# GENERAL INTERNAL MEDICINE REVIEW COURSE

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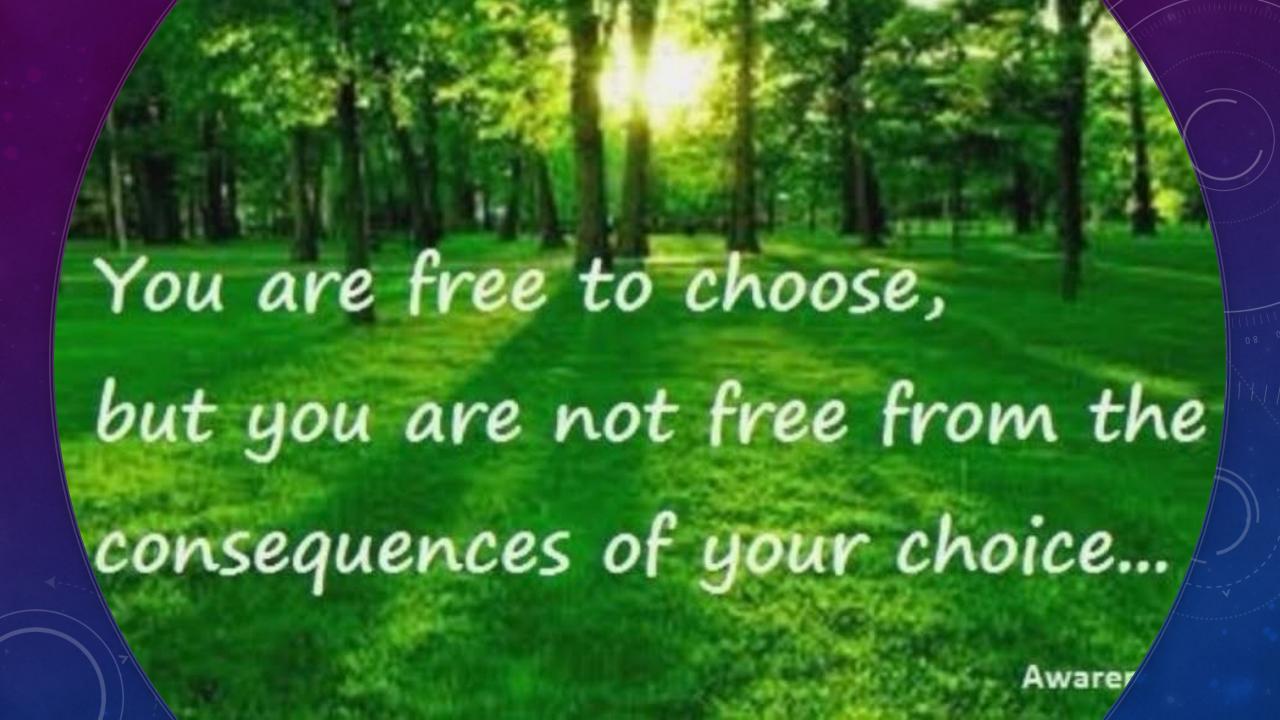
- DUE TO TIME CONSTRAINTS content of some slides will be only discussed briefly but is here so you can STUDY it on your OWN
- Each organ system has multi-year subspecialty training
- Expectations: establish a working diagnosis, initiate treatment, know when to refer to a specialist
- Limitations: diagnostic testing, availability of specialists
- Do the best you can (medical ethics)
  - If it's key to the diagnosis, facilitate external testing
  - Give it your best guess and initiate treatment and assess for response
  - Refer to specialist when indicated
  - See them back to coordinate care

# ENDOCRINE DISORDERS

- Pancreas -> Insulin resistance & Diabetes
- Thyroid gland -> Hypothyroidism and Hyperthyroidism
- Adrenal glands -> Addison's disease / Cushing's disease

#### GOOD HEALTH

- "Do you not know that your body is a temple? Therefore honor God with your body."
  - 1 Corinthians 6:19, 20
- "So whether you eat or drink, or whatever you do, do it all for the glory of God."
  - 1 Corinthians 10:31

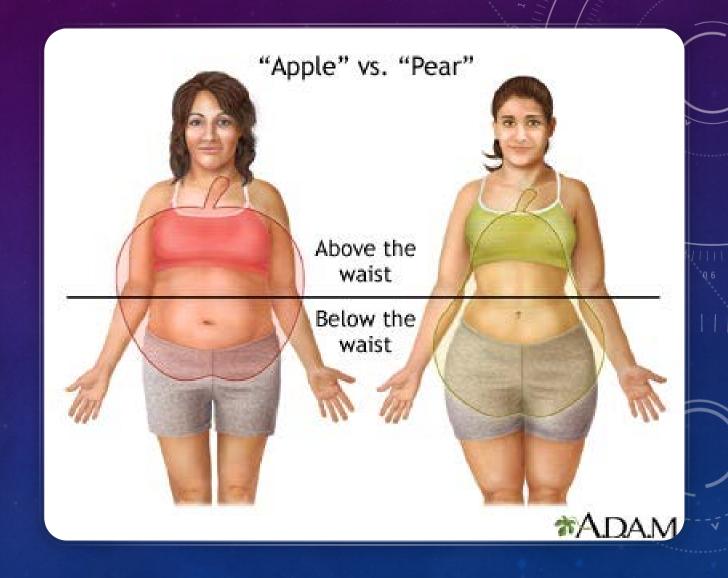


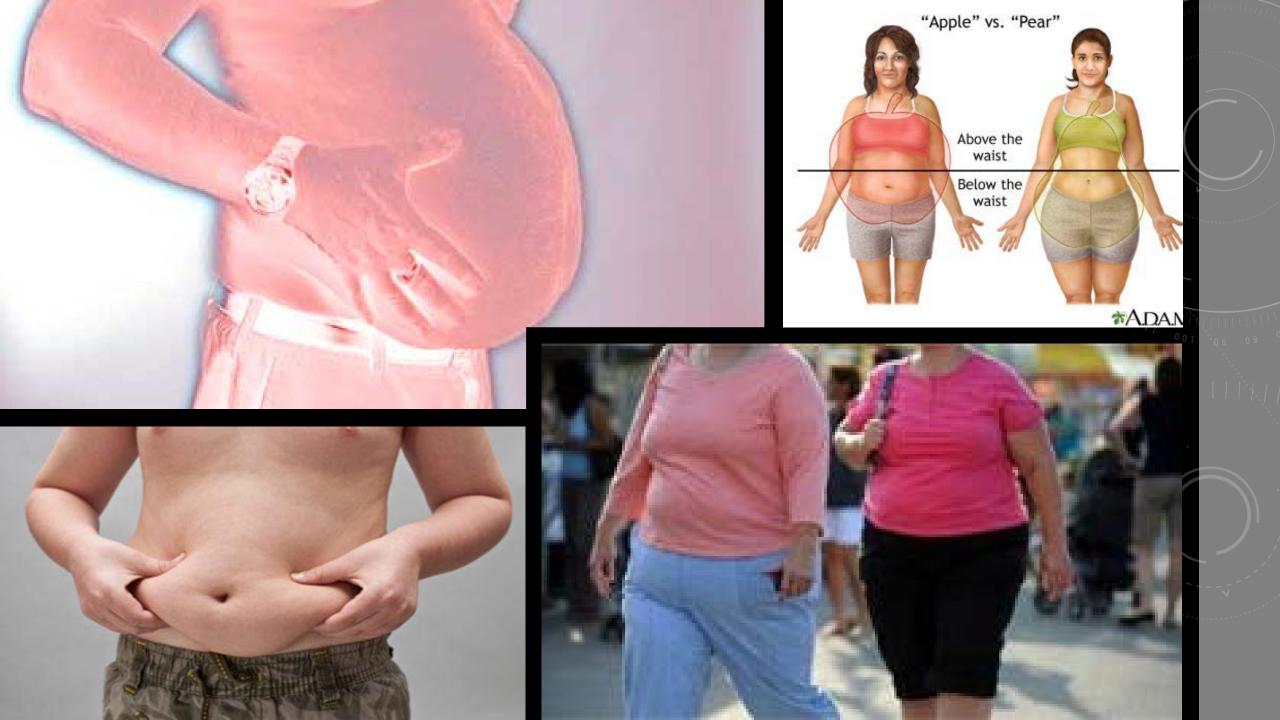
- Syndrome with 4 parts (insulin resistance)
  - Central obesity
  - High blood sugar
  - High blood pressure
  - Abnormal lipids (high trigs and/or low HDL)

- Most develop overt diabetes over time
- Markedly increased risk for cardiovascular events (heart disease & stroke)

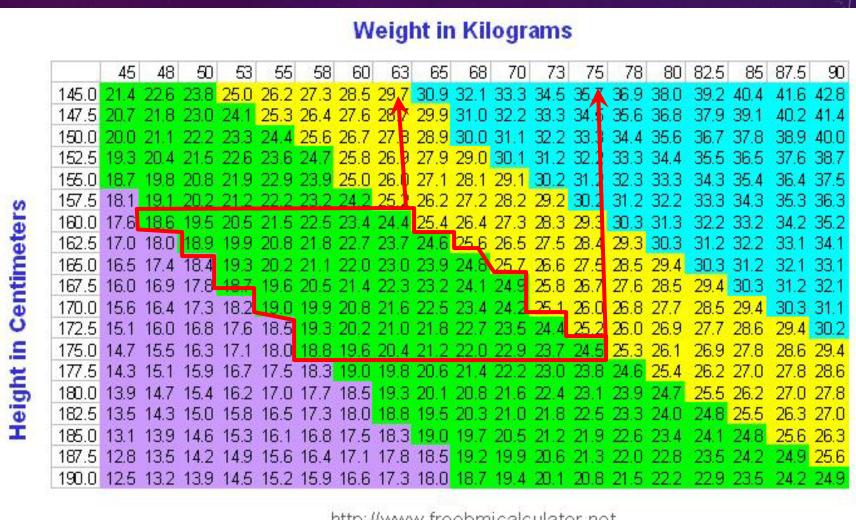
#### CENTRAL OBESITY

- Measured by waist circumference
- Risk of heart attack & diabetes much higher in central obesity
- Measure at belly button
  - Women > 88 cm
  - Men > 102 cm





#### **BODY MASS INDEX**



http://www.freebmicalculator.net

Underweight



Overweight

Obesity

- Syndrome with 4 parts (insulin resistance)
  - Central obesity
  - High blood sugar
  - High blood pressure
  - Abnormal lipids (high trigs and/or low HDL)

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#### HIGH BLOOD SUGAR

- "borderline" or elevated fasting blood sugar
  - Between 100 and 125mg/dL
  - About 10% per year develop full diabetes
- Mildly elevated HgbA1c (5.7% to 6.5%)

- Diabetes
  - FBS above 126mg/dL or HgbA1c above 6.5%
  - RBS above 200mg/dL

- Syndrome with 4 parts (insulin resistance)
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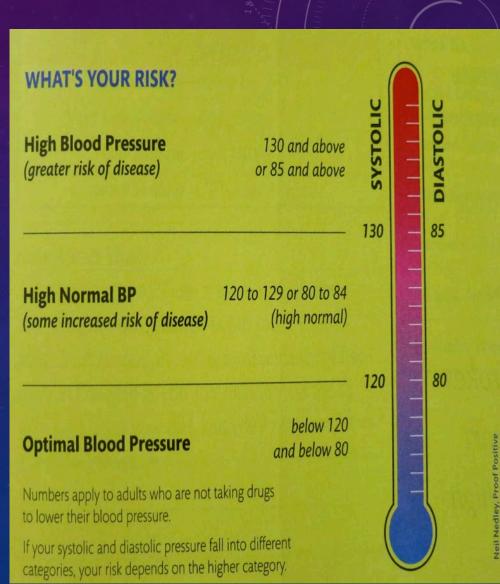
#### HIGH BLOOD PRESSURE

#### Nutrition

 High potassium, low salt diet can improve BP by 10-15 points!

#### Exercise

 Regular exercise can lower BP by another 8 points!



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  - High blood pressure
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#### Elevated triglycerides

 Above 150mg/dL (1.7mmol/dL)

#### Low HDL cholesterol

- Women below 50 mg/dL
- Men below 40 mg/dL

ABNORMAL CHOLESTEROL

- Syndrome with 4 parts
  - Central obesity
  - High blood sugar (including borderline)
  - High blood pressure ("pre-hypertension")
  - Abnormal lipids (high trigs or low HDL)

Any 3 of the 4 equals metabolic syndrome

# WHY DO WE CARE?

- Up to 2x the risk of stroke and heart attack
- Some US studies 2.6 times higher cardiovascular death and 2 times higher all cause mortality EVEN IN THE ABSENCE of baseline cardiovascular disease and diabetes
- Risk of cardiovascular event or death is similar to those with "full" diabetes or hypertension

### Etiology

- Insulin resistance
- Cells have reduced use of insulin & fats
- Pancreas has higher production of insulin

#### **ENERGY EFFICIENCY**

- Example: taking a long road trip
  - How many liters of petrol will you need?
  - Depends on your car
  - Depends on fuel efficiency







#### ENERGY EFFICIENCY

- Example: taking a road trip
  - How many liters of petrol will you need?
  - Depends on your car
  - Depends on fuel efficiency
- Caloric intake
  - Some people **USE** calories (fat, carbohydrates) much more
  - Others EAT more calories than they need
  - Excess calories are "stored" in the body for later use (central obesity)
  - Genetics: Asians and Hispanics more likely

- Syndrome with 4 parts
  - Central obesity
  - High blood pressure
  - High blood sugar
  - Abnormal cholesterol

- Treatment
  - Diet & Lifestyle modification
  - Medications

# MAKE A **NEW START** TODAY!

- **N**utrition
- **E**xercise
- Water
- **S**unlight
- **T**emperance
- Air
- <u>R</u>est
- **T**rust in God



#### SUCCESSFUL WEIGHT CONTROL

Long-term behavioral treatment, whatever form it takes, encourages patients to practice four key behaviors

- 1. Exercise regularly
- 2. Consume a lower-calorie diet
- 3. Monitor weight regularly
- 4. Record food intake and physical activity

#### WEIGHT LOSS

- As little as 5-10% weight loss results in
  - improved blood tests (glucose, cholesterol)
  - improved blood pressure
  - reduced cardiovascular mortality

- Set realistic goals with patients
  - 10% in 3-6 months
  - From 110kg to 100kg or from 100kg to 90kg



THIS ONE
RUNS ON MONEY
AND MAKES
YOU FAT



THIS ONE
RUNS ON FAT
AND SAVES
YOU MONEY



- Treatment Medications
  - Target FBS < 150 and HgbA1c < 7.5%</li>
    - Start with oral hypoglycemics
    - Metformin (first line) + sulfonylurea (if needed)
    - SGLT2 inhibitor (dapagliflozin, empagliflozin, canaglifozin)
    - "glitazones" + sitagliptin
    - Insulins
  - Target BP < 140/85mmHg
    - Diuretics
    - Ace-I or ARB if proteinuria
    - Beta blockers/calcium channel blockers
  - Use aspirin & statins for all if no contraindication

### CVD / ASCVD RISK

- Known atherosclerosis
  - Peripheral vascular disease
  - Prior heart attack
  - Stroke
- Diabetes
- High risk profile (age, family history etc)
  - Framingham, European Heart Score

- Primary Cholesterol target is LDL
  - Latest ACC/AHA guidelines emphasize that <u>statins</u> are the mainstay of therapy and do not encourage other therapies
  - Highly controversial to target a number (LDL < 70) versus high intensity therapy
- Secondary targets
  - Non-HDL cholesterol targets
  - Triglyceride targets

# ATP III CHOLESTEROL GUIDELINES

HMG CoA reductase inhibitors (statins)	Agents and Daily Doses	Lipid/Lipoprotein Effects		Side Effects	Contraindications
	Lovastatin (20-80 mg) Pravastatin (20-40 mg) Simvastatin (20-80 mg) Fluvastatin (20-80 mg) Atorvastatin (10-80 mg) Cerivastatin (0.4-0.8 mg)	LDL HDL TG	↓18-55% ↑5-15% ↓7-30%	Myopathy Increased liver enzymes	Absolute:  • Active or chronic liver disease  Relative:  • Concomitant use of certain drugs*
Bile acid sequestrants	Cholestyramine (4-16 g) Colestipol (5-20 g) Colesevelam (2.6-3.8 g)	LDL HDL TG	↓15-30% ↑3-5% No change or increase	Gastrointestinal distress Constipation Decreased absorption of other drugs	Absolute: • dysbeta- lipoproteinemia • TG >400 mg/dL Relative: • TG >200 mg/dL
Nicotinic acid	Immediate release (crystalline) nicotinic acid (1.5-3 gm), extended release nicotinic acid (Niaspan®) (1-2 g), sustained release nicotinic acid (1-2 g)	LDL HDL TG	↓5.25% ↑15.35% ↓20.50%	Flushing Hyperglycemia Hyperuricemia (or gout) Upper GI distress Hepatotoxicity	Absolute:     Chronic liver disease     Severe gout Relative:     Diabetes     Hyperuricemia     Peptic ulcer disease
Fibric acids	Gemfibrozil (600 mg BID) Fenofibrate (200 mg) Clofibrate (1000 mg BID)		↓5-20% increased in with high TG) ↑10-20% ↓20-50%	Dyspepsia Gallstones Myopathy	Absolute:  • Severe renal disease  • Severe hepatic disease

#### ELEVATED TRIGLYCERIDES

#### Treat elevated triglycerides.

#### ATP III Classification of Serum Triglycerides (mg/dL)

<150	Normal
150-199	Borderline high
200-499	High
≥500	Very high

#### Treatment of elevated triglycerides (≥150 mg/dL)

- Primary aim of therapy is to reach LDL goal
- Intensify weight management
- Increase physical activity
- If triglycerides are ≥200 mg/dL after LDL goal is reached, set secondary goal for non-HDL cholesterol (total – HDL) 30 mg/dL higher than LDL goal.

#### Comparison of LDL Cholesterol and Non-HDL Cholesterol Goals for Three Risk Categories

Risk Category	LDL Goal (mg/dL)	Non-HDL Goal (mg/dL)
CHD and CHD Risk Equivalent (10-year risk for CHD >20%)	<100	<130
Multiple (2+) Risk Factors and 10-year risk <20%	<130	<160
0-1 Risk Factor	<160	<190

If triglycerides 200-499  $\rm mg/dL$  after LDL goal is reached, consider adding drug if needed to reach non-HDL goal:

# If triglycerides 200-499 mg/dL after LDL goal is reached, consider adding drug if needed to reach non-HDL goal:

- intensify therapy with LDL-lowering drug, or
- add nicotinic acid or fibrate to further lower VLDL.

#### If triglycerides >500 mg/dL, first lower triglycerides to prevent pancreatitis:

- very low-fat diet (≤15% of calories from fat)
- · weight management and physical activity
- · fibrate or nicotinic acid
- when triglycerides <500 mg/dL, turn to LDL-lowering therapy.</li>

#### Treatment of low HDL cholesterol (<40 mg/dL)

- First reach LDL goal, then:
- Intensify weight management and increase physical activity
- If triglycerides 200-499 mg/dL, achieve non-HDL goal
- If triglycerides <200 mg/dL (isolated low HDL) in CHD or CHD equivalent consider nicotinic acid or fibrate.

#### METABOLIC SYNDROME - "TIP OF THE ICEBERG"

- People ask me "everything is normal?"
- Disease of lifestyle, carries substantial risk
- Unless you as a doctor emphasize the risk, your patients won't know!
- PREVENTION is BETTER than TREATMENT
- Consider pharmacologic treatment if diet & lifestyle changes don't work <u>after 3-6 months</u>, especially for those who are high risk (asa, statin, metformin)
- ALWAYS treat trigs > 800 (risk of pancreatitis)



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## CLINICAL PRESENTATION

- Classic symptoms
  - Polyuria and polydipsia
  - Nocturia
  - Blurred vision
  - Weight loss
  - Fatigue

### TYPES OF DIABETES

#### Type 1

- Insulin deficiency caused by destruction of the pancreatic beta cells.
- Most often diagnosed in children or adolescents
- Thin or normal weight
- Family history common
- Sudden Onset
- Ketoacidosis common

### Type 2

- Increased peripheral insulin resistance
- Generally occurs in adults
- Often obese
- Family history common
- Gradual onset
- Ketoacidosis rare

### DIAGNOSTIC CRITERIA

	HbA1c (percent)	Fasting Plasma Glucose (mg/dL)	Oral Glucose Tolerance Test (mg/dL)
Diabetes	≥ 6.5	≥ 126	≥ 200
Prediabetes	5.7 <b>—</b> 6.4	100 - 125	140 — 199
Normal	~ 5.7	≤ 99	≤ 139

In the absence of symptoms of hyperglycemia, diagnosis should be confirmed with repeat testing on subsequent day

### SCREENING FOR DIABETES

- Once yearly screening in patients age 40-70 and any one
  - hypertension,
  - hyperlipidemia,
  - BMI ≥25
- Preferred screening tests
  - Fasting plasma glucose
  - Glycosylated hemoglobin (A1C)

### COMMONLY AVAILABLE DIABETES MEDICATIONS

- Metformin
  - DPP4 Inhibitors ("gliptins")
- Sulfonylureas
- Glitazones (Thiazolidinedions)
- GLP1 Receptor Agonists
- SGL2 Inhibitors
- Insulin

### METFORMIN

- Mechanism: Reduces glucose released liver, decreases insulin resistance in muscle cells
- No hypoglycemia
- Helps with weight loss
- Contraindicated with eGRF<30</li>
  - Cr 2.8 in 60year-old 80kg male
- Side effects: GI (Nausea, diarrhea usually at high doses)

# DPP4 INHIBITORS ("GLIPTINS")

- Vildagliptin (Galvus), Sitagliptin (Janumet)
  - Mechanism: Prolongs the action of GLP-1, increases glucose-dependent insulin secretion and decrease glucagon production
- No hypoglycemia
- Renal dose adjustment required (half dose with renal patients), can be used in ESRD
- Few adverse effects

### SULFONYLUREAS

- Glipizide (Novoglip), Glimepiride (Diapride), glibenclamide (Glycoben), Gliclazide
- Mechanism: Stimulates pancreas to increase insulin production
- High risk of hypoglycemia. Avoid in frail elderly
- Safe in kidney disease except glibenclamide
- Side effects: Weight gain

### GLITAZONES (THIAZOLIDINEDIONS)

- Pioglitazone (Tripride)
- Mechanism: Increases insulin sensitivity in adipose tissue and muscle, decreases liver glucose output
- No risk of hypoglycemia
- Generally not recommended in renal impairment due to potential for fluid retention
- Contraindicated in heart failure, hepatic impairment, osteoporosis, history of bladder cancer
- Side effects: weight gain, fluid retention, bone fractures

### GLP1 RECEPTOR AGONISTS

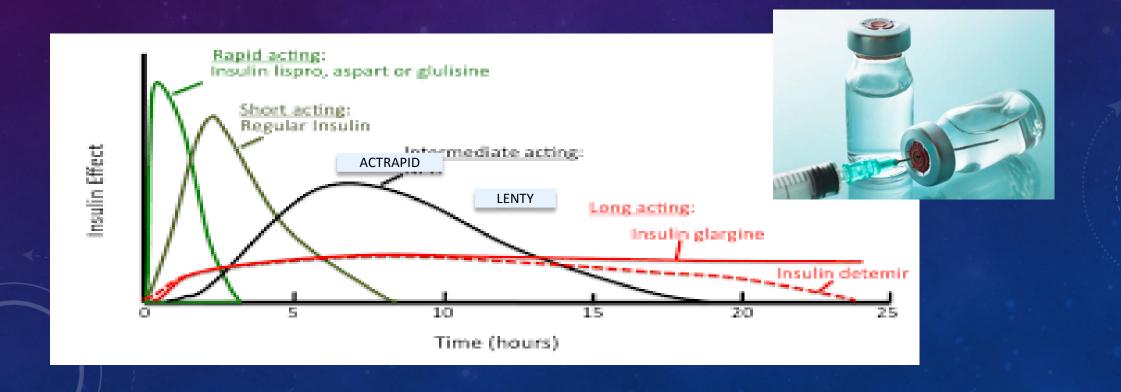
- Lixisenatide, Liraglutide, Exenatide
- Mechanism: Mimics the effect of incretin hormones to increase glucosedependent insulin secretion and decrease glucagon production
- No risk of hypoglycemia
- Helps with weight loss
- Not recommended for eGFR <30</li>
- Side effects: GI (N/V/D), thyroid cancer

### SGL2 INHIBITORS

- Canaglifozin, Empaglifozin, Dapaglifozin
- Mechanism: Inhibits glucose reabsorption in the kidneys
- No hypoglycemia
- Helps with weight loss
- New studies showing mortality benefit in heart failure
- Not recommended with eGFR <30-60 depending on agent</li>
- Risk of genitourinary infections, polyuria, hypovolemia

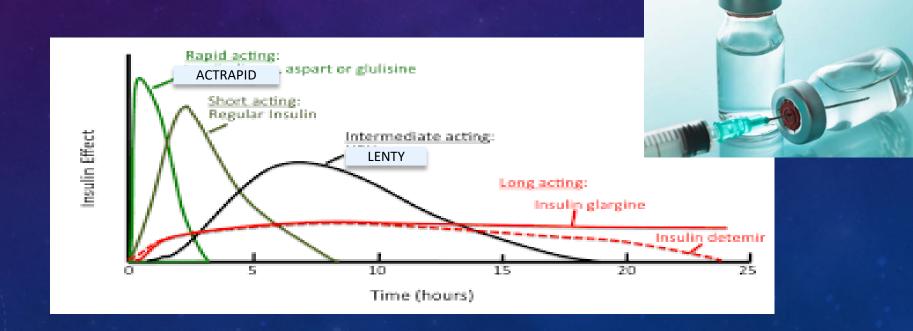
### INSULIN

- Long acting (24 hours): Lantus (Glargine), Detemer
- Intermediate acting (BD dosing): Lente
- Short acting (2-4 hours): Actrapid



### INSULIN

- Side effects: Weight gain, hypoglycemia, hypersensitivity reactions
- Preferred in ESRD
- Requires refrigeration



# MANAGEMENT OF TYPE 2 DIABETES

- Diabetes education
- Low refined carbohydrate diet
  - "Nothing white"
- Weight loss
- Exercise





### CHOICE OF INITIAL THERAPY

- If A1c < 9.0, consider monotherapy
  - Metformin is first line if no contraindications
  - If Metformin contraindicated, consider sulfonylurea
- If A1c >9.0, consider starting with dual therapy
  - Metformin + sulfonylurea or DPP4 inhibitor

### TREATMENT GOAL

- Young patients without established complications should have an A1C goal of 7 to 7.5 if this can be achieved without significant hypoglycemia or other side effects
- Older adults and those with comorbid conditions or limited life expectancy may have A1C targets 8 to 8.5 due to limited likelihood of benefit from intensive therapy balanced against the side effects of medications.

### MANAGEMENT OF PERSISTENT HYPERGLYCEMIA

- Monitor HgbA1c every 3 months (substitute blood sugar log fasting and 2 hrs post prandial)
- For most patients, add a second medication when glycemic treatment goal is not achieved within three months
  - Second line: Metformin + sulfonylurea or DPP4 inhibitor
  - If treatment goal not achieved within another three months, Metformin + sulfonylurea + DPP4 inhibitor

### STARTING INSULIN

- Have patients continue metformin and DPP4 inhibitors while on insulin, stop sulfonylureas
- Start with basal long acting insulin
  - Start with 10-20 units daily
  - Increase by 2 units per day until fasting at goal (100-150mg/dL or 5.5 8.5 mmol/L)
  - Have patients check blood glucose before breakfast and at bedtime before their dose
- If post-prandial blood sugars remain high, start short acting insulin TDS with meals starting 6 units with small meals, 8 units with medium meals and 10 units with big meals.

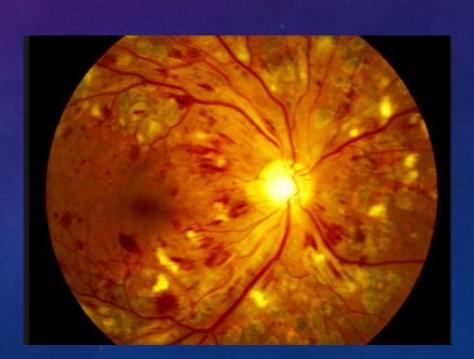
### LONG-TERM COMPLICATIONS OF DIABETES

- Macrovascular Complications
  - Increased risk of cardiovascular, peripheral vascular and cerebrovascular disease — heart attack and stroke
- Microvascular comlications
  - Peripheral neuropathy
  - Diabetic ulcers
  - Chronic Kidney Disease

# LONG-TERM COMPLICATIONS OF DIABETES

### Eye pathology

- Proliferative diabetic retinopathy
- Cataracts
- Glaucoma



### PREVENTION AND SCREENING FOR DIABETES COMPLICATIONS

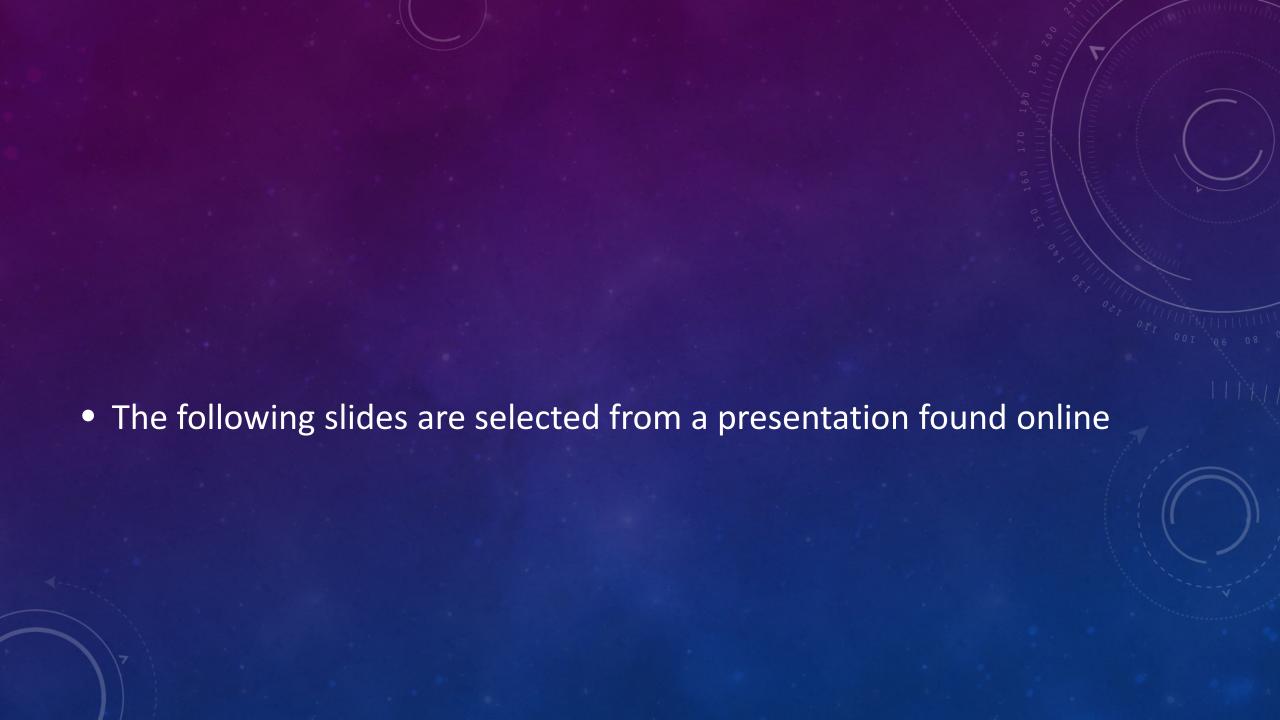
- Risk reduction for microvascular disease
  - Smoking cessation
  - Blood pressure control (ACE-i is often a good first medication for renal protection)
  - Aspirin and statin therapy for high risk patients (monitor lipid profile)
  - Measure urine protein yearly and, if positive, initiate ACE-i to slow renal disease
- Diabetic eye exam yearly
- Routine foot examination for neuropathy, PVD, diabetic ulcers, fungal infections

### TYPE 1 DIABETES

- Confirming the diagnosis:
  - Send out for pancreatic autoantibodies against glutamic acid decarboxylase 65 (GAD65)
- Treatment differences from type 2:
  - Patients will need life-long insulin therapy. This should be initiated on diagnosis of the disease
  - Metformin helpful in increasing insulin sensitivity

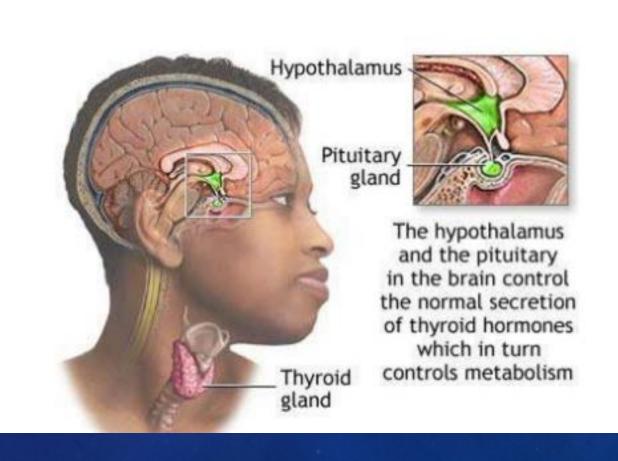
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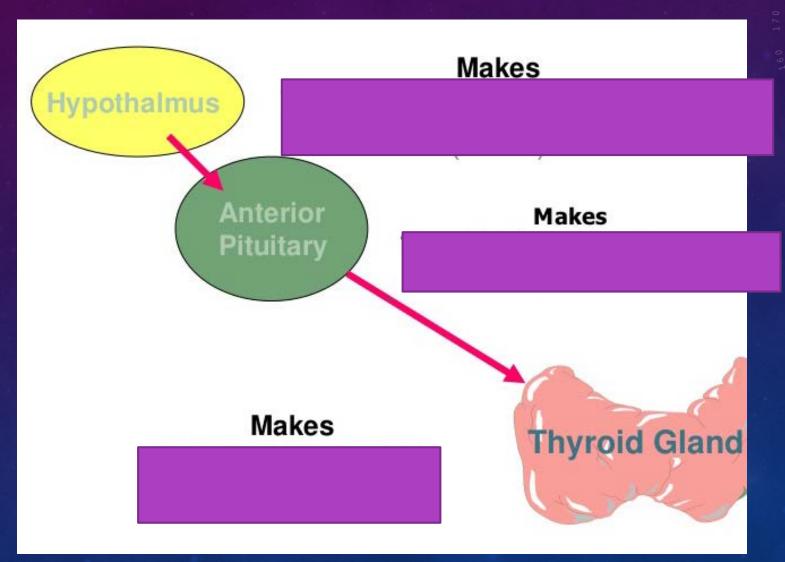




# THYROID PHYSIOLOGY



### HYPOTHALAMUS-PITUITARY-THYROID AXIS



# THYROID HORMONE SYNTHESIS, METABOLISM AND ACTION

- Iodine enters thyroid gland and is used for T3 and T4 production
- Hormones are released from the thyroid and vast majority are protein bound (TBG) and deposited in peripheral cells

T4 has 4 iodine atoms, removal of one produces T3

Total= Bound to TBG

Free= Unbound

### T3 & T4

- Facilitate normal growth and development
- Increase metabolism
- Increase catecholamine effects

### TSH

- Most useful marker of thyroid hormone function
- Released in a pulsatile diurnal rhythm- highest at night

### HYPOTHYROIDISM

Insufficient thyroid hormone

- 1. Primary: thyroid gland failure
- 2. Secondary: pituitary gland failure
- 3. Tertiary: hypothalamus failure

### HYPOTHYROIDISM CAUSES

### Primary hypothyroidism

- Iodine deficiency- most common cause worldwide
- Congenital
- Autoimmune mediated
  - Hashimoto's thyroiditis- B lymphocytes invade thyroid
- latrogenic- post-thyroidectomy or radio-iodine treatment
- Drug-induced Anti-thyroid, lithium, amiodarone
- Severe infection
- Trauma to thyroid/pituitary/hypothalamus
- Pituitary tumour

### HYPERTHYROIDISM CAUSES

Hyperthyroidism (thyrotoxicosis) is excess thyroid hormone

- Autoimmune
  - Graves Disease (76%)
  - F>M, age 20-40
  - IgG auto antibodies bind TSH receptors T3 & T4
  - Leads to gland hyper function
- Toxic adenoma and toxic multinodular goitre
- Viral Thyroiditis (de Quervain's)
  - Fever and ESR- self limiting
- Exogenous Iodine
- Neonatal thyrotoxicosis
- Drugs- Amiodarone
- TSH secreting pituitary adenoma (rare)

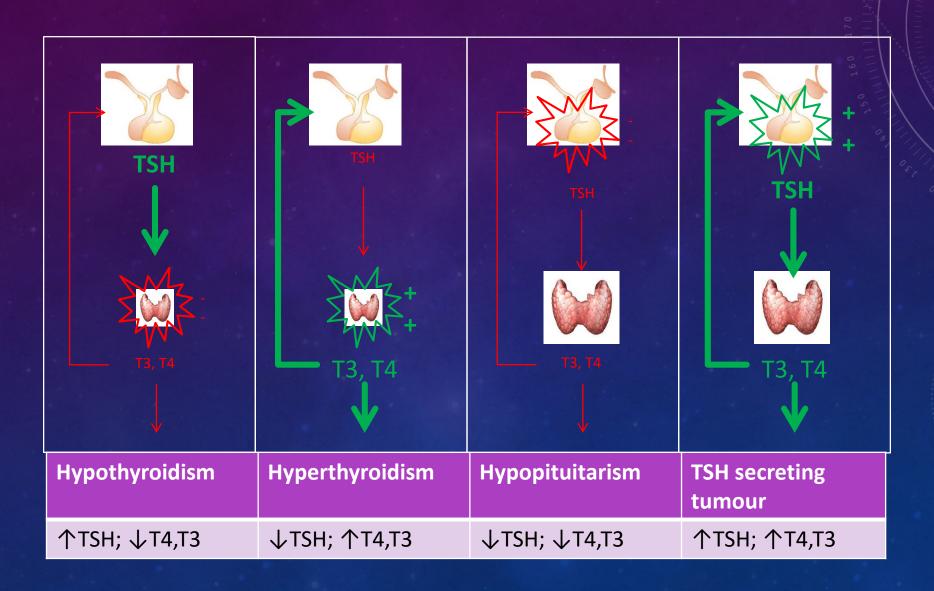
### INVESTIGATING THYROID DISEASE

- TSH- first thing you assess
  - Normal range 0.5-5 μU/ml
  - Supressed= Hyperthyroid
  - Elevated= Hypothyroid

If TSH abnormal request Free T4

- Elevated= Hyperthyroid
- Suppressed= Hypothyroid

### INVESTIGATIONS — TFTS



### HYPOTHYROIDISM - MANAGEMENT

#### Conservative

Lifestyle - smoking cessation, weight loss

#### Medical

- Levothyroxine (T4)
  - Repeat TSH in 6/52
  - Adjust dose according to clinical response and normalisation of TSH
  - Caution in patients with IHD- risk of exacerbation of MI
  - Clinical improvement may not begin for 2/52
  - Symptom resolution 6/12→ if not consider +T3

#### Surgical

 Symptomatic – carpal tunnel decompression, thyroidectomy if compression of local structures

### HYPERTHYROIDISM - MANAGEMENT

#### Conservative

 Smoking cessation – especially with Graves's ophthalmology, associated with worse prognosis

#### Medical

- Symptomatic β-blockers
- Carbimazole, propylthiouracil (50% relapse)
  - Risk of agranulocytosis
- Radio-iodine treatment
- Long term likely to become hypothyroid

### THYROID STORM

- Life threatening emergency (rare) 30% mortality even with early recognition and management
- Exacerbation of thyrotoxicosis precipitated by stress i.e.
  - Surgery
  - Infection
  - Trauma

- Signs
  - Fever
  - Agitation and confusion
  - Tachycardia +/- AF

# THYROID CANCERS

Type of tumour	Frequency (%)	Age at presentation (years)	20 year survival (%)
Papillary	70	20-40	95
Follicular	20	40-60	60
Anaplastic	5	>60	<1
Medullary	5	>40	50
Lymphoma	2	>60	10

 The above slides were selected from a presentation found online

### ENDOCRINE DISORDERS

- Insulin / Pancreas -> Insulin resistance & Diabetes
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### ADRENAL GLANDS

- Insufficient or excess cortisol / aldosterone / sex hormones
- Condensed for this presentation

### ADRENAL INSUFFICIENCY

- Most common clinical scenarios
  - Chronic vague symptoms (weakness, fatigue, falls, dizziness, hypotension)
  - Acute illness (rapid shock and deterioration)
  - HIV and TB associated (persistent tachycardia, hypotension, cyclical decompensation)
  - Frequent or chronic home steroid use (COPD, asthma, autoimmune disease)
- Treatment based on presentation
  - Hospitalized or unstable: Treat immediately with empiric IV steroids
  - Stable or chronic: Check ACTH levels versus empiric treatment
  - May need fludrocortisone for mineralocorticoid action if chronic
  - Continuous low dose replacement versus taper

### ENDOCRINE DISORDERS

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- Not addressed
  - Hormone secreting tumors (neuroendocrine tumors)
  - Gonadal hormone imbalance or failure
  - Pituitary failure / Sheehan's syndrome
  - Calcium homeostasis / parathyroid glands
  - Acromegaly/Gigantism/Dwarfism