Tech Lectures®

For the Pharmacy Technician

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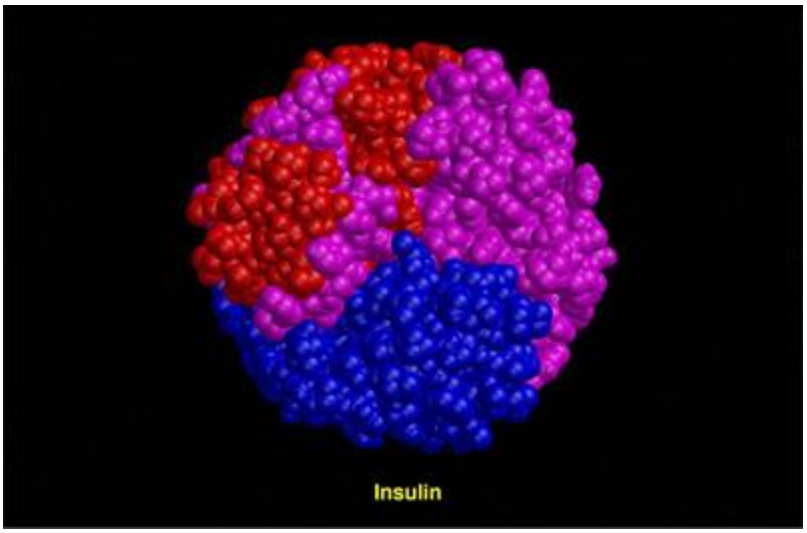


Lecture 2 – About Diabetes

About Diabetes

Terms:

Autoimmune
NIDDM
Beta-cells
Hyperglycemia
Glucosuria
Polydipsia
Insulinplethoric
Asymptomatic
Clinitest
Lipohypertrophy
Hypothermia
Glycogen
Dextrose
Proteinuria
Metabolic Syndrome
IDDM
Ketones
Insulin
Hypoglycemia
Polyuria
Polyphagia
Sympathomimetics
Sulfonylureas
Ketoacidosis
Acetone
Acidemia
Glucose
Retinopathy
Type I & II

At the end of this section, the student should have a basic understanding of:

1. the differentiation between the types of Diabetes Mellitus
2. the Pathophysiology of Diabetes Mellitus
3. the Non-Pharmacological and Pharmacological treatment of Diabetes Mellitus
4. the Pathophysiology and treatment of Ketoacidoses
5. the Terms that apply in this section

Diabetes Mellitus

a. A **complex disorder** of carbohydrate, fat and protein metabolism which is caused by lack of insulin or insufficient use of insulin in the body.

Statistics*

Total prevalence of diabetes

Total: 25.8 million children and adults in the United States—8.3% of the population—have diabetes.

Diagnosed: 18.8 million people

Undiagnosed: 7.0 million people

Pre-diabetes: 79 million people

New Cases: 1.9 million new cases of diabetes are diagnosed in people aged 20 years and older in 2010.

Most current statistics 2010*

Diabetes is likely to be underreported as a cause of death.

leading cause of non-traumatic amputations (60%)

risk for death among people with diabetes is about twice that of people without diabetes

Cost of diabetes in the United States

Total (direct and indirect): $132 billion

Direct medical costs: $92 billion

Indirect costs: $40 billion (disability, work loss, premature mortality)

Among adults with diagnosed diabetes, 16 percent take insulin only, 12 percent take both insulin and oral medication, 57 percent take oral medication only, and 15 percent do not take either insulin or oral medications.

Why?

a. most cases are due to genetic predisposition

b. pancreatic or endocrine disease

c. autoimmune response

- body goes against its own antigen markers on cells and attacks *self* cells

a. precipitated by drug therapy

IDDM (Insulin Dependent Diabetes Mellitus) or Type I

a. 5% to 10% of diabetic population

b. also known as "*juvenile onset diabetes mellitus*"
- usually diagnosed as a juvenile

c. No pancreatic reserve of insulin
- must receive insulin therapy to control the condition

d. Often exhibit wide fluctuation in blood glucose levels
- therefore sometimes called "**brittle diabetes**"

e. more prone to toxic ketones in the blood (*Ketosis*)

Ketones - breakdown products of metabolism. Often acidic in nature. Products may accumulate in body fluids (example: Acetone)

f. patients are often thin

NIDDM (Non insulin dependent Diabetes Mellitus) or Type II

a. usually older onset
   - around age 40 or later

Use to be called Adult onset Diabetes, but recent studies have shown an increase of this type of diabetes in children due to sedentary lifestyle and poor eating habits.

b. vast majority are of this type
   - 90% - 95% of diabetics

c. have some residual pancreatic function
   - may have normal or even high levels of insulin

d. less likely to develop ketosis as in Type I

e. Most diabetics (80%) of this type are *obese* and live *sedentary* lifestyles

b. Some diabetics (5%) of this type are brittle Type II

c. Considered to be associated with Metabolic Syndrome

Gestational Diabetes

is a form of glucose intolerance diagnosed in some women during pregnancy. Gestational diabetes occurs more frequently among African Americans, Hispanic/Latino Americans, and American Indians. It is also more common among obese women and women with a family history of diabetes. During pregnancy, gestational diabetes requires treatment to normalize maternal blood glucose levels to avoid complications in the infant. After pregnancy, 5 to 10 percent of women with gestational diabetes are found to have type 2 diabetes. Women who have had gestational diabetes have a 20 to 50 percent chance of developing diabetes in the next 5 to 10 years.

Metabolic Syndrome

Today risk factors for coronary heart disease and other diseases such as Type II Diabetes can be related to one's characteristics associated with the new term "metabolic syndrome."

Metabolic syndrome is characterized by a group of metabolic risk factors in one person. They include:

- Abdominal obesity (excessive fat tissue in and around the abdomen)
- Atherogenic dyslipidemia (blood fat disorders — high triglycerides, low HDL cholesterol and high LDL cholesterol — that foster plaque buildups in artery walls)
- Elevated blood pressure
- Insulin resistance or glucose intolerance (the body can't properly use insulin or blood sugar)
- Prothrombotic state (e.g., high fibrinogen or plasminogen activator inhibitor–1 in the blood)
- Proinflammatory state (e.g., elevated C-reactive protein in the blood)

The metabolic syndrome has become increasingly common in the United States. It's estimated that over 50 million Americans have it.

The dominant underlying risk factors for this syndrome appear to be abdominal obesity and insulin resistance. Insulin resistance is a generalized metabolic disorder, in which the body can't use insulin efficiently. This is why the metabolic syndrome is also called the insulin resistance syndrome.

Other conditions associated with the syndrome include physical inactivity, aging, hormonal imbalance and genetic predisposition.

Some people are genetically predisposed to insulin resistance. Acquired factors, such as excess body fat and physical inactivity, can elicit insulin resistance and the metabolic syndrome in these people. Most people with insulin resistance have abdominal obesity. The biologic mechanisms at the molecular level between insulin resistance and metabolic risk factors aren't fully understood and appear to be complex.

Metabolic Syndrome is associated with pre-diabetes risk factors which involves impaired glucose tolerance and impaired fasting glucose

- Pre-diabetes is a condition that raises the risk of developing type 2 diabetes, heart disease, and stroke. Some people with pre-diabetes have blood glucose levels higher than normal but not high enough to be classified as diabetes.
- People with pre-diabetes have impaired fasting glucose (IFG) or impaired glucose tolerance (IGT). Some people have both IFG and IGT.
- IFG is a condition in which the fasting blood glucose level is 100 to 125 milligrams per deciliter (mg/dL) after an overnight fast. The level is higher than normal but is not high enough to be classified as diabetes.
- IGT is a condition in which the blood glucose level is 140 to 199 mg/dL after a 2-hour oral glucose tolerance test. This level is higher than normal but not high enough to be classified as diabetes.
- More recent estimates from 1999–2002 indicate that, among U.S. adults age 20 years and older, 26 percent had IFG, which was similar to the prevalence in 1988–1994 (25 percent). Applying this percentage to the entire U.S. population, 54 million American adults had IFG in 2002. Because IGT was not measured in 1999–2002, these data suggest that at least 54 million American adults had pre-diabetes in 2002.
- Progression to diabetes among those with pre-diabetes is not inevitable. Studies have shown that people with pre-diabetes who lose weight and increase their physical activity can prevent or delay diabetes and even return their blood glucose levels to normal.

Pathophysiology of Diabetes

1. ingestion of food causes an increase in blood glucose
2. thereby, triggering release of insulin from the pancreas
    a. *Beta cells* of the Pancreas

Main two functions of Insulin :

1. allows the transfer of Glucose across cell membranes
2. allows the conversion of Glycogen in the liver to Glucose

Glycogen ----------> Glucose --------> Energy

Glycogen: stored form of Glucose
Glucose: end product involving the breakdown of carbohydrate

3. The continued release of insulin causes a reduction in the Blood glucose concentration and eventually produces a hypoglycemic state. This inhibits further insulin release and the release of other hormones
    a. corticosteroids, epinephrine, Glucagon

Food eaten ----> Hyperglycemia ---------->(*release of Insulin*)------->Hypoglycemia

a. increase of Glucose in the blood

Pancreas : a gland situated behind the stomach in front of the 1st and 2nd lumbar vertebrae in a horizontal position

Function: produces pancreatic juices for helping in the digestion of food

Produces **Insulin** & Glucagon which play a role in the regulation of Carbohydrate metabolism

Produce Desmopressin Acetate (anti-diuretic) and Other Hormones

Insulinplethoric: greater insulin but less receptor sites limited to family history

theory: high caloric intake leads to increased insulin levels which leads to "down regulation" of receptor sites

Doodle Space

In the Diabetic

a. ***Deficiency of insulin/or the resistance of tissue to insulin action causes:***

1. **Hyperglycemia**

- high blood glucose stays high even after eating a meal

- when blood glucose level exceeds **180mg/dl**

a. spillage of excess glucose in urine
- *glucosuria*

b. draws body water into the urinary tract

c. cause *polyuria* (> frequency of urination)

d. which causes *polydipsia* (thirst)

e. which may result in electrolyte imbalances/ deficiencies

f. also more receptive to urinary tract infections

2. *Interference* with Glucose utilization

a. which causes other nutrients to break down to provide fuel

- *fasting metabolism*

b. fatty acids are converted to *ketones*

c. proteins are broken down

d. Glycogen (stored form of Glucose) is broken down to Glucose

leads to :

1. Diabetic Ketoacidosis
2. Wasting of muscle tissue
3. Even higher and prolonged levels of glucose
    - free floating Glucose is unable to breakdown

Clinical Symptoms

1. weight loss
2. fatigue
3. constant eating (*polyphagia*)
4. polyuria
5. polydipsia

Successful treatment dependent on:

1. proper dietary management
2. proper exercise program
3. drug therapy
4. close patient monitoring

Normal Glucose levels : 60mg/dl - 180mg/dl or 60 - 180mg%

Diagnosis:
1. Clinical Symptoms
2. Random Glucose levels > 200mg/dl
3. Glucosuria

Drugs that Induce: Phenytoin (less release of Insulin)

Thiazides (adjust dose of anti-diabetic agents)

Birth Control Pills

Gluccocorticosteroids

Sympathomimetics (Diabetics should avoid)

Goals of Therapy : Keep patient Asymptomatic (symptom free)

Good energy level

Euglycemic (60mg to 180mg%)

Maintain normal weight and growth (juveniles)

Patient Education

Components of Therapy:

Diet: well balanced
must eat regularly
need to document diet

Exercise: moderate
before vigorous exercise

a. less insulin or
greater CHO intake

b. do not inject insulin
in thigh

Drugs: Insulin, Oral medications

Long Term Effects: Cataracts (clouding of eye lens)
Retinopathy ----> blindness
Proteinuria
Kidney Failure
Neuropathy
Micro and macro vascular disease
a. gangrene in limbs

Lab Tests:

Urine Tests (detection of Glucosuria)

Advantages: inexpensive

can detect Ketones

Disadvantages: : indirect measure of blood glucose

can't differentiate glucose level

0 - 180mg%
180 - x mg%

no correlation with blood glucose

Products:

Clinitest : false positive - Salicylates
Ascorbic Acid
Cephalosporins

Diastix

Ketodiastix: false positive - inhibited by Ketones
Ascorbic Acid, Salicylates

How Often to test

1. Once daily in AM
2. Occasionally 1 - 2 hours after a meal
3. Type I (if stable) ------> twice a day
   - if not stable ------> qid (ac & hs)
4. In general if ill -------> qid

Home Blood Glucose Monitoring

a. By far the best method

- Will give accurate reading of actual Glucose blood level

b. Indication

- brittle type I
- Pregnant
- Color blind
- ignorance of symptoms of hypo or hyperglycemia

c. Goal of therapy

- random blood Glucose less than 180mg%
- Euglycemic
- Generally test qid
  a. 7 am fasting level
  b. 11am how regular insulin is handling breakfast
  c. 5pm how insulin is handling lunch and NPH break
  d. 10pm how insulin is handling dinner

d. Dose Adjustment

- less than 100mg/dl same dose
- less than 80mg/dl lower dose
- 150mg - 200mg% add 2 units to dose
- greater than 200mg/dl add 4 units to dose

e. Disadvantages

- complex procedure
- compliance
- expense

Ketoacidosis

Causes: reduction of insulin dose
infection and/or stress
unknown
initial manifestation of diabetes
a. diagnosis often occurs

Symptoms: develop over 36 hours

nausea and vomiting
Acetone breath
Hypothermia
Dehydration
Stupor -----> coma

Lab values: Glucose 300 - 800mg/dl
Ketone bodies elevated
pH decreased - Acidemia
WBC usually increased
other electrolyte and enzymes increased

Treatment: Fluid replacement (avoid Dextrose)

Insulin Replacement
0.1 to 0.2units/Kg bolus
0.1 units/Kg IVPB

if no decrease in Glucose level - double rate

Potassium Replacement
Insulin will lower Potassium level

NaHCO3 (Sodium Bicarbonate)
for severe Acidemia (pH less 7.1)
one ampule

Response: Glucose should drop to 75 - 100mg/dl/hr
Ketosis usually reversed in 12 -24 hours
Fluid replacement usually takes 1 - 2 days

Doodle Space

Insulin Therapy

Replacement insulin therapy should mimic normal release patterns.

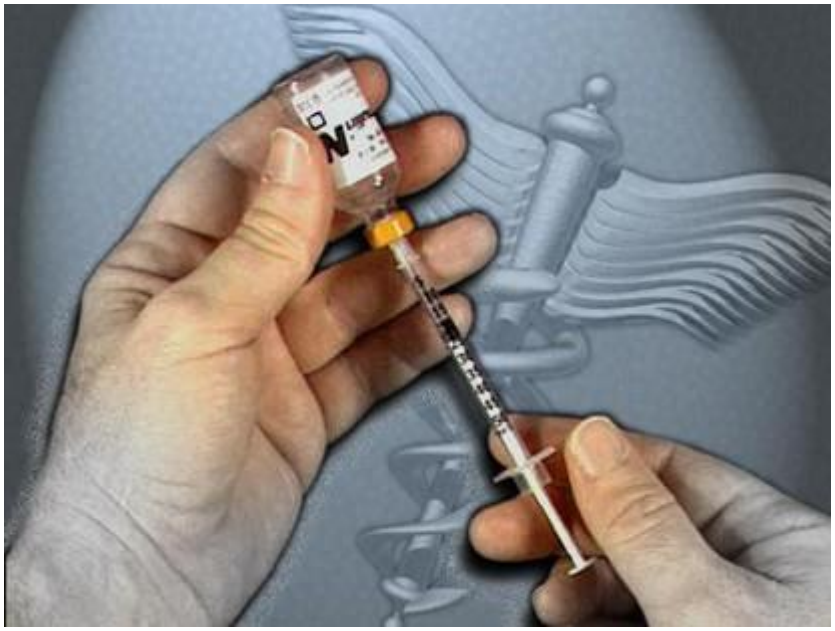
a. Basal insulin, using long-acting insulins (i.e., neutral protamine Hagedorn [NPH], ultralente, glargine) is injected once or twice a day and continued on sick days.

   Basal insulin is the insulin that controls blood glucose levels between meals and overnight. It controls glucose in the fasting state.

b. Bolus (or mealtime) insulin, using short-acting or rapid-acting insulins (i.e., regular, aspart, lispro) covers mealtime carbohydrates and corrects the current glucose level.

   Bolus insulin is the insulin that is released when food is eaten. A bolus is a burst of insulin that is delivered by injection or by the insulin pump

c. The starting dose of 0.15 units per kg per day for augmentation or 0.5 units per kg per day for replacement can be increased several times as needed. About 50 to 60 percent of the total daily insulin requirement should be a basal type, and 40 to 50 percent should be a bolus type.



Onset and Duration of Insulins

Insulin	Onset	Usual effective duration (hours)	Usual maximum duration (hours)
Bolus or mealtime insulin			
Aspart (NovoLog)	5 to 10 minutes	3 to 5	4 to 6
Lispro (Humalog)	< 15 minutes	2 to 4	4 to 6
Regular (Humulin R, Novolin R)	30 to 60 minutes	3 to 6	6 to 10
Basal insulin			
NPH (Humulin N, Novolin N)	2 to 4 hours	10 to 16	14 to 18
Lente (insulin zinc suspension)	3 to 4 hours	12 to 18	16 to 20
Ultralente (extended insulin zinc suspension)	6 to 10 hours	18 to 20	20 to 24
Glargine (Lantus)	1 hour, 6 minutes	24	24
Combinations			
50% NPH/50% regular	30 to 60 minutes	10 to 16	14 to 18
70% NPH/30% regular (Humulin R 70/30, Novolin R 70/30)	30 to 60 minutes	10 to 16	14 to 18
75% NPL/25% lispro (Humalog 75/25)	< 15 minutes	10 to 16	14 to 18
70% APS/30% aspart (NovoLogMix 70/30)	10 to 20 minutes	24	24

Dosage adjustments are always necessary when changing from one type of insulin to another type

Side effects:

a. local reaction

- ***Lipohypertrophy***

a. injection site swelling
b. reason to rotate injection sites

b. Insulin Reactions (too much)

- Hypoglycemia (less than 60mg/dl)

a. night sweats
b. nightmares
c. moody behavior
d. hungry
e. palpitations

Treatment

- sugar cubes
- hard candy
- fruit juice (4 oz)

Dosing Goal of Insulin

mimic body's insulin pattern

maintain blood glucose 60mg/dl to 180mg/dl

Usual Dose

0.5 to 1.0 unit / Kg / day

Oral Hypoglycemic Agents

Classification: Sulfonylureas

First widely used gents that stimulate pancreatic beta cells to secrete insulin

a. some pancreatic function required

b. use limited to Type II (NIDDM)

- does not respond to diet alone
- unwilling to use insulin

c. use of these agents may lead to increased risk of

- liver disease
- cardiovascular death
  a. reason for decline in popularity

d. Protocol for use of Sulfonylureas

- Pt should not be overweight
- Use less than 40 units insulin daily to control

e. Should not take alcohol with these medications

- palpitations
- flushing

Sulfonylureas 1st Generation

Tolinase	Tolazamide	

Sulfonylureas 2nd Generation

Amaryl	glimepiride	
Diabeta, Glynase, Pres-Tab, Micronase	glyburide	
Glucotrol, Glucotrol XL	glipizide	
Diamicron	gliclazide	Not available in US

Classification: Biguanides

Biguanides reduce hepatic glucose output and increase uptake of glucose

Fortamet, Glucophage, Glucopahge XR, Glumetza, Riomet	metformin	

- metformin (Glucophage). Metformin may be the best choice for patients who also have heart failure.

  Most common drug used today

Classification: Meglitinides

Meglitinides help the pancreas produce insulin They are taken with meals to boost the insulin response to each meal.

Prandin	repaglinide	
Starlix	nateglinide	

Classification: Thiazolidinediones

Thiazolidinediones allow greater insulin sensitivity at cell receptor sites thus better use of glucose by the cells.

Actos	pioglitazone		
Avandia	rosiglitazone		

Classification - Alpha-Glucoside Inhibitors

Alpha-glucosidase inhibitors slow the digestion of starch in the small intestine, so that glucose from the starch of a meal enters the bloodstream more slowly, and can be matched more effectively by an impaired insulin response or sensitivity.

Glyset	miglitol	
Precose	acarbose	

Classification - Glucagon-like peptide analogs

The first glucagon-like peptide analogs allows increase in production of insulin from the beta cells of the pancreas.

Byetta	exenatide	

Classification - Dipeptidyl Peptidase 4 Inhibitors

Pramlintide is an injectable medicine for adults with Type 1 and Type 2 diabetes to control blood sugar. It slows down the movement of food through your stomach. This affects how fast sugar enters your blood after eating.

Symlin	pramlintide		

Drug Combinations

Actoplus Met	metformin and pioglitazone	
Avandamet	metformin and rosglitazone	
Avandaryl	glimepiride and rosglitazone	
Duetact	glimepiride and pioglitazone	
Glucovance	glyburide and metformin	
Janumet	metformin and sitagliptin	
Metaglip	glipizide and metformin	
Prandimet	metformin and repaglinide	

End of Lecture 2 - About Diabetes

Lecture 2 - About Diabetes Worksheet

True or False

_____ 1. One of the clinical signs of either type of Diabetes would be lots of energy

_____ 2. Glucophage is the most common drug used today for Type I Diabetes

_____ 3. Urine tests are more advantageous than glucose monitors in that they can look for Ketones

_____ 4. Glargine has the maximum duration of action of 48 hours

_____ 5. Dosage adjustments are not necessary when changing from one type of insulin to another type

_____ 6. An example of a 1st Generation Sulfonylurea would be Micronase

_____ 7. Ingestion of food causes an increase of blood glucose

_____ 8. In some cases, Insulin is not required for Type I diabetes

_____ 9. Glucose allows the transfer of insulin across cell membranes

_____ 10. Diabetic Lipohypertrophy can lead to blindness

_____ 11. People with pre-diabetes have impaired fasting glucose (IFG) or impaired glucose tolerance (IGT) or both.

_____ 12. Home Blood Glucose monitoring is by far the best method of getting an accurate blood glucose level

Answers may be submitted online at the following URL

https://form.jotform.com/241495235881160