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STRESS AND THE DIABETES EPIDEMIC

Key Words: Racial differences, fast foods, exercise and physical fitness, Pima Indians, BMI, waist/hip ratio, accelerated atherosclerosis, neuropathy, retinopathy, nephropathy, pregnancy, Alzheimer's, menopause

Americans are experiencing an explosive increase in the incidence of diabetes that some authorities believe is reaching epidemic proportions. A recent report surveying some 150,000 households revealed that the number of Americans with Type 2 adult onset diabetes has increased by one third in the past eight years. The greatest increase appears to be occurring among 30 to 39-year-olds who registered a staggering 70 percent rise! Type 2 diabetes now affects 6.5 percent of the population compared to less than 5 percent eight years ago.

ALSO INCLUDED IN THIS ISSUE

Ninety two percent of all diabetics suffer from the Type 2 variety. This condition is also referred to as adult onset or non-insulin diabetes because it generally appears after the age of forty and can often be managed by adhering to a diet and/or taking oral medications rather than insulin. This is in contrast to Type 1 or juvenile diabetes which surfaces during childhood and requires daily injections of insulin to maintain life. Type 1 diabetes is a very different disease. It is almost always inherited, invariably occurs if both parents have diabetes, is much more frequent in babies with birth weights over ten pounds and has a higher incidence of vascular complications that can cause blindness, kidney failure, strokes, and heart attacks.

Type 2 adult onset diabetics also tend to have a family history of the disease, but environmental factors rather than genetics probably play a more important role. **What is of great concern is the growing increase of Type 2 diabetes now being seen in twenty-year-olds and even teenagers.**

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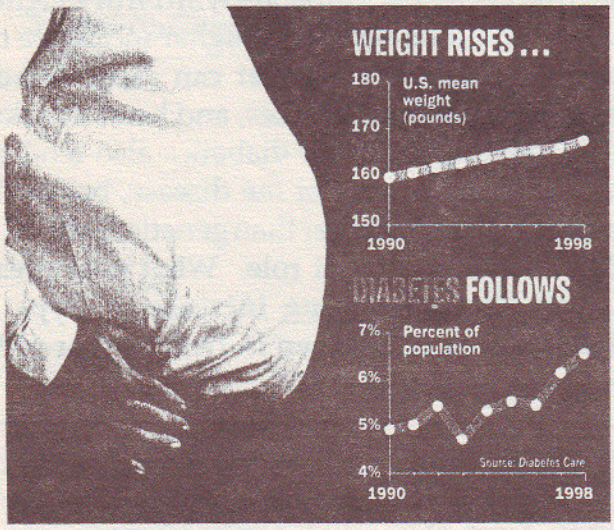
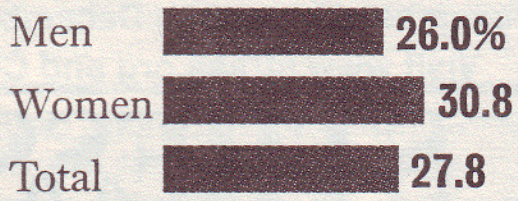
Why The Explosive Increase?

Stressful and sedentary life styles are significant contributors to this growing epidemic, but the most important influence is clearly the increase in obesity. In 1991, there were only seven states with obesity rates over 15 percent. By 1998, forty-five states were now in this category! **In 1991, 12 percent of Americans were obese compared to 18 percent in 1998, a rise of 150 percent during these seven years.**

The correlation between the increase in Type 2 diabetes practically mirrors this rise in corpulence, as indicated in this diagram from a recent article in *Time*.

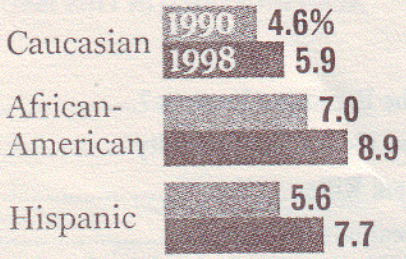


As emphasized in a recent Newsletter, Americans are eating much more now than ever before, and particularly high-calorie fast foods. These are often obtained at drive-in chains to eat in the car to avoid any unnecessary physical activity, which is another contributing factor to obesity. Between a quarter and a third of adult men and women in the U.S. report no significant regular physical activity or exercise.



Although two out of three people trying to lose weight do exercise, less than a third follow the Federal guidelines of 30 minutes a day, five days a week. Walking for shorter periods of time is the most common form of exercise, but averages only two or three times weekly, according to a survey conducted by the Centers for Disease Control. This study also found that overweight adults in Southern states are least likely to exercise, while those in the Midwest are the most active. Education also plays a role. More than three out of four overweight men and women with a college degree exercised regularly, compared to less than half without a high-school diploma

Racial differences also enter the equation. African Americans and Hispanics have higher rates of Type 2 diabetes than Caucasians. Part of the recent rise in diabetes may reflect the steadily increasing percentage of Hispanics and Afro-Americans in the population.



Whether this is due to ethnic eating habits or heredity is not clear, and for some native American Indians, it is a combination of both.

Diabetes, Genes And Heredity

There is a strong family history in patients with Type 1 diabetes, but genetic factors also play a role in the much more common Type 2 variety. Scientists at the Whitehead Center for Genome Research recently identified a variant form of a gene on chromosome 1 that appears to increase the likelihood of Type 2 diabetes by 25 percent. However, it is carried by about 85 percent of the population, the vast majority of whom never develop diabetes, so it must be activated by some external trigger. Certain racial groups do seem to be particularly susceptible to Type 2 diabetes. One example is the tribe of Pima Indians who live in the southwestern portion of the U.S.; half of them now suffer from Type 2 diabetes! This is a fairly recent development that illustrates the interplay between nature and nurture. The ancestors of these Pima tribes lived in an arid, hot and harsh climate, where food was often scarce. During the course of evolution, what has been called a "thrifty gene" may have developed. It's purpose was to lower metabolism during times of famine so the body could maintain normal blood sugar levels despite a markedly reduced caloric intake. The downside of this would be the likelihood of having elevated blood sugars when food was plentiful for lengthy periods of time.

Famine is no longer a problem in a country where Kentucky Fried Chicken, Dunkin Donuts, Big Macs, Whoppers with fries, 40 oz. sodas, pizza and other high calorie - fast food offerings are readily available wherever you turn. The closely related tribes of Pimas living in Mexico who farm and eat traditional foods have much lower rates of diabetes, even though food deprivation is not a problem.

Obesity due to increased caloric intake, and decreased physical activity is not the only explanation. A rise inType 2 diabetes is also being seen in people of normal weight, and the total number of cases is much higher than current statistics suggest. **Many Type 2 diabetics have few symptoms, and are unaware of their condition, which can remain undetected for years.**

The Silent Killer

Type 2 diabetes usually begins very gradually and tends to progress slowly. The disease may be present long before symptoms of thirst, increased urination, fatigue, blurred vision, or weight loss cause patients to seek medical attention. Impotence is often a very early symptom in men, who may chalk it up to age, stress, smoking, or alcohol, or are too embarrassed to seek medical attention. Diabetic women often have vaginal yeast or fungal infections under the breasts or in the groin. Periodontal disease, vision problems, itching, and unusual sensations such as tingling or burning in the extremities may also be signs of Type 2 diabetes that are attributed to other causes or are not investigated thoroughly.

The earlier diabetes is detected and treated, the less the likelihood of developing its devastating complications. Tests to rule out diabetes should be performed whenever any of the above signs or symptoms appear, especially if there is a family history. Testing is fairly simple, and involves measuring blood sugar levels or sugar in the urine after a hearty meal or following the ingestion of a standard amount of sugar in the glucose tolerance test. Even if this is not positive, individuals at increased risk can be identified by administering drugs like cortisone and repeating the test.

A much more sensitive procedure is to demonstrate the presence of insulin resistance. Type 2 diabetes is called non-insulin dependent diabetes because the disorder is due not to lack of insulin, but rather the development of resistance to its effects on muscle and liver cells. This is a major factor in the development of Type 2 diabetes and is more apt to be present in obese people because it appears to contribute to being overweight. There has been increasing concern about the dangers of increased insulin resistance because of evidence that it may play a significant role in the development of hypertension, heart attacks, periodontal disease, acanthosis nigricans and other disorders, even in people who are not obese or overweight.

Insulin Resistance & Syndrome X

Insulin plays a crucial role in regulating metabolic activities. During the digestive process, carbohydrates and proteins are broken down by enzymes in the gastrointestinal tract to smaller glucose and amino acid molecules that can be absorbed into the blood stream. The resultant rise in blood sugar stimulates the pancreas to secrete insulin, which enables these nutrients to enter the cell. In Type 1 diabetes, there is a severe deficiency of insulin production and/or antibodies that block its activities. Type 1 diabetics require daily injections of insulin to stay alive, which is why it is referred to as insulin dependent diabetes (IDDM).

Type 2, or non insulin dependent diabetes (NIDDM) results when cells become resistant to insulin and usually surfaces after the age of 40. It is nine times more common than Type 1 childhood diabetes, but usually much less severe, and can be managed with diet and oral drugs, or relatively small amounts of insulin. **Type 2 diabetics produce normal or even increased amounts of insulin, but abnormalities in liver and muscle cells resist its ability to cause glucose to gain entry into the cell.** Maturity-Onset Diabetes in Youth (MODY) is a rare form of Type 2 diabetes that usually develops in thin teenagers, because of a genetic defect in liver enzyme function. Gestational Diabetes is a another variant which occurs in about one out of 200 pregnancies, usually during the last trimester. Blood sugar levels generally return to normal after delivery, but up to 50 percent of women who are affected will develop Type 2 diabetes within 10 years.

When cells become resistant to insulin, blood levels of insulin rise without any resultant lowering of blood sugar or other signs or symptoms to signal its presence. This condition, which is referred to as Syndrome X, is associated with serious cardiovascular complications and premature death. The scary thing is that insulin resistance can be demonstrated in about a third of the U.S. population, the vast majority of whom are completely unaware that they may be headed for trouble.

In Syndrome X, fasting insulin is elevated despite a normal blood sugar, or insulin levels skyrocket after eating. Although there are no signs or symptoms of its presence, numerous studies show it markedly increases the risk for heart attack, stroke and diabetes Like type 2 diabetes, Syndrome X is higher in Hispanics and certain other demographic groups, and usually results from some combination of inherited and environmental factors. Although obesity alone does not necessarily cause insulin resistance, it can precipitate or aggravate it in genetically predisposed individuals.

The presence of insulin resistance and some idea of its severity can be determined by measuring blood insulin levels in a fasting state and after consuming 75 grams of glucose. Fasting insulin levels over 15 IU or elevations greater than 50 IU two hours after drinking the glucose solution indicate increased insulin secretion due to insulin resistance. However, for practical purposes, you really only need a scale, and a tape measure. Individuals with a body mass index (BMI) over 30 are at increased risk. You can determine your BMI by:

1. multiplying your weight in pounds by 703
2. measure your height in inches and square it
3. divide this number into the first

For example, if you weigh 140 lbs. and are 67 inches tall (5'7"), your BMI would be 22 (98,420 divided by 4,489). A BMI over 25 for women indicates obesity and the likelihood of insulin resistance rises with values over 30.

Although the BMI will tell you how overweight you are, it does not distinguish whether these extra pounds come from more muscle mass, fluid, or fat. **Insulin resistance is most apt to occur in people with central obesity due to increased deposits of fat in the abdomen.** This can be determined by measuring the circumference around your waist and dividing it by the circumference around your hips. A waist/hip ratio greater than 1 for men or .80 for women indicates central obesity, which can also be measured by calipers and electrical impedance. The combination of central obesity and high BMI correlates even more strongly with greater insulin resistance.

Complications Of Diabetes

Long-term insulin resistance, even in the absence of Type 2 diabetes, is a risk factor for future cardiovascular disease in children and adolescents. The vast majority of complications that occur when diabetes does surface result from vascular injuries and nerve damage. Diabetics are two to four times more likely to have cardiovascular problems such as stroke and heart attacks, or impaired circulation in the lower extremities due to accelerated atherosclerosis. Heart attacks account for 60 percent and strokes for 25 percent of diabetic deaths. **A recent study reported that Type 2 diabetics with no history of heart disease had the same risk of heart attack within seven years as nondiabetics with established coronary artery disease.**

Nerve damage occurs in half of Type 2 diabetics within 25 years, particularly in patients whose glucose levels are poorly controlled. Symptoms include numbness, tingling, weakness, and burning sensations, often starting in the toes and fingers and moving up the legs and arms. A more serious condition is neuropathy which causes a loss of sensation, so that heat and pain are no longer perceived. As a result, people may be unaware that a blister or minor wound has become infected. This complication is compounded in diabetes because of circulatory problems resulting from obstructed blood vessels that may be sufficiently severe to cause ischemic ulcerations and tissue damage on their own.

Even trivial traumatic lesions and infections that would normally be readily apparent and easily treated can develop into deep tissue damage. Extensive surgery may be required, and it may be necessary to amputate a foot or leg. Diabetes is responsible for more than half of all the lower limb amputations performed in the U.S. each year. It is estimated that early recognition and aggressive treatment of diabetics who may be at particular risk because of impaired circulation in the lower extremities could prevent at least 50 percent of amputations. Blood vessel obstruction can also damage the eyes and kidneys.

Diabetes accounts for 12,000 to 24,000 cases of blindness every year, and is the leading cause of new cases of blindness in adults aged 20 to 74. Because of the long duration of the disease, **most Type 2 diabetics will develop abnormalities in the blood vessels of the retina at some point in their lives.** However, only a minority will develop diabetic retinopathy severe enough to cause partial or total blindness. About 20 percent of Type 2 diabetics have evidence of some eye damage at the time when the diagnosis is first established. Complaints of blurred vision are particularly common because of fluctuations in blood sugar levels that affect the lens.

The earliest and most common form of eye damage is nonproliferative or background retinopathy. In this disorder, abnormally weakened blood vessels in the retina rupture and leak, leading to the deposition of "waxy" lesions. When these are in the central portion of the retina, they may result in reduced or blurred vision. If weakened blood vessels become blocked and the flow of blood is interrupted, soft "woolly" areas may develop, signalling the development of proliferative retinopathy. This is more dangerous, since new and abnormal blood vessels that grow on the surface of the retina may spread or bleed into the back of the eye. A major hemorrhage and retinal detachment can cause partial or total blindness. Occasionally, the sensation of seeing flashing lights may signal the start of retinal detachment, but most often there are no symptoms of this form of serious progressive retinopathy. Type 2 diabetics are also at increased risk for developing cataracts and certain types of glaucoma.

Kidney disease can also be a very serious complication of diabetes and patients with hypertension, coronary disease, infections or other urinary tract problems are at particular risk. Symptoms include swelling in the feet, fatigue, and pallor due to anemia and/or uremia. In Type 1 diabetes, high blood pressure usually develops once there is kidney damage. Hypertension itself is another major cause of heart attack, stroke, kidney and heart failure.

(*Continued on Page 6*)

Type 2 diabetes can also cause a variety of mental, cognitive, and emotional disturbances. There is a higher than average risk of developing dementia due either to Alzheimer's disease or interference with blood flow to specific sites in the brain. Reduction in attention span and memory that sometimes starts in the seventh and eighth decades can occur in diabetics under the age of 55 who have had the disease for many years.

Since diabetic neuropathy may block anginal pain, patients need to be sensitive to other warning signs of a possible impending heart attack such as sweating, sudden fatigue, and shortness of breath. Type 2 diabetics are also at higher risk for bacterial, fungal, and viral infections. This is particularly true for influenza and complications such as pneumonia, possibly because the effects of protective proteins on the surface of the lung are diminished in diabetics. When diabetes affects nerves in the autonomic nervous system, there may be abnormalities in mechanisms that regulate the control of blood pressure, and bowel and bladder function. Impotence and other forms of sexual dysfunction are not uncommon in males.

Women with Type 2 diabetes face a higher risk for uterine cancer, especially if they are obese and both male and female diabetics appear to have a higher risk for rectal and colon cancers. Preexisting diabetes in pregnant women as well as temporary diabetes that may occur during pregnancy can increase the likelihood of birth defects. Because glucose crosses the placenta, elevated levels cause the fetus to secrete large amounts of insulin. This combination of high blood levels of both glucose and insulin leads to excessive fetal growth, which explains why the incidence of diabetes is higher in newborns weighing 10 or more pounds. Diabetes may also contribute to delayed fetal maturation or death. In addition to endangering the fetus, diabetes presents health risks for expectant mothers, particularly preeclampsia. This condition is associated with a sustained elevation in blood pressure that can have very dangerous consequences.

Diabetes contributes to 187,000 deaths annually and is the sixth leading cause of death by disease in the United States. There are an estimated 15.3 million Americans with Type 2 diabetes and studies suggest that half of them are not aware of their condition. **It takes an average of four to seven years before the diagnosis is confirmed**, usually because of some visual complaint or other complication that prompts a visit to the doctor. During this time period, there can be progressive damage that may be irreversible.

As a result, an international expert committee comprised of representatives from the American Diabetes Association, Centers for Disease Control and the National Institutes of Health has recommended that all adults over the age of 45 should be tested every three years. Testing should be done more frequently in all individuals with a family history of diabetes, marked obesity, or other risk factors for diabetes. The committee urged that physicians replace the current unpleasant oral glucose tolerance test with a simpler, less expensive fasting plasma glucose procedure that costs less than $10 and requires only an eight hour fast before the blood is drawn. The committee also believes that the level of blood sugar formerly considered to be normal is too high and lowered it from 140 mg. to 126 mg. per deciliter. This change is projected to identify 2 million of the 8 million Americans with undiagnosed diabetes.

Not all experts are in favor of these changes. Some are concerned that by lowering the threshold to 126 mg./dl, some people diagnosed as diabetics would normalize on their own and never develop complications. Many may worry unduly or adhere to diets that reduce their quality of life. Others may take medications that could have disturbing side effects. Studies show that early intervention in Type 1 diabetes clearly reduces complications, but the evidence is not as overwhelming in Type 2 patients with only mild blood sugar elevations. The best advice for these individuals may be to eat a healthy diet and exercise in order to avoid obesity and maintain a proper weight.

Stress And Diabetes

Most diabetics know that blood sugar levels are affected by diet, drug dosages and exercise. However, few recognize the important direct and indirect effects of stress. Emotional stress is associated with the increased secretion of hormones like adrenaline and hydrocortisone which can sharply raise blood glucose through various mechanisms. Adrenaline causes the breakdown of carbohydrate stores in the body into glucose to supply fuel for energy to improve muscular strength for flight or fight activities. Since these carbohydrates were originally derived from glucose, this process is known as glycolysis. Hydrocortisone and other glucorticoids increase blood sugar by breaking down protein and fat stores, that supply a new source of glucose, which is why this activity is referred to as gluconeogenesis. **Stress can also contribute to binge eating and other dietary indiscretions that elevate blood sugar, and often disrupts compliance with dietary regimens required to maintain blood sugar within normal limits.** These combined influences frequently result in fluctuating blood sugars that produce anxiety, nervousness, lethargy and fatigue. All of these can generate more stress that further aggravates the problem.

Severe stress that evokes fight or flight responses is not the only culprit. Daily hassles and irritants also raise blood sugar levels. "White coat" hypertension refers to patients whose blood pressures are elevated when taken in the office setting by a physician, but are quite normal during ambulatory monitoring or when measured at home by the patient or family member. In some diabetic patients, the stress associated with a visit to the physician's office can also cause high blood sugar readings due to transient elevations that quickly fall after leaving the office and remain normal. **Such "white coat" diabetics are often told to increase their dosage of insulin or other medications based on these misleading values, resulting in dangerous hypoglycemic reactions due to low blood sugar.** Protein bound glucose and other tests that measure the average level of blood sugar over the preceding weeks or month that confirm normal values can prevent such errors in treatment.

Type 2 diabetes mellitus is now increasingly being viewed as one of several manifestations of a more widespread metabolic disorder known as the insulin resistance syndrome. One of the markers for this is central obesity due to a high waist/hip ratio circumference measurement due to increased abdominal fat. Individuals with increased fat deposits in the buttocks, as seen in some African tribes are not at increased risk for developing diabetes. Why? What is it about central obesity due to increased abdominal fat that makes it so dangerous? "Middle-aged spread" is quite common, but does not have the same dire consequences for everyone. Does heredity predispose to both central obesity and insulin resistance, or could increased secretion of stress hormones be the cause of both?

Cushing's syndrome is a disorder in which increased stimulation of the adrenal cortex results in higher levels of hormones that raise blood glucose, which is why they are classified as glucocorticoids. One of the characteristics of Cushing's is central obesity, and there is often increased insulin resistance and Type 2 diabetes. In Cushing's syndrome due to a pituitary tumor, following its removal, excess abdominal fat stores diminish or disappear, as does insulin resistance and diabetes. Further support comes from a study showing that **men with the highest levels of chronic stress also had the highest cortisol levels and the greatest amount of deep belly fat.**

One explanation may be that fat cells in these abdominal fat depots have the largest number of receptors for cortisol. Scientists suspect that the reason for this may be to provide the liver ready access to this source of fuel in the event that energy is needed for increased physical activity in response to stress. Male and female hormones protect against abdominal fat deposits. **"Middle aged spread" results from the sharp decline in these hormones after the menopause, as well as the increased stresses that accompany what is often called "change of life".**

Book Review

Stress and Health: Research and Clinical Applications, Kenny DT, Carlson JG, McGuigan FJ, Sheppard JL, eds. Harwood Academic Publishers, Amsterdam, 2000. 467 pp., $68.00

The 23 chapters contained in this book represent revisions of selected papers presented at the First International Congress on Stress and Health, a five day meeting that took place in Sydney, Australia in October 1996. They have been grouped into six sections: Introduction; Biological, Physiological and Psychological Bases of Stress; Health Consequences of Stress; Management of Stress and Stress-related Disorders; Stress, Cardiovascular Disease and Cancer; and Occupational Stress. As might be expected in an offering of this sort, writing styles differ. In some instances, the material would appeal to and be readily understood by a lay audience, and in others, considerable knowledge in a specific subject would be required to fully comprehend the contents of the chapter. The editors have done an admirable job in smoothing things out by arranging these contributions on diverse aspects of stress, into a cohesive and attractive arrangement that flows very well.

The section on Management of Stress and Stress-related Disorders is particularly well done and provides a truly global perspective with contributions from distinguished authorities all over the world. Lennart Levi's chapter entitled *Stress management and prevention on a European community level: Options and obstacles* is a particularly valuable summary of his extensive experience in this area. Similarly, the late Hans Eysenck's chapter, *Personality as a risk factor in cancer and coronary heart disease*, reviews the ground breaking research studies conducted by Grossarth-Maticek and Eysenck over the past four decades, vividly illustrating Sir William Osler's advice in 1906 that "It is very often much more important to know what kind of person has the disease, than what kind of disease the patient has". Another welcome contribution is *Measuring stress in the workplace: The Job Stress Survey* by Charles Spielberger, who brings to this subject his vast expertise in the measurement of state and trait anger and anxiety. This new instrument differs from the Karasek-Theorell demand / control model of job strain but appears to be well validated. Another slant on this important subject is provided in Don Byrne's *The Frustration of Success: Type A Behavior, Occupational Stress and Cardiovascular Disease*, which follows up on Ray Rosenman's research and is extremely well written. Space limitations preclude discussing some of the other chapters in this splendid stress potpourri, and I am proud to have mine included among them

I enjoyed participating in this event not only because it provided a place to meet with the above and other old friends, but the opportunity to learn about cutting edge advances in stress research all over the world. This is clearly illustrated in this book, which is highly recommended.

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