DIABETES MELLITUS

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- It is a metabolic disorder of multiple etiology characterized by chronic Hyperglycaemia with disturbances of Carbohydrates, Fats and Protein metabolism resulting from defects in Insulin secretion, Insulin action or Both.

Clinical Features

- Easy Fatigability
- Polyuria
- Polydipsia
- Wasting
- Weight loss
- Air hunger
- Blurred vision
- Poor wound healing

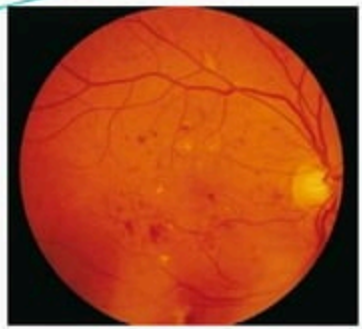
Complications

- Acute :- Diabetic ketoacidosis.
  Hyperglycemic Hyperosmolar state.
- Chronic :-
  A. Microvascular
  B. Macrovascular
  C. Others

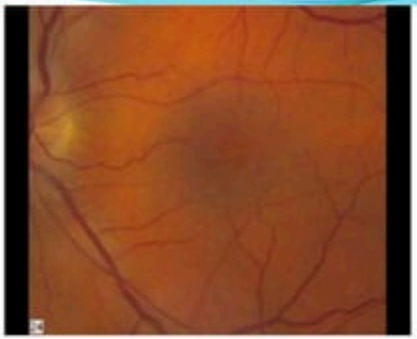
A. **Microvascular complications** :- Retinopathy, Macular edema, Sensory & motor neuropathy, Autonomic neuropathy.

B. **Macrovascular complications** :- Coronary heart disease, Peripheral arterial disease, Cerebrovascular disease.

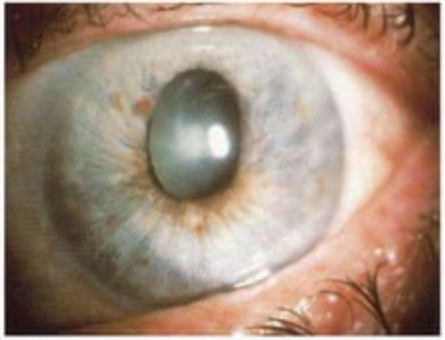
C. **Others** :- Cataract, Glaucoma, Periodontal disease, Hearing loss, Gastroparesis, Diarrhea, Uropathy, Sexual dysfunction, Acanthosis nigricans, Necrobiosis lipoidica, Vitiligo etc....



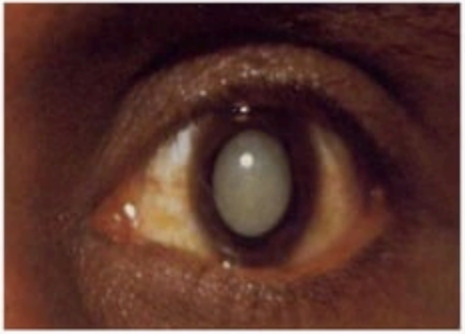
Retinopathy



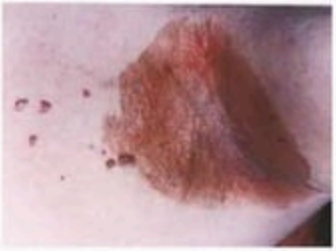
Macular edema



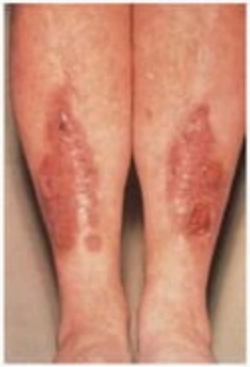
Glaucoma



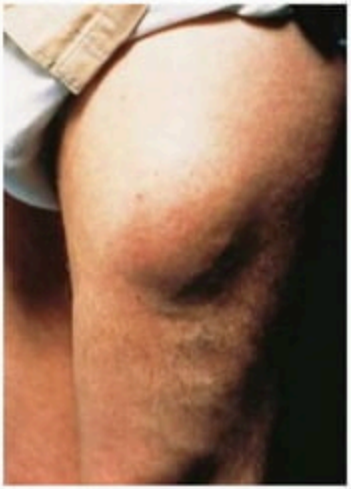
Cataract



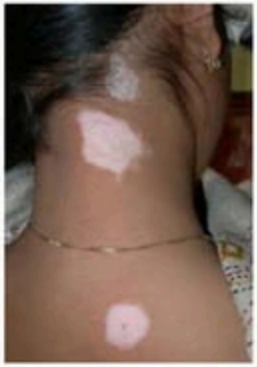
Acanthosis nigricans



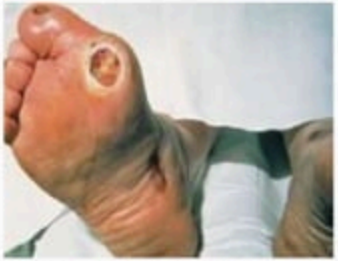
Necrobiosis lipoidica



Lipohypertrophy



Vitiligo



Neuropathic foot ulcer

Types

- Type 1 :- IDDM also called Juvenile Diabetes
- Type2 :- NIDDM
- Type3 :- Gestational Diabetes
- Type4 :- Other Specific Types

Type 1

- Insulin Dependent Diabetes Mellitus.
- Also called Juvenile Diabetes
- Common among 10-14 yrs of age group.
- Accounts for 5%-10% of all diagnosed cases of Diabetes Mellitus.
- 90% is Autoimmune mediated.

  10% is Idiopathic.

Type 2

- Non Insulin Dependent Diabetes Mellitus.
- Common among adults and elderly people.
- Accounts for about 90-95% of all the diagnosed cases of Diabetes.
- Begins as Insulin resistance, as the need for insulin rises, the pancreas gradually loses it's ability to produce insulin.

Type 3

- Gestational Diabetes.
- It is a condition of Glucose Intolerance diagnosed in some women during pregnancy.
- Common in African americans, Latino americans, American Indians, Obese and women with family history of Diabetes.
- After pregnancy, 5-10% of women with Gestational Diabetes are found to develop Type 2 Diabetes.

Other Specific Types

- Genetic defects of Beta-cell function.
- Genetic defect in insulin action.
- Pancreatic diseases.
- Excess endogenous production of hormonal antagonist to Insulin.
- Drug- Induced.
- Viral infections.
- Latent Autoimmune Diabetes in Adults (LADA).
- Modified Onset of Diabetes in Young (MODY).

Risk Factors

- Host Factors
  - Age
  - Sex
  - Genetic Factors
  - Genetic Markers:- HLA-B8, HLA-B15, HLA-DR3 and HLA-DR4
  - Immune mechanism
  - Maternal Diabetes
  - Obesity

Environmental Factors

- Sedentary life style
- Diet rich in Saturated Fatty acids
- Decreased consumption of Diatary Fibers
- Malnutrition
- Alcohol
- Chemical agents
- Stress
- Other factors

Diagnosis of Diabetes Mellitus

Values for diagnosis of diabetes mellitus and other categories of hyperglycaemia

	Glucose concentration, mmol l^{-1} (mg dl^{-1})		
	Whole blood		Plasma[a]
	Venous	Capillary	Venous
Diabetes Mellitus:			
Fasting	≥ 6.1 (≥ 110)	≥ 6.1 (≥ 110)	≥ 7.0 (≥ 126)
or			
2-h post glucose load	≥ 10.0 (≥ 180)	≥ 11.1 (≥ 200)	≥ 11.1 (≥ 200)
or both			
Impaired Glucose Tolerance (IGT):			
Fasting (if measured)	< 6.1 (< 110)	< 6.1 (< 110)	< 7.0 (< 126)
and			
2-h post glucose load	≥ 6.7 (≥ 120) and < 10.0 (< 180)	≥ 7.8 (≥ 140) and < 11.1 (< 200)	≥ 7.8 (≥ 140) and < 11.1 (< 200)
Impaired Fasting Glycaemia (IFG):			
Fasting	≥ 5.6 (≥ 100) and < 6.1 (< 110)	≥ 5.6 (≥ 100) and < 6.1 (< 110)	≥ 6.1 (≥ 110) and < 7.0 (< 126)
and (if measured)			
2-h post glucose load	< 6.7 (< 120)	< 7.8 (< 140)	< 7.8 (< 140)

Screening

- Urine examination:- LAck of Sensitivity
  Gives too many "False Negatives"
- Blood Sugar Testing:-
  - RBS - >200mg/dl with symptoms & signs of diabetes.
  - FBS - >126mg/dl
  - PPBS - >200mg/dl
  - Glycated Haemoglobin - >6.5%

- Target Population:-
  - More than 40yrs
  - Family history of Diabetes
  - Obese
  - HDL <35mg/dl and Triglycerides >250mg/dl
  - Women who had baby weighing >4.0kg
  - Women who show excess weight gain during pregnancy
  - Patients with Premature Atherosclerosis

Management of DM

- The major components of the treatment of diabetes are:

A	• **Diet and Exercise**
B	• **Oral hypoglycaemic therapy**
C	• **Insulin Therapy**

A. Diet

- Diet is a basic part of management in every case. Treatment cannot be effective unless adequate attention is given to ensuring appropriate nutrition.

- **Dietary treatment should aim at:**
  - ensuring weight control
  - providing nutritional requirements
  - allowing good glycaemic control with blood glucose levels as close to normal as possible
  - correcting any associated blood lipid abnormalities

Exercise

- Physical activity promotes weight reduction and improves insulin sensitivity, thus lowering blood glucose levels.
- Together with dietary treatment, a programme of regular physical activity and exercise should be considered for each person. Such a programme must be tailored to the individual's health status and fitness.
- People should, however, be educated about the potential risk of hypoglycaemia and how to avoid it.

B. Oral Anti-Diabetic Agents

- There are currently four classes of oral anti-diabetic agents:

i. Biguanides
ii. Insulin Secretagogues – Sulphonylureas
iii. Insulin Secretagogues – Non-sulphonylureas
iv. α-glucosidase inhibitors
v. Thiazolidinediones (TZDs)

B.1 Oral Agent Monotherapy

- If glycaemic control is not achieved (HbA1c > 6.5% and/or; FPG > 7.0 mmol/L or; RPG >11.0mmol/L) with lifestyle modification within 1 –3 months, ORAL ANTI-DIABETIC AGENT should be initiated.

- In the presence of marked hyperglycaemia in newly diagnosed symptomatic type 2 diabetes (HbA1c > 8%, FPG > 11.1 mmol/L, or RPG > 14 mmol/L), oral anti-diabetic agents can be considered at the outset together with lifestyle modification.

B.1 Oral Agent Monotherapy (cont.)

As first line therapy:

- Obese type 2 patients, consider use of metformin, *acarbose* or TZD.
- Non-obese type 2 patients, consider the use of metformin or insulin secretagogues
- Metformin is the drug of choice in overweight/obese patients. TZDs and acarbose are acceptable alternatives in those who are intolerant to metformin.
- If monotherapy fails, a combination of TZDs, acarbose and metformin is recommended. If targets are still not achieved, insulin secretagogues may be added

B.2 Combination Oral Agents

Combination oral agents is indicated in:

- Newly diagnosed symptomatic patients with HbA1c >10
- Patients who are not reaching targets after 3 months on monotherapy

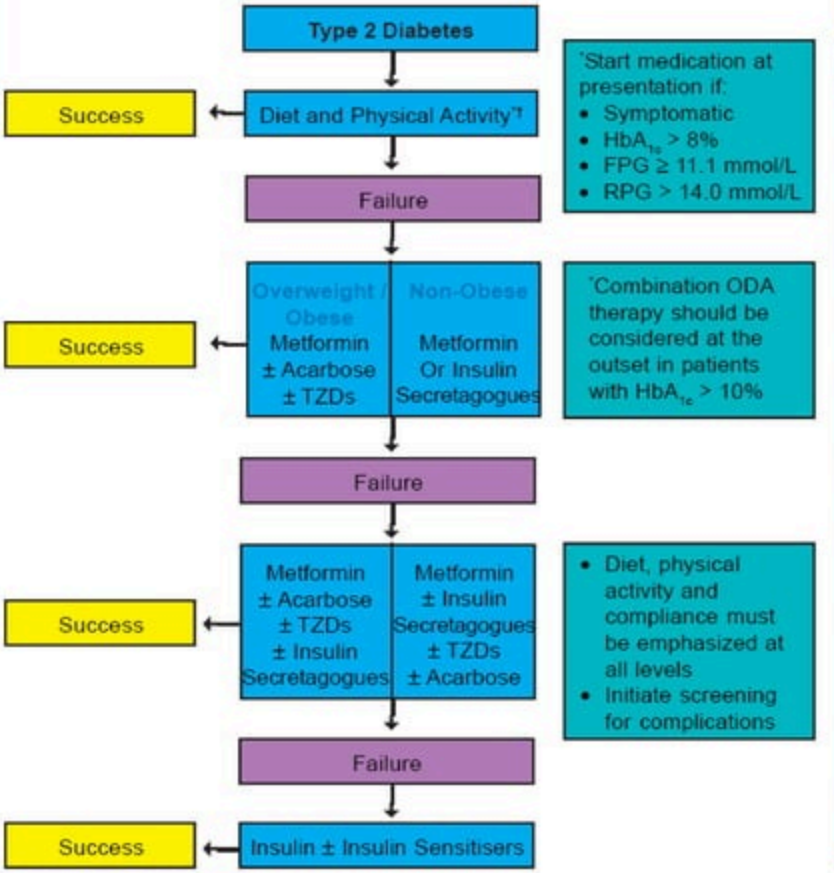
B.3 Combination Oral Agents and Insulin

- If targets have not been reached after optimal dose of combination therapy for 3 months, consider adding intermediate-acting/long-acting insulin (BIDS).

- Combination of insulin+ oral anti-diabetic agents (BIDS) has been shown to improve glycaemic control in those not achieving target despite maximal combination oral anti-diabetic agents.

- Combining insulin and the following oral anti-diabetic agents has been shown to be effective in people with type 2 diabetes:
  - Biguanide (metformin)
  - Insulin secretagogues (sulphonylureas)
  - Insulin sensitizers (TZDs)*(the combination of a TZD plus insulin is* not an approved indication)
  - α-glucosidase inhibitor (acarbose)

- Insulin dose can be increased until target FPG is achieved.



Diabetes Management Algorithm

AGENTS & ACTIONS

Drug Class	Drug Name	Brand Name	Mechanism of Action
Biguanides	Metformin	Glucophage®	Inhibit glucose production by the liver
Sulfonylureas (second-generation)	Glimepiride Glipizide Glyburide	Amaryl® Glucotrol® Diabeta®, Glynase PresTab®, Micronase®	Increase insulin secretion by pancreatic beta cells
Meglitinides	Repaglinide Nateglinide	Prandin® Starlix®	Increase insulin secretion by pancreatic beta cells
Thiazolidinediones (TZDs)	Pioglitazone Rosiglitazone	Actos® Avandia®	Increase glucose uptake by skeletal muscle
Alpha-glucosidase inhibitors	Acarbose Miglitol	Precose® Glyset®	Inhibit carbohydrate absorption in the small intestine

C. Insulin Therapy

Short-term use:

- Acute illness, surgery, stress and emergencies
- Pregnancy
- Breast-feeding
- Insulin may be used as initial therapy in type 2 diabetes
- in marked hyperglycaemia
- Severe metabolic decompensation (diabetic ketoacidosis, hyperosmolar nonketotic coma, lactic acidosis, severe hypertriglyceridaemia)

Long-term use:

- If targets have not been reached after optimal dose of combination therapy or BIDS, consider change to multi-dose insulin therapy. When initiating this,insulin secretagogues should be stopped and insulin sensitisers e.g. Metformin or TZDs, can be continued.

Self-Care

- Patients should be educated to practice self-care. This allows the patient to assume responsibility and control of his / her own diabetes management. Self-care should include:

  - Blood glucose monitoring
  - Body weight monitoring
  - Foot-care
  - Personal hygiene
  - Healthy lifestyle/diet or physical activity
  - Identify targets for control
  - Stopping smoking
  - Carrying Diabetic Identity card

Prevention

- PRIMARY PREVENTION
  - Population Strategy
  - High-Risk Strategy
- SECONDARY PREVENTION
- TERTIARY PREVENTION

Primary Prevention

- POPULATION STRATEGY
  - The scope for primary prevention of IDDM is limited.
  - Based on Elimination of environmental risk factors , development of prevention programmes for NIDDM is possible.
- HIGH-RISK STRATEGY
  - Effectively directed at TARGET POPULATION groups.
  - No special high risk strategy for IDDM.
  - Risk of Diabetes in NIDDM can be reduced by correcting sedentary lifestyle, over nutrition, obesity, and avoiding alcohol, smoking & OCPs.

Secondary Prevention

Aims :-

- To maintain blood glucose levels as close within normal limits.
- To maintain ideal body weight.

Treatment :-

- Diet alone – small balanced meals more frequently.
- Diet and Oral Antidiabetic drugs.
- Diet and Insulin.
- Combination of Oral Antidiabetic drugs and Insulin.

Oral Antidiabetic drugs

Oral Hypoglycaemic Medications

AGENTS & ACTIONS

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Sulfonylureas (second-generation)	Glimepiride Glipizide Glyburide	Amaryl® Glucotrol® Diabeta®, Glynase PresTab®, Micronase®	Increase insulin secretion by pancreatic beta cells
Meglitinides	Repaglinide Nateglinide	Prandin® Starlix®	Increase insulin secretion by pancreatic beta cells
Thiazolidinediones (TZDs)	Pioglitazone Rosiglitazone	Actos® Avandia®	Increase glucose uptake by skeletal muscle
Alpha-glucosidase inhibitors	Acarbose Miglitol	Precose® Glyset®	Inhibit carbohydrate absorption in the small intestine

Tertiary Prevention

Aim:- Prevention of complications from occurring.

The main objective at the tertiary level is to organize specialized clinics and units capable of providing diagnostic and management skills at high order.

Also to be involved in Epidemiological research.

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Thank You.