The History of Diabetes

We tend to think of the 20th and 21st centuries as the greatest eras of medical discoveries and advances in the treatment of human diseases, and a very strong case can be made for this. On the other hand, we also tend to think that ancient or native people didn't know much about disease and had to rely on "magic", a few herbs or just plain luck to stay healthy. This is not actually a valid way of looking at the history of medicine, as it turns out.

Ancient physicians and healers appear to have known more about the body, more about diagnosis and more about treatment plans than they have been given credit for. For example, approximately 25% of modern prescription medications have at least one plant or herb-derived substance as ingredients[1] and there is a growing number of plant-based medicines used to treat cancer—these include taxol-based (from the yew tree) and etoposide- based (from the Mayapple) chemotherapeutic agents. The field of ethnobotany specializes in talking to native and traditional healers in part to determine which plants should be further investigated for anti-cancer, anti-diabetes, antibiotic and other properties. We are also learning that older concepts regarding nutrition (an apple a day ie. eat well) or lifestyle habits (early to bed, early to rise ie. get your rest!) have real value for many people. Hippocrates, the "Father of Modern Medicine", besides being responsible for the Hippocratic oath, is also reputed to have stated "Let food be thy medicine, and let medicine be thy food."[2] The concepts that nutrition, relaxation, meditation and continued physical activity can lead to a healthier life are undergoing a worldwide resurgence. The growing consensus among medical scientists and physicians is that ancient medicines and ancient approaches may need to be re-examined, even if it is not stated that way.

Ancient Descriptions of Diabetes

The first known reference to diabetes is found in an Egyptian papyrus, the Ebers papyrus, dated to about 1500 BCE: this papyrus mentions a conditions associated with increased volume and an increased frequency of urination along with excessive thirst and severe weight loss.[3] Relating to the point made earlier about the older concepts of nutrition, the ancient Egyptian physicians recommended a diet of whole wheat grains.

In India at about the same time, physicians found that the urine from people with diabetes attracted ants—this provided the first clinical test for diabetes—the physicians would pour out the urine and see if the ants were attracted to it! If they were attracted, the diagnosis was "madhumeha" which can be translated as "honey urine". Patients with madhumeha exhibited extreme thirst, bad breath (probably the "acetone" breath of advanced ketosis) and excessive urination. The Western name for this condition—diabetes—was coined by the ancient Greek physician Apollonius of Memphis in the 3rd century BCE. The word "diabetes" is Greek for "to pass through". The early Greeks believed that diabetes was a disorder of the kidneys. Later Greek physicians were able

to distinguish between what we today call diabetes mellitus and another disorder, diabetes insipidus, which is also characterized by extreme thirst and frequent urination, but is based on a completely different hormonal disorder. An interesting fact is that Galen, a famous Roman physician, reported seeing only two cases of diabetes in his whole career—so while diabetes was recognized and known, it was a very rare occurrence.[4]

By the 5th century, Ayurvedic physicians in India had determined that there were at least two types of diabetes—one which developed in the young (Type 1 diabetes or what used to be called juvenile onset diabetes) and one which was associated with obesity and occurred in adults (Type 2 diabetes). Chinese physicians noted that individuals with diabetes were wealthier and heavier—and were more likely to suffer infections.

The “Middle Ages” of Diabetes

During the early history of diabetes, most physicians believed that the kidneys were diseased. In the late 18th century, however, an English physician noticed that diabetes developed in individuals after an injury to the pancreas. At about the same time, another English physician identified sugar in the urine of patients with diabetes. By the 19th century, sugar in the urine was the definitive diagnostic test for diabetes. The main treatment for diabetes during much of this time was a low calorie, high protein, low carbohydrate diet along possibly with agents such as digitalis and opium to suppress appetite.[3]

The Discovery of Insulin

Throughout the 18th though the 19th centuries, physicians began to gain a greater understanding of the biology of diabetes. By the late 19th century, the substance that was deficient in diabetes (still unknown at that point) was identified as being produced by the pancreas and specific areas of the pancreas (the islet cells) were thought to be the ones deficient in diabetes. Other researchers made progress in identifying this substance but the final credit for discovering insulin is given to Frederick Banting and Charles Best, working in Toronto, Canada. The first insulin treatment was done by Banting and Best in Toronto in 1922. They successfully treated a 14-year old boy with Type 1 diabetes.

The First Hypoglycemics

Hypoglycemics are drugs that lower blood glucose (blood sugar) levels. They were first discovered because these drugs produced lower blood sugars as a side effect. (It is not widely known, but many modern drugs are “discovered” because while they were

initially used to treat one condition, they produced side effects that were useful for other conditions…in other words, they were discovered essentially by mistake!)

The first class of hypoglycemic that were developed during the 20th century were the monoguanidines and the biguanidines—the biguanides are still commonly prescribed today and include Metformin. Sulfonylurea drugs (including Glipizide and Tolbutamide) and other classes such as the Thiazolidinediones, the DPP-4 inhibitors, the GLP-1 inhibitors and others followed.

Insulin

For a good deal of the 19th and 20th centuries, diabetics who required insulin relied on insulin derived from cows or pigs. Vey luckily, nature is pretty conservative when it comes to the types of molecules it uses—in other words, if one substance works in one species, it is likely to work in another species in much the same way—nature doesn't spend a lot of time re-inventing a wheel that already works pretty well! Cow insulin differed from human insulin in only 3 places (3 different amino acids, the basic building blocks of a protein such as insulin). Pig insulin differed in only one place. While insulin from cows and pigs usually worked very well, there were significant numbers of people who developed immune responses, making the insulin less effective. This lead to the development of recombinant-DNA based production of human insulin. In this process, the human gene that codes for insulin is inserted into bacteria—the bacteria are then essentially turned into insulin-making factories.

The Development of Lab Tests for Diabetes Diagnosis and Management

Lab tests for glucose (blood sugar) have been known for some time, but monitoring for patients with diabetes was complicated until the development in 1965 of a home blood sugar testing strip. Since that time, the medical device industry has improved monitoring to the point where anyone with a blood glucose monitor can get an accurate and inexpensive test of their blood sugar at any time of the day or night.

Also during the 1960s, the discovery of a form of glycosylated hemoglobin, A1c, lead to the development of a test which was able to streamline monitoring the average blood sugar levels for the past 3 months. Glycosylated hemoglobin is a form of hemoglobin (the oxygen carrying molecule in the red blood cells) that has sugar molecules chemically attached to it. As red blood cells age (they survive on average, for 3 months) the hemoglobin picks up sugar molecules from the blood—the more sugar in the blood, the greater the number of sugar molecules attached to hemoglobin. This characteristic allows a physician to monitor how well a person is controlling their blood sugars and is valuable as a diagnostic lab test as well.

Current Status of Diabetes Research

Currently, the emphasis of much of the research is on the development of more hypoglycemic agents to control diabetes. This, however, is a treatment, not a cure. Research into a cure for diabetes centers around pancreas and islet cell (the cellular source of insulin) transplants. As with all transplants, the key is to find a way to reduce rejection of the tissue. With the completion of the Human Genome Project in 2003, it is hoped and believed that a better understanding of the genetics of diabetes may lead to better methods of detection, treatment and prevention.[3]

A good deal of current research goes into prevention of diabetes. Methods of prevention are actually well known and include improving an individual's diet, nutrition and level of physical fitness and activity. In a study begun in 1993, three approaches to prevention and treatment were studied.[3] 3,234 obese patients with signs of prediabetes were treated with:

1. "Intensive" dietary, nutritional and exercise-based lifestyle modifications and no medications
2. Metformin plus standard care (monitoring blood glucose, A1c levels, moderate dietary and lifestyle modifications)
3. Placebo plus standard care (monitoring blood glucose, A1c levels, moderate dietary and lifestyle modifications)

In the first group, the "intensive" dietary, nutritional and exercise-based lifestyle group, 14% developed diabetes. This was in contrast to 29% of the placebo group and 22% of the metformin- treated group who developed diabetes. The study clearly indicated that losing weight, eating healthy foods and exercising routinely could drop the risk of diabetes by about half.

Diabetes Today

Today, with the world-wide adoption and spread of western dietary habits, obesity and diabetes is reaching epidemic proportions.[3,5] While research in the prevention and treatment of diabetes continues, the fact is that we know how to prevent diabetes. Utilizing and "spreading the word" about prevention is critical, however. Diet, nutrition and exercise can prevent diabetes in many, if not most people. According to the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK): "You don't have to knock yourself out to prevent diabetes. The key is: small steps that lead to big rewards."[6]