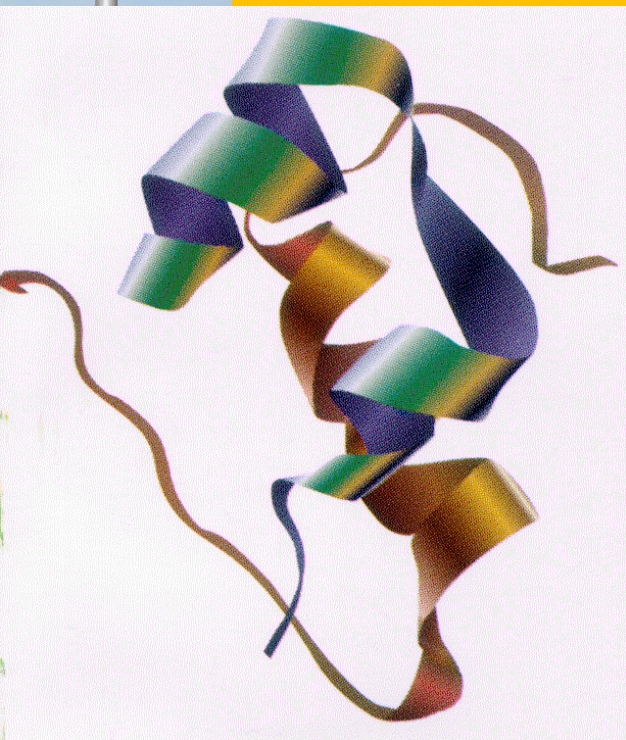




# Diabetes 2016: A Primer



## Characterizing and Treating Diabetes

**Barry H Ginsberg, MD, PhD**  
**Diabetes Technology Consultants**



# Barry H Ginsberg, MD, PhD

**65-72 MD, PhD (Molecular Biology) Einstein Col of Med**

**72-74 Internal Medicine, Beth Israel Boston (Harvard)**

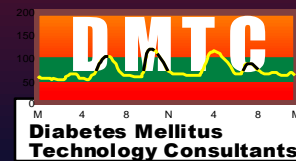
**74-77 Endocrine, Diabetes Branch, NIDDKD, NIH**

**77-90 Prof of Medicine and Biochemistry Univ of Iowa**

**83-90 PI DCCT at Iowa**

**90-07 VP WW Medical Affairs, Diabetes, Becton Dickinson**

**07- President Diabetes Technology Consultants**





# Diabetes, A Primer

## Topics:

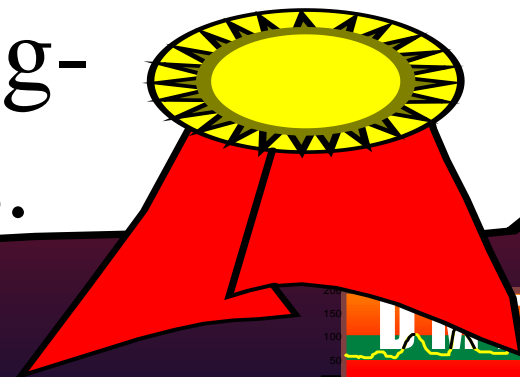
- What is diabetes?
- Why is it bad?
- How do we treat and monitor?





# What is Diabetes?

A disease characterized by high blood glucose (sugar), associated with abnormalities in metabolism and often associated with long-term complications.



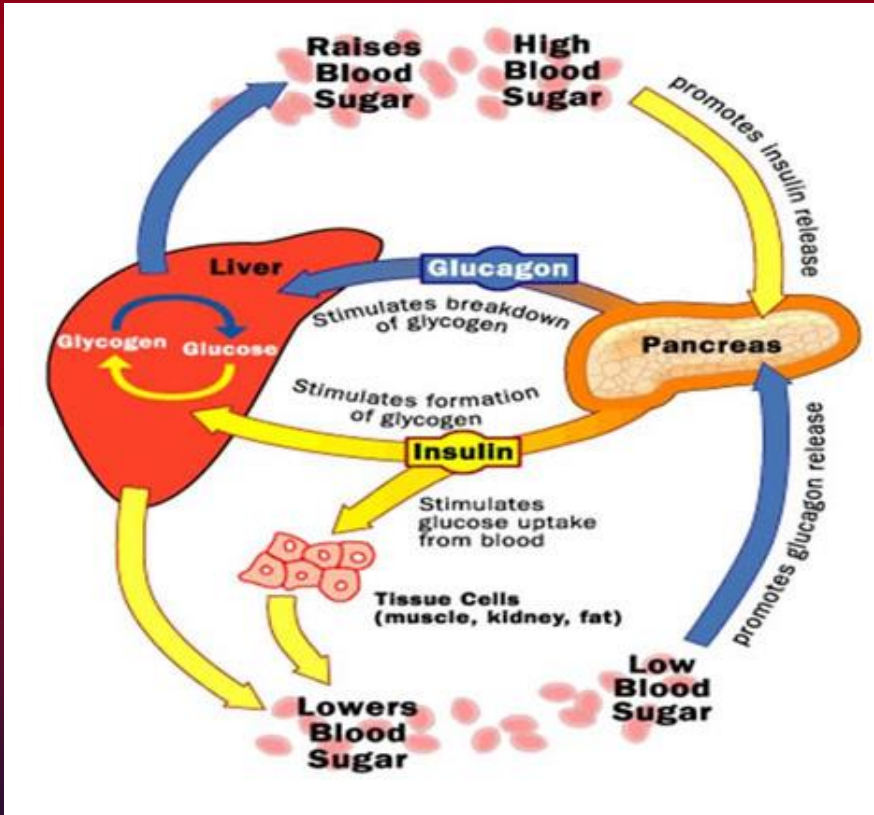


# Glucose Regulation

## Two Sources of Energy: Glucose and Fat

### Glucose Raised

- Food
- Liver
- Glucagon
- Adrenaline
- Cortisol
- Growth Hormone



### Glucose Lowered

- Storage in Liver
- Conversion to Fat
- Exercise
- Urine
- Metabolism
- Insulin



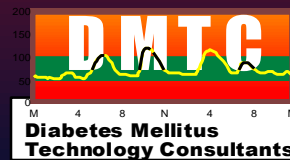
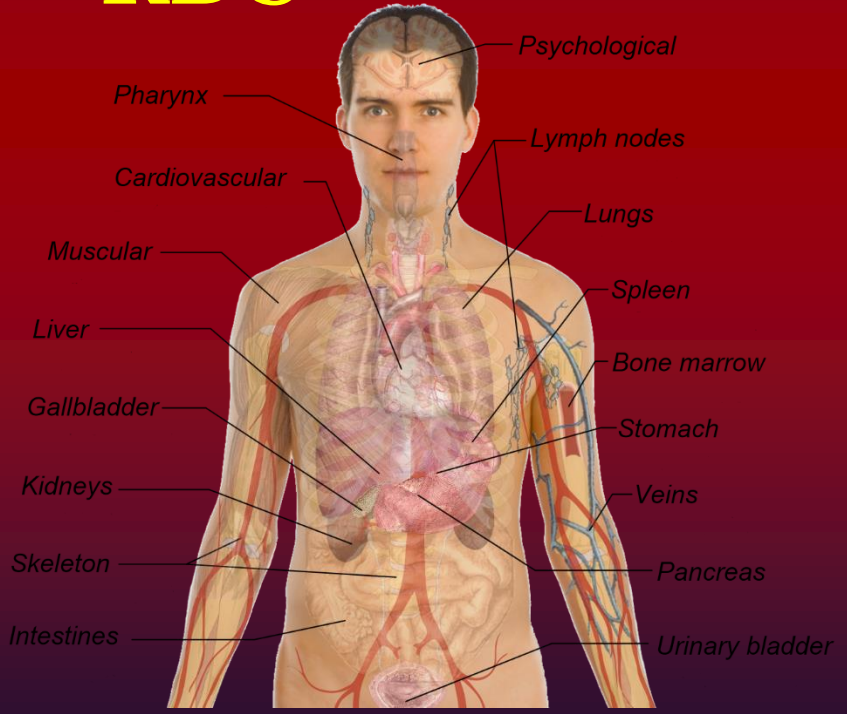


# Cellular Energy

**Glucose**  
**Brain**  
**RBC**

**Fat**  
**Heart**

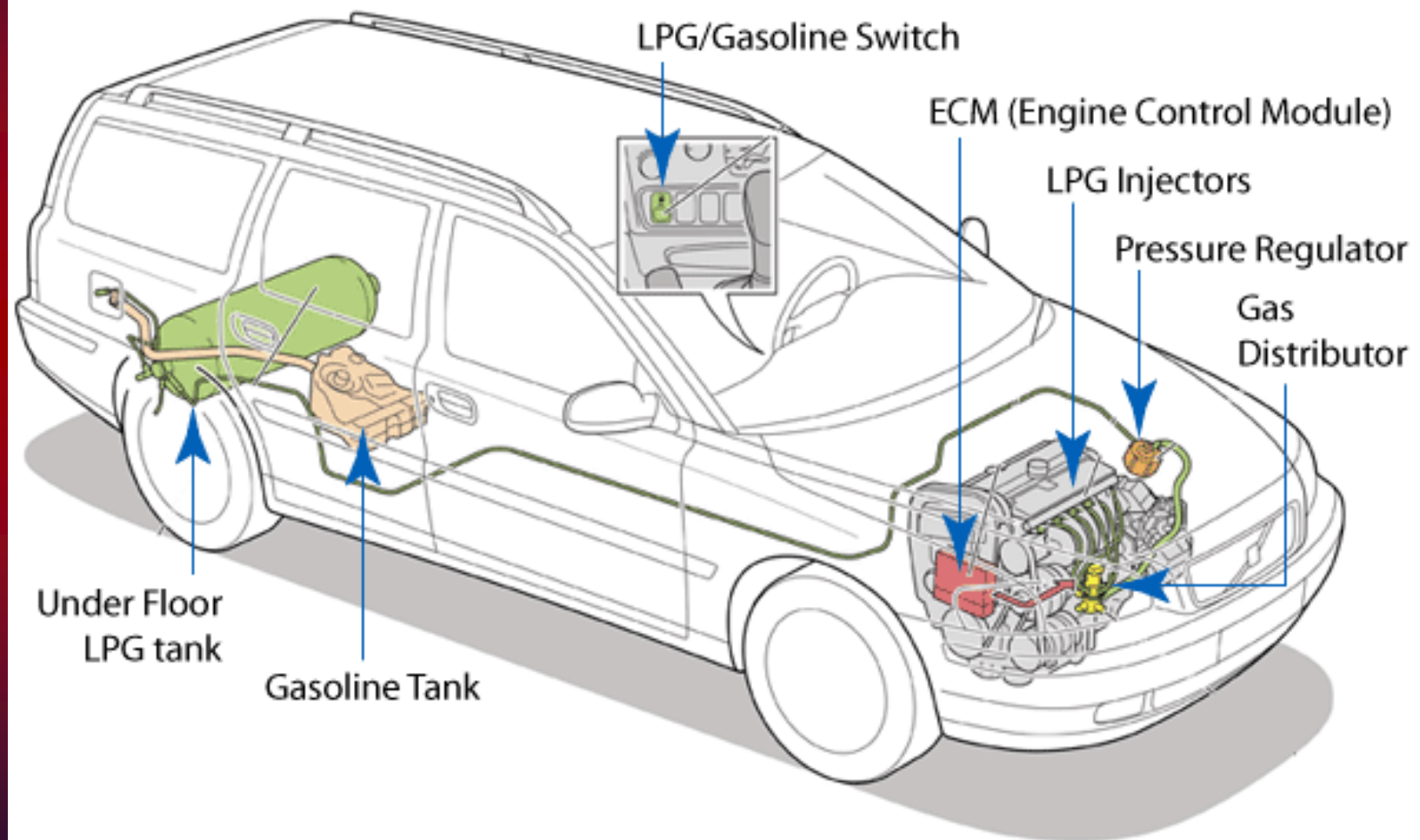
**Both**  
**Muscle**  
**Liver**  
**Fat**  
**Lungs**  
**Kidneys**  
**Skin**  
**GI Tract**  
**Immune**





# Energy Sources for Cars

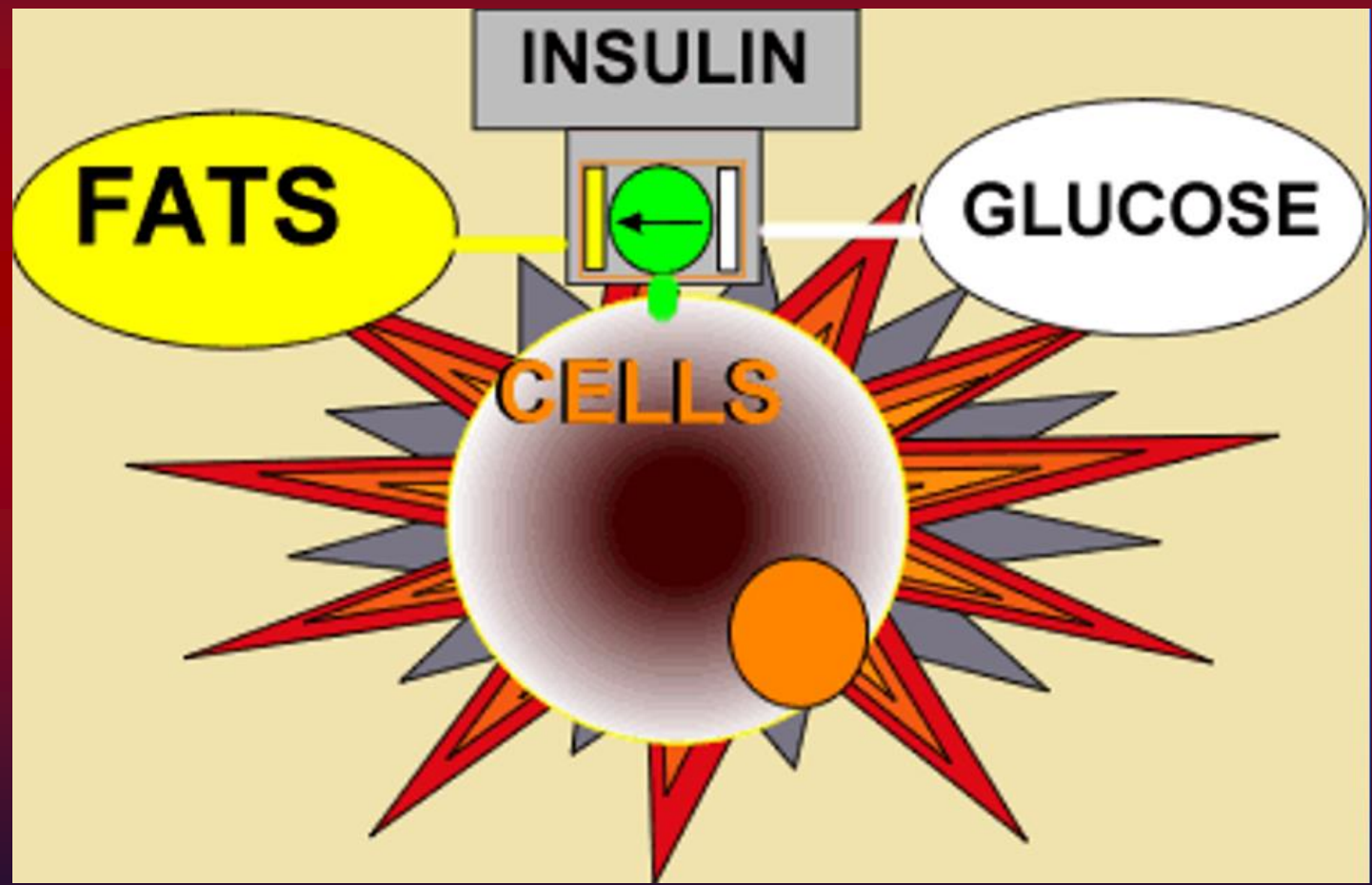
## Volvo Bi-fuel System





# Energy Sources for Life

## Glucose, Insulin & Energy

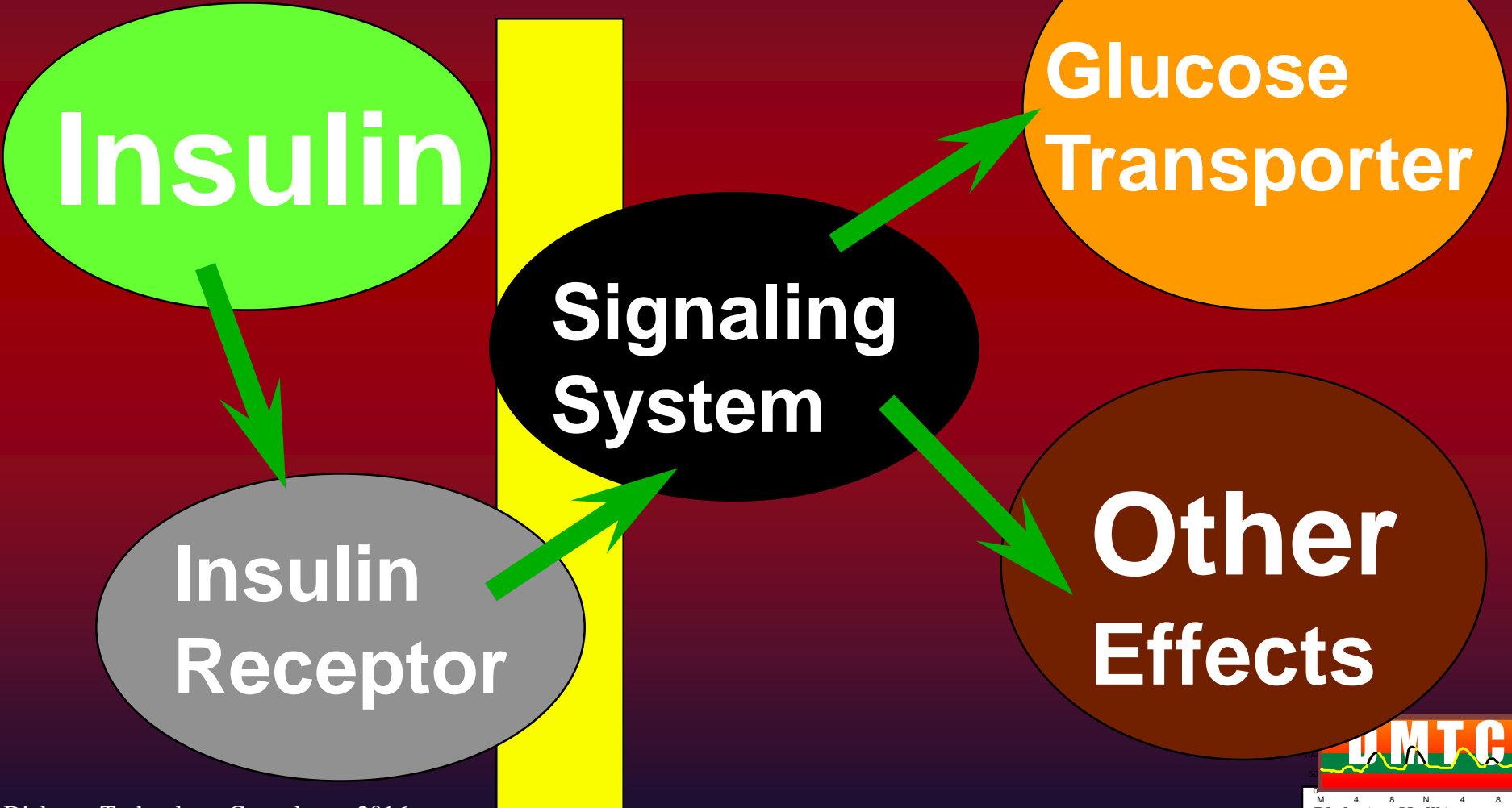






# Causes of Type 2 Diabetes

## Insulin Action

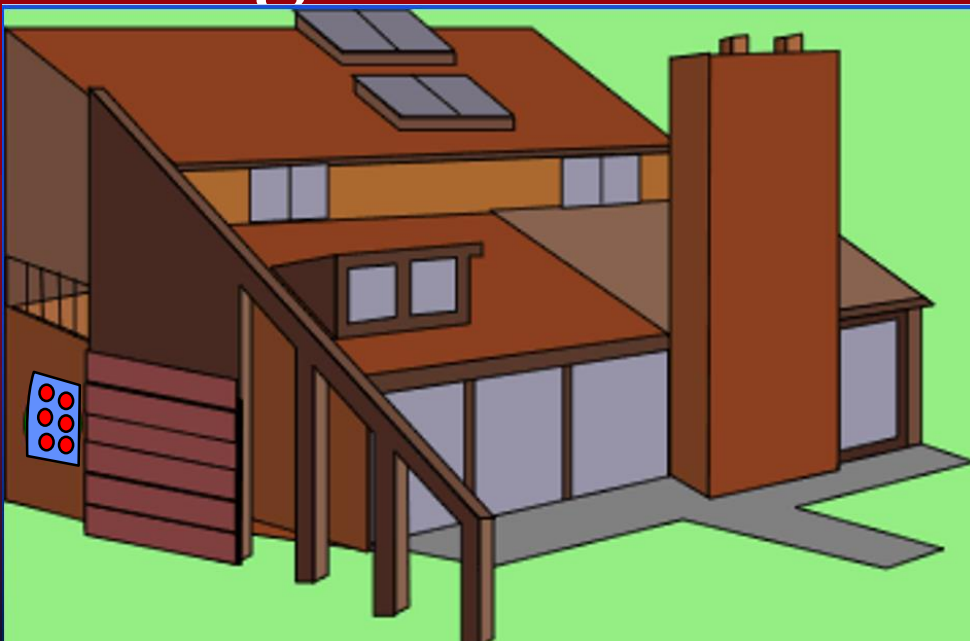




# Causes of Type 2 Diabetes

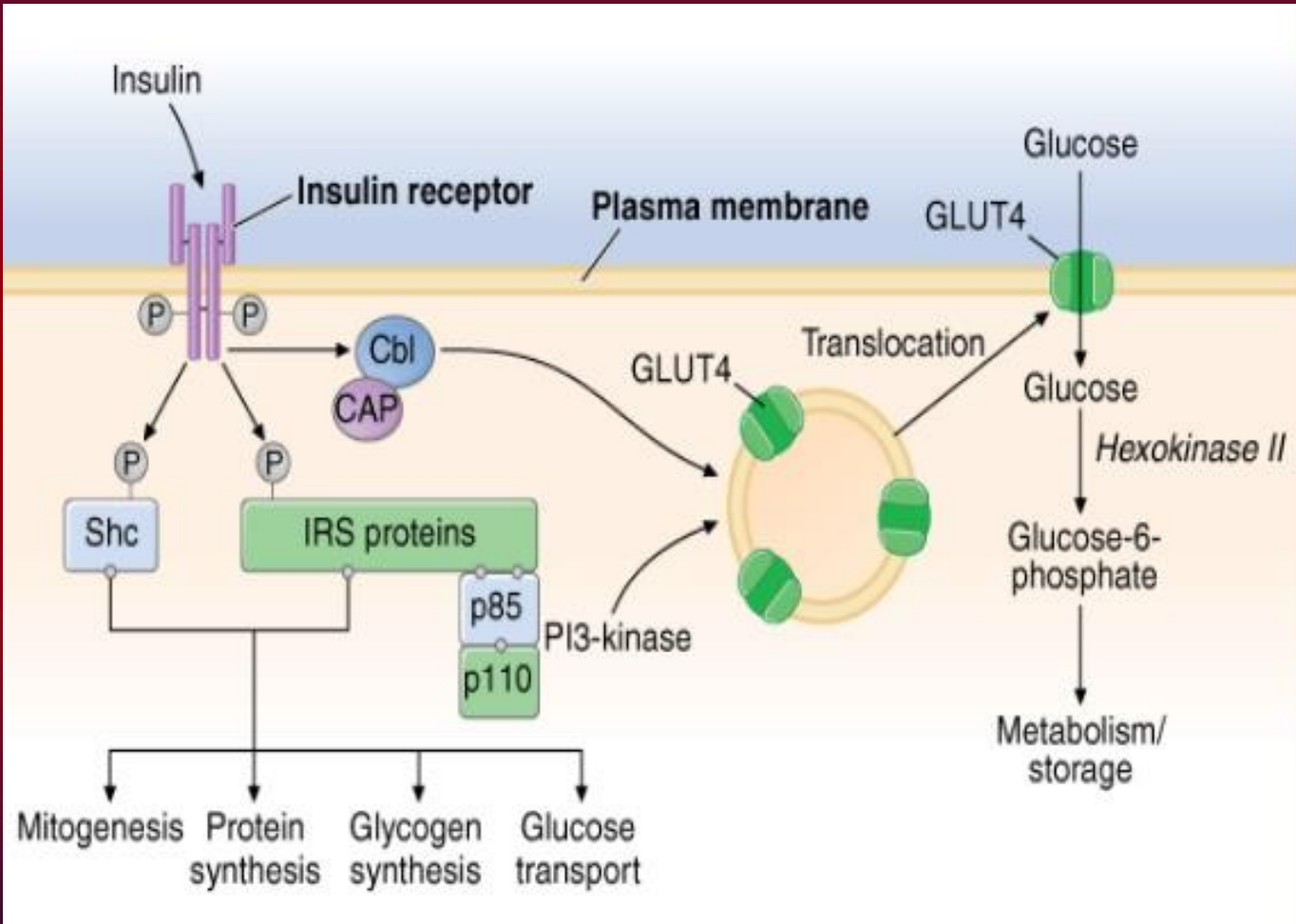
## Insulin Action:

- Insulin needs to pass **its signal** into the cell
- Similar to the signal of a external garage doorkey!



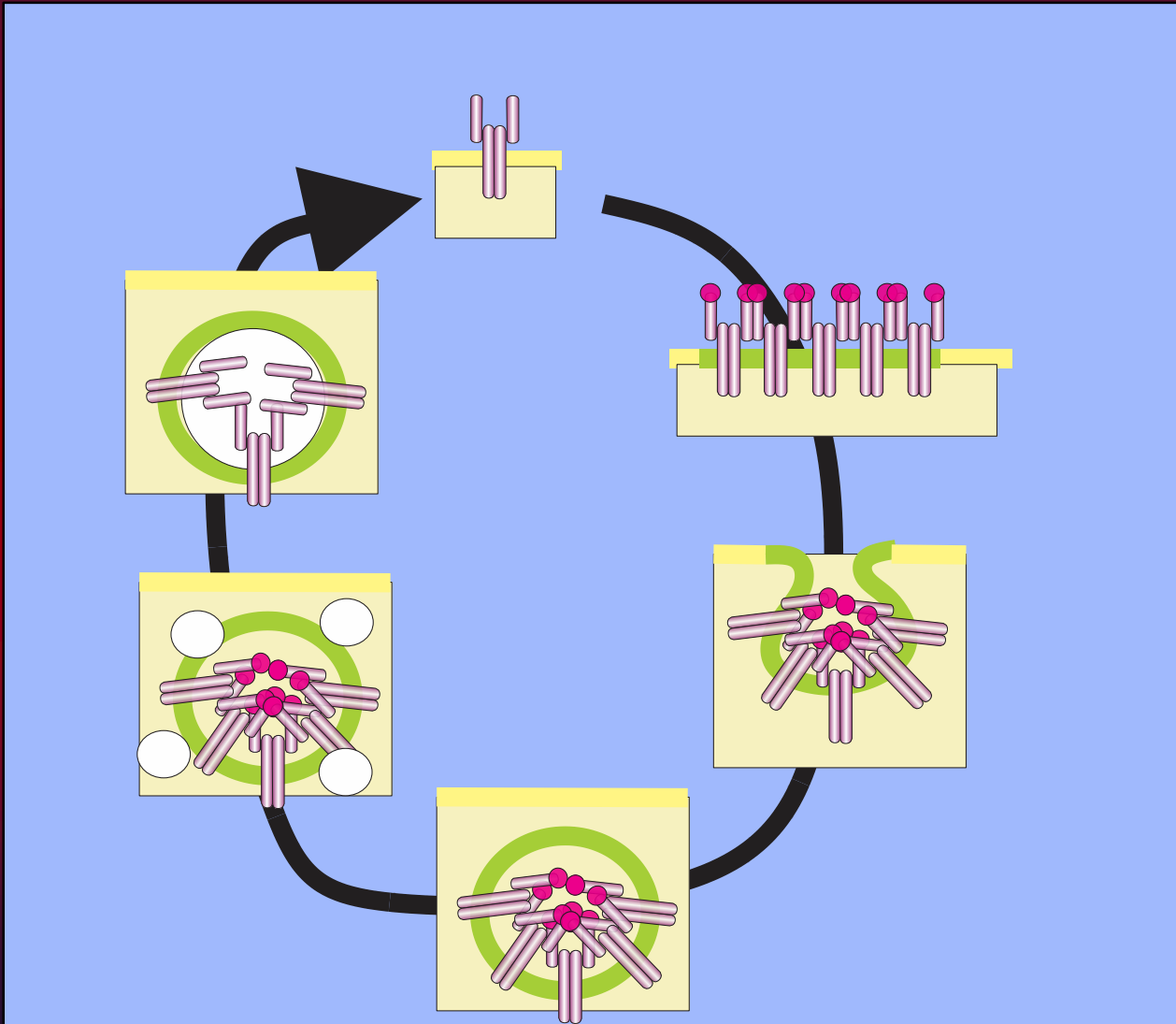


# Insulin Receptor Activity





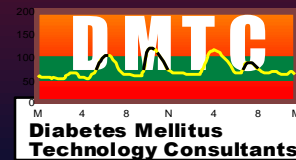
# Insulin Receptor Regulation





# Types of Diabetes

- **Type 1** **~1.9M**  
(pancreatic destruction)  
Insulin dependent (IDDM), JODM
- **Type 2** **~29M**  
(insulin resistant) (~8 M undiagnosed)  
Non-insulin dependent (NIDDM), AODM
- **Gestational** **~200K**
- **PreDiabetes** **~30M**





# Symptoms of Diabetes: Type 1

- Classically called the 3 P's:
- Polyuria: excess urination  
**Named for this symptom**
- Polydipsia: excess drinking
- Polyphagia: excess eating
- Weight loss: water weight



# Common Symptoms: Type 2

- **Nonspecific**

**Infections**

**Poor healing**

**Tiredness**

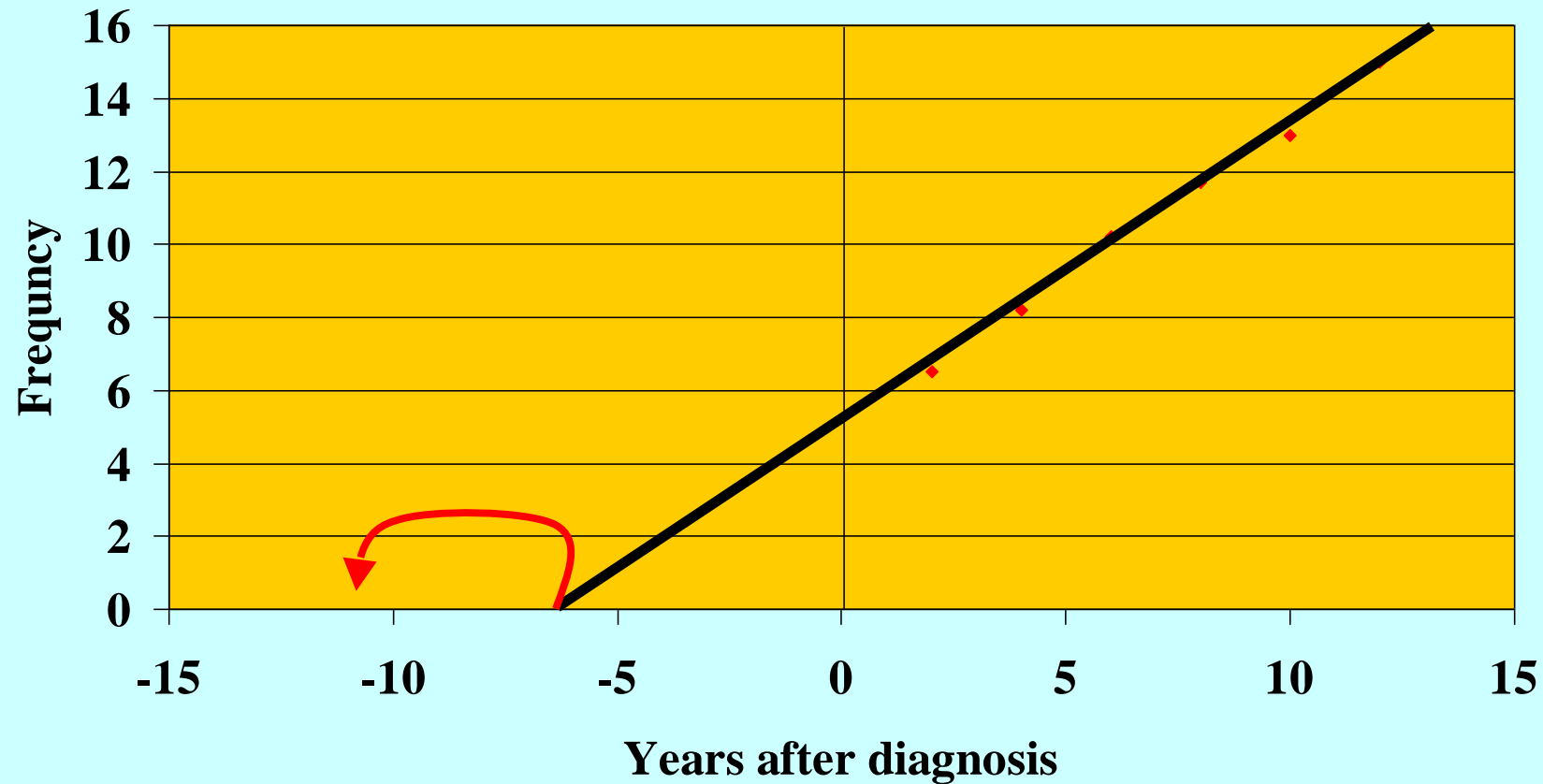
**Blurred vision**



# Type 2 Diabetes Starts 11 Years Before Diagnosis



## Retinopathy in Type 2







# Diagnosing Diabetes:

- **Random blood glucose** **>200 S/2**
- **Fasting blood glucose** **>126 S/2**
- **Postprandial blood glucose** **>200**
- **Glucose Tolerance Test**
- **Hemoglobin A1c** **>6.5**



# Diagnosing Diabetes:

## Pre-Diabetes

### Impaired Glucose Tolerance (oGTT)

- Normal fasting, 2hr post-prandial  $\geq 140$

### Impaired Fasting Glucose

- Fasting  $> 100$ , 2hr post-prandial  $< 140$

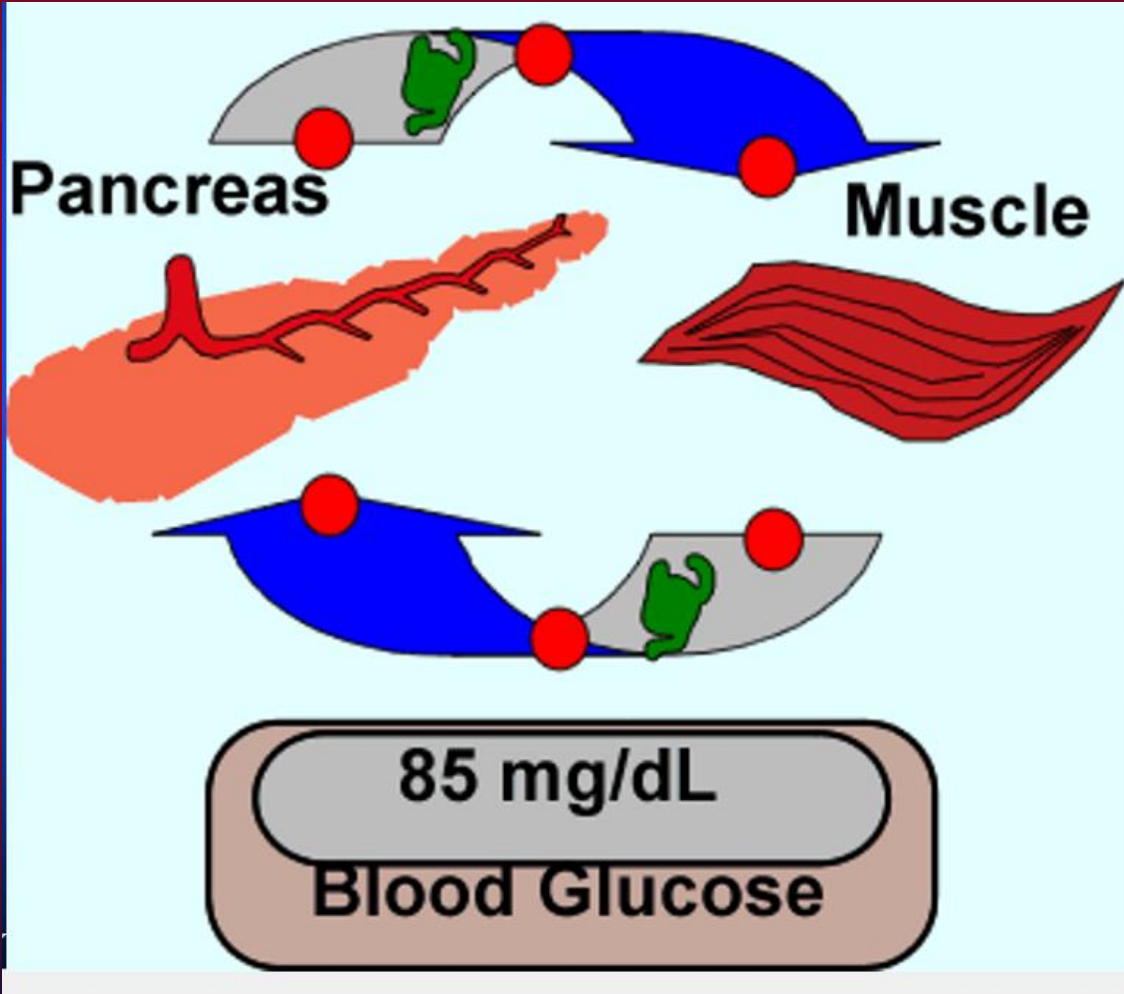
## Risks

- Increased cardiovascular risk
- Many go onto DM within 5 years (6%/year)



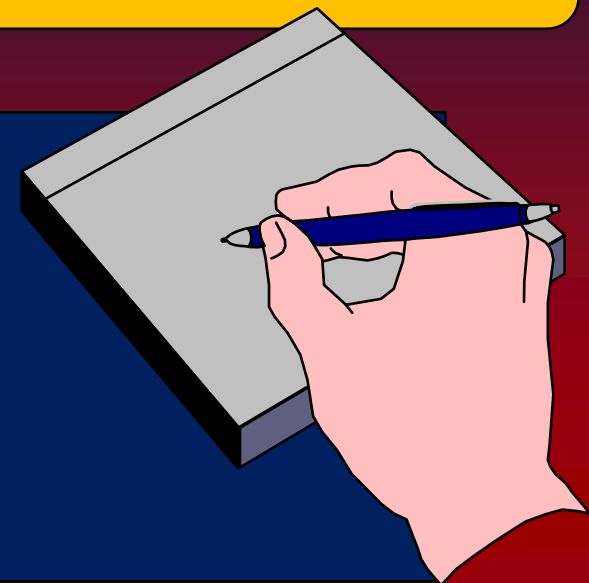
# Causes of Diabetes

## Blood Glucose Control





# Causes of Diabetes



- **Lack of insulin**

  - Failure of secretion**

    - Complete** Type 1

    - Partial** Type 2

- **Insulin resistance**

  - Error in insulin recognition** Type 1

  - Error in insulin action** Type 2

- **Hepatic gluconeogenesis**





# Causes of Diabetes

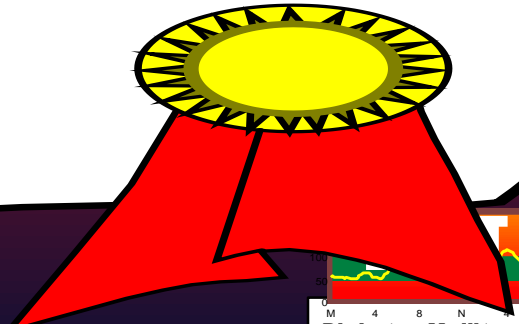
## Type 1

**5% of all diabetes**

**Generally younger**

**Normal weight**

**Genetic**



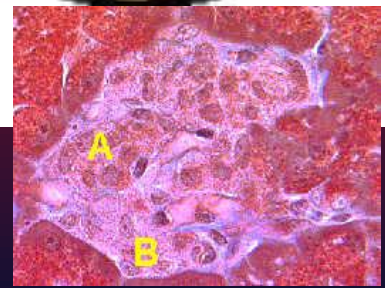


# Causes of Type 1 Diabetes

## Pancreas:



- Mostly digestive organ (>99%)
- Insulin secreted by Islets of Langerhans(<1%)

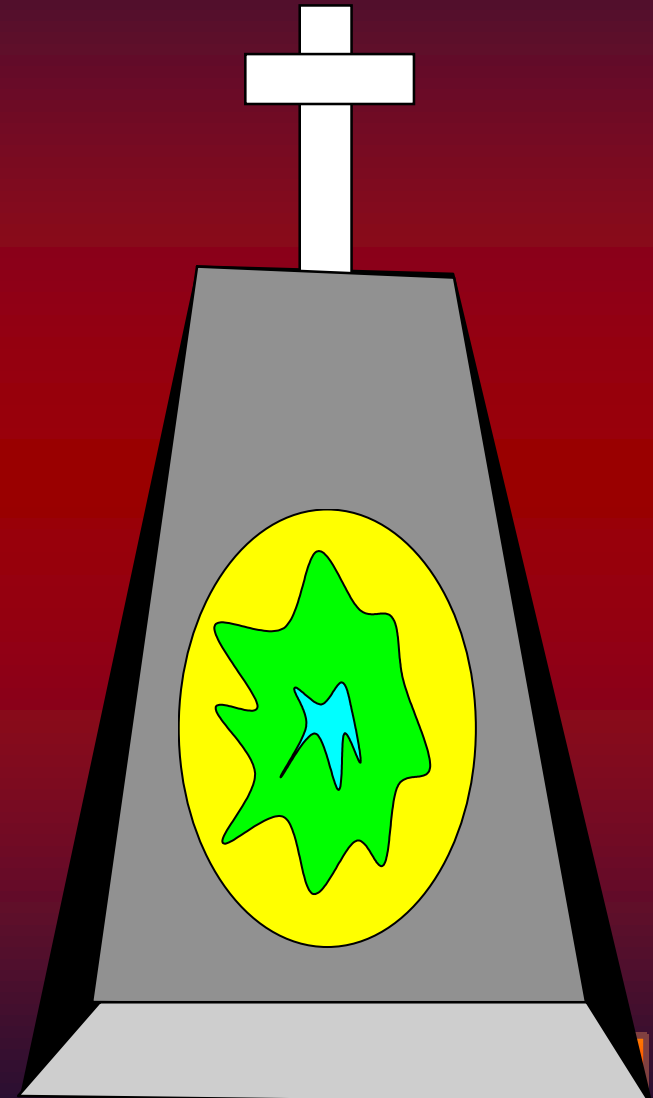




# Causes of Type 1 Diabetes

## Death of an Islet

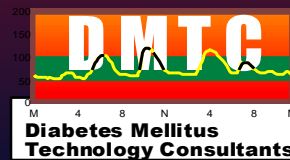
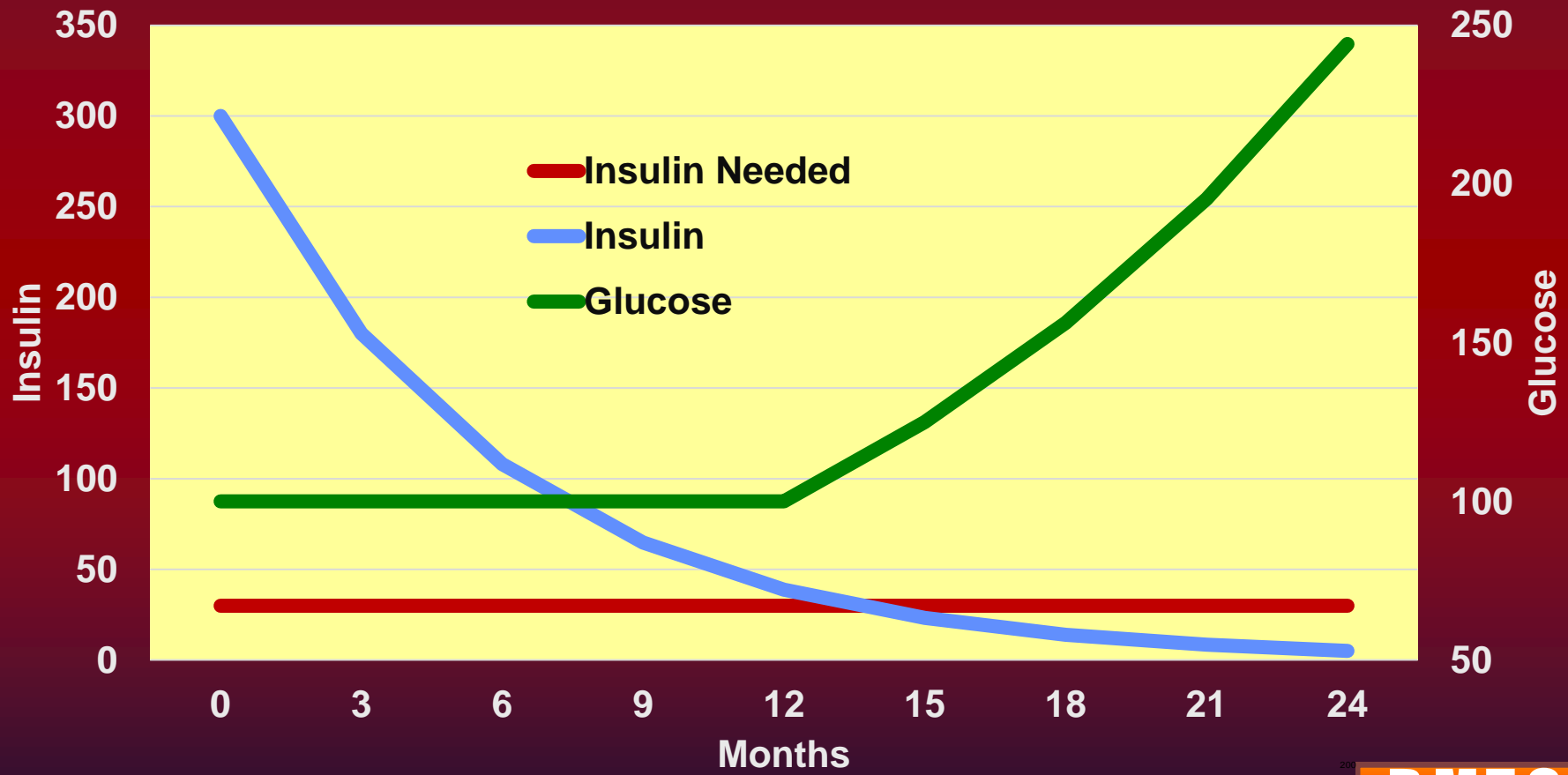
- Genetics
- Virus Infection
- Immune Problems  
(Autoimmune)





# Causes of Type 1 Diabetes

## Insulin Secretion







# Causes of Type 2 Diabetes

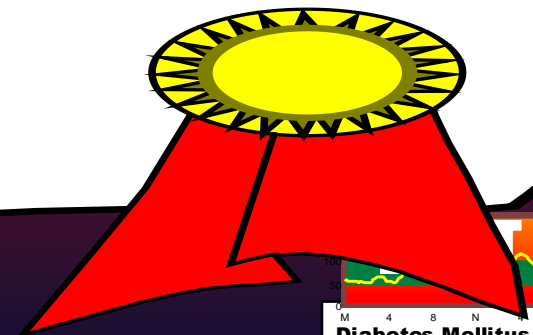
## Type 2

**95% of all diabetes**

**Generally older**

**Usually obese**

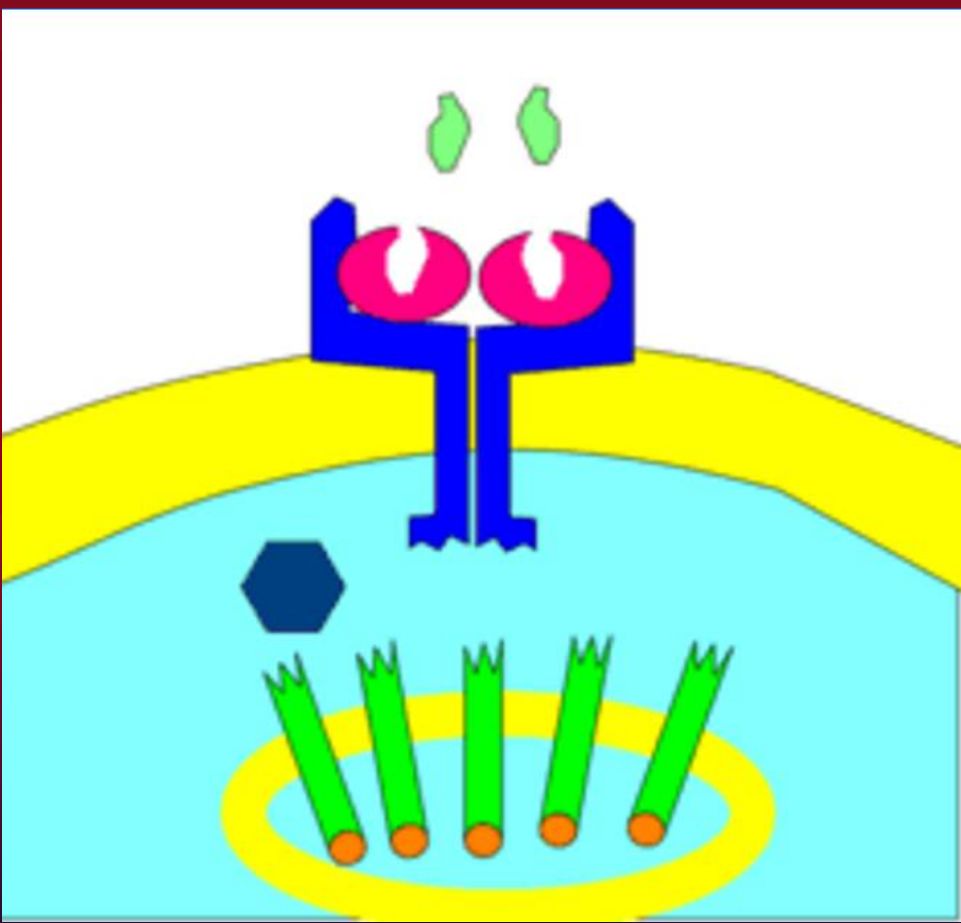
**Genetic**





# Insulin Resistance

## Components of cellular insulin response:

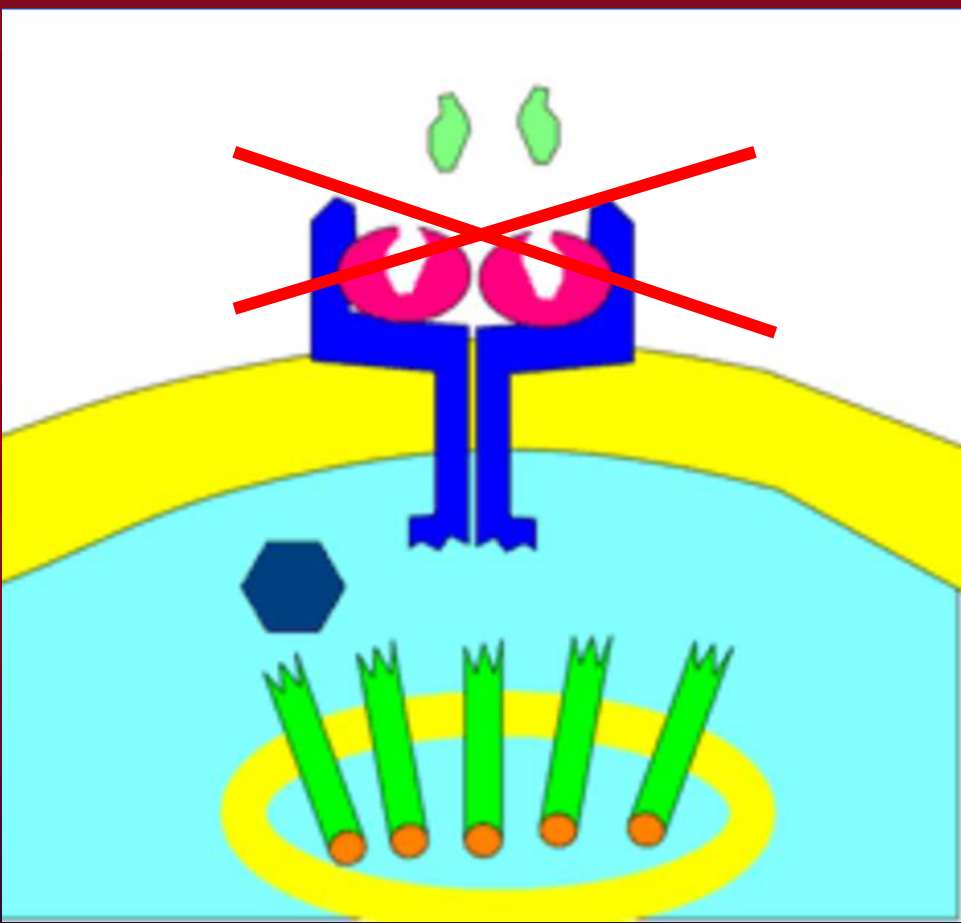


- Receptor
- Binding
- Transmembrane
- Tyrosine Kinase
- Signal Proteins
- Glucose Transporter
- Translocation
- Glucose Transport

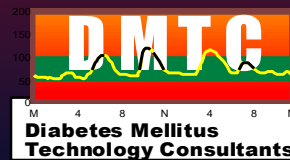


# Insulin Resistance

## Components of cellular insulin response:



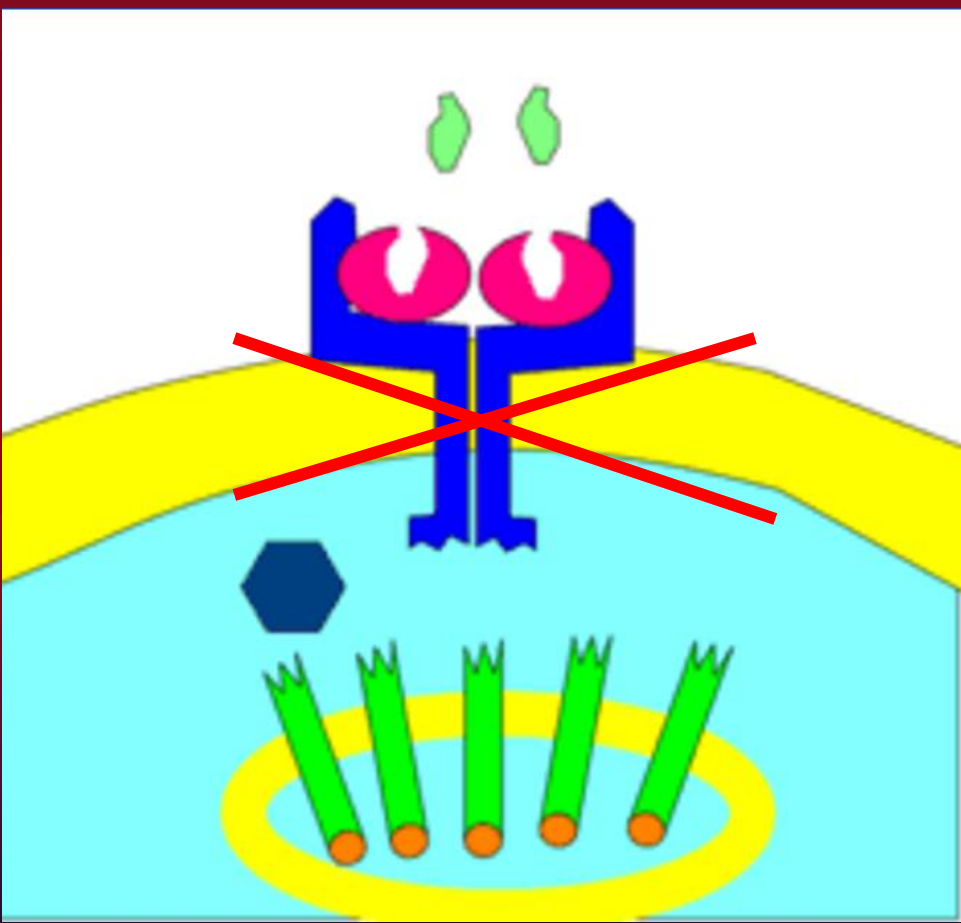
- Receptor
- Binding
- Transmembrane
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- Glucose Transporter
- Translocation
- Glucose Transport





# Insulin Resistance

## Components of cellular insulin response:

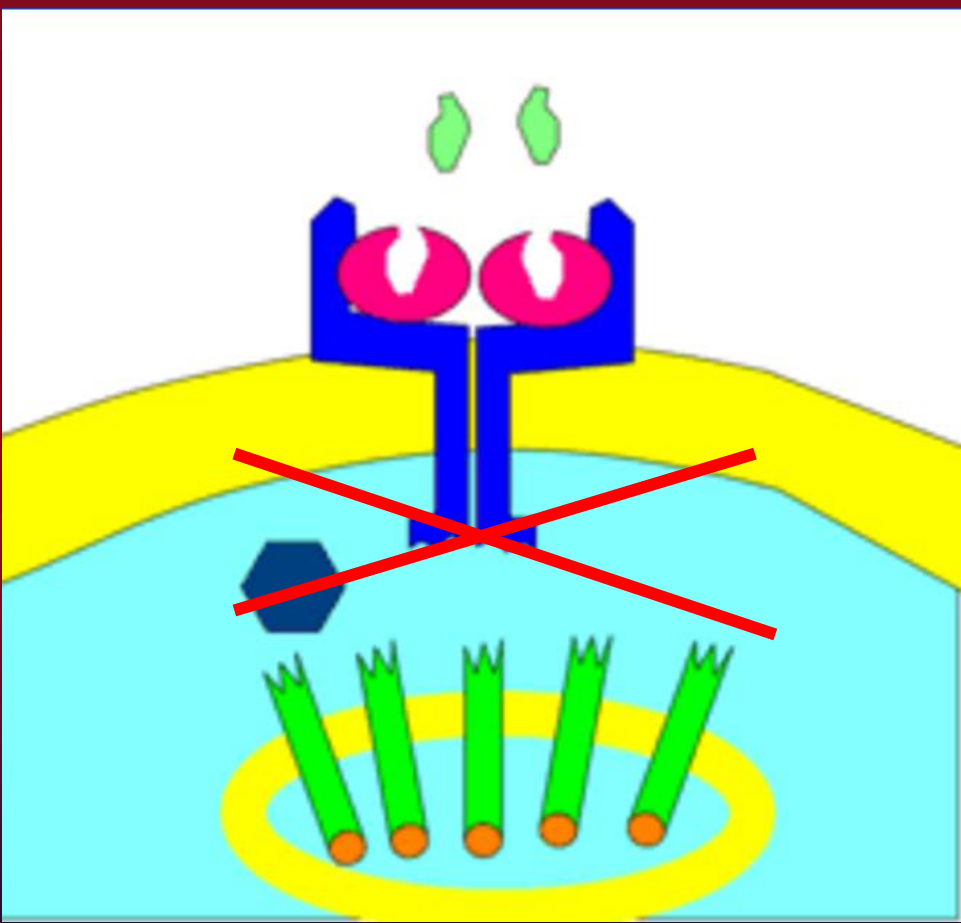


- Receptor
- Binding
- Transmembrane
- Tyrosine Kinase
- Signal Proteins
- Glucose Transporter
- Translocation
- Glucose Transport



# Insulin Resistance

## Components of cellular insulin response:

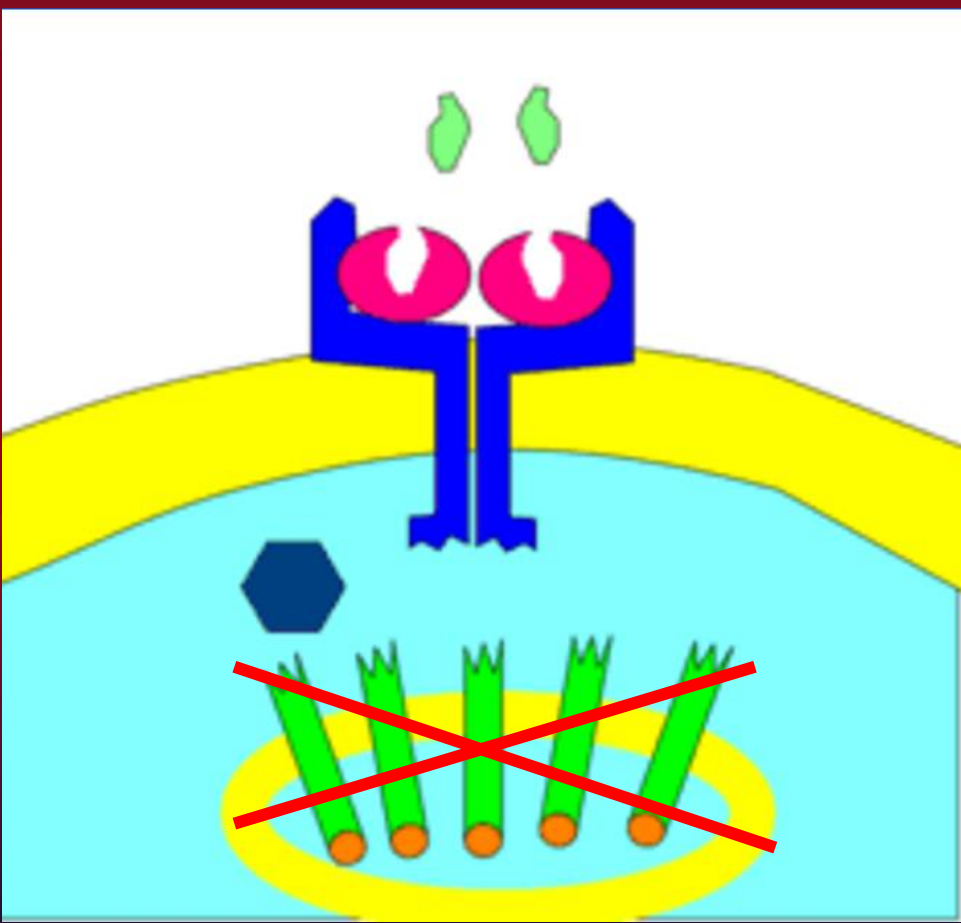


- Receptor
- Binding
- Transmembrane
- Tyrosine Kinase
- Signal Proteins
- Glucose Transporter
- Translocation
- Glucose Transport

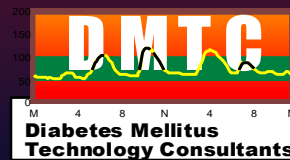


# Insulin Resistance

## Components of cellular insulin response:



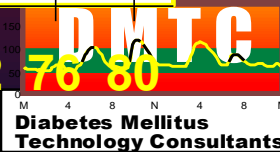
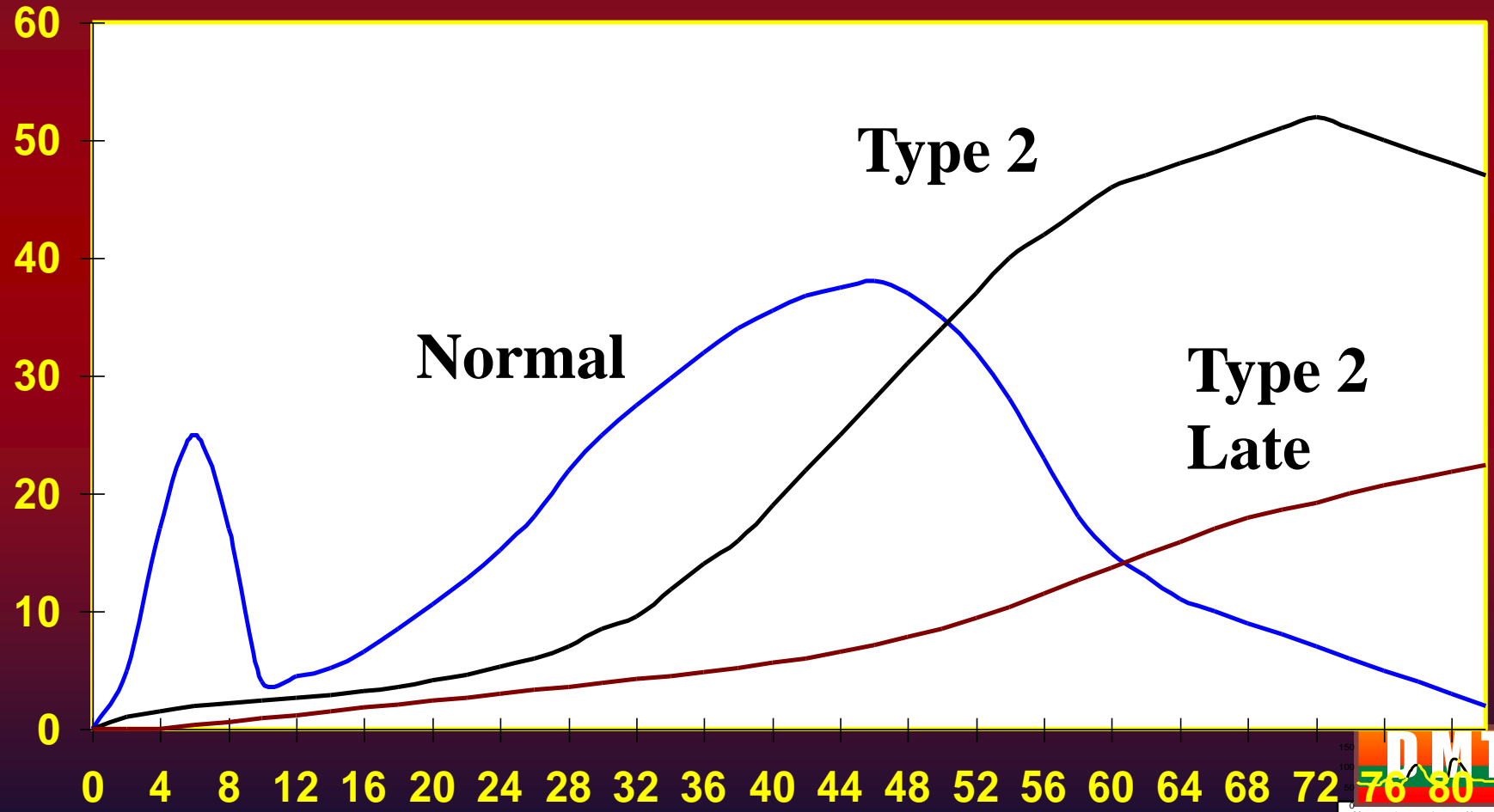
- Receptor
- Binding
- Transmembrane
- Tyrosine Kinase
- Signal Proteins
- Glucose Transporter
- Translocation
- Glucose Transport





# Insulin Insufficiency

## Insulin Secretion





# Causes of Type 2 Diabetes

## Hepatic Gluconeogenesis

- Liver makes more sugar
- Leads to high fasting BG







# Distribution of Diabetes

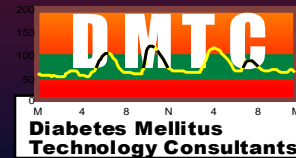
## Epidemiology of Type 2

- **Non-Caucasian disease**
- **Oriental “descent”**
  - Native Americans (20-50%)
  - Western Hispanics (10-15%)
  - Orientals (10-15%)
- **Asian Indians ~ 25%**
- **Africans (Negroid) ~10%**



# Why is Diabetes Bad?

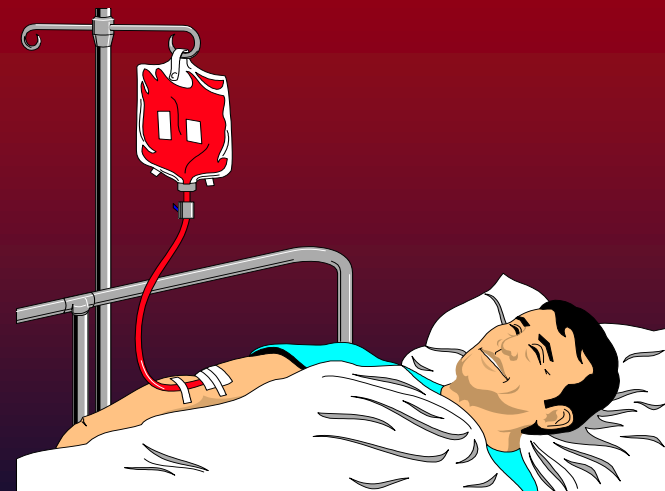
- Acute Complications
  - Long-term Complications
  - Economics
  - Secondary Prevention
- Bad News
- Good News





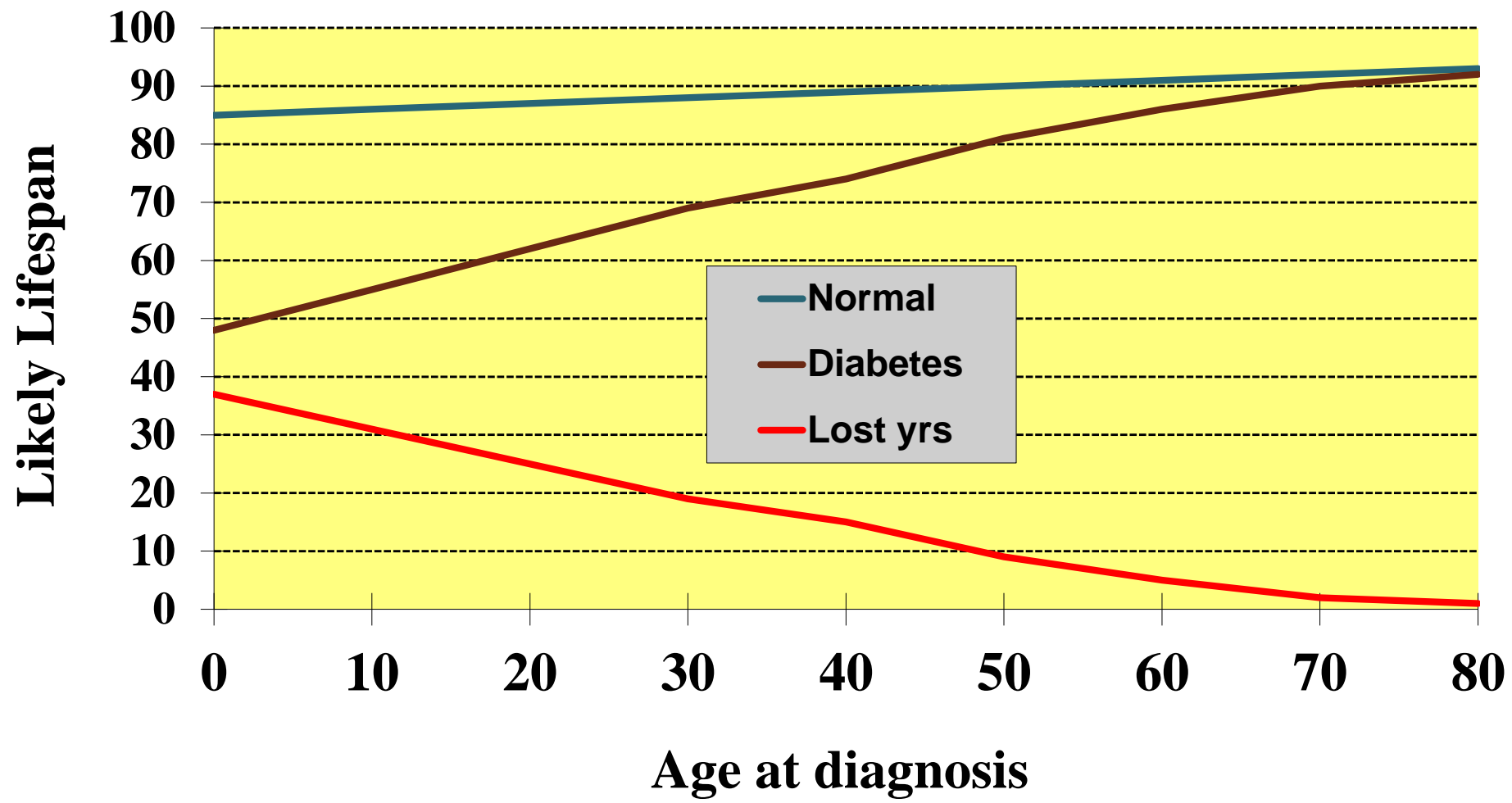
# Acute Complications

- Infections, Dental, Poor wound healing
- Type 1  
Ketoacidosis
- Type 2  
NonKetotic hyperosmosis





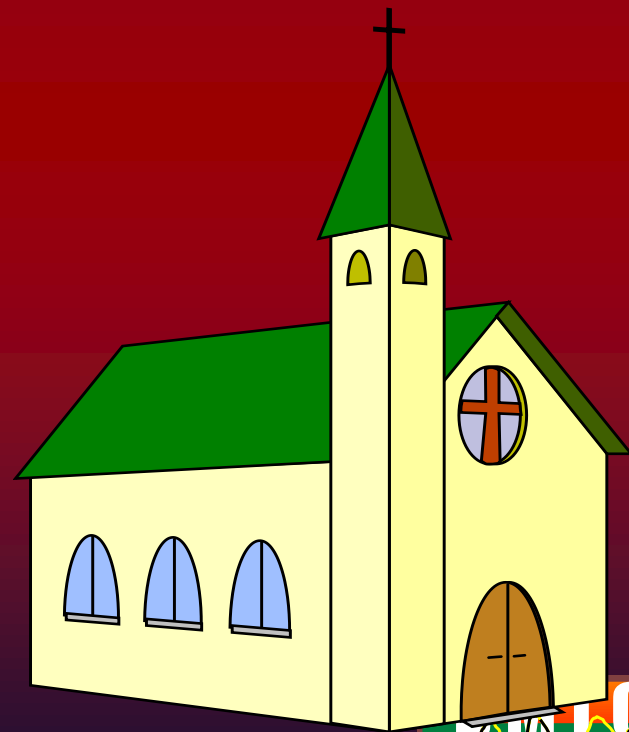
# Death From Diabetes





# Death From Diabetes

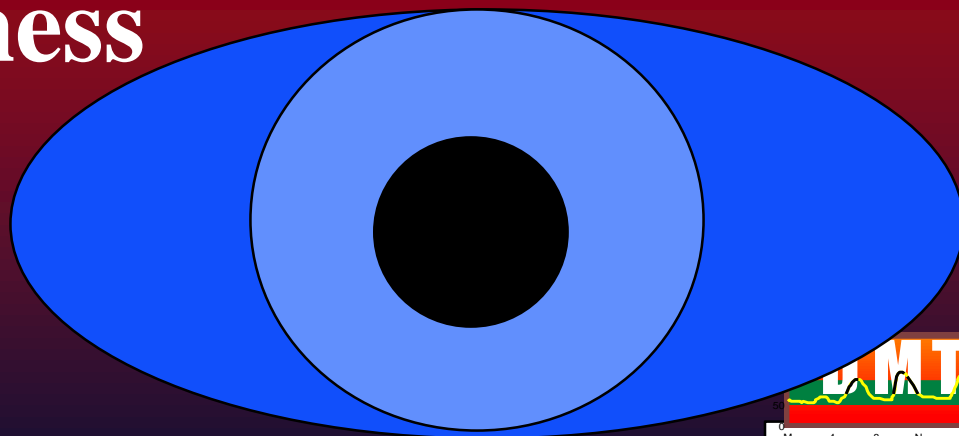
- Third leading cause of death
- Heart disease
- Kidney failure





# Eye disease

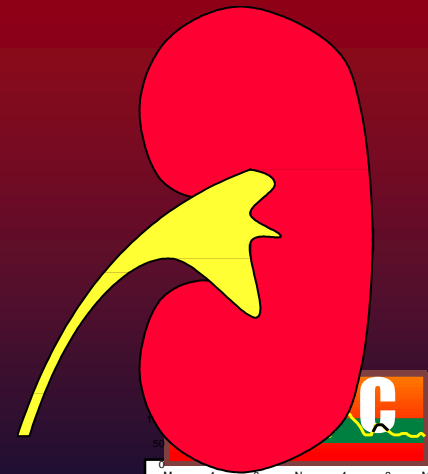
- **Blurred vision**
- **Cataracts**
- **Retinopathy**
- **Leading cause of acquired blindness**
- **17 x more blindness**





# Diabetic Kidney disease

- 33% of all dialysis and transplantation
- 25 x more renal failure
- High blood pressure
- Swelling





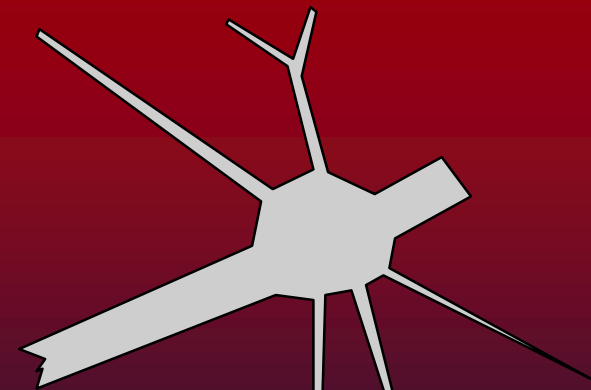
# Diabetic Nerve Disease

- **Types of nerves involved:**

**Peripheral**

**Autonomic**

**Usually not brain or spine directly**



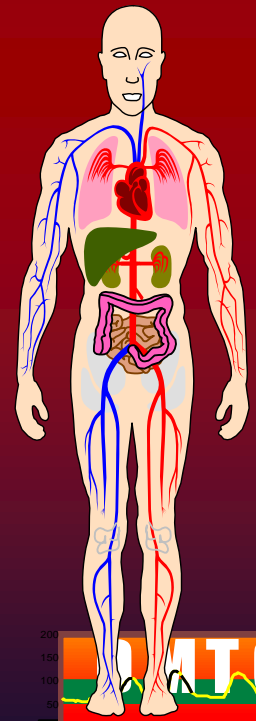
Diabetes Mellitus  
Technology Consultants



# Cardiovascular Disease



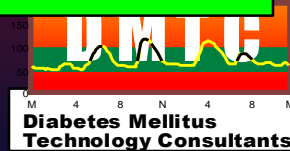
- Heart attacks up 2-20 x
- Females lose protection
- Vascular ds up 2-5 x
- Strokes up 2-6 x
- May be due to post-prandial blood glucose





# Diabetic Foot

- Nerve & CV disease
- 50% of non-military amputations
- 50% preventable



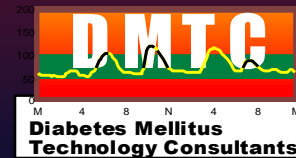


# Economic Cost of Diabetes (2012)

- 20% of total health care cost in US
- \$245 Billion/yr (176 direct, 69 indirect)
- Cost of care

Direct 20%

Complications 80%





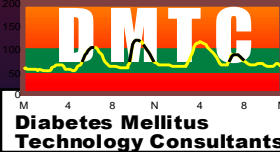
# Diabetes Control and Complications Trial and EDIC

- 1441 patients type 1 diabetes
- **Demonstrated:**
  - 1.8% decrease in Hb A1c in experimental group
  - Eye disease: 76% reduction
  - Kidney disease: 50% reduction
  - Nerve disease: 60% reduction
  - CVD: 57% reduction (EDIC)
- **Very Cost Effective**



# Why Treat Diabetes?

- **Type 1 :**
  - Survival
  - Feel better
  - Prevent complications
- **Type 2**
  - Feel better
  - Prevent complications





# Treating Diabetes

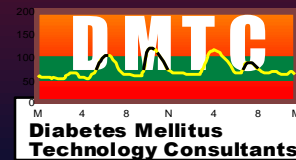
- **Nutrition / Exercise**
- **Glucose Monitoring**
- **Team Care / Education**
- **Lipids / BP**





# Therapy of Type 1 DM

- **Insulin**





# Therapy of Type 2 DM

- Orals / Combination
- Insulin







# GLYCEMIC CONTROL ALGORITHM

## LIFESTYLE MODIFICATION

(Including Medically Assisted Weight Loss)

ENTRY A1c < 7.5%

ENTRY A1c ≥ 7.5%

ENTRY A1c > 9.0%

### MONOTHERAPY\*

- ✓ Metformin
- ✓ GLP-1 RA
- ✓ DPP4-i
- ✓ AG-i
- ⚠ SGLT-2\*\*
- ⚠ TZD
- ⚠ SU/GLN

If A1c > 6.5% in 3 months add second drug (Dual Therapy)



### DUAL THERAPY\*

- GLP-1 RA ✓
- DPP4-i ✓
- TZD ⚠
- \*\* SGLT-2 ⚠
- Basal insulin ⚠
- Colesvelam ✓
- Bromocriptine QR ✓
- AG-i ✓
- SU/GLN ⚠

MET or other first-line agent

If not at goal in 3 months proceed to triple therapy



### TRIPLE THERAPY\*

- GLP-1 RA ✓
- TZD ⚠
- \*\* SGLT-2 ⚠
- Basal insulin ⚠
- DPP4-i ✓
- Colesvelam ✓
- Bromocriptine QR ✓
- AG-i ✓
- SU/GLN ⚠

MET or other first-line agent

If not at goal in 3 months proceed to or intensify insulin therapy



NO SYMPTOMS

SYMPTOMS

DUAL THERAPY OR TRIPLE THERAPY

INSULIN ± OTHER AGENTS

ADD OR INTENSIFY INSULIN

### LEGEND

- ✓ = Few adverse events or possible benefits
- ⚠ = Use with caution

\* Order of medications listed are a suggested hierarchy of usage

\*\* Based upon phase 3 clinical trials data

PROGRESSION OF DISEASE



# Therapeutic Modalities

Oral agents fall into three broad categories:

- **Agents that increase insulin secretion:**

Sulfonylureas

Metiglinides

Incretins

- **Agents that lower insulin resistance:**

Biguanides

Thiazoladinediones

- **Others**

Alpha Glycosidase Inhibitors

SGTL2 Inhibitors





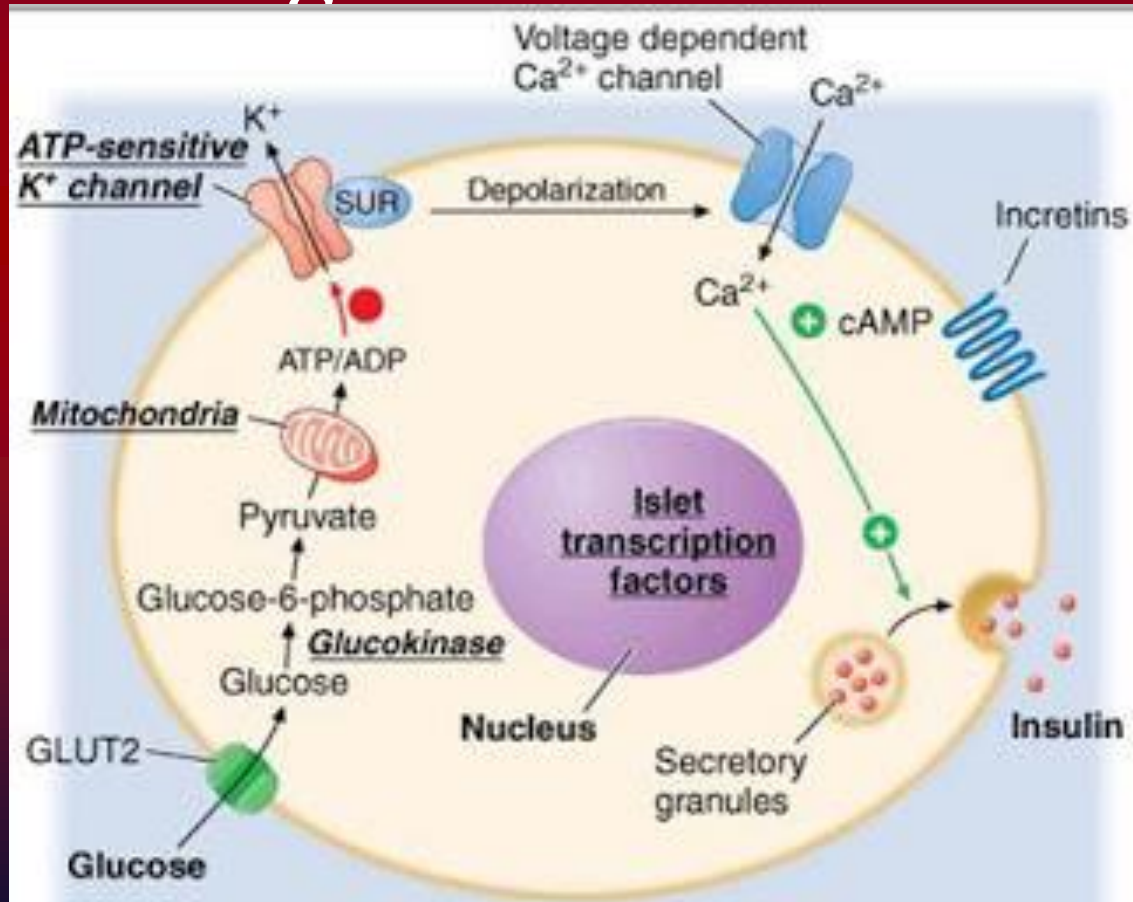
# Properties of Oral Agents

Agent	Effective-ness	Safety	Cost	Side effects
Sulfonylurea	Green	Yellow	Green	Yellow
Metiglinide	Green	Yellow	Yellow	Yellow
Biguanide	Green	Yellow	Green	Red
AGI	Red	Green	Green	Red
Glitazone	Yellow	Yellow	Red	Green
Incretin	Green	Green	Red	Green
SGTL2	Green	Green	Red	Yellow

# Sulfonylureas, diabetes pills



- Stimulate islets to produce insulin but need functioning beta cells





# Sulfonylureas, Specific drugs

- **Sulfonylureas**

Very cost effective (\$6/mo/HbA1c drop)

Payers like them

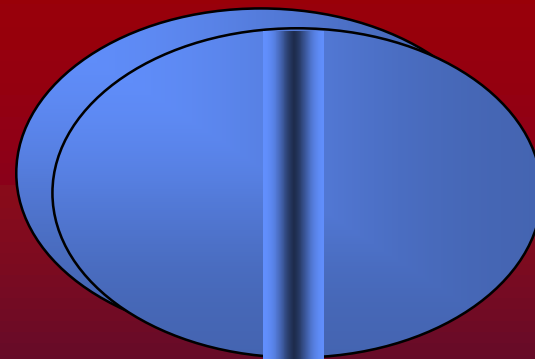
- **Hypoglycemia**

Often no SMBG

Often no education: frightening

- **Weight gain**

- **Increased CV disease**



# Incretins- Candidate hormones

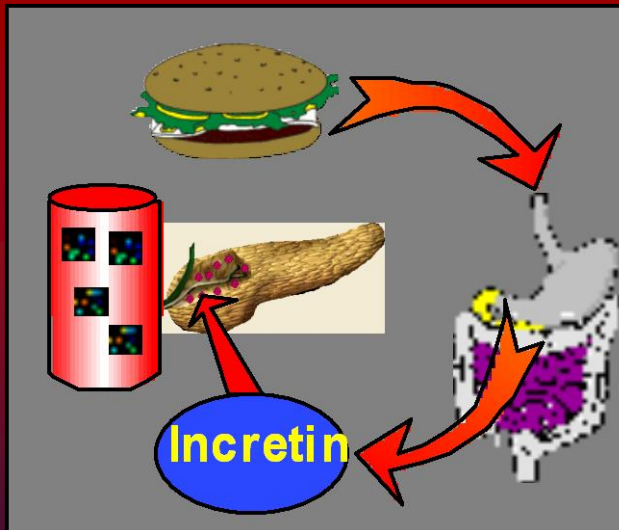


- **Postulate:**

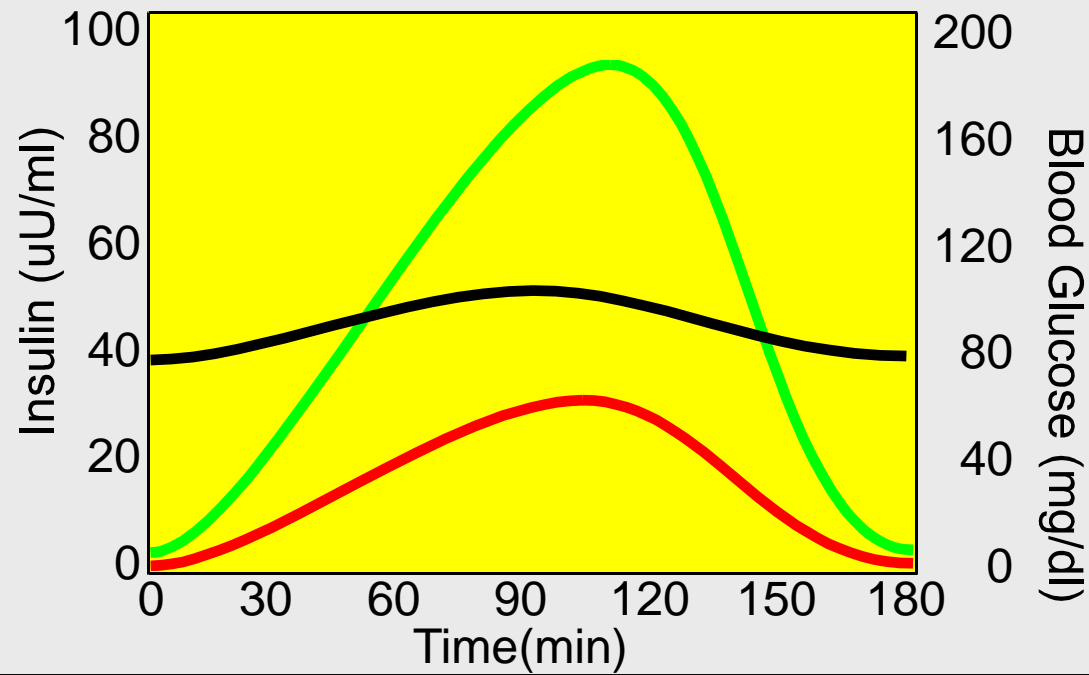
There was one or more hormones that turned up the “gain” on the pancreas.

When there is normal BG, no insulin secretion

When the BG rises, in the presence of an Incretin, the pancreas makes more insulin



## Insulin Response to Glucose





# Incretins

- **GLIP-1 (Glucagon-Like Intestinal Peptide**

GLIP-1 is an incretin

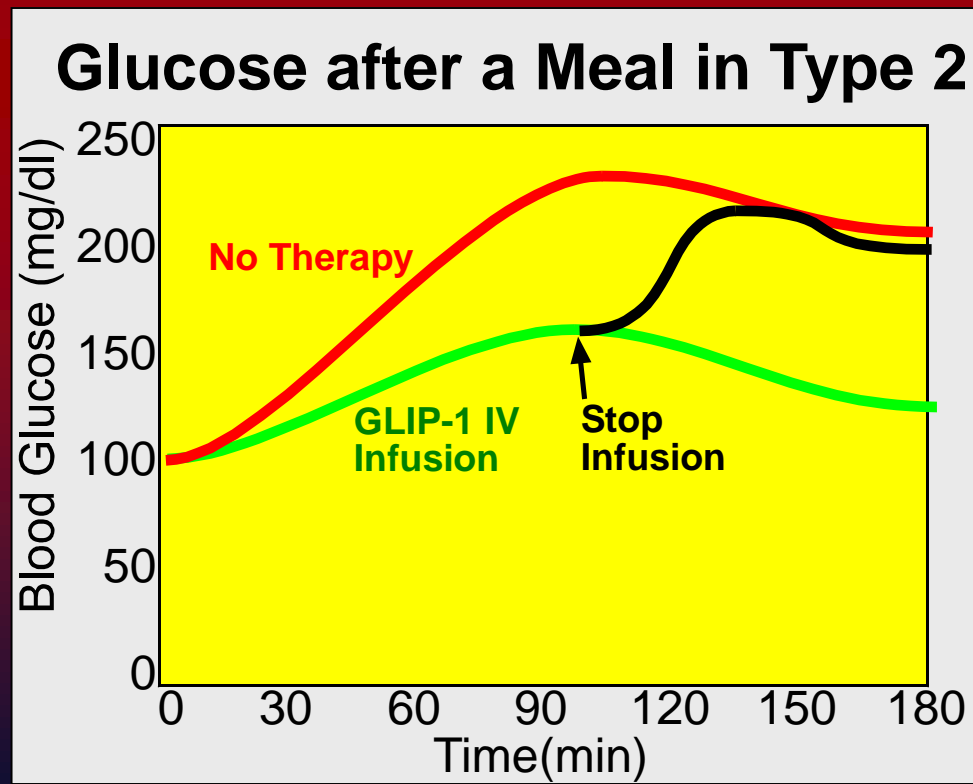
Made by gut in response to eating

Parenteral

Destroyed in 2-3 min

Destroyed by DPP-4

Need a way to keep it acting longer





# Incretin action

- **Three Approaches**

  - Change structure so DPP-4 cannot destroy

  - Slow release formulation

  - Inhibit DPP-4

- **Exenatide-accidental discovery (Byetta, Bidureon)**

  - Gila Monster can go for 2 weeks without food

  - Study Gila Monster metabolism

  - Found hormone in saliva that works just like GLIP-1

  - Not degraded by DPP-4

  - Lasts 12 hours, Called Byetta

  - Needs to be injected every 12 hrs

  - No hypoglycemia







# Other Incretins

- **Bidureon**

Long-acting form of Exentide (1x week)

Uses nanoparticles

- **GLIP analogs**

Liraglutide add fatty acid

Trulicity add polyethene glycol

- **DPP-4 inhibitors (CD26)**

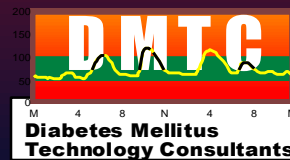
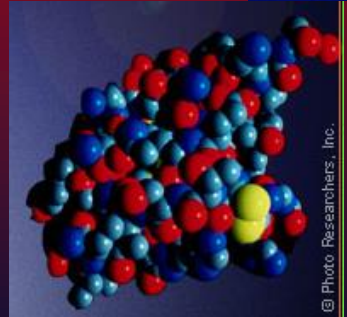
Januvia, Onglyza

Very popular

Lowers A1c by ~1%

Expensive

- **All no hypoglycemia**





# Lowering Insulin Resistance

- **Diet / Exercise**
- **Biguanides  
(Metformin)**
- **Thiazolidinediones  
(Pioglitazone)  
(Rosiglitazone)**
- **All no hypoglycemia**





# Biguanides: Metformin

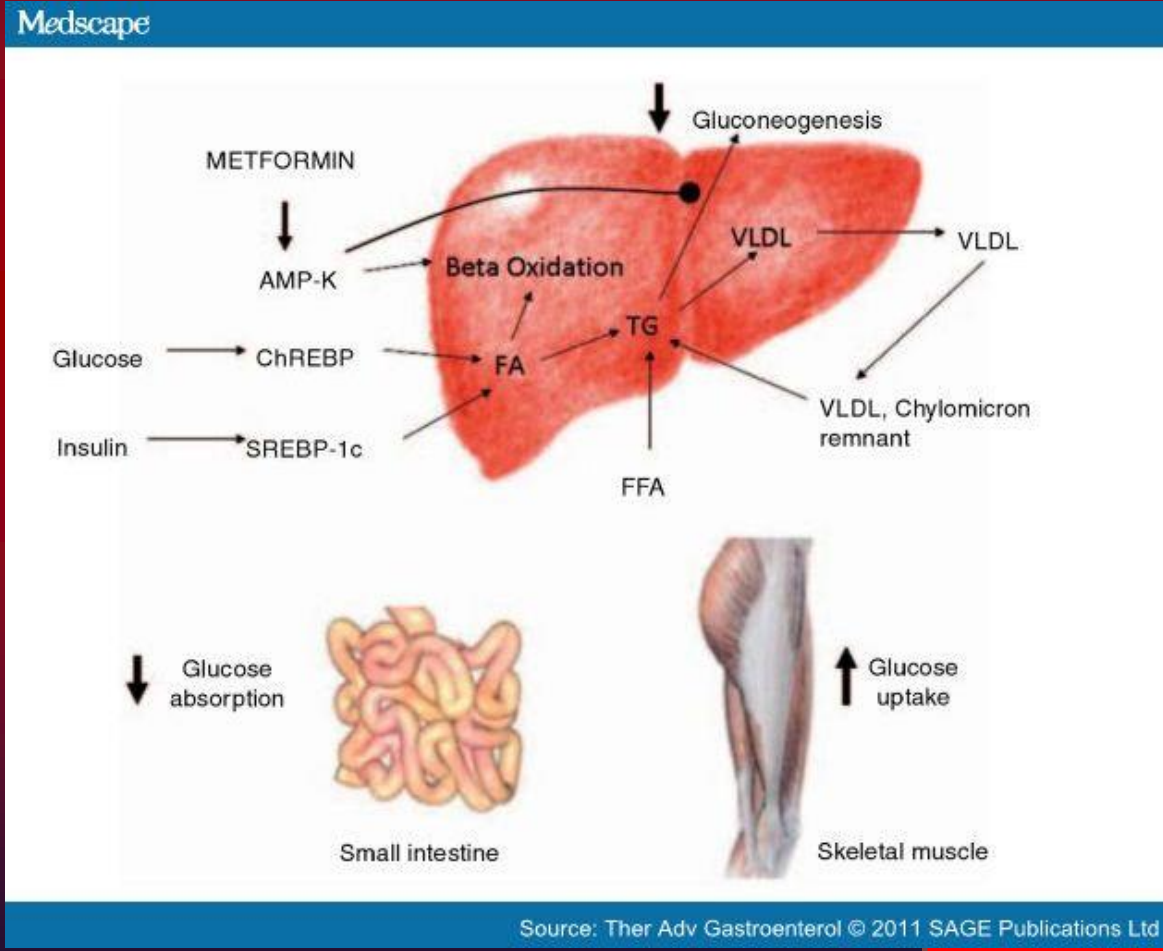
- Most popular diabetes medication

Inhibits oxidative phosphorylation

Liver

Muscle

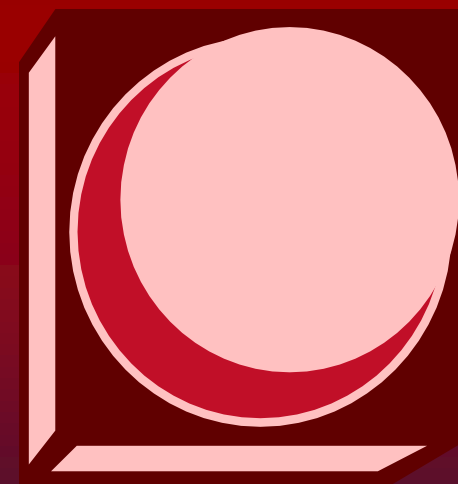
Slows gut absorption of glucose





# Biguanides: Metformin

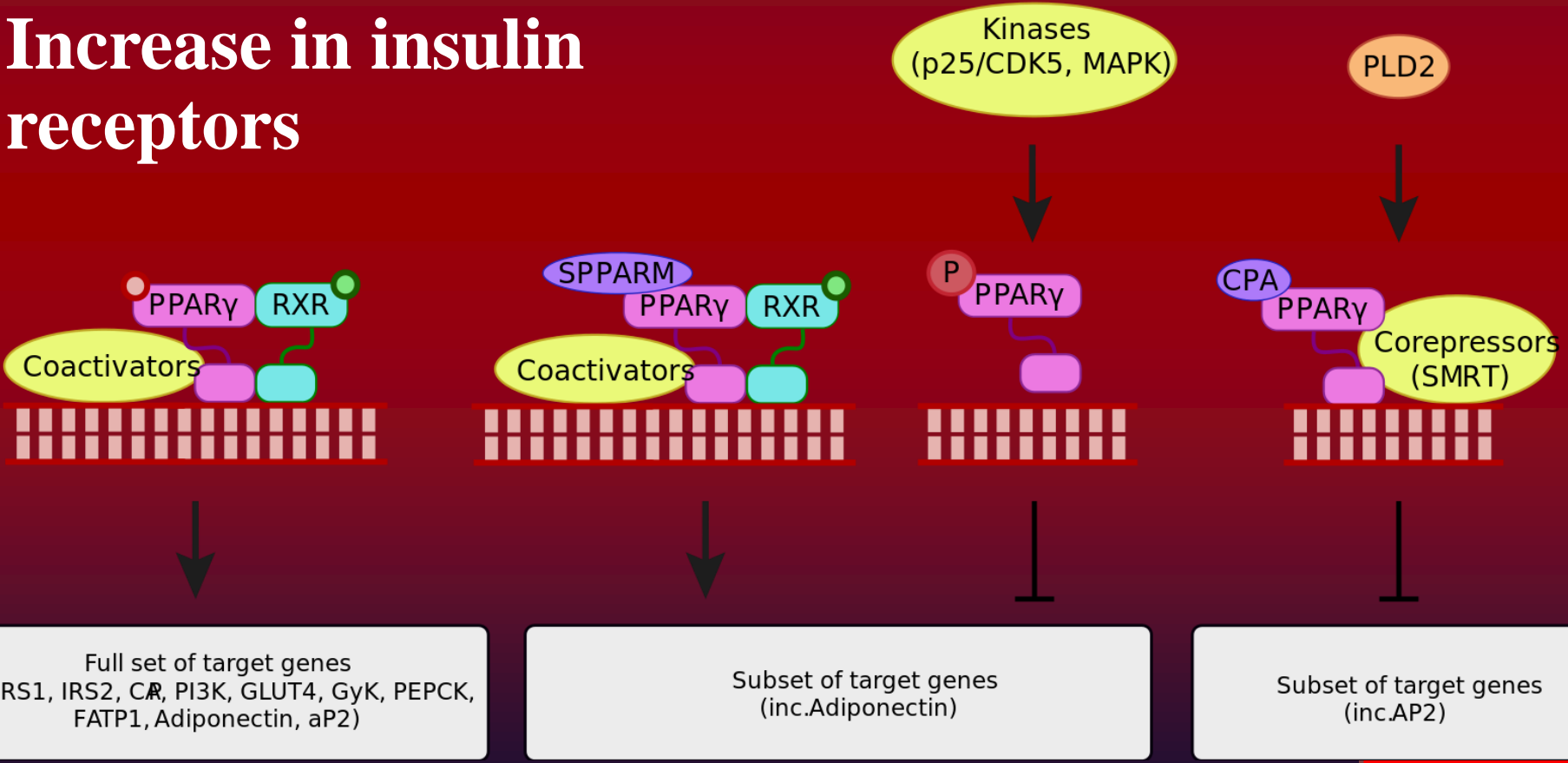
- Most effective in obese
- Generally reduces BG by 60 mg/dl
- Weight gain uncommon
- Little or no hypoglycemia
- GI side effect
- Generic, very inexpensive
- Rare lactic acidosis





# Glitazones

- Called insulin sensitivity enhancers (  $\gamma$  PPAR )
- Increases fat storage, lowers blood FFA
- Increase in insulin receptors





# Glitazones

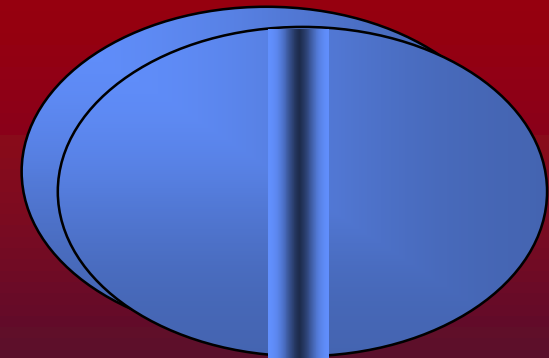
- **Less effective than Metformin or SU**
- **Water retentions**
- **Greenstick fractures**
- **Bad Rep based on faulty meta-analysis**





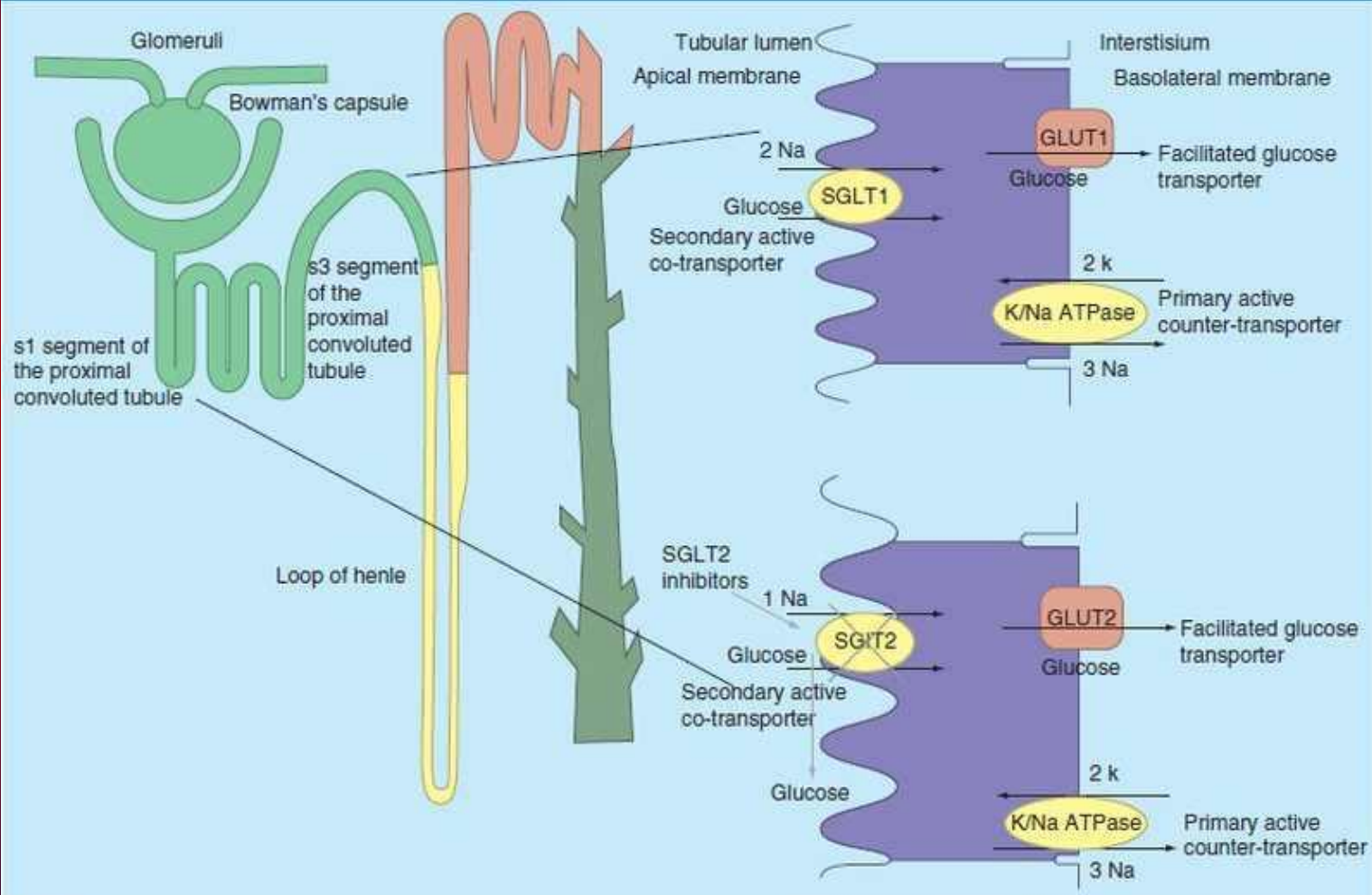
# SGLT2 Inhibitors

- **New drug**
- **Blocks glucose reabsorption by kidney**
- **Excrete excess glucose**
- **Good second drug**





# SGLT2 Inhibitors







# Biochemistry of Insulin

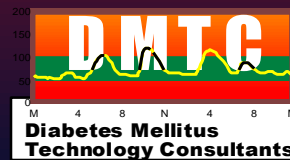
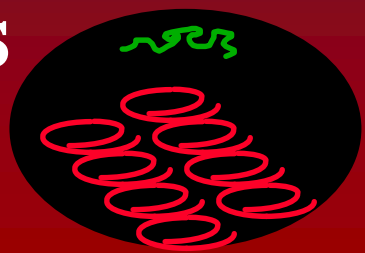
- **Small protein made by pancreas**
- **Cannot be taken by mouth as it will be digested by the stomach**
- **Usually injected**





# Recombinant DNA Insulin

- Make gene for insulin
- Insert into unicellular organisms
  - Bacteria (Lilly/Sanofi)
  - Fungus (Novo)
- Unicell will make proinsulin or chains
- Purify, Transform



# Pharmacological Actions of Insulin



- **Lowers blood sugar**
- **Therapeutic Index (TI):**  
**Toxic dose of a drug**  
**Therapeutic dose of a drug**
- **Some therapeutic indices**  
**Penicillin = ~1,000,000**  
**Digitalis = ~5**  
**Insulin = ~1.5**

# Pharmacological Actions of Insulin



- **Remember 2 things:**
- **Insulin saves lives**
- **Insulin is one of the most dangerous drugs that we use**





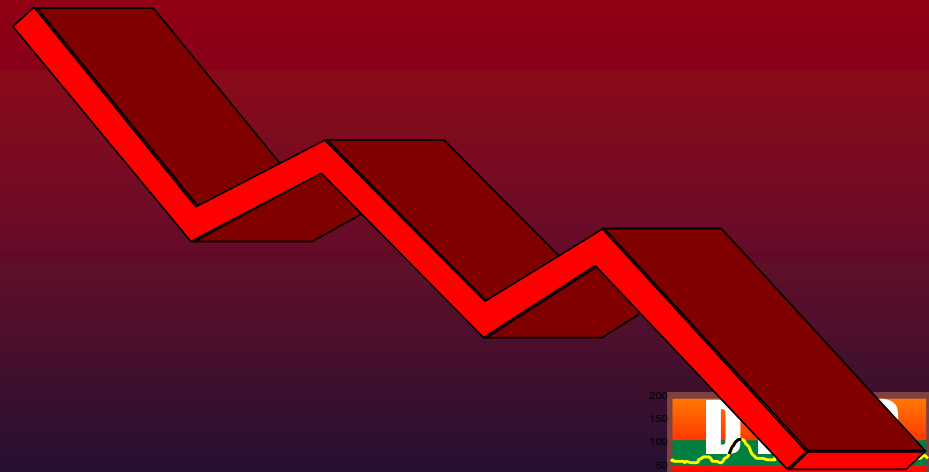
# Clinical Actions of Insulin

- **Lowers blood sugar**

Lowers elevated blood sugar

No limit on action, can lower sugar too much, *ie* hypoglycemia

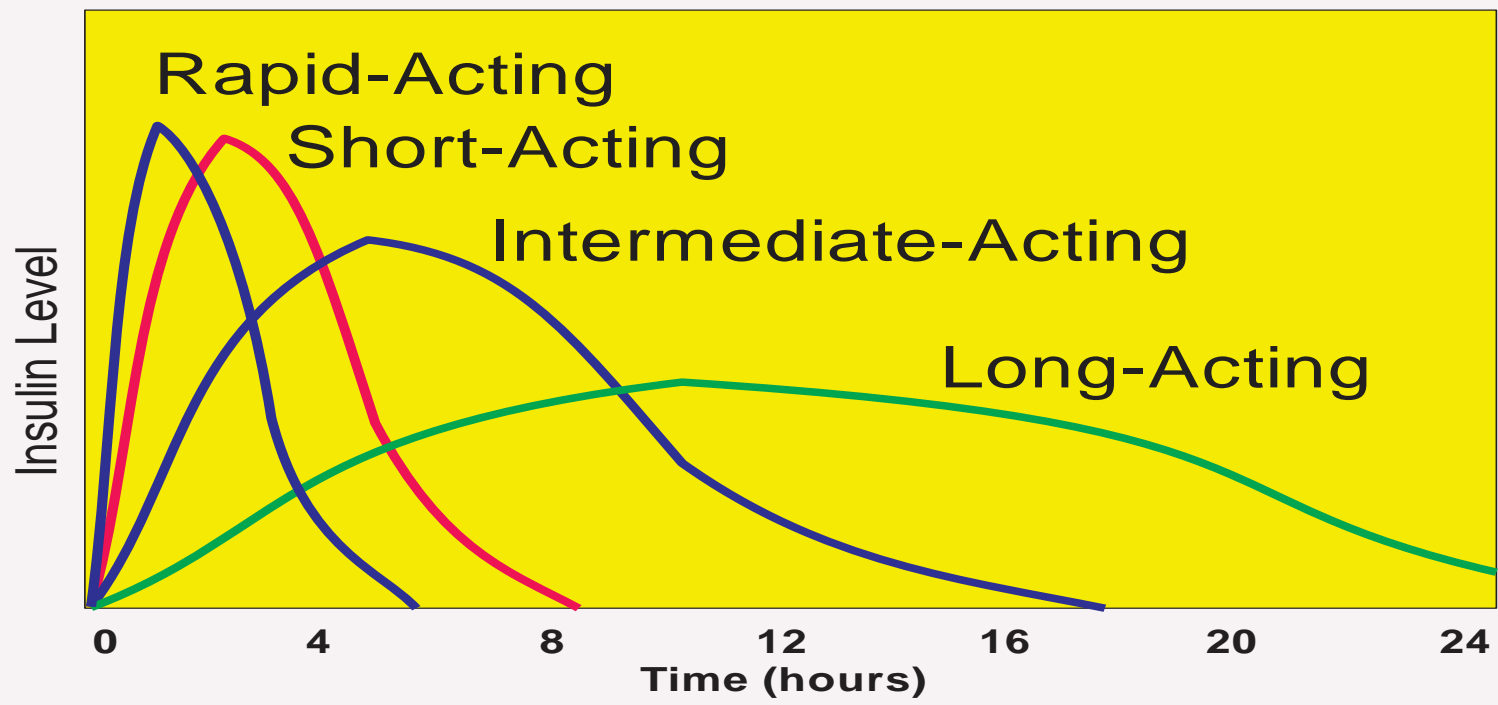
- **Lowers blood fats**



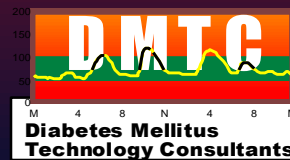


# Classes of Insulin

## Classes of Insulin



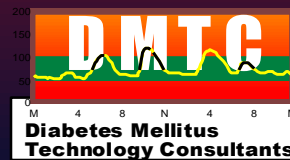
- |        |         |     |          |
|--------|---------|-----|----------|
| Lispro | Regular | NPH | Glargine |
| Aspart |         |     | Detimer  |
|        |         |     | Deglutec |





# Insulin Preparations

- **Physiologic**
  - Low Concentration**
    - Monomer
    - Blood form
  - High Concentration**
    - Hexamer
    - Beta cell
    - Bottle

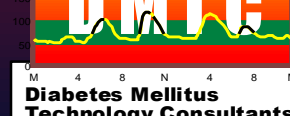
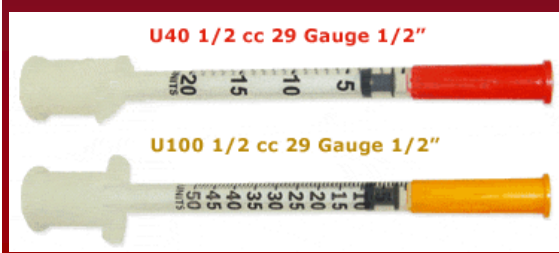




# Insulin Preparations

## Concentrations

- **U40**  
Animals  
Poor countries
- **U100**  
Everywhere else
- **U200, U300**  
New formulations
- **U500**  
For large doses

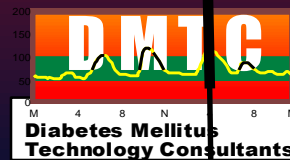






# Pharmacology of Insulin

- **Types of insulin**
- **Action of each type of insulin**

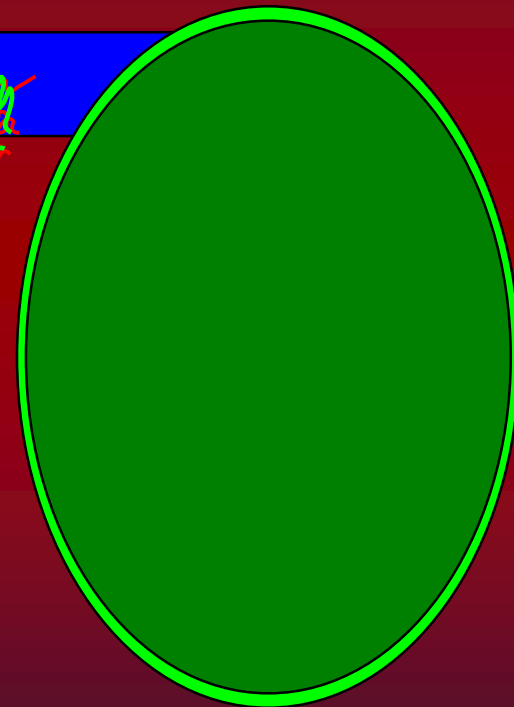
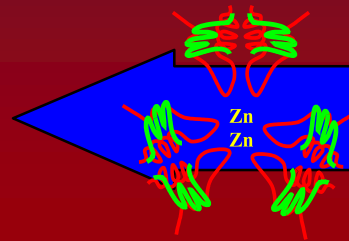




# Types of Insulin

## Short Acting Insulin

- Regular or CZI
- Onset 15-30 minutes
- Peak action 90-120'
- Lasts 6-8 hours



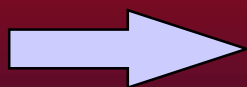


# Rapid Acting Insulin

## Regular Insulin: Factors in Absorption

- Hexamer is injected prep
- Monomer only is absorbed
- Slow step in absorption is

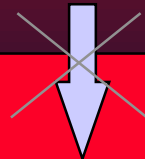
Hexamer



Dimer



Monomer





# Rapid Acting Insulin

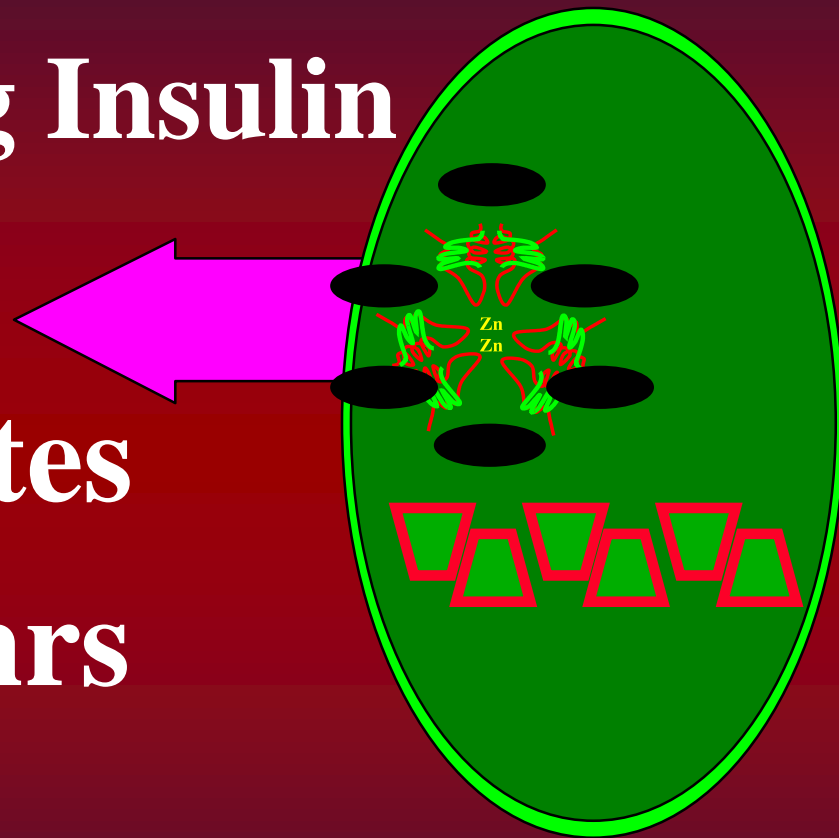
- Change insulin gene to block hexamers
- **Lispro** (B28 Pro, B29 Lys > B28 Lys, B29 Pro)  
Lys-Pro forms less monomers
- **Aspart** (B28 Pro > B28 Asp)  
B28 Aspart forms less monomers
- Acts about twice as fast as regular
- Better BG control, less hypoglycemia
- Taking over CZI, >2-4x price



# Types of Insulin

## Intermediate Acting Insulin

- NPH
- Onset 30-60 minutes
- Peak action 7-12 hrs
- Lasts 14-18 hours

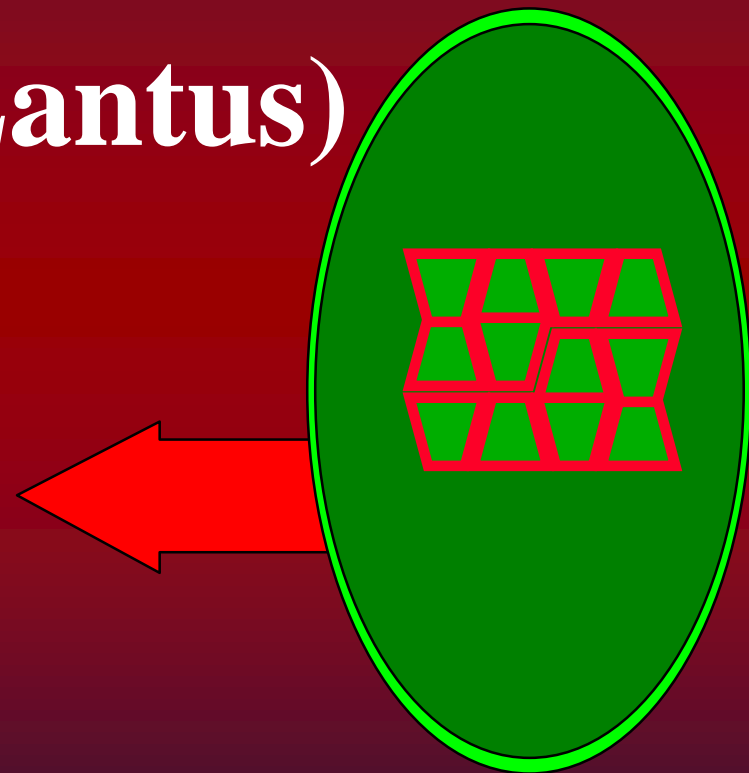




# Glargine: Lantus

## Long Acting Insulin

- **Glargine Insulin (Lantus)**
- **Soluble insulin**
- **Onset 2-4 hours**
- **No peak action**
- **Lasts 20-24 hours**





# Types of Insulin

## Lantus Insulin

- **Factors in Absorption**

Insoluble due to change in pH

Soluble in vial at acid pH

Cannot be mixed

Precipitates under the skin at neutral pH

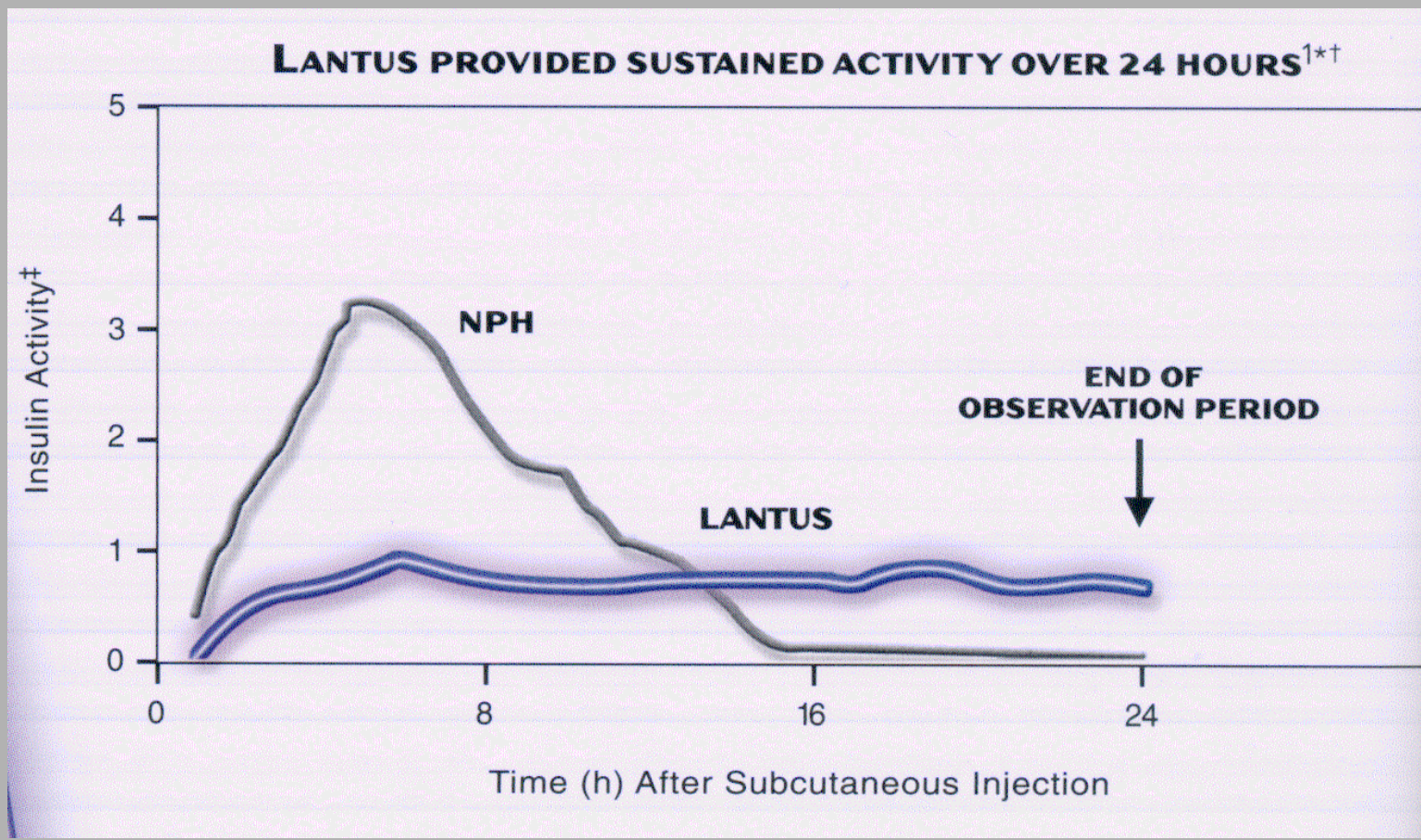
Very fine particles

Reproducible



# Types of Insulin

## Lantus



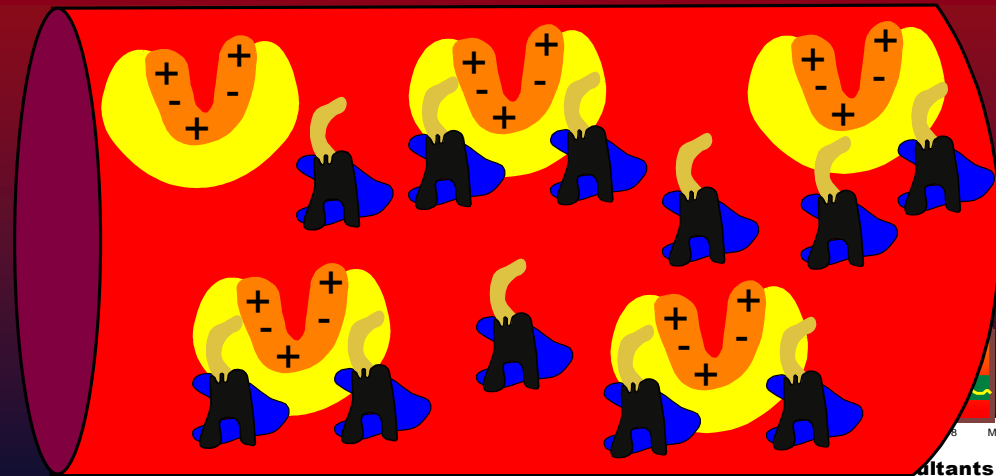
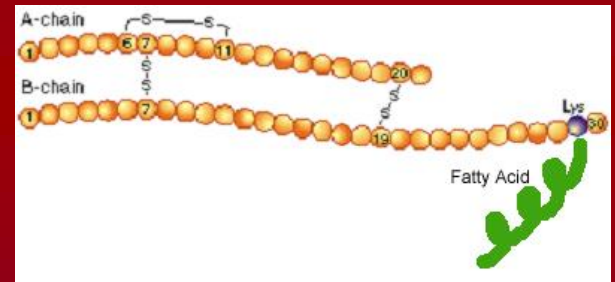




# Detemir/ Deglutec

## Long Acting Insulin

- Add fatty acid to B29 Lysine
- Binds to Albumin
  - Inactive while bound
  - Slows activity
- Soluble insulin
- Detemir lasts 16-20 hr
- Deglutec lasts 36-48 hr





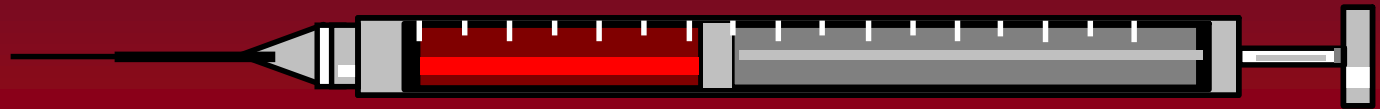
# Insulin Packaging

- Vial ( 10 cc)
  - Pump
  - Syringe
- Cartridge
  - Pen
  - 1.5 cc
  - 3.0 cc
  - Mixtures





# Clinical Use of Insulin



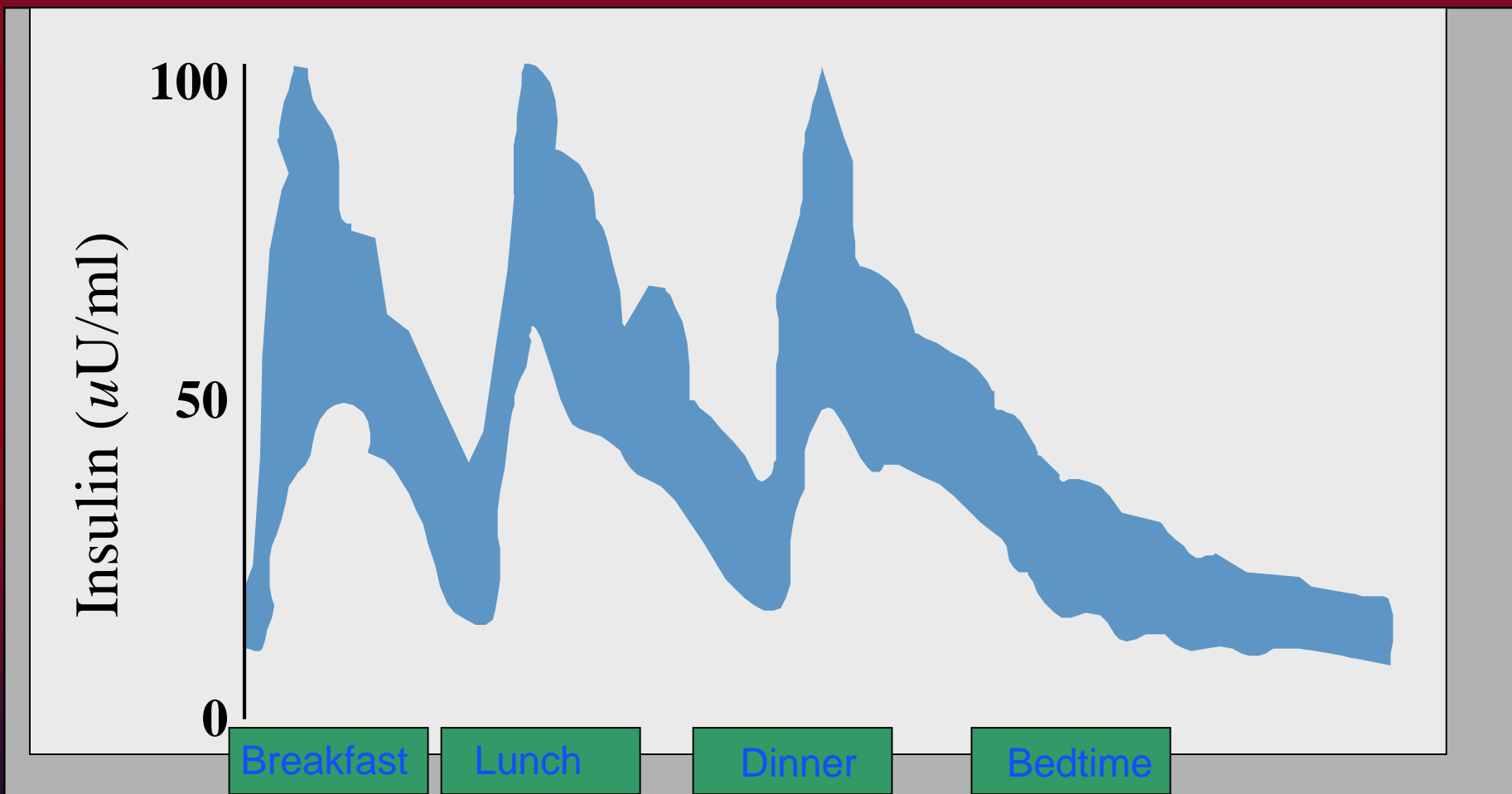
## Food vs Insulin

- Match food to insulin:  
**Conventional Rx**
- Match insulin to food:  
**Intensive Rx**



# Clinical Use of Insulin

## Normal Insulin Secretion





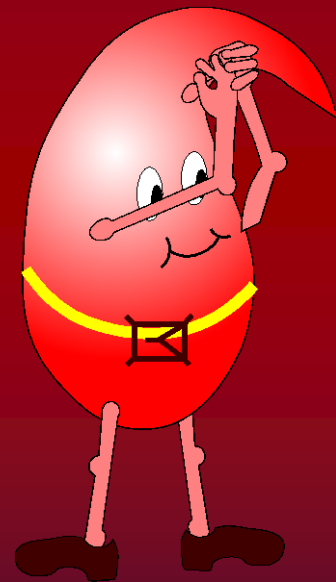
# PreMix Insulin

- **2 shots/day**
- **Start 2/3 AM, 1/3 PM**
- **70/30 or 75/25 (NPH/Reg) in AM**
- **50/50 in PM**
  
- **6 meals to match**



# Synonyms

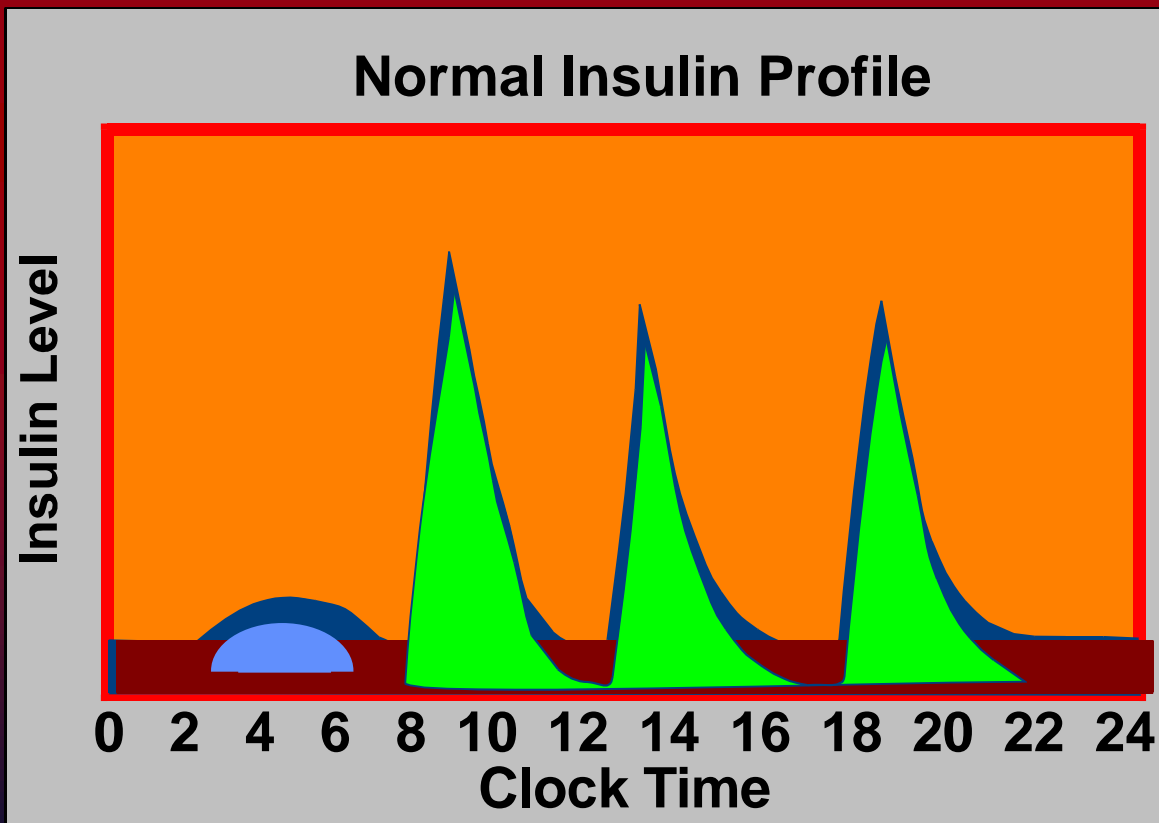
- Intensive insulin therapy
- Basal-bolus therapy
- Physiological insulin therapy
- Functional insulin therapy





# How FIT Works

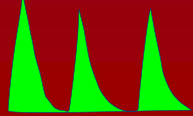
- Replace insulin physiologically
- Give patients flexibility in their regimen



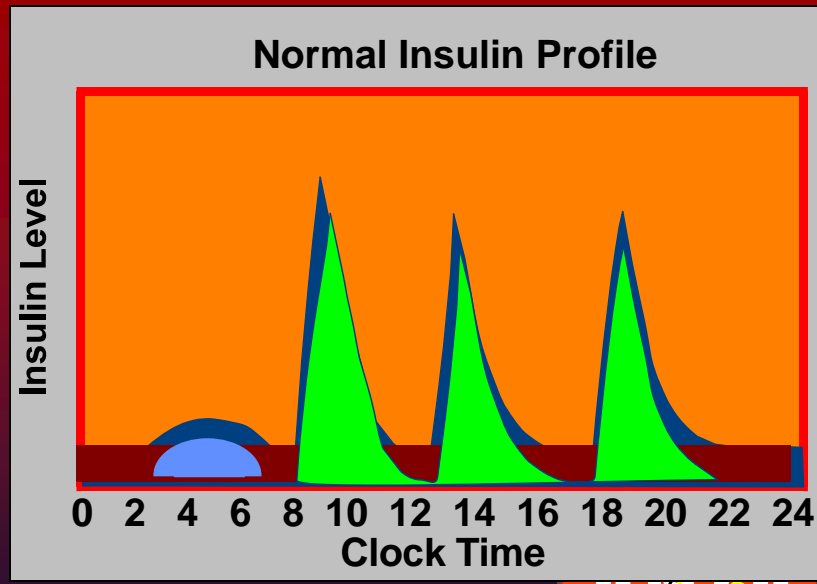


# Role of Basal and Bolus

- **Basal**
  - Covers baseline needs
  - Hepatic gluconeogenesis
  - Pump: change for exercise

- **Bolus** 
  - Covers food from each meal
  - Non pump: change for exercise

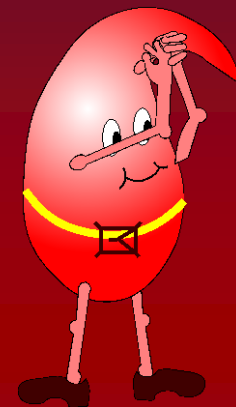
- **Dawn** 







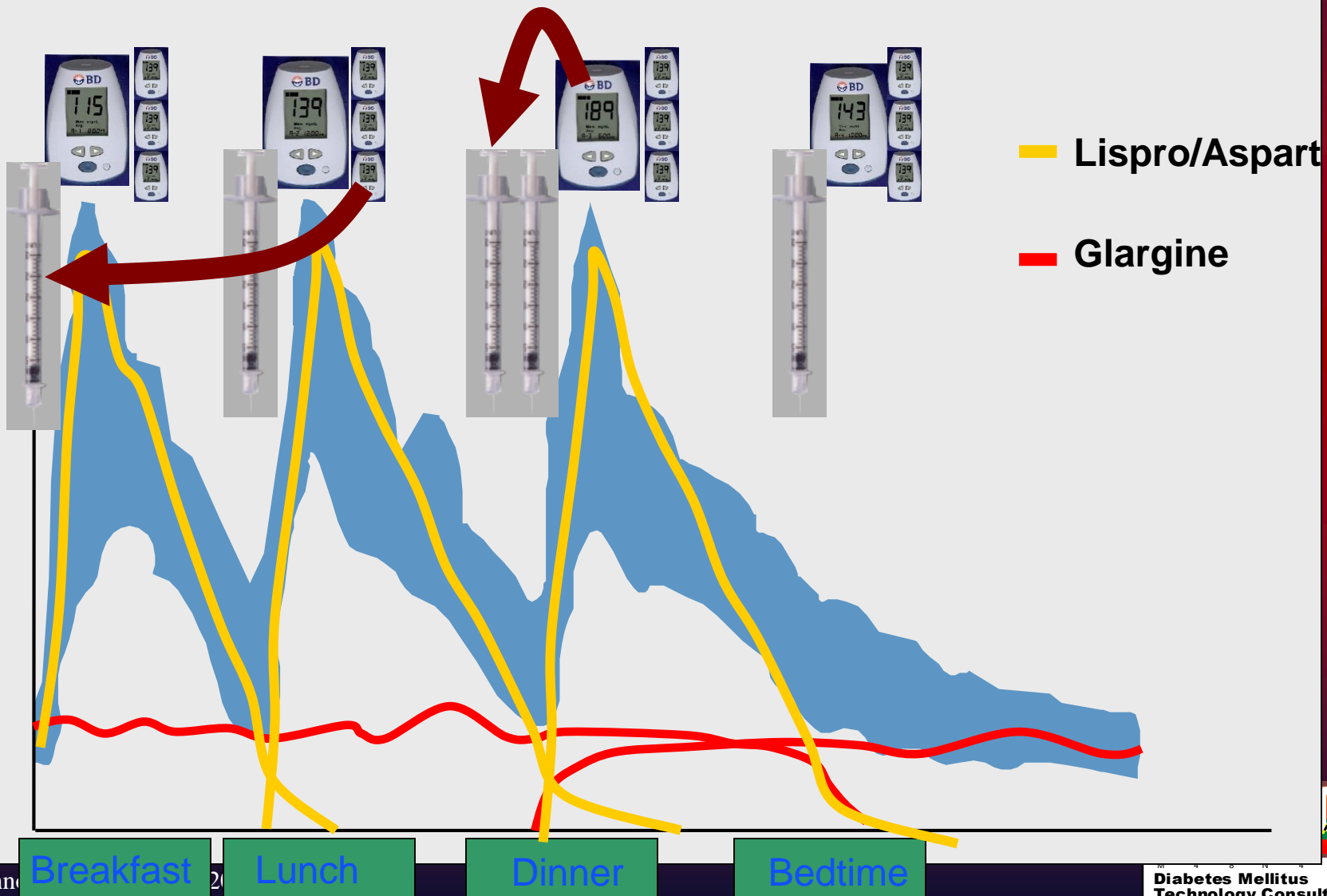
# Advantages



- **Better control of blood glucose**
- **Easier to understand**
- **More freedom in lifestyle**
  - Change you food quantity
  - Change food timing
  - Vary exercise
- **Blood glucose monitoring is central to good control and serves a dual-function**
  - Correction doses
  - Adjustments to therapy



# Flexible Insulin Therapy (FIT)





# Total Bolus

- **Bolus = Food Bolus + Correction Dose**
- **Bolus**
  - = **[Carb]/[Carb to Insulin Ratio]**
  - + **[BG-Target]/ISF**
  - **Remaining active insulin** (subtract only from correction)

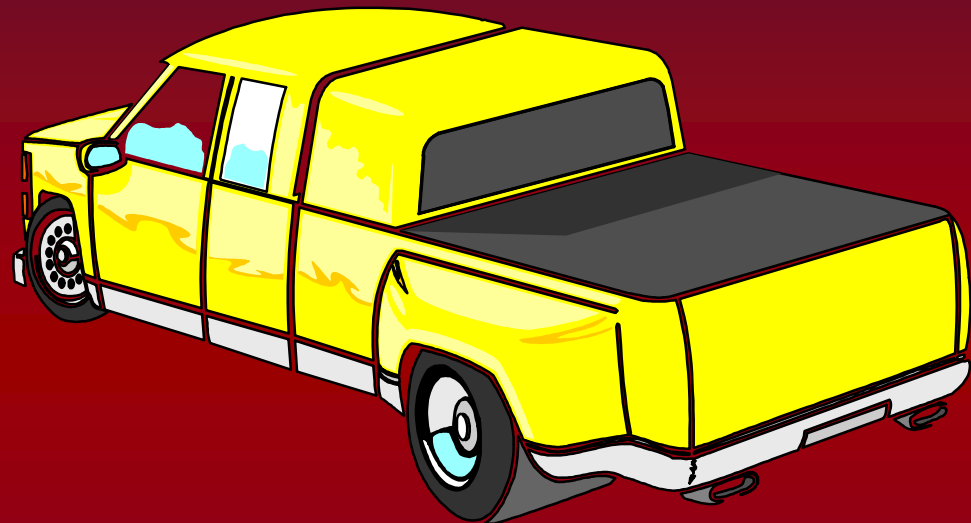
- **Very Complicated**





# Insulin Delivery

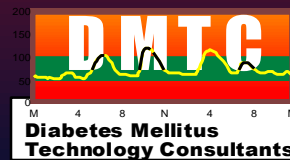
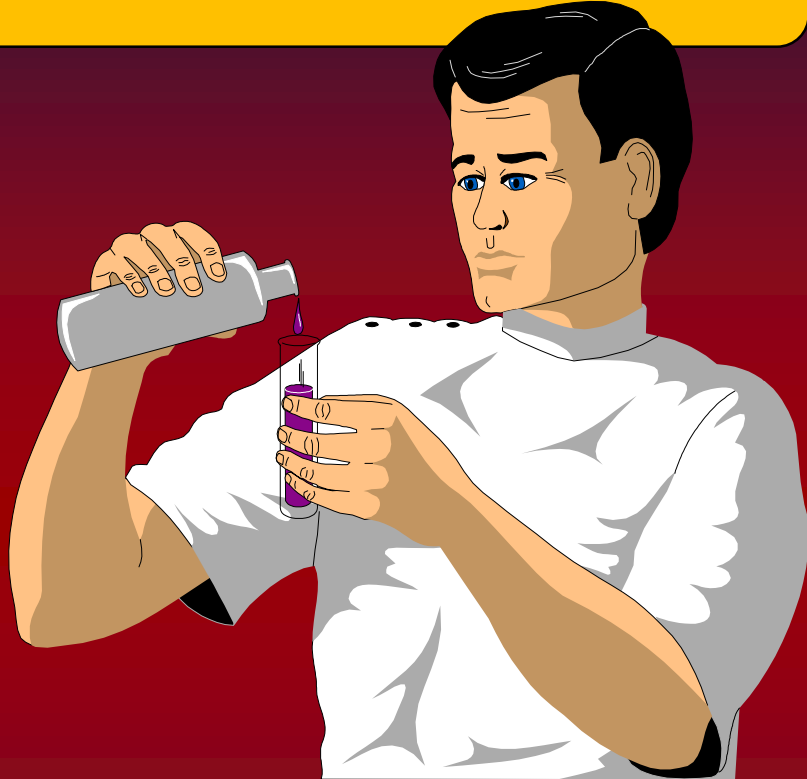
- Methods
- Technique
- Devices





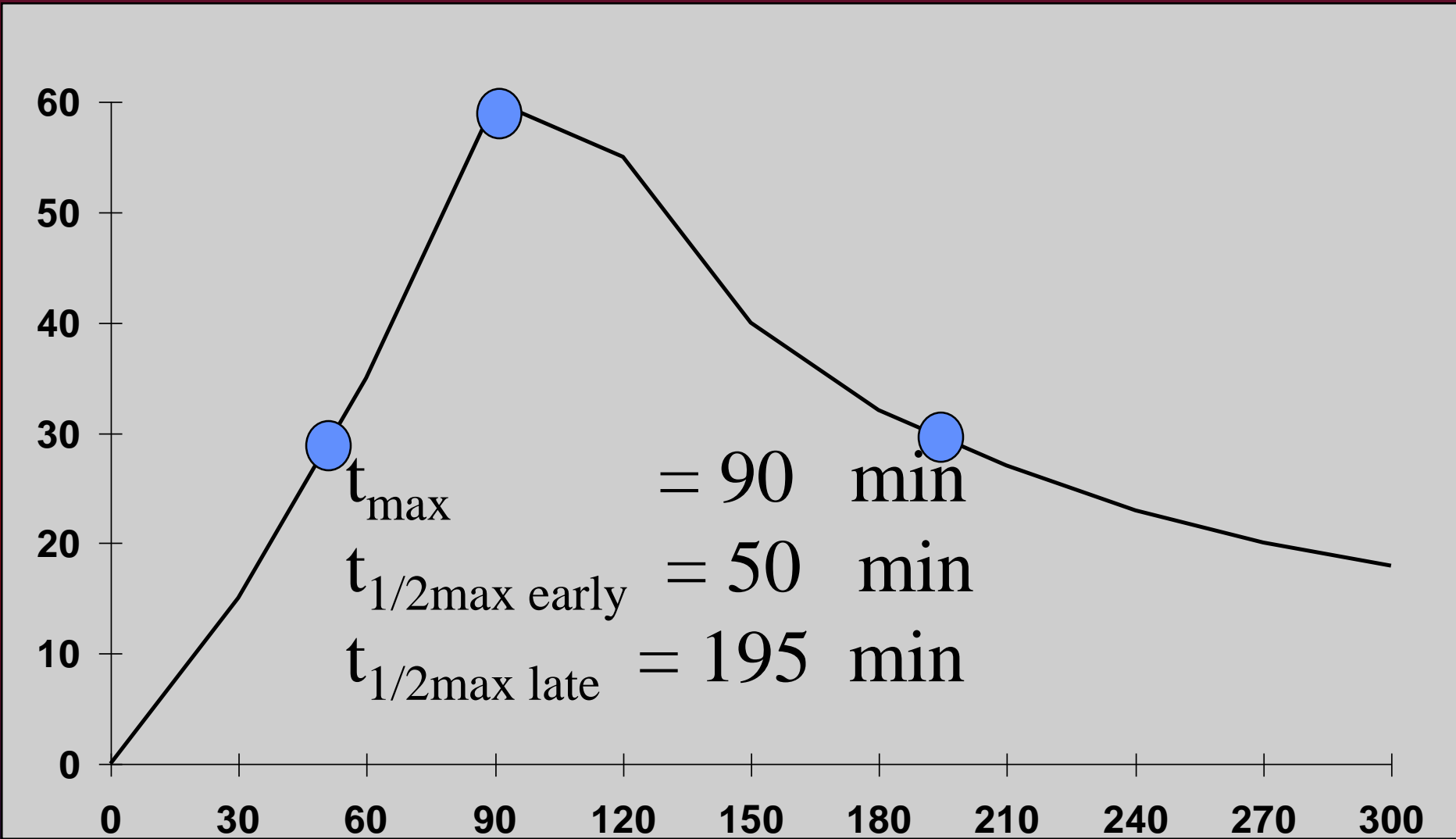
# Insulin Delivery Methods

- Intravenous
- Intramuscular
- Subcutaneous
- Pulmonary
- Research Methods
  - Trans-membrane
  - Oral
  - Nasal
  - Intradermal



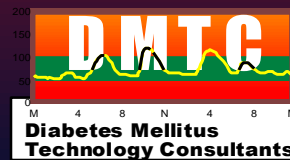
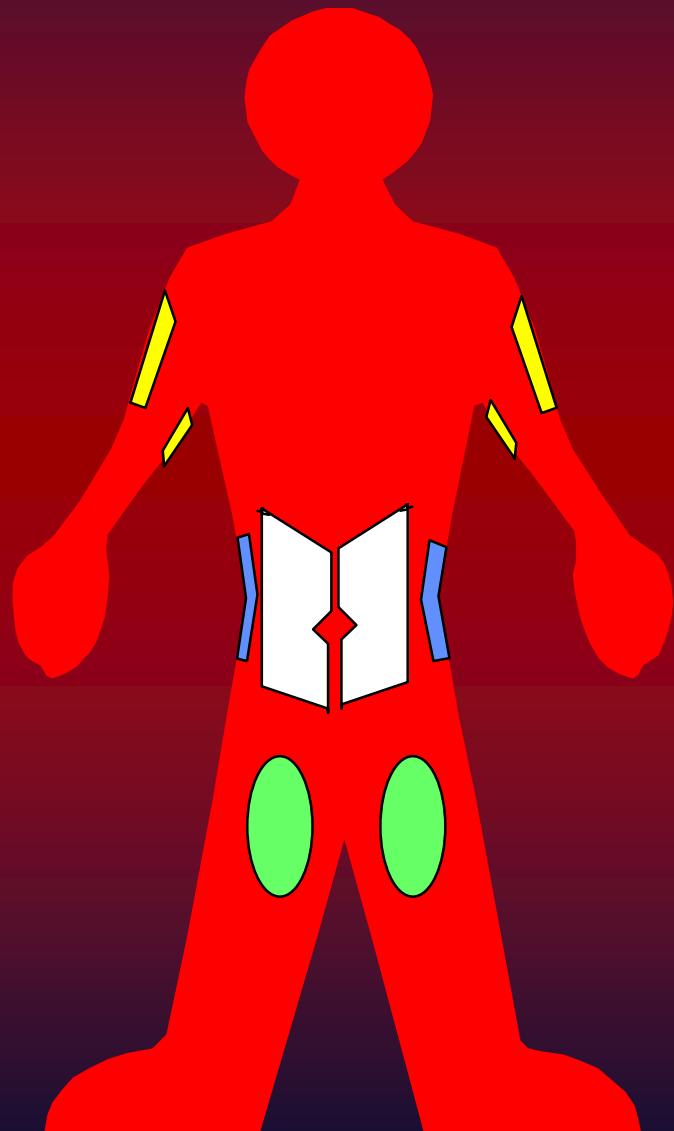


# Subcutaneous Insulin



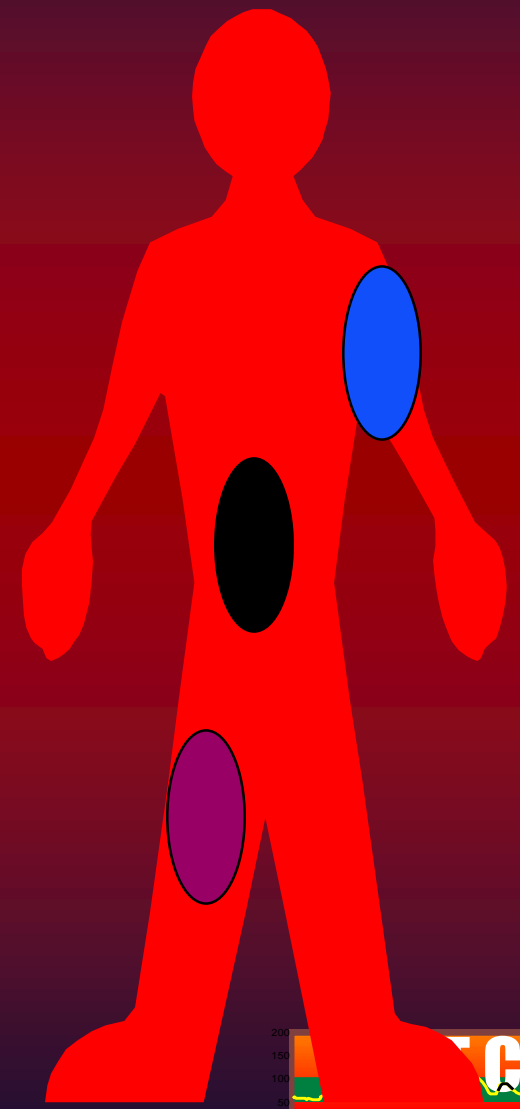
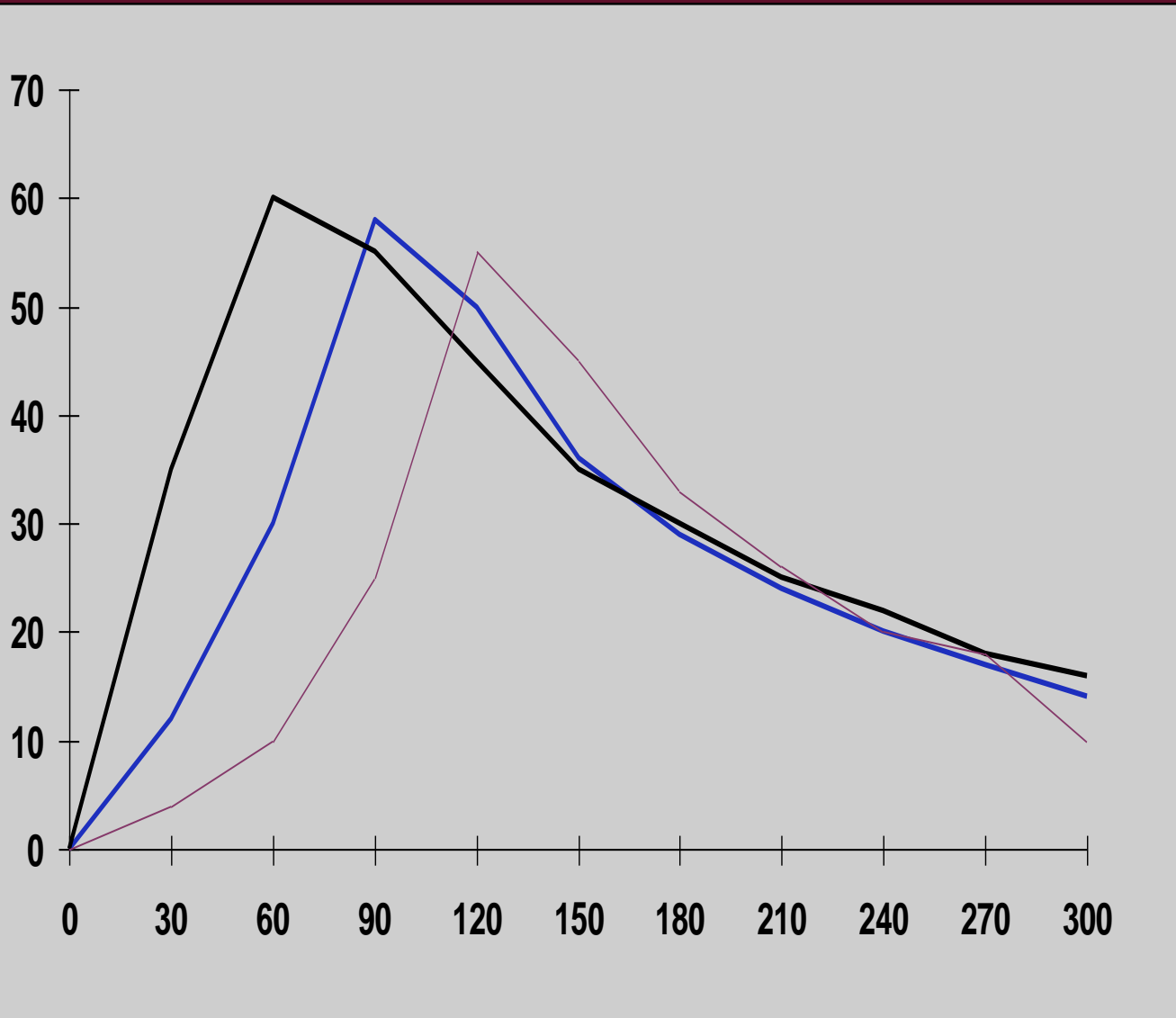


# Insulin Injection Sites





# Insulin Injection Sites

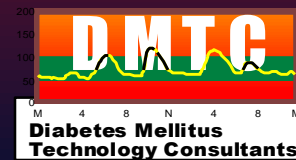






# Insulin Injection Technique

- Insulin can have erratic absorption
- May be due to intramuscular injection
- Can prevent this with pinch up
- Short needles may help
- recommend that patients always pinch up with a two finger technique
- Can see results with CAT Scan





# Insulin Injection Sites

**Average  
thickness of  
subcutaneous  
tissue  
(men/women)**

**9/15**

**14/23**

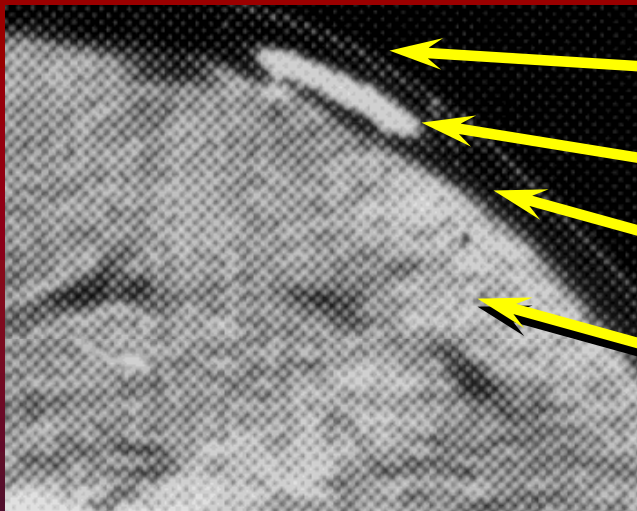
**7/14**





# Insulin Injection Sites

- CAT scan of injection into lateral thigh using pinch up technique and 12.7 mm needle:



**Skin**

**Insulin**

**Fat**

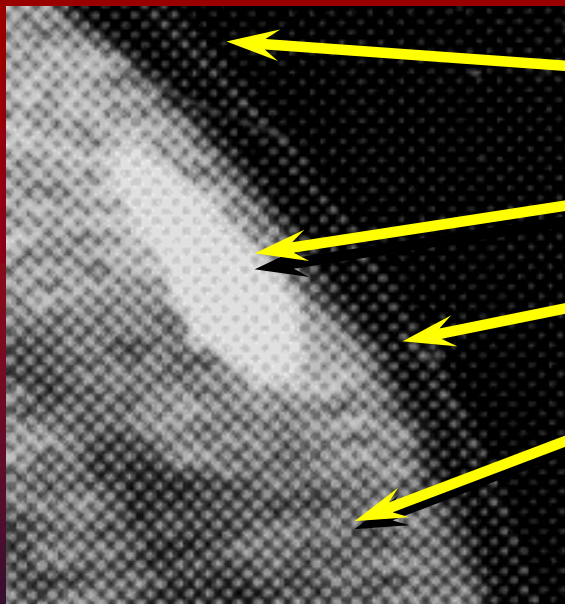
**Muscle**

- Injection is into subcutaneous tissue



# Insulin Injection Sites

- CAT scan of injection into lateral thigh using no pinch up technique and 12.7 mm needle:



**Skin**

**Insulin**

**Fat**

**Muscle**

- Injection is into muscle, even an 8 mm needle would deliver into muscle



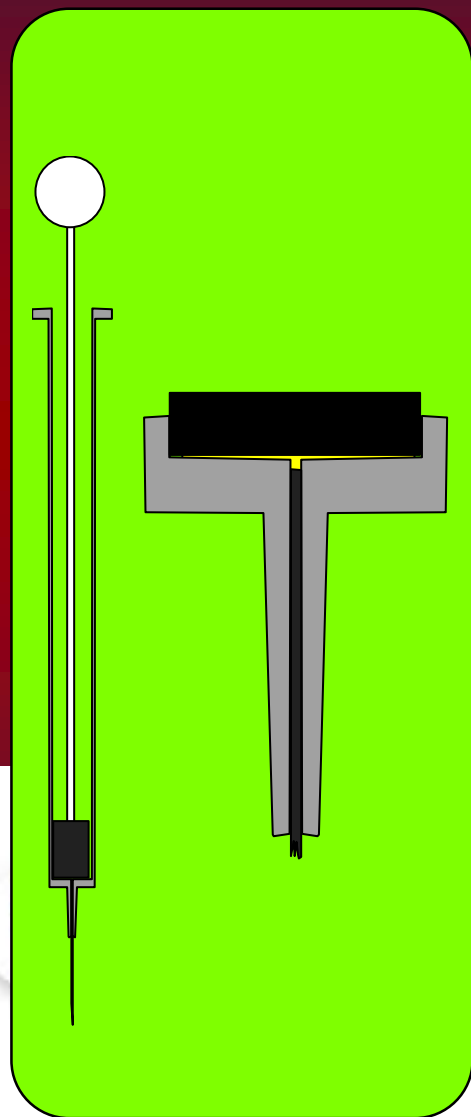
# Insulin Delivery Devices

- Syringe
- ~~Jet Injector~~
- Pen
- Pump



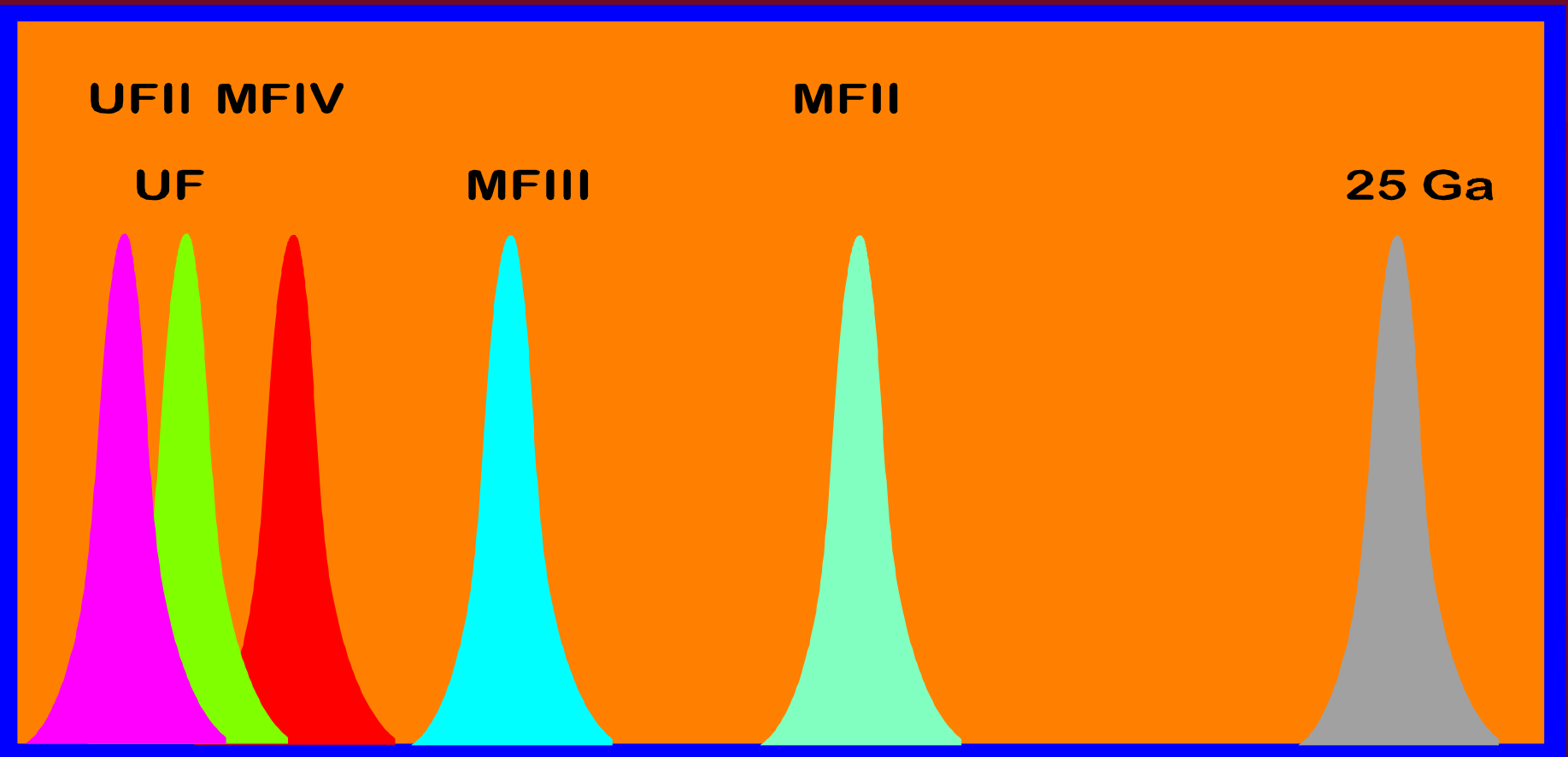
# Integral Barrel Syringe

- Integrates needle with syringe
- No dead space (0.1 U)
- Small gauge needles, but generally not less than 32

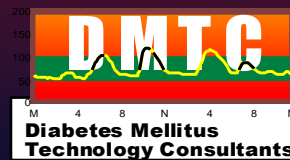




# Cannula Gauge



## Relative Pain





# Cannula Length

- 12.7 mm
- 8 mm (most common)
- 6 mm
- 4, 5 mm (pen needle)





# Cannula Geometry

- Three “GRIND” angles

  - Primary grind

  - Secondary grind

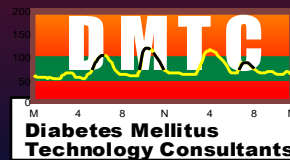
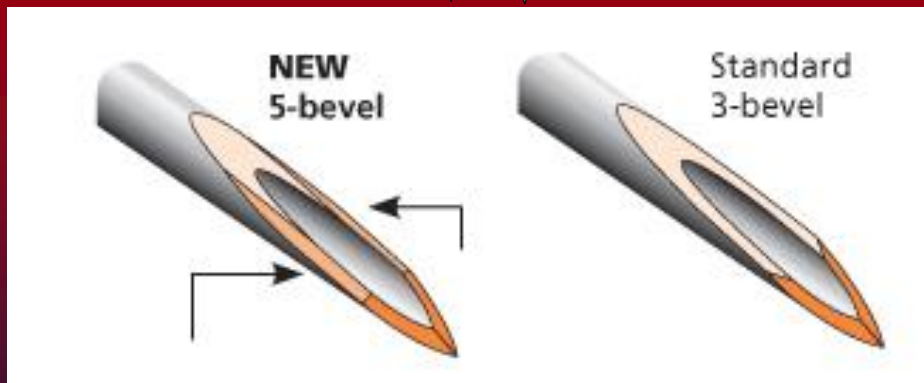
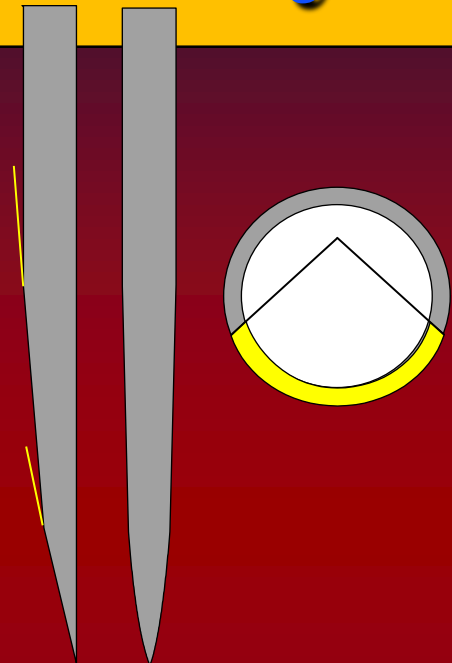
  - Roll angle

- Five Grind angles

  - 3 above

  - 2 side cuts(BD)

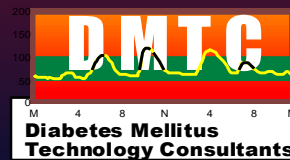
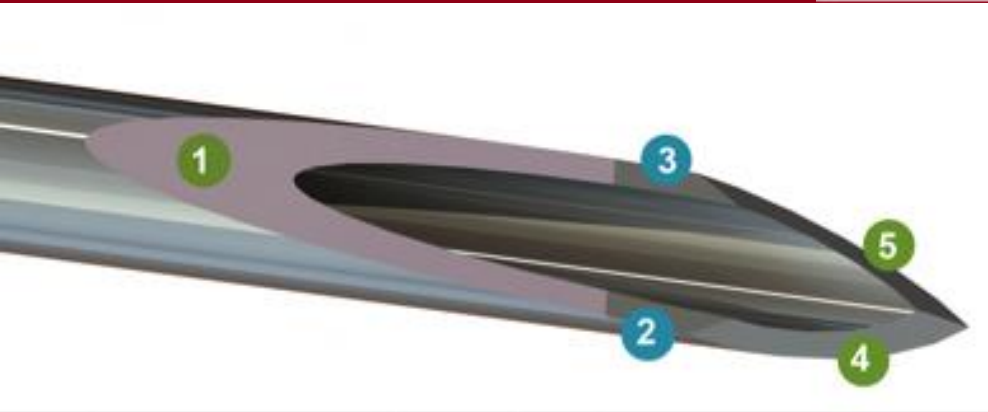
  - Tertiary Grind (CareFine)





# Cannula Geometry

## Creating a very sharp device





# Syringes

- **Advantages**

Reliable

Ability to mix freely

- **Disadvantages**

Cmplicated

Many “pieces”

“Druggy”

Limited thinness



# Insulin Pens-Principle

- **Types of pens:**

Reusable:

Insulin in cartridges

Load cartridge into pen

Disposable pens

- **Place new needle onto pen**

- **Dial dose**

- **Press plunger, deliver insulin**





# Insulin Pens-Devices

- Novo I first pen
- Novo II-IV, Echo, Jr
- Sanofi ClickStar
- Lilly Luxura
- AutoPen
  
- KwikPen
- FlexPen
- SoloStar





# Insulin Pens-Uses

- **Convenient, Limited cartridges**  
Regular, Rapid Analog  
NPH, Lantus, Detimir , Deglutec  
70/30, 75/25  
(90/10, 80/20, 60/40 in Europe/Canada)
- **Intensive Insulin Therapy**
- **Elderly type 2**



# Insulin Pumps

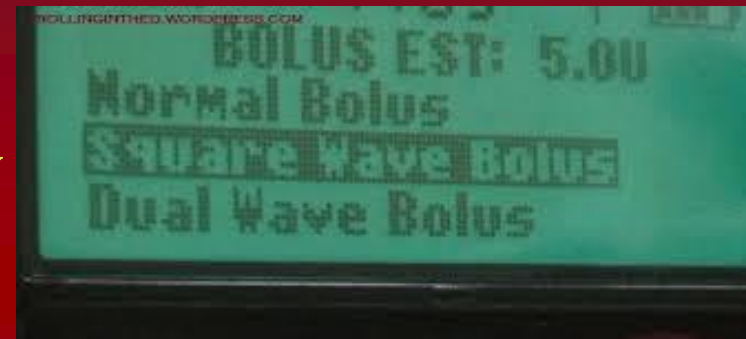
- Principles
- Devices
- Uses





# Insulin Pump-Principles

- Intensive insulin therapy
- Basal insulin
  - 5-24 basal settings per day
- Bolus insulin
  - Square wave
  - Dual waves
  - Delayed
- Mostly Type 1

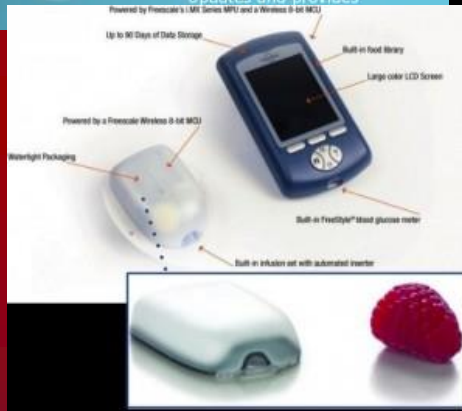






# Insulin Pump-Devices

- **ReUsable**
  - Medtronic
  - JNJ Animas
- **Patch**
  - Roche
  - Debiotech
- **Disposable**
  - Insulet
  - Valeritas
  - CeQur
  - Calibra





# Insulin Pump - Uses

- Lots of work
- Very expensive (~\$9/day)
- Very good control
- About 350,000 in US and slowly growing



# Monitoring Diabetes

- **SMBG**
- **Glycated Proteins**

Date	AM	Noon	PM	qHS	Comm
Jan 15, 2014	124	278	98	167	AM ex
Jan 16, 2014	141	223	126	154	Lunch
Jan 17, 2014	109	187	54	112	eat





# SMBG

- **Critical for decisions**

Patient, at each meal

Patient, pattern changes

Clinical, at each visit

- **Often inaccurate**

Patient skills

Verification





# SMBG Methods

- ~~Reflectance meter~~
- Sensor
- Both use same basic chemistry



- Measure:  
Production of electrons



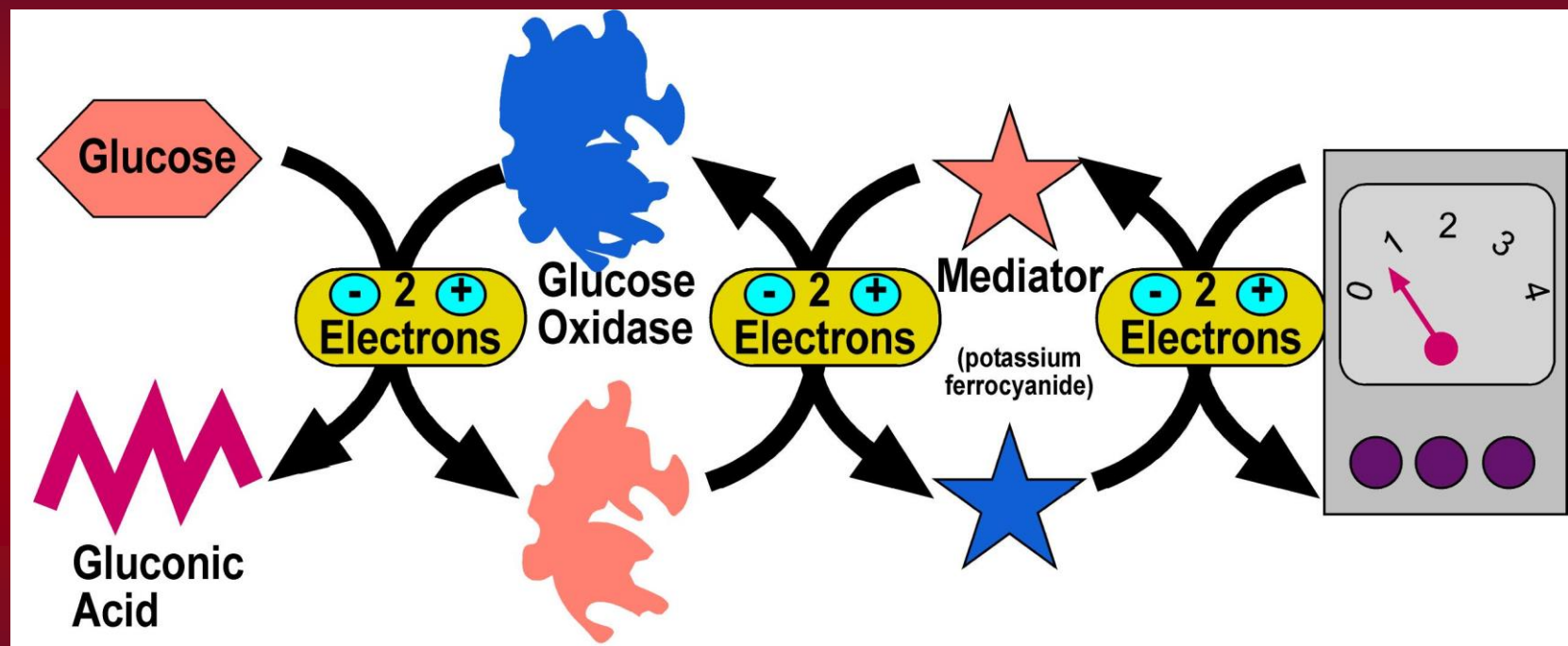
# Sensors

- Oxygen normally acts as electron acceptor
- Use chemical electron acceptor (often ferrocene)
- Couple electron acceptor to electric current meter.





# Chemistry of a Biosensor





# SMBG in Practice

- Obtain a sample
- Measure sample
- Record result
- Use data







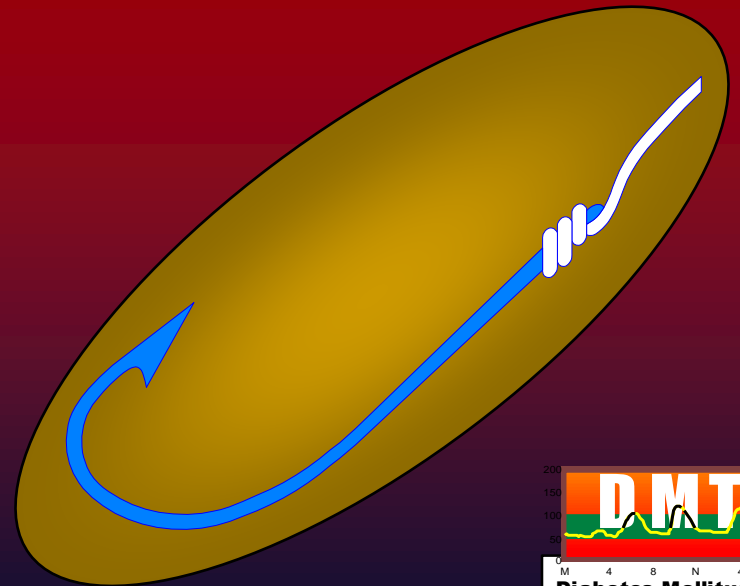
# Obtain a Sample

- Usually with lancer/lancet
- Amount of blood needed varies with meter
- Most onerous part of diabetes

Painful

Messy

Embarrassing





# Painless Glucose Monitoring

- Sample size has diminished greatly

1980 Eytone		30.0 $\mu\text{L}$
1984 Accucheck 2		15.0 $\mu\text{L}$
1990 One Touch		5.0 $\mu\text{L}$
1998 AC CC		4.0 $\mu\text{L}$
2001 OT Ultra		1.0 $\mu\text{L}$
2003 BD Logic		0.3 $\mu\text{L}$



# Painless Glucose Monitoring

- Pain is related to sampling device:

Depth of penetration

Lancet gauge

Bounce-back

Wobble

} Sample Size





# Measuring the Sample

## Meter Read:

- Calibration
- Time for reading
- Size of meter
- Size of display
- Self-loading strips
- Plasma vs blood reading





# Correction Doses

- If the blood glucose before a meal is too low or too high, the patient may try to correct for this by altering their insulin dose.
- For short acting insulin this is easy: each insulin only works until the next meal.
- If the blood glucose is too high, extra insulin is taken; if too low less insulin is taken.

Date	AM	Noon	PM	qHS	Comm
Jan 15, 2014	124	278	98	167	AM ex
Jan 16, 2014	285				



# SMBG, Pattern Changes

- Based on a 3 day pattern for high blood sugar or 2 day for a low blood sugar
- Usually change by only 1-2 units



# SMIBG, Pattern Changes

- Look for patterns in last 3 days

**Breakfast: Slightly high**

**Lunch: High**

**Supper: OK, variable**

**Bedtime: Slightly high**

Date	AM	Noon	PM	qHS	Comm
Jan 15, 2014	124	278	98	167	AM ex
Jan 16, 2014	141	223	126	154	Lunch
Jan 17, 2014	155	187	54	112	eat





# Using SMBG

- type 1
- type 2, using insulin
- type 2, oral agents / diet





# Role of Verified Data

- Patient BG falsified
- Lowered if high
- Raised if low
- Made up
- Deleted
- Overall 65% incorrect

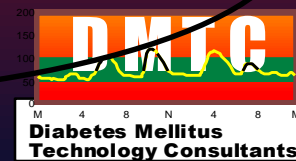
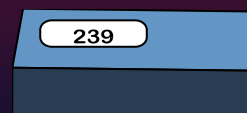
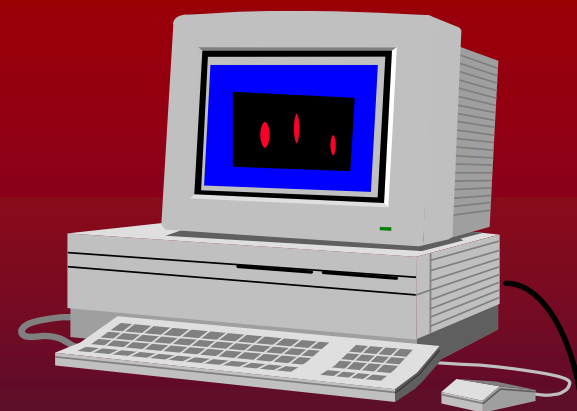
189?  
No, 89  
is better





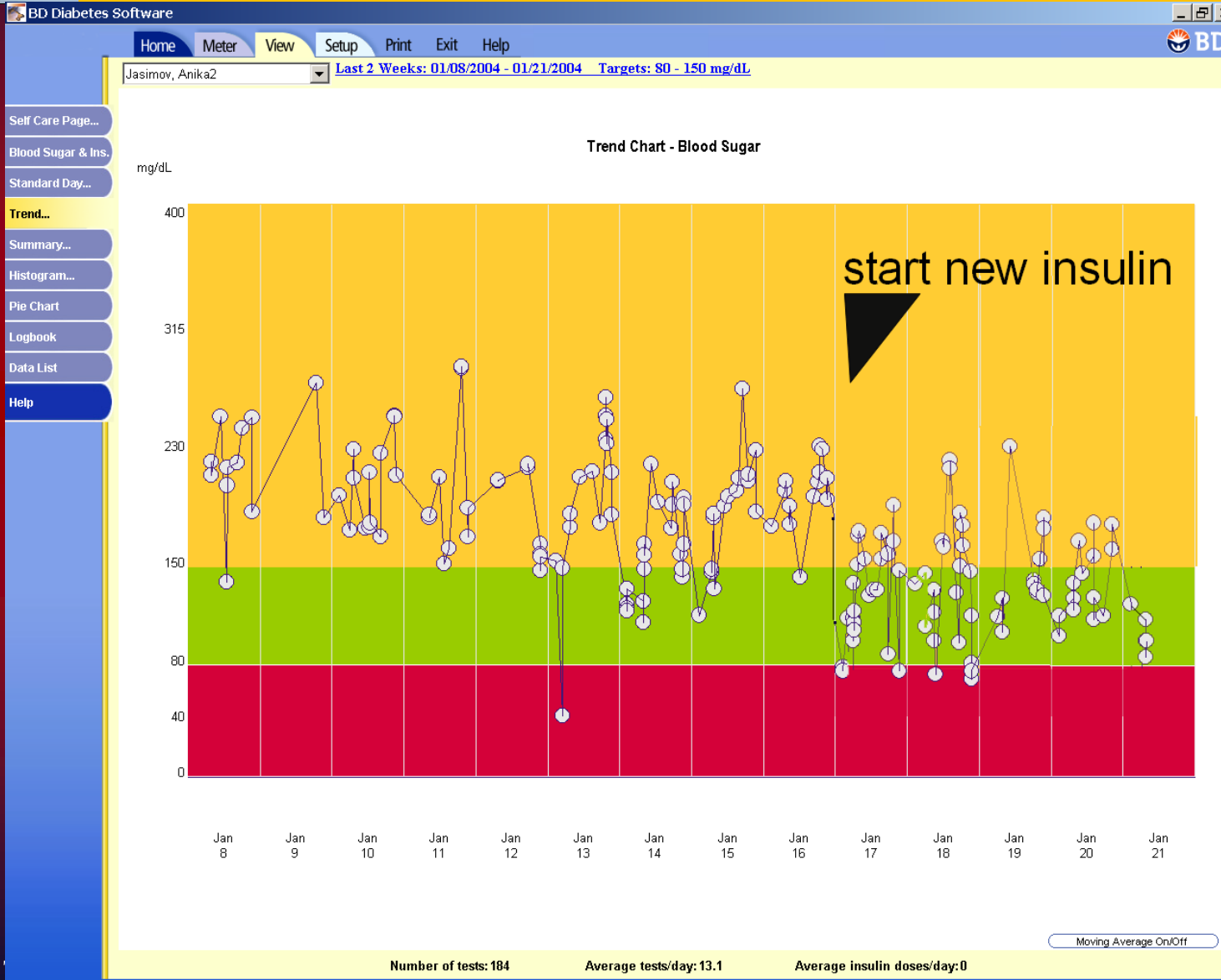
# Computerized SMBG

- Avoids Patient falsifications
- Becoming more popular



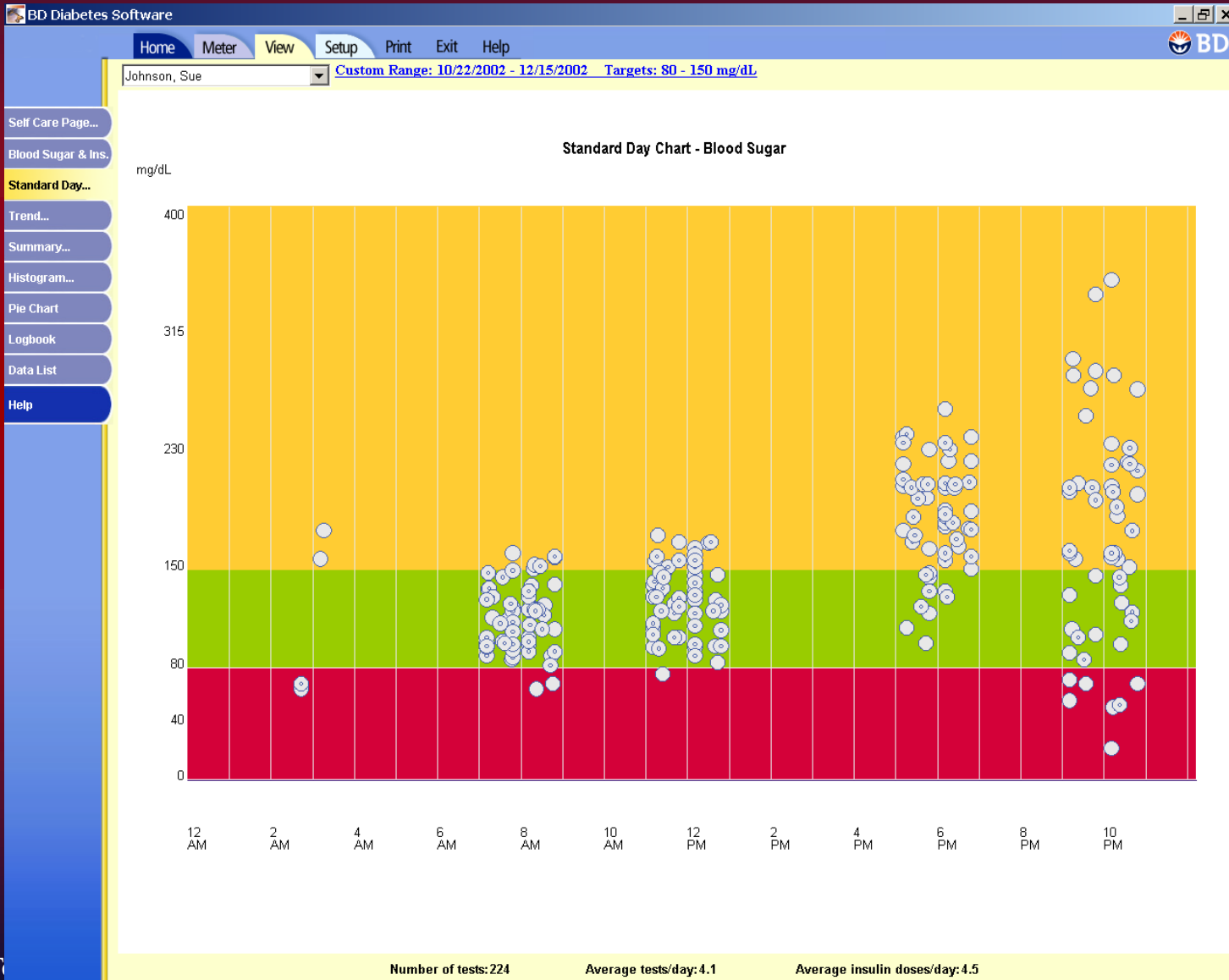


# Trend





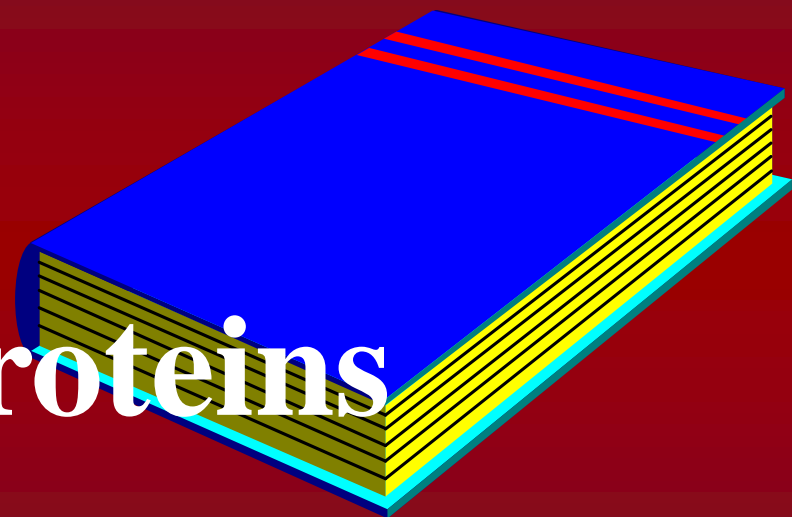
# Standard Day





# Glycated Proteins: Topics

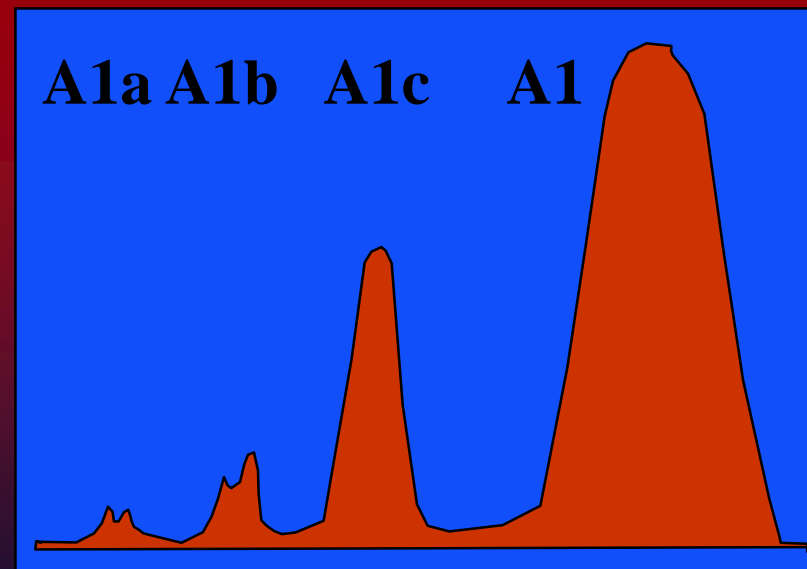
- Hemoglobin A1c
- Fructosamine
- Other glycated proteins





# Hemoglobin A1c

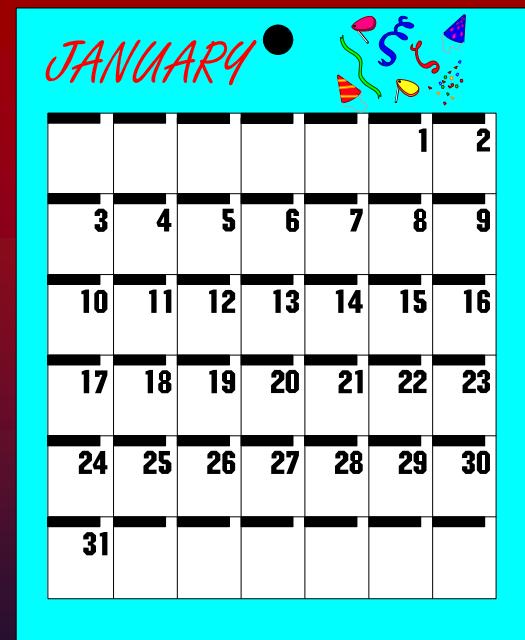
- Adduct of glucose onto hemoglobin
- Measures average blood sugar over 2-3 months
- Most common test
- Reported as % of hemoglobin A





# Hemoglobin A1c

- Should be measured
- 3-4 times per year in type 1
- 2-3 times per year in type 2
- After major change in therapy





# Fructosamine

- Adduct of glucose onto mixture of proteins in serum, mostly albumin
- Measures average blood sugar over 10-15 days
- Used less commonly
- Reported as absolute value







# Fructosamine

- Should be measured:
- 10-12 times per year in type 1
- 4-6 times per year in type 2
- After major change in therapy





# Other Glycated Proteins

- **Virtually every protein in body**
- **May be part of aging**
- **Lipoproteins, Collagen**



# Summary

- **Diabetes is:**

- ❖ **Common**
- ❖ **Serious**
- ❖ **Treatable**
- ❖ **A lifestyle disease**