GASTRIC EMPTYING IN ETHNIC POPULATIONS: POSSIBLE RELATIONSHIP TO DEVELOPMENT OF DIABETES AND METABOLIC SYNDROME

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Direct as well as indirect evidence suggests that rapid gastric emptying may be occurring in Mexican Americans, American Indians, and other ethnic groups. Mexican Americans have been shown to have a more rapid rate of gastric emptying compared to non-Hispanic Whites after matching for weight, sex, and body mass index. Indirect evidence also suggests that American Indians and other ethnic groups may have an accelerated rate of gastric emptying of carbohydrate solutions. The rate of gastric emptying of carbohydrate-containing meals has been demonstrated to positively correlate with postprandial glucose levels (r=.58, P<.05). Accelerated absorption of carbohydrates following rapid gastric emptying in these ethnic groups could be a contributing factor to the increased risk of diabetes and metabolic syndrome. An abnormally accelerated gastric emptying of rapidly absorbed processed carbohydrates could be a genetic adaptation related to the paucity of rapidly absorbed carbohydrates in the native diets of certain ethnic populations. Further investigation is required to study gastric emptying in these different ethnic groups by using scintigraphy or other accurate methods. Ethnic populations with a high incidence of diabetes and impaired glucose tolerance might particularly benefit from therapeutic approaches with agents that slow gastric emptying. (*Ethn Dis*. 2006;16:682–692)

Key Words: American Indian, Diabetes, Ethnic Populations, Gastric Emptying, Metabolic Syndrome, Mexican American

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INTRODUCTION

Certain ethnic populations, such as American Indian, Mexican Americans, Pacific Islanders, Ethiopian migrants to Israel, and Australian Aborigines have a high incidence of type 2 diabetes. Nondiabetic subjects in these populations have abnormally high postprandial glucose and insulin levels after ingestion of an oral glucose load.[1–5] A more rapid rate of gastric emptying of ingested carbohydrates has been described in patients with type 2 diabetes[6–9] as well as in nondiabetic Mexican Americans in comparison with non-Hispanic Whites.[10,11] A rapid rate of gastric emptying may contribute to the postprandial rise in plasma glucose levels in certain ethnic groups.[10,12,13] The rate of gastric emptying after eating significantly correlates with postprandial glucose levels. In 1993, Horowitz et al studied the relationship of gastric emptying to postprandial glucose levels in normal subjects after ingestion of an oral glucose tolerance beverage containing 75 g of glucose in 350 mL of water.[12] In this study, a direct correlation was observed between the area under the glucose curve from 0–30 minutes and the amount of the glucose meal emptied from the stomach at 30 minutes (r=.58, P<.05). A similar correlation of gastric emptying with postprandial glucose levels was also reported by Schwartz et al (r=.51, P<.05).[10] The positive correlation of the rate of gastric emptying with postprandial plasma glucose levels clearly demonstrates the role of gastric emptying in postprandial glucose homeostasis.

The close association of gastric emptying rates to postprandial glucose levels has implications for disease risk. For example, elevated postprandial glucose levels after an oral glucose tolerance test are associated with a significantly increased death from coronary artery disease and overall increased risk of death.[14–21] In another study, glucose levels 90 minutes after administration of a glucose load were shown to be predictive for the development of hypertension three to eight years later.[22,23] A recent study of 234 men with suspected coronary artery disease who underwent angiography has also shown that postprandial glucose levels at two hours after administration of an oral glucose tolerance beverage correlated more strongly with the extent of coronary artery disease (r=.667) than fasting glucose (r=−.03), hemoglobin A1C (HbA1C) (r=.561), postprandial insulin levels (r=.221), or fasting insulin levels (r=.297).[20]

Postprandial plasma glucose levels following an oral glucose load are also considered by many investigators to be a better marker of diabetic control than fasting plasma glucose in type 2 diabetes.[24] Postprandial glucose levels have also been shown to be a greater contributor to HbA1C than fasting glucose levels.[25] This association is important because a 1% decrease in HbA1C is associated a 21% reduction in deaths related to diabetes, a 14% reduction in myocardial infarction, and a 37% reduction in microvascular complications. Glucose levels after an oral glucose load appear to be relevant to normal postprandial physiology. Glucose levels after ingestion of oral glucose correlate closely with glucose levels reached after a mixed meal.[26]

Unfortunately, few gastric emptying studies have been performed in ethnic populations that are at high risk of developing diabetes. An abnormally rapid gastric emptying rate of carbohy-

This article will review the few gastric emptying studies that have been performed in ethnic populations and will also review findings in populations in which indirect evidence points to the possible occurrence of an abnormally rapid rate of gastric emptying.

drates in certain ethnic populations could be a significant factor contributing to the well-known increased risk of diabetes and obesity in these populations. An abnormally accelerated gastric emptying of rapidly absorbed processed carbohydrates could reflect a lack of genetic adaptation related to the paucity of rapidly absorbed carbohydrates in the native diets of certain ethnic populations. This article will review the few gastric emptying studies that have been performed in ethnic populations and will also review findings in populations in which indirect evidence points to the possible occurrence of an abnormally rapid rate of gastric emptying.

GASTRIC EMPTYING IN MEXICAN AMERICANS

Nondiabetic Mexican Americans are more insulin resistant and have a higher incidence of diabetes than age- and weight-matched non-Hispanic Caucasians.[27–29] The incidence of type 2 diabetes in Mexican Americans is ≈2.5 times greater than that of non-Hispanic Caucasians.[30] Much of this increased risk of diabetes is thought to be contributed by 31% admixture American Indian genes occurring in Mexican Americans.[31] The increased incidence of type 2 diabetes in Mexican

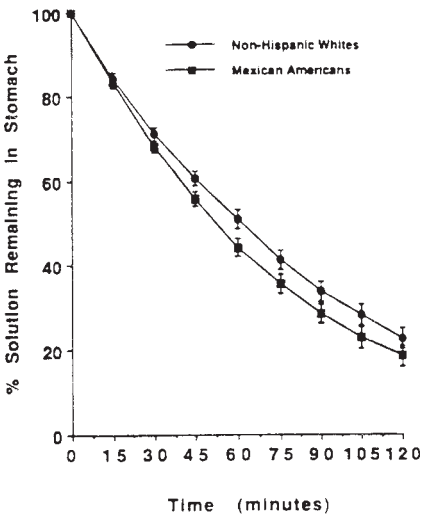

Fig 1. The percentage of glucose solution remaining in the stomach following ingestion of a 50 g glucose solution in 450 mL in 32 Mexican Americans and 31 non-Hispanic White controls matched for age, sex and body mass index. Reprinted with permission from Springer Science and Business Media. From Gastric emptying in Mexican Americans compared with Non-Hispanic Whites. *Digestive Diseases and Sciences*. 1995: 624–630

Americans is approximately midway between non-Hispanic Whites and Pima Indians, who have a five times higher incidence of type 2 diabetes.[30] Similar to native American Indians, Mexican Americans have higher postprandial insulin responses to an oral glucose load compared to matched non-Hispanic Whites after correction for weight and body mass index (BMI).[4] Gestational diabetes also occurs three times more frequently in Mexican Americans than in non-Hispanic Caucasians.[32]

Mexican Americans empty a 50-g liquid (620 mmol/L) glucose meal 15%–20% more rapidly from their stomachs than non-Hispanic Whites who were matched for age, sex, and BMI as shown in Figure 1 ($P<.05$).[10] This study used scintigraphic gastric emptying methods, which are considered the gold standard method of assessing the rate of gastric emptying.[33] This method is based on the use of technetium-99m (^{99m}Tc), which is used to label the ingested meal. After ingestion of the labeled meal, scintigraphy is used to image the stomach and to noninvasively and quantitatively determine the rate of gastric emptying. Another observation from this study was the significant correlation of the rate of gastric emptying with postprandial glucose levels ($r=.51$, $P<.05$).[10]

In a separate study, gastric emptying of beer, which naturally contains liquid carbohydrates, was also shown to be accelerated in Mexican Americans compared to non-Hispanic Whites ($P=.0492$)[11] (See Figure 2A). Partial correlation coefficients (adjusted for ethnicity, sex, age, and BMI) showed the gastric half-emptying time was inversely related to the incremental levels of glucose ($r=-.709$, $P=.0010$) and alcohol ($r=-.650$, $P=.0035$).[11] Postprandial insulin and glucose levels were also significantly higher in Mexican Americans compared with non-Hispanic Whites after drinking beer (Figures 2B and 2C).[11]

Based on the results in Mexican Americans, an accelerated rate of gastric emptying in Mexican Americans is likely to be at least partially responsible for the postprandial hyperinsulinemia reported in the Mexican American population.[4,34] A rapid rate of gastric emptying may also be related to the increased incidence of diabetes and obesity in the Mexican American population in a changing environment with an increasing abundance of rapidly absorbed carbohydrates. The Mexican American population might particularly benefit from therapeutic interventions aimed at slowing the rate of gastric emptying.[35,36]

STUDIES OF GASTRIC EMPTYING IN AMERICAN INDIANS

As previously described, North American Indian populations have

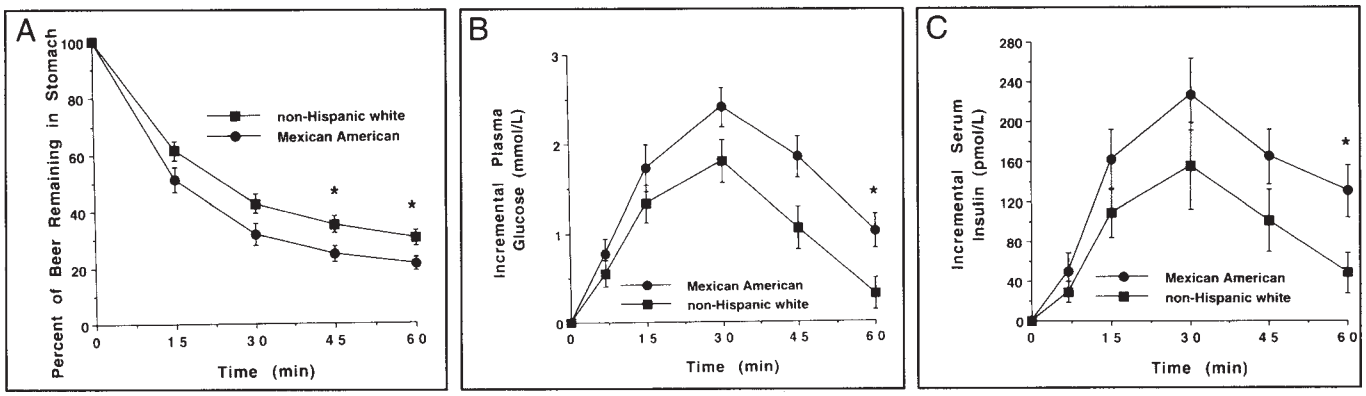

Fig 2. The percentage of beer remaining in the stomach following the ingestion of beer in Mexican Americans compared with non-Hispanic Whites. Reprinted with permission from Elsevier. From Schwartz JG, Salman UA. Gastric emptying of beer in Mexican Americans compared with Non-Hispanic Whites. *Metabolism*. 1996: 1174–1178

a high incidence of diabetes.[37,38] No recent studies of gastric emptying have been performed in American Indian populations with the gold standard method of scintigraphy.

The few gastric emptying studies that have been performed in American Indians have not used optimal methods, however indirect evidence suggests that accelerated gastric emptying may be occurring in American Indians. The gastric emptying studies that have been performed in American Indians and the indirect evidence of accelerated gastric emptying in American Indians will be reviewed in the following section.

Three studies of gastric emptying performed >20 years ago have been reported in Pima Indians. The Pima Indians of Arizona are a relatively homogeneous population with one of the highest reported incidences of type 2 diabetes in the world.[37] The first report of gastric emptying in this population performed in 1972 used a traditional radiographic technique. In this study, Pima Indians were reported to have an accelerated gastric emptying rate of a barium meal.[39] This study briefly described the incidental finding of rapid gastric emptying in Pima Indians as part of a description of the x-ray manifestations of diseases in American Indians of the Southwest.

Another study specifically examined gastric emptying in Pima Indians.[40] In this 1984 study, 17 obese Pima Indians and 9 nonobese Pima Indians were studied. Distilled water (250 mL) was placed in the stomach of Pima Indians by gastrointestinal intubation along with phenol red dye as a marker of gastric emptying. The fractional emptying rate of the water was higher in the obese subjects than in the nonobese subjects (11.7 ± 1.63%/min vs 7.5 ± 1.6%/min) but not significantly different. From this study, the investigators concluded that obesity per se did not affect the rate of gastric emptying in Pima Indians. This study did not assess the gastric emptying rate of calorie-containing liquid meals, and no comparison was made with non-Pima Indian control subjects. Therefore, no conclusion from this study can be made as to how Pima Indians would empty a calorie-containing meal compared to nonobese Caucasian subjects. In a subsequent study, a 75-g glucose solution was administered to obese and nonobese Pima Indians as well as nonobese Caucasians by using the phenol dye dilution technique with intubation.[41] This study also found no significant differences between the obese and nonobese Pima Indian groups. Nonobese Pima Indians emptied the glucose solution at a rate of 3.0% emptying of the ingested meal/min compared to an emptying rate of 3.5% of the ingested meal/min in obese Pima Indians. Nonobese Caucasians had an even greater rate of gastric emptying of 4.8% of the ingested meal/min. All of the gastric emptying rates reported in this study are extremely high for a 75-g glucose solution compared to more recent studies that used scintigraphic methods. For example, in the Pima Indian study, nonobese Caucasian subjects had <20% of 75-g glucose solution remaining in the stomach at one hour, which indicates rapid gastric emptying compared with rates reported in recent studies with the gold standard scintigraphic method. In these more recent scintigraphic studies, normal subjects who were administered a similar 75-g glucose solution had an average of 70% of the glucose solution remaining in their stomach at one hour. In this more recent scintigraphic study, the fractional gastric emptying rate was .5% per minute in normal healthy subjects, which is much lower than those reported in the previously described study that used intubation, which had a 4.8% per minute fractional emptying rate for a similar 75-g glucose solution. The gastric emptying

rates reported in the Pima Indian study calculate a gastric emptying rate of 14 kcal per minute, which is much more rapid than the 1.7–2 kcal per minute reported for normal subjects with recent scintigraphic studies.[42,43] Because the results in this early study comparing Pima Indians to nonobese Caucasians with the intubation technique vary so greatly from more recent research with scintigraphic techniques, it brings into question the accuracy and reliability of these initial gastric emptying studies. Additional studies in Pima Indians and other ethnic populations at high risk of diabetes and metabolic syndrome should be performed with liquid nutrient meals using image-based gold standard scintigraphic techniques.[41]

Although interpreting these prior gastric emptying studies in Pima Indians is difficult, other indirect evidence supports the occurrence of an abnormally rapid rate of gastric emptying in American Indians. This indirect evidence is based on the postprandial measurement of the hormone, glucose-dependent insulinotropic polypeptide, (GIP).[44] This hormone is released from the small intestine at a rate that corresponds to the absorption of nutrients in the small intestine. Since nutrient absorption is rapid once nutrients have been emptied from the stomach into the small intestine, postprandial GIP levels provide a marker of the rate of gastric emptying.[45,46]

Evidence of the close association of postprandial blood levels of GIP with gastric emptying comes from many studies. For example, postprandial GIP levels mirror the rate of direct glucose infusion into the duodenum in healthy male volunteers.[47] When glucose was infused into the duodenum through a catheter at a rate of 1.1 kcal/min, GIP levels rose rapidly and reached a plateau at ≈400 pg/mL. When the glucose infusion was increased to a rate of 2.2 kcal/min, GIP levels reached a plateau at ≈800 pg/mL. This study clearly demonstrates the linear relationship of duodenal glucose absorption with GIP levels and suggests that GIP is a fairly good indirect marker of the rate of gastric emptying. Much other evidence exists of the close correlation of GIP with gastric emptying. For instance, patients with known gastric dumping syndrome have significantly elevated postprandial GIP levels.[48] Subjects with type 2 diabetes have elevated postprandial levels of GIP,[49,50] and these postprandial GIP levels are correlated with accelerated gastric emptying in type 2 diabetic subjects.[46]

Support for the occurrence of rapid gastric emptying in American Indians comes from a study in which postprandial GIP levels were compared between American Indians and Caucasians. In this study, postprandial GIP, insulin, and glucose levels were measured in 25 lean Caucasians, 22 obese nondiabetic Caucasians, and 8 obese American Indians after administration of a liquid 75-g glucose meal. The American Indians in this study were members of the Paiute, Washoe, and Shoshone Indian tribes from the Nevada region of the United States. Lean American Indians were not studied because of the high prevalence of obesity in the American Indian populations from this region. The obese American Indians in this study had much higher postprandial GIP levels compared with matched obese Caucasians ($P<.01$) (Figure 3). Postprandial insulin levels were also moderately elevated ($P<.05$) in the obese American Indians compared with obese Caucasians, while postprandial glucose levels were not statistically different between the two groups. Based on average changes during the first hour of the study, American Indians and Caucasians had similar postprandial increments in glucose (97 ± 19 vs 93 ± 8 mg/dL/min) and moderately greater postprandial increments of serum insulin (285 ± 52 vs 225 ± 34 μU/mL/min, $P<.01$), while GIP levels were more than twice as high in the obese American Indians compared with the obese Caucasian group (3764 ± 769 vs 1487 ± 235 pg/mL/min, $P<0.001$).[44] Based on all previously described studies of postprandial GIP levels, the elevated postprandial GIP levels in these American Indians suggests that their gastric emptying rate was approximately twice as rapid compared with matched Caucasians.

Other evidence in this study suggests that this abnormally rapid gastric emptying in American Indians may be specific to carbohydrates. For example, as part of the same study, American Indians were also administered a liquid mixed meal with a nutrient content of 14% protein, 32% fat, and 54% carbohydrate with a total of 500 kcal. With this mixed liquid meal, the average GIP levels during the first hour were only slightly higher in the obese American Indians compared to obese Caucasians (GIP 4599 ± 615 vs 3738 ± 396 pg/mL/min).[44] This finding suggests that gastric emptying of the meal composed only of liquid glucose was different in Pima Indians compared to obese Caucasians, while gastric emptying of the liquid mixed meal was more similar between these two groups. This evidence of rapid gastric emptying in American Indians is consistent with the previously described studies in Mexican Americans by Schwartz et al.[10,11]

Other indirect evidence is also consistent with the occurrence of rapid gastric emptying in American Indian populations. For example, native American Indian populations have elevated postprandial levels of insulin.[2] One possibility is that these postprandial insulin levels could be a response of the body to an abnormally rapid rate of entry of the glucose into the blood following rapid gastric emptying. For example, both normal and prediabetic Pima Indians have a hyperinsulinemic response after administration of a 100-g glucose solution compared with

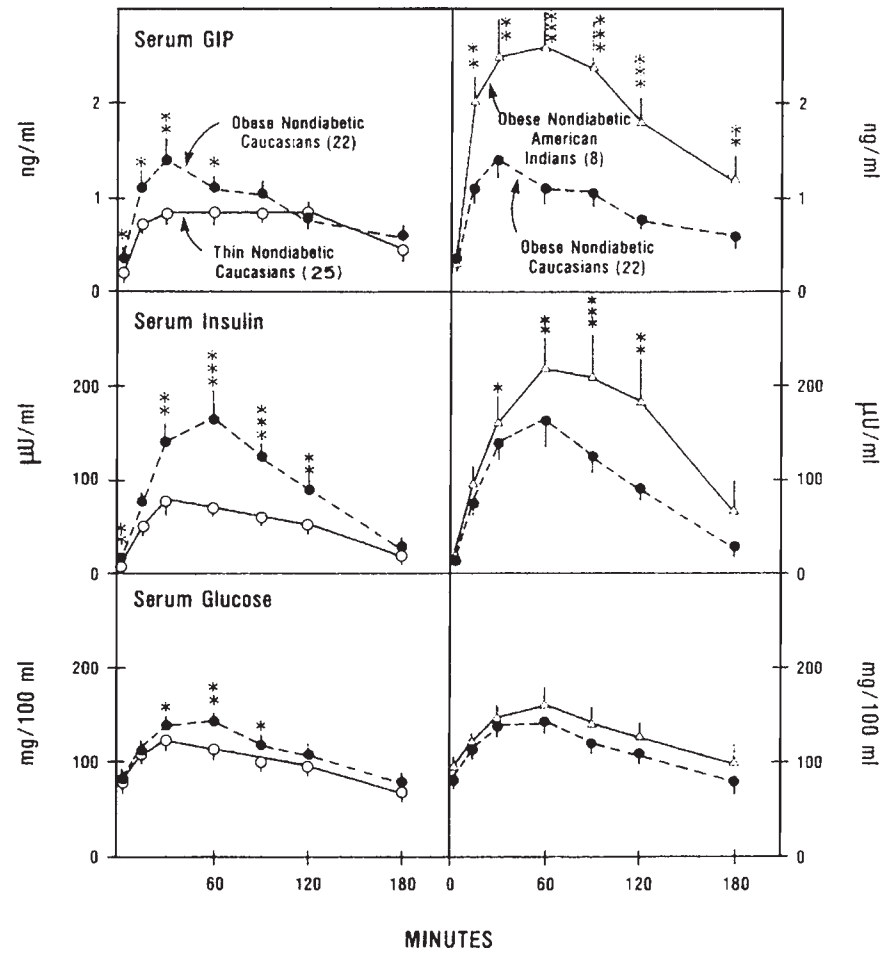

Fig 3. Postprandial GIP levels are very high in obese American Indians following administration of oral glucose. Although GIP and insulin levels were higher in obese, non-diabetic Caucasians compared to thin, non-diabetic Caucasians, GIP levels in North American Indians were much higher than those of obese Caucasians. GIP has been shown to correlate with the rate of gastric emptying in previous studies. Reprinted with permission from the Endocrine Society. From Mazzaferri E, Starich G, Lardinois C, Bowen G. Gastric inhibitory polypeptide responses to nutrients in Caucasians and American Indians with obesity and noninsulin-dependent diabetes mellitus. *J Clin Endocrinol Metab*. 1985;61(2):313–321

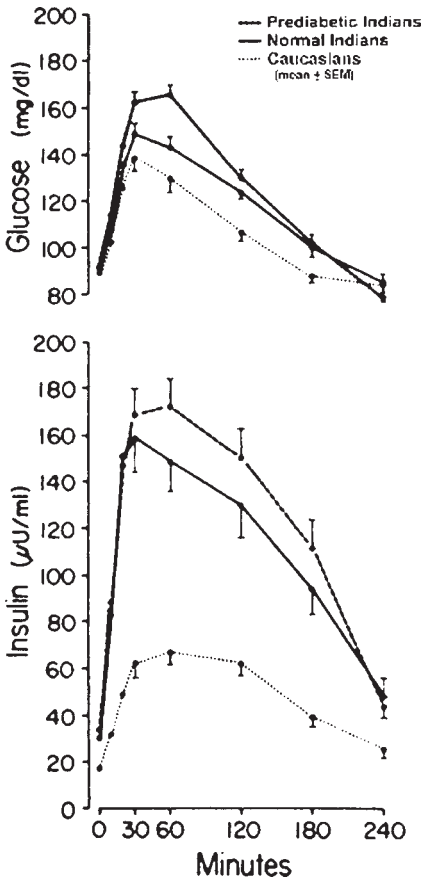

Fig 4. Normal and prediabetic Pima Indians demonstrate a hyperinsulinemic response to an oral glucose load compared to normal Caucasians. The mechanism of the hyperinsulinemia was considered unexplained by the authors. Rapid gastric emptying could be contributing to this hyperinsulinemic response. Reprinted with permission from the American Diabetes Association from Aronoff SL, Bennett PH, Gorden P, Rushforth N, Miller M. Unexplained hyperinsulinemia in normal and "prediabetic" Pima Indians compared with normal Caucasians. An example of racial differences in insulin secretion. *Diabetes*. 1977;26 (9):827–840

nondiabetic Caucasians.[2] In this study, 26 normal Pima Indians, 32 prediabetic Pima Indians, and 29 nondiabetic Caucasians without a family history of diabetes were studied. The subjects were classified on the basis of a 75-g OGTT. The normal Pima subjects were classified on the basis of a plasma glucose ≤140 mg/dL at two hours and no evidence of diabetes in either parent. The prediabetic subjects were classified as prediabetic by having a two-hour plasma glucose ≤140 mg/dL and having at least one parent with plasma glucose levels >275 mg/dL at two hours after an oral 75-g glucose tolerance test. Plasma insulin and glucose were measured at baseline and at 30-minute intervals during the four hours of the study. Both the prediabetic and normal Pima Indians had greatly elevated postprandial insulin levels compared to Caucasians, as shown in Figure 4. The mechanism for this postprandial hyperinsulinemia was considered to be unexplained.[2] Although several possible mechanisms were suggested in this article, such as a genetic decrease in insulin sensitivity in this population, one explanation not considered by the authors was the possibility that an excessively rapid rate of gastric emptying in Pima Indians

resulted in an elevated postprandial insulin response. If rapid gastric emptying is occurring in Pima Indians, the postprandial insulin elevation could simply be a normal physiologic response to control blood glucose levels, which is required by the rapid entrance of glucose into circulation following rapid absorption of nutrients by the duodenum.

Pima and other American Indians groups have been exposed to a more processed modern diet for at least the last 50 years, which could be altering their normal responses to an oral glucose load. For this reason, knowing how American Indians, living a more traditional native lifestyle, respond to oral glucose loading in terms of gastric emptying and postprandial insulin responses is important. The Dogrib Indians of the Northwest Territories of Canada were still living a traditional lifestyle in the late 1980s. At that time, type 2 diabetes was a rarity among them. These Dogrib Indians had normal fasting glucose and insulin values, and they were not overweight. Because of these characteristics, the Dogrib Indians were considered to be ideal candidates for investigating the etiology of type 2 diabetes in the American Indian population. After administration of an oral glucose tolerance test containing 100 g of glucose, these Dogrib Indians experienced a large rise in plasma insulin levels after one hour (Figure 5).[3,51] This postprandial rise in insulin was almost as high as that occurring in Navaho Indians who were obese and at high risk of developing diabetes.

This massive rise of insulin in the Dogrib Indians after administration of an oral glucose load was not explained by a lack of prior carbohydrate consumption as it occurred even in those subjects that had consumed >240 g of carbohydrate the day before the study. This massive rise in postprandial insulin in Dogrib Indian subjects may be due to an excessively rapid gastric emptying rate after ingestion of the oral glucose solution. The hyperinsulinemic response could be viewed as a normal physiologic response required to control blood glucose levels following an excessively rapid rate of glucose entry into the blood.

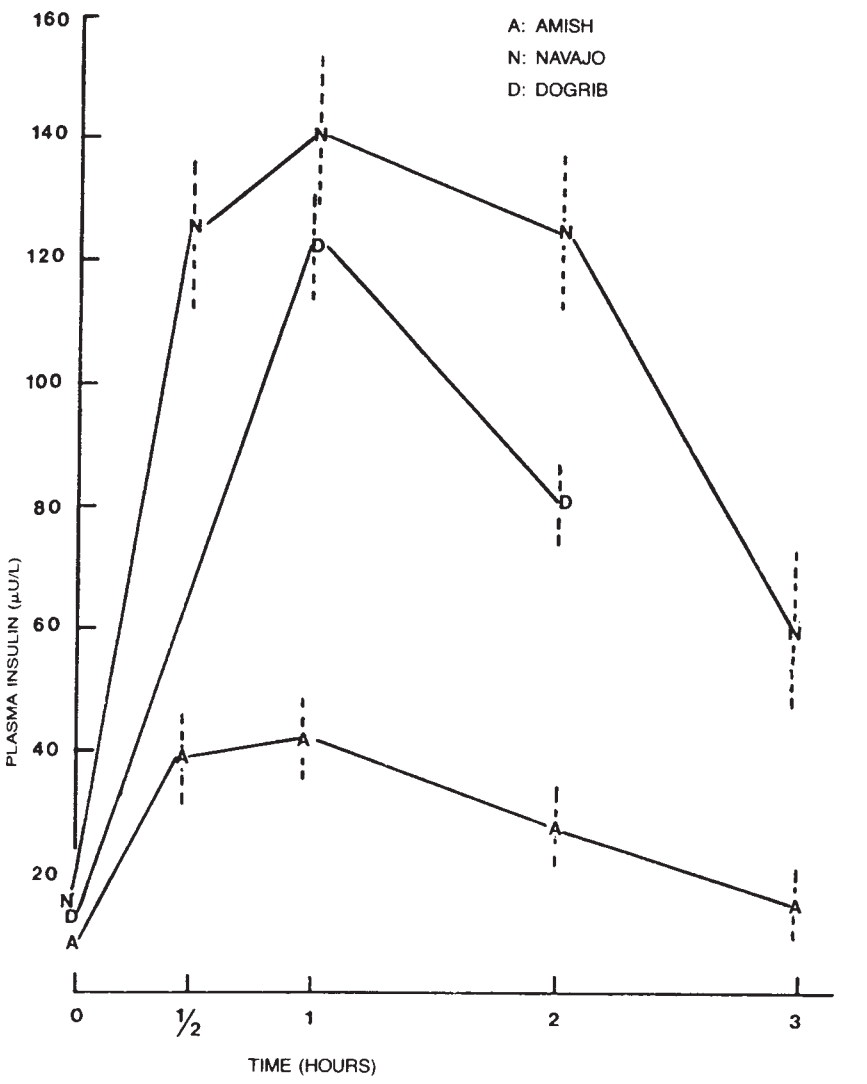

Fig 5. Note the high postprandial insulin levels in two American Indian populations, the Navajo and the Dogrib. This elevation is particularly interesting in the Dogrib Indians because of their low carbohydrate diet and little change in their diet for the last 1000 years. Reprinted with permission from Taylor and Francis group, LLC. From Szathmary EJ. The impact of low carbohydrate consumption on glucose tolerance, insulin concentration and insulin response to glucose challenge in Dogrib Indians. *Med Anthropology*. 1989 (11):329–359

If rapid gastric emptying is occurring in Dogrib Indians and other American Indian populations, it might be due to a lack of genetic adaptation to processed carbohydrate ingestion. Dogrib Indians are a population whose original native diet consisted primarily of meat and fish, such as were available aboriginally in the arctic and subarctic.[3]

Indirect evidence described in this section suggests that gastric emptying of carbohydrates may be more rapid in American Indians than in nondiabetic Caucasians. Abnormally rapid gastric emptying of carbohydrates could provide an explanation for the

hyperinsulinemic response observed after carbohydrate ingestion in American Indians and the high incidence of diabetes and obesity in these populations. Unfortunately, no recent gastric emptying studies using current methods have examined gastric emptying of carbohydrate meals or liquid glucose in these populations. High-quality scintigraphic gastric emptying studies should be performed in these American Indian populations. Studies of this type could provide explanations for the increased incidence of obesity and diabetes in these populations upon exposure to diets of highly processed carbohydrates. American Indians could benefit from recently approved medications that slow the rate of gastric emptying following meal ingestion.[35,36]

ETHIOPIAN IMMIGRANTS

Indirect evidence also suggests that rapid gastric emptying may be occurring in other ethnic populations. One such population is Ethiopians who have migrated to Israel in the last two decades. These immigrants have a high incidence of diabetes, which develops shortly after their migration to Israel. Nine percent of 158 Ethiopians that had recently immigrated to Israel who were administered an oral glucose tolerance test were found to have diabetes and another 9% were found to have impaired glucose tolerance based on two-hour glucose values.[52] These immigrants were relatively young for development of type 2 diabetes (<30 years of age) and all had a BMI <27. These rates of diabetes and impaired glucose tolerance are high compared to the nonimmigrant Ethiopian populations living in northern Ethiopia. Even more unusual and interesting to the investigators who have studied this immigrant population, 13 of 158 Ethiopian immigrants tested had the unusual occurrence of normal fasting glucose and an extremely high one-hour glucose value (390 mg/dL) that could not be classified as either diabetes or impaired glucose tolerance because their two-hour glucose values were normal. These 13 young Ethiopians had an average fasting glucose value of 76 mg/dL with extremely high average one-hour glucose levels of 390 mg/dL, while their two-hour glucose level returned to near-normal levels of 117 mg/dL. Unfortunately, neither insulin nor GIP levels were measured in these studies.

One explanation for the severe glucose excursions at one hour could be that the Ethiopian migrants have a rapid rate of gastric emptying and a subsequent rapid rate of intestinal glucose absorption. An alternative explanation is that this group has severe insulin resistance, which allows glucose to become elevated at one hour but somehow permits the return of glucose levels to near-normal levels by two hours. However if this degree of insulin resistance were present, blood glucose would be unlikely to return to near-normal levels by two hours. These high one-hour glucose levels followed by normal glucose levels at two hours suggest that gastric emptying rates may be rapid in this ethnic group. Two years after discovering these metabolic anomalies in the Ethiopian immigrants, these same Ethiopian immigrants were restudied and compared to immigrants that had recently arrived in Israel who were living under the same conditions.[53] These two-year immigrants had significantly elevated blood pressures, lipidemia, fasting insulinemia, and HbA1C levels compared to newly arrived immigrants.[53]

POSSIBLE MECHANISMS OF ABNORMALLY RAPID GASTRIC EMPTYING IN NATIVE POPULATIONS

The recent conversion of many native peoples from a hunter-gatherer diet to a processed carbohydrate diet is associated with a high incidence of diabetes and obesity in these populations. These populations include native Americans, Pacific Islanders, and Australian aborigines as well as many others.[54–56] A lack of adaptation to a Western processed food diet could be manifested by lack of appropriate hormonal responses required to control the rate of gastric emptying of highly processed and rapidly absorbable carbohydrates. This lack of appropriate hormonal responses may be the mechanism that results in an abnormally rapid gastric emptying of processed carbohydrates in certain ethnic groups. The highly processed Western diet is a different diet from the hunter-gatherer diet of human populations before the agricultural revolution 10,000 years ago.[57] An excellent review discussing the likely nutrient content of the Paleolithic hunter-gatherer diet has recently been published.[57]

Conversion of native peoples from a Paleolithic diet to a Western diet containing high-carbohydrate, processed foods that do not strongly stimulate cholecystokinin (CCK) and other GI hormones could result in rapid gastric emptying and elevated postprandial glucose and insulin levels. Foods in the native diet, on the other hand, are more likely to stimulate normal GI hormones such as CCK, leading to a more controlled rate of gastric emptying.[58,59] For example, Pima Indians had an agricultural system that provided them with extremely low glycemic carbohydrates such as beans, which are also strong stimulators of CCK secretion.[60] CCK has many actions, of which one of its most important is slowing the rate of gastric emptying.[61,62]

Excessively rapid gastric emptying of processed carbohydrates could lead to elevated postprandial glucose and insulin levels and predispose these native populations to the development of obesity, coronary artery disease, and diabetes.[63] The greatly increased intake of snacks high in processed carbohydrates and

liquid carbohydrates, such as soda beverages, which are now increasingly consumed in Western societies, could have significant detrimental effects in ethnic populations that are less genetically adapted to these foods. Dietary interventions in these populations may be particularly important, as studies have shown that sugary beverages contribute 9.5% of total energy intake of American Indian children.[64,65] Genetically based decreased gastrointestinal hormone response to high-carbohydrate foods could also explain the increased incidence of gallbladder disease in these American Indian populations. Several recent studies have demonstrated that in normal subjects, CCK release is moderately stimulated by eating carbohydrate-containing foods.[66,67] Decreased gallbladder contraction in response to meals is thought to a factor leading to gallstone formation.[68] Pima Indians and other native American Indian populations as well as Mexican Americans have a high incidence of gallbladder disease.[69,70]

Beneficial Effect of Native Foods on Postprandial Glycemia

When ethnic populations return to a diet that resembles either their native hunter-gatherer diets or their native agricultural diet, remarkable improvements occur in their glucose and lipid blood levels. This beneficial effect of native diets has been shown in native Hawaiians, Pima Indians, and other native peoples.[58,71,72] Native diets are traditionally composed of low saturated-fat meats containing higher levels of omega-3 lipids and monounsaturated lipids and other high-fiber, low-glycemic-index foods.[57,73] Native diets are often composed of beans and unsaturated fats as well as other foods that are naturally strong stimulators of CCK secretion.[60,74] Other potential advantages of native diets is that spices and herbs contained in these native diets have been associated with slowing the rate of gastric emptying.[75–79]

Comparison Gastric Emptying Studies between Ethnic Populations

Existing evidence suggests the possibility that gastric emptying of nutrients varies between ethnic populations. Based on this preliminary evidence, more studies are required to compare gastric emptying rates between ethnic populations. One potential method for comparing the gastric emptying patterns between different ethnic populations would be through the use of a standardized glucose-containing beverage. This beverage should have a physiologic osmolality (<650 mmol/L) that does not trigger nonspecific slowing of gastric emptying from high osmolality.[80] Schwartz et al have already described the use of a 50-g glucose beverage contained in 450 mL of water for comparison of gastric emptying between Mexican Americans and non-Hispanic Whites.[10] This beverage can be easily and accurately reproduced worldwide so that standardized gastric emptying rate comparisons can be made of different ethnic populations. These gastric emptying studies can be performed by adding ^{99m}Tc-SC to the beverage and acquiring one-minute scintigraphic images in the anterior and posterior positions at serial time points. Ideally, this gastric emptying information can be compared simultaneously with obtained blood glucose and insulin levels. These studies will permit comparisons of the rates of gastric emptying in ethnic populations worldwide.

Potential Therapeutic Approaches

If rapid gastric emptying of liquid carbohydrates or highly processed solid carbohydrates is occurring in certain ethnic populations, several therapeutic strategies may be particularly effective in these populations. These strategies could include agents that delay the rate of gastric emptying after a meal and methods that block the absorption of carbohydrates after meal ingestion.

Agents that slow gastric emptying could either prevent the development of diabetes and/or metabolic syndrome or have a beneficial effect on subjects who already have diabetes. With the recent commercial availability and Food and Drug Aministration (FDA) approval of two different therapeutic peptides, pramlintide and exendin-4, for the treatment of diabetes, a pharmacologic approach that specifically delays gastric emptying could be useful for the treatment and/or prevention of diabetes in ethnic populations.[35,81] Both of these agents exert their effect on postprandial glucose levels at least in part by slowing the rate of gastric emptying. These agents may be particularly effective for treatment of certain ethnic populations if they are shown to have a more rapid rate of gastric emptying compared with non-Hispanic Whites. These agents might also prove useful to treat metabolic syndrome in these populations. Oral agents that stimulate CCK may also be used for treatment or prevention of type 2 diabetes. Oral ingestion of potato-derived trypsin inhibitor, PI2, with a mixed liquid meal has been shown to stimulate CCK, slow gastric emptying, and result in lower postprandial glucose levels in type 2 diabetic patients.[82]

Agents that delay absorption of carbohydrate in the intestine may also be useful for treatment or prevention of type 2 diabetes. Recently, studies have shown that prolonged treatment with the clinically available, FDA-approved glucosidase inhibitor acarbose, which blocks the rapid absorption of carbohydrate in the small intestine and also delays gastric emptying,[83,84] was associated with prevention in the progression of patients with impaired glucose toler-

Another approach to treatment of ethnic populations with rapid gastric emptying is to encourage the increased consumption of high-fiber, low-glycemic-index foods similar to the low-glycemic-index foods consumed in native diets.

ance to diabetes.[85] Surprisingly, acarbose was also associated with a 34% relative risk reduction in the development of hypertension in patients with impaired glucose tolerance who were treated with acarbose over a 3.3-year period (P=.006).[86] In addition, use of acarbose was also associated with a 49% relative risk reduction in the development of cardiovascular events in these patients (P=.03).

Another approach to treatment of ethnic populations with rapid gastric emptying is to encourage the increased consumption of high-fiber, low-glycemic-index foods similar to the low-glycemic-index foods consumed in native diets. These foods are not only slowly absorbed in the small intestine after emptying because of their higher fiber content, but they also have factors that stimulate hormones such as CCK that slow gastric emptying. As previously discussed, beans are effective stimulators of CCK secretion. Foods with high lectin content are also associated with delayed gastric emptying because of CCK stimulation.[87]

SUMMARY

Minimal direct and moderate indirect evidence suggests that rapid gastric emptying may be occurring in American Indians, Mexican Americans, and other ethnic groups. Much more investigation is required to study gastric emptying in these groups by using scintigraphic or other accurate techniques. Gastric emptying studies in other populations with a high incidence of type 2 diabetes and metabolic syndrome, such as African Americans and Asian Indians, should also be undertaken. These studies should specifically examine the gastric emptying of carbohydrates.[88,89] No comparative gastric emptying studies in these other populations can be found in the medical literature. Ethnic populations with high incidences of diabetes and impaired glucose tolerance might particularly benefit from therapeutic approaches with agents that slow gastric emptying.

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Manuscript draft: Phillips
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