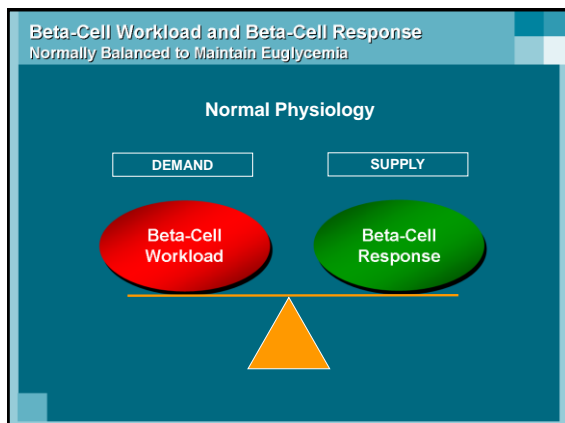


Principles of Basal-Bolus Insulin Therapy and Carbohydrate Counting

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Disclosures

- I do not have any relevant financial relationships with any commercial interests.



Types of Diabetes Mellitus

- The classification of diabetes includes four clinical classes
 - Type 1 diabetes
 - Type 2 diabetes
 - Other specific types of diabetes due to other causes, eg., genetic defects in β -cell function
 - Gestational diabetes mellitus (GDM)

Diagnosis of Diabetes Mellitus

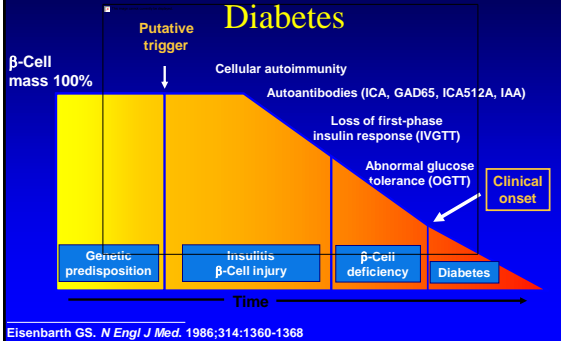
Criteria for Diagnosis

- Symptoms of diabetes and a casual plasma glucose ≥ 200 mg/dl (11.1 mmol/l) (classic symptoms of diabetes include polyuria, polydipsia, and unexplained weight loss) or
- FPG ≥ 126 mg/dl (7.0 mmol/l) (fasting is defined as no caloric intake for at least 8h) or
- 2-h plasma glucose ≥ 200 mg/dl (11.1 mmol/l) during OGTT (75-g glucose load)

Type 1 Diabetes Mellitus

- Absolute deficiency of insulin usually due to autoimmune destruction of the insulin-producing beta cells in the pancreas

Natural History of “Pre”–Type 1 Diabetes



Type 2 Diabetes Mellitus

- A disease characterized by a relative deficiency of insulin production relative to need and by a relative resistance to the action of insulin
- Both genetic and environmental factors contribute to development of this disease

Risk Factors - Type 2 Diabetes

- Age > 45 years
- Overweight (BMI > 25 kg/m²)
- Family history of diabetes
- Habitual physical inactivity
- Certain ethnic groups (African Americans, Latinos, Native Americans, Pacific Islanders)
- Previously identified IFG or IGT
- History of GDM or delivery of infant > 9 lb

Risk Factors - Type 2 Diabetes (continued)

- Hypertension (\geq 140/90 mmHg in adults or on therapy for hypertension)
- HDL cholesterol < 35 mg/dl and/or triglycerides > 250 mg/dl
- Polycystic ovary syndrome
- History of vascular disease

Insulin Resistance: Definitions

Insulin Sensitivity

- Ability of insulin to lower circulating glucose concentrations
 - stimulate glucose utilization: muscle plus fat
 - suppress glucose production: liver

Insulin Resistance

- Condition of low insulin sensitivity

©1998 PDC

Insulin Resistance: Inherited and Acquired Influences

Inherited

Rare mutations

- Insulin receptor
- Glucose transporter
- Signaling proteins

Common forms

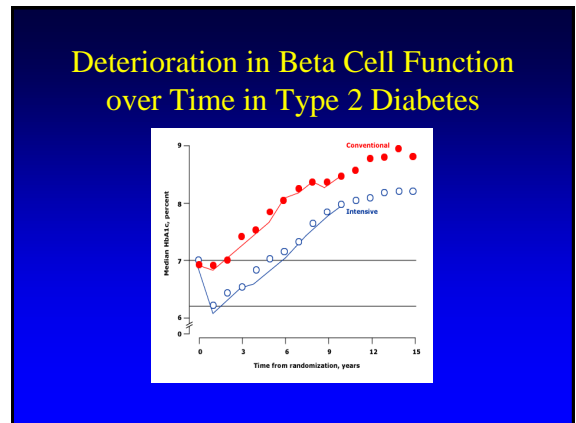
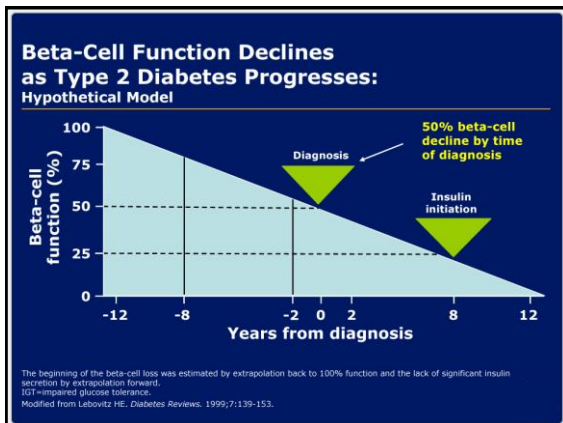
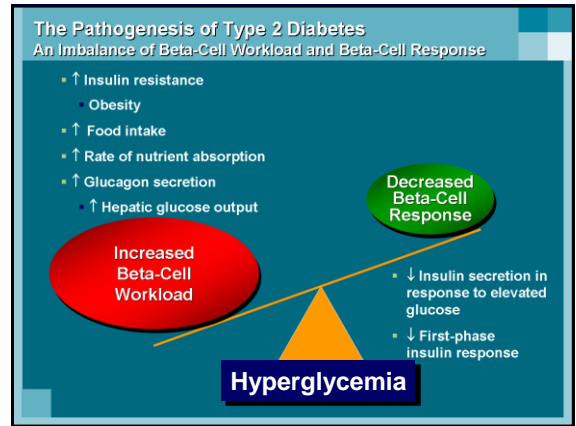
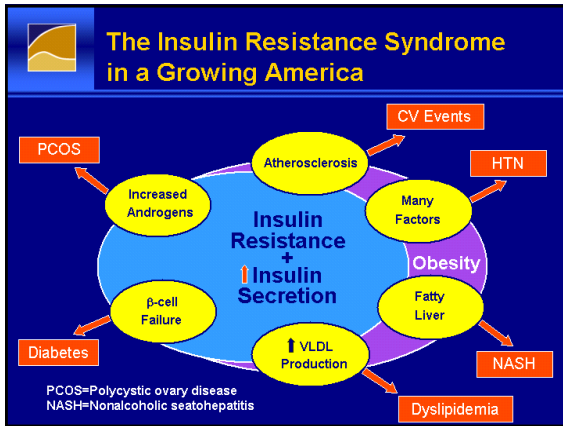
- Largely unidentified

Acquired

- Inactivity
- Overeating
- Aging
- Medications
- Hyperglycemia
- Fatty acids

Insulin Resistance

©1998 PDC



Type 2 Diabetes ... A Progressive Disease

Over time, most patients will need insulin to control glucose

- ## Other Types of Diabetes Mellitus
- Genetic defects in beta-cell function (such as specific MODY types)
 - Endocrinopathies
 - Exocrine pancreas diseases (such as chronic pancreatitis)
 - Drug or chemical induced
 - Other rare forms

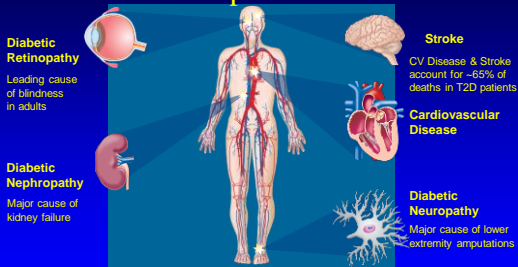
Acute Diabetic Complications

- Hyperglycemia
- Hypoglycemia
- Diabetic ketoacidosis
- Hyperosmotic hyperglycemic nonketotic state

Chronic Complications

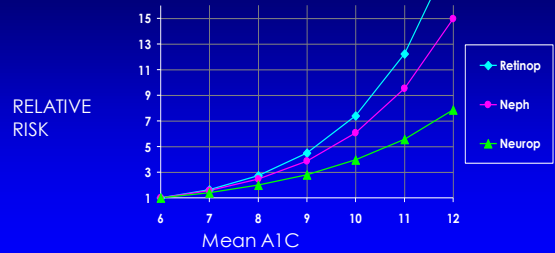
- Microvascular
 - Retinopathy
 - Nephropathy
 - Neuropathy
 - Peripheral
 - Autonomic
 - Other
- Macrovascular
 - Coronary Artery Disease
 - Cerebrovascular Disease
 - Peripheral Vascular Disease

Diabetes is Associated with Serious Complications



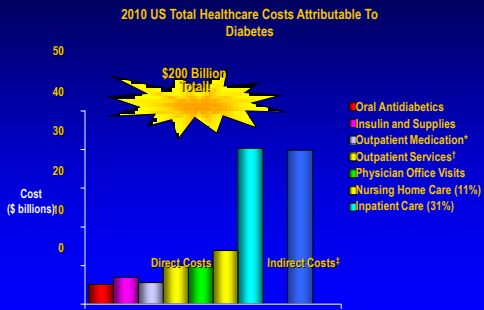
CV = cardiovascular
National Institute of Diabetes and Digestive and Kidney Diseases. National Diabetes Statistics fact sheet: general information and national estimates on diabetes in the United States, 2005. Bethesda, MD: U.S. Department of Health and Human Services, National Institute of Health, 2005.

Relative Risk of Progression of Diabetes Complications (DCCT)



DCCT Research Group, *N Engl J Med* 1993; 329:977-986.

42% Of Diabetes Costs Related To Hospitalization And Long-Term Care



ADA and AACE/ACE Guidelines: Treatment Goals for A1C, FPG, and PPG

Parameter	Normal ^{1,2} Level	ADA ³ Goal	AACE/ACE ² Goal
FPG, mg/dL	<100	90–130	<110
PPG, mg/dL	<140	<180	<140
A1C, %	4–6	<7 ^a	≤6.5

^aThe goal for an individual patient is to achieve an A1C as close to normal (<6%) as possible without significant hypoglycemia.

FPG=fasting plasma glucose; PPG=postprandial glucose; ADA=American Diabetes Association; AACE=American Association of Clinical Endocrinologists; ACE=American College of Endocrinology.
1. Adapted from Buse J et al. In: *Williams Textbook of Endocrinology*, 10th ed, 2003. Permission requested.
2. AACE Diabetes Mellitus Clinical Practice Guidelines Task Force. *Endocr Pract* 2007;13(suppl):13-68.
3. ADA. *Diabetes Care* 2007;30:S4-S41.

Patient Education in Diabetes

ADA National Standards for DSME*

*Diabetes Self-Management Education (DSME)

Should include	May include
DSME team Patient, RN, RD, physician (endocrinologist where possible)	Psychologist, exercise physiologist, ophthalmologist, optometrist, pharmacist, podiatrist, and other health care providers
Written curriculum <ul style="list-style-type: none"> • Insulin administration • Nutritional management • Glucose monitoring 	<ul style="list-style-type: none"> • Diabetes disease process • Physical activity guidance • Other monitoring (urine ketones, etc) • Prevention, detection, and treatment of complications • Goal setting and problem solving • Preconception and prenatal care

Mensing C et al. *Diabetes Care*. 2004;27(suppl 1):S143-S150

Nutrition Plan

ADA Recommendations

	Energy Intake
Saturated fat	<10%
Protein	15%–20%
Carbohydrates and monounsaturated fat	60%–70%
<ul style="list-style-type: none"> – Amount of monounsaturated fat varied according to metabolic needs and weight management goals – Carbohydrates from whole grains, fruit, and vegetables – Total amount of carbohydrate more important than source or type—sugar acceptable in moderation 	

American Diabetes Association. *Diabetes Care*. 2004;27(suppl 1):S36-S46

Treatment of Type 1 Diabetes

- Insulin replacement is essential
- Food intake, insulin, and exercise must be balanced carefully
- No accepted preventive measures (yet)

Treatment of Type 2 Diabetes

- Diet and exercise are the first interventions for prevention or treatment
- Oral medications
- Injectable medications other than insulin
- Insulin

Insulin Therapy in Type 2 Diabetes

Indications

- Significant hyperglycemia at presentation
- Hyperglycemia on maximal doses of oral agents
- Decompensation
 - Acute injury, stress, infection, myocardial ischemia
 - Severe hyperglycemia with ketonemia and/or ketonuria
 - Uncontrolled weight loss
 - Use of diabetogenic medications (eg, corticosteroids)
- Surgery
- Pregnancy

Possible Barriers to the Initiation of Insulin

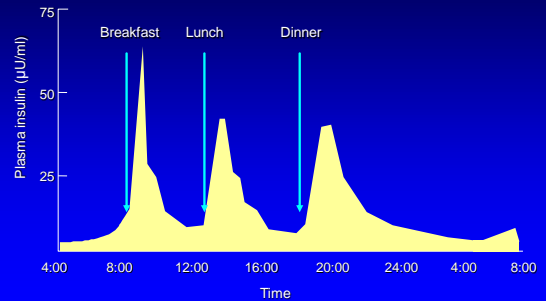


Korytkowski M. *Int J Diab*. 2002;26(suppl 3):S18-S24.
 Lennie AC. *Diab*. 2001;24:1728-1733.
 Snoek FJ. *Int J Clin Pract Suppl*. 2002;129:80-84.

Insulin

- The most powerful tool for controlling blood glucose
- Used in type 1 and type 2 diabetes
- Use of insulin does not mean a patient has type 1 diabetes or that they will never get off insulin

Physiological Serum Insulin Secretion Profile



Different Types of Insulin

- Rapid Acting Analogs
 - Lispro
 - Aspart
 - Glulisine
- Short Acting
 - Regular (R – U100 or U500)
- Intermediate Acting
 - NPH
- Long Acting Analogs
 - Glargine
 - Detemir

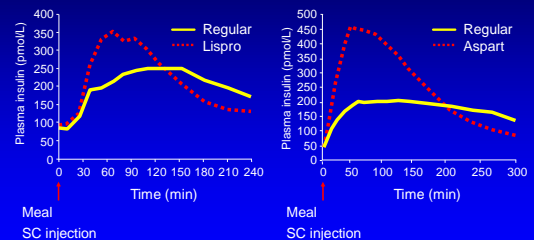
Different Types of Insulin

- Pre-Mixed Insulins
 - 70% NPH & 30% regular
 - 75% lispro protamine & 25% lispro
 - 50% NPH & 50% regular
 - 50% lispro protamine & 50% lispro
 - 70% aspart protamine & 30% aspart

Comparison of Human Insulins / Analogues

Insulin preparations	Onset of action	Peak	Duration of action
Regular	30–60 min	2–4 h	6–10 h
NPH	1–2 h	4–8 h	10–20 h
Lispro/aspart	5–15 min	1–2 h	4–6 h
Glargine	1–2 h	Flat	~24 h

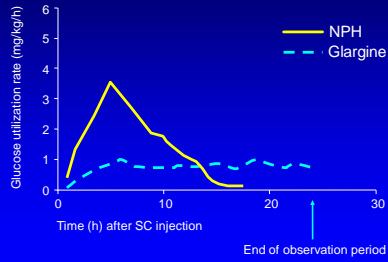
Short-Acting Insulin Analogs Lispro and Aspart Plasma Insulin Profiles



Heinemann, et al. *Diabet Med.* 1996;13:625–629; Mudalier, et al. *Diabetes Care.* 1999;22:1501–1506.

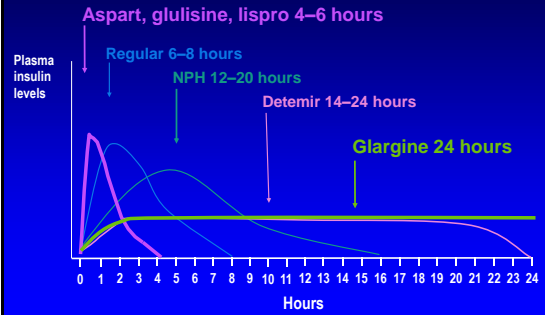
Glargine vs NPH Insulin in Type 1 Diabetes

Action Profiles by Glucose Clamp



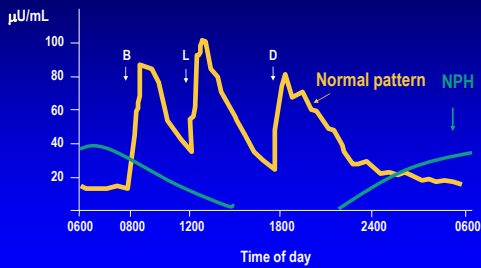
Lepore, et al. *Diabetes*. 1999;48(suppl 1):A97.

Action Profiles of Insulins



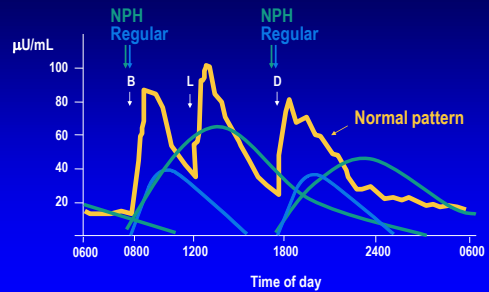
Evening Basal Insulin

Bedtime NPH



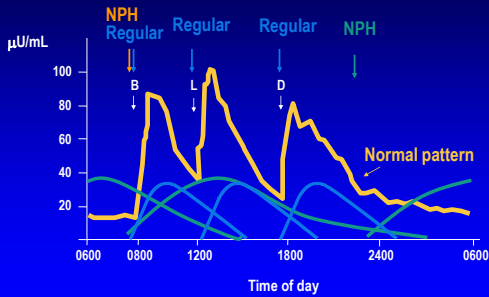
Split-Mixed Regimen

Human Insulins

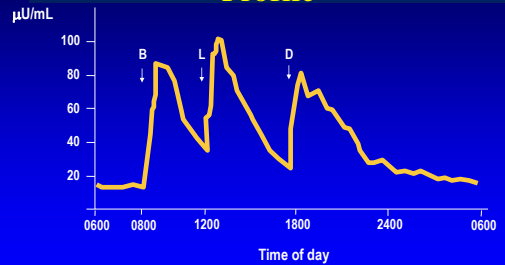


Multiple Daily Injections

Human Insulins



Normal Daily Plasma Insulin Profile



Polonsky KS et al. *N Engl J Med*. 1988;318:1231-1239

The Basal/Bolus Insulin Concept

- Basal insulin
 - Suppresses glucose production between meals and overnight
 - 40% to 50% of daily needs
- Bolus insulin (mealtime)
 - Limits hyperglycemia after meals
 - Immediate rise and sharp peak at 1 hour
 - 10% to 20% of total daily insulin requirement at each meal

Starting Multidose Insulin

- Starting insulin dose is based on weight
 - 0.2 x wgt. in lbs. or 0.45 x wgt. in kg
- Bolus dose (aspart/lispro) = 20% of starting dose at each meal
- Basal dose (glargine/NPH) = 40% of starting dose at bedtime

Key Parameters: Carbohydrate to Insulin Ratio

- Amount of carbohydrate metabolized by one unit of insulin
- Insulin given with meals is based on carbohydrates in the meal (pump can do calculation)
- Estimated at 500/TDD, often about 15:1 for type 1 diabetes patients

Carbohydrate to Insulin Ratio

Total Daily Insulin Dose	500 Rule	450 Rule
	Grams of Carb per Unit of Rapid-acting Insulin	Grams of Carb per Unit of Regular Insulin
20	25	23
25	20	18
30	17	15
35	14	13

Adapted from Pocket Pancreas, © 1994, Diabetes Services, Inc.

Alternative for Estimating the Carbohydrate to Insulin Ratio (CIR)

Individually determined

$$\text{CIR} = (2.8 \times \text{wgt in lbs}) / \text{TDD}$$

Anywhere from 5 to 25 g CHO is covered by 1 unit of insulin

Using Carbohydrate Counting

- To calculate insulin dose for a carbohydrate choice:
 - Divide the total grams of carbs by carb-to-insulin ratio (for example, 15 grams per 1 unit).
 - Example – eight crackers:
 1. Total carbs = 44 g.
 2. 44 divided by 15 = 2.94 (round to 3.0).
 3. Therefore, 8 crackers would require 3 units.

Key Parameters: Correction Factor

- Describes by how much blood sugar is lowered by one unit of insulin
- Used to calculate amount of insulin to reduce an elevated blood sugar to target
- Used to calculate amount of insulin to subtract from a meal dose to raise a low blood sugar to target

Insulin Correction Factor or Sensitivity Factor

Total Daily Insulin Dose	1800 Rule	1500 Rule
	Point Drop per Unit of Rapid-acting Insulin	Point Drop per Unit of Regular Insulin
20	90 mg/dL	75 mg/dL
25	72 mg/dL	60 mg/dL
30	60 mg/dL	50 mg/dL
35	51 mg/dL	43 mg/dL

Adapted from Type 1 Diabetes - a Guide for Children, Adolescents, Young Adults and Their Caregivers; Ragnar Hanas MD, PhD; 2005, Marlowe & Company, NY.

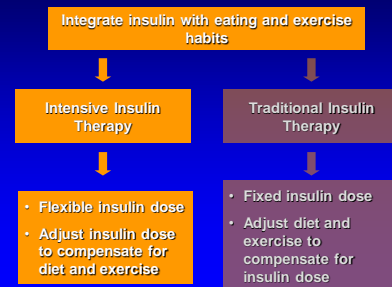
Total Insulin Bolus Administered Equals

Meal insulin dose based on carbohydrate counting

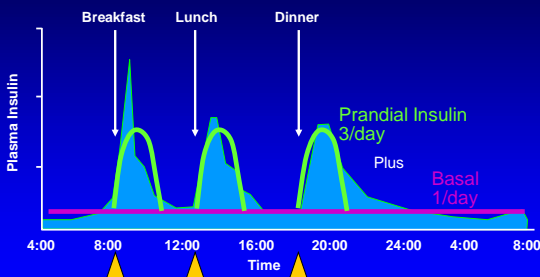
+

Correction dose calculated from blood sugar value and target

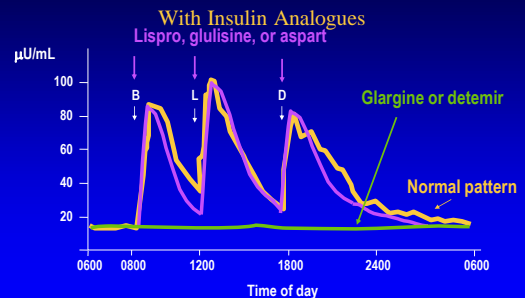
Integrating Insulin Therapy With Lifestyle in Diabetes Mellitus



Mimicking Physiology: Basal and Prandial Insulin



Basal-Bolus Insulin Treatment



B=breakfast; L=lunch; D=dinner

Thank you
and
Happy Nutrition Month

Any questions?