

Complications

- **1-ACUTE COMPLICATIONS**
- **1-Diabetic Ketoacidosis** DKA develops most commonly in patients with T1DM, it can be seen in patients with T2DM, especially during acute illness.
- mortality in developed countries is 5-10% and is higher in the elderly
- DKA is defined as being present in patients with absolute or relative insulin deficiency when the following criteria are met:
- **1-Hyperglycemia:** plasma glucose levels greater than 250 mg/dL
- **2-Ketosis:** moderate to severe ketonemia (ketone levels positive at a serum dilution of $\geq 1 : 2$, or serum β -hydroxybutyrate concentration > 0.5 mmol/L) and moderate ketonuria (2+ to 3+)
- **3- metabolic Acidosis:** pH less than or equal to 7.3 and/or bicarbonate less than or equal to 15 mEq/L
- **AVERAGE LOSS OF FLUID AND ELECTROLYTES IN ADULT DIABETIC KETOACIDOSIS OF MODERATE SEVERITY**
- Water: 6 litres
- 3 litres extracellular -replace with saline
- 3 litres intracellular -replace with dextrose
- Sodium: 500 mmol
- Chloride: 400 mmol
- Potassium: 350 mmol

• **CLINICAL FEATURES OF DIABETIC KETOACIDOSIS**

• **Symptoms**

- Polyuria, thirst
- Weight loss
- Weakness
- Nausea, vomiting
- Leg cramps
- Blurred vision
- Abdominal pain

• **Signs**

- Dehydration
- Hypotension (postural or supine)
- Cold extremities/peripheral cyanosis
- Tachycardia
- Air hunger (Kussmaul breathing)
- Smell of acetone
- Hypothermia
- Confusion, drowsiness, coma (10%)

MANAGEMENT OF DIABETIC KETOACIDOSIS

- **1-Fluid replacement**
- **0.9% saline (NaCl) i.v.**
 - 1 litre over 30 minutes
 - 1 litre over 1 hr
 - 1 litre over 2 hrs
 - 1 litre over next 2-4 hrs
- **When blood glucose < 15 mmol/l (270 mg/dl)**
 - Switch to 5% dextrose, 1 litre 8-hourly
 - If still dehydrated, continue 0.9% saline and add 5% dextrose 1 litre per 12 hrs
- **Typical requirement is 6 litres in first 24 hrs but avoid fluid overload in elderly patients**
- **Subsequent fluid requirement should be based on clinical response including urine output**

- **2-Insulin** 50 units soluble insulin in 50 ml 0.9% saline i.v. via infusion pump
 - 6 units/hr initially
 - 3 units/hr when blood glucose < 15 mmol/l (270 mg/dl)
 - 2 units/hr if blood glucose declines < 10 mmol/l (180 mg/dl)
- Check blood glucose hourly initially-if no reduction in first hour, rate of insulin infusion should be increased
- Aim for fall in blood glucose of 3-6 mmol/l (~55-110 mg/dl) per hour(OR a loading dose of 10-20 units of soluble insulin can be given by intramuscular injection, immediately followed by 5 units hourly)
- **3-Potassium** None in first litre of i.v fluid unless < 3.0 mmol/l
- If plasma potassium < 3.5 mmol/l, give 40 mmol added potassium
 - Give in 1 litre of fluid
 - Avoid infusion rate of > 20 mmol/hr
- If plasma potassium is 3.5-5.0 mmol/l, give 20 mmol added potassium
- If plasma potassium is > 5.0 mmol/l, or patient is anuric, give no added potassium
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- **4-ADDITIONAL PROCEDURES IN THE MANAGEMENT OF DKA**
- ***Catheterisation if no urine passed after 3 hrs**
- ***Nasogastric tube to keep stomach empty in unconscious or semiconscious patients, or if vomiting is protracted**
- ***Central venous line if cardiovascular system compromised, to allow fluid replacement to be adjusted accurately**
- ***Plasma expander if systolic BP is < 90 mmHg or does not rise with i.v. saline**
- ***Antibiotic if infection demonstrated or suspected**
- ***ECG monitoring in severe cases**
- **5-Bicarbonate**
- **In patients who are severely acidotic ($[H^+] > 100$ nmol/l, pH < 7.0) the infusion of sodium bicarbonate (300 ml 1.26% over 30 minutes into a large vein**

- **COMPLICATIONS DKA**
- **1-Cerebral oedem**
 - May be caused by very rapid reduction of blood glucose, use of hypotonic fluids and/or bicarbonate
 - High mortality
 - Treat with mannitol, oxygen
- **2-Acute respiratory distress syndrome**
- **3-Thromboembolism**
- **4-Disseminated intravascular coagulation (rare)**
- **5-Acute circulatory failure**

- **2-NON-KETOTIC HYPEROSMOLAR DIABETIC COMA**
- characterised by severe hyperglycaemia (> 50 mmol/l (900 mg/dl)) without significant hyperketonaemia or acidosis. Severe dehydration and pre-renal uraemia are common. It usually affects elderly patients, many with previously undiagnosed diabetes. Mortality is high (40%). Treatment differs from ketoacidosis in two main respects. Firstly, these patients are usually relatively sensitive to insulin and approximately half the dose of insulin recommended for the treatment of ketoacidosis should usually be employed (3 units/hr). Secondly, the plasma osmolality should be measured or, less accurately, calculated using the following formula based on plasma values in mmol/l: $\text{osmolality} = 2\{\text{Na}\} + 2\{\text{k}\} + \text{glucose} + \text{urea}$ (in mmol-l)

- The normal value is 280-300 mmol/kg and the conscious level is depressed when it is high (> 340 mmol/kg). The patient should be given 0.45% saline until the osmolality approaches normal, when isotonic (0.9%) saline should be substituted. The rate of fluid replacement should be regulated on the basis of the central venous pressure, and plasma sodium concentration checked frequently. Thromboembolic complications are common, and prophylactic subcutaneous low molecular weight heparin is recommended.

- **3-LACTIC ACIDOSIS**
- is likely to be taking metformin for type 2 diabetes and is very ill and overbreathing but not as profoundly dehydrated. The patient's breath does not smell of acetone, and ketonuria is mild or even absent, yet the plasma bicarbonate and pH are markedly reduced ($H^+ > 63$ mmol/l, $pH < 7.2$) and the anion gap is increased
- The diagnosis is confirmed by a high (usually > 5.0 mmol/l) concentration of lactic acid in the blood. Treatment is **with intravenous sodium bicarbonate sufficient to raise the arterial pH to above 7.2**, along with insulin and glucose. Despite energetic treatment, the mortality in this condition **is $> 50\%$** . Sodium dichloroacetate may be given to lower blood lactate
- **4-recurrent uti, genital infection, skin infection**

- **5—HYPOGLYCAEMIA** Hypoglycemia is considered present when serum glucose level is less than 50 mg/dL
- COMMON SYMPTOMS OF HYPOGLYCAEMIA
- **Autonomic**
- Sweating
- Trembling
- Pounding heart
- Hunger
- Anxiety
- **Neuroglycopenic**
- Confusion
- Drowsiness
- Speech difficulty
- Inability to concentrate
- Incoordination
- **Non-specific**
- Nausea
- Tiredness
- Headache

- **Causes of hypoglycaemia**
- Missed, delayed or inadequate meal
- Unexpected or unusual exercise
- Alcohol
- Errors in oral hypoglycaemic agent or insulin dose/schedule/administration
- Poorly designed insulin regimen, particularly if predisposing to nocturnal hyperinsulinaemia
- Lipohypertrophy at injection sites causing variable insulin absorption
- Gastroparesis due to autonomic neuropathy
- Malabsorption, e.g. coeliac disease
- Unrecognised other endocrine disorder, e.g. Addison's disease
- Factitious (deliberately induced)
- Breast feeding by diabetic mother
- **Investigation 3 criteria** (clinical feature ,low bl.sugar ,response to glucose intake

- **Risk factors for severe hypoglycaemia**
- Strict glycaemic control
- Impaired awareness of hypoglycaemia
- Age (very young and elderly)
- Increasing duration of diabetes
- Sleep
- C-peptide negativity
- History of previous hypoglycaemia
- Renal impairment
- Angiotensin-converting enzyme (ACE) genotype

MORBIDITY OF SEVERE HYPOGLYCAEMIA IN DIABETIC PATIENTS

CNS :Impaired cognitive function

- Coma
- Convulsions
- Transient ischaemic attack, stroke
- Intellectual decline
- Brain damage (rare)
- Focal neurological lesions (rare)

Heart : Cardiac arrhythmias Myocardial ischaemia

Eye :Vitreous haemorrhage ,? Worsening of retinopathy

Other: Hypothermia ,Accidents (including road traffic accidents) with injury

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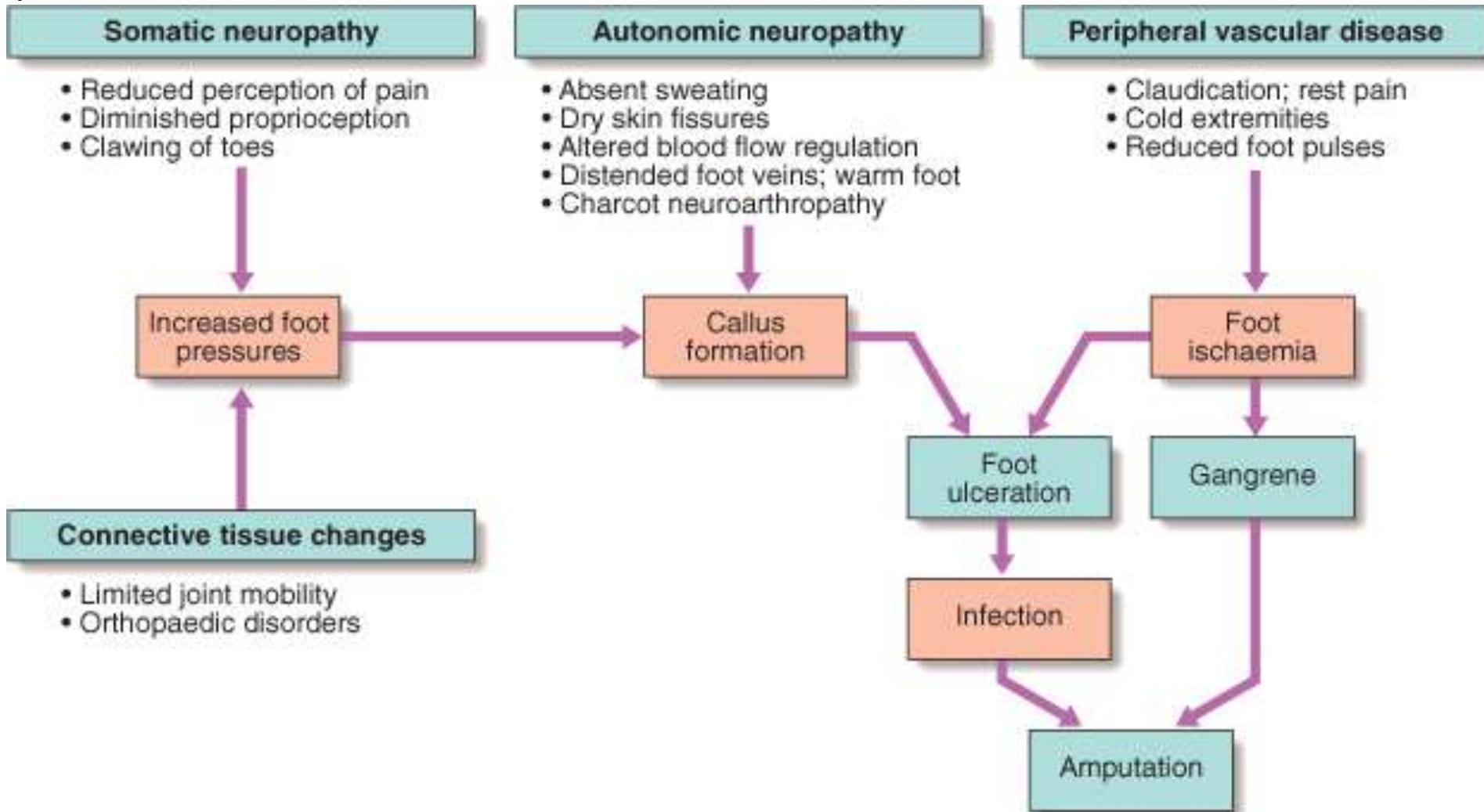
- Treatment
- **1-oral carbohydrate** if hypoglycaemia is recognised early. If the adult patient is unable to swallow,
- **2-intravenous glucose** (30-50 ml of 20-50% dextrose) or
- **3- glucagon (1 mg by intramuscular injection)** should be administered. The recommended dose of intravenous dextrose in children is 0.2 g/kg.
- As soon as the patient is able to swallow, glucose should be given orally. Full recovery may not occur immediately and reversal of cognitive impairment may not be complete until 60 minutes after normoglycaemia is restored. Further, when hypoglycaemia has occurred in a patient using a long- or intermediate-acting insulin or a long-acting sulphonylurea, such as glibenclamide, the possibility of recurrence so should follow the state few days and to prevent this a 10% dextrose infusion, titrated to the patient's blood glucose, may be necessary. The development of cerebral oedema should be considered in patients who fail to regain consciousness after blood glucose is restored to normal. Other causes of impaired consciousness, such as alcohol intoxication, a post-ictal state or cerebral haemorrhage, should be excluded. Cerebral oedema has a high mortality and morbidity, and requires urgent treatment with mannitol and high-dose oxygen.
- Unless the reason for a hypoglycaemic episode is clear, the patient should reduce the next dose of insulin by 10-20%

- **CHRONIC COMPLICATIONS OF DIABETES**
- **Microvascular**
- **1= Retinopathy, cataract** Diabetic retinopathy is one of the most common causes of blindness in adults between 30 and 65 years of age (Microaneurysms Retinal haemorrhages ,Exudates ,Cotton wool spots ,Venous changes,Neovascularisation ,Pre-retinal haemorrhage ,Vitreous haemorrhage ,Fibrosis)
- **2=Nephropathy DM is** the most common causes of end-stage renal failure ,Microalbuminuria is an important indicator of risk of developing overt diabetic nephropathy ,
- Management :
- control bl.sugar ,HT,UTI,decreaseprotein in diet ,stop smoking , giving ACEI

- **3=DIABETIC NEUROPATHY:**
- HISTOPATHOLOGY
- Axonal degeneration of both myelinated and unmyelinated fibres
 - Early: axon shrinkage
 - Later: axonal fragmentation; regeneration
- Thickening of Schwann cell basal lamina
- Patchy, segmental demyelination
- Thickening of basement membrane and microthrombi in intraneural capillaries
- **CLASSIFICATION OF DIABETIC NEUROPATHY**
- **Somatic** Polyneuropathy
 - Symmetrical, mainly sensory and distal
 - Asymmetrical, mainly motor and proximal (including amyotrophy)
- Mononeuropathy (including mononeuritis multiplex)
- **Visceral (autonomic)**
- **Cardiovascular** (Postural hypotension ,Resting tachycardia ,Fixed heart rate ,)
- **Gastrointestinal**(gastroparesis; altered bowel habit, Nocturnal diarrhoea ± faecal incontinence Constipation, due to colonic atony
- **Genitourinary** (Difficulty in micturition, urinary incontinence, recurrent infection, due to atonic bladder
- Erectile dysfunction and retrograde ejaculation
- **Sudomotor**(Gustatory sweating ,Nocturnal sweats without hypoglycaemia ,Anhidrosis; fissures in the feet
- **Vasomotor**(Feet feel cold, due to loss of skin vasomotor responses ,Dependent oedema, due to loss of vasomotor tone and increased vascular permeability ,Bullous formation (
- **Pupillary** (Decreased pupil size ,Resistance to mydriatics ,Delayed or absent reflexes to light

Condition	Management
Pain and paraesthesiae from peripheral somatic neuropathies	Intensive insulin therapy (strict glycaemic control) Tricyclic antidepressants (amitriptyline, imipramine) Anticonvulsants (gabapentin, carbamazepine, phenytoin, pregabalin) Substance P depletor capsaicin-topical Opiates (tramadol, oxycodone) Membrane stabilisers (mexiletine, intravenous lidocaine) Antioxidant (α -lipoic acid)
Postural hypotension	Support stockings, Fludrocortisone, (midodrine) Non-steroidal anti-inflammatory drugs (NSAIDs)
Gastroparesis	Dopamine antagonists (metoclopramide, domperidone) Erythromycin
Diarrhoea (p. 869)	Loperamide, Broad-spectrum antibiotics, Clonidine, Octreotide
Constipation	Stimulant laxatives (senna)
Atonic bladder	Intermittent self-catheterisation (p. 1199)
Excessive sweating	Anticholinergic drugs (propantheline, poldine) Clonidine Topical antimuscarinic agent (glycopyrrolate cream)
Erectile dysfunction (impotence)	Phosphodiesterase inhibitors (sildenafil, vardenafil, tadalafil) -oral Dopamine agonist (apomorphine)-sublingual intra-urethral administration of pellets (MUSE) Vacuum tumescence devices

4=DIABETIC FOOT Foot ulceration occurs as a result of trauma or infection in the presence of neuropathy and/or peripheral vascular disease with infection occurring as a secondary phenomenon following disruption of the protective epidermis. In most cases all three components are involved but sometimes neuropathy or ischaemia may predominate



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- **Macrovascular complication**
- **Coronary circulation** Myocardial ischaemia/infarction
- **Cerebral circulation** Transient ischaemic attack ,Stroke
- **Peripheral circulation** Claudication ,Ischaemia

MANAGEMENT OF DIABETES

in NIDDM 1-diet and lifestyle advice alone 50% of new case

2- oral anti-diabetic drugs 25%,

3- insulin 25%.

In IDDM (diet +insulin)

- The goals of therapy for type 1 or type 2 DM are to:
- **(1) eliminate** symptoms related to hyperglycemia,
- **(2) reduce** or eliminate the long-term microvascular and macrovascular complications of DM,
- **(3) allow** the patient to achieve as normal a lifestyle as possible.

- **there are 3 line of treatment**
- **1-Non medical treatment** :education ,nutrition, exercise,
- **:education** : care of diabetes during illness, and medications to lower the plasma
- Glucoseself-monitoring of blood glucose;urine ketone
- monitoring (type 1 DM);insulin administration;guidelines for diabetes
- management during illnesses;management of hypoglycemia;
- foot and skin care;diabetes management before, during, and after exercise;
- and risk factor–modifying activities
- **nutrition** *Nutritional Recommendations for All Persons with Diabetes* Percentage of energy intake
 - *Carbohydrate 50%
 - * Fat 35
 - *Protein 15%
 - *Use of caloric sweeteners, including sucrose, is acceptable.
 - * Fiber (20–35 g/d) and sodium less than (3000 mg/d) levels as recommendedfor the general healthy population
 - *Cholesterol intake less than 300 mg/d
- **Exercise** Exercise has multiple positive benefits including cardiovascular risk reduction, reduced blood pressure, maintenance of muscle mass, reduction in body fat, and weight loss. For individuals with type 1 or type 2 DM, exercise is also useful for lowering plasma glucose (during and following exercise) and increasing insulin sensitivity.
- **Treatment associated conditon** increase morbidity and mortality(HT ,obesity ,hypercholestremia ,smoking ,alcohol.....)

- To avoid exercise-related hyper- or hypoglycemia, individuals with
- type 1 DM should: (1) monitor blood glucose before, during, and after
- exercise;(2) delay exercise if blood glucose is 14 mmol/L (250 mg/
- dL), 5.5 mmol/L (100 mg/dL), or if ketones are present;(3) monitor
- glucose during exercise and ingest carbohydrate to prevent
- hypoglycemia;(
- 4) decrease insulin doses (based on previous experience) before
- exercise and inject insulin into a nonexercising area;and (5) learn
- individual glucose responses to different types of exercise and increase
- food intake for up to 24 h after exercise, depending on intensity and
- duration of exercise. In individuals with type 2 DM, exercise-related
- hypoglycemia is less common but

- **FACTORS ASSOCIATED WITH INCREASED MORTALITY AND MORBIDITY IN PEOPLE WITH DIABETES**

- **Duration of diabetes**
- **Early age at onset of disease**
- **High glycated haemoglobin (HbA_{1c})**
- **Raised blood pressure**
- **Proteinuria; microalbuminuria**
- **Dyslipidaemia**
- **Obesity**