

# Diabetes Mellitus

Arden Gregory RN, PhD, CDDN  
Statewide Nursing Coordinator

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## Course Objectives

- Define/Characterize Diabetes Mellitus (DM)
- Review the incidence of DM
- Examine carbohydrate/glucose digestion, absorption & metabolism
- Analyze the hormones/chemicals involved in glucose digestion, absorption & metabolism
- Examine insulin functions in detail

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## Course Objectives

- Review DM risk factors
- Consider possible causes of DM
- Examine DM pathology by DM type
- List and study Sx of DM & Tx complications
- Examine DM complications
- Review DM Tx Modalities

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## Definition

- A complex group of metabolic diseases in which a person has elevated blood sugar concentration (hyperglycemia of  $\geq 126$  mg/dl or  $HbA_{1c} \geq 6.5$ )

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## Who, When, What <sup>(3)</sup>



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## STATISTICS

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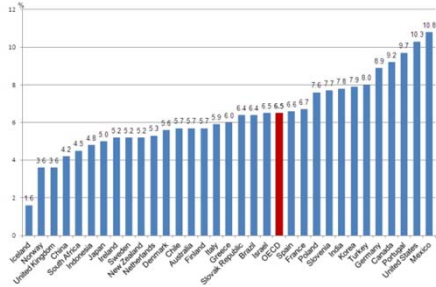
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### Prevalence of Diabetes by Country



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### Epidemiology - World

- In 2011, 366 million had DM. Estimated that 1/2 (183 million) are undiagnosed
- DM caused 4.6 million deaths in 2011
- Prediction: by 2030, 552 million will have DM.

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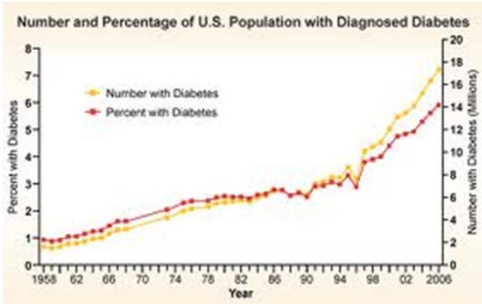
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## Epidemiology – U.S. <sup>(1)</sup>

- 25.8 million = 8.3% of population (2011)
- 18.8 million diagnosed; 7.0 million undiagnosed (2011)
- Prediabetes affects 35% of adults 20+

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## Epidemiology – U.S. <sup>(2)</sup>

- Age (2011)
  - 215,000 < 20 years (2.6%) (about 1 in 400)
  - 10.9 million > 65 (26.9%) (Types 1 & 2)
- Gender
  - Males: 13.0 million or 11.8% of pop. age 20 or older
  - Females: 12.6 million or 10.8% of pop. age 20 or older

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## Epidemiology – U.S. <sup>(4)</sup>

- Morbidity/Mortality – 2007
  - 71,382 deaths (6<sup>th</sup> leading cause of death)
  - Contributed to 160,022 deaths
- Overall death risk  $\cong$  2x of those without DM
- Life expectancy shorted by 5 - 10 years
- Cost (2007): Total - \$174 billion [\$116 billion medical direct; \$58 billion indirect (disability, work loss, premature mortality)]

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## Epidemiology – U.S. <sup>(5)</sup>

- DM Complications (2005-2008) Leading cause
  - new blindness 4.2 million (28.5%) with DM 39+ had diabetic retinopathy
  - nontraumatic lower-limb amputation (> 60%)
  - kidney failure (44% of new cases in 2008 & any given year > 50,000 DM on dialysis or transplant)
  - 2 – 12X the risk for heart disease
  - 2 – 4X the risk for stroke

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## Epidemiology – U.S. <sup>(6)</sup>

- Developmental Disabilities & DM: No statistics were found but source after source state that the chance of diabetes prevalence, causative conditions, complications and Tx difficulty is higher in those with DD.

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## BLOOD SUGAR ANATOMY & PHYSIOLOGY

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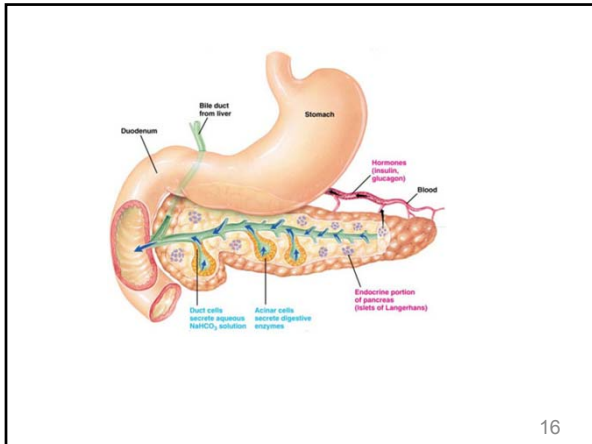
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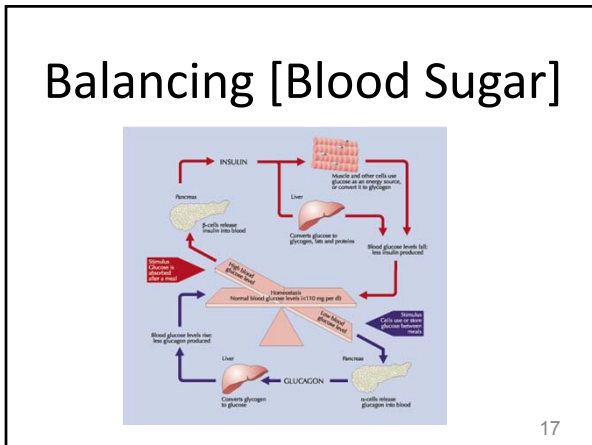
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**Table 1: Digestive Chemicals & Sources**

<u>Cell/Hormone</u>	<u>Sources</u>	<u>Action</u>
• □: Glucagon		• ↑ [blood glucose]
• □: Insulin & Amylin		• ↓ [blood glucose]
• PP: Pancreatic Polypeptide		• ↓ [blood glucose]
• □: Ghrelin		• ↑ [blood glucose]
• Δ: Somatostatin		• ↓ [blood glucose]
• Mucosa L cells: GLP-1		• ↓ [blood glucose]
• Mucosa K cells: GIP		• ↓ [blood glucose]
• Brush border: □ glucosidases		• ↑ [blood glucose]

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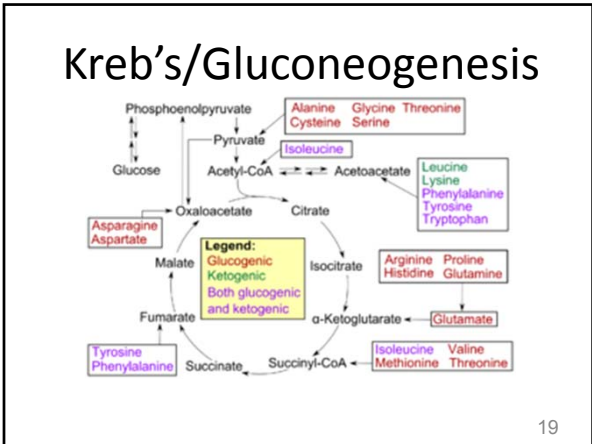
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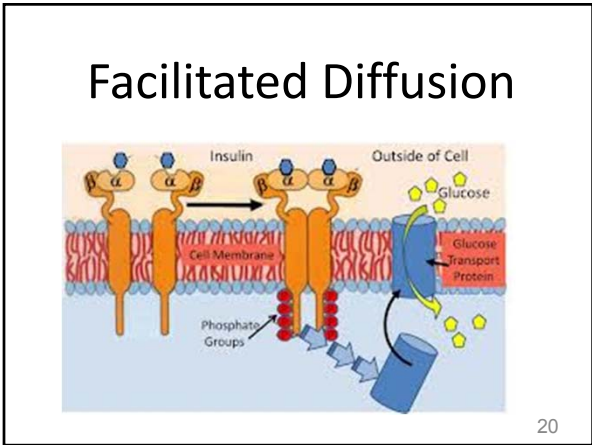
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### Table 2 - Insulin Functions

<ul style="list-style-type: none"> <li>• <b>↓ [blood glucose]</b> <ul style="list-style-type: none"> <li>➢ Facilitated diffusion</li> <li>➢ ↑ glucogen synthesis</li> <li>➢ ↑ esterification fatty acids</li> <li>➢ ↓ lipolysis</li> <li>➢ ↓ proteolysis*</li> <li>➢ ↑ amino acid uptake</li> <li>➢ ↓ (inhibits) glucagon release</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• <b>Not [blood glucose] related</b> <ul style="list-style-type: none"> <li>➢ ↓ autophagy</li> <li>➢ ↑ K<sup>+</sup> uptake</li> <li>➢ ↓ in arterial muscle tone</li> <li>➢ ↑ secretion of gastric HCl</li> <li>➢ ↓ blood pressure</li> <li>➢ ↓ renal Na<sup>+</sup> excretion</li> <li>➢ ↑ K<sup>+</sup> excretion/↓ blood [K<sup>+</sup>]</li> </ul> </li> </ul>
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## RISK FACTORS

### Type 1

- Family History
- Possible genetic precursors

### Type 2

- Obesity\*
- Adipose tissue distribution
- Inactivity
- Family history of Type 2 DM
- Ethnicity
- Age
- Prediabetes
- Gestational diabetes
- Large baby (> 9 lbs)

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## ETIOLOGY/CONDITIONS

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### Etiology/Conditions → DM <sup>(1)</sup>

- Genetic defects in  $\beta$  cell function
- Exocrine Pancreatic Defects
  - Chronic pancreatitis
  - Pancreatectomy
  - Pancreatic neoplasm
  - Cystic Fibrosis
  - Hemochromatosis
  - Fibrocalculous pancreatopathy

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**Etiology/Conditions → DM** (2)

- Endocrinopathies
  - Cushing Syndrome
  - Hyperthyroidism
  - Growth Hormone excess (acromegaly)
  - Pheochromocytoma

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**Etiology/Conditions → DM** (5)

- Drugs
  - Atypical antipsychotics
  - □-adrenergic agonists
  - Calcium Channel blockers
  - Corticosteroids
  - Niacin
  - Phenothiazines
  - Thiazide diuretics
  - Thyroid hormone
  - Phenytoin
  - Statins
  - Estrogen

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**DM PATHOLOGY**

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### TYPE 1 – Insufficient Insulin

- $\square$  cells destroyed in antigen-antibody reaction
- DM occurs when 80 – 90%  $\square$  cells destroyed

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### TYPE 2 – Resistance/Reduction

(1)

- Insulin resistance
- Contributing Factors:
  - Defective insulin or receptor & post-receptor defects  $\rightarrow$  inability to initiate facilitated diffusion.
  - $\downarrow$  intracellular fat & muscle glucose from insulin lack/resistance. Initiates  $\uparrow$  liver glycogenolysis to  $\uparrow$  [blood glucose]
  - Insulin resistance  $\rightarrow$   $\uparrow$  lipolysis

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## Types 1 & 2 DM SYMPTOMS

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## Osmotic Pressure & DM

**Fig 1**  
Osmotic Pressure

The diagram shows a container divided by a vertical membrane. The left side is labeled 'Sugar Solution' and contains several black dots representing sugar molecules. The right side is labeled 'Plain Water' and is empty. The membrane is labeled 'Membrane permeable to water but not to sugar'. Three arrows point from the plain water side to the sugar solution side, with the text 'Flow of water through membrane into sugar solution via osmotic pressure'.

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## Kidney Nephron

The diagram shows a cross-section of a nephron. It includes the renal corpuscle (glomerulus and Bowman's capsule), the proximal convoluted tubule, the loop of Henle, the distal convoluted tubule, and the collecting duct. The parts are numbered 1 through 13.

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## DM Symptoms <sup>(1)</sup>

Symptom	Type		Symptom	Type	
	1	2		1	2
Hyperglycemia	✓	✓	Weight loss	✓	✓
Glycosuria	✓	✓	Fatigue	✓	✓
Polydipsia (thirst)	✓	✓	Blurred vision	✓	✓
Polyuria (frequent urination)	✓	✓	Slow healing/freq infections	✓	✓
Polyphagia (hunger)	✓	✓	Acanthosis nigricans	✓	✓

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## DM Symptoms <sup>(2)</sup>

Symptom	Type	
	1	2
Lethargy	✓	
Stupor	✓	
Ketoacidosis (DKA)	✓	unusual
Abdominal pain	✓	
Nausea/Vomiting	✓	
Hyperosmolar Hyperglycemic Nonketotic State (HHNK)		rare

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## Diabetic Ketoacidosis Sx

- Kussmaul breathing  
– $H_2O + CO_2 \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$
- Fruity (alcohol) smelling breath
- Dry skin & mouth
- Flushed face
- Nausea & vomiting
- Stomach pain

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## HHNK Sx

- Severe hyperglycemia
- Extreme dehydration
- Hyperosmolar plasma
- Altered consciousness, confusion or disorientation to coma without significant ketosis (seizures & death)

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## Hypoglycemic Symptoms

(1)

- Sweating
- Hunger
- Weakness
- Anxiety
- Dizziness/lightheaded
- Pale skin
- Shakiness
- Rapid or irregular HR
- Fatigue
- Headache
- Blurred vision
- Irritability

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## Hypoglycemic Symptoms

(2)

Later Symptoms (mistaken for intoxication)

- Lethargy
- Confusion
- Behavior Change
- Poor coordination
- Convulsions

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## Hyperglycemic Symptoms

- Frequent urination
- Increased thirst
- Blurred vision
- Fatigue
- Nausea
- Irritability
- Hunger
- Difficulty concentrating

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# COMPLICATIONS

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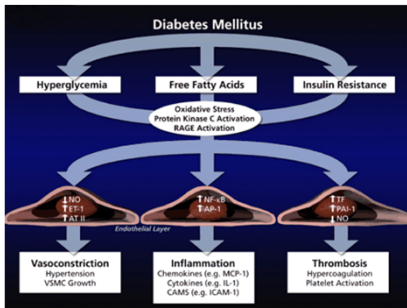
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## Diabetic Vascular Disease



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## Macroangiopathy

- Stroke & Cerebrovascular Disease
- Coronary artery Disease

(These are large vessel diseases → decreased blood supply (ischemia) from atherosclerosis secondary to vessel endothelial dysfunction plus: procoagulant state and antifibrinolytic state)

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# Microangiopathy

- Retinopathy
- Nephropathy

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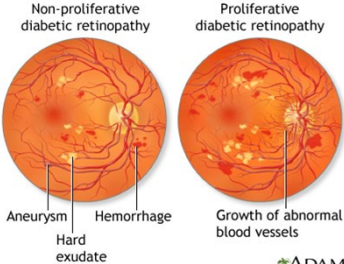
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# Retinopathy

Non-proliferative diabetic retinopathy      Proliferative diabetic retinopathy



Aneurysm      Hemorrhage      Growth of abnormal blood vessels  
Hard exudate

ADAM

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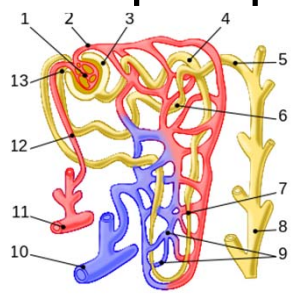
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# DM Nephropathy



1 2 3 4 5  
13 6  
12 7  
11 8  
10 9

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## Autonomic Neuropathy

- Gastroparesis
- Diarrhea
- Impotence/Sexual dysfunction
- Orthostatic Hypotension

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## Peripheral Neuropathy & Microangiopathy

- Light touch, vibratory & temp sensation
- Lost foot proprioception & possible eventual ataxia, gait problems
- Ulceration
- Necrosis



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## Blood Pressure/Hypertension

Circulatory System (CS)	Change	B/P change
Heart stroke volume	↑ ↓	↑ ↓
Heart Rate	↑ ↓	↑ ↓
Artery volume	↑ ↓	↓ ↑
Blood Volume:	↑ ↓	↓ ↑

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# TREATMENT

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# DM Diagnosis

- History & Physical
- Diagnostic Tests – [blood sugar]
  - Random blood sugars
  - Fasting blood sugar
  - Glycohemoglobin (HbA<sub>1C</sub>)
  - Fructosamine Assay
  - C-Peptide Assay (Connecting Peptide Assay)

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**Exercise**  
Regular exercise helps your body lower blood sugars, promote weight loss, reduce stress and enhance overall fitness.

**Healthy Weight**  
Maintaining a healthy weight is especially important in the control of Type 2 Diabetes.

**Take Medication if needed**  
Type 1 Diabetes always requires daily injections of insulin. Type 2 Diabetes is controlled through exercise and meal planning and may require medications and/or insulin to assist the body in making or using insulin more effectively.

**Education**  
All people with diabetes need to learn about their condition in order to make healthy lifestyle choices and manage their diabetes.

**Eat a Healthy diet**  
What, when and how much you eat plays an important role in regulating how well your body manages blood sugar levels.

**Lifestyle Management**  
Learning to reduce stress levels in day-to-day life can help people with diabetes better manage their disease.

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# Treatment Approach

- T1DM – Absolute insulin lack
- T2DM – Cellular resistance & relative insulin lack
- Balance insulin production/admin with insulin need
- Treatment modalities:
  - Medications – Insulin and oral antidiabetics (monitored)
  - Diet – monitored & goal directed
  - Exercise – monitored and goal directed

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# DM MEDICATIONS

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## Insulins - Rapid & Short Acting

Name	Onset	Peak	Duration
<b>Rapid -Acting</b>			
Humalog/Lispro	15 – 30"	30 – 90"	3 – 5 hours
Novolog/Aspart	10 – 20"	40 – 50"	3 – 5 hours
Apidra/Glulisine	20 - 30"	30 – 90"	1 – 1½ hours
<b>Short -Acting</b>			
Regular/Humulin	30" – 1 hour	2 – 5 hours	5 – 8 hours
Velsulin (pump)	30" – 1 hour	2 – 3 hours	2 – 3 hours

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### Insulins – Intermediate & Long-Acting

Name	Onset	Peak	Duration
<b>Intermediate-Acting</b>			
NPH (N)	1 – 2 hrs	4 – 12 hrs	18 – 24 hrs
Lente (L)	1 – 2½ hrs	3 – 10 hrs	18 – 24 hrs
<b>Long-Acting</b>			
Ultralente (U)	30" – 3 hrs	10 – 20 hrs	20 – 36 hrs
Lantus	1 – 1½ hrs	No peak	20 – 24 hrs
Levemir/Detemir	1 – 2 hrs	6 – 8 hrs	Up to 24 hrs

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### Insulins – Pre-Mixed

Name	Onset	Peak	Duration
Humulin 70/30	30"	2 – 4 hrs	14 – 24 hrs
Novolin 70/30	30"	2 – 12 hrs	Up to 24 hrs
Novolog 70/30	10 – 20"	1 – 4 hrs	Up to 24 hrs
Humulin 50/50	30"	2 – 5 hrs	18 – 24 hrs
Humalog mix 75/25	15"	30" – 2 ½ hrs	16 – 20 hrs

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### Self Administration

- Injection using 31 gauge, 5/16" long needle @ 90° angle for most; 45° for thin people
- Self injection, rotation of abdomen & thighs
- Tissue damage eventually leads to:
  - Hardened skin with lumps & dimpling
  - Weakened underlying fatty tissue (lipodystrophy)
  - ↓ insulin absorption → difficulty in controlling [blood glucose] levels

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### Oral Antidiabetic Agents - List

- $\alpha$ -glucosidase inhibitors – Acarbose, Miglitol
- Biguanide – Metformin HCl
- Glucagon-Like Peptide (GLP-1) agonists – Exenatide, Liraglutide
- Dipeptidyl peptidase-4 inhibitors - Linagliptin, Sitagliptin, Saxagliptin
- Human Amylin Analogue – Pramlintide
- Meglitnide/Meglitnide derivative – Repaglinide, Nateglinide

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### Oral Antidiabetic Agents - List

- Combination Medications
  - Metformin HCl & Linagliptin
  - Metformin HCl & Sitagliptin
- Weight Loss Drugs
  - Lorcaserin/Belviq®
  - Phentermine/Topiramate

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### Diabetes and Obesity

- Does obesity cause DM-Type 2?
- Developed eating habits early in life
- Body Mass Index
- Losing weight is simple, not easy
- Life-style change

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### Diabetes and Obesity (2)

- BODY FAT % RANGES FOR MEN

RATING	AGE				
	20-29	30-39	40-49	50-59	60+
LOW	<13	<14	<16	<17	<18
NORMAL	14-20	15-21	17-23	18-24	19-25
MODERATE	21-23	22-24	24-26	25-27	26-28
HIGH	>23	>24	>26	>27	>28

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### Diabetes and Obesity (3)

- BODY FAT % RANGES FOR WOMEN

RATING	AGE				
	20-29	30-39	40-49	50-59	60+
LOW	<19	<20	<21	<22	<23
NORMAL	20-28	21-29	22-30	23-31	24-32
MODERATE	29-31	30-32	31-33	32-33	33-35
HIGH	>31	>32	>33	>34	>35

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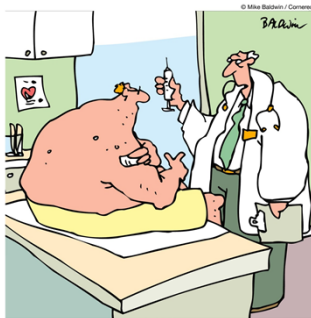
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"It wasn't really insulin. You don't have diabetes yet. It was just a warning shot."

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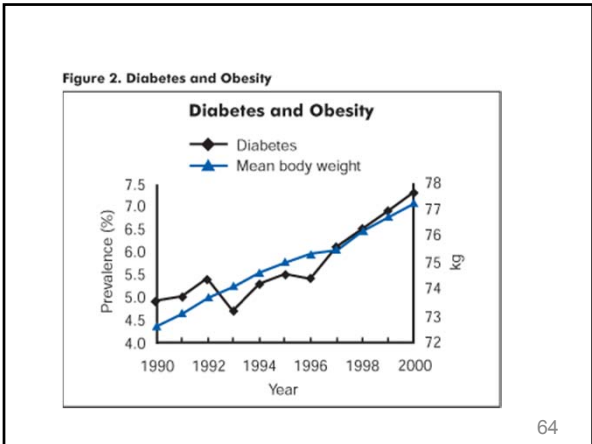
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# Diet

# **DIABETES &**

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- ## Diet - Sources <sup>(1)</sup>
- Nutritionist/Dietitian
  - Sources:
    - American Diabetics Association:  
[www.diabetics.org](http://www.diabetics.org)
    - Academy of Nutrition and Dietetics (was American Dietetic Association)  
[www.eatright.org](http://www.eatright.org)
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## Diet – Intake Amount <sup>(2)</sup>

- Recommended caloric intake:
  - ♂, active ♀ – 15 calories/lb body weight
  - Most ♀, sedentary ♂, & adults ↑ 55 - 13 cal/lb
  - Sedentary ♀, obese adults – 10 cal/lb
  - Pregnant, lactating ♀ - 15 – 17 cal/lb
  - Example: 200 lb ♂ needs to eat 2000 cal daily to maintain his weight

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## Diet - Tracking <sup>(3)</sup>

- Counting calories
- Exchange lists
- Glycemic Index

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## Diet – Exchange List <sup>(4)</sup>

GROUP	CHO	PROTEINS	FAT	CALORIES
Starch/Bread	15/0.529	3/0.106	TRACE	80
<u>Meat</u>				
Very Lean		7/0.247	0-1/0.035	35
Lean		7/0.247	3/0.106	55
Med-Fat		7/0.247	5/0.176	75
High-Fat		7/0.247	8/0.282	100

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## Diet – Exchange List

(5)

GROUP	CHO	PROTEINS	FAT	CALORIES
Vegetable	5/0.176	2		25
Fruit	15/0.529			60
<u>Milk</u>				
Skim	12/0.423	8/0.282	0-3/0.106	90
Low-Fat	12/0.423	8/0.282	5/0.176	120
Whole	12/0.423	8/0.282	8/0.282	150
Fat			5/0.176	45

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## Diet – Exchange List

(6)

- Food exchange lists extensive
- To be determined (dietitian)
  - Caloric intake
  - amount of CHO, P & F
  - Minimize Na, fats, cholesterol,
  - Appropriate fiber amount

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## Diet – Glycemic Index <sup>(7)</sup>

- Glycemic Index – Measure of how quickly blood glucose level rises compared to glucose standard of 100 after eating a particular food. 95 is high GI value; 20 is low

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## Diet – Glycemic Index <sup>(8)</sup>

- Index tied to serving size in grams
- GI charts list foods much like exchange lists
- Problems: amt CHO actually consumed; insulin production; variability of foods; person response; impact speed/persistence

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## Diet - Timing <sup>(9)</sup>

- Meal timing
  - For diabetics – important
  - Especially important for those using long acting insulin
  - Intensive insulin therapy more flexible

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## Exercise **DIABETES &**

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www.glasbergen.com

GLASBERGEN

“What fits your busy schedule better, exercising one hour a day or being dead 24 hours a day?”

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### EXERCISE AND RISK OF DIABETES

Decrease risk of developing diabetes by 50% in those with high risk defined by:

- High blood pressure
- Family history
- Obesity

Relative risk of developing diabetes

Kcal of Exercise per week	Relative risk of developing diabetes
500	1.00
3500	0.52

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### Exercise & Type 2 Diabetes

Group	Percent reduction in incidence of type 2 diabetes
Diet/exercise vs placebo	58%
Metformin vs placebo	31%
Diet/exercise vs Metformin	39%

Source: Knowler et al., 2002. Randomized clinical trial with average 2.8-year follow-up period.

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### Exercise Benefits <sup>(1)</sup>

- Improves body insulin use
- Aerobic exercise can ↓ risk of T2DM
- Aerobic exercise can ↓ complication risk
- May delay/prevent T2DM
- Empties liver glycogen reserves
- ↓ [blood sugar] & fatty acid levels
- ↓ □ cell workload/excessive production

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### Exercise Benefits <sup>(2)</sup>

- Weight loss and control
- Combats health conditions & diseases
- ↑energy, muscle strength, endurance partly do to ↑ body efficiency
- Improves mood
- Promotes better sleep

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### Exercise elements <sup>(2)</sup>

- Mode: walking, swimming, jogging, etc
- Frequency: How often exercise occurs
- Duration: How long exercise lasts
- Intensity: How “hard” exercise is
- Intensity can replace duration somewhat but be careful

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## Easy Exercise

- Walk while talking on phone
- Don't use TV remote
- Wash car
- Park car at far end of shopping center lot
- Yard work
- Use stairs

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## Exercise Planning <sup>(1)</sup>

- SEE PHYSICIAN FIRST!
- Determine best exercise mode
- Schedule food intake, exercise & medication
- Be care of intense exercise
- With regular exercise, medications may have to be reduced. Check with physician
- Learn what exercise does to [blood sugar]

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## Exercise Planning <sup>(2)</sup>

- Have CHO-based food available after exercise
- May need to add CHO to meals
- With MD, adjust insulin as necessary
- Track exercise (intensity, duration, frequency)

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### Exercise Cautions <sup>(1)</sup>

- Wear medical alert ID (RoadID.com)
- Exercising when medication is @ peak effect
- Exercising when [blood glucose] is very high
- Watch for Symptoms of hypoglycemia (restoring of body balance can take 24 hours)
- Check [blood sugar] before, during, & after (learn how exercise effects body)

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### Exercise Cautions <sup>(2)</sup>

- Carry small CHO snack such as fruit or fruit drink for possible hypoglycemia during exercise
- Too much exercise (intensity/duration) can cause catecholamine production to ↑ [blood glucose]

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### Exercise Cautions <sup>(3)</sup>

- Don't exercise with DM-T1 & positive ketone test & [blood glucose] > 250 mg/dl
- If insulin injection necessary, use abdomen rather than arm or leg to absorb insulin more evenly
- Start hydrated and stay hydrated

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## Exercise Measures

Determining Target Range	
INTENSITY	% MAX HEART RATE
Very light	< 35
Light	35 – 54
Moderate	55 – 70
Hard	71 – 90
Very Hard	> 90
Maximal	100

220 – age. Ex: moderate  $[220 - \text{age}] \times 0.55$  to  $[220 - \text{age}] \times 0.70$

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## Bariatric Surgery <sup>(1)</sup>

- Considered appropriate when BMI is:
  - 30 – 35 with significant comorbidities
  - 35 & up with serious coexisting medical conditions such as diabetes
  - 35 – 40 when no comorbidities are present

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## Bariatric Surgery <sup>(2)</sup>

- Bariatric Surgery not 1 specific procedure
  - Gastric band (implanted)
  - Partial gastrectomy (“sleeve” gastrectomy or biliopancreatic diversion with duodenal switch)
  - Resection & re-routing of small intestine to small stomach pouch (gastric bypass)
  - Can → long term significant weight loss

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## Bariatric Surgery <sup>(3)</sup>

- Bariatric Surgery can result in:
  - Significant long-term weight loss
  - Diabetic resolution/cure
  - Improved cardiovascular risk
  - Reduction of mortality rates from 23 to 40%
- Study showed no survival benefit among older, severely obese people

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## DM & Developmental Disabilities <sup>(1)</sup>

- Incidence of obesity in DD individuals 4x more common than general population
- Problems:
  - Access to healthcare for screening & treatment
  - Inability of those with DD to self manage
  - Inability to understand
  - Flawed view of disease

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## DM & Developmental Disabilities <sup>(2)</sup>

- Source: Prevent, Understand, and Live with Diabetes: A Guide for Individuals with Developmental Disabilities, ARC of New Jersey, 985 Livingston Ave, North Brunswick, NJ 08902
- To request copy call (732) 246-2525, ext. 35 or email [info@arcnj.org](mailto:info@arcnj.org)
- February 2012 document

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**DM & Developmental Disabilities** <sup>(3)</sup>

- This guide is for the individual with DM.
- It used relatively simple language and pictures
- It talks about DM prevention, warning signs, blood sugar testing, and living with diabetes.
- It is also available in Spanish

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