DM TBL

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Readiness Assessment TEST

1. **A 24-year-old woman comes to your clinic because she is worried she might have diabetes. She is overweight with a BMI of 28. She is healthy otherwise and has been trying to lose weight over that last few months. Her father was recently diagnosed with diabetes at the age of 65 and her mother has hypertension**

Which of the following would be the most suitable recommendations?

a. She is still too young to start diabetic testing. You inform her to live her life without concern and come back at 45 for testing then

b. She is at increased risk for diabetes. You request diabetes screening tests and encourage her to continue weight loss and to increase physical activity

c. She is at increased risk for diabetes. However, she is trying to lose weight and diabetic testing can be delayed till she reaches her weight loss goals

d. You are not concerned as she appears healthy and is not complaining of any symptoms to suggest diabetes. You reassure her that she does not need testing

2. A 42-year-old man with a history of sickle cell disease presents to your clinic to follow up on diabetic testing he had done. Here are his results:

- **FPG 138 mg/dl [7.6 mmol/L]**
- **OGTT 250mg/dl [13.8mmol/L]**
- **HgA1c 5.7%**

What do you tell the patient?

a. You are diabetic as you have two abnormal tests in the diabetic range.

b. You have prediabetes as your HgA1c is in the prediabetes range

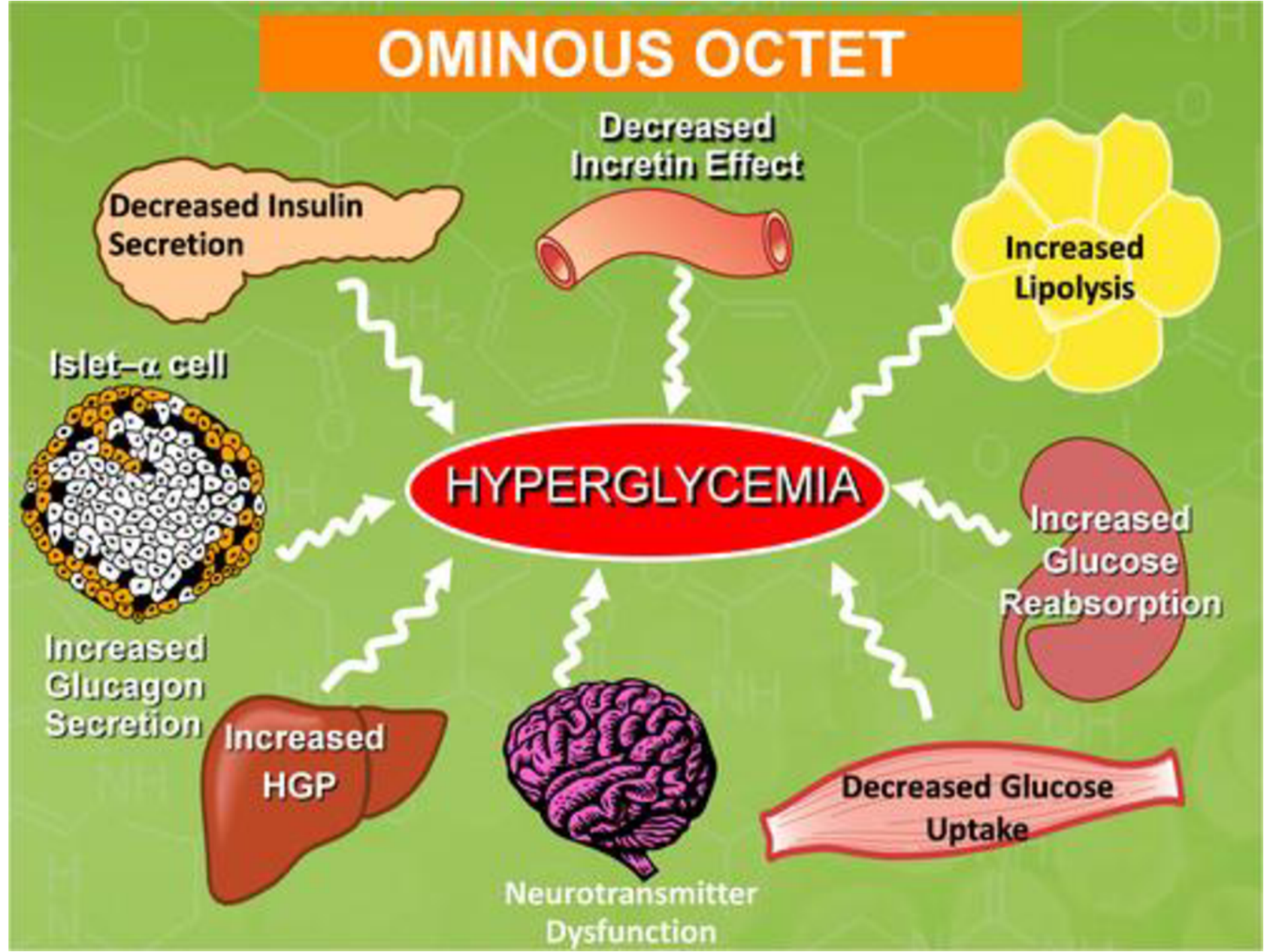
c. Your blood tests are confusing and need to be repeated to make a diagnosis

d. Monitor your blood sugar at home and we will make a diagnosis from that

DM Mechanism

http://mediacenter.novomedlink.com/v/diabetes-pathophysiology

OMINOUS OCTET



3. Which one of the following is true concerning the use of hemoglobin A1c levels t diagnose diabetes mellitus?

a. A level >6.0% is diagnostic of diabetes mellitus

b. Results can be misleading in patients with sickle cell disease

c. One abnormal Hg A1c result is sufficient to make a diagnosis

d. D) The test is useful to diagnose diabetes during pregnancy

Diagnostic Criteria and limitations

Screening for diabetes

Table 2.2—Criteria for testing for diabetes or prediabetes in asymptomatic adults

1. Testing should be considered in all adults who are overweight (BMI ≥25 kg/m^2 or ≥23 kg/m^2 in Asian Americans) and have additional risk factors:
   - physical inactivity
   - first-degree relative with diabetes
   - high-risk race/ethnicity (e.g., African American, Latino, Native American, Asian American, Pacific Islander)
   - women who delivered a baby weighing >9 lb or were diagnosed with GDM
   - hypertension (≥140/90 mmHg or on therapy for hypertension)
   - HDL cholesterol level <35 mg/dL (0.90 mmol/L) and/or a triglyceride level >250 mg/dL (2.82 mmol/L)
   - women with polycystic ovary syndrome
   - A1C ≥5.7% (39 mmol/mol), IGT, or IFG on previous testing
   - other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans)
   - history of CVD
2. For all patients, testing should begin at age 45 years.
3. 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 (e.g., those with prediabetes should be tested yearly) and risk status.

Diabetes

Table 2.1—Criteria for the diagnosis of diabetes

FPG ≥126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.*

OR

2-h PG ≥200 mg/dL (11.1 mmol/L) during an OGTT. The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.*

OR

A1C ≥6.5% (48 mmol/mol). The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*

OR

In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (11.1 mmol/L).

*In the absence of unequivocal hyperglycemia, results should be confirmed by repeat testing.

Prediabetes

Table 2.3—Categories of increased risk for diabetes (prediabetes)*
FPG 100 mg/dL (5.6 mmol/L) to 125 mg/dL (6.9 mmol/L) (IFG)
OR
2-h PG in the 75-g OGTT 140 mg/dL (7.8 mmol/L) to 199 mg/dL (11.0 mmol/L) (IGT)
OR
A1C 5.7–6.4% (39–46 mmol/mol)

*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.

To test for prediabetes, all these tests are equally appropriate.

Prediabetes

- Should be counseled on lifestyle changes.
- 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)

HbA1C values are influenced by red cell survival

- Falsely high values in patients with iron, vitamin B12, or folate deficiency anemia.
- Falsely low values in patients with hemolysis or anemia and those treated for iron, vitamin B12, or folate deficiency, and patients treated with erythropoietin.

Glycemic Targets

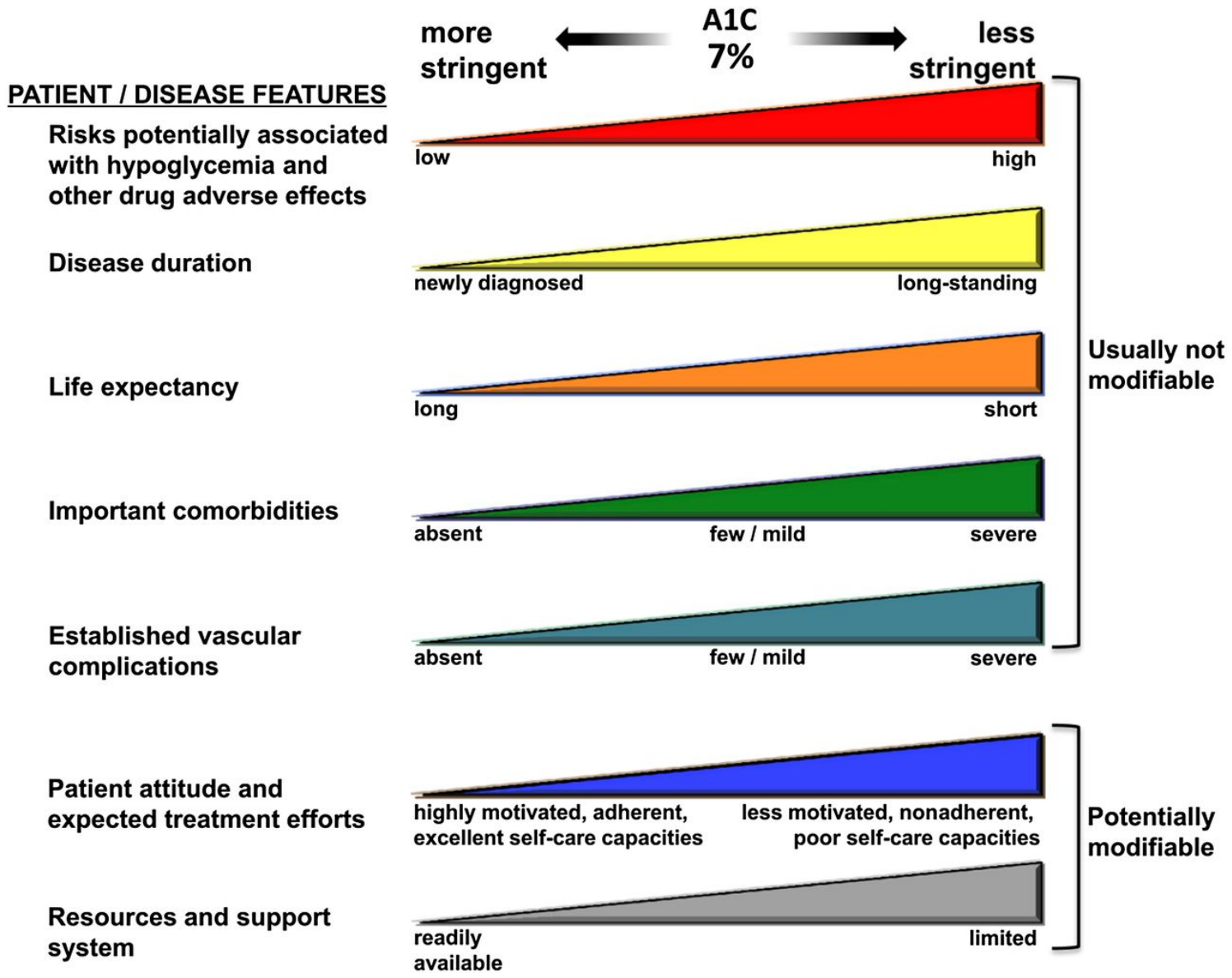
Blood Glucose Targets for Non-Pregnant Adults With Diabetes

A1C <7.0% (53 mmol/L)

Fasting 4.4-7.2 mmol/L (80-130 mg/Dl)

Postprandial <10.0 mmol/L (<180 mg/dL)

Approach to the management of hyperglycemia



Life Style Modification

For all patients, advise for

Weight Management (in overweight/obese patients can improve insulin sensitivity targeting a loss of 7% of body weight)

Exercise (walking 150 mins / week)

Diet (Provided by a Dietitian**)**

Can reduce HbA1C by 1-2%

Problems

Poor adherence over time

When to add Metformin in pre-diabetes?

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

4. A 55-year-old female presents for annual checkup. She developed diabetes mellitus at the age of 45. Currently, she is treated with Metformin 2g . Over the last one year, she has suffered from episodes of dysuria and has received treatment for cystitis on four separate occasions. Her blood pressure is 126/76 mmHg.

Investigations show:

HbA1C: 7.2 %

Urea: 4.5mmol/L (2.5 – 7.5)

Creatinine: 90 mmol/L (60 – 110) (GFR60)

Urinalysis: [Glucose 1+ WBC: nil RBC: nil]

24 hr urine protein: …… 260 mg/ 24 hrs (≤ 150)

<u>What would be the best therapeutic option to deal with her results?</u>

a. Improve glycemic control
b. Prescribe a low protein diet
c. Treat with ACE inhibitor
d. Use prophylactic antibiotics

5. A 62-year-old man with type 2 diabetes and a BMI of 33 has been controlled on Metformin 2g for 2 years. In the last two visits his HgA1c has been 8%. You would like to add a second glucose lowering medication. Knowing that he drives on a regular basis to AlQaseem for work, he is a smoker and on an ACE inhibitor and statin

<u>What would be your preferred second medication be?</u>

a. NPH insulin

b. Glyburide

c. Insulin Glargine

d. Liraglutide

6. A 58-year-old female with a 12-year history of hypertension and diabetes, has been treated with metformin 2g, gliclazide 90 mg, atorvastatin 20mg, lisinopril 10 mg, aspirin 81 mg and amlodipine 10 mg daily for the last two years.

At annual review her blood pressure is 138/87 mmHg, fundi reveal background diabetic retinopathy. Her results show:

HbA1c	6.9%	(3.8-6.4)
Urea	12.5 mmol/L	(2.5-7.5)
Creatinine	176 µmol/L	(60-110) (GFR 25)
Cholesterol	4.8 mmol/L	

You decided to discontinue one of her medications.

<u>Which of the following drugs should be withdrawn?</u>

a. Atorvastatin
b. Gliclazide
c. Llisinopril
d. Metformin

7. A 39 y.o. woman with type 2 diabetes on metformin and an ACE inhibitor attends your clinic for her routine follow up. Her BP is 128/65 and her Hg A1c is 7.9.%. Her kidney profile is as follows:

Creatinine	100 µmol/L	(60-110) (GFR 56)
Albumin / Creatinine Ratio	10.5 mgA/gCr	(0-30)

You decided to add a second medication to help bring her HgA1c closer to target.

What is your preferred medication class?

a. Alfa glucoside inhibitors (Acarbose)
b. Thiazolidinediones (Pioglitazone)
c. Sulfonylureas (Gleglazide)
d. SGLT2 inhibitors (Empagliflazin)

Oral Medication in Type 2 DM

Biguanides

Medications: Metformin

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

Sulphonylureas

Medications: Glibenclamide, Glipizide, Glimepiride, Gliclazide

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

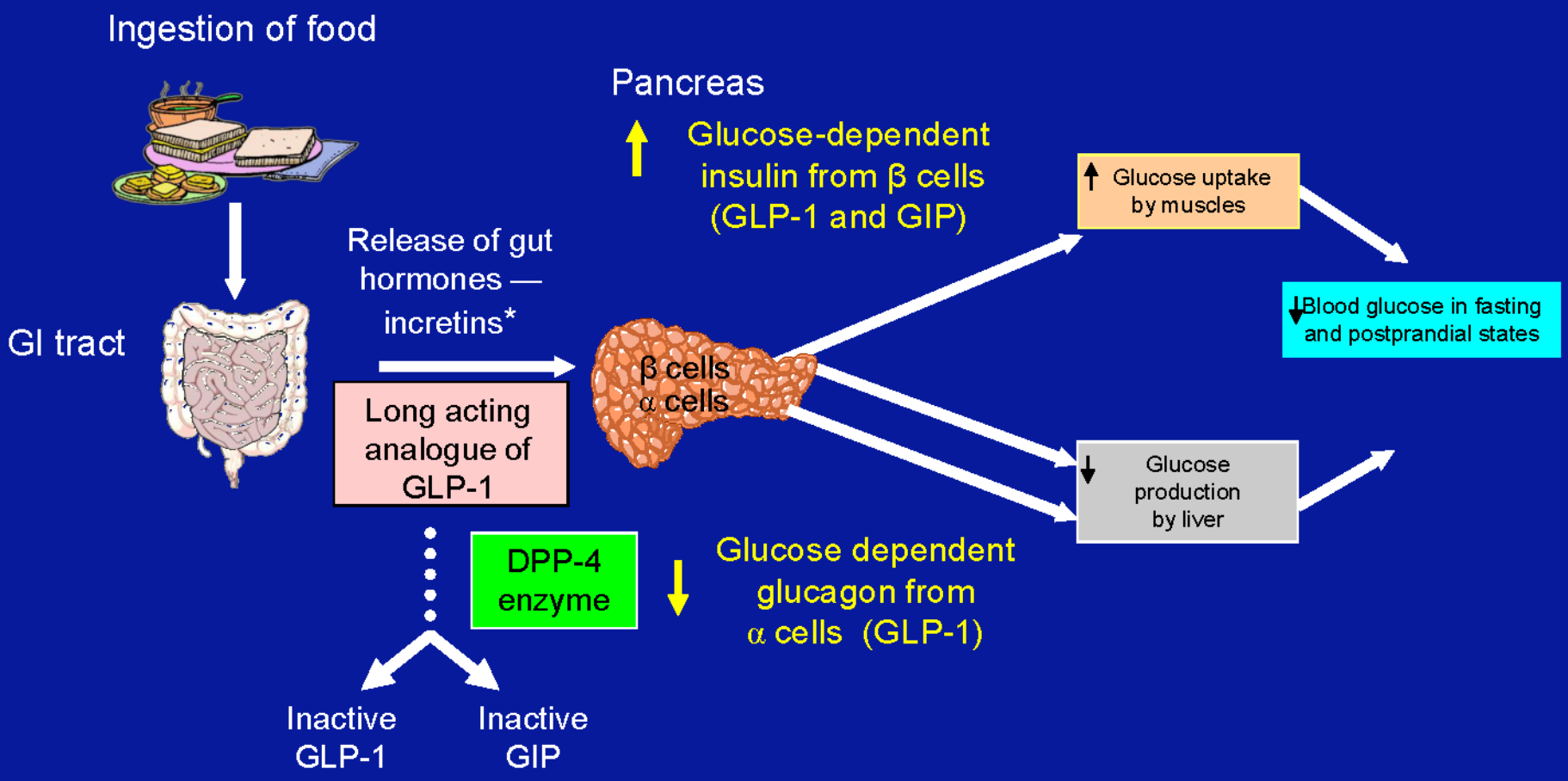
Thiazolidinediones

Medications: Pioglitazones

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

INCRETINS

Role of Incretins in Glucose Homeostasis



*Incretins are also released throughout the day at basal levels.

Adapted from Kieffer TJ, Habener JF. *Endocr Rev*. 1999;20:876–913; Ahrén B. *Curr Diab Rep*. 2003;2:365–372; Drucker DJ. *Diabetes Care*. 2003;26:2929–2940; Holst JJ. *Diabetes Metab Res Rev*. 2002;18:430–441.

INCRETINS

- 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.

Glucagon-like Peptide-1 (GLP-1)

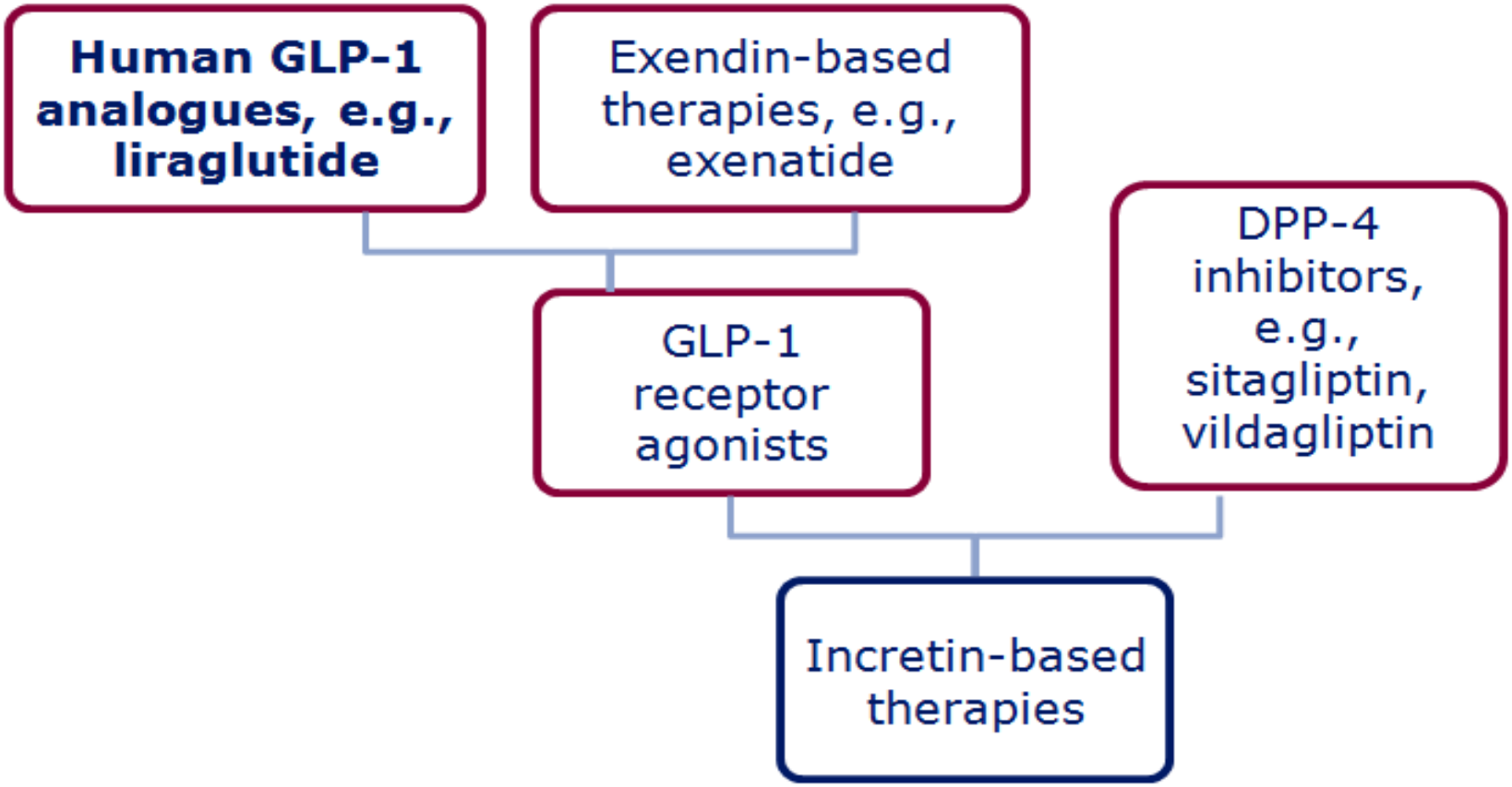
- secreted throughout the day by intestinal mucosa in response to oral glucose in the gut
- stimulates all steps of insulin biosynthesis
- provides continued and augmented release of insulin without overproduction
- acts on islet alpha cells, causing strong inhibition of postprandial glucagon secretion
- slows gastric emptying and acts on brain to promote early satiety

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

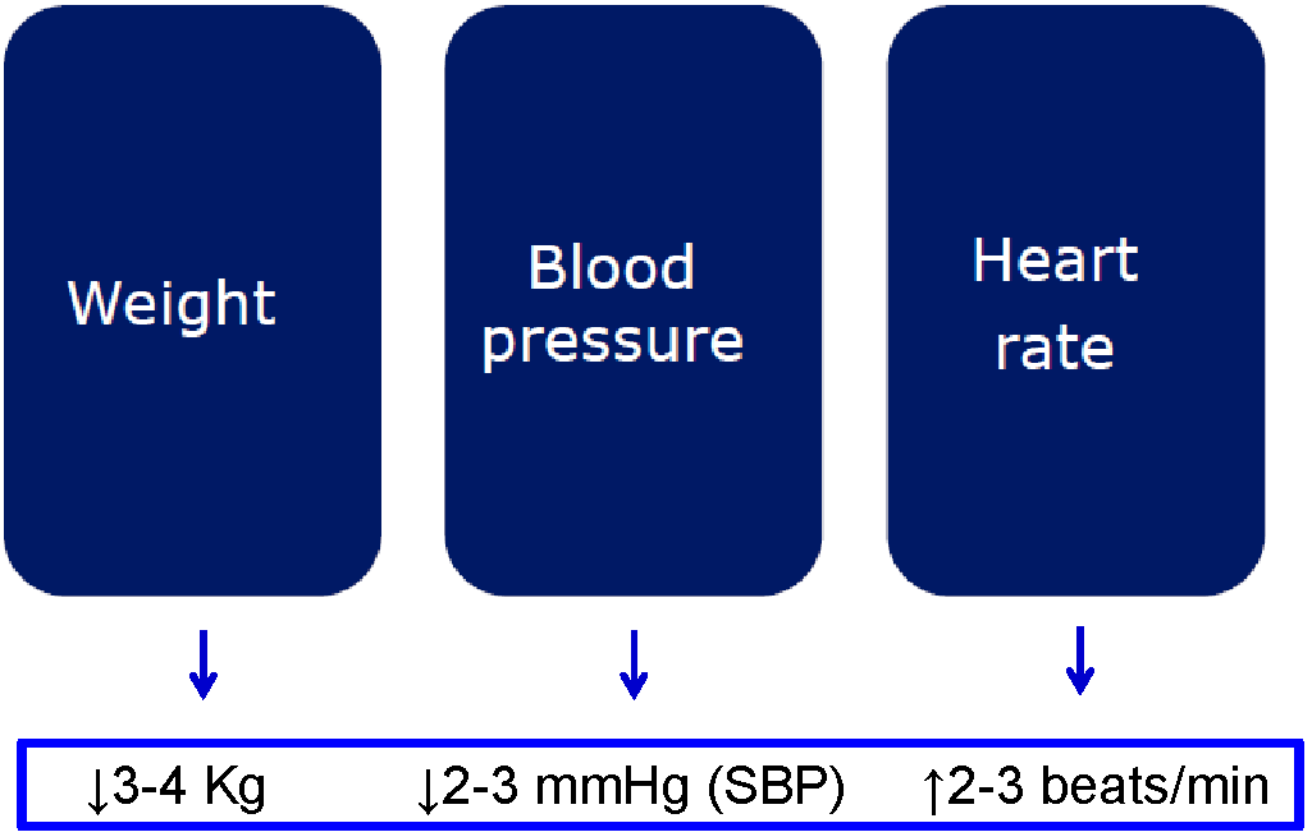


Wick & Newlin. *J Am Acad Nurse Pract* 2009;21:623–30; White. *J Am Pharm Assoc* 2009;49(Suppl. 1):S30–40

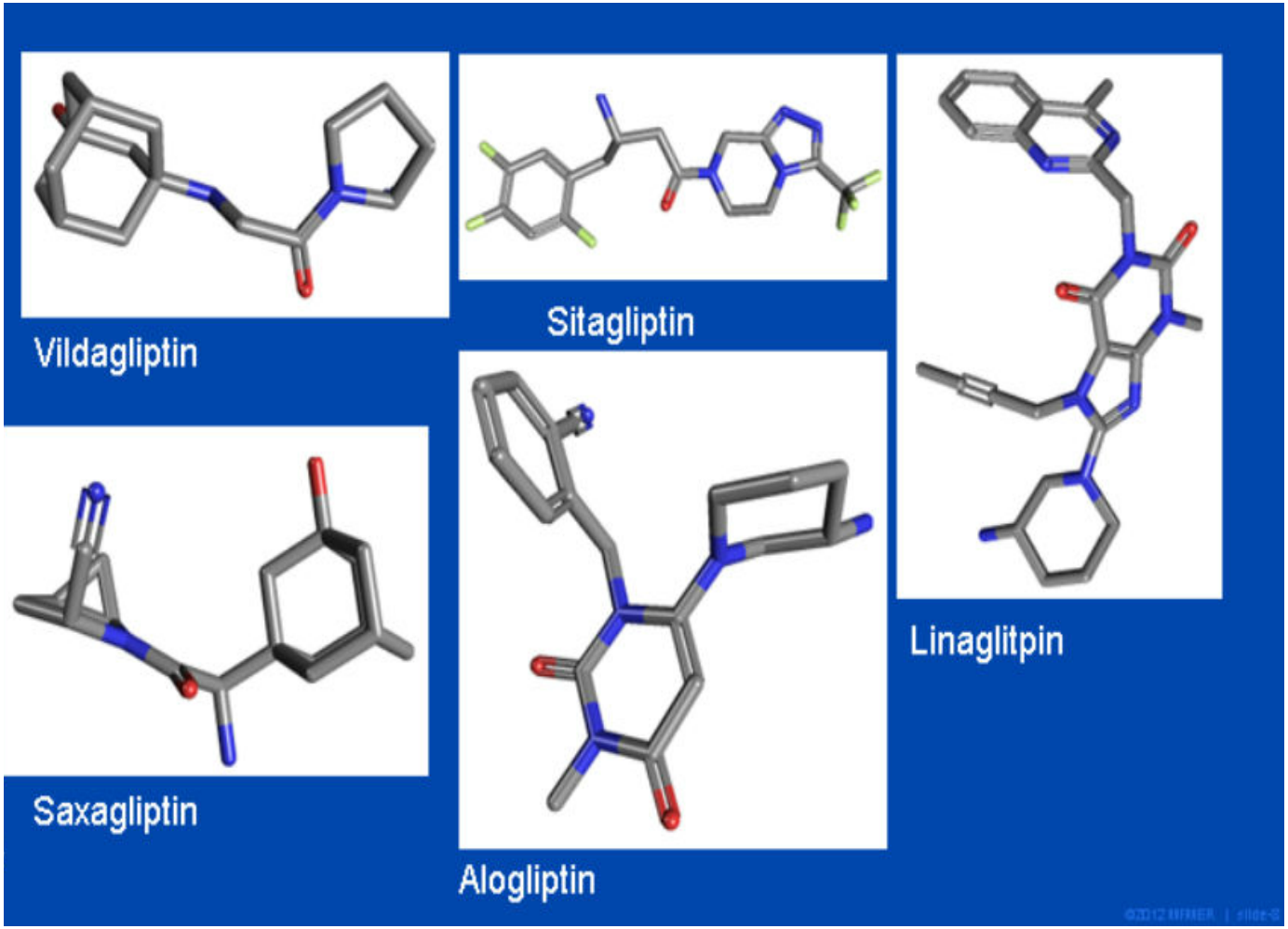
GLP-1 analogues

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

Non glucose effects of GLP-1 receptor agonists



DPP 4 inhibitors



DPP4 –inhibitors

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?

SGLT2 inhibitors

- Promotes the renal excretion of glucose
- Modestly reduces (limited by filtered load)
- Dose not cause hypoglycemia
- Empagliflozin -- CVD
- Main use as third line
- ? Safety of prolonged glucoseuria

Ominous Octet

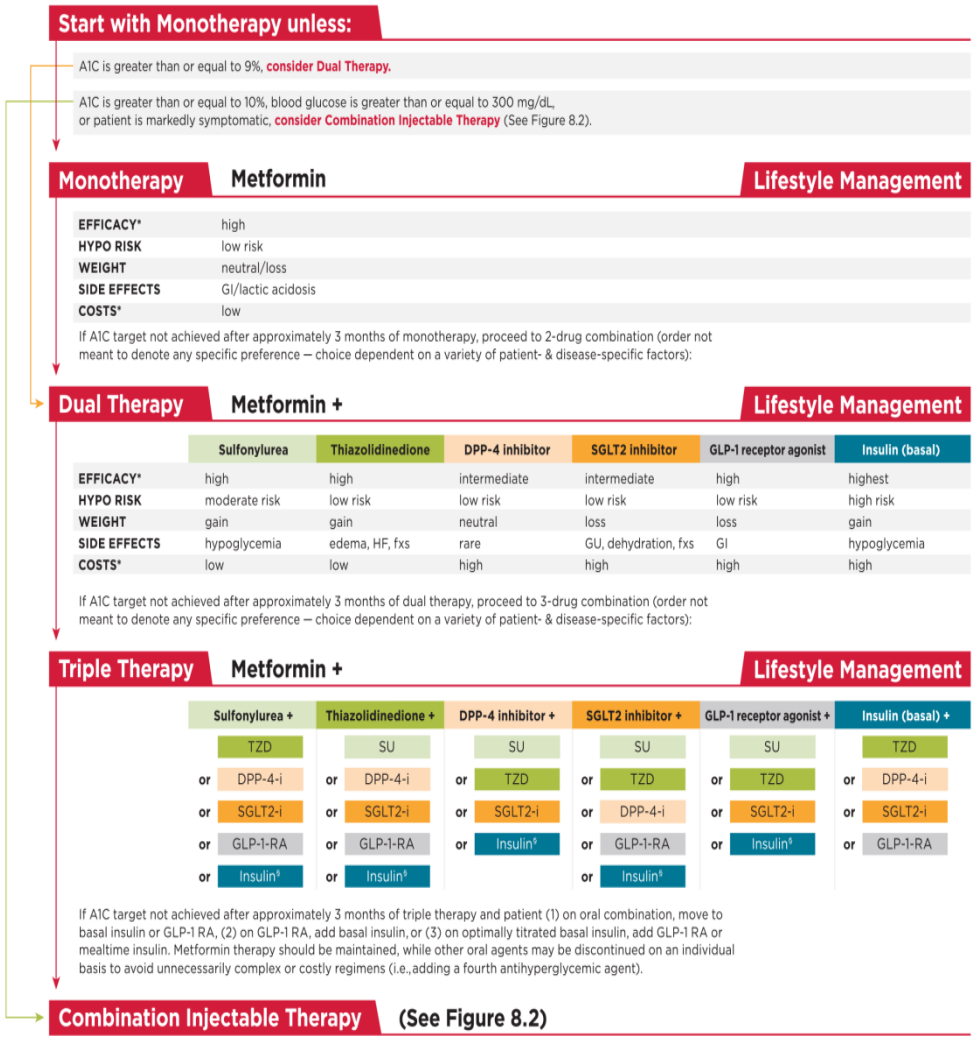
Organ/Cell	Pathophysiology	Medication
1. Muscle	Decreased glucose uptake	Metformin/TZDs/Insulin
2. Liver	Increased gluconeogenesis	Metformin/TZDs/Insulin
3. β Cells	Impaired insulin secretion	Sulphonylureas/DPP-4 Inhibitors/ GLP-1 receptor agonists/Insulin
4. α cells	Increased glucagon secretion	DPP-4 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

Caution and Contraindications

- **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.

Individualized Therapy

Antihyperglycemic Therapy in T2DM



Start with Monotherapy unless:

A1C is greater than or equal to 9%, **consider Dual Therapy.**

A1C is greater than or equal to 10%, blood glucose is greater than or equal to 300 mg/dL, or patient is markedly symptomatic, **consider Combination Injectable Therapy** (See Figure 8.2).

Monotherapy — Metformin — Lifestyle Management

EFFICACY*	high
HYPO RISK	low risk
WEIGHT	neutral/loss
SIDE EFFECTS	GI/lactic acidosis
COSTS*	low

If A1C target not achieved after approximately 3 months of monotherapy, proceed to 2-drug combination (order not meant to denote any specific preference — choice dependent on a variety of patient- & disease-specific factors):

Dual Therapy — Metformin + — Lifestyle Management

	Sulfonylurea	Thiazolidinedione	DPP-4 inhibitor	SGLT2 inhibitor	GLP-1 receptor agonist	Insulin (basal)
EFFICACY*	high	high	intermediate	intermediate	high	highest
HYPO RISK	moderate risk	low risk	low risk	low risk	low risk	high risk
WEIGHT	gain	gain	neutral	loss	loss	gain
SIDE EFFECTS	hypoglycemia	edema, HF, fxs	rare	GU, dehydration, fxs	GI	hypoglycemia
COSTS*	low	low	high	high	high	high

If A1C target not achieved after approximately 3 months of dual therapy, proceed to 3-drug combination (order not meant to denote any specific preference — choice dependent on a variety of patient- & disease-specific factors):

Triple Therapy — Metformin + — Lifestyle Management

Sulfonylurea +	Thiazolidinedione +	DPP-4 inhibitor +	SGLT2 inhibitor +	GLP-1 receptor agonist +	Insulin (basal) +
TZD	SU	SU	SU	SU	TZD
or DPP-4-i	or DPP-4-i	or TZD	or TZD	or TZD	or DPP-4-i
or SGLT2-i	or SGLT2-i	or SGLT2-i	or DPP-4-i	or SGLT2-i	or SGLT2-i
or GLP-1-RA	or GLP-1-RA	or Insulin[§]	or GLP-1-RA	or Insulin[§]	or GLP-1-RA
or Insulin[§]	or Insulin[§]		or Insulin[§]		

If A1C target not achieved after approximately 3 months of triple therapy and patient (1) on oral combination, move to basal insulin or GLP-1 RA, (2) on GLP-1 RA, add basal insulin, or (3) on optimally titrated basal insulin, add GLP-1 RA or mealtime insulin. Metformin therapy should be maintained, while other oral agents may be discontinued on an individual basis to avoid unnecessarily complex or costly regimens (i.e., adding a fourth antihyperglycemic agent).

Combination Injectable Therapy (See Figure 8.2)

8. A 42-year-old man presents to clinic for routine follow up of diabetes.He is taking:

- Metformin 500 mg three times daily
- Gliclazide 120 mg once daily
- Ramipril 10 mg once daily.

His lifestyle is still sensible. Investigations show:

- Fasting plasma glucose is 18.7 mmol/l
- HbA_{1c} 12.4%
- Urinalysis shows 4+ glucose (negative for ketones).

What is the most appropriate regimen of treatment you recommend to him?

a. Start glitazones like pioglitazone
b. Increase the dose of metformin and gliclazide
c. Start insulin therapy
d. Start DPP 4 inhibitor like sitagliptin

9. You are thinking about adjusting a type 2 diabetic insulin to improve his blood glucose. He is on Insulin Glargine 12 unit but his post prandial readings are always high ranging between (13.7 mmol/L – 17.3 mmol/L)

Which of the following insulin types is appropriate to control such levels?

a. Insulin mixed
b. Insulin NPH
c. Insulin Aspart
d. Insulin Detemir

Insulin therapy

INSULIN AS INITIAL THERAPY

- Glycated hemoglobin (A1C) >10 percent
- Fasting plasma glucose >13.9 mmol/L (>250 mg/dL)
- Random glucose consistently >16.7 mmol/L (>300 mg/dL)
- Ketonuria, or Unplanned weight loss with hyperglycemia (catabolism)

TREATMENT REGIMENS

Conventional Insulin Therapy

Two injections of NPH and Regular Insulin

Mixed Insulin

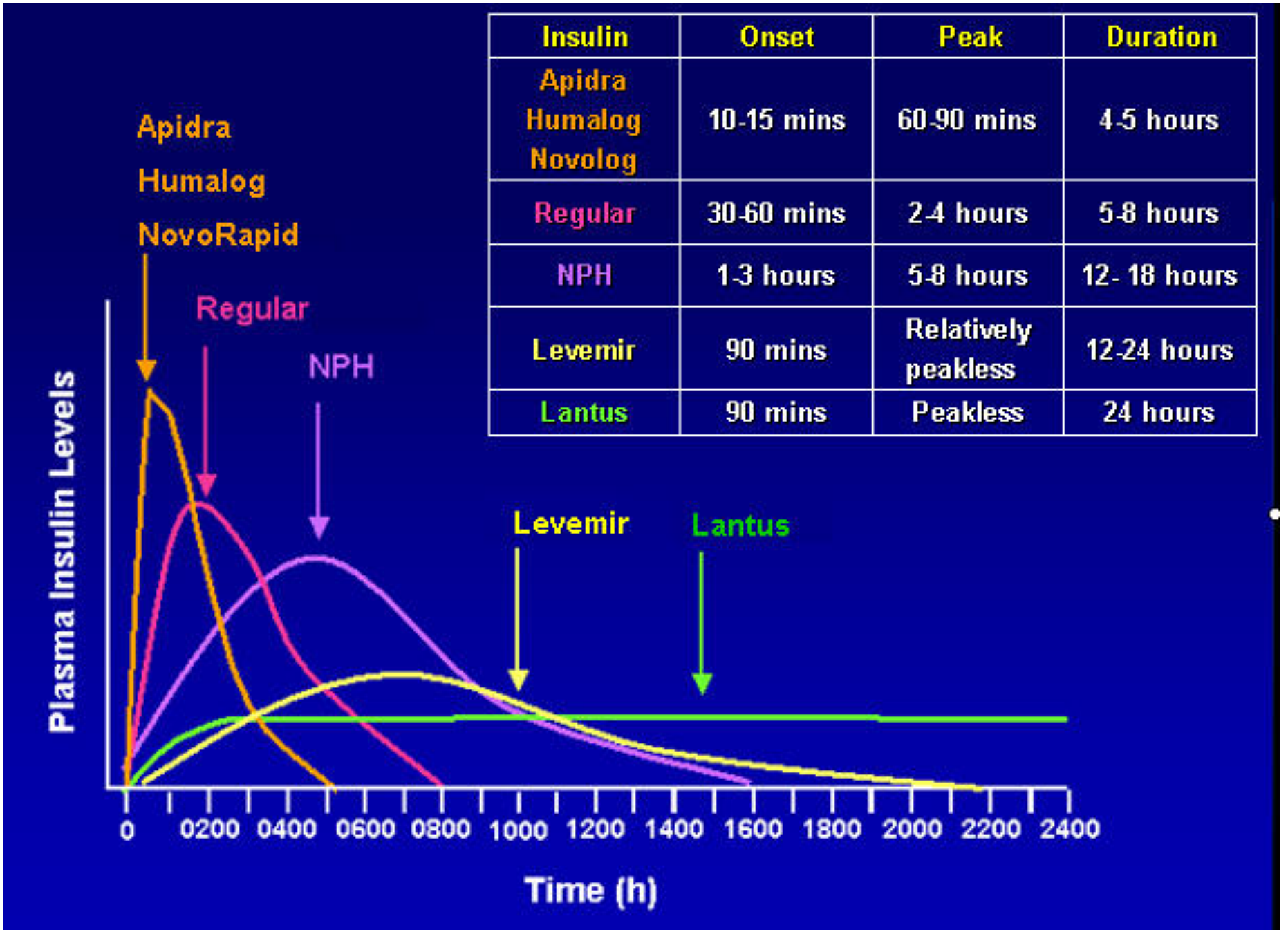
Two injections of 70/30 or 60/40 or 50/50

Multiple Insulin Injections

1 or 2 injections of NPH plus 3 injections of Regular or Rapid Insulin

One injection of Glargine or Detemir plus 3 injections of rapid insulin(Lispro /Aspart)

Insulin	Onset	Peak	Duration
Apidra Humalog Novolog	10-15 mins	60-90 mins	4-5 hours
Regular	30-60 mins	2-4 hours	5-8 hours
NPH	1-3 hours	5-8 hours	12- 18 hours
Levemir	90 mins	Relatively peakless	12-24 hours
Lantus	90 mins	Peakless	24 hours



Initiation and adjustment of insulin regimens (Multiple injections)

Long acting insulin (Glargine) at bedtime 10 U or 0.2 U/Kg

↓

Check FG, increase by 2 U every 3-4 days until FG 80 – 130 mg/dl

↓

If hypoglycaemia occurs, or FG < 70 mg/dl reduce bedtime by 4 units or 10 % which is greater.

↓

If FG in range, check 2 hrs after breakfast, lunch and dinner and add rapid (Aspart) insulin. Begin with 4 U before each. Adjust by 2 U every 3-4 days Untill 2hpp < 180 mg/dl .

↓

Usually the dose of rapid insulin is near equal or higher than dose of Long acting insulin

DM visits

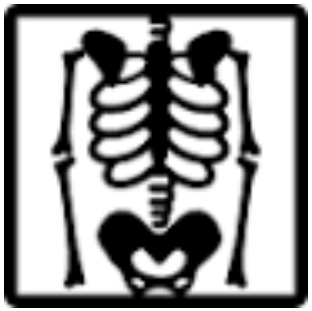
- Diabetes care is a team work
- Individualize management
- Set Target goals
  - **Glycaemic Targets**
  - **BP goals**
  - **Lipid goals**
- Education
- Is associated with increased use of primary and preventive services and lower use of acute, inpatient hospital services.

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

Investigation

- FPG and 2 hr PP
- Midstream Urine (for Ketones, protein, pus cells,…)
- Urea and Creatinine
- Lipid Profile (total cholesterol, LDLc, HDLc and triglycerides)
- HbA1C (every 3 m for insulin / every 6 m for controlled)
- Test for Microalbuminuria or Albumin to creatinine ratio / 24 hr urine collection for protein / Creatinine Clearance
- ECG
- Chest X-Ray



Yearly Check Up

Investigations

- HbA1C
- Urea and Creatinine
- Lipid Profile (Cholesterol, Triglyceride, LDL-C and HDL-C)
- Albumin to creatinine ratio / 24 hour urine collection for protein (Microalbuminuria 30 -<300 mg while Macroalbuminyria ≥ 300 mg).

Check :

- Eye: Fundus Examination / eye referral
- Feet : Visual inspection and Neurovascular status

10. The post postpartum care of a patient who developed GDM in the last month of her pregnancy would include the following:

a. A OGTT at 12 weeks, if negative screening every 3 years, instructions to maintain a healthy weight
b. OGTT 7 days after delivery, only test again if she gets pregnant, advised to live a healthy lifestyle
c. Do a fasting blood test 6 weeks postpartum, if negative repeat in another 6 months, keep a healthy weight
d. Fasting blood test at 6 weeks postpartum, must take metformin as she is at increased risk for developing diabetes


THE END