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# CARDIOVASCULAR DISEASE PREVENTION AND CONTROL IN DIABETES

## The WHO CINDI Programme Guidelines for Intervention

Editors:

David R. MacLean, M.D.,
Dalhousie University,
Halifax, N.S.,
Canada.

Igor Glasunov, M.D.,
WHO CINDI Program,
WHO regional Office for Europe,
Copenhagen, Denmark.

# Contents

# Foreword

The purpose of this document is to provide guidelines to members of the WHO CINDI programme in the management of cardiovascular disease and its risk factors in people with diabetes. It forms part of the programme material which has been developed by the Working Group for the implementation of the St Vincent Declaration in CINDI. The contents were originally prepared for a meeting, held in London in 1994, to redraft the guidelines for Cardiovascular Disease in Diabetes which originally appeared in the St Vincent Implementation Document of 1991.

It is recognized that the treatment of diabetes and its cardiovascular disease complications varies quite significantly between the various countries of the CINDI Programme and is influenced, in great measure, by the availability of resources and facilities. As a consequence, this document should be used as a guide to be tailored as appropriate to local conditions.

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**Dr I. Glasunov**
Regional Adviser, Countrywide Integrated Noncommunicable Diseases Intervention (CINDI) Programme, WHO Regional Office for Europe

**Professor A. Gries**
Diabetes Forschungsinstitut, Universität Düsseldorf, Düsseldorf, Germany

**Professor H. Janka**
Zentralkrankenhaus Bremen-Nord, Bremen, Germany

**Dr I. Kalo**
Consultant, Quality of Care and Technologies, WHO Regional Office for Europe

**Professor H. Keen**
Guy's Hospital Medical School, London, United Kingdom

**Dr D. MacLean**
Faculty of Medicine, Dalhousie University, Halifax, Nova Scotia, Canada

**Professor Meng Tan**
Faculty of Medicine, Dalhousie University, Halifax, Nova Scotia, Canada

**Professor J. S. Yudkin**
University College London, United Kingdom

# Introduction

Diabetes places a great burden at both the individual and societal level in most countries of the world particularly the developed nations. It is one of the top ten leading causes of death, despite the fact that mortality data tend to underestimate the impact of diabetes as it is frequently under-reported on death certificates[1]. Diabetes is a major cause of disability, particularly in the middle years of life. It is one of the dominant risk factors for the development of cardiovascular disease and adverse outcomes of pregnancy. It is the single largest contributor to the development of blindness, end-stage renal disease and nontraumatic amputations. This high disease burden is not spread equally throughout society, being greater in disadvantaged populations such as individuals of lower socioeconomic status and the elderly. The costs to health care systems and societies in general associated with the care of people with diabetes and its complications is truly massive. In Great Britain for example, it is estimated that approximately 5% of total health care expenditures are devoted to the care of people with diabetes[2], while in the United States the amount is approximately 15% of health care expenditures[3].

# Diabetes as a health policy issue

Of the two major types of diabetes, insulin dependent diabetes mellitus (IDDM) and non-insulin dependent diabetes mellitus (NIDDM), the latter accounts for 85% of total cases. From an epidemiological perspective there are significant geographical differences around the world in the incidence and prevalence of both major types of diabetes. In addition there have been significant changes with respect to the secular trends concerning this disease with increasing incidence in many populations around the world. These observations suggest that there are powerful environmental factors at play which, in combination with individual genetic endowment, are responsible for the development of this disease. As a consequence the prevention and control of diabetes and its complications may be possible[1].

## The Potential of Prevention

There is an ever growing body of literature which supports the feasibility of prevention of diabetes and its complications. Obesity particularly of the abdominal type has been implicated as a risk factor for NIDDM, although the mechanisms where by it influences glucose intolerance are poorly understood[4]. There is general agreement that diet modification is a cornerstone in the prevention of diabetes, although the exact nature of the diet

[1] Prevention in this context is interpreted broadly to include primary prevention i.e. the reduction in incidence of diabetes; secondary prevention i.e. the improvement in metabolic control and the prevention of complications in individuals with the disease; and tertiary prevention i.e. the early identification and treatment of complications.

remains controversial[5].Studies have demonstrated that sustained physical activity is associated with a reduced incidence of NIDDM which along with other work suggests that the prevention of NIDDM is possible[6,7]. With regard to IDDM much more information is now available regarding the role of the body's immune response in association with environmental factors in the development of this disease suggesting the possibility of effective preventive strategies being developed[8,9]. There is an increasing body of evidence supporting benefits of taking action for secondary prevention[10],including the benefits of good metabolic control for the prevention of adverse pregnancy outcomes and ketoacidosis.

There is strong evidence of the benefit of early identification and treatment of diabetic complications. This includes the prevention of blindness, amputation and end-stage renal disease along with a growing body of information supporting CVD risk factor reduction efforts for the prevention of coronary artery disease, stroke and peripheral vascular disease in people with diabetes.[11,12]

Over the past number of decades much has been learned about the etiology and treatment of diabetes. Although much more is still to be understood, it is clear that much can be done to reduce its burden, not only by discovering new treatment approaches but also by ensuring effective and efficient use of those therapeutic approaches which we now know will work.

# Factors related to the development of cardiovascular disease in people with diabetes

About 75% of people with diabetes die from cardiovascular disease, principally coronary heart disease. There is a two to fourfold excess in deaths due to coronary heart disease (CHD) in people with diabetes as compared to those without the disease. The great excess of deaths attributable to this disease in people with both major types of diabetes as compared to populations without the condition is due to atherosclerosis. Autopsy studies have demonstrated that atherosclerosis in individuals with diabetes is a more extensive and accelerated process than in individuals without the disease. Extensive disease has been demonstrated in the major coronary arteries of individuals with IDDM before the age of 15 years. The extent and severity of atherosclerosis in the aorta and in cerebral and peripheral arteries of the lower extremities are also increased in people with diabetes.

## Cardiovascular Disease Risk and Diabetes

There are a number of known environmental factors which in interaction with an individuals' genetic make up, increase significantly the susceptibility of people with diabetes to the development of cardiovascular disease. One third of individuals with IDDM die of coronary heart disease (CHD) by the age of 55 years.[13] Renal disease is the leading cause of death of people with IDDM with CHD becoming a more common cause of death the longer individuals have the disease. With NIDDM, CHD is the leading cause of death regardless of the duration of the disease.

The relative excess of atherosclerosis in people with diabetes appears to be greater in women than men, eliminated the comparative advantage enjoyed by women who do not have diabetes. This observation is more apparent with IDDM than NIDDM.[14] It would appear that the impact of the known risk factors to heart disease is amplified in people with diabetes.

## Environmental Factors

The main factors which increase the susceptibility of people with diabetes to CHD are dyslipidemia, hyperinsulinemia, high blood pressure, central obesity, smoking, a positive family history of atherosclerosis and sedentary living.

The dyslipidemia of diabetes include hypertriglyceridemia, low levels of HDL cholesterol, increased levels and alterations of the composition of LDL cholesterol with a predominance of triglyceride-rich small, dense LDL particles, and an increase in apolipoproteins B and E. These changes are more prominent with poor metabolic control.

High blood pressure is more prevalent in people with diabetes than the general population. Its role as a risk factor for the development CHD in people with diabetes appears to be at least as strong as with the general population.

Hyperinsulinemia in the general population is a weak and inconsistent risk factor for the development of CHD, independent of other risk factors. Hyperinsulinemia in individuals with NIDDM is related to CHD and there is concern that the exogenous insulin use in IDDM may predispose these individuals to CHD. However, this issue is not yet resolved.

Impaired insulin action\insulin resistance in NIDDM is related to central\abdominal obesity leading to hyperinsulinemia which has been associated with high blood pressure and

dyslipidemia. Each of these factors are strongly associated with the development of atherosclerosis. There is growing evidence that insulin resistance may be a common thread running through atherosclerosis, CHD, and NIDDM.

Central/abdominal obesity as opposed to peripheral obesity is the major weight related factor associated with the development of CHD in diabetes. Of importance is visceral abdominal adiposity which is best detected by a CT scan and is the form of fat deposition which is most clearly associated with hyperinsulinemia and the development of insulin resistance found in NIDDM.

There is strong evidence that cigarette smoking, which is as prevalent in people with diabetes as it is in the general population, strongly increases the susceptibility of myocardial infarction and the complications of peripheral vascular disease in people with diabetes. It appears that women with diabetes who smoke are more susceptible to the development of these conditions than men. Smoking is associated with unfavourable lipid profiles particularly low levels of HDL cholesterol and increased levels of lp(a).

Physical inactivity/sedentary living has been strongly associated in many epidemiological studies with an increased incidence of CHD in people with diabetes as well as the general population. For people with IDDM, exercise increases insulin sensitivity and may reduce insulin requirements along with other beneficial effects on the cardiovascular system through the improvement in lipid profiles, the control of body weight and high blood pressure. For people with NIDDM regular exercise lowers blood glucose and glycosylated haemoglobin levels, lowers fasting and postprandial plasma insulin levels, improves insulin sensitivity and weight control, reduces total and excess abdominal fat, improves adverse plasma lipoprotein profiles along with some blood coagulation parameters and high blood pressure.

Renal disease and the presence of proteinuria are strongly associated with CHD in IDDM. The development of renal disease is associated with other risk factors for CHD i.e. increased fibrinogen levels, platelet aggregation and elevated blood pressure.

## Genetic Factors:

### *IDDM*

IDDM occurs in most racial and ethnic groups but the risk appears to be highest among white populations. These differences result from differing exposure patterns to environmental factor and in all likelihood from a differing prevalence of genetic susceptibility. IDDM clusters in families with the risk to siblings by age 50 years of approximately 10% or about twenty times that of the general population. The concordance rate for monozygotic twins is approximately 25-50%. There appears to be a greater risk to the offspring of fathers with diabetes that mothers. The risk to the offspring is inversely associated with the age of diagnosis of the parent.

The risk of an individual developing IDDM appears to be determined by an HLA gene(HLA-B and DR) or one closely linked to the HLA region.(the short arm of chromosome 6) However most individuals with an at risk HLA gene do not develop IDDM. Genetic studies suggest there are likely non-HLA loci, yet to be identified, involved with the IDDM susceptible genotype.

### *NIDDM*

There is a large variability in the occurrence of NIDDM in different racial groups worldwide suggesting an important role for environmental factors in the development of this condition. These conclusions have been reinforced by the finding from twin studies.

No single gene locus has been identified that contributes significantly to the susceptibility for NIDDM. However many of the risk factors for NIDDM such as obesity and hyperinsulinemia may be under genetic influence.

# Health care policies for diabetes prevention and control

Health policy for diabetes prevention and control requires a public health perspective which strikes the right balance between high risk and population approaches. However at present diabetes tends to be viewed largely as a clinical issue to be dealt with primarily in the clinical setting of doctors offices, clinics and hospitals. Clearly these services and facilities are essential for the care and well being of those with diabetes. However if there is to be a public health approach to this problem, particularly one where the prevention of diabetes and its complications plays a prominent role, then a much broader perspective is needed. This perspective will need to be incorporated not only in the development of public policy but also be accepted by the public. Because diabetes is a chronic disease with a long period of development it is seen by many in society as inevitable and therefore not necessarily preventable or postponable. Health care professionals and diabetes patient organizations can have significant impact to bring about changes in these views. In this context it is critical requirement that there be the development and strengthening of cooperative efforts among the primary care, public health and health promotion sectors.

There is an emerging consensus of the potential for the prevention of diabetes and its complications. Also being identified is the need for improved approaches to clinical assessment and management of the disease along with the provision of a continuity of care and the control of risk factors to prevent or delay the onset of complications particularly ischaemic heart disease, stroke and peripheral vascular disease.

There are a number of key facts which are important for those concerned with the prevention and control of diabetes. Cholesterol lowering in non-diabetic subjects has been shown to reduce coronary events and deaths[15], while blood pressure reduction in non-diabetic subjects is of benefit in reducing coronary heart disease and stroke[16]. Although no studies have confirmed these findings in people with diabetes, the same benefits seem likely. Smoking cessation for all people with diabetes can be calculated to reduce coronary deaths by 15% and all deaths by 16% in the diabetic population. Treating people in the top fifth of blood pressure distribution would reduce coronary deaths by 6% and all deaths by 4%. Treating people in the top fifth of distribution of total cholesterol would reduce coronary deaths by 5% and all deaths by 0.5%. Population approaches aimed at reducing levels of blood pressure and cholesterol for all people with diabetes might have two to three times the potential benefit of a strategy targeting high risk individuals[17].

# Management of cardiovascular disease in people with diabetes

## Preclinical Cardiovascular Disease

Advances in diagnostic methodology now make possible accurate noninvasive detection of asymptomatic or preclinical cardiovascular disease such as left ventricular hypertrophy, peripheral arterial vessel disease (PVD), carotid atherosclerosis, and renal dysfunction. The presence of one of this abnormality carries a markedly increased risk for symptomatic morbidity as well as cardiovascular mortality[18,19]. It has been recommended that all physician offices providing routine care to adult diabetic patients should be able to measure ankle and brachial blood pressure for ankle brachial index (ABI) to detect PVD[20]. All patients with confirmed preclinical cardiovascular disease should be especially carefully screened and monitored for risk factors and accordingly aggressively treated.

## Diagnosis

Evidence of cardiovascular disease should be specifically sought by clinical enquiry, physical examinations and non-invasive techniques, such as electrocardiography and Doppler sonographic devices if available. Diabetic patients should be investigated as vigorously as is warranted by existing evidence. Special procedures may be used, such as duplexsonographic examinations, radionuclide scanning, echocardiography, and coronary angiography where available.

Since a considerable number of NIDDM patients have already significant coronary artery disease at diabetes diagnosis, investigations should be started early.

## Management of Clinical Signs and Symptoms

Symptoms of angina are treated with nitrates, calcium antagonists and beta-blockers. Cardioselective betablockers should be used to minimize non-cardiac side-effects. There are significant differences between the available calcium channel blockers in their suppression of sinoatrial node function and myocardial contractility.

Surgical treatment or angioplasty of coronary disease should be considered when medical treatment has failed to relieve symptoms if available. Several studies have suggested that coronary atherosclerosis in the diabetic patient is more severe and diffusely distributed. However, there appears to be no increase in operative mortality and the adequacy of symptom relief is similar to that achieved for non-diabetic patients. The resulting improvement in quality of life is comparable, so that the clinical indications for coronary surgery, coronary angioplasty and coronary stent implantation in patients with diabetes are identical to those for the general population.

### *Myocardial infarction*

Acute myocardial infarction carries twice the mortality of that in the general population. Contributory factors may include coexistent diabetic cardiomyopathy, blunting of cardiac reflexes by autonomic neuropathy, and adverse metabolic effects.

Acute myocardial infarction in diabetic patients should be managed with tight control of blood glucose and potassium levels and prompt treatment of cardiac failure. The benefit of fibrinolytic therapy appears to be greater among the diabetic

patients. This therapy saves a substantial amount of lives in the younger and middle age group[21]. There is evidence that streptokinase is underused in diabetes.

Silent myocardial ischemia and silent myocardial infarction are more common in people with diabetes, have a worse prognosis in diabetes than in the general population, and angioplasty or coronary surgery can prolong survival in this group.

*Cardiac failure*

The diabetic patients, particularly the elderly, are prone to cardiac failure. In addition to coronary heart disease and hypertension, diabetic cardiomyopathy and autonomic neuropathy may contribute. Management of cardiac failure involves improved glycemic control, treatment of hypertension and the use of angiotensin converting enzyme inhibitors, digoxin and diuretics. Patients with symptomatic arrhythmia require evaluation, the benefit-to-risk ratio of antiarrhythmic therapy and/or anticoagulation has to be judged individually.

## Secondary Prevention

Diabetic patients with existing cardiovascular disease should be investigated and managed as vigorously as is warranted by existing evidence. Since a considerable number of NIDDM patients have already significant coronary artery disease at diabetes diagnosis, intervention should be started early, probably already in the prediabetic state.

There is evidence that primary risk factors continue to operate, although their effect is proportionately less, depending on the degree of cardiac and vascular damage (which ultimately dominates prognosis). Thus, risk factors should still be sought and corrected to a degree compatible with the patient's age and physical condition. In addition, measures to revascularize the

myocardium, the carotid and peripheral arteries should always be considered. Preventive measures for the diabetic patient should also include physical retraining programmes and the use of low doses of aspirin. Particularly at this stage, all diabetic patients should be offered an education including the individual patient's problem, the options for investigation and treatment, and secondary prevention advice.

Patients with a history of ischemic foot lesions require preventive foot care and lifelong surveillance.

# Management of Risk Factors

## Dyslipidemias

### *Dietary Treatment*

It is well established that a diet high in total/saturated fat and cholesterol can raise serum total cholesterol, especially LDL-cholesterol. Many clinical trials in humans have clearly demonstrated that lowering serum total/LDL-cholesterol can result in a decrease in mortality due to coronary artery disease (CAD), overt manifestations (angina, positive exercise stress tests, etc.) of CAD, and slow-down in the progression as well as regression of coronary atherosclerosis. Although these studies were done in people at risk for CAD but without diabetes, it is generally accepted that these findings apply to people with diabetes who have a higher risk for CAD. The subgroup analysis of the 4S study of cholesterol lowering in secondary prevention in NIDDM showed similar benefits to the whole study group.

A major goal in the treatment of CAD in people with diabetes, therefore, is the reduction in total/saturated fat as well as cholesterol intake. It is also recommended that non-pharmacological measures in the treatment of CAD in people with diabetes should include weight reduction in those who are obese and physical exercise in all who can do it. Reduction in total fat intake and physical exercise can lead to weight reduction. Weight reduction and physical exercise can lower serum triglycerides and LDL-cholesterol and raise HDL-cholesterol.

Total caloric intake should enable the person with diabetes to attain and maintain ideal body weight. Caloric restriction is indicated in those who need weight reduction. Not more than 30%

of the total caloric intake should come from fat in the diet. Not more than 10% of the total caloric intake should come from saturated fat in the diet. Reduction of saturated fat intake to <70% can lead to further reduction in the serum total and LDL cholesterol.

Daily cholesterol intake should be <300 mg. Further reduction to <200 mg may also reduce the serum total and LDL cholesterol further. Protein intake should aim for 0.8g/Kg ideal body weight.

The remainder of the calories should come from carbohydrates (50-60% of total caloric intake). Most of the carbohydrate should come from complex carbohydrate as part of the overall plan to control glycemia. Foods high in soluble fibre are recommended as they can lower serum total and LDL cholesterol as well as have a beneficial effect on the glycemic effect of the meal. For people with diabetes and hypertension, sodium reduction to <2400 mg/day is recommended.

Guidelines to facilitate the choice of nutritionally adequate meals from a variety of foods that meet the person with diabetes' food preference, socioeconomic means, cultural and religious background should be provided.

Optimal dietary therapy includes a referral to a registered dietician who can enable and empower the person with diabetes to adhere to an acceptable and practical meal plan that achieves the goal of eating healthy as part of the overall plan to reduce CAD.

A program for physical exercise should be an integral part of the non-pharmacologic therapy. Here, the preference of the person with diabetes and the practical aspects of the exercise program should be emphasized.

One life-style change that is important in reducing the risk for CAD is cessation of cigarette smoking for those who smoke

cigarettes. Cessation of smoking is often accompanied by weight gain which can be distressing to those people with diabetes who are trying to lose weight. Meal planning and eating healthy should address this problem.

*Drug Therapy*

It is generally recommended that the initial approach to managing dyslipidemias in people with diabetes is non-pharmacological therapy (diet and exercise) and control of the hyperglycemia. There are two exceptions when drug therapy is used with the non-pharmacological therapy initially. First, the person with diabetes has hypercholesterolemia and/or hypertriglyceridemia and is already on the recommended diet and has close to normal blood glucose control. Second, the patient has massive hypertriglyceridemia (except in diabetic ketoacidosis) where there is a risk for pancreatitis.

After non-pharmacological therapy has been used for up to six months and the person with diabetes has been compliant, drug therapy is considered for treatment of the dyslipidemia. The choice of lipid altering drug depends on the pattern of dyslipidemia. For each pattern several drugs are available and the final choice depends on several factors, i.e. efficacy, safety, cost and availability.

## Target Lipid Levels

Target serum lipid levels for adults with diabetes have been recommended:

| | Risk for adults with diabetes | | |
|---|---|---|---|
| Lipid(mmol/L) | Acceptable High | Borderline | |
| Total cholesterol | < 5.2 | 5.2-6.2 | > 6.2 |
| LDL-cholesterol | < 3.4 | 3.4-4.1 | > 4.1 |
| HDL-cholesterol | > 0.9 | - | < 0.9 |
| Triglycerides | < 2.3 | 2.3-4.5 | > 4.5 |

For adults with diabetes who are at high risk for CAD, the desirable serum LDL cholesterol is 2.6 mmol/L and triglycerides 1.7 mmol/L.

## Elevated serum triglycerides and/or reduced HDL-cholesterol

The drugs that can be used are fibric acid derivatives and niacin. Fibric acid derivatives include gemfibrozil, fenofibrate and bezafibrate. They lower serum triglycerides 30-40% and LDL-cholesterol 10-25% and raise HDL-cholesterol 10-15% (depending on the drug). They do not affect glycemic control.

Niacin or nicotinic acid lowers serum triglycerides 20-50% and LDL-cholesterol 15-25% and raise HDL-cholesterol 15-30%. Niacin can cause hyperglycemia and in one study 6% of non-diabetic patients developed clinical diabetes during 2.5 years of niacin therapy. For this reason, niacin is no the first line drug and is recommended for use with caution in people with diabetes who are resistant to other forms of lipid altering drugs. However,

niacin is a cost-effective drug for lowering elevated serum triglycerides and cholesterol and raising HDL-cholesterol.

## Elevated LDL-cholesterol

The drugs that can be used are HMG-CoA reductase inhibitors, bile acid resin binders, niacin, fibric acid derivatives and probucol.

HMGCoA reductase inhibitors are the drugs of choice as they can lower LDL-cholesterol by 30-40%, lower triglycerides 10-25% and raise HDL-cholesterol 5-10%.

Bile acid resin binders can lower LDL-cholesterol by 15-20%. A potential side-effect of bile acid resin binders is hypertriglyceridemia and should, therefore, be used carefully in hypertriglyceridemic patients. Its effect on serum HDL-cholesterol is minimal.

Niacin is also an effective drug in lowering LDL-cholesterol and has the advantage of raising HDL-cholesterol significantly. Its lipid altering capabilities are discussed above.

Fibric acid derivatives can also lower serum LDL-cholesterol, but their effects are not as great as the other drugs above.

Probucol can lower LDL-cholesterol by 10-20%. Because it lowers HDL-cholesterol (20-30%) its use is not widespread. However, its anti-oxidant capability may be beneficial.

## Elevated serum LDL-cholesterol and triglycerides

The drugs that can be used are HMGCoA reductase inhibitors, fibric acid derivatives, niacin and combinations of lipid altering

drugs. The choice depends on which lipid fraction is elevated. If the major lipid elevation is LDL-cholesterol, HMG-CoA reductase inhibitors are preferred. If the major lipid elevation is triglycerides, fibric acid derivatives are preferred. combination therapy can include fibric acid derivatives and bile acid resin binders to lower both serum triglycerides and LDL-cholesterol.

## High Blood Pressure

### *Non-Pharmacologic Measures*

Initial advice should concentrate on lifestyle and non-pharmacological advice dealing with the following where appropriate. Weight reduction, where possible. Dietary sodium reduction, even if only to the range of 80-120 mmol/day[22]. Increased physical activity where practicable. Avoidance of excess alcohol. Avoidance of excessive caffeine, especially in smokers.

### *Choice of Drug*

Thiazides may be used but only on low dosage, not exceeding 2.5 mg/day of bendrofluazide or its equivalent. Cardioselective beta-blockers may be used. Combinations of thiazides and beta-blockers should be avoided in view of their effect on glucose tolerance.

Calcium antagonists are valuable, especially where systolic hypertension is predominant, and probably have little effect on glucose tolerance, except possibly for nifedipine. ACE inhibitors are effective in many patients, especially as detailed below. Alpha-blockers appear promising but long-term data in diabetes are limited.

There are a number of key facts that are important to bear in mind with the treatment of risk factors of people with diabetes.

Blood pressure should be measured at least annually in all people with diabetes. Equipment should be tested regularly. Unless clinically urgent, multiple measurements should be taken before initiation of therapy.

Guidelines provided by the Keen Working Party Report[23], based on level of risk, recommend drug treatment in any NIDDM subject with blood pressure over 160/90, or over 140/90 in the presence of kidney or other organ damage.

Blood pressure lowering its of clearest benefit in people with IDDM with proteinuria, where strict criteria for target levels can be applied[24,25]. Similar considerations appear logical in microalbuminuric people with IDDM, but non-insulin dependent diabetic patients with nephropathy are generally older, and such rigorous targets may be inappropriate.

With hypertension in NIDDM subjects non-pharmacological measures should be used initially and before automatic drug prescription[26]. These include weight loss, mild sodium restriction, increased exercise, reduction of excessive alcohol intake and avoidance of excessive caffeine (especially in smokers).

Optimal drug therapy for hypertension in NIDDM is unknown and requires individual selection to optimise benefit and minimise risk of side-effects or toxicity. In non-diabetic subjects, beta blockers and thiazides, but no other classes of drugs, have been shown to reduce cardiovascular mortality. Both of these groups of drugs may induce adverse metabolic and other effects in people with diabetes, but their separate monitored use in low dose is reasonable. The efficacy of angiotensin converting enzyme inhibitors and of alpha blockers on improving outcome in people with diabetes needs further investigation.

# Smoking

Smoking is an important risk factor in people with diabetes, not only for cardiovascular disease, but also, in some studies, for retinopathy and nephropathy[27]. Smoking is also the most clearly reversible of all risk factors, and emphasis on preventing people with diabetes from starting to smoke, and on smoking cessation for those that do, should be a major priority. Emphasis on other risk factors should not divert attention from this message.

The major potential beneficial impact on cardiovascular risk is that of smoking cessation. Powerful programmes of education must be supplemented by increasing the availability of nicotine replacement therapy to diabetic patients. At present, diabetes is a caution, but not a contraindication, for nicotine replacement therapy, based on risk in people with peripheral vascular disease, and on the possibility that nicotine antagonises the action of insulin, although probably less than do cigarettes themselves. It is recommended making nicotine replacement therapy widely available to diabetic subjects, including its availability on prescription, for physician supervision and dosage adjustment if necessary.

There are a number of key facts which pertain to the issue of smoking with respect to people with diabetes. Smoking is the major reversible risk factor for cardiovascular disease in diabetic subjects. Smoking cessation for all people with diabetes can be calculated to reduce coronary deaths by 15% and all deaths by 16% in the diabetic population. Smoking prevention and cessation are amongst the highest priorities in the prevention of cardiovascular disease in people with and without diabetes. Nicotine replacement therapy is of proven benefit in people without diabetes. There is a strong case for extending this to diabetic patients and making it available on prescription.

# Physical activity and diabetes

It is generally recognized that physical inactivity is a potent risk factor contributing to the development of cardiovascular disease in the general population as well as for people with diabetes.[28] There now appears to be consensus that regular physical exercise has many real and potential benefits for people with diabetes, particularly for the prevention and control of cardiovascular disease and its risk factors. Specific exercise recommendations have been made for people with insulin-dependent (IDDM) and non-insulin-dependent (NIDDM) diabetes mellitus.[29]

***Exercise and IDDM:***

People with IDDM should be encouraged to participate in all forms of physical activity which is consistent with their lifestyle choices. This includes competitive sports. There is little evidence to support that regular exercise will improve glycemic control in people with IDDM, however exercise does appear to increase insulin sensitivity and may reduce insulin requirements. (and thereby possibly reducing any potentially deleterious effects of exogenous insulin on the cardiovascular system?) Exercise may have other beneficial effects on the cardiovascular system through the improvement in lipid profiles, particularly a decrease in LDL cholesterol and an increase in HDL cholesterol.[30] As with people who do not have diabetes, regular exercise carried out by people with IDDM can be beneficial in the control of body weight and high blood pressure.

Regular physical exercise by individuals with IDDM should be undertaken with due caution to avoid possible injury or harm. Complication of exercise include hypoglycaemia ( the most common risk), hyperglycaemia and ketosis, cardiovascular

ischemia and arrhythmia, retinal detachment and intraocular haemorrhage, lower extremity injury due to peripheral neuropathy or vascular disease. As a consequence caution should be used in recommending exercise in individuals with IDDM with proliferative retinopathy, severe peripheral neuropathy, nephropathy with heavy proteinuria, coronary artery disease, particularly those with unstable angina or heart failure and cerebrovascular disease with recurrent transient ischemic attacks.[31]

The metabolic response to exercise is determined by many factors such as fitness level, duration and intensity of the exercise and the timing of the activity in relation to insulin administration and meals. Thus, for people with IDDM, exercise recommendations need to be specifically tailored to the individual. Self monitoring of blood glucose is very important to allow the individual to adjust diet and insulin dosage to ensure that hypoglycaemia is avoided. Blood glucose concentrations should be monitored before, during, and after exercise. This is particularly true when new exercise programs are being initiated. Each individual needs to learn how they respond to different types and intensity of exercise. If blood glucose is less than 5.6 mmol/l (100mg/dl), a carbohydrate snack should be eaten before exercise. Exercise should be avoided at the time of peak insulin action and when it involves muscles into which short-acting insulin has recently been injected.[32]

### *Exercise and NIDDM*

For people with NIDDM regular exercise should be encouraged as a means of lowering blood glucose and glycosylated haemoglobin levels, lowering fasting and postprandial plasm insulin levels, improving insulin sensitivity, and increasing energy expenditure as a adjunct to diet for weight control and as a means of reducing a number of cardiovascular disease risk factors such as total and excess abdominal fat, adverse plasma lipoprotein profiles, some blood coagulation parameters and high blood pressure.[33]

Numerous epidemiological studies have demonstrated that NIDDM is more prevalent in sedentary individuals, independent of age and body mass index. Other studies have demonstrated a reduced incidence of NIDDM in individuals who exercise.[34] Therefore regular physical activity may be important to the primary prevention of NIDDM for a significant proportion of the population.

As with people with IDDM exercise should be undertaken by individuals with NIDDM with due regard to the prevention of complications. Although the risk of hypoglycaemia is reduced in people with NIDDM as compared to those with IDDM, individuals about to begin an exercise program should be assessed clinically for the presence of high blood pressure, neuropathy, retinopathy, nephropathy, and silent ischemic heart disease. An exercise stress test is recommended for all individuals over the age of 35 years.

There are a number of goals for the treatment of people with diabetes. It is critical to have appropriate regular physical exercise become part of the usual activities of daily living of people with diabetes and have appropriate regular physical activity recommended as part of the usual care received of people with diabetes, particularly for the prevention and control of macrovascular complications.

The following recommendations with regard to exercise are suggested to improve glycemic control and reduce cardiovascular risk factors in people with diabetes. An exercise program should include aerobic exercise at 50-70% of the individuals maximum oxygen uptake.(or to sustained maximum heart rate = 220 - persons age). The duration of the exercise be 20-45 minutes and be carried out at least three times per week. An exercise program include low-intensity warm-up and cool-down exercises. The exercise program be appropriate to the individuals' general physical condition and lifestyle. All individuals with diabetes should use proper footwear, avoid exercising in extreme heat or

cold, and inspect their feet daily and after exercise. Exercising should be avoided during periods of poor metabolic control.

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