Therapeutic areas – Part 3

Module 4 Topic 5

Respiratory Disorders

Cough

- Sudden, forceful expulsion of air from the lungs
- Purpose - to clear material from the airways and to protect the lungs
- Types - dry (unproductive) or productive
- Common causes
  - For **acute cough**
    - An upper respiratory infection (URI), including acute bronchitis
    - Postnasal drip (drainage of secretions from the nose down the throat, or pharynx)
    - Pneumonia

Cough (contd)

- Causes for **chronic cough**
  - Chronic bronchitis
  - Gastroesophageal reflux (GERD)
  - Tuberculosis
  - Lung cancer
- Treatment of Cough
  - Treat the underlying disorder e.g. infections
  - Cough suppressants - antitussives e.g. dextromethorphan
  - Expectorants e.g. guaifenesin
  - Decongestants e.g. phenylephrine for cough caused by postnasal drip

Acute Bronchitis

- Inflammation of the trachea and the airways (bronchi)
- Usually caused by viral infections
- Treatments, such as antipyretics and antitussives are used for symptom relief; Antibiotics are usually not needed
- **Bacterial bronchitis** occasionally follows a viral upper respiratory infection; treated with azithromycin or clarithromycin

Asthma

- Condition in which the airways narrow (bronchoconstriction) in response to certain stimuli
- Asthma triggers
  - Allergens e.g. dust mites, secretions from cockroaches, feathers and animal dander
  - Infections e.g. colds, bronchitis
  - Irritants e.g. smoke from tobacco, fumes, cold air; and stomach acid
  - Exercise (called exercise-induced asthma)
  - Stress and anxiety
  - Aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs)
- Status asthmaticus - severe, intense, prolonged airway narrowing that is resistant to treatment

Asthma (contd)

- **Treatment**
  - Bronchodilators e.g. salbutamol
  - Corticosteroids
  - Methylxanthines e.g. theophylline
- **Prevention**
  - Leukotriene Modifiers e.g. montelukast
  - Mast Cell Stabilizers e.g. sodium cromoglycate

Pneumonia

- Acute inflammation of the lungs due to infection
- Types
  - Community-acquired
  - Hospital-acquired (including ventilator-acquired and postoperative pneumonia)
  - Bacterial causes - S. pneumoniae, H. influenzae, C. pneumoniae, and M. pneumoniae
  - Viral causes - respiratory syncytial virus (RSV), adenovirus, influenza viruses, metapneumovirus, parainfluenza viruses, and coronavirus (SARS)
  - Treatment - Antibiotics, Antivirals Supportive measures
- Also, pneumonia in immunocompromised patients, including patients with HIV infection and aspiration pneumonia

What is High Blood Pressure?

- Blood pressure is the force exerted on the arterial walls by flowing blood
- High blood pressure (hypertension) indicates that blood pressure - is consistently high.
- Blood pressure is recorded as two numbers:
- Systolic blood pressure (the upper number) - indicates how much pressure your blood is exerting against artery walls when the heart beats.
- Diastolic blood pressure (the lower number) - indicates how much pressure your blood is exerting against your artery walls while the heart is resting between beats

Hypertension

Blood Pressure Category	Systolic mm Hg (upper #)		Diastolic mm Hg (lower #)
Normal	less than 120	and	less than 80
Prehypertension	120 – 139	or	80 – 89
High Blood Pressure (Hypertension) Stage 1	140 – 159	or	90 – 99
High Blood Pressure (Hypertension) Stage 2	160 or higher	or	100 or higher
Hypertensive crisis (Emergency care needed)	Higher than 180	or	Higher than 110

Pathophysiology of hypertension

- Pathophysiology still uncertain
- A small number of patients (2% and 5%) have an underlying renal or adrenal disease (**Secondary HT**)
- In the remainder, no clear identifiable cause is found (**Essential HT**)
- Many interrelated factors contribute to the raised blood pressure in hypertensive patients, and their relative roles may differ between individuals

Hypertension Complications

Mainly diseases due to target organ damage

- Heart
  - Coronary artery disease
  - Left ventricular hypertrophy
  - Heart failure
- Brain cerebrovascular
  - Stroke
  - Dementia
- Kidneys - nephrosclerosis
- Eyes retinopathy
- Peripheral Vascular Disease, erectile dysfunction

Lifestyle modification

- Weight loss
- Exercise
- Low salt diet
- Stress management and relaxation therapy
- Stop smoking
- Decreased alcohol intake

Pharmacotherapy of hypertension

Drug Class	Mode of action	Major side effects
Diuretics - Thiazides, Furosemide, K sparing	Increase Na and water excretion, reduce blood volume	Eletrolyte imbalance, hyperglycaemia, hyperuricemia
ACE inhibitors – Enalapril, Ramipril	Inhibit synthesis of Angiotensin II – decrease in peripheral resistance	Cough, angioedema, hypotensiondysgeusia
Angiotensin AT1 blockers – valsartan, telmisartan, Olmesartan	Blocks binding of Angiotensin II to its receptors	Low incidence of above side effects of ACE inhibitors
Beta blockers- Propranolol, Atenolol	Block beta receptors, reduced force and rate of contraction	Fatigue, lethargy, loss of libido

Pharmacotherapy of hypertension

Drug Class	Mode of action	Major side effects
Alpha blockers – Prazocin, Terazocin	Blocking of alpha receptors in smooth muscles – vasodilatation	Headache, dry mouth, postural hypotension
Ca channel blockers – Nifedipine, verapamil	Blocks influx of Ca++ in smooth muscle cells, vasodilation	Dizziness, fatigue, headache, itching
Vasodilators – Nitrates	Vasodilation	Palpitation, tachycardia, Na retention
K channel blockers - Minoxidil	Vasodilation	Hair growth
Centrally acting – Clonidine, methyldopa	Act on central α2A receptors to decrease sympathetic outflow – fall in BP	Cognitive impairment, postural hypotension, rebound hypertension

LIPIDS: Composition, Types and Function

What are lipids?

- Lipids are chemical compounds which are present in two forms in the body viz.
  - Triglycerides
  - Cholesterol

Triglycerides

- They are a combination of glycerol and fatty acids
- They provide energy for different metabolic process
- Excess triglycerides are stored in adipose tissues

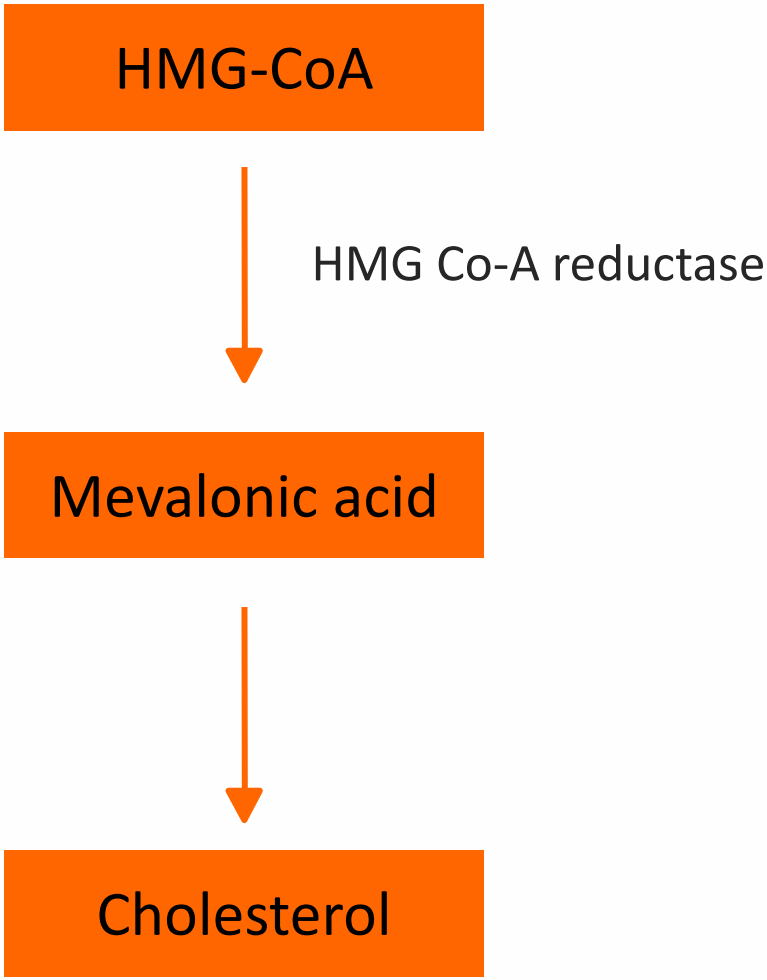
Cholesterol

- It is chemically a sterol and is found widely in animal tissues
- It is present in egg yolk, various oils, liver, kidneys and adrenal glands
- Cholesterol is utilized by liver to synthesize various bile salts and bile acids which help in metabolism of nutrients as well as drugs.
- Cholesterol is useful in cell wall synthesis
- Cholesterol is used by liver for synthesis of steroids and sex hormones

What do you mean by 'useful cholesterol' and 'harmful cholesterol'?

- Excess of LDL is dangerous as it leads to atherosclerosis. LDL is therefore harmful and LDL cholesterol is harmful cholesterol.
- On the contrary, function of HDL is to pick up excess cholesterol from the tissues and transport back to liver. HDL is therefore a good cholesterol.

How is cholesterol synthesized in liver



What are normal levels of lipids in the blood?

Normal levels of lipids are as follows:

Lipoproteins	Desired Concentrations In Blood
Total cholesterol	< 200mg/dl
LDL	< 130 mg/dl
HDL	> 60mg/dl
Triglycerides	< 200mg/dl

LIPID Disorders

Hyperlipidemia

- Hyper+ lipid + emia = excess of cholesterol/ triglycerides in the blood.

Hypercholesterolemia

- Higher than normal levels (> 200mg/dl) of cholesterol in the blood.

Hypertriglyceridemia

- Higher than normal levels (> 200mg/dl) of triglycerides in the blood

Excess lipid levels may

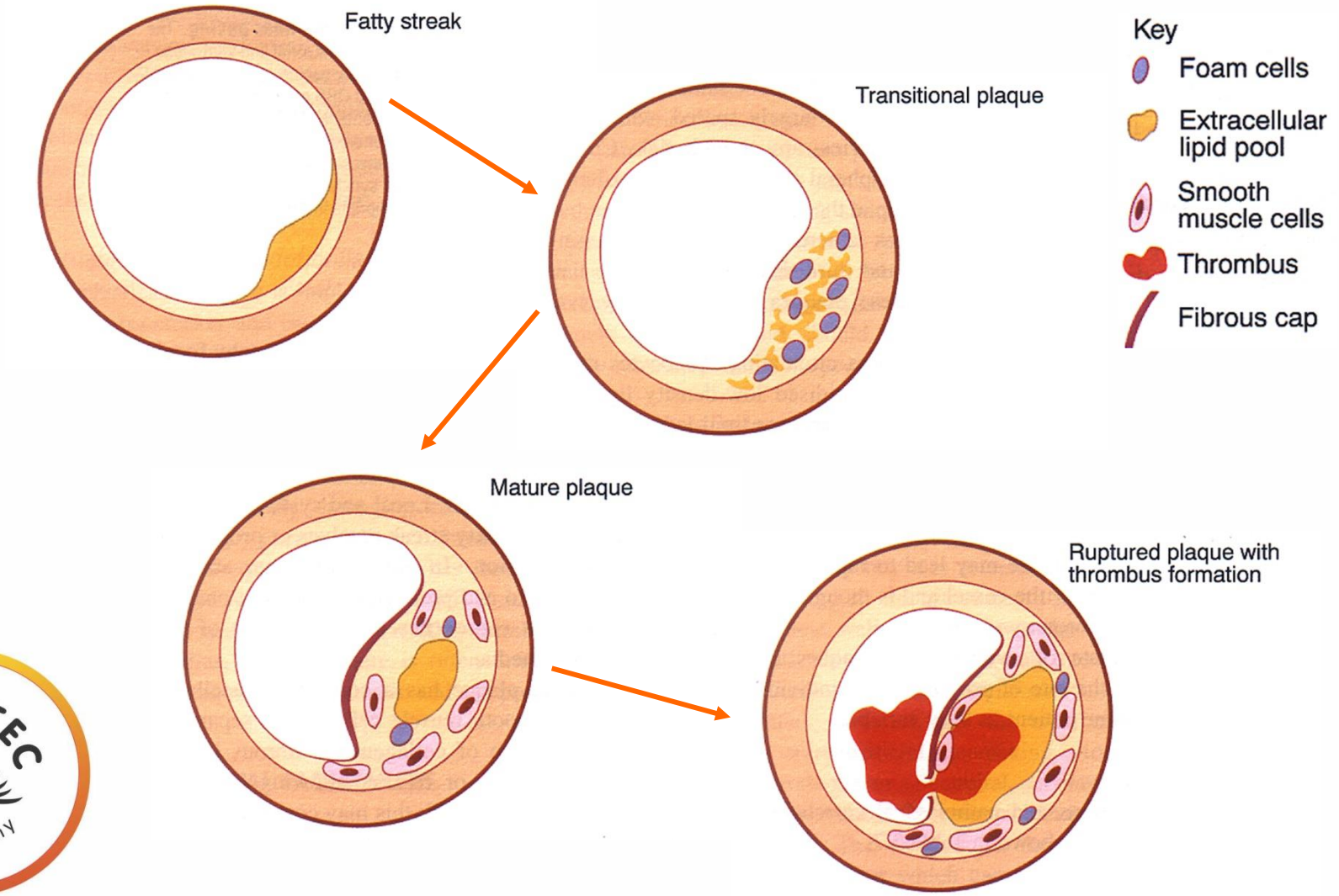
- Enhance atherosclerosis
- Lead to coronary artery disease
- Aggravate diabetic complications leading to accelerated atherosclerosis

Atherosclerosis

What is atherosclerosis?

- It is a disease of arteries which is characterized by thickening of the vessel and lipid accumulation in the innermost layer of the blood vessel
- The lipid deposits, ultimately results in the formation of a yellow patch called 'plaque' on the inner surface

Process of Atherosclerosis



Management of Hyperlipidemia

- Reduce saturated fat intake to provide about only 30% of total fat intake
- Reduce total fat intake to provide only about 30% of energy intake
- Reduce alcohol intake

Lipid-Lowering drugs

- HMG CoA reductase inhibitors (e.g, simvastatin, pravastatin, atorvastatin)
  - Inhibit cholesterol biosynthesis in the liver
  - LDL reduction 25-45%
- Bile acid sequestrant resins (e.g cholestyramine, colestipol)
  - Block intestinal reabsorption of bile acids
  - LDL reductions by 10-35%, HDL increased by 5%
- Nicotinic acid
  - Activate LPL
  - TG reduced by 20- 80%, LDL reduced by 10-15%

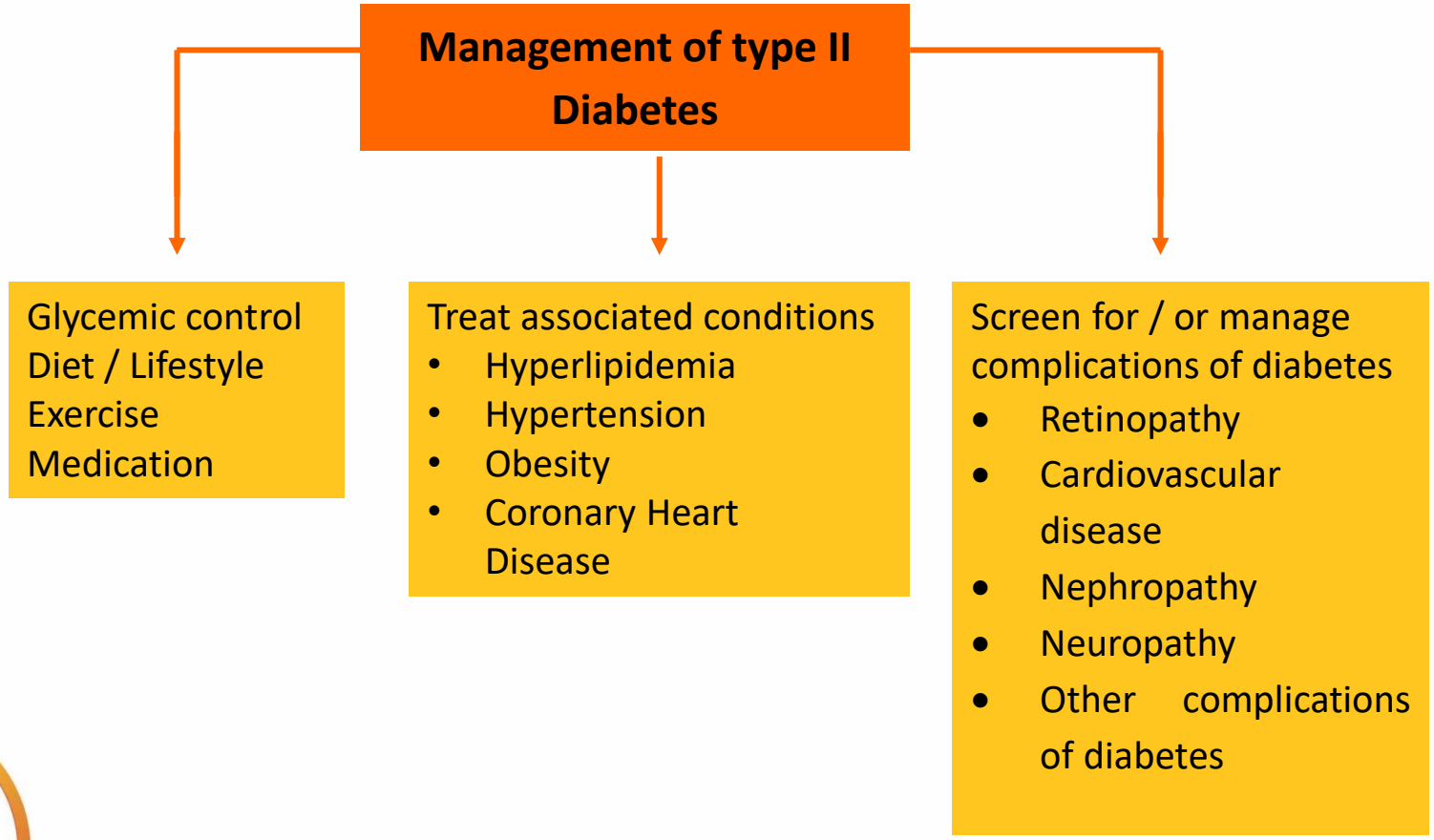
Diabetes mellitus

- Disorder of carbohydrate metabolism , results from inadequate production or underutilization of insulin
- Characterized by glucosuria and hyperglycemia
- Symptoms: polyuria, polydipsia, polyphagia, and possibly itching
- Complications:
  - **Diabetic Retinopathy**, **Diabetic neuropathy, Diabetic nephropathy, Foot ulcers**,
  - Peripheral vascular disease & gangrene,
  - Impotence,
  - delayed gastric emptying & impaired bladder function,
  - Increased risk of infection of skin, oral and vaginal candidiasis

Diabetes mellitus - Overview

- Two forms
  - Type 1 - patient secretes no insulin. Cause is felt to be autoimmune.
  - Patient needs insulin regularly
  - Type 2 - patient secretes insufficient amounts of insulin and insulin receptors are resistant to circulating insulin

Diabetes mellitus - Overview



Diabetes mellitus - Overview

Diet recommendations:

- Weight reduction in obese patients & maintenance of appropriate weight
- Carbohydrates should provide 45 - 60 % of daily caloric intake depending on severity of diabetes
- Restriction of saturated fat to < 10 % of daily caloric intake
- Increased use of monounsaturated fats (e.g. olive oil, peanut oil)
- Decreased cholesterol intake to < 200 mg/d
- Sodium restriction in patients with / prone to hypertension

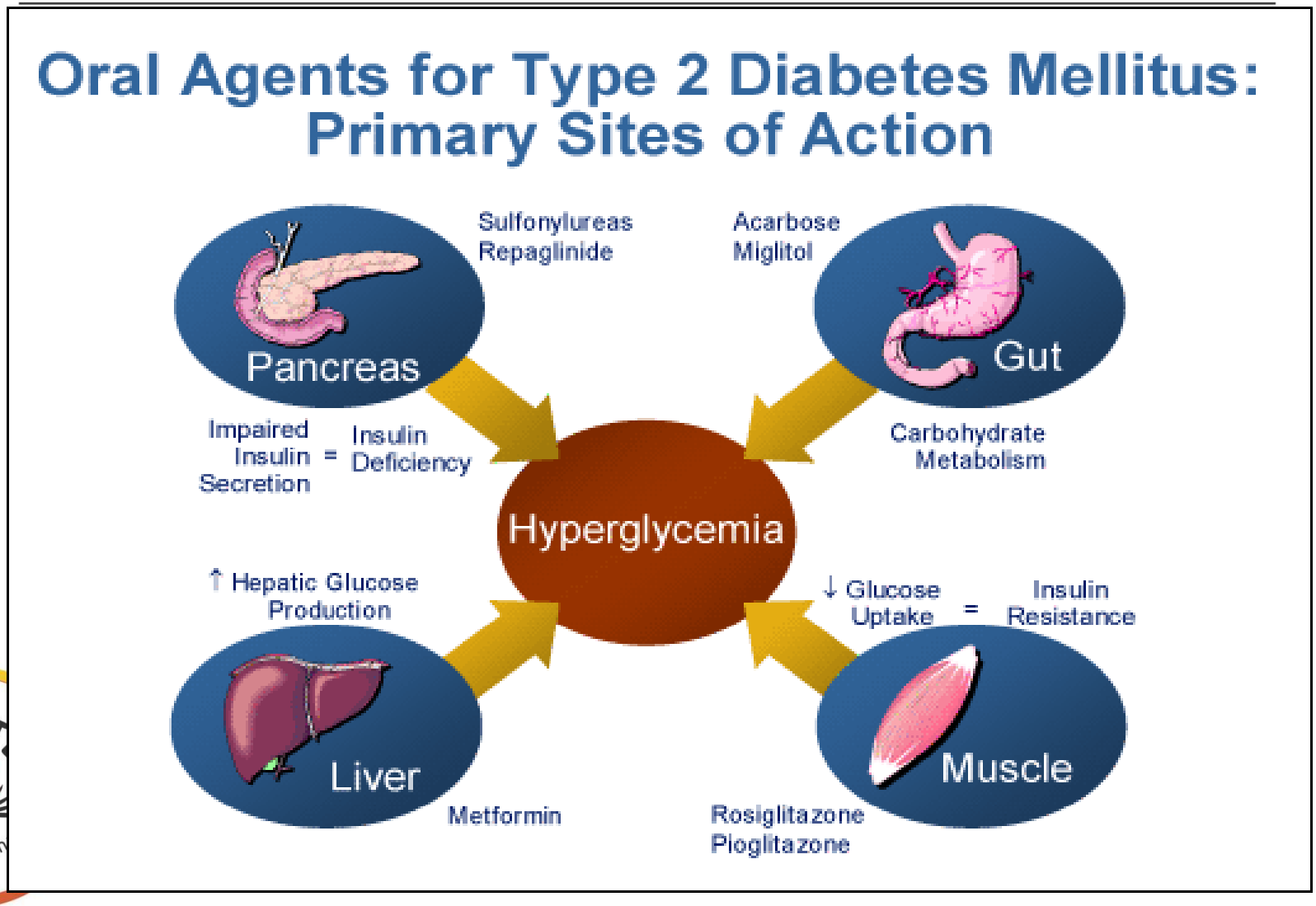
Diabetes mellitus - Overview

Oral hypoglycaemic agents

- **Sulfonylureas** e.g. glyburide, glipizide, glimperide
- **Biguanides** e.g. metformin
- **Meglitinides** e.g. repaglinide, nateglinide
- **Alpha-glucosidase Inhibitors** e.g. acarbose, miglitol
- **Thiazolidinediones** (peroxisome proliferator-activated receptor g i.e. ppr g inhibitors) e.g. pioglitazone, rosiglitazone
- **Dipeptidyl peptidase IV** (DPP-4 Inhibitors) e.g. sitagliptin, saxagliptin, linagliptin
- **GLP-1 receptor agonists** e.g. exenatide, liraglutide
- **SGLT2 inhibitors** e.g. canagliflozin, dapagliflozin
- **Amylin agonist** e.g. pramlintide
- **Combination Medicines**

SGLT2 = Sodium Glucose Cotransporter 2 (located in the kidneys)

Diabetes mellitus - Overview



Endocrinology

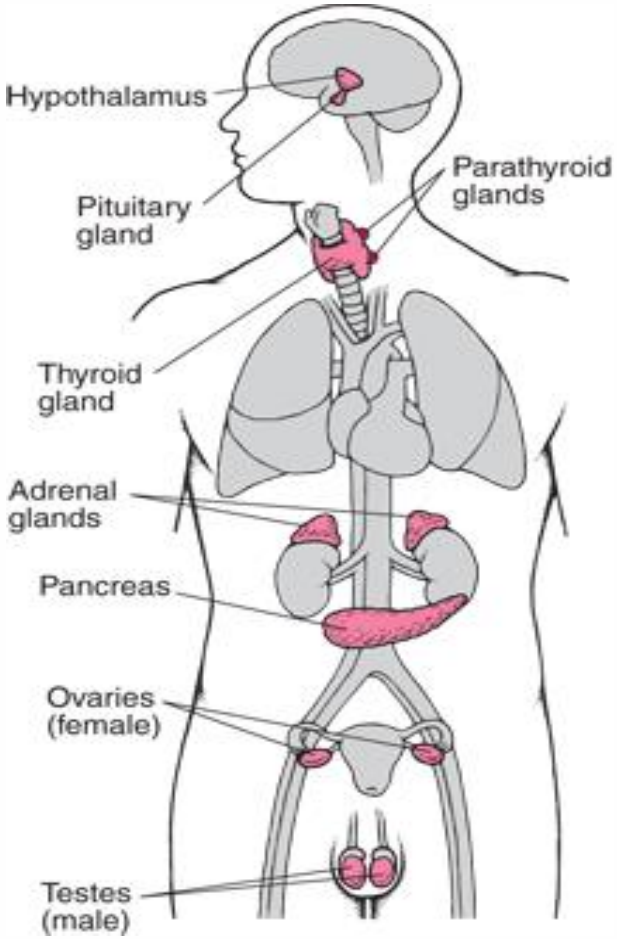
- Endocrine system consists of a group of glands and organs that regulate and control various body functions by producing and secreting hormones
- hormones serve as messengers, controlling and coordinating activities throughout the body
- *Endocrine* glands release their hormones directly into the *bloodstream*

Major Endocrine Glands

- Hypothalamus
- Pituitary gland
- Thyroid gland
- Parathyroid glands
- Islet cells of the pancreas
- Adrenal glands
- Testes in men, and the ovaries in women
- Pancreas is both an endocrine and exocrine gland

Endocrinology

Major Endocrine Glands



Major Hormones

Produced by	Hormone	Function
Hypothalamus	Thyrotropin-releasing hormone	Stimulates the release of thyroid-stimulating hormone and prolactin
	Gonadotropin-releasing hormone	Stimulates release of luteinizing hormone and follicle-stimulating hormone
	Corticotropin-releasing hormone	Stimulates release of adrenocorticotropic hormone
	Growth hormone–releasing hormone	Stimulates release of growth hormone
	Somatostatin	Inhibits release of growth hormone, thyroid-stimulating hormone, and insulin

Major Hormones

Produced by	Hormone	Function
Pituitary gland	Vasopressin (antidiuretic hormone)	Causes kidneys to retain water and, along with aldosterone, helps control blood pressure
	Corticotropin (ACTH)	Controls the production and secretion of hormones by the adrenal glands
	Growth hormone	Controls growth and development Promotes protein production
	Luteinizing hormone and follicle-stimulating hormone	Control reproductive functions, including the production of sperm and semen in men and egg maturation and menstrual cycles in women Control male and female sexual characteristics (including hair distribution, muscle formation, skin texture and thickness, voice, and perhaps even personality traits)
	Oxytocin	Causes muscles of the uterus to contract during childbirth and after delivery and stimulates contractions of milk ducts in the breast, which move milk to the nipple
	Prolactin	Starts and maintains milk production in the ductal glands of the breast (mammary glands)
	Thyroid-stimulating hormone	Stimulates the production and secretion of hormones by the thyroid gland

Major Hormones

Produced by	Hormone	Function
Parathyroid glands	Parathyroid hormone	Controls bone formation and the excretion of calcium and phosphorus
Thyroid gland	Thyroid hormone	Regulates the rate at which the body functions (metabolic rate)
	Calcitonin	Tends to decrease blood calcium levels and helps regulate calcium balance
Adrenal glands	Aldosterone	Helps regulate salt and water balance by causing the kidneys to retain salt and water and excrete potassium
	Cortisol	Has widespread effects throughout the body Especially has anti-inflammatory action Maintains blood sugar level, blood pressure, and muscle strength Helps control salt and water balance
	Dehydroepiandrosterone (DHEA)	Has effects on bone, mood, and the immune system
	Epinephrine and norepinephrine	Stimulate the heart, lungs, blood vessels, and nervous system

Major Hormones

Produced by	Hormone	Function
Pancreas	Glucagon	Raises the blood sugar level
	Insulin	Lowers the blood sugar level Affects the processing (metabolism) of sugar, protein, and fat throughout the body
Kidneys	Erythropoietin	Stimulates red blood cell production
	Renin	Controls blood pressure
Ovaries	Estrogen	Controls the development of female sex characteristics and the reproductive system
	Progesterone	Prepares the lining of the uterus for implantation of a fertilized egg and readies the breasts to secrete milk
Testes	Testosterone	Controls the development of male sex characteristics and the reproductive sy

Endocrine disorders

- Hyperthyroidism
- Hypothyroidism
- Cushing disease (Oversecretion of glucocorticoids)
- Addison disease
- Acromegaly
- Short stature in children
- Diabetes mellitus