Diabetes

Saturday, December 6, 2014
6:38 PM

Learning Objectives:
- actions of insulin with reference to glucose, fat, & protein metabolism
- counter-regulatory hormones
- actions of glucagon, epinephrine, GH, & glucocorticoids on blood glucose
- role of incretin in glucose regulation
- pathophysiology & clinical presentation of DM1 vs. DM2
- diagnosis of DM
- lab values of IFG vs. IGT vs. DM
- risk factors for DM2
- Hb A1c goal
- when a pregnant woman should be screened for DM/gestational DM
- complications of gestational DM on mother and fetus
- causes & diagnosis & clinical manifestation of DKA & HHS
- microvascular & macrovascular complications of DM

Endocrine System
- feedback regulation
- hormones *(free vs. bound)*
- receptors *(#, affinity, pH)*

Glucose Regulators
- I/A
- GLP1/GIP
- G
- GH
- E *(Catecholamines)*
- Cortisol *(Glucocorticoids)*

COUNTER-REGULATORY HORMONES

Hormone	Cell Source
I/A	β
G	α
GLP1	L
GIP	K

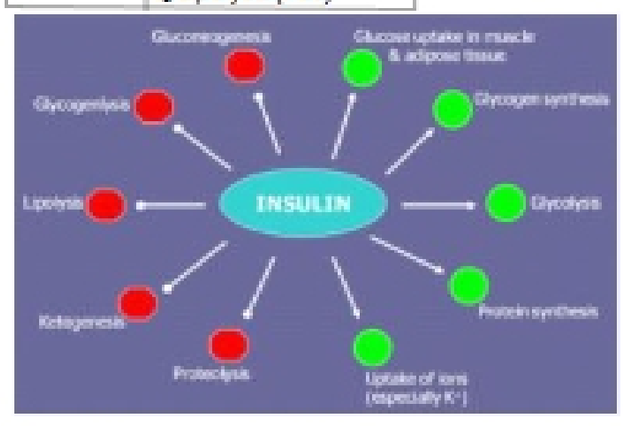
State	I, G/E	Main Process	Glucose Source
Fed	↑I, ↓G/E	Glycolysis	diet
Overnight Fast (<24 hrs)	↓I, ↑G/E	Glycogenolysis	Glycogen
Prolonged Fasting (>24hrs)	↓I, ↑G/E	GNG	AAs
Starvation	↓I, ↑G/E	Ketogenesis	FAs
Stress (E,Cortisol,GH)	↓I, ↑G/E		

Glucose	(+) I/A, GLP1/GIP (-) G/E

Fed	I/A	Builds up	↓Glucose/↑Glycogen	↓AA/↑Protein	↓KB↓FA/↑TG	↑ATP
Fasting	G/E	Breaks down	↑Glucose/↓Glycogen	↑AA/↓Protein	↑KB↑FA/↓TG	↓ATP

Insulin Effects

↓Ions (K+)	↑uptake
↓*Glucose*	↑*GLUT-4 uptake (m/a)*
↓*AAs*	↑*Proteins* ↓*Proteolysis*
↓*KBs/FAs*	↑LPL ↓*Lipolysis (HSL)*



GLUT-4 - Insulin-dependent glucose transporter
PROINSULIN = Insulin + C-Peptide (β-cells)
INSULIN - *(in response to Glucose)*
AMYLIN - secreted w/Insulin *(in response to Glucose)*
INCRETINS (GLP1/GIP) - ↑Insulin *(in response to Glucose)*
DPP4 - quickly kills Incretins

Fed

A	↓G, slows stomach emptying, satiety
GLP1	↑I, ↓G, slows stomach emptying, satiety
GIP	↑I

Stress

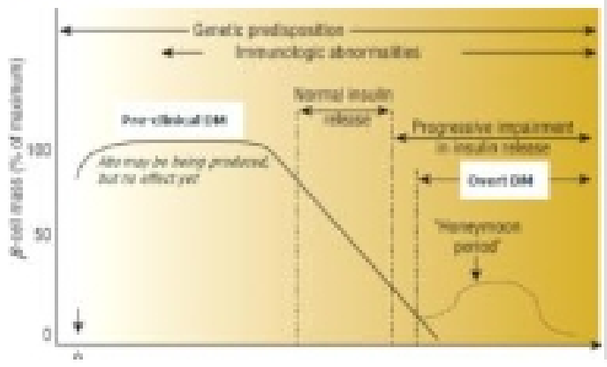
E *(Catecholamines)*	↓I, ↑G	mins
Cortisol *(Glucocorticoids)*	↑G	hours
GH	↑G	hours

Types of DM
- DM1/2
- Disease
- Drug
- GDM
- MODY
- Pre-DM: (IFG/IGT)

GDM = Gestational DM
MODY = Maturity Onset DM of Youth

IFG = Impaired Fasting Glucose
IGT = Impaired Glucose Tolerance

	DM1 *(5-10%)*	DM2* *(90-95%)*
Age	<30	>30
Onset	Acute	Gradual
Body Type	Lean	Obese
Pathophysiology	- β-cell destruction (NO Insulin) 1) AUTOIMMUNE - cell-mediated, genetic, environmental Targets: - Islet-cell (ICA)* - Glutamic Acid Decarboxylase (GAD) - Tyrosine Phosphatase-related islet antigen (IA2) - Insulin (I) 2) LADA - autoimmune; failure of oral meds..needs Insulin 3) IDIOPATHIC - NOT autoimmune (Africans, Asians)	- β-cell dysfunction (↓Insulin) 1) ↓1st ↑2nd-phase release 2) Degeneration: -age -genetic -Glucotoxicity -Lipotoxicity -Insulin-Resistance -↓Incretins 3) Long-term Insulin-Resistance:



I	Glucose
high	< 140
low	> 140

- Insulin-Resistance *(obesity, metabolic syndrome)*

Liver	↑Glucose
Muscle*	↓Intracellular Insulin signaling
Adipose	↑FAs ↓Adiponectin

- ↑G

Epidemiology
**28% do not know they have DM*

Disease-Induced DM

Endo	?	- Cushing's - Acromegaly
Exo	Pancreas	- Pancreatitis - Cystic Fibrosis

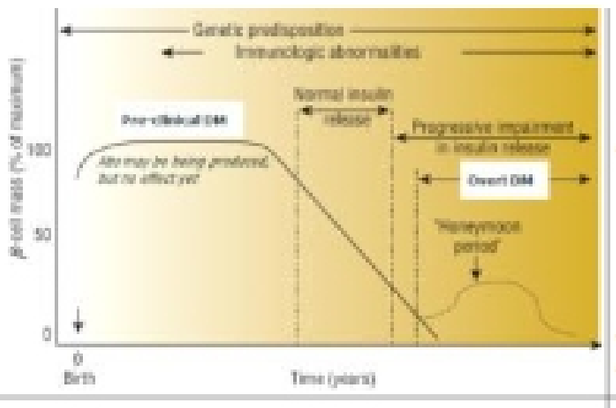
Drug-Induced DM
- Corticosteroids
- Niacin
- Olanzapine

GDM
Screening: 24-28 wks

1-Step	2hr 75g OGTT after fast	FPG > 92 1hr > 180 2hr > 153
2-Step	1hr 50g OGTT after fed + 3hr 100g OGTT after fast	50 > 140 3hr > 140

Risks:

Mother	- HTN - DM *(postpartum)*
Fetus	- ↑Insulin

		- Insulin-Resistance *(obesity, metabolic syndrome)* - ↑G - ↓GLP1/GIP
Clinical Manifestations	- lethargy - polyuria (frequent urination) - polydipsia (thirst) - polyphagia (↑appetite) - weight loss - DKA	- asymp - lethargy - polyuria (frequent urination) - polydipsia (thirst) - nocturia - blurred vision - dry skin
Screening		45+ yr — every 3yrs BMI >25 + Risk Factor: — Dx younger - pregnant - 1st° relative w/DM - AA, Latino, Native, Asian, Pacific Islander - postpartum DM/GDM - HTN, Lipids, PCOS - ↓HDL, ↑TG - A1c 5.7%, IFG, IGT - CVD 10+ yr + BMI >85th percentile + 2 Risk Factors: — every 3 yrs - 1st/2nd° relative w/DM2 - AA, Latino, Native, Asian, Pacific Islander - HTN, Lipids, PCOS - maternal DM/GDM

I	Glucose	
high	< 140	
low	> 140	

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Risks:

Mother	- HTN - DM *(postpartum)*
Fetus	- ↑insulin - ↑birth weight *(macrosomia)* - fetal death

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MODY
- ↓Insulin *(NO insulin-Resistance)*
- genetic

Pre-DM (IFG/IGT)
**should be tested yearly*

Diagnosis

	Fasting PG	Random PG	2hr Post-OGTT	A1c
---	70-100	<140	<140	<5.7
IFG	100-125	<140	<140	5.7-6.4
IGT	70-100	140-199	140-199	5.7-6.4
DM	126+	200+	200+	6.5+ (goal<7)

COMPLICATIONS

DKA = Diabetic Ketoacidosis
HHS = Hyperosmolar Hyperglycemic State

Acute

	DKA *(Biochem Triad)*	HHS
Causes	- untreated DM - Pancreatitis - Stroke (CVA) - MI - Infection - meds	- untreated DM - Pancreatitis - Stroke (CVA) - MI - Infection - meds
Clinical Manifestation	Symptoms: - polyuria *(frequency)*, - polydipsia *(thirst)*, - dehydration, - weak, - Δmental status, - coma, - weight loss, - N/V, - abdominal pain Physical Findings: - poor turgor, - ↑HR, - HoTN, - Kussmaul respirations, - shock **Biochem Triad:** 1) Hyperglycemia 2) Ketonemia 3) Metabolic Acidosis	Symptoms: - polyuria *(frequency)*, - polydipsia *(thirst)*, - dehydration, - weak, - Δmental status, - coma Physical Findings: - poor turgor, - ↑HR, - HoTN
Diagnosis	BG > 250; HCO_3^- < 15; pH < 7.3 - Ketonemia - Anion Gap - (↑K^+)	BG > 600; Osm > 230

Chronic

(Micro)	(Micro)	(Micro)	(Macro)
NEUROpathy	**NEPHROpathy** **leading cause of ESRD*	**RETINOpathy** **leading cause of blindness*	**CVD**
1) nerve damage 2) vessel wall thickening *(↓blood flow to nerve)* 3) Schwann cell de-myelination	1) Δ Glomerulus - Δbasement membrane - ↓blood flow - proteinuria	1) hyperglycemia 2) hemmorhage/ischemia 3) neovascularization/detachment 4) blindness	- CHD - CVD - PVD

Peripheral	Autonomic
- bilateral poor circulation/paresthesias (tingling) - foot ulcers - amputations	- GI (gastroparesis, constipation) - GU (neurogenic bladder, ED) - CV (↑HR, ortho HoTN) - sweat (sudomotor)

2) Albuminuria
3) Albumin:Creatinine

Urine Spot Collection

Normal	< 30
Micro	30-300
Macro	>300