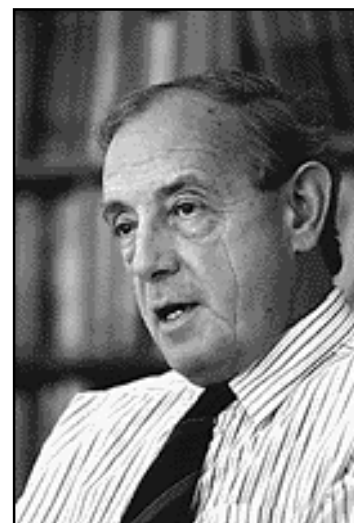
By studying Pima Indian volunteers, Dr. Clifton Bogardus and his colleagues established that glucose not needed for immediate energy is converted to glycogen and stored in skeletal muscle. However, several enzymes that drive this natural process appear different in insulin resistant people, according to the researchers, and they continue to study the biochemistry of insulin resistance to understand this breakdown and how it might be repaired.

By studying Pima Indian volunteers, researchers have determined that diabetes runs in families, as does insulin resistance, and obesity. Scientists believe that some people also have a gene that makes them more likely to have the kidney disease that occurs in people who have had diabetes a long time. Looking for these genes is a key part of the search now being conducted by NIH and the Pima Indians.

Researchers are working on this complex genetic puzzle by studying blood drawn from every member of the Pima community who comes into the NIH clinic at Hu Hu Kam Memorial Hospital for an examination. Blood is checked for healthy levels of blood sugar, cholesterol and other nutrients. Then, each person's blood and serum are typed and some is reduced to a very small pellet of DNA, the genetic material that instructs a person's cells to function one way or another. When NIH researchers find a family with one parent who is diabetic and one who is not, they are able to study the genes of both parents and their children in an effort to find the gene or genes shared by those who have diabetes.

After finding these genes, scientists hope to break the codes that cause insulin resistance, obesity, diabetes and kidney disease of diabetes. "If we can locate the genes contributing to disease--some enzyme being made or not being made," explains Dr. Knowler, "we can identify which people are at high risk for the disease and figure out ways to intervene." Finding these genes will help doctors identify youngsters at risk and begin prevention before disease sets in.

Another important finding has already made a difference in how diabetes patients are treated. The



Dr. Peter Bennett, Chief of the Phoenix Epidemiology and Clinical Research Branch of NIDDK



The Gila River Arts and Crafts Center at Sacaton, Arizona

complications that come with long-term diabetes--kidney disease, eye disease, and amputations caused by nerve damage--are the major reasons for illness and death among the Pima Indians. When Dr. Knowler began his research in Phoenix, few understood what he and his colleagues would discover by working with Pima volunteers: that high blood pressure predicts complications of diabetes such as eye and kidney disease, and that lowering blood pressure may slow the onset of diabetes and the progress of already existing kidney disease. Because of this work, doctors today are not only aware of the need to treat high blood pressure in people with diabetes, but they begin treating it sooner than in the past.

"Our greatest pride," says Dr. Knowler, "is in conducting research that affects clinical practice."

Other research with important implications for future generations is Dr. David Pettitt's study of high blood sugar and diabetes in pregnant women. By working with Pima volunteers, Dr. Pettitt found that children born to diabetic women are more likely to be overweight and more likely to develop diabetes than children of women who have not developed diabetes.

Dr. Eric Ravussin conducts studies that measure food intake, metabolism, and energy expenditure to evaluate their interaction and contribution to a genetic predisposition to obesity.

Now NIH and the Pima Indians are building on these accomplishments. "The search goes forward on two fronts," says Dr. Knowler. "We're working hard on the genetics of the disease. We're optimistic we will find one or more genes. It's still hard to predict how we might prevent diabetes, but we might, for example, be able eventually to correct the genetic difference that causes disease. More immediately, identifying the diabetes genes would allow us to identify the people most likely to get the disease."

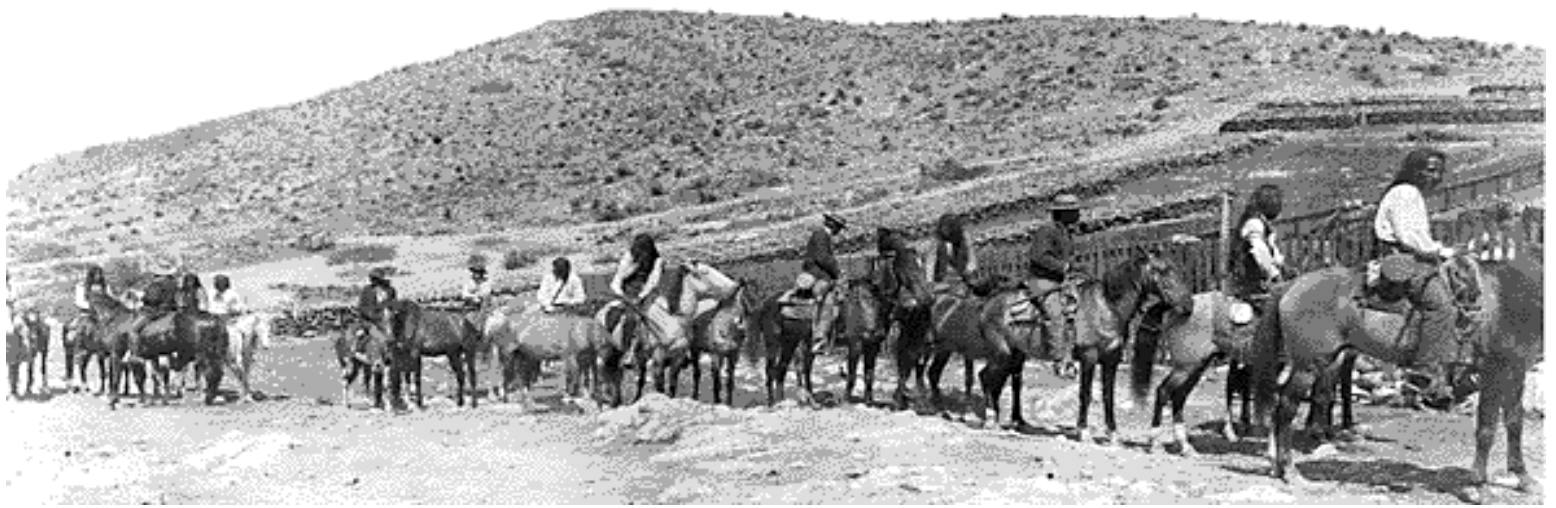


Luis Morago, a noted scout for the U.S. Army in 1872 (Smithsonian Institution)

The second strategy is to encourage those who are at high risk to change behaviors that can lead to diabetes, such as eating a high fat diet, being physically inactive, and being overweight.

The NIH has begun a major nation-wide program to prevent diabetes in people who increase exercise and eat lower fat foods. Fifty percent of the volunteers will be American Indians and other minorities, and once again, the Pima Indians will be prominent among them. Health for this and future generations: that's the NIH-Pima goal.

-- Jane DeMouy



Pima Scouts in 1886 (Smithsonian Institution)