Objectives:

- Epidemiology of Diabetes in Saudi Arabia and worldwide
- Diagnosis of diabetes, recent guidelines for diagnosis and classification
- Screening for diabetes
- Highlight on pre-diabetes and prevention of diabetes complications
- Approach to a diabetic patient in a clinic
- Role of diabetes team in management of diabetes and Goals to be achieved in managing HbA1C, LDL, HDL, Trig. and for Blood Glucose
- Important aspects of the clinical examination, focusing on LL examination, Eye, ...
- Essential Investigations (regular visits and annual medical checkup)
- Update in Management of type 2 diabetes that includes education, lifestyle modification, role of diet and exercise
- Highlights for oral medications like Biguanides, Sulphonylurea, Glitazones, Incretins, DPP 4 inhibitors, Meglitinides, Liraglutide, Insulin types
- Annual medical check up
- **Practical: Examination of the lower limbs in a diabetic patient. Method of Examination**

References : guidelines, Slides

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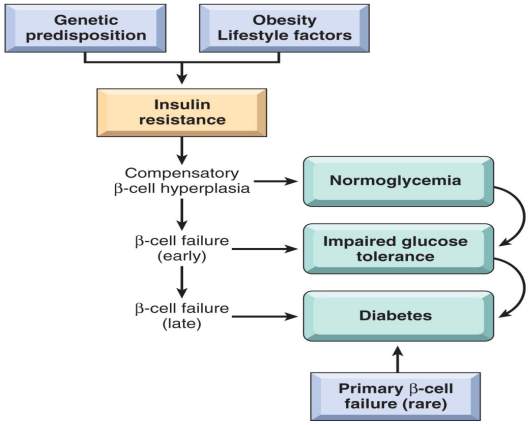
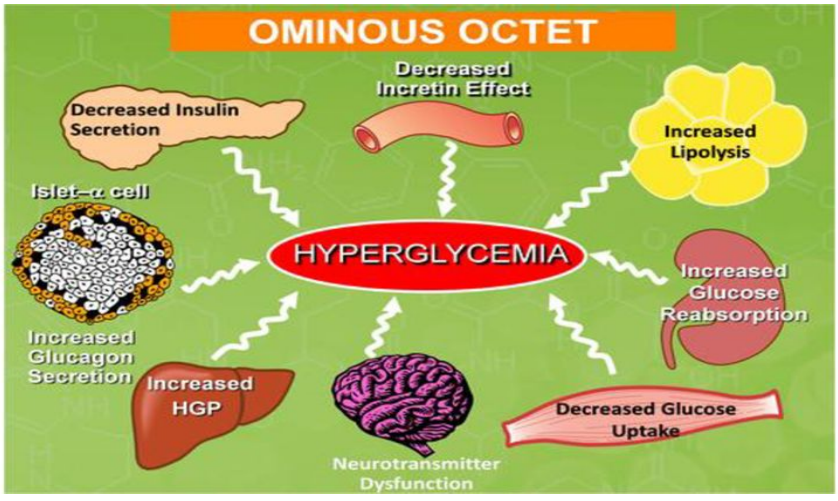
[Color index : Important | Notes | Extra]

❖ Introduction:

- There are several types DM mainly:
  - DM 1: due to autoimmune β -cell destruction, usually leading to absolute insulin deficiency)
  - DM 2: due to a progressive loss of β -cell insulin secretion frequently on the background of insulin resistance
  - Gestational (GDM): diabetes diagnosed in the second or third trimester of pregnancy that was not clearly overt diabetes prior to gestation (can increase the risk of having DM for the mom and child)
  - Specific types of diabetes due to other causes, e.g., monogenic diabetes syndromes (such as MODY) or other underlying causes
- Mechanism of DM (type 2) check image:
  - Usually 50% of beta cells are functioning at time of diagnosis



- The eight factors that cause hyperglycemia (Ominous Octet): will be discussed further in medications:



❖ Epidemiology

- **Worldwide**
  - The global prevalence of diabetes among adults over 18 years of age has risen from 4.7% in 1980 to 8.5% in 2014 (WHO)
  - Diabetes prevalence has been rising more rapidly in middle- and low-income countries.
  - WHO projects that diabetes will be the seventh leading cause of death in 2030

- **Saudi Arabia**
  - A study of 17232 subjects between the ages of 30-70 years conducted between 1995 and 2000 in KSA of selected households during 5-year period found out:
  - The overall prevalence of DM obtained was 23.7% in KSA.
  - The prevalence in males and females were 26.2% and 21.5% respectively (p<0.00001).
  - A large number of diabetics 1116 (27.9%) were unaware of having DM.

❖ Screening for DM:

- Criteria for Testing for Diabetes or Prediabetes in Asymptomatic **Adults**:

1) Testing should be considered in overweight or obese (BMI ≥25 kg/m^2 or ≥23 kg/m^2 in Asian Americans) adults who have one or more of the following risk factors:
   - A) First-degree relative with diabetes
   - B) High-risk race/ethnicity (e.g., African American, Latino, Native American, Asian American, Pacific Islander)
   - C) History of CVD
   - D) Hypertension (≥140/90 mmHg or on therapy for hypertension)
   - E) Women with polycystic ovary syndrome
   - F) HDL cholesterol level <35 mg/dL (0.90 mmol/L) and/or a triglyceride level >250 mg/dL (2.82 mmol/L)
   - G) Physical inactivity
   - H) Other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans

2) Patients with prediabetes (A1C ≥5.7% [39 mmol/mol], IGT, or IFG) should be tested yearly.

3) Women who were diagnosed with GDM or delivered a baby weighing > 9lb should have lifelong testing at least every 3 years.

4) For all other patients, testing should begin at age 45 years.

5) If results are normal, testing should be repeated at a minimum of 3-year intervals, with consideration of more frequent testing depending on initial results and risk status.

- Risk-Based Screening for Type 2 Diabetes or Prediabetes in Asymptomatic **Children** and Adolescents in a Clinical Setting (<18 yrs):

TABLE 1. Criteria for the Screening and Diagnosis of Diabetes

	Prediabetes	Diabetes
A1C	5.7–6.4%*	≥6.5%†
FPG	100–125 mg/dL (5.6–6.9 mmol/L)*	≥126 mg/dL (7.0 mmol/L)†
OGTT	140–199 mg/dL (7.8–11.0 mmol/L)*	≥200 mg/dL (11.1 mmol/L)†
RPG	—	≥200 mg/dL (11.1 mmol/L)‡

**For all three tests, risk is continuous, extending below the lower limit of the range and becoming disproportionately greater at the higher end of the range. †In the absence of unequivocal hyperglycemia, results should be confirmed by repeat testing. ‡Only diagnostic in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis. RPG, random plasma glucose.*

Criteria

- Overweight (BMI >85th percentile for age and sex, weight for height >85th percentile, or weight >120% of ideal for height) **A**

Plus one or more additional risk factors based on the strength of their association with diabetes as indicated by evidence grades:

- Maternal history of diabetes or GDM during the child's gestation **A**
- Family history of type 2 diabetes in first- or second-degree relative **A**
- Race/ethnicity (Native American, African American, Latino, Asian American, Pacific Islander) **A**
- Signs of insulin resistance or conditions associated with insulin resistance (acanthosis nigricans, hypertension, dyslipidemia, polycystic ovary syndrome, or small-for-gestational-age birth weight) **B**

❖ Diagnosing Prediabetes and Diabetes:

- A1C 5.7 - 6.4 % or (39-46 mmol/mol) for prediabetes or 6.5% (48 mmol/mol) for diabetes

❖ Prediabetes:

- Persons with prediabetes [Impaired Glucose Tolerance (IGT) or Impaired Fasting Glucose (IFG)] should not be viewed as a clinical entity but rather as an increased risk for diabetes and cardiovascular disease (CVD), should be counseled on lifestyle changes.
  - Weight Management (in overweight/obese patients can improve insulin sensitivity)
  - Exercise (walking 150 minutes/week)
  - Diet (Provided by a Dietitian)
  - Can reduce HbA1C by 1-2% but may face poor adherence over time
- Three large studies of lifestyle intervention has shown sustained reduction in the rate of conversion to type 2 diabetes,
  - 43% reduction at 20 years in the Da Qing study.
  - 43% reduction at 7 years in the Finnish Diabetes Prevention Study (FDPS).
  - 34% reduction at 10 years in the U.S. Diabetes Prevention Program Study (DPPS) .
- A consensus panel felt that Metformin should be the choice of drug considered
- **When to add Metformin in prediabetes?**
- In addition to lifestyle counseling, Metformin is considered in IFG plus:
  - Hypertension
  - Low HDL cholesterol
  - Elevated triglycerides
  - Family history of diabetes (first-degree relative)
  - Obese
  - Hx of GDM
  - Under 60 years of age

❖ Prevention of Diabetes Complications

Microvascular Complications

- Diabetic kidney disease (DKD): presence of albuminuria and/ or reduced eGFR in the absence of signs or symptoms of other primary causes of kidney damage.
- occurs in 20–40% of patients with diabetes
- typically develops after diabetes duration of 10 years in type 1 diabetes, but may be present at diagnosis of type 2 diabetes and can progress to ESRD (Leading cause of ESRD in US)
- At least once a year, assess urinary albumin (e.g., spot UACR) and eGFR in patients with type 1 diabetes with duration of ≥5 years, and in all patients with T2DM at time of diagnosis

Treatment is control glucose level and blood pressure levels.

Diabetic Retinopathy

- Screening: 5 years or more T1DM, T2DM at time of diagnosis.
- If there is no evidence of retinopathy and glycemia is well controlled, then exams every 1–2 years may be considered, if not it should be in shorter periods.
- Promptly refer patients with any level of **macular edema**, severe nonproliferative diabetic retinopathy or any proliferative diabetic retinopathy to an ophthalmologist

Neuropathy

- Screening: 5 years or more T1DM, T2DM at time of diagnosis.
- History and assessment of either temperature or pinprick sensation (small-fiber function) and vibration sensation using a 128-Hz tuning fork. All patients should have annual 10-g monofilament testing
- Either pregabalin or duloxetine are recommended as initial pharmacologic treatments for neuropathic pain in diabetes.
- For peripheral neuropathy:
    - Small-fiber function: pinprick and temperature sensation
    - Large-fiber function: vibration perception and 10-g monofilament
    - Protective sensation: 10-g monofilament

Foot Care

- Perform a comprehensive foot evaluation at least annually to identify risk factors for ulcers and amputations
- The examination should include inspection of the skin, assessment of foot deformities, neurological assessment and vascular assessment including pulses in the legs and feet

A complete medical evaluation should be performed at the initial visit to:

Confirm the diagnosis and classify diabetes.
Evaluate for diabetes complications and potential comorbid conditions.

Consider screening patients with T1DM for autoimmune thyroid disease and celiac disease soon after diagnosis.

Diabetes is associated with increased risk of cancers of the liver, pancreas, endometrium, colon/rectum, breast, and bladder. Patients with diabetes should be encouraged to undergo recommended age- and sex-appropriate cancer screenings and to reduce their modifiable cancer risk factors (obesity, physical inactivity, and smoking).

A follow up visit should be arranged.

❖ Approach to management (الدكتور شرح وركز كثير عالمانجمنت)

- Diabetes management is a team work
- Individualize management
- Set Target goals:
  - Glycaemic Targets
  - BP goals
  - Lipid goals
- Education
  - associated with increased use of primary and preventive services and lower use of acute, inpatient hospital services.
- Physical Examination:
  - Height and Weight (BMI)
  - Blood Pressure (2 readings)
  - Fundus Examination (Hard and soft exudates, new vessel formation, macular oedema....)
  - Cardiac examination
  - Lower Limbs:
    - Skin Examination
    - Evaluation of pulses
    - Foot Examination
    - Neurologic Examination
- LAB EVALUATION:
  - FPG and 2 hrPP
  - Lipid Profile (total cholesterol, LDLc, HDLc and triglycerides)*
  - HbA1C (every 3 m for insulin / every 6 m for controlled) *
  - Midstream Urine (for Ketones, protein, pus cells,...)
  - Urea and Creatinine*
  - Test for Microalbuminuria (30-300 mg) or macroalbuminuria (≥300 mg)/ Albumin to creatinine ratio / 24 hr urine collection for protein / Creatinine Clearance*
  - ECG
  - Chest X-Ray

* Yearly check up important + Eye: Fundus Examination / eye referral + Feet : Visual inspection and Neurovascular status

- Current Treatment Goals for Glycaemic Control:

  In the guideline follow ADA (preprandial 80*-130)

	ADA[1]	ACE[2]
HbA1c	< 7.0% *(general goal)*	≤ 6.5%
Preprandial plasma glucose	70–130 mg/dL (3.9–7.2 mmol/L)	< 110 mg/dL (< 6.1 mmol/L)
Postprandial plasma glucose	< 180 mg/dL (< 10.0 mmol/L)	< 140 mg/dL (< 7.8 mmol/L)

ACE=American College of Endocrinology; ADA=American Diabetes Association; HbA1c=hemoglobin A1c;
Adapted from: [1]ADA / EASD consensus statement: Nathan DM, et al. *Diabetes Care*. 32:193–203;
[2]American Association of Clinical Endocrinologists, American College of Endocrinology. *Endocr Pract*. 2002; 8 (Suppl 1): 5–11;

Diabetes Medical Evaluation:

TABLE 4. Components of the Comprehensive Diabetes Medical Evaluation at Initial and Follow-up Visits

		INITIAL VISIT	EVERY FOLLOW-UP VISIT	ANNUAL VISIT
PAST MEDICAL AND FAMILY HISTORY	**Diabetes history**			
	▪ Characteristics at onset (e.g., age, symptoms)	✓		
	▪ Review of previous treatment regimens and response	✓		
	▪ Assess frequency/cause/severity of past hospitalizations	✓		
	Family history			
	▪ Family history of diabetes in a first-degree relative	✓		
	▪ Family history of autoimmune disorder	✓		
	Personal history of complications and common comorbidities			
	▪ Macrovascular and microvascular	✓		
	▪ Common comorbidities	✓		
	▪ Presence of hemoglobinopathies or anemias	✓		
	▪ High blood pressure or abnormal lipids	✓		
	▪ Last dental visit	✓		✓
	▪ Last dilated eye exam	✓		✓
	▪ Visits to specialists	✓	✓	✓
	Interval history			
	▪ Changes in medical/family history since last visit		✓	✓
SOCIAL HISTORY	**Assess lifestyle and behavior patterns**			
	▪ Eating patterns and weight history	✓	✓	✓
	▪ Sleep behaviors and physical activity	✓	✓	✓
	▪ Familiarity with carbohydrate counting in type 1 diabetes	✓		
	▪ Tobacco, alcohol, and substance use	✓		
	▪ Identify existing social supports	✓		
	Interval history			
	▪ Changes in social history since last visit		✓	✓
MEDICATIONS AND VACCINATIONS	▪ Medication-taking behavior	✓	✓	✓
	▪ Medication intolerance or side effects	✓	✓	✓
	▪ Complementary and alternative medicine use	✓	✓	✓
	▪ Vaccination history and needs	✓		✓
TECHNOLOGY USE	▪ Assess use of health apps, online education, patient portals, etc.	✓		✓
	▪ Glucose monitoring (meter/CGM): results and data use	✓	✓	✓
	▪ Review insulin pump settings	✓	✓	✓
SCREENING	**Psychosocial conditions**			
	▪ Screen for depression, anxiety, and disordered eating; refer for further assessment or intervention if warranted	✓		✓
	▪ Consider assessment for cognitive impairment*	✓		✓
	Diabetes self-management education and support			
	▪ History of dietitian/diabetes educator visits	✓	✓	✓
	▪ Screen for barriers to diabetes self-management	✓		✓
	▪ Refer or offer local resources and support as needed	✓	✓	✓
	Hypoglycemia			
	▪ Timing of episodes, awareness, frequency and causes	✓	✓	✓
	Pregnancy planning			
	▪ For women with childbearing capacity, review contraceptive needs and preconception planning	✓	✓	✓

TABLE 4. Components of the Comprehensive Diabetes Medical Evaluation at Initial and Follow-up Visits, *continued from p. 5*

		INITIAL VISIT	EVERY FOLLOW-UP VISIT	ANNUAL VISIT
PHYSICAL EXAMINATION	▪ Height, weight, and BMI; growth/pubertal development in children and adolescents	✓	✓	✓
	▪ Blood pressure determination	✓	✓	✓
	▪ Orthostatic blood pressure measures (when indicated)	✓		
	▪ Fundoscopic examination (refer to eye specialist)	✓		✓
	▪ Thyroid palpation	✓		✓
	▪ Skin examination (e.g., acanthosis nigricans, insulin injection or insertion sites, lipodystrophy)	✓	✓	✓
	▪ Comprehensive foot examination			
	• Visual inspection (e.g., skin integrity, callous formation, foot deformity or ulcer, toenails)	✓	✓	✓
	• Screen for PAD (pedal pulses; refer for ABI if diminished)	✓		✓
	• Determination of temperature, vibration or pinprick sensation, and 10-g monofilament exam	✓		✓
LABORATORY EVALUATION	▪ A1C, if the results are not available within the past 3 months	✓	✓	✓
	▪ If not performed/available within the past year			
	• Lipid profile, including total, LDL, and HDL cholesterol and triglycerides#	✓		✓^
	• Liver function tests#	✓		✓
	• Spot urinary albumin-to-creatinine ratio	✓		✓
	• Serum creatinine and estimated glomerular filtration rate†	✓		✓
	• Thyroid-stimulating hormone in patients with type 1 diabetes#	✓		✓
	• Vitamin B12 if on metformin (when indicated)	✓		
	• Serum potassium levels in patients on ACE inhibitors, ARBs, or diuretics†	✓		✓
ASSESSMENT AND PLAN	**Goal setting**			
	▪ Set A1C/blood glucose target and monitoring frequency	✓	✓	✓
	▪ If hypertension diagnosed, establish blood pressure goal	✓		✓
	▪ Incorporate new members to the care team as needed	✓	✓	✓
	▪ Diabetes education and self-management support needs	✓	✓	✓
	Cardiovascular risk assessment and staging of CKD			
	▪ History of ASCVD	✓	✓	✓
	▪ Presence of ASCVD risk factors (see Table 9.2)	✓	✓	✓
	▪ Staging of CKD (see Table 10.1)†	✓	✓	✓
	Therapeutic treatment plan			
	▪ Lifestyle management	✓	✓	✓
	▪ Pharmacologic therapy	✓	✓	✓
	▪ Referrals to specialists (including dietitian and diabetes educator) as needed	✓	✓	✓
	▪ Use of glucose monitoring and insulin delivery devices	✓	✓	✓

*Tables 9.2 and 10. 1 are in the full 2018 Standards of Care. *≥65 years. †May be needed more frequently in patients with known CKD or with changes in medications that affect kidney function and serum potassium (see Table 10.2 in the full Standards of Care). #May also need to be checked after initiation or dose changes of medications that affect these laboratory values (i.e., diabetes, blood pressure, cholesterol, or thyroid medications). ^In people without dyslipidemia and not on cholesterol-lowering therapy, testing may be less frequent. ABI, ankle-brachial pressure index.*

Management of T2DM:

In short, we should **start with lifestyle modification and looking at HbA1c levels:**

IF A1c levels are <9% and there are no metformin CI, we start with metformin alone and monitor after 3 months. If the results after 3 months did not reach the goal, or the A1c levels at the first visit were 10%>A1c≥9%, Dual therapy ⟶ 3 months goal not achieved ⟶ Triple therapy ⟶ 3 months not achieved or first presentation with A1c 10%≥, blood glucose 300 mg/dl⟶ injectable therapy

Other oral medication:

Acabose:

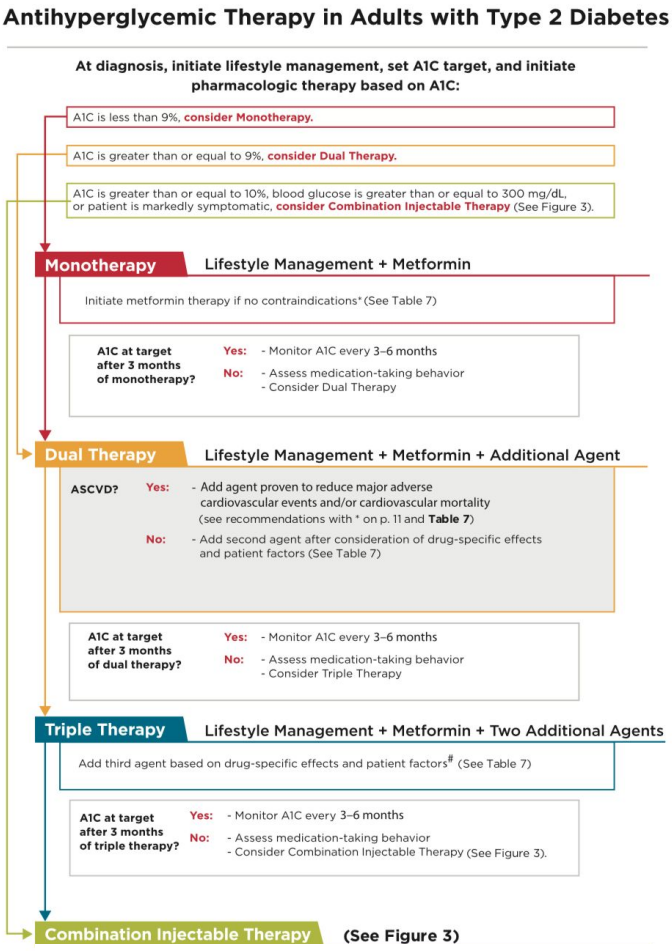
Class: alpha-glucosidase inhibitor

Dose: 50-100 mg TDS

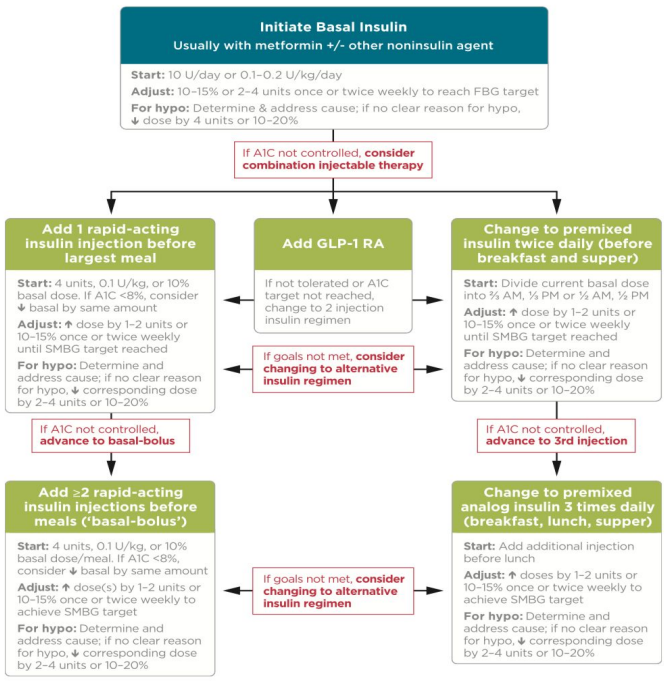
Side effects: Flatulence & Diarrhoea.

Regarding Triple therapy:

GLP-1 agonist and DDP-4 inhibitor Should NOT be prescribed together.



Injectable therapy



Medications Used in T2DM management:

❖ Biguanides (Metformin): choose as initial therapy

- Acts by reducing hepatic glucose production (main), Other:
  - Reduces appetite & may delay absorption
  - Improves peripheral insulin sensitivity
- **NO** hypoglycemia and mild weight loss
- Contraindications: kidney, liver, cardiopulmonary dysfunction or alcohol abuse (Lactic acidosis risk). Contraindicated in pregnancy also.
- Start with 500 mg once or twice/day with meals and increase every few days till reach maximum dose of 2 gm/day.

Advantages	Disadvantages
▪ Oral	▪ GI disturbance
▪ Low cost	▪ B12 deficiency
▪ Decrease macrovascular complications?	▪ Lactic acidosis
▪ Decrease hepatic gluconeogenesis	▪ Contraindications
▪ Once daily dosing	

Sulfonylureas (Glibenclamide, Glimepiride, Glipizide, Gliclazide...)

Advantages	Disadvantages
▪ Oral	▪ Hypoglycaemia
▪ Low cost	▪ Weight gain
▪ Decrease microvascular complications	▪ β-cell failure?
▪ Once daily dosing	▪ CV risk?

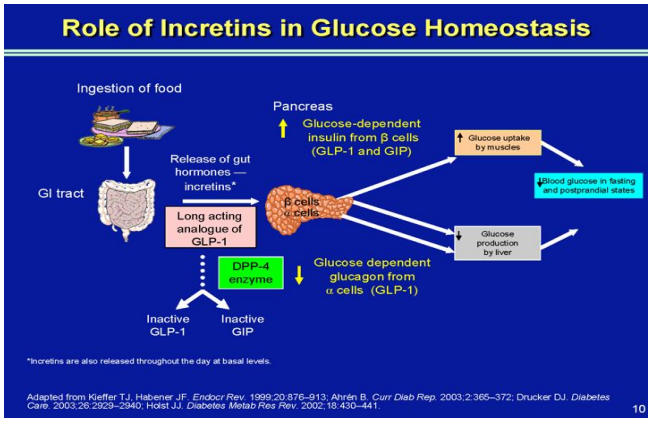
Thiazolidinediones (TZD) (Pioglitazone)

- Dose: 15-30 mg OD
- Promotes glucose uptake by skeletal muscles and adipose tissue
- Used in combination with metformin and sulphonylurea
- Periodic monitoring of liver enzymes
- Not given in patients with heart failure
- Recently, debate about increase incidence of bladder cancer.

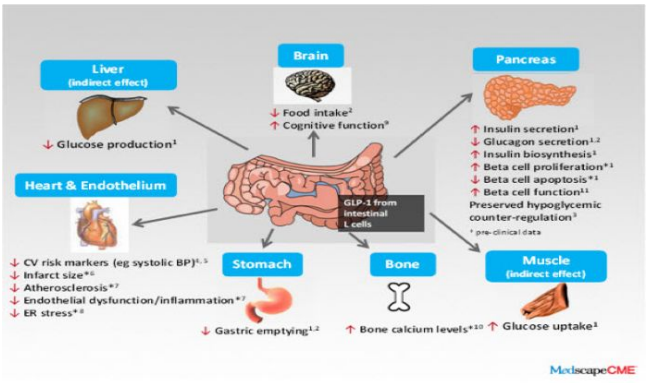
Advantages	Disadvantages
▪ Target insulin resistance	▪ Fluid retention/CCF
▪ β-cell preservation?	▪ Weight gain
▪ Vascular protection?	▪ Bone fractures
▪ Decrease hepatic gluconeogenesis	▪ Bladder cancer?
▪ Once daily dosing	▪ Costly

Physiology of Incretins (GLP-1) and DPP-4 :

- Role of incretins (Rt image): The incretin system is impaired in patients with T2DM, which, as a consequence of its insulinotropic actions, contributes to fasting and postprandial hyperglycemia.
- The impairment of GLP-1 secretion varies directly with the degree of insulin resistance; those who are more insulin resistant have a lower rise in GLP-1 in response to a meal.

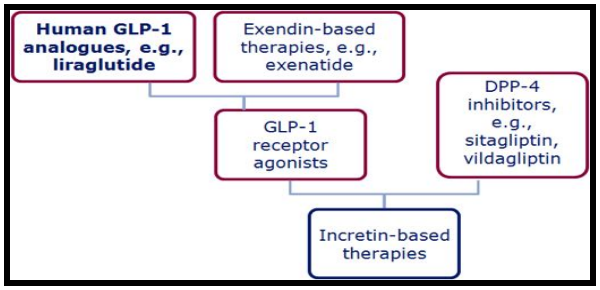


- Effects of GLP-1:
  - GLP-1 is secreted throughout the day by intestinal mucosa in response to oral glucose in the gut.
  - GLP-1 causes anabolic actions on the synthesis of insulin in beta cells by stimulating all steps of insulin biosynthesis.
  - GLP-1 provides continued and augmented release of insulin for secretion in response to glucose without overproduction that could lead to hypoglycemia.
  - GLP-1 also acts on islet alpha cells, causing strong inhibition of postprandial glucagon secretion.
  - GLP-1 slows gastric emptying and acts on brain to promote early satiety with reduced food intake



- Dipeptidyl Peptidase-4 (DPP-4):
  - Within minutes of secretion or exogenous administration, GLP-1 is rapidly degraded by dipeptidyl peptidase-4 (DPP-4).
  - DPP-4 is found in many body tissues, including liver, renal, and intestinal brush- border membranes; lymphocytes; and endothelial cells.

The family of incretin-based therapies:



A) GLP-1 agonist:

- Exendin-based therapy have ~ 50% sequence identity to human GLP-1
- Human GLP-1 analogues (liraglutide) which have share a much higher percentage of amino acids with human GLP-1 (97%)
- Liraglutide:
  - SC, 0.6,1.2 -1.8 mg once daily
  - For overweight / obese type 2 patients Combined with Metformin +/- Pioglitazone
- NON glucose effects of GLP-1 agonist:
  - Weight: ↓ 3-4 kg; BP: ↓ 2-3 mmhg (SBP); Heart rate: ↑ 2-3 beats/min

Main advantages	Main disadvantages
Low risk of hypoglycaemia	Injection required
Weight loss	Limited long-term clinical experience at present
Lower blood pressure	Antibody formation (significance?)
CVD protective?	Link to pancreatic/medullary C-cell cancer and pancreatitis?
	Expensive

Main advantages	Main disadvantages
Low risk of hypoglycaemia	Limited long-term clinical experience
Weight neutral	Pancreatitis/Pancreatic Ca?
No drug interactions	Expensive
Fixed dose combinations with Metformin available	Heart Failure?

B) DPP-4 inhibitor

- Sitagliptin (Januvia), 100 mg OD
    - Other DPP-4 inhibitors, Vildagliptin, Saxagliptin,Alogliptin, Linagliptin
    - Type 2 diabetes only
    - Monotherapy with Metformin or TZD
    - Weight neutral
    - Does not cause hypoglycemia

Which antidiabetic Drugs are contraindicated or should be only very cautiously when the following Co-Morbidity is present?

- Chronic Kidney Failure: Metformin,Acarbose,Sitagliptin,Insulin & SUs (reduced dosage)
- Heart Failure: TZDs
- Osteoporosis: TZDs
- Myocardial Infarction: Hypoglycemias should be avoided when Insulin or SUs are taken.
- Elderly people (>70 years): Hypoglycemias should be avoided when Insulin or SUs are taken.

❖ Ominous Octet & MEdications:

Ominous Octet

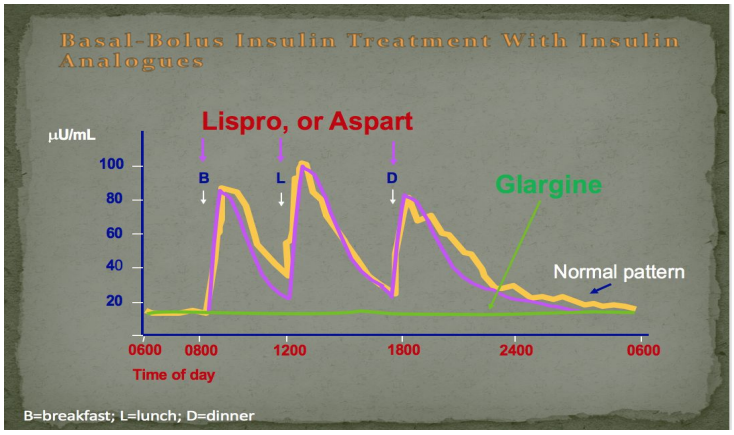
Organ/Cell	Pathophysiology	Medication
1. Muscle	Decreased glucose uptake	Metformin/TZDs/Insulin
2. Liver	Increased gluconeogenesis	Metformin/TZDs/Insulin
3. β Cells	Impaired insulin secretion	Sulphonylureas/DPP-4 Inhibitors/ GLP-1 receptor agonists/Insulin
4. α cells	Increased glucagon secretion	DPP-4 inhibitors/ GLP- receptor agonists
5. Fat	Increased lipolysis and decreased glucose uptake	TZDs
6. Intestine	Decreased/Impaired incretin effect?	DPP-4 Inhibitors/ GLP-1 receptor agonists (α- glucosidase inhibitors)
7. Kidney	Increased glucose reabsorption	SGLT-2 inhibitors
8. Brain	Neurotransmitter dysfunction	GLP-1 receptor agonists/ Bromocriptine

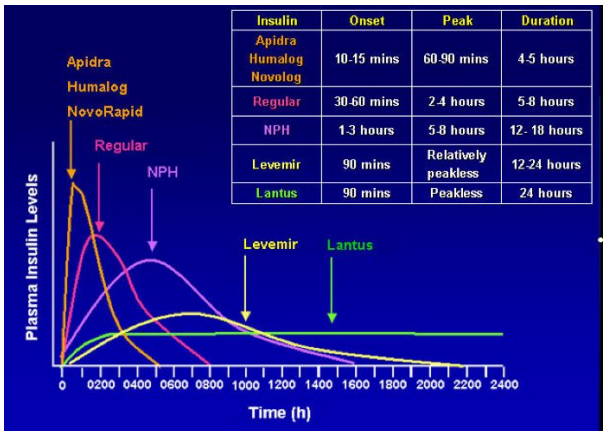
❖ Insulin:

- History
    - 1982 – Human insulin approved
    - 1996 – First rapid acting insulin analogue approved
    - 2004 – First long acting insulin analogue approved
- Powerful agent, inexpensive
- Necessary in 20-30%
- Weight gain, Hypoglycemia, and High level of patient fear

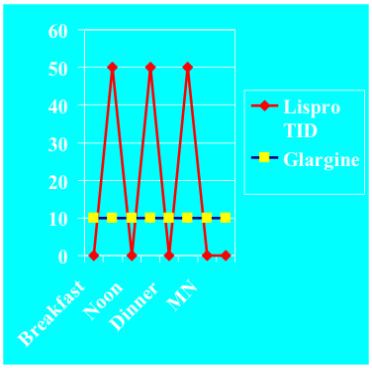
- **Indication in T2DM:**
  - If HbA1c is ≥ 9 %
  - After maximum metformin and sulfonylurea
  - You should consider adding Insulin and taper the Sulphonylurea.
- **T1DM Regimen:**
  - Conventional Insulin Therapy: Two injections of NPH (intermediate acting) and Regular (short acting) Insulin
  - Mixed Insulin: Two injections of 70/30 or 60/40 or 50/50 (NPH/Regular)
  - Multiple Insulin Injections:
    - 1 or 2 injections of NPH plus 3 injections of Regular or Rapid Insulin.
    - One injection of long acting (Glargine or Detemir) plus 3 injections of rapid insulin (Lispro/Aspart).
  - INSULIN GLARGINE (LANTUS)
    - The first clear long-acting insulin
    - Acidic (pH of 4) when injected it is neutralized by the body, causing Glargine crystals to be precipitated and slowly absorbed.
    - It is taken once a day
    - Being acidic, cannot be mixed with other insulin

- **Comparison between different types of insulin in terms of their durations:**

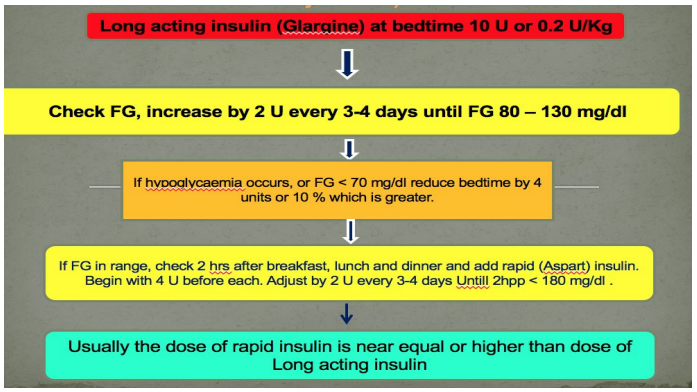




- **Glargine/ Lispro:**
  - Avoids fasting hyperinsulinaemiaand hypoglycemia
  - Can mimic pancreatic ß-cell insulin secretion
  - 36% had hypoglycemia vs 50% on NPH.
  - Dose: Glargine 50% and Lispro 50%



❖ Initiation and adjustment of insulin regimens (Multiple injections):



- **Insulin administration:**
  - Do not mix Glargine with other insulin products.
  - Insulin site should be clean, but wiping with alcohol is not needed.
  - Syringe reuse acceptable but meticulous attention to cleanliness is needed.
  - Insulin pens improve the dose accuracy.
  - Injection site rotation reduces the lipoatrophy.
  - Abdomen region has a faster absorption rate than the Arm, which is faster than the leg.

❖ CVD Treatment in Diabetic patients

- **Antiplatelet agents**
  - Consider Aspirin therapy (75–162 mg/day) as a primary prevention strategy in those with type 1 or type 2 diabetes at increased cardiovascular risk (10-year risk 10%).
  - This includes most men 50 years of age or women 50 years of age who have at least one additional major risk factor(family history of CVD, hypertension, smoking, dyslipidemia, or albuminuria).
- **Statins and Diabetes**
  - Diabetics < 40 years with no CV risk factors, No statin.
  - Statin therapy should be added to lifestyle therapy, for diabetic patients with no additional atherosclerotic CV disease risk factors 40-75 years (A) and < 40 years (B).
  - qFor patients with diabetes aged 40–75 years with additional atherosclerotic cardiovascular disease risk factors, consider using high-intensity statin and lifestyle therapy. (B)
  - The addition of Ezetimibe to moderate-intensity statin has been shown to provide additional CV benefit compared with moderate-intensity statin alone and may be considered for patients with a recent acute coronary syndrome with LDL cholesterol > 50 mg/dL (1.3 mmol/L) or for those patients who cannot tolerate high intensity statin therapy. (A)

TABLE 8. Recommendations for Statin and Combination Treatment in Adults With Diabetes

Age	ASCVD	Recommended statin intensity^ and combination treatment*
<40 years	No	None†
	Yes	High • If LDL cholesterol ≥70 mg/dL (3.9 mmol/L) despite maximally tolerated statin dose, consider adding additional LDL-lowering therapy (such as ezetimibe or PCSK9 inhibitor)#
≥40 years	No	Moderate‡
	Yes	High • If LDL cholesterol ≥70 mg/dL (3.9 mmol/L) despite maximally tolerated statin dose, consider adding additional LDL-lowering therapy (such as ezetimibe or PCSK9 inhibitor)

**In addition to lifestyle therapy. ^For patients who do not tolerate the intended intensity of statin, the maximally tolerated statin dose should be used. †Moderate-intensity statin may be considered based on risk-benefit profile and presence of ASCVD risk factors. ASCVD risk factors include LDL cholesterol ≥100 mg/dL (2.6 mmol/L), high blood pressure, smoking, CKD, albuminuria, and family history of premature ASCVD. ‡High-intensity statin may be considered based on risk-benefit profile and presence of ASCVD risk factors. #Adults aged <40 years with prevalent ASCVD were not well represented in clinical trials of nonstatin–based LDL reduction. Before initiating combination lipid-lowering therapy, consider the potential for further ASCVD risk reduction, drug-specific adverse effects, and patient preferences.*

  - **Statin and Fibrate**
    - Statin and Fenofibrate may be considered for men with both triglyceride level ≥ 204 mg/dL(2.3mmol/L) and HDL cholesterol level < 34 mg/dL(0.9 mmol/L). (B)

- Combination therapy (statin/niacin) has not been shown to provide additional cardiovascular benefit above statin therapy alone and may increase the risk of stroke and is not generally recommended. (A)

❖ **Vaccinations:** Influenza vaccine (yearly) + Pneumococcal vaccine (once in lifetime)

- Targets in DM

- BP < 140 / 90
- HbA1C≤ 7 % (European Diab. Soc. ≤ 6.5 %)
- LDL-C < 100 mg/dl (2.6 mmol/L)
- HDL-C > 40 mg/dl (males) , > 50 mg/dl (females)
- TG < 150 mg/dl (1.7 mmol/L)

- 2009 - A new **meta-analysis** suggests that intensively controlling blood glucose levels (HbA1c) to < 7.0%, significantly reduces the risk of (MI) and (CHD) events and has no effect on all-cause mortality and Stroke. The findings include UKPDS, ADVANCE, VADT, ACCORD, and PROACTIVE studies.
- The concerns stemmed particularly from the (ACCORD) and (ADVANCE) and (VADT) which showed no significant response on Macrovascular Outcomes.
- **ACCORD**, on the other hand, was stopped early because of an increased risk of death in patients who underwent intensive blood glucose lowering.

❖ History of developed medication for Diabetes: