

# Diabetes Update

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# Review of the stats

- Approximately 20.8 million people in the United States have diabetes (10% have type 1 and 90 % have type 2)
- 7 % of US population
- 14.6 million have been diagnosed with diabetes, 6.2 million people (or nearly one-third) are unaware that they have the disease.
- Gestational diabetes affects about 4% of all pregnant women - about 135,000 cases in the United States each year.

## Diagnostic Criteria of DM

- Two Fasting plasma glucose  $\geq 126$  mg/dl with fasting defined as no oral intake for at least 8 hours
- Symptoms of diabetes plus casual plasma glucose concentration  $\geq 200$  mg/dl
- 2-hr PG  $\geq 200$ mg/dl during an OGTT using 75 g of Glucose

# Pre-DM Diagnostic Criteria

- FBG of 100-125 mg/dL
- PBG of 141-199 mg/dL
- 41 million Americans who have pre-diabetes

# Type?

- Labs indicate Type 1
  - Elevated GAD (Glutamic Decarboxylase) antibody normal 0-1.4
  - DKA
- Labs indicate Type 2
  - C-peptide normal 0.8-3.5
  - Not fasting lab
  - Need corresponding glucose

# Current Insulin's

American Diabetes Association, 2004

<b>Insulin Preparation</b>	<b>Name</b>	<b>Onset of Action</b>	<b>Peak Duration</b>	<b>Effective Duration</b>
Rapid-acting Analogs	Humalog (lispro), Novolog (aspart), Apidra (glulisine)	5-15 minutes	30-90 minutes	3-5 hrs
Short-Acting Analogs	Regular	30-60 minutes	2-3 hrs	5-8 hrs
Intermediate Acting	NPH	2-4 hrs	4-10 hrs	10-16 hrs
Long Acting	Lantus (glargine)	2-4 hrs	Peakless	20-24 hrs

# New Insulin's

- Levemir (Detemir)
  - New basal insulin
  - Used for all Medicaid patients in Iowa
- Exubera
  - Inhaled bolus insulin
  - Comes in 1 mg or 3 mg blister pack
  - 1 mg blister pack=3 units insulin

# Exubera Pics



# Exubera

## Advantages (per Pfizer)

- Improved pt convenience
- Faster onset of action compared to Regular SC insulin
- No needles risk of infection
- Potential earlier onset of insulin therapy in Type 2 diabetes mellitus

## Disadvantages

- Long term effect with lungs unclear
- Cannot use if smoker, start smoking, or if you quit smoking less than 6 months ago
- Adaptation of dose unclear in smokers, asthma, pneumonia and COPD
- Inhalation devices clumsy bulky, fragile and/or weighty
- Larger dose necessary compared to SC insulin
- Difficult to achieve with pts on large doses of insulin
- Not approved for children, pregnancy or teenagers

# Levemir (Determir)

- Basal Insulin with relatively flat action profile
- Clear, colorless
- Cannot be mixed with other insulins
- Slow systemic absorption
- Mean duration of 5-7 hrs at the lowest dose and 23.2 hrs at its highest dose
- Steady state levels reached after 2-3 days depending on dosage and frequency



# Levemir/Detemir

## Advantages

- Shown to have less night time hypoglycemia than NPH
- Shown to have less major hypoglycemia than lantus (glargine)
- Less weight gain than NPH

## Disadvantages

- Cannot be mixed
- No studies show large improvements in glycemic control
- More shots of basal insulin-most patients will need BID dose

Russel-Jones, et al. (2005) *Diabetologia* 48 (Suppl 1), A92. (meta)  
Pieber et al. (2005). *Diabetologia* 48 (Suppl 1), A92

# New Class of Drugs deals with incretin Hormones

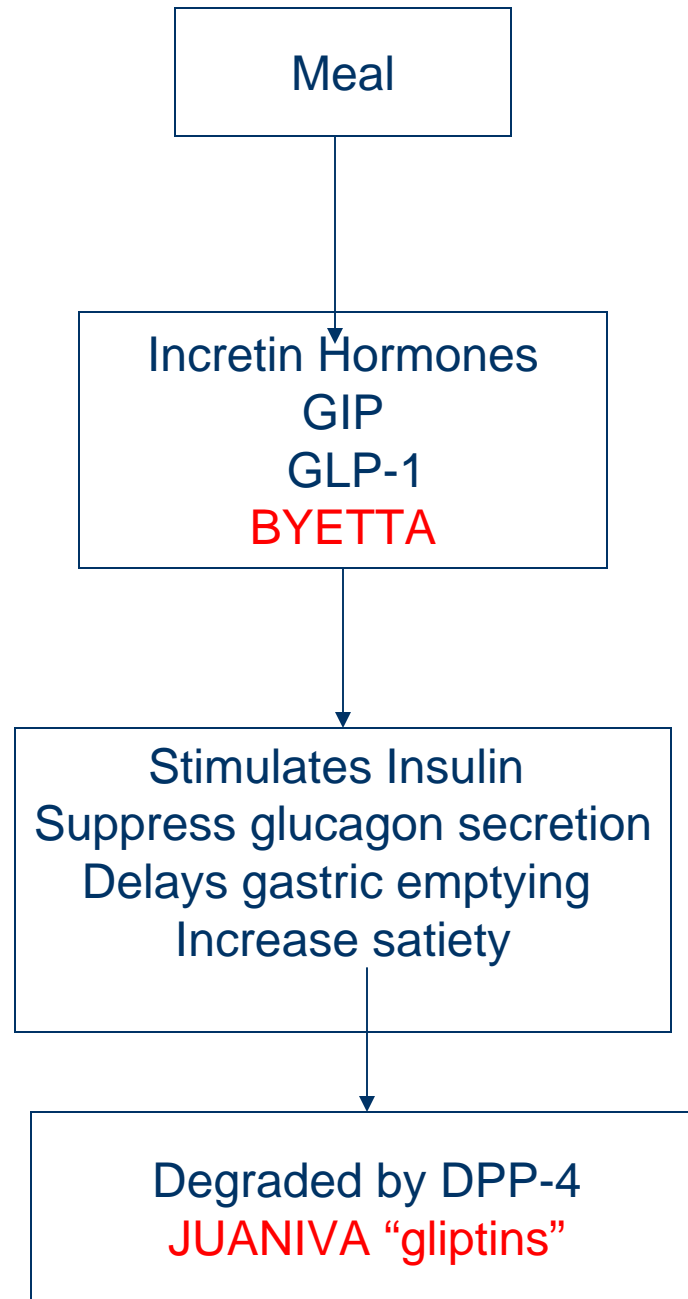
- Byetta (Exentide)
  - Derived from a chemical found in the saliva of the Gila monster, a venomous lizard
  - Mimics the incretin hormone GLP-1
  - Injectable
  - Type 2 DM
- Januvia (sitagliptin phosphate)
  - DDP-IV (dipeptidyl-peptidase IV) inhibitor
  - Oral
  - Type 2 DM
- Amylin
  - Islet amyloid polypeptide
  - Type 1 DM
  - Injectable

# Review Incretin Hormones

- Incretin hormones are secreted from the gut in response to a meal.
- GIP (Glucose dependent insulinotropic polypeptide), synthesized in duodenal and jejunal enteroendocrine K cells in proximal small bowel.
- GLP-1 (Glucagon like peptide), made from enter endocrine L cells in distal ileum and colon

# Incretin Hormones

- Plasma levels of GLP-1 are low in fasting state 5-10 pmol/L and increases rapidly after eating 15-50 pmol/L.
- GIP receptors are located in islet beta cells, adipose tissue and CNS.
- GLP-1 receptor is expressed in islet alpha and beta cells and peripheral system.
- Both GIP and GLP-1 are found to be low in people with diabetes



Meal

Incretin Hormones  
GIP  
GLP-1  
BYETTA

Stimulates Insulin  
Suppress glucagon secretion  
Delays gastric emptying  
Increase satiety

Degraded by DPP-4  
JUANIVA "gliptins"

# Byetta

## Advantages

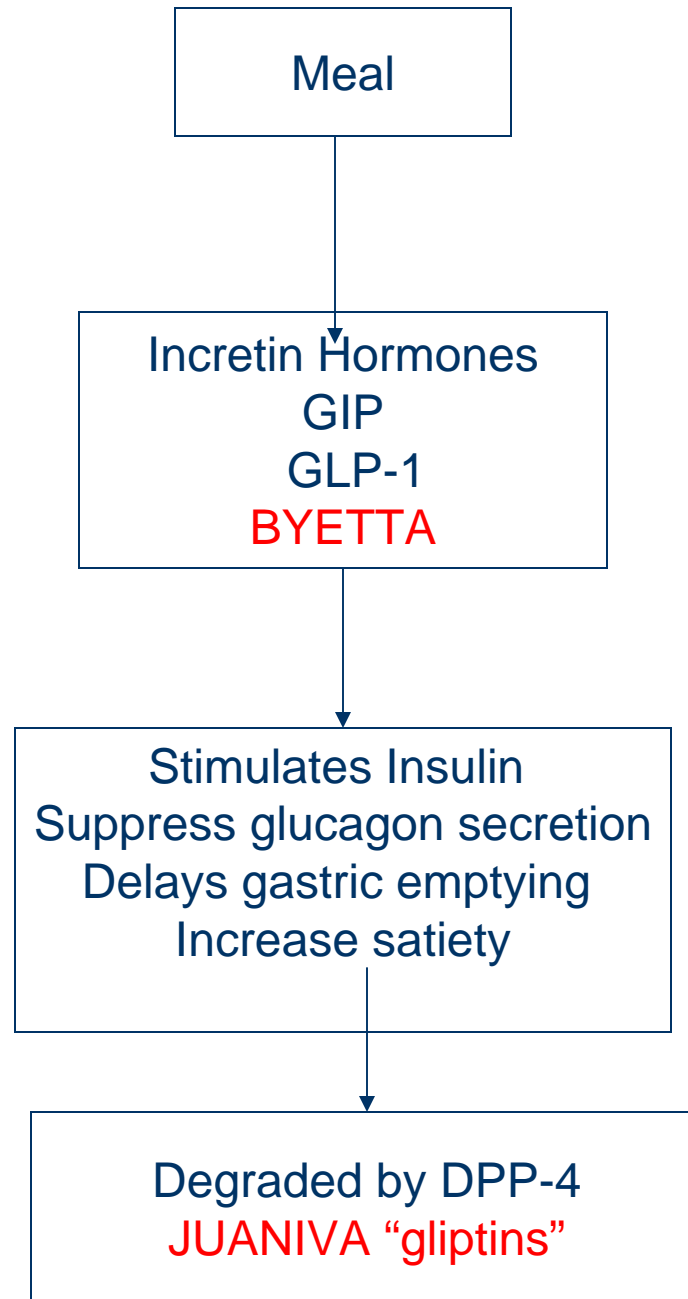
- Decrease appetite and reduce weight
- Enhances glucose induced insulin secretion
- Slows nutrient absorption by gut
- Possible beta cell preservation
- Possible benefit on triglycerides

## Disadvantages

- Injection
- Nausea
- Hypoglycemia when used with sulfonylurea
- Not yet approved as monotherapy (being used)

# DPP-4

- Inhibiting DPP-4 elevates endogenous or exogenous GLP-1 levels by slowing the rate of degradation and inactivation



Meal

Incretin Hormones  
GIP  
GLP-1  
BYETTA

Stimulates Insulin  
Suppress glucagon secretion  
Delays gastric emptying  
Increase satiety

Degraded by DPP-4  
JUANIVA "gliptins"

# DDP-4 (Januvia)

## Advantages

- Oral bioavailability
- Decreases Hba1c by 0.5-1%
- Minimal hypoglycemic events
- Weight neutrality
- Can be combined with metformin or a TZD.

Diabetes Care, Volume 26, Number 10, October 2003.

## Disadvantages

- Durability of Glycemic control
- DPP-4 inhibitors do not lower the blood glucose to a greater extent as compared to existing therapies
- Cost
- Long term safety data

Agent	Max dose	Hba1c ↓%	Cost /yr \$
Glyburide	10 bid	1.5-2	130
Glipizide	20 bid	1.5-2	175
Glimiperide	8 qd	1.5-2	330
Repaglinide	4 tid	1.5-2	910
Nateglinide	120 tid	0.5-1	1100
Metformin	850 tid	1.5-2	600
Glucophage XR	2000 qd	1.5-2	1000
Rosiglitazone	4 bid	1.5	1875
Pioglitazone	45 qd	1.5	2110
Acarbose	100 tid	0.5-1	700
Exenatide	10mcg bid	1	1800
Sitagliptin	100,200	0.7	1700

# Amylin

- 37 AA peptide co-secreted with insulin and deficient in individuals with diabetes
- Amylin (Pramlintide) is a synthetic analog
- More commonly used in Type 1 DM, who have failed to achieve desired glucose control despite optimal insulin therapy (example: overweight Type 1)
- Can be used with Type 2 if on mealtime insulin
- When initiating reduce current insulin dose by 50% to avoid hypoglycemia

# Amylin

## Advantages

- Weight management when nutrition, exercise and insulin fail to control blood sugars
- Control post-prandial glucose

## Disadvantages

- Injections
- Cost (5 mL vial contains 3000 mcg costs \$104)
- Nausea, headache
- Avoid in gastroparesis
- Contraindicated in hypoglycemia unawareness
- Cannot mix with insulin

# Real time Glucose Monitoring



- Can be used with MiniMed Paradigm 522 or 722
- System takes measurements continuously and displays updated glucose values every five minutes
- Alarms are designed to warn you of low and high glucose levels

# Real Time Glucose Monitoring

## Advantages

- Alarms during night time lows
- Snap shot picture in time
- Identify lows/highs for those that can't feel them

## Disadvantages

- Patients start to react to every high/low blood sugar
- Cost- \$1000 sensor & \$35/sensor needle changed every 3 days ~\$350/month
- Not covered by most insurance companies



**Thank you!**



- Questions?