

# An Evaluation of Three Models for High-prevalence Diabetes Rates in Native Populations

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## INTRODUCTION

Non insulin-dependent Diabetes Mellitus (NIDDM), more commonly known as Type 2 Diabetes, greatly affects many Native American groups when compared to the U.S. population as a whole. A genetic basis was proposed in the early 1960s, suggesting that certain hunter/gatherer populations had developed an adaptation to their “feast or famine” existence. The hypothesis claimed that this adaptation led to obesity and diabetes when these people transitioned to sedentary lifestyles and a high-calorie diet.

Even though this “thrifty genotype” hypothesis has gained wide acceptance in scientific circles and among Native Americans, the responsible genes have yet to be discovered. Other hypotheses for the origins of Type II Diabetes in certain Native American populations have begun to gain a foothold, and are better supported by experimental data. These hypotheses focus on nutritional issues during fetal development, and lead to very different approaches for treatment and intervention. The recent availability of Indian Gaming revenue could provide additional resources for implementing such intervention programs.

## THE THRIFTY GENOTYPE MODEL

As early as 1962, a genetically-based etiology for the Type 2 Diabetes epidemic among many Native American populations was proposed (Benyshek 2001:30). The hypothesis rests upon the assumption that the first Americans encountered severe “feast-or-famine” conditions while migrating from Asia to North America. Those who could more readily store blood sugar in fat cells when food was available were better able to survive long periods without food by living off the stored energy source. This natural selection for an energy-thrifty genotype resulted in a valuable trait, which carried the first Americans through thousands of difficult years on the new continent.

Unfortunately, this same trait became a liability when Native Americans adopted a western-style diet and a more sedentary life way. Their highly efficient metabolisms were ill-prepared for a high-fat, high-calorie diet, and the results were obesity and diabetes.

This hypothesis was echoed and supported for decades, resulting in a theme that appears repeatedly in the scientific literature: “Diabetes is inevitable, uncontrollable, and unpreventable in high-prevalence communities” (Benyshek 2005:195).

While studies have shown a significant genetic connection for some of the rarest forms of diabetes (Benyshek, et al. 2001:32), the search for a gene (or combination of genes) which causes Type 2 Diabetes has so far come up empty (Martin 2004:2).

This lack of supporting genetic evidence hasn't slowed the “thrifty genotype” juggernaut, however. Only a few years ago, Elbein (1997:1891S) began an article discussing the genetics of diabetes by claiming that Type 2 Diabetes is strongly inherited, yet the concluding paragraph of the same paper contains the following sentence: “To date, success in identifying a cause for the bulk of NIDDM is limited.”

While there is a dearth of evidence in favor of the “thrifty genotype” hypothesis, considerable evidence exists which undermines it. Two related Native American tribes, the Dogrib of Canada and the San Carlos Apache of the American Southwest, have similar histories since arriving on the continent. They are descended from common ancestors who crossed the Bering Strait, they both lived a hunter/gatherer existence for several thousand years, and they both transitioned to a western lifestyle (including a high-calorie diet) in the twentieth century. Even so, the San Carlos Apache suffer a high prevalence of NIDDM, while only 1.5% of the Dogrib had Type 2 Diabetes in 1999 (Benyshek, et al. 2001:43).

Little about the “thrifty genotype” model is questioned, including its foundational assumption that hunter/gatherer populations commonly suffer periods of starvation. A large

body of archaeological data suggests the opposite: It was prehistoric agricultural societies that experienced severe and frequent periods of starvation (Benyshek, et al. 2001:34).

The staying power of such a straightforward and believable hypothesis has significantly affected the types of intervention programs deployed in high-prevalence communities. The assumption that Native Americans possess an inherited predisposition for diabetes permeates such programs, and as a result they present life-long lifestyle changes as the only effective method for controlling symptoms (Benyshek, et al. 2001:28). Not surprisingly, no prevention program in Indian country has resulted in a net reduction of diabetes (Benyshek 2005:194).

#### THE THRIFTY PHENOTYPE MODEL

In the early 1990's, British researchers put forth the "thrifty phenotype" hypothesis, based on findings that suggested fetal undernutrition leads to Type 2 Diabetes in adulthood (Benyshek, et al. 2001:35). Experimental research on rats supported this, demonstrating that gestational protein malnutrition stunts fetal growth, induces glucose intolerance, and results in decreased insulin secretory capacity in the offspring (Benyshek, et al. 2001:36). There is an inverse correlation between birth weights in stunted offspring and the severity of both insulin resistance and glucose intolerance they experience (Martin 2004).

All of the Native American groups that show a high-prevalence of Type 2 Diabetes experienced a period of prolonged starvation in the late 19th century (mostly due to forced marches and camp internment by the U.S. Government). The generation of children born during this time is the first with a significant increase in the incidence of Type 2 Diabetes (Martin 2005).

The "thrifty phenotype" hypothesis presents a substantiated model by which fetal protein undernutrition leads to elevated glucose levels in later life, but it fails to explain how diabetes could be passed on to subsequent generations (Benyshek, et al. 2001:37). Nevertheless, it

clearly underscores the importance of quality prenatal care, which necessarily includes a sufficient and balanced diet.

## THE MULTIGENERATIONAL MODEL

Building on the work of Barker and others, John Martin, Daniel Benyshek, and their colleagues identified the next step in the puzzle: How a disease with fetal origins is passed on to later generations.

Experimental studies using rats at Arizona State University showed that insulin-deficient, gestationally-diabetic females born to protein malnourished mothers also give birth to stunted offspring when they are fed a high-fat, low protein diet during pregnancy. These offspring are all insulin resistant and hyperinsulinemic, i.e., they are capable of secreting large amounts of insulin (Martin 2005). When females from these stunted offspring are fed the same diet during pregnancy, they too give birth to rats that are also insulin resistant and hyperinsulinemic (Martin 2004). As long as similar diets are eaten, the cycle continues.

It is interesting to note that while the gestational conditions that create the first generation of diabetic-prone offspring are dominated by undernutrition, the subsequent generations of affected offspring experience overnutrition in the womb. The mother's gestational diabetes ensures a glucose-rich environment for the fetus, resulting in increased bone growth, more fat cells, and a larger pancreas (Martin 2005).

Martin's (2000:744) data clearly support the multigenerational hypothesis, and manage to expose a major flaw in the "thrifty genotype" model at the same time. The experiments developed insulin resistance through multiple generations of a population of rats that were genetically normal.

The most stunning result of the animal research at ASU came next. By placing insulin-resistant females from the study on a 30% calorie-restricted diet (compared to the control group)

during pregnancy, they were able to break the cycle. The offspring of the restricted-diet females were normal: Their birth weights were normal, and they were neither hyperinsulinemic nor insulin-resistant (Martin 2004).

The conclusive results of these experiments carry a strong implication for human intervention. Martin (2004) argues that community health programs that focus on controlling body weight prior to pregnancy and weight gain during pregnancy, combined with monitoring and control of blood glucose throughout pregnancy, may prove quite effective in reducing the incidence of diabetes in high-prevalence Native American communities.

#### AN APPROACH FOR INTERVENTION

Benyshek, Martin, and Johnson (2001:48) make a compelling argument that prenatal monitoring and control of a mother's blood glucose levels can break the familial cycle of Type 2 Diabetes. Improved prenatal care featuring such monitoring would thus seem like an obvious goal, and even those who still doubt the fetal origin etiology could not oppose such programs when "normoglycemia during pregnancy appears to be a consistent and unqualified goal in obstetric medicine" (Benyshek, et al. 2001:49).

Prenatal care is the key to reducing the incidence and prevalence of Type 2 diabetes, and the necessary behaviors should be much easier to inspire and maintain. Convincing a soon-to-be mother to accept some self-sacrifice during the nine months of pregnancy on behalf of their unborn child should be simple, compared to the impossible task of compelling an entire population to change their eating and exercise habits for the rest of their lives. Benyshek (2005:194) reported that non-compliance with prevention recommendations has exceeded 80% in some high-prevalence Native communities with active diabetes prevention and management programs.

Any effective plan for reducing diabetes within high-prevalence Native American groups must account for much more than the likely etiology and the best treatment. It must also consider: The culture and its likely response to interference from people outside the community; the political environment; and the resources available to those hoping to make a difference.

While non-native researchers and medical professionals may have a lot of the answers, they will still likely be viewed as outsiders. I believe that successful intervention programs must arise from within the Native American communities. Relationships must be built between the scientific community and Native Americans in a position to create such programs from the inside.

It is also important to account for the political climate. Martin (2005) indicated that influential persons within Native American communities are much more concerned about treating the more senior members who display the most serious symptoms (which often translates to themselves). Any proposed new intervention policy must not reduce any diabetes management programs already in place. Instead, it should probably increase their funding and scope of the existing programs, to minimize opposition to the new prenatal intervention programs.

The recent availability of revenue from Indian gaming creates new opportunities for combating diabetes in Native American communities. With greater financial resources, intervention programs could be created which address the management of adults already suffering from diabetes, and provide the necessary enhanced prenatal care at the same time.

## CONCLUSION

The multigenerational, fetal-origin theory for the etiology of the Type 2 diabetes epidemic in Native American populations is well-supported by experimental data on animals, and also fits very well with the histories of those Native populations with a high prevalence of Type 2

Diabetes. These same experiments have also provided a method for interrupting the cycle, allowing a new generation to be born free of the yoke of diabetes.

The successful breaking of the cycle of diabetes in rats holds great promise for applying these same methods to humans. Prenatal monitoring and control of blood sugar during the entire pregnancy for women who are insulin resistant might well break the observed diabetes cycle in Native American communities.

The ultimate challenge will be the implementation of such programs in the face of a widely-held belief in the genetic origins of diabetes, cultural pressures to hide pregnancies, and political pressures to spend healthcare dollars elsewhere.

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