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News

The University of Texas Health Science Center at Dallas
5323 Harry Hines Boulevard Dallas, Texas 75235 (214)688-3404

CONTACT: Christopher Land
Office: 214/688-3404
Home: 214/239-5104

*****Team of top experts on diabetes and obesity probe the plight of the Pima Indians.

DALLAS--For more than 2,000 years the Pima Indians have lived in a remote river valley in the Arizona desert. Genetically isolated, they survived by adapting to cycles of feast and famine. Now, however, the "River People" have fallen prey to the twin maladies of diabetes and obesity.

With the highest rate of diabetes ever recorded, the Pimas are receiving special attention from some of the world's top scientists in an unprecedented effort that may reap benefits for all mankind.

Fifty percent of the Pimas aged 35 years and older are diabetic--15 times the overall U.S. rate--and almost all adult Pimas are obese. Because of this extraordinarily high incidence of diabetes and obesity, the Pima Indians are an ideal population for study of these important related diseases, notes Dr. Roger Unger, professor of medicine at The University of Texas Southwestern Medical School and Senior Medical Investigator at the Dallas Veterans Administration Hospital. As a result, the National Institutes of Health (NIH) is currently funding a research unit for the study of human diabetes in Phoenix with UT Southwestern Medical School as the contracting institution and Dr. Unger, an internationally recognized diabetes researcher, as the principal investigator.

Diabetes--a metabolic disease characterized by high blood sugar--and obesity both increased in the United States during the last 30 years. According to the American Diabetes Association, diabetes now ranks as the third leading cause of death in the U.S. and as the leading cause of new cases of blindness.

Indian tribes in the Southwest have been especially hard hit. This major effort creates a research unit in this area capable of attracting the world's top experts on diabetes and related disorders to Phoenix for interdisciplinary conferences and collaborative projects. So far, scientists at 16 different institutions have agreed to collaborate, including: the University of Geneva, Switzerland; the University of Chicago; the University of California at San Diego; Harvard University; the Salk Institute in California; and the Bronx, N.Y., VA Hospital. The group of scientists includes two recent Nobel prize winners.

"This effort may be unique in medical history because we are assembling from all over the world the scientific talent required to explore a problem in a single population," Dr. Unger says. "The research unit now has at its disposal the most distinguished panel of collaborators that can be assembled for such a collective research effort."

The first two years of the contract have proven the feasibility of the project, he continues. "Indeed, this may be a preferred method for the solution of certain types of medical problems."

The diabetes unit is located in the Phoenix Clinical Research Center, an NIH-supported facility directed by the pre-eminent epidemiologist Dr. Peter Bennett. By studying the Pimas for over a decade, Bennett has produced "the most comprehensive epidemiological data ever compiled on diabetes in a population," Unger says.

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Writing about his studies in a recent issue of "Diabetes Forecast," Dr. Bennett said: "While we still do not know the basic reason why so many of the Pimas develop diabetes, it is unequivocally clear that there is an inherited predisposition to the disease. Following whole families over a long period of time will ultimately enable us to determine what proportion of the children of various types of parents--two diabetic parents or a diabetic mother and a non-diabetic father, for example--will subsequently develop the disease. In this way, just how diabetes is inherited will become apparent."

Research efforts are concentrating on the Pimas because they are a genetically homogeneous population. Archaeological evidence indicates the tribe has lived in the same river valley for more than 2,000 years. In fact, they call themselves the "River People" and several centuries before the time of Christ their ancestors were irrigating fields of corn by means of a remarkably well-engineered canal system. Since that time most Pimas have married within the tribe. And most eat the same foods and have basically the same lifestyle. So they are a homogeneous population in terms of the two key factors thought to be involved in development of diabetes and obesity--heredity and diet.

Of course this is not the case in the general American population, which is a "melting pot" full of people of Oriental, African, and Northern and Southern European origins, among others. And Americans in general have a wide range of diets and lifestyles, which again makes it difficult to get any reliable scientific data. "There are so many different factors involved when you study the general population that it becomes very hard to interpret your data," Dr. Unger explains.

Further complicating such studies is the fact that diabetes is not one but several different diseases with similar symptoms. The chance of finding one defect, or one group of defects, that cause or contribute to diabetes and obesity is much greater in a homogeneous population such as the Pimas. "I think it's clear that you can only get so far if you just study the people who happen to live around your medical center," Dr. Unger says. "You really need special populations to study certain problems."

The majority of diabetic Pimas develop the disease as adults. Thus, they are said to have "adult-onset" diabetes. About 90 percent of U.S. diabetics suffer from this form of the disease, so results from the Pima studies should be applicable to a large majority of all diabetics.

When diabetics of the adult-onset variety gain weight, their diabetes often gets worse; when they lose weight, their condition improves. Sometimes all evidence of diabetes vanishes in those with milder forms of the disease if their weight is corrected. Obesity clearly is one of the risk factors for adult-onset diabetes. But of course there are plenty of obese people who are not diabetic. Genetic risk factors are also involved.

Although Pimas usually are not diabetic until adulthood, many of them do become obese in adolescence. Dr. Unger believes this is a growing problem in the general U.S. population too:

"I think there has been an increase of obesity in the young here in the United States to the point that it has become a terribly serious problem. I'm not talking about the middle-aged person who gets a little heavy around the waist. I'm talking about people under 35 who are massively obese. I believe this is a relatively recent phenomenon. And when this generation reaches middle-age, they may be susceptible to a number of serious health problems including diabetes.

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"Obesity on the scale that it exists in the United States is pretty unique," he continues. "It's not really seen in any other country, at least not to this degree. I think it's a shock to people coming from overseas when they see how much obesity there is in this country."

The ability to get fat was of survival value to the Pimas when their crops were failing an average of once every five years because of drought. Those who became fat during times of plenty had a better chance of surviving periods of famine.

The desert rat has made a similar adjustment to life in the arid Southwest. When it rains and there is a lot of food available, the desert rat eats and eats and gets very fat. When the dry season comes, he has stored enough fat to survive till the next rainy season. But if you put the desert rat in a cage and give him plenty of food year round, he "gets so fat he can barely move," Dr. Unger says.

Researchers have theorized that this may be analogous to what is happening to the Pimas and some other Americans who have what one scientist labeled "thrifty genes," that is, genetic factors that in the past would have enabled them to survive when food was scarce, but now are contributing to their obesity because food is plentiful.

In this analogy the "cage" is the American lifestyle and diet, with food always available. The situation is especially harmful to young Americans. "From an early age these kids are surrounded with easily available food," notes Dr. Unger. "In the past people had to go to a lot of trouble to get food, but now there are vending machines everywhere and fast-food places surround the campuses of most high schools and colleges."

Those who don't have the genetic capacity to get fat will stay relatively thin even when they overeat. This has been tested by a group at the University of Vermont now collaborating in the Pima study. The Vermont researchers fed lean prisoners a very high-calorie diet--about three times their normal intake. The prisoners gained only about 15 pounds and then their weight leveled off. In order to maintain the extra weight, the prisoners had to stay on a high-calorie diet. In contrast, an obese Pima can maintain a weight of 300 to 400 pounds on a relatively small number of calories per day.

Some of the Pimas have been able to lose up to 100 pounds by spending several months in the Phoenix Clinical Research Center where their diet can be rigidly controlled. In these patients the investigators are studying differences in fat and sugar metabolism before and after the weight loss to determine why losing weight produces such marked improvement in diabetics.

The various participating research groups are also conducting further studies of glucagon and somatostatin, two hormones known to be involved in the syndrome of diabetes and obesity. Dr. Unger has produced evidence that both hormones play important roles in the regulation of blood sugar levels and may be useful in treating diabetes. In addition, preliminary studies indicate that somatostatin may have the ability to slow down the absorption of sugars and fats in the gastrointestinal tract and in this manner it may play a key role in obesity. "It's possible that abnormalities in somatostatin are present in both diabetes and obesity," Dr. Unger says.

Much of the work on these and the other studies going on at the Phoenix center is performed by an "on-site" staff of medical scientists, which includes Drs. Murugasu Nagulesparan, Barbara Howard, David Mott and Frank Kosmakos. Together with scientists at the 16 participating institutions, this outstanding team of researchers is following leads that may result in improved treatment and prevention of diabetes and obesity.

Eventually, the genetics and lifestyle of this small, isolated tribe in the Arizona desert may provide a key to survival for the world's diabetic population.

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