

What am I taking?

An overview of diabetes medications

Hispanic Health Council

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Outline

- Introduction/Diabetes Review
- Review Current Guidelines
- Review Treatment Strategies
 - Insulins
 - Inhaled and injected
 - Oral Medications

Introduction

- Diabetes Mellitus affects ~20 million
- 6th leading cause of death
- Leading cause of:
 - Blindness in adults
 - ESRD
 - Nerve damage
 - Lower extremity amputations
- Increases risk of stroke and MI 4-fold

Diagnosis

- Fasting glucose \geq 126 mg/dL
- Any plasma glucose \geq 200 mg/dL
- Glucose Tolerance Test

Pathophysiology

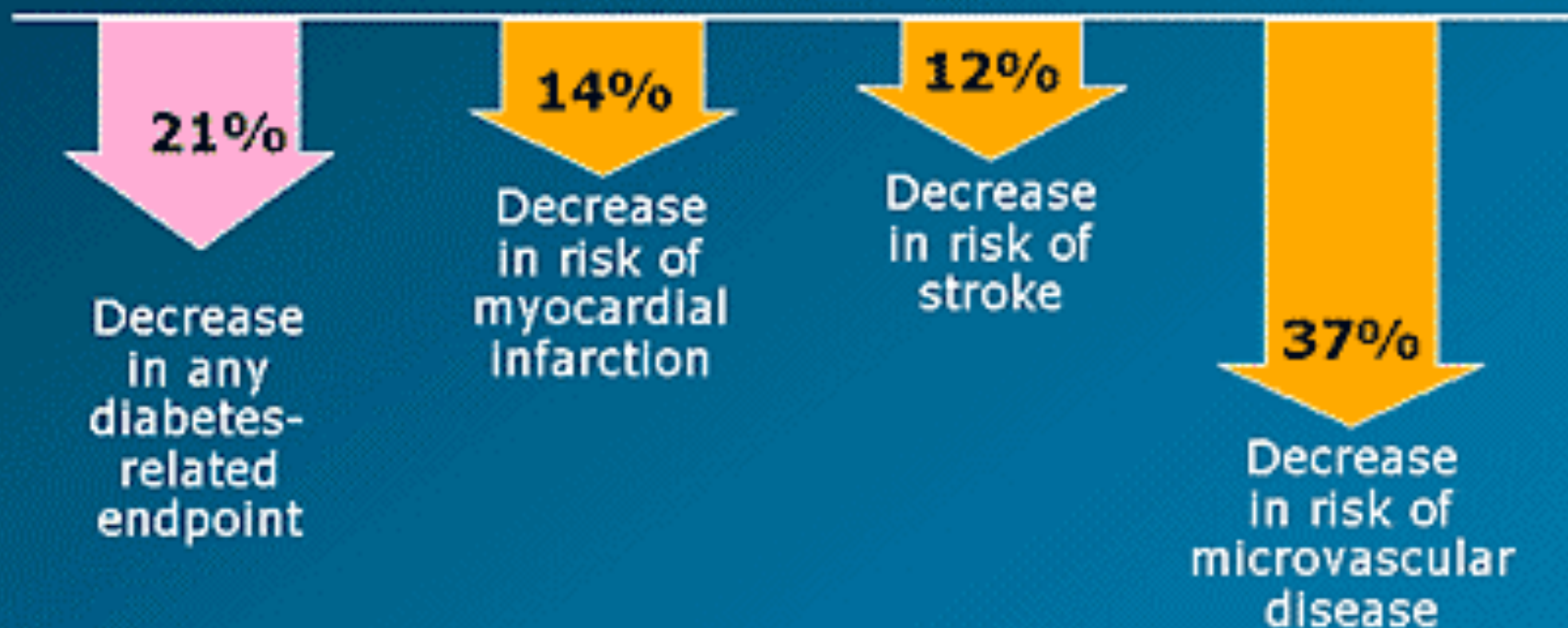
- Type I DM is absolute insulin deficiency
 - Must have insulin at all times
- Type II DM is combination of:
 - Insulin Resistance
 - Beta cell failure

Complications

- Microvascular:
 - Retinopathy
 - Nephropathy
 - Neuropathy
- Macrovascular:
 - Coronary artery disease
 - Cerebrovascular disease
 - Peripheral vascular disease

UKPDS 35: Tight Glycemic Control Prevents Complications

Every 1% drop in HbA1c resulted in:



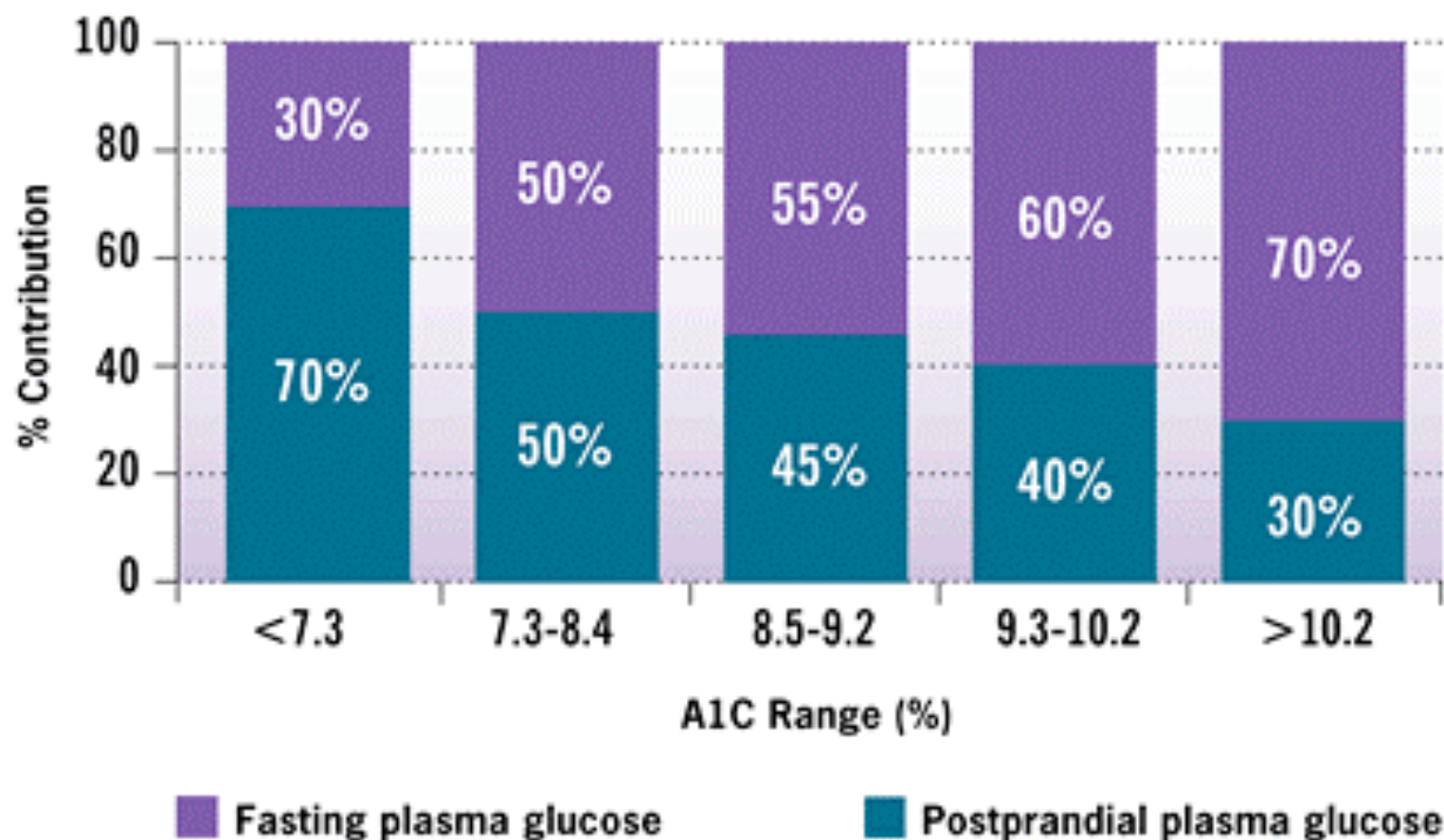
N=3642

Stratton IM et al. *BMJ*. 2000;321:405-412.

Outpatient Glycemic Goals

	<u>ADA</u>	<u>AACE</u>
HbA1C (%)	<7.0	<6.5
Pre-prandial glucose (mg/dL)	<130	<110
2-hr post-prandial glucose (mg/dL)	<180	<140

POSTPRANDIAL AND FASTING GLUCOSE CONTRIBUTION TO A1C



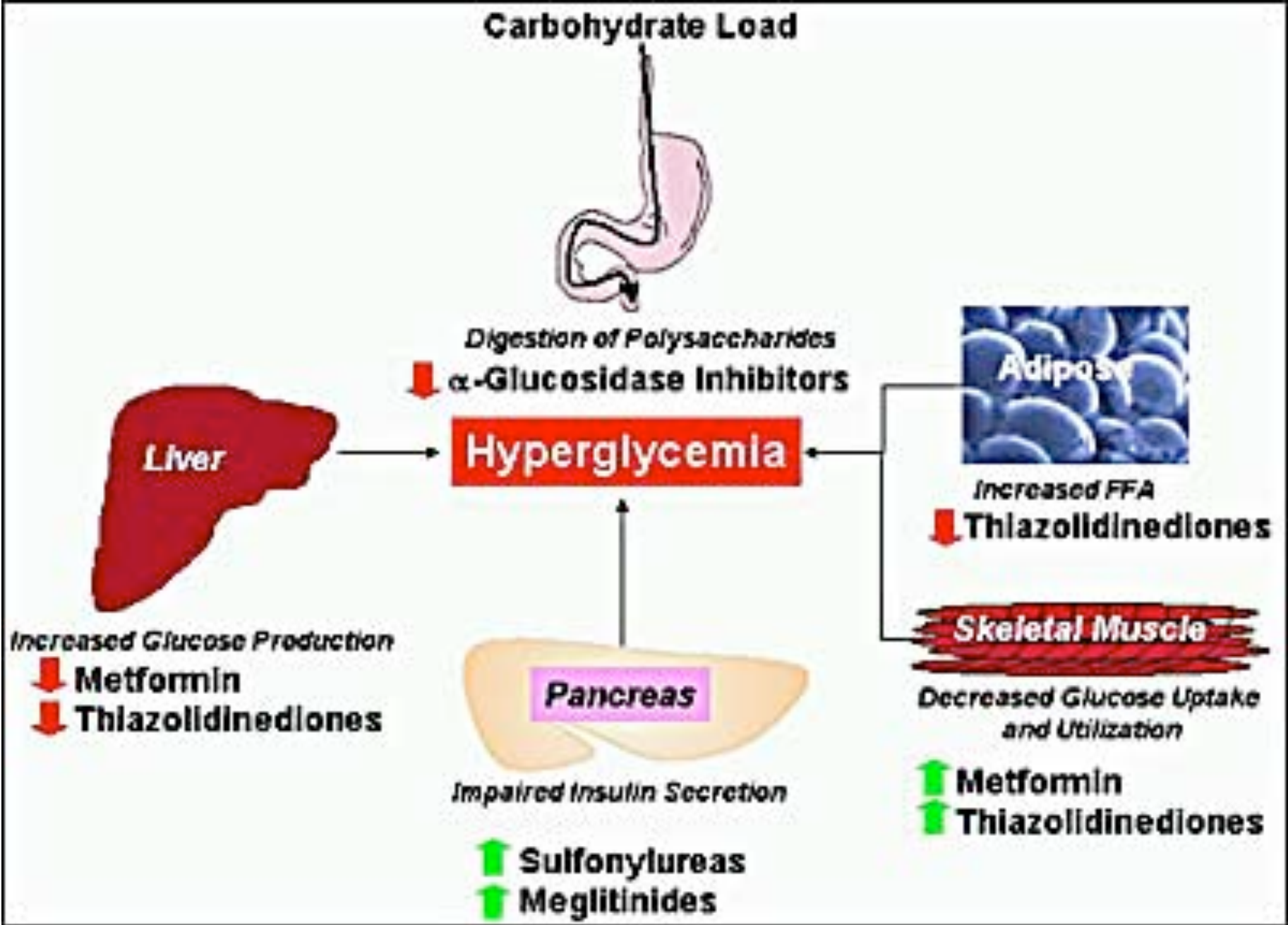
Treatment Options for Type 2 Diabetes: *Where Are We Now?*



?
Inhaled insulin
Insulin analogs
Gut peptides



1922 1950s 1982-85 1995 1996 2001 2003 →



Treatments Strategies

Can consider combination oral therapy initially:

- Need sulfonylurea or insulin to get rapid control
- ? β -cell stabilization with TZDs

Add-on therapy:

- Orals ok when A1C <9%
- When A1C >9%, really probably need insulin

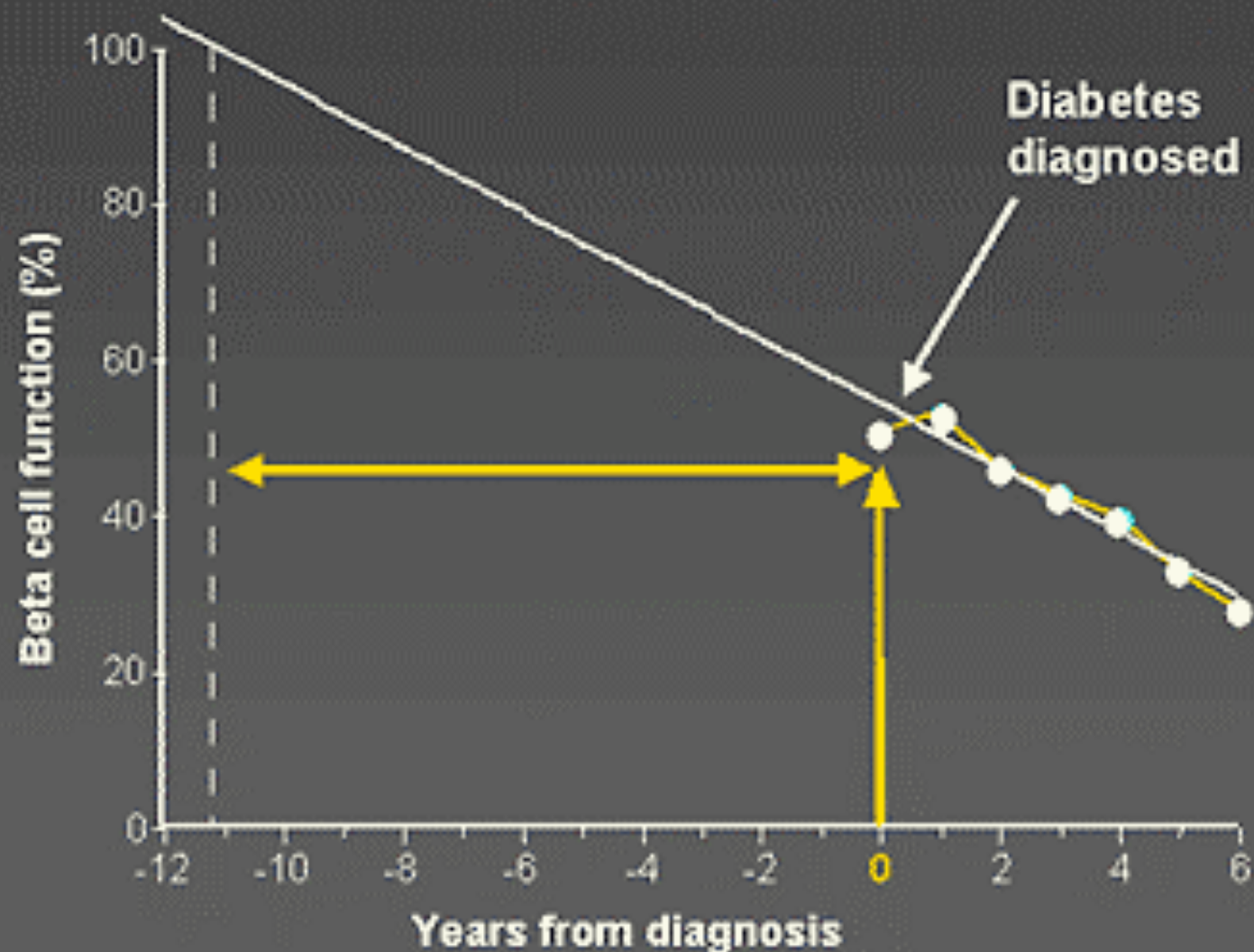
What are the options?

- **Injectable**
 - Insulin
 - Byetta
 - Symlin
- **Oral**
 - Biguanides
 - Sulfonylureas
 - TZDs
 - DPP IV inhibitors
- **Inhaled**
 - Insulin

What am I taking?

- What does the medication do?
- How do I use it?
- What precautions/contraindications are there?
- What are the side effects?

Progressive Loss of Beta-Cell Function Over Time



Insulin	Onset	Peak	Duration
Regular (Humulin-R Novolin-R)	30 min	2-4 hr	6-8hr
NPH (Humulin-N Novolin-N)	2 hrs	4-6 hrs	8-12 hrs
Lispro (Humalog) Aspart (Novolog) Glulisine (Apidra)	15 min	60-90 min	2-4hr
Glargine (Lantus)	2 hr	None	24 hr
Levemir (Detemir)	2-4 hr	May peak at 6-8 hrs	12-24 hrs (dose dependent)

Insulin: What does it do?

- Replaces insulin not being produced by the pancreas
- Overcome insulin resistance

Insulin: How do I use it?

Vial and Syringe

1000u per vial

Pen

SoloStar: Lantus and Apidra

FlexPen: Levemir, Novolog, Novolog 70/30

Pen: Humalog, Humalog 75/25, Humulin N

Memoir/Luxura: Humalog

Insulin: How do I use it?

- Syringes
 - Capacity
 - 30u, 50u, 100u
 - Gauge
 - 31/30/28
- Pen needles
 - Will fit all pen devices
- Disposal of needles

Insulin:

Precautions/Contraindications

- Sensitivity to drug/class/components
- Not for IV use
- Caution in renal or liver insufficiency

Insulin: What are the side effects?

- Hypoglycemia
- Local infection
- Lipohypertrophy
- Weight gain

Exubera: What does it do?

- Inhaled insulin
- Similar action to Regular
- Meant for mealtime dosing

Exubera: How do I use it?

- Inhaler
- 1, 3mg blister packs
- 1mg = 3u
- 3mg = 8u
- Three 1mg blisters DO NOT equal one 3mg blister

Exubera:

Precautions/Contraindications

- Smoking within 6 months
- $FEV_1 < 70\%$ predicted
- Poorly controlled asthma
- Clinically significant COPD

Exubera:

What are the side effects?

- Hypoglycemia
 - Incidence similar to regular insulin
- Chest Pain
 - Majority (>90%) mild to moderate
 - Not associated with increase risk of heart disease
- Dry Mouth
- Cough
 - Occurred within seconds to minutes after inhalation
 - Usually mild
 - Decreased with continued use
 - Only 1.2% of patients dropped out of study because of cough

Exubera:

What are the side effects?

- Shortness of breath
 - Usually mild to moderate
 - Only 0.4% of patients discontinued treatment
- Decrease in lung function
 - Very small
 - Occurred within first few weeks on treatment
 - Did not progress over 2 years
 - Completely reversible after 6 weeks when stopped treatment

Byetta: What does it do?

- Effects:
 - Restores first-phase insulin secretion
 - Reduces postprandial blood glucose
 - Lowers glucagon levels
 - Reduces food intake
 - Slows gastric emptying
- Weight loss
- A1c reduction = 1.3%
- Increases insulin sensitivity

Byetta: How do I use it?

- Injectable only
 - Prefilled pen
 - 5mcg x 1 month
 - 10mcg thereafter
- Twice daily
 - 30-45 minutes prior to meal
 - Breakfast and Dinner
- Storage
 - Can be stored at room temperature

Byetta:

Precautions/Contraindications

- Contraindications:
 - Type I DM
 - End-stage/severe renal disease (CrCl<30)
 - Severe GI disease

Byetta: What are the side effects?

- Hypoglycemia
 - With SU and insulin
 - Decrease does of SU or insulin at start
- Nausea
- Vomiting, diarrhea, feeling jittery, dizziness, headache, dyspepsia
- Slows gastric emptying
 - Meds dependent on threshold concentrations (i.e. antibiotics) should be taken 1 hour before

Drug Class	Mechanism	Duration to maximum effect	Contraindications	Major side effects	A1C reduction
Sulfonylureas (Glipizide, Glimepride, Glyburide)	Increase β -cell insulin secretion (long-acting)	1 week	Hypersensitivity Renal insufficiency (60-90% renal clearance)	Hypoglycemia	1-2% (2% mono, 1% add-on)
DPP IV inhibitors (Januvia)	Decr incretin metabolism (long-acting)	1 week	Hypersensitivity (renal dosing)	Rhinitis	0.6-1.2%
Metformin (Glucophage, Riomet)	Decrease hepatic glucose production	2 weeks	Cr > 1.4 (females) Cr > 1.5 (males) CHF Active liver disease (LFTs >2.5x ULN)	Lactic Acidosis (rare)	1-2% (2% mono, 1% add-on)
TZDs (Actos, Avandia)	Increase peripheral glucose uptake (Muscle)	8-12 weeks	CHF (NYHA III or IV) Active liver disease (LFTs >2.5x ULN)	Edema Weight gain	1-2% (2% mono, 1% add-on)

Symmlin: What does it do?

- Synthetic analog of Amylin
- Neurohormone cosecreted with insulin by beta cells
- Secretion mirrors that of insulin
- Effects:
 - Slows gastric emptying
 - Suppresses postprandial glucagon secretion
 - Suppresses appetite/enhances satiety

Symmlin: What does it do?

- Results in reduction of postprandial hyperglycemia
- Reduces glucose fluctuations
- Lowers mealtime insulin requirement
- Avg. weight loss 3-6 lbs at 6 months
- Avg. A1C reduction 0.5% at 6 months

SymLin: How do I use it?

- Indicated for Type 1 or Type 2 DM patients taking mealtime insulin
- Injectable only
- Must be taken immediately before meal
- Should not be mixed with insulin
- Meal must contain minimum of 30g CHO

Symlin: How do I use it?

- Type I:
 - Reduce mealtime insulin by 50%
 - Start with 15mcg injection (2.5 units)
 - Titrate dose up by 15mcg (2.5 units) every 3-7 days as tolerated
 - Max dose 60mcg (10 units)
 - Once Symlin dose stabilized, adjust insulin for optimal glucose control
- Type II:
 - Reduce mealtime insulin by 50%
 - Start with 60mcg injection (10 units)
 - Titrate dose up to 120mcg (20 units) after 3-7 days as tolerated
 - Max dose 120mcg (20 units)
 - Once Symlin dose stabilized, adjust insulin for optimal glucose control

Symlin:

Precautions/Contraindications

- Gastroparesis
- Hypersensitivity
- Pediatrics
- Hypoglycemic unawareness
- GI motility-altering agent use

Symlin: What are the side effects?

- Hypoglycemia
- Nausea
- Headache
- Vomiting

Metformin: What does it do?

- Insulin sensitizer
 - Decrease insulin resistance
- Decrease hepatic glucose production
- Decrease intestinal glucose absorption

Metformin: How do I use it?

- Oral
 - 500, 850, 1000
 - ER 500, 750
- Liquid form
 - Riomet: 500mg/5cc
- Daily or split dosing
 - Max 2000mg/day

Metformin:

Precautions/Contraindications

- Black Box Warning: lactic acidosis
- Renal dysfunction
- CHF requiring medication
- Acidosis: metabolic/keto/lactic
- Iodinated contrast
 - Recheck Cr prior to restarting
- Caution
 - Elderly
 - Impaired liver function
 - Alcohol use

Metformin:

What are the side effects?

- Lactic Acidosis and Anemia
- GI
 - Diarrhea, flatulence, N/V, indigestion, abdominal discomfort, anorexia
 - Give at meals
 - Use ER preparation

Sulfonylureas: What does it do?

- Increases insulin production
 - Stimulates beta cell

SU: How do I use it?

- Glipizide (Glucotrol)
 - 5, 10
 - 2.5, 5, 10 ER
 - Metaglip (2.5/250, 2.5/500, 5/500)
- Glimeperide (Amaryl)
 - 1,2,3,4,6,8
- Glyburide (DiaBeta, Micronase)
 - 1.25, 2.5, 5
 - Glucovance (1.25/250, 2.5/500, 5/500)

SU: Precautions/Contraindications

- Near-term pregnancy
- Caution with liver dysfunction
- Caution in elderly
- Caution in renal dysfunction

SU: What are the side effects?

- Hypoglycemia
- Diarrhea
- Nausea
- Dizziness
- Nervousness
- Tremor

TZDs: What does it do?

- Increases insulin sensitivity

TZDs: How do I use it?

- Avandia
 - 2, 4, 8mg
 - Daily or BID (2 and 4mg only)
 - Max daily 8mg
- Actos
 - 15, 30, 45mg
 - Daily
 - Max daily 45mg
- No adjustment for renal dysfunction

TZDs:

Precautions/Contraindications

- Black Box warning
 - May cause or exacerbate CHF
- Contraindicated in CHF NYHA Class III-IV
- Contraindicated if ALT >2.5x ULN
- Edema, CHF, impaired liver fxn, sulfonylurea/insulin use, CHF risk factors

TZDs: What are the side effects?

- Edema/fluid retention/weight gain
- Angina
- MI (Avandia only)
- Pleural effusion or pulmonary edema
- Hepatotoxicity
- URI/headache

Januvia: What does it do?

- Inhibits DPP IV / incretin metabolism
- Increases insulin synthesis and release
- Decreases glucagon levels

Januvia: How do I use it?

- Oral
 - 25, 50, 100mg tabs
 - Initial dose 100mg daily
 - Take in am
 - Renal dosing
 - 50mg daily for CrCl 30-50
 - 25mg daily for CrCl <30

Januvia:

Precautions/Contraindications

- Type 1 DM
- Diabetic ketoacidosis

Januvia: What are the side effects?

- Rhinitis
- URI
- Headache
- Diarrhea
- Abdominal pain
- Arthralgia