Consequences of Diabetes on Nutritional Status  

Module 21.1  

Medical Nutrition in Diabetes Mellitus  

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Learning Objectives  

1. Definition of diabetes mellitus  
2. Criteria for the diagnosis of diabetes mellitus  
3. Medical nutrition therapy for diabetes  
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   3.2. Meal/insulin timing  
   3.3. Physical activity/exercise  
   3.4. Weight management  
   3.5. Nutritional content  
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Key messages

- Diabetes mellitus is a complex disease with metabolic and nutritional consequences;
- The nutrition prescription for patients with diabetes should target glycaemic control, blood pressure, and low-density lipoprotein cholesterol;
- The nutritional prescription should be individualized to optimally manage pre-existing diabetes-related complications, avoid those at which the patient is at risk, and optimize other concomitant conditions;
- The process by which nutrition is individualized, based on medical, lifestyle, and personal factors, is known as medical nutrition therapy and is a cornerstone of diabetes management and education;
- Promoting dietary compliance is important to optimize glycaemic control and to avoid acute and chronic complications.
1. Definitions of Diabetes Mellitus Type 1 (DMT1) and 2 (Dmt2)

The term diabetes mellitus (DM) describes several conditions associated with altered carbohydrate metabolism characterized by hyperglycaemia. DM results from a relative or absolute impairment in insulin secretion, along with varying degrees of peripheral resistance to insulin action (1).

DMT1 is defined by autoimmune destruction of the pancreatic beta cells, leading to absolute insulin deficiency. DMT2 is characterized by hyperglycaemia and variable degrees of insulin resistance. In the long term, hyperglycaemia can impair pancreatic beta cell function and lead to insulin deficiency. DMT2 is a common disorder strictly associated with obesity. Patients suffering from DM are at increased risk of macro- and micro-vascular complications, e.g. cardiovascular disease (CVD), cerebrovascular disease, peripheral vascular disease, central and peripheral neuropathy, retinopathy, nephropathy and gastrointestinal problems. These complications are of major importance, since they impair function and quality of life as well as reducing life expectancy.

2. Diagnosis of DM

The diagnosis of diabetes can be established with any of the following criteria (2):

<table>
<thead>
<tr>
<th>Criteria for the diagnosis of diabetes</th>
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</thead>
<tbody>
<tr>
<td>1. HbA1c ≥6.5 %</td>
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<tr>
<td>OR</td>
</tr>
<tr>
<td>2. FPG ≥126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least eight hours.*</td>
</tr>
<tr>
<td>OR</td>
</tr>
<tr>
<td>3. Two-hour plasma glucose ≥200 mg/dL (11.1 mmol/L) during an OGTT. The test should be performed using a glucose load containing the equivalent of 75-gram anhydrous glucose dissolved in water.*</td>
</tr>
<tr>
<td>OR</td>
</tr>
<tr>
<td>4. In a patient with classic symptoms of hyperglycaemia or hyperglycaemic crisis, a random plasma glucose ≥ 200 mg/dL (11.1 mmol/L).</td>
</tr>
</tbody>
</table>

HbA1c: glycated haemoglobin; FPG: fasting plasma glucose; OGTT: oral glucose tolerance test.

Criteria 2 and 3 were recommended by the American Diabetes Association (ADA) in 2003 for diagnosing diabetes (3). The use of an HbA1c value of ≥6.5 percent (≥48 mmol/mol) was proposed in 2009 by an International Expert Committee to diagnose diabetes (4), the ADA, EASD (European Association for the Study of Diabetes), and WHO confirmed the decision (5, 6).

In the absence of overt hyperglycaemia, criteria 1 to 3 should be confirmed by repeating the test. However, if two different tests (e.g., FPG and HbA1c) are available and are concordant for the diagnosis of diabetes, additional testing is not needed. If two different tests are discordant, the test that is diagnostic of diabetes should be repeated to confirm the diagnosis (7). The importance of confirming the diagnosis by repeated measurements is highlighted by the finding that the prevalence of diabetes decreased when the diagnosis is based on two abnormal measurements rather than on one single abnormal test (8).

Since the different tests (FPG, two-hour plasma glucose and HbA1c) represent different physiological phenomena, each test will identify different proportions of the population with
diabetes. It has been suggested that the shift from using the FPG to using HbA1c to diagnose diabetes may decrease the proportion of patients screening positive (7, 9). However, in another study the use of HbA1c and FPG was concordant in the diagnosis of DM in 98% of the population investigated (10). For this reason, in 2011 the WHO concluded that an HbA1c value of <6.5 % (48 mmol/mol) does not exclude diabetes if diagnosed using plasma glucose levels (6).

In addition to diabetes, four additional categories have been identified with respect to glucose metabolism, as shown in Table 2 (3, 5, 7, 11, 12).

### Table 2

<table>
<thead>
<tr>
<th>Categories at normal or increased risk for diabetes</th>
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<tbody>
<tr>
<td>Normal glucose level</td>
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<tr>
<td>• FPG &lt;100 mg/dL (5.6 mmol/L).</td>
</tr>
<tr>
<td>• Two-hour glucose during OGTT &lt;140 mg/dL (7.8 mmol/L).</td>
</tr>
<tr>
<td>Increased risk for diabetes (prediabetes)</td>
</tr>
<tr>
<td>• IFG – FPG 100-125 mg/dL (5.6-6.9 mmol/L).</td>
</tr>
<tr>
<td>• IGT – Two-hour plasma glucose value during a 75 g OGTT 140-199 mg/dL (7.8-11.0 mmol/L).</td>
</tr>
<tr>
<td>• HbA1c 5.7-6.4% (39-46 mmol/mol) or 6.0-6.4% in (4) (42-46 mmol/mol).</td>
</tr>
</tbody>
</table>

FPG: fasting plasma glucose; OGTT: oral glucose tolerance test; IFG: impaired fasting glucose; IGT: impaired glucose tolerance.

Impaired fasting glucose (IFG) is defined as a fasting plasma glucose of 110-125 mg/dL (6.1 to 6.9 mmol/L) (2, 13).

Impaired glucose tolerance (IGT) is defined as a FPG <126 (7.0 mmol/L), and a two-hour, post-OGTT glucose ≥140 mg/dL (7.8 mmol/L) but <200 mg/dL (11.05 mmol/L). HbA1c levels in the range of 5.7-6.4% (39 to 46 mmol/mol) or 6.0-6.4% (42 to 46 mmol/mol) according to the International Expert Committee report (4) are associated with the highest risk of developing diabetes, although the risk increases progressively for HbA1c levels lower than 6.5 percent (48 mmol/mol).

### 3. Target of Nutrition Therapy in DM

Diet is very important in the treatment of diabetes. In this setting nutrition should be targeted at the control of glycated haemoglobin and of body weight by integrating with diabetes therapy and physical activity, at the management of blood pressure and of low-density lipoprotein (LDL)-cholesterol. Nutritional prescription should be individualized to the individual’s needs in order to maintain optimal blood glucose levels, to manage risk factors and to prevent/delay acute and chronic diabetic complications. In addition, personal and cultural preferences should be considered and addressed in order to restrict food choice only when strictly necessary. The relative impact of each nutritional goal varies in different patients according to the individual’s characteristics.

The nutrition prescription for patients with diabetes is an integral component of diabetes management and diabetes self-management education (14), and should be managed by a registered dietitian from the time of diagnosis of DM, and based on medical, lifestyle, and personal factors.

The effectiveness of nutrition therapy is demonstrated by randomized controlled trials which have shown a decrease in HbA1c of approximately 0.3-1 % in patients with DMT1 (15, 16) and by 1-2% in DMT2 (17). Glycaemic control is tightly linked to the development
and progression of neuropathy, nephropathy, retinopathy in both DMT1 and 2, and of coronary artery disease in patients with DMT1 (18, 19). Diabetes nutrition therapy both for DMT1 and 2 should be directed at increasing patients' adherence to the meal plan, at adjusting insulin dose for meal size and content, at regulating food and/or insulin in response to hypo/hyperglycaemia and before physical activity, at managing weight changes while achieving glycaemic control and at preventing acute and chronic complications.

To achieve these goals, the key points of diabetes nutrition therapy include consistency in daily carbohydrate intake, meal/insulin timing, weight management and physical activity, energy balance (caloric intake balanced with caloric expenditure) and nutritional content (balance of selected protein, carbohydrates, and fats).

### 3.1. Consistency of Daily Carbohydrate Intake

Variations in daily carbohydrate intake can result in unstable glucose control and in hypoglycaemia in DMT1. Basal-bolus insulin therapy allows for some flexibility in the carbohydrate content of meals as well as short-acting insulin analogues or insulin pumps. For patients receiving fixed doses of short- and intermediate-acting insulin, however, day-to-day regularity in the amount and source of carbohydrate at meals and snacks is important. Regularity in daily carbohydrate intake in these patients has been associated with a lower HbA1c level, while variations in calorie, protein or fat intake did not affect it (20).

Several approaches are known to plan meals in order to achieve carbohydrate consistency, including basic and advanced carbohydrate counting and sample menus. The best approach for each patient is determined depending on his/her lifestyle and learning capabilities. Patients using carbohydrate counting consume a predetermined daily amount of carbohydrate at meals and in snacks, calculated in grams of carbohydrate per food portion (21). The calculated carbohydrate intake is derived from an optimal percentage of total calories from carbohydrates, based on nutrition goals and the usual eating pattern. Patients need to be comfortable with simple arithmetical computations and must be trained by a dietician to set appropriate meal and snack targets and to measure or estimate portion sizes and read food labels. Another basic approach to achieve carbohydrate consistency is by using sample menus, which specify the time and amounts of food to be eaten at each meal and snack. For type 1 diabetic patients, menus are developed to meet calorie needs, to provide consistent carbohydrate intake at meals and snacks and to meet individual food preferences and diabetes nutrition therapy goals. Advanced carbohydrate counting approaches are based on a more detailed way of counting carbohydrates to maintain good glucose control by matching mealtime insulin doses to the amount of carbohydrate ingested.

### 3.2. Meal/Insulin Timing

Meal timing at regular intervals has traditionally been a cornerstone for diabetic patients treated with fixed doses of short- and intermediate-acting insulin to achieve goals for glycaemic control without hypoglycaemia (21). Newer rapidly-acting insulins, however, allow for more flexibility in meal schedules and content. Traditional insulin regimens were characterized by the injection of roughly the same amount of insulin at the same time each day, without taking into account the amount and timing of carbohydrate intake. This was associated with fluctuations in blood glucose profiles, exposing the patients to the risk of hyper- and hypoglycaemia.
The flexibility of intensive therapy regimens with newer insulins allows determination of the amount of short- or rapid-acting insulin needed to cover an established amount of carbohydrate. A significant inter- and intra-individual variability at different meals in the carbohydrate-insulin ratio has however been described. Familiarity with carbohydrate counting approaches becomes essential in making insulin therapy adjustments.

3.3. Weight Management and Physical Activity

The success of dietary intervention, which is strategic in achieving and maintaining an appropriate body weight especially in DMT2, is associated with many patient related factors. Self-monitoring for dietary intake and weight can be helpful in achieving and maintaining weight loss. Self-monitoring for dietary intake include consciousness of eating behaviour, refusal of food offered by others, stopping eating when appropriate and provision of structured meal plans. Exercise is a significant component of diabetes management. Benefits of exercise include improved glycaemic control, weight control, reduction in co-morbidities (hypertension, dyslipidaemia, and cardiovascular disease), improved mood, and quality of life (22, 23). These beneficial effects are more evident in DMT2. Diabetic patients should perform 30-60 minutes of moderate-intensity aerobic activity on most days of the week (to a minimum total of 150 minutes of moderate-intensity aerobic exercise per week) (13, 24). Vigorous exercise should be avoided in the presence of advanced microvascular complications and of established coronary heart disease. More exercise may be beneficial for achieving and maintaining long-term weight loss. This should be considered comprehensively when periodically adjusting the plan for dietary and pharmacological interventions to optimize glucose control.

3.4. Energy Balance

The importance of caloric intake depends on several factors, including current weight, weight history, fat distribution and waist circumference, lean muscle mass, genetics and glycaemic control. Lowering caloric intake and inducing weight loss are of major importance for overweight and obese patients with DMT2. It is known also that modest weight loss is associated with a reduction in clinical risk factors for cardiovascular disease (25).

3.5. Nutritional Content

The optimal mix of macronutrients for patients with DMT1 and 2 is so far controversial (16, 26) as the ideal percentage of calories from carbohydrate, protein, and fat may vary depending on the individual’s eating patterns, preferences and targets for metabolic control. In this view, several different eating patterns (low fat, low carbohydrate, Mediterranean) can be accepted (16, 27).

3.5.1. Carbohydrates

Variations in carbohydrate intake can deeply impact glucose control, particularly in DMT1. In this context, definitive evidence on the ideal amount of carbohydrates for diabetic patients is lacking. However, monitoring carbohydrate intake (by basic or advanced carbohydrate counting) is a very important strategy to improve and maintain glycaemic control. Amongst the different carbohydrates, intake from fruits, vegetables, whole grains and legumes should be encouraged (16).
3.5.2. Glycaemic Index and Glycaemic Load

Foods containing the same amount of carbohydrate can differentially impact plasma glucose levels because of different glycaemic index and/or glycaemic load:
Notably, glycaemic index is determined by the incremental rise in blood glucose after ingestion of a portion of the test food containing 50 g of carbohydrate, compared with the same amount of carbohydrate from a reference food, which is usually white bread or glucose (28, 29). Some examples of low-glycaemic index foods include non-starchy vegetables, nuts and legumes. High glycaemic index foods include white bread, and other refined products made from grains.
In addition to the quality of carbohydrates ingested (i.e. the glycaemic index), the quantity of carbohydrates also influences the blood glucose response. In this view, the glycaemic load is the product of the glycaemic index value of a food and its total carbohydrate content (30). Although glycaemic index and glycaemic load may have a deeper impact on metabolic control than glycaemic control alone, a modest additional benefit for glycaemic control has been shown in DM when substituting low-glycaemic load foods for higher glycaemic-load foods (31). In subjects at increased risk for diabetes low glycaemic index diets have been associated with improvement of cardiovascular risk factors (32). The difficulty in defining the effects of glycaemic index and glycaemic load in clinical trials lies on the fact that their effect is hardly dissectible from that of fibre.

3.5.3. Fibre

Fibre and whole grain intake should be at least equivalent to that recommended for the general population (14 grams per 1000 calories daily or about 25 g/day for adult women and 38 g/day for adult men) (13). Their effect on glycaemic control is modest, however they may improve serum cholesterol and cardiovascular risk factors.

3.5.4. Sucrose, Fructose and Non-nutritive Sweeteners

Intake of sucrose, a disaccharide composed of glucose and fructose, does not significantly impact glucose control at up to 35% of total daily calories, although care should be taken to avoid excess calories (33); sucrose can be substituted for other carbohydrates (e.g. starch) in the meal plan or, if added, covered with insulin. Intake of fructose from fruits (“free fructose”) may improve glycaemic control as compared with sucrose or starch without adversely affecting triglycerides as long as it does not exceed 12% of total caloric content (16). Non-nutritive sweeteners may reduce calorie intake if used to replace caloric sweeteners, although the evidence in terms of weight reduction is limited (34).

3.5.5. Protein

The ideal amount of dietary protein to be consumed in patients without kidney disease in order to reach and maintain an optimal glucose control is uncertain (16). Furthermore, it is unclear whether a low protein diet contributes with other measures (e.g. angiotensin-converting enzyme (ACE) inhibition and aggressive control of blood pressure and blood glucose) to reduce cardiovascular risk and to preserve renal function. Thus, protein intake should be individualized. In the presence of kidney disease (e.g. macro- or microalbuminuria) a reduction of dietary protein intake is not recommended. Patients should be encouraged to substitute lean meats, fish, eggs, beans, peas, soy products, and nuts and seeds for red meat (16). In DMT2 dietary proteins stimulate insulin secretion and this should be taken into account in the presence of recurrent hypoglycaemia.

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3.5.6. Fat
As for proteins and carbohydrates, the ideal quantity of fat to be consumed in the diet in DM is uncertain (16). In contrast, the type of fat consumed is more important than quantity in terms of metabolic control and of cardiovascular risk management. Saturated fats and trans fatty acids increase the risk of cardiovascular disease; in contrast, monounsaturated and polyunsaturated fats show a protective effect. Saturated fats should be replaced with monounsaturated and polyunsaturated fatty acids. An increased consumption of foods containing omega-3 polyunsaturated fatty acids is recommended; the general suggestion to assume at least two servings of fish per week applies also to diabetic patients. Trans fatty acid consumption should be sharply limited.

3.5.7. Micronutrients
Specific deficits in selected vitamins and minerals have been associated with diabetes. Vitamin D (cholecalciferol) is a lipid-soluble vitamin, which also acts as a hormone. The major function of vitamin D is maintenance of calcium-phosphorus homeostasis and promotion of bone mineralization. It has been suggested that low levels of vitamin D and calcium may predispose to DMT1 and 2 by promoting inflammation and destruction of beta cells (35). In addition, low vitamin D is associated with insulin resistance, development of albuminuria, cardiovascular disease and higher HbA1c levels. Although several prospective observational studies have shown an inverse relationship between circulating 25-hydroxyvitamin D levels and risk of DMT2, intervention studies are scarce and mostly inconclusive. Currently vitamin D supplementation is encouraged only in patients who show evidence of reduced plasma concentrations. The intake of calcium in adults ≥50 years should be 1200 mg/day and that of vitamin D 800-1000 IU, to maintain hydroxy-vitamin D levels above 30 ng/ml.
Chromium and magnesium have been associated with insulin sensitivity and glucose metabolism and their deficits could impact glucose control. However, in the absence of documented deficiencies no clear benefits from routine vitamin or mineral supplementation has been shown in diabetic patients (16). Currently, it is suggested that food choice is optimized in order to satisfy recommended dietary allowance for all micronutrients and vitamins.

3.5.8. Alcohol
Alcohol intake should be limited to no more than one drink (10g alcohol) per day for women or two drinks per day for men; alcohol should be consumed with food. Because of an increased risk of delayed hypoglycaemia particularly if associated with insulin therapy and secretagogues, patients with DMT1 should closely monitor blood glucose to assess any immediate or delayed effects of alcohol intake on blood glucose levels (16).

3.6. Dietary Patterns
In order to promote dietary compliance and to individualize the nutritional prescription a variety of dietary patterns can be accepted to achieve glycaemic control and to target a desirable body weight in DMT1 and 2, including Mediterranean, vegetarian, vegan, low fat, and low carbohydrate diets (16). In DMT1 day-to-day carbohydrate consistency should be emphasized if an intensive insulin therapy regimen is prescribed. In DMT2 monitoring dietary intake and weight can be a helpful strategy to achieve weight loss.
4. Specific Situations

4.1. Acute Complications

4.1.1. Hypoglycaemia

Hypoglycaemia can be a frequent event if the patient is not well trained to match hypoglycaemic therapy with diet and physical activity. Overtreating hypoglycaemia can result in undesired hyperglycaemia and increased calorie intake, resulting in weight gain; therefore in case of frequent hypoglycaemic episodes, review and potential revision of any hypoglycaemic therapy should be performed.

In case of hypoglycaemia (blood glucose <70 mg/dL), in the range of glucose levels between 51 to 70 mg/dL, intake of 10 to 15 g of fast-acting carbohydrate is recommended, and of 20 to 30 g of fast-acting carbohydrate if blood glucose levels fall ≤50 mg/dL. Retesting 15 minutes after ingestion and repeating treatment as needed based on blood sugar levels is recommended. Once blood glucose is >70 mg/dL, an appropriate insulin dose to cover carbohydrate intake at the next meal should be administered (36).

4.1.2. Diabetic Ketoacidosis (DKA) and Hyperosmolar Hyperglycaemic State (HHS)

Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycaemic state (HHS) are two of the most dangerous acute complications of DM. Each of them represents an extreme in the spectrum of hyperglycaemia and there may be considerable diagnostic overlap between them.

The main differences between DKA and HHS consist in the presence of ketoacidosis and, usually, the degree of hyperglycaemia (37, 38). In DKA, metabolic acidosis is often the major finding, while the serum glucose concentration is generally below 800 mg/dL (44.4 mmol/L). Serum glucose may be normal or minimally elevated in patients with euglycaemic DKA. From a pathophysiologic perspective, DKA is a typical complication of DMT1 caused by severe insulin deficiency. Its typical presentation includes hyperglycaemia, glycosuria, polyuria and loss of fluids and electrolytes, including sodium and potassium, although their serum levels are influenced by water balance. Phosphorus and magnesium deficiency also develop. While the typical total body deficits of electrolytes are similar, total body water deficit is much more marked in HHS than in DKA (9 vs. 6 litres).

HHS is typically a complication of DMT2. In HHS there is a relative insulin deficiency leading to hyperglycaemia without ketoacidosis. It is usually precipitated by intercurrent illnesses such as infection or acute myocardial infarction. Blood glucose levels are exceedingly high, causing an osmotic diuresis and severe salt and water deficiency. The serum glucose concentration frequently exceeds 1000 mg/dL (56 mmol/L), the plasma osmolality (Posm) may reach 380 mOsmol/kg, and neurologic abnormalities are frequently present (including coma in 25-50% of cases). The definitions and clinical features proposed by the American Diabetes Association (ADA) for DKA and HHS are shown in Table 3 (39).
Table 3
**Typical laboratory and patient characteristics of DKA and HHS**

<table>
<thead>
<tr>
<th></th>
<th>DKA</th>
<th></th>
<th>HHS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mild</td>
<td>Moderate</td>
<td>Severe</td>
</tr>
<tr>
<td>Plasma glucose (mg/dL)</td>
<td>&gt;250</td>
<td>&gt;250</td>
<td>&gt;250</td>
</tr>
<tr>
<td>Plasma glucose (mmol/L)</td>
<td>&gt;13.9</td>
<td>&gt;13.9</td>
<td>&gt;13.9</td>
</tr>
<tr>
<td>Arterial pH</td>
<td>7.25 to 7.30</td>
<td>7.00 to 7.24</td>
<td>&lt;7.00</td>
</tr>
<tr>
<td>Serum bicarbonate (mEq/L)</td>
<td>15 to 18</td>
<td>10 to &lt;15</td>
<td>&lt;10</td>
</tr>
<tr>
<td>Urine ketones</td>
<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>Effective serum osmolality (mOsm/kg)</td>
<td>Variable</td>
<td>Variable</td>
<td>Variable</td>
</tr>
<tr>
<td>Anion gap</td>
<td>&gt;10</td>
<td>&gt;12</td>
<td>&gt;12</td>
</tr>
<tr>
<td>Alteration in sensoria or mental obtundation</td>
<td>Alert</td>
<td>Alert/drowsy</td>
<td>Stupor/coma</td>
</tr>
</tbody>
</table>

Anion gap calculation: \((\text{Na}^+ - (\text{Cl}^- + \text{HCO}_3^-))\) (mEq/L).

The treatment of DKA and HHS is similar, including fluids and potassium replacement and intravenous administration of regular insulin or of insulin analogues according to established algorithms. Frequent monitoring is essential, and underlying precipitating events should be identified and corrected. Intravenous (IV) fluid replacement to correct both hypovolaemia and hyperosmolality should be undertaken vigorously within the first 24 hours to correct estimated deficits, with care to avoid an exceedingly rapid reduction in serum osmolality, which can precipitate cerebral oedema. Indications for sodium bicarbonate administration to help correct the metabolic acidosis are controversial. Monitoring involves hourly glucose measurement until stability, basic blood chemistry profile and venous pH (for DKA) every two to four hours. The course of metabolic acidosis can be assessed by direct measurement of the serum anion gap.

### 4.2. Chronic Complications

Both macrovascular (atherosclerosis) and microvascular complications (retinopathy, nephropathy, and neuropathy) strongly contribute to the burden of diabetes morbidity. Glucose control is highly related to the development and progression of microvascular complications; in DMT2, both macrovascular and microvascular complications may be present at the time of diagnosis (40) and altered glucose levels along with atherogenic dyslipidaemia and hypertension together increase the risk of macrovascular disease. Therefore, non-pharmacological interventions (medical nutrition therapy, exercise and weight reduction) in combination with pharmacological interventions (aggressive management of blood glucose, blood pressure, and lipids and use of the renin-angiotensin-aldosterone system blockers) can prevent or delay the onset of complications.

The beneficial effects of strict glycaemic control on microvascular complications have been demonstrated both in DMT1 and 2 by several prospective, randomized clinical trials, which have shown that intensive therapy aimed at lowering HbA1c minimizes the risks for retinopathy, nephropathy and neuropathy (18, 41) both in DMT1 and 2 and decreases the risk for cardiovascular disease in DMT1 (19). These benefits have to be considered in front
of the higher risk of severe hypoglycaemia associated with intensive therapy, particularly in DMT1.

Prevention of cardiovascular disease is a priority in DM patients, especially type 2. To this aim, aggressive reduction of modifiable risk factors, including comprehensive smoking cessation, aggressive management of hypertension and cholesterol lowering (with a target of low-density lipoprotein ≤100 mg/dL), should be undertaken (42). As a matter of fact, intensive glycaemic alone control does not conclusively impact on cardiovascular outcomes in DMT2.

Lifestyle interventions (medical nutrition therapy, weight loss, increased physical activity) are the first steps to be undertaken in all patients affected by DM. Among complications with nutritional impact gastrointestinal autonomic neuropathy is worth a special mention.

4.2.1. Diabetic Autonomic Neuropathy

Diabetic autonomic neuropathy describes a wide spectrum of symptoms affecting many organs, including the cardiovascular, gastrointestinal, genitourinary, and neuroendocrine systems. These abnormalities are most probably related to autonomic neuropathy of the enteric nervous system.

Poor glucose control and cardiovascular risk factors are associated with the development of diabetic neuropathy (43). In DMT1 intensive insulin therapy reduced cardiovascular autonomic neuropathy incidence by 53% (44), this beneficial effect persisting for up to 14 years (45). In DMT2 intensive therapy consisting of lifestyle intervention (including diet, exercise and smoking cessation) combined with pharmacological treatment (multiple agents to achieve several therapeutic goals) has been shown to result in a delayed rate of progression of autonomic neuropathy, a phenomenon with a metabolic memory of 13.3 years (46).

Gastrointestinal autonomic neuropathy is of particular interest as it may affect spontaneous nutritional intake and nutritional status. The prevalence of gastrointestinal autonomic neuropathy is unknown. Its clinical manifestations are shown in Table 4.
Table 4
Abnormalities of gastrointestinal function in DM related to autonomic neuropathy of the enteric nervous system

<table>
<thead>
<tr>
<th>Complication</th>
<th>Pathophysiology</th>
<th>Clinical manifestations</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastro-oesophageal reflux disease</td>
<td>- Decreased lower oesophageal sphincter (LES) pressure</td>
<td>Pyrosis Regurgitation</td>
<td>Optimize glucose control</td>
</tr>
<tr>
<td></td>
<td>- Increased number of transient LES relaxations due to hyperglycaemia</td>
<td></td>
<td>Lifestyle and dietary modifications</td>
</tr>
<tr>
<td></td>
<td>- Impaired clearance function of the tubular oesophagus</td>
<td></td>
<td>Antacids</td>
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<td></td>
<td>- Delayed gastric emptying</td>
<td></td>
<td>Surface agents and alginates</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Histamine 2 receptor antagonists</td>
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<td></td>
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<td></td>
<td>Proton pump inhibitors</td>
</tr>
<tr>
<td>Gastroparesis</td>
<td>- Impaired neural control of gastric function</td>
<td>Nausea Vomiting Abdominal pain Early satiety Postprandial fullness Bloating</td>
<td>Optimize glucose control</td>
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<td></td>
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<td></td>
<td>Lifestyle and dietary modifications</td>
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<td></td>
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<td>Antiemetic and prokinetic agents</td>
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<td></td>
<td></td>
<td></td>
<td>Discontinue incretin-based therapy</td>
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<tr>
<td>Diabetic diarrhoea</td>
<td>- Disordered motility</td>
<td>Watery diarrhoea Faecal incontinence</td>
<td>Hydration and correction of electrolyte and nutrient deficiency</td>
</tr>
<tr>
<td></td>
<td>– Increased intestinal secretion</td>
<td>Constipation</td>
<td>Treatment of the underlying cause</td>
</tr>
<tr>
<td></td>
<td>– Small intestinal bacterial overgrowth</td>
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<td></td>
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<tr>
<td></td>
<td>– Faecal incontinence</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>– Medications (metformin, artificial sweeteners)</td>
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Gastro-oesophageal reflux disease (GORD) is characterized by the retrograde passage of gastric contents into the oesophagus. In DM, GORD may be caused by multiple mechanisms as listed in **Table 4**. Its most common clinical manifestations include pyrosis and regurgitation. The treatment of GORD in DM does not differ from that of GORD in the general adult population and is summarized in **Table 4**.

Gastroparesis is characterized by anorexia, nausea, vomiting, early satiety, postprandial fullness and, in severe cases, weight loss. A strong association between acute and chronic elevations of blood glucose and delayed gastric emptying has been described (47). Dietary modifications are the first step in treating gastroparesis; they consist of a limitation of fatty foods and carbonated beverages, elimination of alcohol and fractionation of meals (small, frequent meals, low in fat, containing only soluble fibre and of liquid/semiliquid consistence). Concomitant measures include optimization of glucose control and adequate hydration. In the case of failure of dietary modifications, pharmaceutical treatment with prokinetics (metoclopramide, domperidone and erythromycin) to increase the rate of gastric emptying can be prescribed (48).

In case of failure of pharmacotherapy in patients with abdominal pain and nausea a gastrostomy tube for decompression can be considered. In the presence of unintentional loss of 10% or more of the usual body weight during a period of three to six months, and/or two or more hospitalizations for refractory symptoms in 6 months, then enteral nutrition through a jejunostomy can be justified.

Clinical manifestations of diabetic enteropathy include chronic constipation, diarrhoea and rarely steatorrhoea, or even incontinence. Diabetic diarrhoea may be secondary to a variety of factors including intestinal dysmotility causing either delayed or accelerated...
small bowel transit, intestinal oversecretion, bacterial overgrowth, pancreatic exocrine insufficiency, faecal incontinence due to anorectal dysfunction and/or bile salt malabsorption secondary to accelerated small bowel transit or bile acid deconjugation due to bacterial overgrowth, medications (metformin and artificial sweeteners, sorbitol and polyols). Both diarrhoea and gastroparesis can adversely affect glycaemic control determining both hyper- and hypoglycaemia. Management of diabetic autonomic enteropathy depends on the causal factors responsible for the diarrhoea (49). It should begin with general measures such as hydration and correction of electrolyte and nutrient deficiency and with symptomatic treatment of diarrhoea. Treatment of the underlying cause should be directed at correcting aberrant motility and may include rotating antibiotics for bacterial overgrowth.

### 5. Summary

Diabetes mellitus is a complex disease with various metabolic and nutritional consequences. Diet and physical activity are crucial in the comprehensive treatment of diabetes, especially of DMT1, and are two important components of the medical nutritional therapy for a diabetic patient. The nutritional plan should be targeted not only at optimizing glycated haemoglobin, but also at managing plasma lipids and blood pressure. The prescription must be personalized to each individual's needs and preferences in order to minimize the incidence of acute and chronic diabetic complications.

### 6. References


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