Exercise and Diabetes

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The number of individuals with diabetes has become a world wide epidemic and continues to increase at an alarming rate. King H, Aubert R, Herman WH (1998) estimated that insulin deficiency afflicts 150 million people worldwide which includes 16 million Americans. They projected that by the year 2025 the number of diabetics worldwide will be over 300 million. Exercise has been shown to have a beneficial effect on the disease. Not only can it prevent diabetes but has also been used as a method of treatment for those that are already diabetic. This review looks at several current articles that address the issue of exercise and diabetes.
Merck defines diabetes as “A syndrome characterized by hyperglycemia resulting from impaired insulin secretion and/or effectiveness… with complications including retinopathy, nephropathy, atherosclerotic coronary and peripheral arterial disease, and peripheral and autonomic neuropathies.” This review of literature will first present the basic physiology associated with the two types of diabetes. Then it will review several current articles examining the benefits of exercise on diabetes. The articles will focus primarily on Type II diabetes although the results are similar in Type 1 patients. The studies presented will look at exercise and diabetes in conjunction with different areas such as: acute and chronic exercise, exercise and medications, elderly, adolescents, and the morbid obese.

Type 1 or insulin-dependent diabetes afflicts the beta cells of the islets of Langerhans in the pancreas which are responsible for the production of insulin. Mathis D, Vence L, & Benoist C. (2001) stated that those with Type 1 diabetes have two distinct phases. At first, insulitis occurs in which leukocytes invade the islets. Next is diabetes, the point at which most of the B-cells have been killed off and the body is no longer capable of producing a sufficient amount of insulin to help regulate the blood glucose levels leading to hyperglycemia. Individuals must take insulin to prevent the development of ketoacidosis. Once insulin is injected it travels to the receptor cells and facilitates the transport of glucose into the cells. Type 1 diabetes typically appears in children or young adults and comprises 5 – 10 % of all diabetics. Common symptoms include: weight loss, hunger, thirst, and increased urination.
Type II, or non-insulin dependent diabetes, differs from that of Type I diabetes in that the factors involved here are predominantly the result of environmental factors such as physical inactivity and obesity. Therefore, it is generally scene but not limited to, individuals that are older and less active. However, Zimmet P, Alberti K, & Shaw J. (2001) describe a serious new epidemic with Type II diabetes in children and various ethnic groups not previously scene until now demonstrating the global effect of a sedentary lifestyle and obesity. Brooks G, Fahey T, White T, Baldwin KM. (2000) characterize the non-insulin-dependent diabetes as excessive hepatic glucose production, insulin resistance, and secretory function problems with the B-cells. Kruszynska YT, et al. (1996) describes the physiological development of Type II as a progression. It starts with the inability of insulin to do its job (insulin resistance). The B-cells sensing this send more insulin (hyperinsulinemia). Blood glucose is regulated and levels are returned to normal. The B-cells after time become exhausted (B-cell decompensation). Glucose levels elevate (impaired glucose tolerance), B-cells fail, and the end result is Type II diabetes. This progression is a result of glucose influx, increased glucose output by the liver, decreased glucose uptake by the muscle adipose, and a decrease in insulin secretion by the pancreas. As mentioned previously this is scene in inactive individuals because the body’s insulin can not meet the demands of the excess glucose and therefore can not transport the glucose into the cell. The encouraging thing about Type II diabetes is that it can be regulated through lifestyle changes which will be clearly scene in the articles presented.
Another important issue to address when discussing diabetes is individuals with impaired glucose tolerance. (IGT) is someone that has not reached the diabetic glucose levels but is very closer to making the transition into that category. Blood glucose levels for someone with (IGT) are 141 – 199 mg/dl 2 hr. post. One is considered diabetic when they reach the 200 mg/dl 2 hr. post. This group does not suffer the microvascular complications associated with those that have diabetes. Individuals with (IGT) have little room for error and must be careful. One way of looking at this is to imagine one is standing on a cliff. He/she can either take a step off or step back. Individuals with (IGT) that become diabetic take that step off the cliff and the ones that exercise and watch their diet take the step back.

The Finnish diabetes prevention study by Tuomilehto et al. (2001) was the first long term intervention study that looked at the relationship between exercise and diabetes. The study was very well-controlled and contained a large sample number (522). The study was a six year study composed of 522 middle aged overweight subjects with (IGT). The breakdown was 172 men and 350 women all with a body mass index greater than 25 and between the ages of 40 -65 years old with the mean age being 55. Participants were excluded from the study if they were diagnosed with diabetes, had a chronic disease that would make survival for the six years unlikely, or any other characteristic that would interfere with the study. The subjects were randomly assigned to either the control group or the intervention group and there was no significant difference between base line measurements.
The control group subjects were given limited help compared to the intervention group. They were given basic oral and written information about diet and exercise at base line and yearly follow up visits. They developed a three-day food diary at base line and at each yearly visit. However, no individualized exercise and diet programs were developed for the individuals in the control group.

The subjects in the intervention group on the other hand, were given a detailed plan on how to achieve their weight loss and exercise goals. Their short term and long term goals were to reduce weight by 5% or more, total intake of fat to less than 30% of total energy consumed, intake of saturated fat to less than 10% of total energy consumed, increase fiber intake to at least 15 grams per 1000 kcal, and moderate exercise for a minimum of 30 minutes per day. Each subject in the intervention group also had to record a three day food log four times a year which was in turn analyzed by a nutritionist whom they met with seven times the first year and one session every three months thereafter. The subjects were given advice on proper endurance activities in order to increase aerobic capacity and cardiovascular fitness. They were also offered personal resistance training through a circuit routine consisting of high repetitions and short rest periods.

The results in the study showed that the intervention group decreased in several categories when compared to the control group. The intervention group decreased in waist circumference, fasting plasma glucose concentration, plasma glucose concentration two hours after oral glucose ingestion, and serum insulin levels. The examiners also noted a significant decrease in weight, triglyceride concentrations, and blood pressure.
The intervention group demonstrated a 58% decrease in diabetes when compared to the control group. A 63% decrease in men and a 54% decrease in women. These results give merit to the fact that the prevention of diabetes and controlling diabetes itself can be attained through a nonpharmacological approach. These findings are also comparable to previous studies from Holland and United States. These studies will be presented in the following sections.

The Netherlands completed a similar study to that of the Finnish study. Menisk M, Feskens E, Sairs W, deBruin T, & Blaak EE (2002) evaluated a lifestyle intervention program on Dutch subjects with impaired glucose tolerance. This was a three year study comprised of 144 subjects (64 men and 50 women) over 40 years old and with a body mass index above 25 kg/m. They were randomly place into either a control group or an intervention group. Subjects were excluded if the had diabetes, participated in regular exercise within the last year, or had some other medical condition that would not allow them to participate.

The intervention group consisted of a diet and physical activity. Subjects had to adhere to the recommendations of Dutch Nutrition Council and consisted of: carbohydrate intake of at least 55% of total energy intake, total fat intake of less than 30-35% with less than 10% coming from saturated fat, cholesterol intake of less than 33 mg/MJ, and protein intake of 10-15% and dietary fiber consisting of at least 3 g/MJ. Initial goals were to achieve at least a 5-10% weight loss during the first year. Subjects were not allowed to use low calorie diets or other weight loss agents. Participants were also recommended to quit smoking and avoid alcohol intake. A dietician analyzed a
three day food record at base line and appointments were made every three months after. Physical activity for at least 30 min at moderate intensity for 5 days a week was incorporated as recommended by the American College of Sports Medicine. Training sessions consisting of aerobic and resistance training were supervised by trainers experienced in working with middle-aged people.

The control group was given limited information on the benefits of a healthy diet, weight loss, and physical activity. In addition, no individualized routines were given as compared to the intervention group which received much personal attention. The subjects’ only requirement was to schedule a visit after one year so that measurements can be taken.

Both the intervention group and the control group presented with similar findings at base line. Data was analyzed following one year and there was only a 10% present drop out rate. Results indicated that after one year the intervention group had significant decreases in the following: reduction in body weight, decrease in waist circumference and sagittal and transverse abdominal diameter. Insulin resistance as indicated by the HOMA index also decreased in the intervention group which was associated with an increase in fiber. Whereas the insulinogenic index, a predictor of B-cell function did not change. Smaller changes were scene in glucose levels and insulin levels however; even small changes in the body can have a big metabolic impact. The reduction in abdominal obesity is important because it is correlated with progression to Type II diabetes. The diets also improved in the intervention group following the one year. Subjects in this group slowly replaced saturated fats with polyunsaturated fats and carbohydrates which
can affect glucose metabolism. Fiber intake was also increased in the intervention group. Overall, these individuals were able to maintain much healthier eating habits and adhered to it for the duration of the study. The Netherlands study did conclude that physical activity is conjunction with a healthy diet can improve glucose tolerance and insulin sensitivity.

The American Diabetes Prevention Research Group [ADPRG], (2002) presented another study examining the effects of lifestyle intervention and drug metformin (glucophage). Metformin suppress endogenous glucose production which is the main determinant of fasting plasma glucose concentrations. It does not increase insulin like other similar drugs. Metformin helps the body respond to insulin through decreasing the amount of sugar the liver make and decreasing the amount of sugar the intestines absorb and not causing hypoglycemia.

The (ADPRG) performed a 4 year intervention study on 3234 subjects. These subjects were older than 25 years old, had a body mass index greater than 24, had glucose levels that categorized them as impaired glucose tolerant, and were from various ethnic groups. None of the subjects fell into the diabetic category. Subjects were excluded if they were taking medications that may alter glucose levels or had a serious illness that would interfere with their ability to participate in the study. An effort was made to include individuals from differing racial or ethnic minority groups. Participants were assigned to one of three groups through random selection.

The first group (N=1073) administered metformin at a dose of 850 mg once daily taken orally plus basic lifestyle recommendations. After one month, dosage was
increased to 850 mg twice daily unless gastrointestinal problems warranted a longer initial period. Adherence to the program was monitored through quarterly pill counts and structured interviews. The lifestyle recommendations consisted of a yearly 20-30 minute session focusing on the benefits of a healthy lifestyle. These subjects were recommended to follow the Food Guide Pyramid to reduce their weight and encouraged to increase their activity. The second group (N=1082) consisted of standard lifestyle recommendations plus a placebo twice daily.

The third group (N=1079) in this study was an intensive program of lifestyle modification. There initial goals included: achieve and maintain reduction of at least 7% of initial body weight through a low calorie, low fat diet and perform physical activity of moderate intensity at least 150 minutes per week. The participants were given a 16 lesson curriculum covering diet, exercise, and behavior modification in order to achieve their goals. Individual sessions performed monthly and group sessions to reinforce behavioral changes were designed.

At base line all three groups were comparable. The results of the (ADPRG) were fifty percent of the individuals in the lifestyle intervention group achieved their goal weight loss of 7 percent or more by the end. The average weight loss between the three groups was 0.1, 2.1, and 5.6 kg in the placebo, metformin, and lifestyle intervention groups. The proportion of participants in the lifestyle intervention group that met the 150 minutes of physical activity per week was 74 percent. Dietary changes also changed more dramatically in the lifestyle intervention group. The average decrease in calories by
the placebo group was 249 kcal, the metformin group was 296, and the largest decrease was by the lifestyle intervention group at 450 kcal. The number of participants that took at least 80 percent of their medication was slightly higher in the placebo group than in the metformin. The findings also showed that the incidence of diabetes was much less in the lifestyle intervention group than in the others. Diabetes was 58 percent lower in the lifestyle intervention group and 31 percent lower in the metformin group when compared to the placebo (see figure 1). The lifestyle intervention group had a 39 percent lower incidence than the metformin group. Metformin was found to work better in participants with a lower base-line glucose concentration. The benefits of metformin were more visible in individuals with higher body mass indexes and higher fasting glucose concentrations. The only adverse affects of the result were some gastrointestinal problems due to the metformin and musculoskeletal injuries with the exercise. There were no significant findings between sex or race or ethnic group.

Lott et al. (2001) looked at the gender differences in glucose and insulin response to strength training in 65 to 75 year olds. They also looked at the how long to produce a response after training. The study was a 6 month whole body strength training program in which the participants met three times a week. Intensity was based on a one rep max. All participants were untrained prior to the study for at least 6 months. Participants were thoroughly screened by means of physical exam, extensive medical history, and measured aerobic capacity for any medical difficulties. None of the participants suffered from hypertension, coronary heart disease, or any other orthopedic problems and none were smokers. The twenty untrained participants were composed of twelve men (2 IGT /
2 Type II) and eleven women (3 IGT). Aerobic capacity was used to verify the participants were not aerobically fit. The subjects met with a dietician whom informed them to keep a 5 day food record and to ingest 150 g of carbohydrates per day and to avoid alcohol. All subjects were given an oral glucose tolerance test to measure insulin response. Fat mass and fat free mass were also determined by a dual energy x-ray absorptimetry. Strength tests were administered for the legs using the leg press and knee extension and for the upper body using the chest press, lateral pulldown, military press, tricep and bicep curls. Strength training was changed three months into the six month study to avoid staleness.

The results discover by Lott et al. were that there were no significant differences between the two genders. At base-line women as expected were shorter, weighed less, had lower aerobic capacity, lower total body mass and fat free muscle, and a greater % body fat then men. After the six months there were no significant changes in body mass index, total body mass, or total fat mass. Men had greater increase in strength than women; however women also saw significant strength gains. When strength was divided by fat free mass, men had more significant increase than did the women in upper body strength. There were no significant differences between the two groups when looking at nutrition. The study also did not find any significant change between the two sexes when it came to plasma glucose response or fasting glucose when administered the oral glucose tolerance test after training. Looking at plasma insulin response between men and women, it was recorded that men had a reduced insulin response at fasting and at the 90 minute time point. Women at these time points showed an increase in plasma insulin
response. Hersey et al. (1994) found similar gender results in their study which looked at
endurance exercise training and plasma insulin response in 70 – 90 year olds. On the
other hand, Ryan A, Pratley R, Goldberg A, & Elahi D (1996) examined postmenopausal
women and found a decrease in plasma insulin response. It was difficult for Lott et al. to
make an assumption on how long the training effects lasted in regards to insulin and
glucose because the findings showed no significant changes 1, 2, or 3 days after the last
training session.

Schmitz et al. tested the effect physical activity had on insulin sensitivity in
children ranging from the ages of 10 – 16 years old. Their euglycemic insulin clamp
study was a cross sectional analysis consisting of 357 black and white non-obese
children. The children received a physical exam from a pediatrician that included
anthropometric and blood pressure measurements. The children were placed in a Tanner
stage based upon their sexual maturation. Other measurements recorded were height and
weight, body fat, waist circumference, and physical activity. Physical activity was
measured by the Paffenbarger physical activity survey and was expressed in kilocalories
expended per day. Physical activity consisted of leisure time, stair climbing, and
walking. The physical activity scores then were categorized into quartiles for the total
sample. Besides the basic measurements previously mentioned, Schmitz et al. also
analyzed the following: fat-free mass, body mass index, fasting insulin, insulin
sensitivity, LDL, HDL, Triglycerides, and total cholesterol.

The results showed that there was wide range of children spread out between the
four quartile categories. Older children were found in the higher quartiles than the
younger children. The lower physical activity quartiles also saw more girls and Caucasians. There were no findings in the different Tanner stages. Body fat decreased and fat-free mass increased the higher quartile achieved. Physical activity was correlated with fasting insulin and insulin sensitivity with children that had above median systolic blood pressure or above median percentage body fat. Whereas, physical activity was correlated with fat-free mass in children with below median systolic blood pressure and percentage body fat. The other physiological areas observed did not see any significant differences with physical activity. Similar to the previous studies there was a positive correlation between physical activity and how it affects fasting insulin and insulin sensitivity. One speculation why this occurs is that because of the enhanced glucose transport and use of glycogen due to exercise. Exercise also increases the amount of fat-free mass therefore increasing the amount of muscle available for glucose transport.

Kitamura et al. (2002) tested the effects of aerobic and resistance exercise training on insulin action in the elderly. They looked at testing the previous hypothesis that insulin sensitivity increased with aerobic training. In addition, increased fat-free mass would improve insulin action and glucose disposal with resistance training. It is understood that as one ages, insulin action decreases and is exacerbated with the lack of physical activity. Kitamura et al. has previously shown that aerobic exercise training increases insulin action by converting low- oxidative fibers to moderate oxidative fibers which contain higher concentrations of GLUT-4.

The participants in this study were fourteen healthy males ages 65 – 73. The participants did not exercise regularly and underwent a thorough medical screening. Any
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of the individuals that had significant abnormalities or disease were excluded from the study. They were then randomly divided into two groups consisting of resistance training only and aerobic and resistance training. Subjects met three times a week for one hour for a total of twelve weeks.

The resistance training only group (N=7) used eight different hydraulic resistance machines. Subjects performed two sets of twenty on the machines at a rate of 30-60 percent of their one rep max assessed at the beginning.

The combined group (N=7) used the same hydraulic resistance machines in conjunction with aerobic exercise. They performed these exercises in a circuit manner in which they would alternate from resistance training to aerobic training every thirty seconds. Participants were asked to complete the maximum number of repetitions at each hydraulic station.

After the twelve weeks of training, the fourteen participants were measured for the following: sensitivity and responsiveness to insulin (euglycemic clamp), body composition, VO2 max, and muscle strength. These findings were compared to their initial levels measured before training began. There were no baseline differences between the two groups.

Kitamura et al. found that body mass index and body weight did not change significantly between the two groups. There was no significant change in fasting plasma glucose and plasma insulin concentrations either. Their study found that there was a significant improvement in glucose infusion rate per body weight at both insulin infusion rates (40mU/m2/min & 400 mU/m2/min) in the combined group where the resistance
only group was not significant. The glucose infusion rate was then calculated per fat-free mass which showed improvement in the insulin action the combined group but not in the resistance only group. The combined group improved insulin sensitivity qualitatively whereas any of the increases in insulin sensitivity scene in the resistance only group can be due to increased muscle mass. Kitamura et al. concluded that the combined training of resistance and aerobic improved insulin sensitivity and resistance only did not alter insulin sensitivity.

Polyzogopolou E, Kalfarentzos F, Vagenakis A, & Alexandrides TK (2003) examined the effect of Bariatric surgery on Type II diabetes over the course of twelve months. The examiners theorized the surgery “reduces the total caloric intake and particularly carbohydrate consumption in part due to dumping syndrome, leading to weight loss and reduction in insulin resistance.” The examiners wanted to investigate if after gastric bypass surgery, normal glucose response and euglycemia can be attained following weight loss in morbid obese (BMI > 40) patients. This is the first study to show that lost glucose induced acute insulin response in patients with accelerated type II diabetes is reversible.

The patients consisted of twenty five morbid obese individuals. Twelve patients had type II diabetes, five had (IGT), and eight with normal glucose levels underwent a biliopancreatic diversion with gastric bypass surgery. The eight patients with normal glucose levels matched the other patients with regards to BMI, age, and sex. A control group of twelve patients with normal BMI were used for comparison.
The examiners used an intravenous glucose tolerance test to analyze their data which were carried out at three, six, and twelve months postoperatively. The quantitative insulin sensitivity check index (QUICKI) assessed insulin sensitivity ($1/\log [\text{fasting insulin}] + \log [\text{fasting glucose}]$). Body composition and fat-free mass were analyzed using a body composition analyzer.

The three groups (diabetic, IGT, and NGT) with morbid obesity had a similar preoperative BMI and higher BMI than that of the control group. Polyzogopolou et al. postoperative results showed that body weight and BMI decreased significantly in all patients. Also, all three operative groups showed a decrease in fat mass and fat-free mass. All patients in the diabetes group demonstrated normal fasting glucose levels after three months postop. Fasting plasma insulin levels declined in all groups initially and normalized three months following surgery. After the three month period insulin sensitivity became normal in all three groups. Acute insulin response was restored at the three month mark in diabetic patients that previously lacked this response and continued to improve throughout the 12 months. Acute insulin response was similar in all three groups by the twelfth month. Despite the fact the patients were still obese after twelve months (BMI 30), there were no cases of diabetes and acute insulin response along with insulin sensitivity returned to normal. The most important findings in this study were the fact that the surgery returns to normal the B-cells acute insulin response to glucose and insulin sensitivity.

After reviewing these articles it can be concluded that exercise improves glycemic control, reduces abdominal adipose tissue, and increases lean muscle mass. In addition,
resistance training when combined with aerobic training yields greater results for diabetics and there are both acute and long term effects. Exercise equals insulin which is a much more cost effective way of managing those that have diabetes or that are susceptible of acquiring it.

The studies from Tuomilehto et al. (Finland), Mensik et al.(Holland), and Diabetes Prevention Program Research Group (United States) proved that diabetes can be maintained through environmental changes in different societies and ethnic groups. It is not a local but a global problem which can benefit from a worldwide lifestyle intervention. A difference between the Finnish, American, and Holland study was the degree of obesity studied. The average BMI was 29.5 kg/m2 in the Holland study, 31.2 kg/m2 in the Finnish study, and 33.9 kg/m2 in the American study. The findings prove that even with lower degrees of obesity (Holland) significant improvements can be made. Also addressed was gender differences response to exercise. Lott et al. concluded in their findings, similar to Hersey et al., that men’s insulin response may be more favorable than that of women following exercise but are conflicting to some other studies. Schmitz et al. proved that being a physically active child lowers fasting glucose levels and increase insulin sensitivity. Therefore, it supports the theory that children that are active at a young age are more likely to avoid diabetes and other health complications when they are older. It was also established by Kitamura et al. that resistance training combined with aerobic training yielded greater benefits then either of the two programs alone. In the combined group there was a higher glucose infusion rate and increased insulin action. The final research article presented was by Polyzogopoulou et al. and looked at the
effects of gastric bypass surgery on the morbid obese patients with type II diabetes. It was concluded that significant changes were made even at the three month postoperative. The most important finding was that beside weight loss, euglycemia, and insulin sensitivity, a normal B-cell acute insulin response to glucose was achieved. This information was important because it shows that previously lost acute insulin response can be retained with type II diabetics.

From an economic standpoint, diabetes is proving to be a world wide epidemic. Diabetes has the highest direct economic effect costing billions of dollars annually (see figure 2). The American Diabetes Association examined the hospitalization costs for chronic complications of diabetes in the United States. The complications associated with diabetes are: renal disease, ophthalmic disease, neurological disease, peripheral vascular disease, and cardiovascular disease. Cardiovascular disease accounts for sixty four percent of the total costs. Peripheral vascular disease is the leading cause of lower limb amputations per year. Retinopathy is the leading cause of new blindness in people ages 20-74. Renal disease is the leading cause of end-stage renal failure which accounts for forty percent of new cases. The individuals with diabetes generally do not just have diabetes. They acquire several different complications and many of the eventually are categorized as having metabolic syndrome or “syndrome X”.
References


Figure 1. Cumulative incidence of Diabetes According to Study Group.

The diagnosis of diabetes was based on the criteria of the American Diabetes Association. The incidence of diabetes differed significantly among the three groups (P<0.001 for each comparison).

Figure 2.