



DIABETES MELLITUS

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Diabetes mellitus

- Diabetes mellitus is a syndrome characterized by abnormal carbohydrate and lipid metabolism.
- It is associated with small vessel changes in the kidney, eye and nerves, and accelerated atherosclerosis.
- There are two major types of overt diabetes mellitus:
 - type 1 or insulin – dependent (IDDM);
 - type 2 or non – insulin dependent (NIDDM).
- Screening: - Individuals who are members of high–risk ethnic groups;
 - Risk factors: obesity, previous or potential abnormality of glucose intolerance, or a history of gestational diabetes should be screened for NIDDM biennially by measurements of fasting blood glucose;

Diabetes mellitus - diagnostic criteria

National Diabetes Data Group - at least one of the following criteria:

1. Presence of classic symptoms (e.g., polyuria, polydipsia, weight loss, ketonuria) together with random blood glucose > 200 mg/dl
2. Fasting plasma glucose > 126 mg/dl or fasting venous whole blood > 126 mg/dl or fasting capillary whole blood > 110 mg/dl *on more than one occasion*
3. Abnormal oral glucose tolerance test (OGTT): the OGTT may be used to make the diagnosis of diabetes when FG is greater than 110 but less than 126 mg/dl. A positive diagnosis requires that both the 2 – hour sample and one other sample between 0 and 2 hours exceed 200 mg/dl.

[Type 1 and type 2 diabetes]

Type 1 diabetes:

- require insulin to sustain life and develop ketoacidosis in its absence
- onset before the age of 35s
- thin patients

Type 2 diabetes:

- do not require insulin to sustain life and, except under extraordinarily stressful conditions (e.g., auto accident, surgery, febrile illness, or death of a spouse), do not develop ketoacidosis
- onset after the age of 35s
- fat patients

Gestational diabetes

- Gestational diabetes develops during pregnancy in a previously normal woman and occurs in 1 to 2 % of all pregnancies
- All women should be screened for diabetes by measurement of FG between weeks 24 and 28 of pregnancy
- Earlier screening include:
 - glycosuria;
 - diabetes in a first-degree relative;
 - morbid obstetrical history: previous stillbirth, spontaneous abortion, fetal malformation;
 - infant weighing more than 9 pounds at birth;
 - maternal obesity;
 - maternal age over 30 years and parity of 5 or more.

[Impaired glucose tolerance]

- An FG less than 126 but an OGTT intermediate between normal and overt diabetes are classified as having impaired glucose intolerance.
- Findings on OGTT include a 2 – hour blood glucose less than 200 mg/dl and more than 180 mg/dl on a least two intermediate times.
- This defines the potential risk for atherosclerotic cardiovascular diseases but do not develop characteristic diabetic microangiopathy in the absence of further deterioration in glucose tolerance.

[Secondary diabetes]

- pancreatic disease
- Cushing's syndrome
- Pheocromocitoma
- acromegaly
- genetics defects
- medications that increase blood glucose: phenylephrine, glucocorticoids, sympatomimetics drugs, potassium

Management of type 1 diabetes

Goals: to improve patient well being and to prevent acute and chronic complications.

Methods: controlling blood glucose levels and ameliorating risk factors.

Four interventions should be used to control blood glucose levels in type 1 diabetes:

- diet
- exercise
- insulin
- education

Management of type 1 diabetes - diet

- Fats should not comprise more than 30 % of the daily caloric allowance;
- “Prudent diet” (low in saturated fats and cholesterol) is desirable;
- Concentrated, refined carbohydrates should be discouraged;
- Inclusion of 25 to 35 grams of fiber per day generally produces benefits;
- Decrease daily caloric intake by 500 cal to obtain 1–1,5 lb weight gain per week;

Management of type 1 diabetes

Insulin therapy

Type of insulin	Onset	Action (hrs)	Duration (hrs)
Insuline glulizine	Ultrarapide	0,5 - 1	0,5 -1
Regular crystalline	Rapid	2 - 4	5 - 7
Semilente	Raid	2 - 4	12 - 16
Lente	Intermediate	6 - 12	24 - 28
Basal	Prolonged	14 - 24	36 +

Management of type 1 diabetes Insulin therapy

Insulin regimens:

1. One daily injection of lente/basal insulin (< 10%);
2. Split-mixed insulin or glulisine: both an intermediate and short-acting insulin are administered from 30 to 60 minutes before breakfast and again 30 to 60 minutes before the evening meal.

2/3 intermediate	2/3 before breakfast	1/3 before evening
1/3 short-acting	1/2 before breakfast	1/2 before evening

3. Lente/basal insulin plus regular insulin at mealtime: a single daily injection of long-acting lente/basal insulin provides the basal background and regular insulin is administered 30 to 60 minutes before each major meal.

Management of type 1 diabetes Insulin therapy

4. Regular insulin with meals (tid) plus intermediate insulin at night: flexibility but demands constant attention because of the frequency of insulin administration.
5. Continuous subcutaneous insulin infusion with monitoring: provide a continuous dose of regular insulin and deliver on demand a pre-programmed dose at mealtime.

Management of type 1 diabetes

Monitoring

- measurements of urine ketones and blood glucose;
- urine glucose testing is unreliable in IDDM. Urine glucose concentrations correlate poorly with blood glucose levels;
- urinary ketones should be determined during an intercurrent illness;
- self-blood glucose monitoring;
- haemoglobin aA1c values are a representation of the glycemia during the previous 6 to 8 weeks;

Management of type 1 diabetes

Metabolic complications

1. **Fasting hyperglycemias (Somogyi phenomenon versus the dawn phenomenon):** nightmares, morning headaches, and wide fluctuations in FG, useful indicators of nocturnal hypoglycemia.
2. **Ketoacidosis:** always be treated in the hospital; suspect ketosis: rapid breathing, high blood glucose, infection or encounter other major stress.

Management of type 1 diabetes

Follow-up

- Patients with type 1 diabetes should be seen at least 4 to 6 months.
- Routine physical examination include: blood pressure measurements, fundoscopic examination, foot examination, brief neurological exam including testing of peripheral light touch, pin prick, proprioception, vibrator sensation, and deep tendon reflexes as well as cardiac examination and assessment of peripheral pulses and bruits.
- Patients with duration of disease greater than 10 years, annual ophthalmologic examinations and measurement of serum creatinine are essential.
- Urine should be tested for protein excretion.
- The patient understands that insulin and diet should be periodically reviewed.

Management of type 2 diabetes

- Type 2 diabetes, also known as non–insulin–dependent diabetes mellitus (NIDDM), is characterized path physiologically by insulin resistance and impaired insulin secretion in, response to glucose.
- Hereditary predisposition plays a large role in the development of type 2 diabetes.
- Type 2 diabetes may faces extreme manifestation of a spectrum of metabolic disorders characterized by insulin resistance, obesity, hypertension, and atherogenic lipid changes including high triglyceride levels and low levels of high–density lipoprotein (HDL) cholesterol.

Management of type 2 diabetes

Three major elements in the treatment of type 2 diabetes:

1. Glycemic control;
2. Risk factor management;
3. Specific efforts to retard and treat complications.

Diet- objectives:

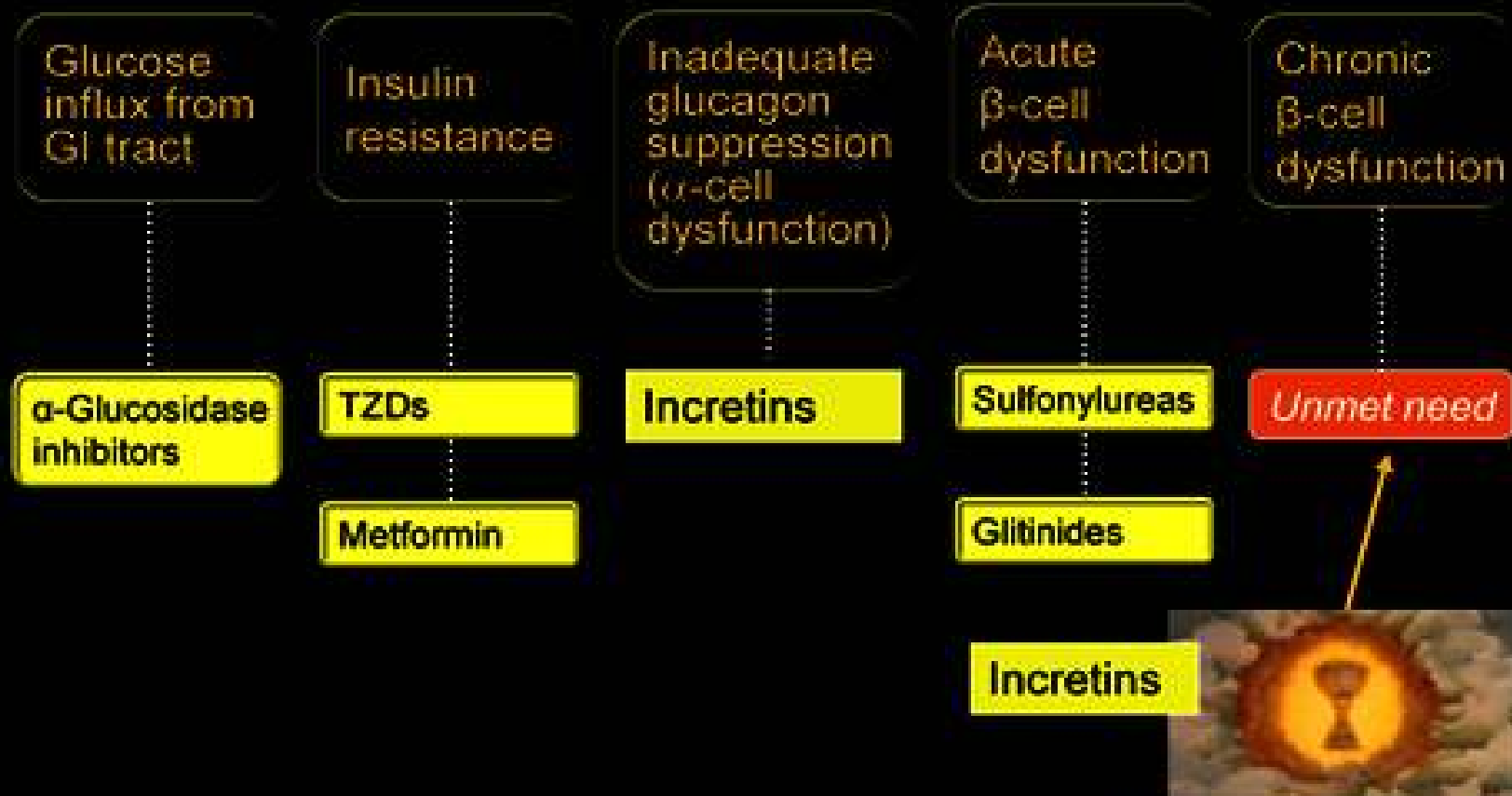
- decrease insulin resistance,
- delay the onset to atherosclerotic cardiovascular diseases,
- the achievement of ideal body weight,
- amelioration of atherosclerotic risk factors.

Management of type 2 diabetes

Diet

- Low in total fat (< 40 % of calories) and saturated fat (< 10 % of calories) and high (55–65% calories) in carbohydrate.
- Starches such as potatoes, bread, pasta, and rice should comprise the bulk of carbohydrate calories.
- Diets high in sucrose will increase plasma triglyceride levels, which have an independent predictive value for coronary heart disease in diabetics.
- Inclusion of fiber will decrease postprandial glycemic index and may improve fasting blood glucose and plasma lipids levels.
- Cholesterol consumption should be restricted to less than 300 mg/day.

Traditional Therapies Do Not Address the Complete Metabolic Needs of Type 2 Diabetes



Dajaj M, et al. *J Clin Endocrinol Metab*. 2004;89:200-206
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The Holy Grail!

Management of type 2 diabetes

Hypoglycemic drugs

Drugs	tablet size mg)	Equivalent dose (mg)	Dosage range (mg/day)	Duration Action,hrs	Doses/day
First generation tolbutamide (ordinate, others) not in use	250, 500	1000	500 – 3000	6 – 12	2 – 3
Second generation glipizide (glucotrol)	5, 10	5	2.5 – 10.0	12 – 24	1 – 2
(diabiten, mycronase) Glibenclamide	1.25, 2.5, 5	5	1.25 – 20.00	12 – 24	1 – 2
Glyclazide MR (Diaprel, Diamicron)	30, 60	30	30-120	24	1
Glyburide (amaryl)	1,2,3,4	4	1 - 8	12 - 24	1 - 2
Short effect Repaglynide (Novonorm)	0,5, 1, 2, 3		0,5 - 9	1 - 2	3

Management of complications of diabetes - micro vascular complication

- **Retinopathy:** proliferate retinopathy, neo-vascularization with retinal detachment and vitreous haemorrhages, occurs in up to 60% of type 1 and 30 % of type 2 diabetics and can lead to blindness. The rate of progression from background to proliferate retinopathy can be decreased significantly by keeping systolic blood pressure (BP) less than 140 mmHg and diastolic BP less than 85 to 90 mmHg.
- **Nephropathy:** low-protein (< 10 % of calories) diets retard the progression of nephropathy; angiotensine-converting enzyme (ACEI) inhibitors decrease micro-albuminuria in diabetics and may be particularly valuable in treating hypertension in diabetics. Haemodialysis, chronic ambulatory peritoneal dialysis (card), and renal transplantation have all been used in the treatment of diabetic end – stage renal disease.

Management of complications of diabetes - microvascular complication

Neuropathy:

- Diabetic gastro paresis and nocturnal diarrhoea are the most common presentations of gastrointestinal neuropathy.

Metoclopramide may be useful in treating gastro paresis

Erythromycin may help control nocturnal diarrhoea

- Cardiovascular: tachycardia, bradycardia, increased orthostatic BP changes

- Sensory neuropathy is burning pain in the soles of the feet, usually greater at night than during the day loss of the Achilles tendon reflex.

Fluphenazine (prolixin), 10 mg every morning or twice a day

Amitriptyline (Elavil), 25 to 75 mg at bedtime

- Bilateral muscle weakness and wasting, often of the interosseous muscles of the hands or proximal muscles of the lower extremities, can also occur as a result of diabetes. No specific therapy is available.

Management of complications of diabetes · macrovascular complication

- The reason atherosclerosis occurs at an accelerated rate in diabetes is not known, this is why the cholesterol goal level in all diabetics should be lower than 230 mg/dl.
- Hypertriglyceridemia has an independent predictive value in diabetics, efforts should be made to maintain triglyceride concentration below 350 mg/dl.
- Dietary restriction of saturated fat and refined carbohydrates is the principal therapy.
- Omega – 3 fatty acid elements also lower triglyceride levels.

Management of complications of diabetes - macrovascular complication

Pharmacologic treatment of high cholesterol levels poses unique problems:

- resins (cholestyramine, colestipol) may increase triglycerides levels
- nicotin acid causes a deterioration of blood glucose control
- fibric acid (gemfibrozil) may actually increase low-density lipoprotein cholesterol levels on hypertriglyceridemic patients
- HMC – CoA production inhibitors (lovastatin) are as useful in the diabetic as in the nondiabetic and do not appear to involve any additional symptoms.

Diabetic ulcer and foot care

Is estimated that 50% of all amputations in the diabetic can be prevented "diabetic ulcers" occur in patients with sensory neuropathy and impaired circulation. The sulfonylurea has a propensity to induce unanticipated hypoglycemia at visual doses. Older patients and those with hepatic or renal impairment are particularly at risk.

In addition, a wide variety of drugs can potentate sulfonylurea action, including propranololum, phenylbutazone, salicylates, and clofibrate.

Postprandial hypoglycemia

- There is considerable controversy above the three principal types of postprandial hypoglycemia: alimentary, early diabetic and functional hypoglycemia. Nonetheless, many people are plagued by adrenergic symptoms occurring 2 to 5 hours after eating.
- Postprandial hypoglycemia can occur before the onset of overt diabetes mellitus. The defect is thought to be delayed and increased insulin release, resulting symptomatic hypoglycemia 3 to 5 hours after eating.
- Treatment includes weight reduction if obesity is present and dietary modification including carbohydrate restriction (60–100 g/day) and increased protein (100–200 g/day) divided among three meals and three snacks.



Obesity

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Nutritional steady state for a healthy life

Energy balance is energy requirements are conceded by no excess and in context of whole body metabolic changes determined by:

- Food intake → basal metabolism – 1200 – 1500 cal/day thermogenesis. Dynamic specific activity of core external influences

- Global caloric requirement:

- depends on: age, sex, weight

- 1900 – 2400 cal/day (= 10.000 kj)

Energy:

- Carbohydrate generates 4 cal/gr.
- Protein → 4 cal/gr.
- Fat → 9 cal/gr.
- Alcohol's → 7 cal/gr.

Qualitative requirements

- **Carbohydrates** – 4 – 7 g/kgc/day
 - 40 – 50% cal/d
 - Minimally → risk of ketosis
 - Excess → hyper secretion of INS – lipogenesis
- **Fat** – 2 g/kgc/day
 - 30 – 40% cal/d
 - lipophylic vitamins
 - Ns. Fatty acids – exces → ats, gall – blade stones
- **Protein** – 1 – 2 g/kgc/d
 - 12 – 15% cal/d
 - Minimally – active mass muscle, enzyme
 - Protein per day in renal damage, 0, 5/kgc/d.

[Normal weight]

- After insurance co. – means body weight which protects you against degenerative diseases, aging and assures the highest longevity. Ideal weight → the lowest risk
- Lorenz: $W_{Ideal} = h - 160 - a$
- W = weight h = height a = age
- BMI (body mass index) = W/h^2

Obesity

A state, with multiple causes, manifested by increasing of fatty tissue.

Clinical examination particularly:

We have to search

- risk factors for obesity
- obesity like a risk factor (i.e. cardio–vascular disorder)

Interrogation

- Thru shape of obesity curve in time:
- continuously
- periodically
- rapidly (1 – 2 kg/d. → hiperhydration)

Circumstances:

- Psychological
- Sexually
- Orally pills
- Stop smoking – low physical act.
- Pregnancy / teenage
- Corticoids, hormones, sedative
- Venous system troubles
- Food behaviour

Obesity - Risk factors



- 1) Genetic (tendencies or sundry) \pm Hypogenous
- 2) Food hyper caloric
- 3) Sedentary
- 4) Alcohol intake (> 300 g/d)
- 5) Behaviour trouble by stress
- 6) Specific period of life (teens, pregnancy)
- 7) Pills
- 8) No smoke
- 9) Endocrinal. Syndrome (hyperthyroidic, hypothyroidic
Cushing)

Obesity - Cardio-vascular risk

- 1) Increase morbidity and mortality
- 2) Independent risk fact. for i.e.
- 3) Increase of weight 15% – high cardio-vascular risk X 3 – 4
- 4) Induce left ventricular hypertrophy
- 5) Android obesity – metabolic syndrome metabolic that includes:
NIDDM, HLP, ats with hyperinsulinemia and insulin resistance
- 6) Benefits of lowing obesity:
 - Increase respiratory function
 - Low arthritis
 - Low left ventricle hypertrophy
 - Low cardio-vascular risk
 - Low mortality
 - Low atheroma plaque

Obesity

Clinical exam.

- quantify the obesity
- Feature of obesity – android, gynoide, mixed
- Adiposity without obesity → endocrinopathy (h. Thyr, Cushing)

Complications

Mecanical → arthritis, trophicity troubles on legs

Cutaneous infection

Ventilator insufficiency → COPD

Metabolic:

- 1) diabetes mellitus insulin resistance
- 2) hyperlipidemia 26 – 38% of obese
- 3) Risk of atherosclerosis gall bladder stones

Obesity - treatment

1) **Diet:** Hypo cal. diet. 500 – 1000 kcal/day, no carbohydrates, moderate fat, normal proteins

2) **Sport**

3) **Psychological therapy**

4) **Medication:** – 1 isomer 1 de (isolipan)‘, 2 cps/daily on meals

List of food:

1) Large and free utilisation

– Meat, egg, haves

2) With limits – cheese, fresh fruit (200 g/d.)

3) Forbidden

– Bread, pates, sugar, milk complete formula

– Butter, bacon

– Alcohol

– Salt

Weight-Loss Myths Refuted in New Review

- For overweight children, involving the family and home environment in weight-loss efforts is ideal.
- Providing actual meals or meal replacements works better for weight loss than does general advice about food choices.
- Both weight-loss drugs and bariatric surgery can help achieve long-term weight loss in some individuals.

Decreasing in weight – weakening

Evolutions in practice we must determine the causes:

1) diseases with apetic:

- energy requirements
- hypertiroidism, growing, fever
- medications (ca, lyl. H.)
- physical activity
- digestive lost: enteropathies, steatorrhea, parasitosis
- iatrogenie – diuretics

2) diseases without apetic:

- physically
- gastro – enteral causes – ulcer, enteropathies, subocclusion, –
general diseases – cancer, leukemias, chronic infections, tb.
- cr. renal failure, cr. cardiac f., cr. liver dis, poisoning – alcohol
we treat basic disease.

Decreasing in weight – weakening

Clinics: – lost in weight (– 20% sever defficiency)

– skin fold over

>8mm cq – rhythm of lowing → attention

– with astenia, weakness, – oedema with exicosis → thirst

– another signs: – thin skin, rare bais, depapilat tongue, osteoporosis

– tendency of infectious, anaemic sdr., visceral plosis, sexual trouble

Laboratory:

– hypoglicemia (possible diabetes of starvation)

– hypoproteinemia < 60 g%, low serines

– feriprive anaemia

– hypolipemia

– hyper k → thirst

– chronic alcoholism:

– mixed pathogeny (primary and secondary)

– energy aport

– excess of utilisation of adn with production of lactic acid

– excess of acetaldehyd – toxic effect

Decreasing in weight – weakening

Pay attention to:

- low bowel capacity
- atrophic gastric mucosal
- atonia
- disendocrynopathy
- other organic troubles

Principles:

- progressive, pleasant
- major – proteins – 1.5 g on 2 days
- high calorics – low volumes
- dietetically, 5 – 6 meals/day
- 500 cal/3 – 5 days – > 3500 cal/days
- concentrates – (dusty milk)
- high vitamins