Diabetes Overview –The Nitty Gritty

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www.DiabetesEd.net

Course Objectives

1. Discuss the current epidemiologic impact of diabetes.
2. Describe the pathway of pathophysiological defects associated with the development of diabetes mellitus.
3. Describe and differentiate between the different types: prediabetes, Type 1, Type 2, LADA and GDM
4. Describe the laboratory tests used for the diagnosis of Diabetes Mellitus including FBG, OGTT, hemoglobin, A1C and antibody testing
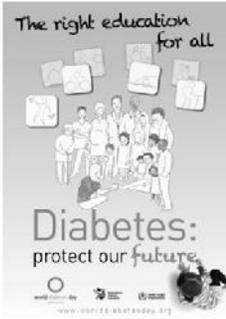

Global Epidemic

▸ Every 10 seconds
 ▸ 1 person dies with diabetes
 ▸ 2 people develop diabetes
▸ Every year
 ▸ 3 million deaths
 ▸ 6 million new cases
▸ World Diabetes Day is November 14
▸ March is ADA Sound the Alert Day "find people w/ undetected diabetes"

World Diabetes Day
November 14

The right education for all

Diabetes: protect our future

The right environment for all

Diabetes: protect our future

IDF.Org

Off to the right start

Healthy Living and Diabetes is the World Diabetes Day theme for 2014-2016. This year's activities and materials focus on the importance of starting the day with a healthy breakfast.

Read more

CDC Announces

35% of Americans will have Diabetes by 2050

Boyle, Thompson, Barker, Williamson
2010, Oct 22:8(1)29
www.pophealthmetrics.com

Diabetes in America 2014

- 29 million or > 9.3%
- 27% don't know they have it
- 37% of US adults have pre diabetes (79 mil)

Diabetes

| 1994 | 2000 | 2009 |

No Data ☐ <4.5% ☐ 4.5-5.9% ☐ 6.0-7.4% ☐ 7.5-8.9% ☐ ≥9.0% ☐

CDC's Division of Diabetes Translation. National Diabetes Surveillance System available at http://www.cdc.gov/diabetes/statistics

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Age-adjusted Diabetes Prevalence

20 yrs or older, by race/ethnicity— U.S. 20014

Age-adjusted* percentage of people aged 20 years or older with diagnosed diabetes, by race/ethnicity, United States, 2010–2012

Non-Hispanic whites	7.6
Asian Americans	9.0
Hispanics	12.8
Non-Hispanic blacks	13.2
American Indians/Alaska Natives	15.9

*Based on the 2000 U.S. standard population.
Source: 2010–2012 National Health Interview Survey and 2012 Indian Health Service's National Patient Information Reporting System.

- Among Hispanic adults, the age-adjusted rate of diagnosed diabetes was 8.5% for Central and South Americans, 9.3% for Cubans, 13.9% for Mexican Americans, and 14.8% for Puerto Ricans.
- Among Asian American adults, the age-adjusted rate of diagnosed diabetes was 4.4% for Chinese, 11.3% for Filipinos, 13.0% for Asian Indians, and 8.8% for other Asians.
- Among American Indian and Alaska Native adults, the age-adjusted rate of diagnosed diabetes varied by region from 6.0% among Alaska Natives to 24.1% among American Indians in southern Arizona.

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Obesity and Economics in America

- 68% overweight or obese
  - 34% BMI 30 +, 34% BMI 25-29
- 1/3 of all overwt people don't get diabetes
- We burn 100 cals less a day at work
- Overall, food costs ~ 10-15% of income
- Calorie Intake is on the rise

Average Daily Per Capita Calories Adjusted for Waste. Source: Economic Research Service of the United States Department ...

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Human Proinsulin Molecule

- Beta – insulin - 60%
- Alpha – glucagon 30%
- Delta –somatostatin 10%

1 Surgeons remove the pancreas from a human cadaver.

Insulin Secretion by the β-Cell
Roles of Glucose, K+, and Ca^{2+}

Glucose entry

GLUT2 glucose transporter

Glucokinase

Glucose metabolism

ADP/ATP

Insulin secretion

Insulin secretory granules

Ca^{2+}

Ca^{2+}

Ca^{2+}

Ca^{2+}

Ca^{2+}

K+

K+ K+

ADP/ATP

SUR 1 Kir 6.2

Calcium channel opens

Potassium (K$_{ATP}$) channel closes

K+

Sulfonylureas close K+ channels

Insulin Action in Muscle and Fat Cells
Mobilization of GLUT4 to the Cell Surface

Plasma membrane

Insulin receptor – tyrosine kinase

Intracellular signaling cascades - phosphorylation

Intracellular GLUT4 vesicles

Insulin

GLUT4 vesicle mobilization to plasma membrane

GLUT4 vesicle integration into plasma membrane

Glucose entry into cell via GLUT4

GLUT4=glucose transporter 4

Insulin (blue) binding with insulin receptors (yellow)

Insulin binding activates tyrosine kinase > phosphorylation cascade > downstream signaling molecules > translocation of Glut 4 to cell membrane > activation of glycogen synthesis   (tk -high affinity cell surface receptors)

Pancreas – Hormones that lower BG

Beta Cells - Insulin

- Anabolic hormone - helps store glucose as glycogen in muscle, liver
  ‣ secreted in response to elevated glucose
  ‣ halts breakdown of glycogen in liver
  ‣ increases protein synthesis, fat storage
  ‣ powerful hypoglycemic

Beta Cells - Amylin

- secreted in 1:1 ratio with insulin
- Causes satiety
- Lowers post-prandial glucagon response
- Slows gastric emptying
- Type 1 make none
- Type 2 make less than normal amounts

Pancreas – Hormone Raises BG
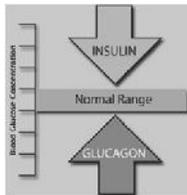
Alpha cells - Glucagon

Opposes action of insulin at the liver

- stimulated in response to low glucose levels
- stimulates liver to convert glycogen to glucose
- inhibits liver from glucose uptake
- causes hyperglycemia

Hormones Effect on Glucose

Hormone	Effect
Glucagon (pancreas)	↑
Stress hormones (kidney)	↑
Epinephrine (kidney)	↑
Insulin (pancreas)	↓
Amylin (pancreas)	↓
Gut hormones - incretins (GLP-1) released by L cells of intestinal mucosa, beta cell has receptors)	↓

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Signs of Diabetes

Polyuria	➡ Glycosuria, H_2O losses
Polydipsia	➡ Dehydration
Polyphasia	➡ Fuel Depletion
Weight loss	➡ Loss of body tissue, H_2O
Fatigue	➡ Poor energy utilization
Skin and other infections	➡ Hyperglycemia increases incidence of infection
Blurry vision	➡ Osmotic changes

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Natural History of Diabetes

Normal
FBG <100
Random <140
A1c <5.7%

Yes!

Prediabetes
FBG 100-125
Random 140 - 199
A1c ~ 5.7- 6.4%
50% working pancreas

NO

Diabetes
FBG 126 +
Random 200 +
A1c 6.5% or +
20% working pancreas

Development of type 2 diabetes happens over years or decades
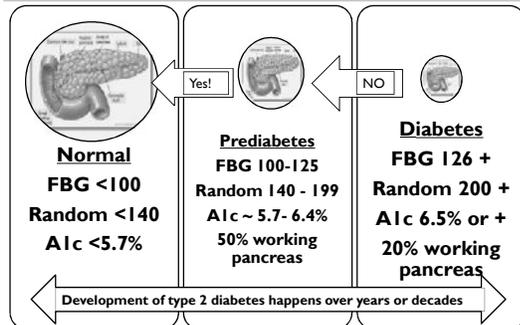
Diagnostic Criteria

▸ All test should be repeated in the absence of unequivocal hyperglycemia

▸ If test abnormal, repeat same test to confirm diagnosis on a different day

▸ If one test normal, the other abnormal, repeat the abnormal test to determine status

▸ Medicare still using fasting as criteria for reimbursement for education

What Kind of Diabetes?

AJ, a 22 year old female admitted to the ICU with a blood glucose of 476 mg/dl and a pH of 7.1.

▸ What further questions and or testing to determine if patient type 1 or type 2 diabetes?

▸ What other tests/ screenings?

Type 1 Diabetes

Type 1 Diabetes Facts

- As many as **3 million Americans** may have type 1 diabetes.
- Each year, approximately **80 people per day** are diagnosed with type 1 diabetes in the U.S.
- Approximately **85 percent** of people living with type 1 diabetes are adults, and **15 percent** are children.
- The rate of type 1 diabetes incidence among children under age 14 is estimated to **increase by 3 percent annually** worldwide.
- Type 1 diabetes accounts for **$14.9 billion** in healthcare costs in the U.S. each year.

Source: JDRF

Type 1 Rates Increasing Globally

- 23% rise in type 1 diabetes incidence from 2001-2009
- Why?
  - Autoimmune disease rates increasing over all
  - Changes in environmental exposure and gut bacteria?
  - Hygiene hypothesis
  - Obesity?

Incidence of Type 1 in Youth

- **General Pop 0.3%**
- **Sibling 4%**
- **Mother 2-3%**
- **Father 6-8%**
- Rate doubling every 20 yrs
- Many trials underway to detect and prevent (Trial Net)

Type 1 – 10% of all Diabetes Genetics and Risk Factors

➢ Auto-immune pancreatic beta cells destruction
➢ Most commonly expressed at age 10-14
➢ Insulin sensitive (require 0.5 - 1.0 units/kg/day)

- Combo of genes and environment:
  - Autoimmunity tends to run in families
  - Higher rates in non breastfed infants
  - Viral triggers: congenital rubella, coxsackie virus B, cytomegalovirus, adenovirus and mumps.

Type 1 Diabetes – Genetics and Risk Factors

▸ Combo of genes and disease susceptibility
▸ Risk Factors:
  ▸ Autoimmunity tends to run in families
  ▸ Higher rates in non breastfed infant
  ▸ Viral triggers: congenital rubella, coxsackie virus B, cytomegalovirus, adenovirus and mumps.
▸ Living longer (avg age expectancy 68.5)

How do we know someone has Type 1 vs Type 2?

▸ Type 1
  ▸ Positive antibodies
    ▸ GAD
    ▸ ICA
    ▸ IAA and others
▸ Younger people develop quickly
▸ Older people take longer to develop
▸ Body wt and presentation

Autoantibodies Assoc w/ Type 1

Panel of autoantibodies –
- GAD65 - Glutamic acid decarboxylase –
- ICA - Islet Cell Cytoplasmic Autoantibodies
- IAA - Insulin Autoantibodies

Diabetes Education

Type 1 Diabetes Associated with other immune conditions

- Celiac disease (gluten intolerance)
- Thyroid disease
- Addison's Disease
- Rheumatoid arthritis
- Other

Diabetes Education

What Does Type 1 Look Like?

Bret Michaels

Halle Berry

Sharon Stone

Mary Tyler Moore

From Debbie Nagata's slide collection

Adam Morrison

Nick Jonas

Justice Sonia Sotomayor

Diabetes Education

What Kind of Diabetes?

AJ, a 22 year old female admitted to the ICU with a blood glucose of 476 mg/dl and a pH of 7.1.

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‣ What other tests/ screenings?

Diabetes Lab Evaluation - ADA

Test	Frequency
‣ A1c	Dx and 2-4 x's a yr
‣ Fasting lipid profile	Dx and Annually
‣ Microalbuminuria	Dx and annually
‣ Creatinine / GFR	Dx and Annually
‣ Thyroid Stimulating Hormone	Dx and Annually
(type 1 over 50, hyperlipidemia, women >50)	
‣ Screen for Celiac Disease	Type 1 Dx, repeat prn
‣ Liver function test	Annually

ADA Clinical Practice Recommendations

Comprehensive Diabetes Evaluation – Referrals - ADA

‣ Annual dilated eye exam

‣ Family planning women of reproductive age

‣ Registered Dietitian for MNT

‣ Diabetes Self-Mgmt Program

‣ Dental exam

‣ Mental Health Professional, if needed

ADA Clinical Practice Recommendations

Type 1 in Hospital

- 43 yr old admitted to evaluate angina.
- Morning blood sugar is 92.
- Based on Regular insulin sliding scale, no insulin required.
- Breakfast tray shows up and patient says, I need my insulin shot before I eat.

  What do you say?

Type 1 Summary

- Autoimmune pancreatic destruction
- Need insulin replacement therapy
- Often first present in DKA
- At risk for other autoimmune diseases

What kind of Diabetes?

- Pt is 58, states she has had type 1 diabetes for 18 years. Quit smoking a year ago and gained about 20 lbs. BMI 25.
- Meds
  - Humalog 18-23 units before each meal
  - Lantus 28 units at bedtime
  - Metformin 500mg TID
- What tests would you recommend?
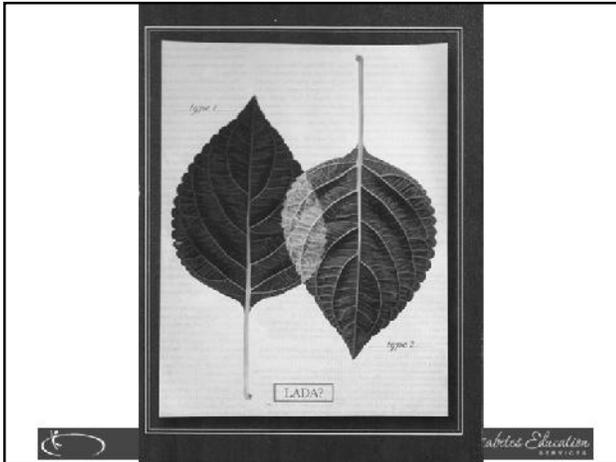
What type of Diabetes?

‣ 72 Years old
‣ A1c 3 months prior 6.2%
‣ A1c now 13.9%
‣ BMI 24.5
‣ Lost about 10 pounds over last month

Latent AutoImmunity Diabetes in Adults (LADA)

‣ Antibody positive to 1-2 of below
  ‣ GAD-65 autoantibodies
  ‣ Insulin Autoantibodies
  ‣ Islet Cell antigen-2
‣ Adult Age at onset
‣ Usually need insulin w/in first 6 months of diagnosis
‣ Early insulin therapy may preserve beta cell function

Diabetes Care 26:536-538, 2003
Jerry P. Palmer, MD and Irl B. Hirsch, MD

LADA Clinical Features Compared to Type 2

Feature	LADA	Type 2
▸ Age <50	63%	19%
▸ Acute hyperglycemia	66	24
▸ BMI < 25	33	13
▸ Hx of autoimmune dx	27	12
▸ Family hx autoimmune	46	35

Practical Diabetology March 08, Unger MD

Life Study – Mrs. Jones

Mrs. Jones is 62 years old, overweight and complaining of feeling tired and urinating several times a night. She is admitted with a urinary tract Infection. Her WBC is 12.3, glucose 237. She is hypertensive with a history of gestational diabetes. No ketones in urine.

▸ What are her risk factors, signs of diabetes
▸ What type of diabetes does she have?
▸ Does she have insulin resistance?

Patti Labelle "divabetic" -- that's a mix of diabetic and diva

BMI – Visual Image

BMI 17.5 / BMI 18.5 / BMI 22.0 / BMI 24.9 / BMI 30 / BMI 40
Underweight — **Normal** — **Overweight**
← Anorexia / Lowest Normal / Middle Normal / Highest Normal / Obesity / Morbid Obesity →
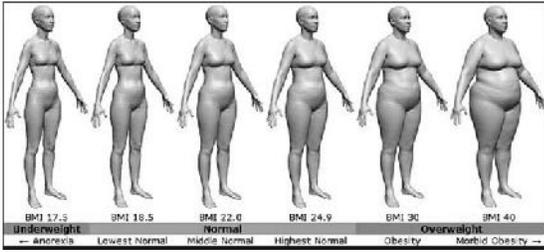
Diabetes 2 - Who is at Risk?
(ADA Clinical Practice Guidelines)

1. Testing should be considered in all adults who are overweight (BMI ≥ 25) and have additional **risk factors**:

   ‣ First-degree relative w/ diabetes
   ‣ Member of a high-risk ethnic population
   ‣ Habitual physical inactivity
   ‣ PreDiabetes
   ‣ History of heart disease

Diabetes 2 - Who is at Risk?
(ADA Clinical Practice Guidelines)

Risk factors cont'd

‣ HTN - BP > 140/90
‣ HDL < 35 or triglycerides > 250
‣ baby >9 lb or history of Gestational Diabetes Mellitus (GDM
‣ Polycystic ovary syndrome (PCOS)
‣ Other conditions assoc w/ insulin resistance:
   ‣ Severe obesity, acanthosis nigricans (AN)

Acanthosis Nigricans

Acanthosis Nigricans (AN)

‣ Signals high insulin levels in bloodstream
‣ Patches of darkened skin over parts of body that bend or rub against each other
  ‣ Neck, underarm, waistline, groin, knuckles, elbows, toes
  ‣ Skin tags on neck and darkened areas around eyes, nose and cheeks.
‣ No cure, lesions regress with treatment of insulin resistance

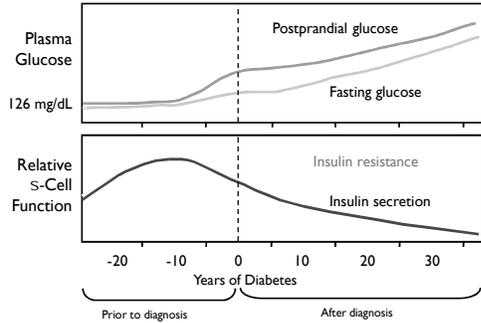---

What is Type 2 Diabetes?

‣ Complex metabolic disorder ….
  (Insulin resistance and deficiency)

with social, behavioral and environmental risk factors unmasking the effects of genetic susceptibility.

New Diagnosis?
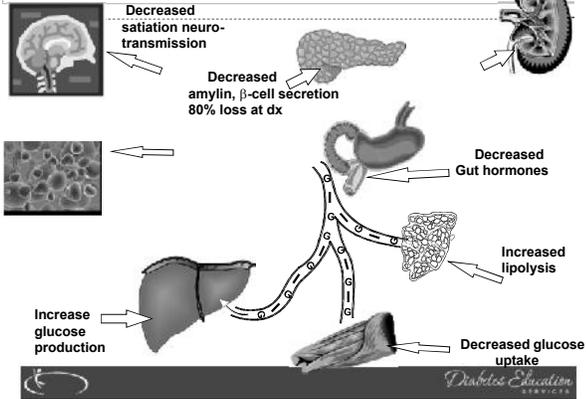Call 800 – DIABETES to request "Getting Started Kit"
www.Diabetes.org

Natural Progression of Type 2 Diabetes

Plasma Glucose

Postprandial glucose

126 mg/dL

Fasting glucose

Relative ß-Cell Function

Insulin resistance

Insulin secretion

-20 -10 0 10 20 30

Years of Diabetes

Prior to diagnosis

After diagnosis

Adapted from Bergenstal et al. 2000; International Diabetes Center.

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Ominous Octet

Decreased satiation neuro-transmission

Decreased amylin, β-cell secretion 80% loss at dx

Decreased Gut hormones

Increased lipolysis

Increase glucose production

Decreased glucose uptake

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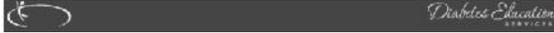
What Do You Say?
Mrs. Jones asks you

‣ What is type 2 diabetes?
‣ Will this go away?
‣ Will I get complications?
‣ Will I need to take diabetes medication for the rest of my life?
‣ How come I got diabetes?
‣ Do I have to check my blood sugars?

Diabetes Education SERVICES

Overcoming barriers

- Confront the key misbelief. Ask the question, does dm cause complications?
- Offer pts evidence based hope message –
- Frequent contact
- Paired glucose testing

- Ask pt, "Tell me 1 thing that is driving you crazy about your diabetes"
- Discuss medication beliefs
- To improve outcomes, see pts more often

Bill Polonsky, PhD, CDE

Comparison of Type 1, Type 2, LADA

	Type 1	Type 2	LADA
Obesity	x	xxx	x
Insulin dependence	xxx	30%	6mos
Respond to oral agents	0	xxx	x
Ketosis	xxx	x	x
Antibodies present	xxx	0	xx
Typical Age of onset	teens	adult	adult
Insulin Resistance	0	xxx	x

Diabetes is also associated with

- Fatty liver disease
- Obstructive sleep apnea
- Cancer; pancreas, liver, breast
- Alzheimer's
- Depression

Other Types of Diabetes

‣ Gestational
‣ Other specific types of diabetes

Gestational DM ~ 7% of all Pregnancies

‣ GDM prevalence increased by
  ‣ ~10–100% during the past 20 yrs
‣ Native Americans, Asians, Hispanics, African-American women at highest risk
‣ Immediately after pregnancy, 5% to 10% of GDM diagnosed with type 2 diabetes
‣ Within 5 years, 50% chance of developing DM in next 5 years.

Increasing Prevalence –
A public health perspective

‣ Body weight before and during pregnancy influences risk of GDM and future diabetes
‣ Children born to women with GDM at greater risk of diabetes
‣ Focus on prevention

Diabetes in pregnant mothers associated with …

- Offspring
  - Fetal Complications
  - Obesity and diabetes later in life
- Mother
  - More complicated pregnancy and delivery
  - Diabetes later in life

- Intrauterine environment is important

Screen Pregnant Women Before 13 weeks

- Screen for undiagnosed Type 2 at the first prenatal visit using standard risk factors.
- Women found to have diabetes at their initial prenatal visit treated as "Diabetes in Pregnancy"
- If normal, recheck at 24-28 weeks

Postpartum after GDM

- 50% risk of getting diabetes in 5 years
- Screen at 6-12 wks post partum
- Repeat at 3 yr intervals or signs of DM
  - Encourage Breast Feeding
  - Encourage weight control
  - Encourage exercise
  - Make sure connected with health care
  - Lipid profile/ follow BP
  - Preconception counseling

Start Metformin therapy

‣ For women with PreDiabetes and History of GDM

Other Specific Types of DM

‣ Medications such as: steroids, protease inhibitors and Prograf*
‣ Secondary to Agent Orange
‣ Liver failure
‣ TPN or tube feedings
‣ Pancreatic cancers or removal
‣ Cystic fibrosis, pancreatitis
‣ Other

Regardless of the cause, hyperglycemia needs to be treated.

Key points

- Be a Diabetes Detective
- At the center of pathophysiology of diabetes is someone living with it everyday.
- Diabetes is a lot of work.
- Focus on successes
- Coach and support

out beyond ideas
of wrongdoing
and rightdoing,
there is a field.

i'll meet you there
-rumi

- Rumi, 13th Century Mystic Poet.

People with diabetes often feel judged by others, including providers, family, friends and even sometimes by diabetes educators.

Thank You

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SERVICES

- www.DiabetesEd.net

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