

# DIABETES MELLITUS:

## WHAT IT IS AND WHAT CAN BE DONE ABOUT IT

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# **DIABETES MELLITUS:**

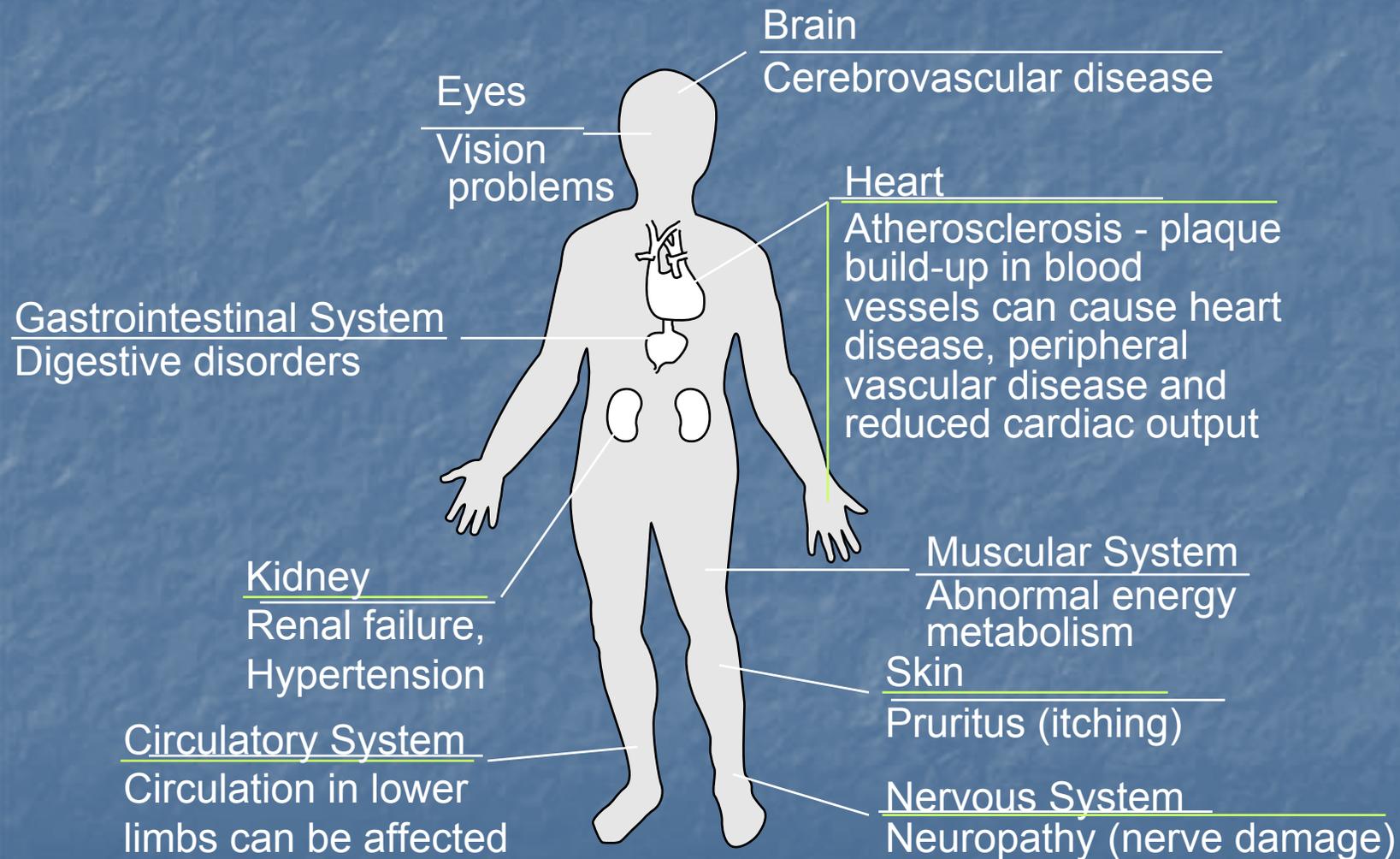
**WHAT IT IS  
(CLINICALLY)**

# DEFINITION

Diabetes mellitus is a disease that is defined by increased blood glucose levels and associated with:

- a) small blood vessel complications involving the eyes, kidneys and nerves;
- b) large blood vessel complications involving the heart, brain and legs.

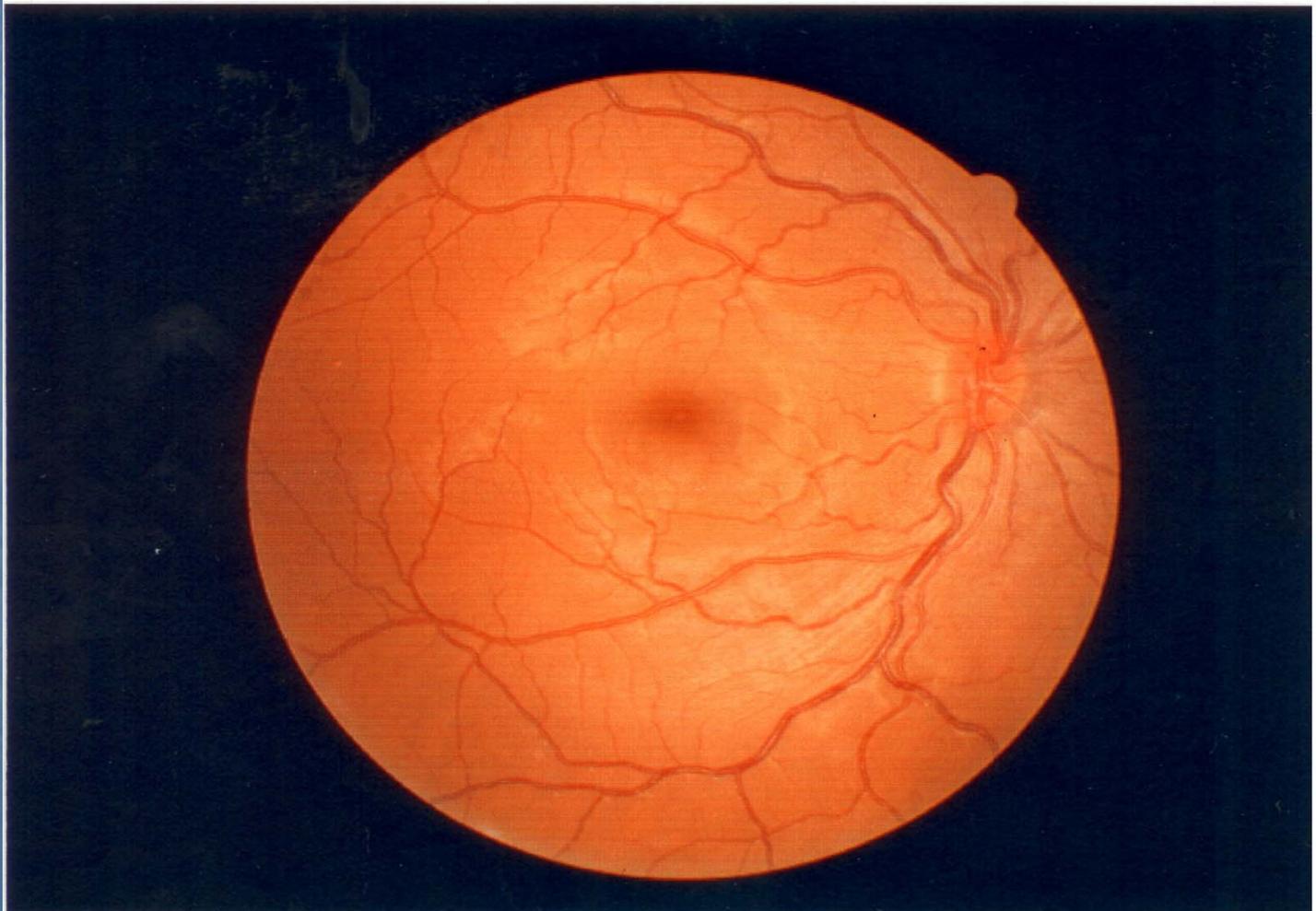
# Possible Complications of Diabetes



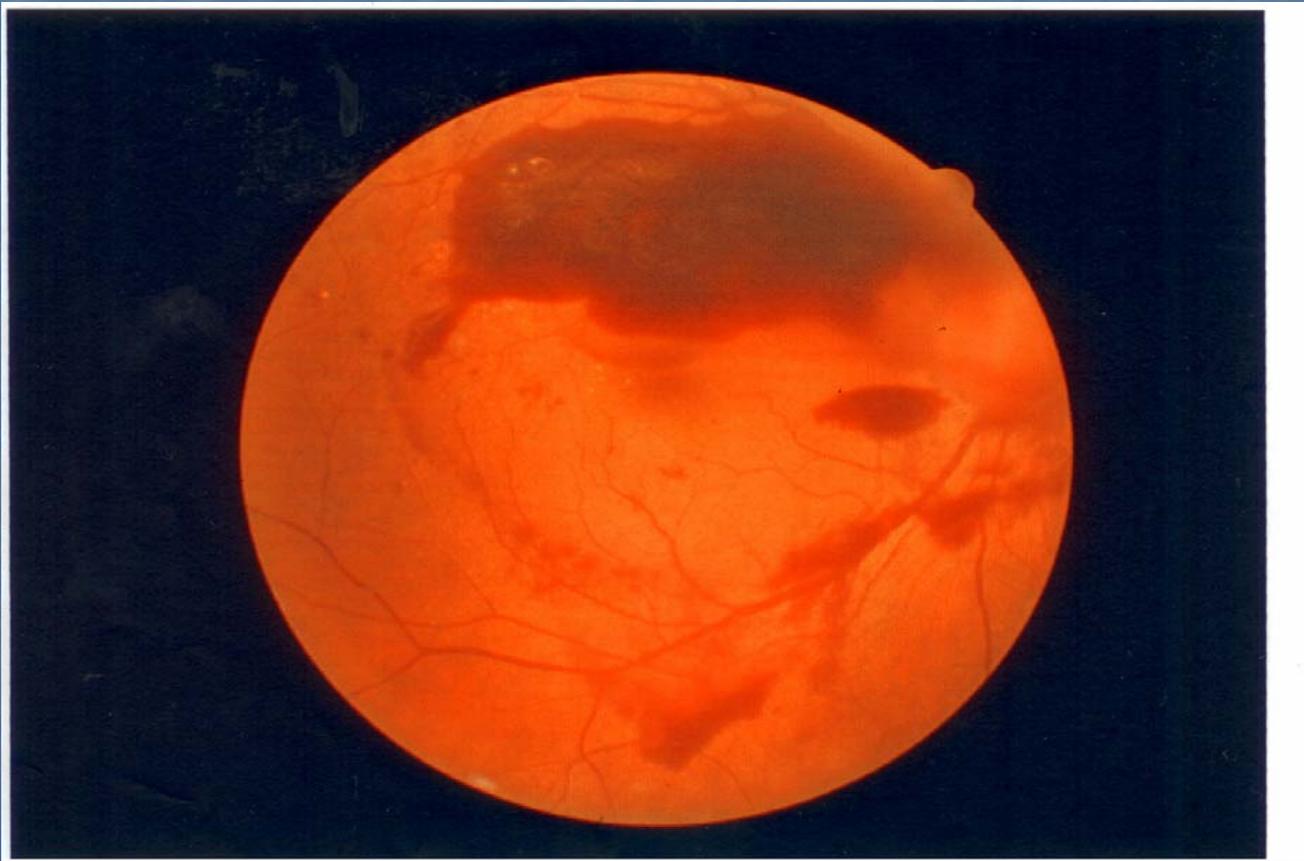
# DIABETIC EYE DISEASE

Leading cause of blindness  
in this country in people  
between the ages of 20 and  
74 years

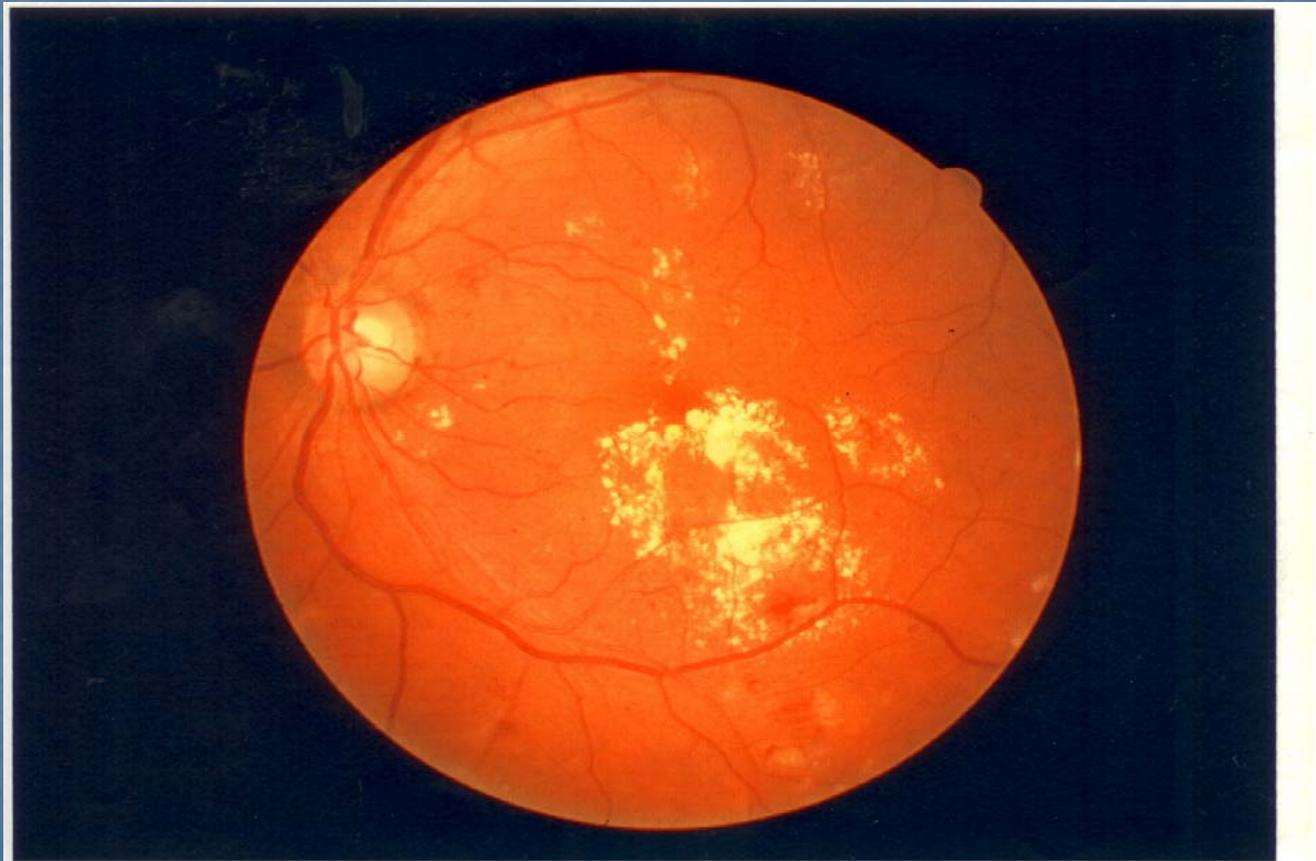
# Normal Retina



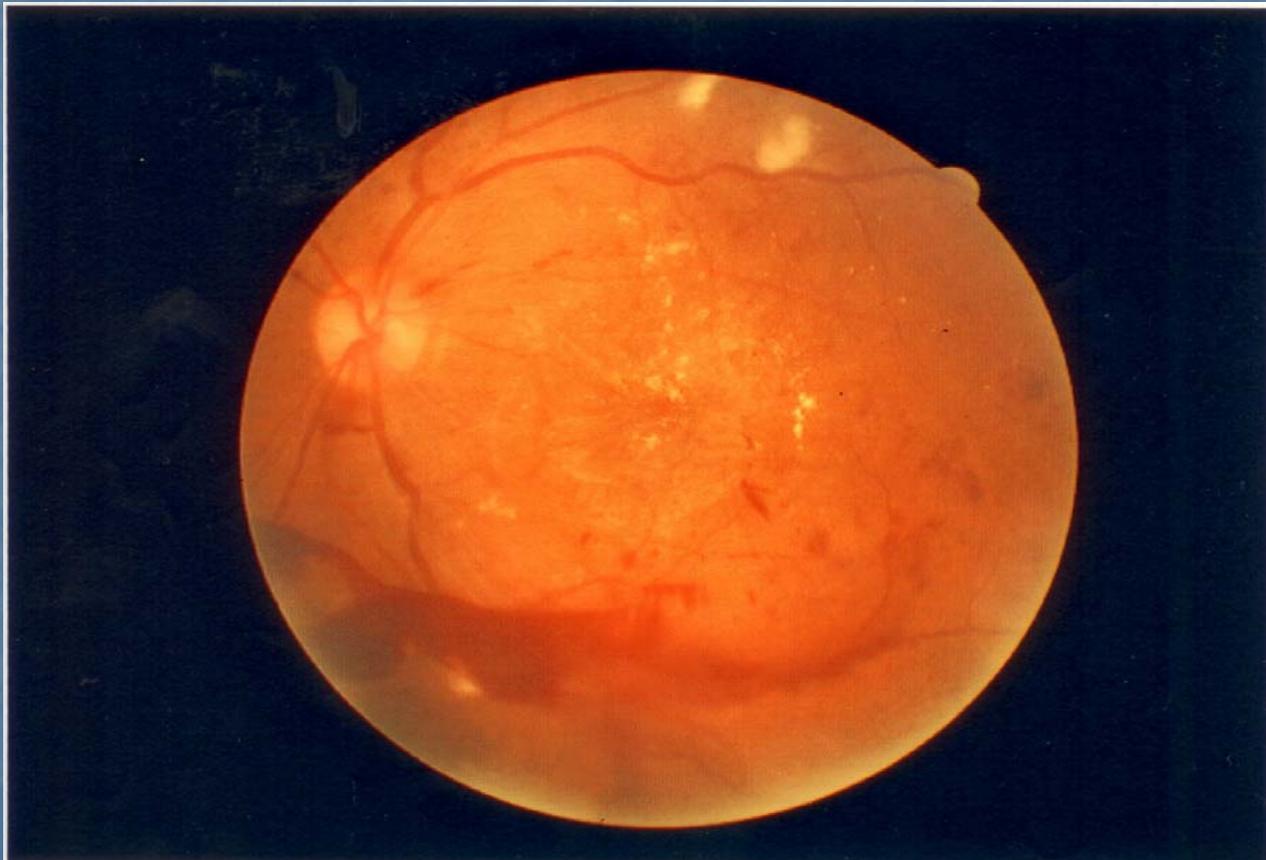
# Hemorrhage



# Macular Edema

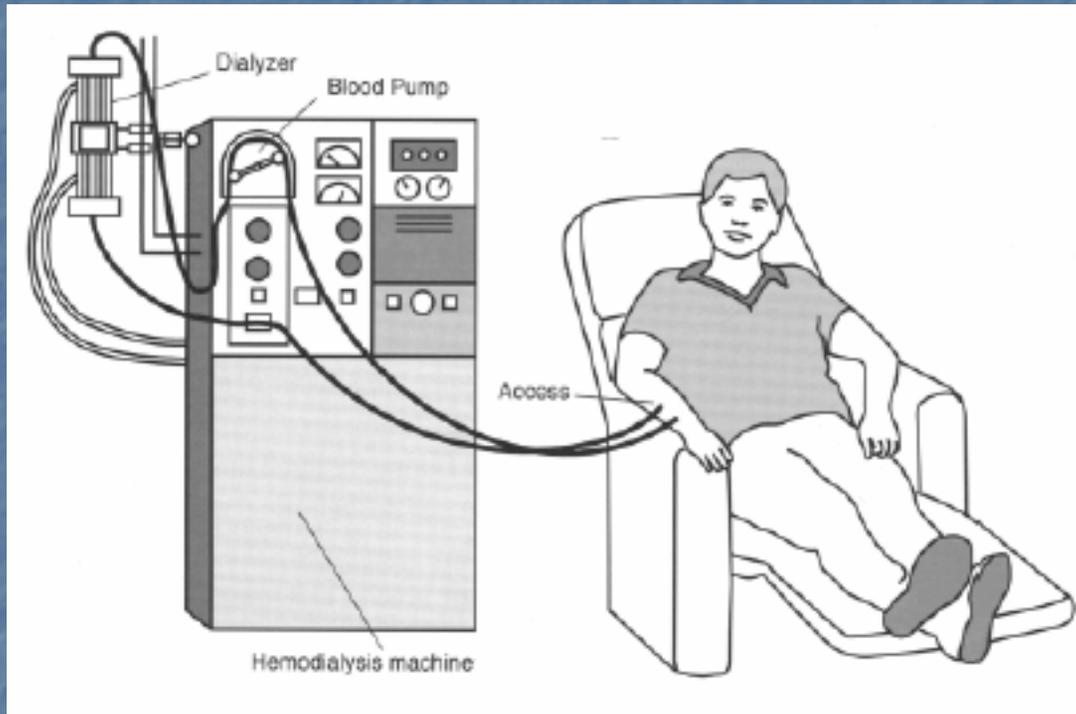


# Hemorrhage & Macular Edema

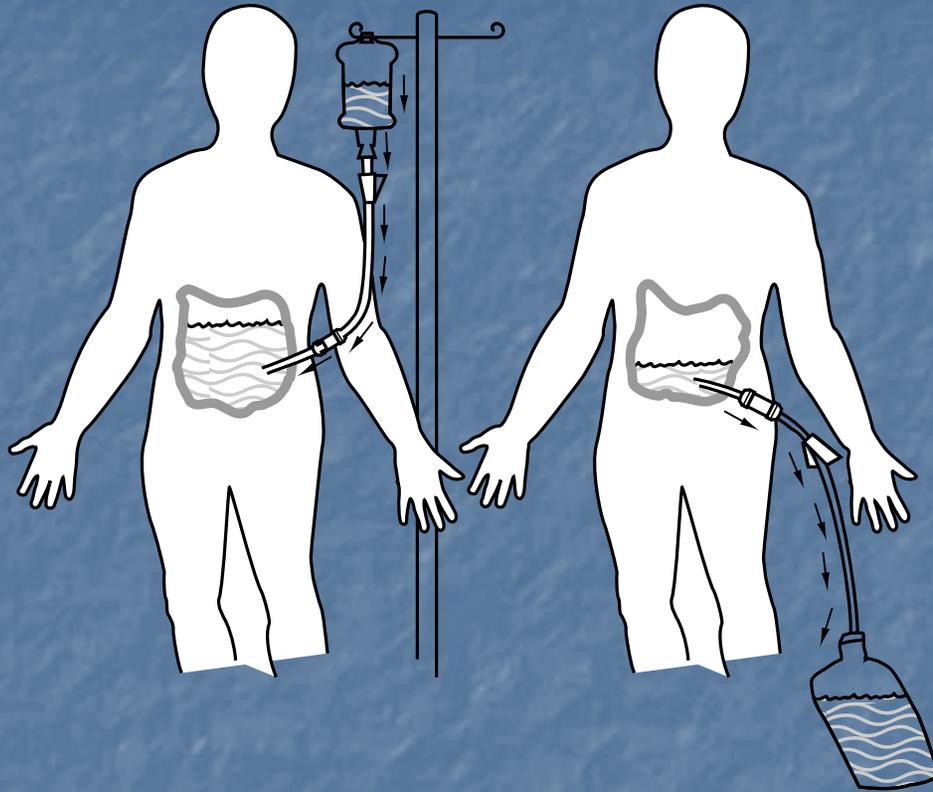


# DIABETIC KIDNEY DISEASE

Although only approximately 7%-8% of our population is known to have diabetes mellitus, almost half of the patients going onto dialysis have kidney failure secondary to diabetes.



# Patient doing PD Exchange



The peritoneal cavity is filled with dialysate, using gravity.

At the end of the exchange, the dialysate is drained into the bag, again using gravity.

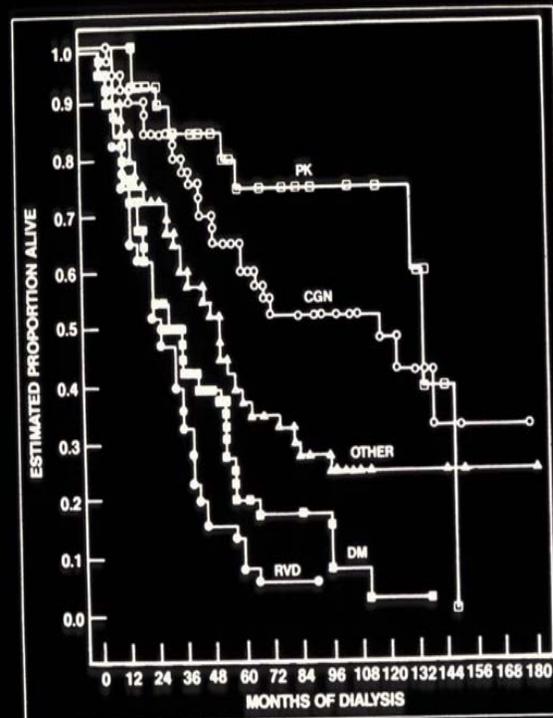


Figure 1. Survival estimates are plotted by renal diagnoses. PK = polycystic kidney disease; CGN = chronic glomerulonephritis; DM = diabetes mellitus; RVD = renal vascular disease; other = all other diagnoses.

Am J of Medicine 84:855-62, 1988

**DIABETIC  
NERVE  
DISEASE**

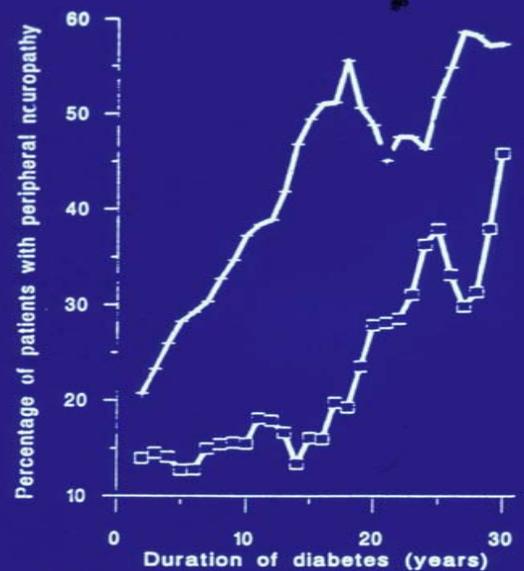
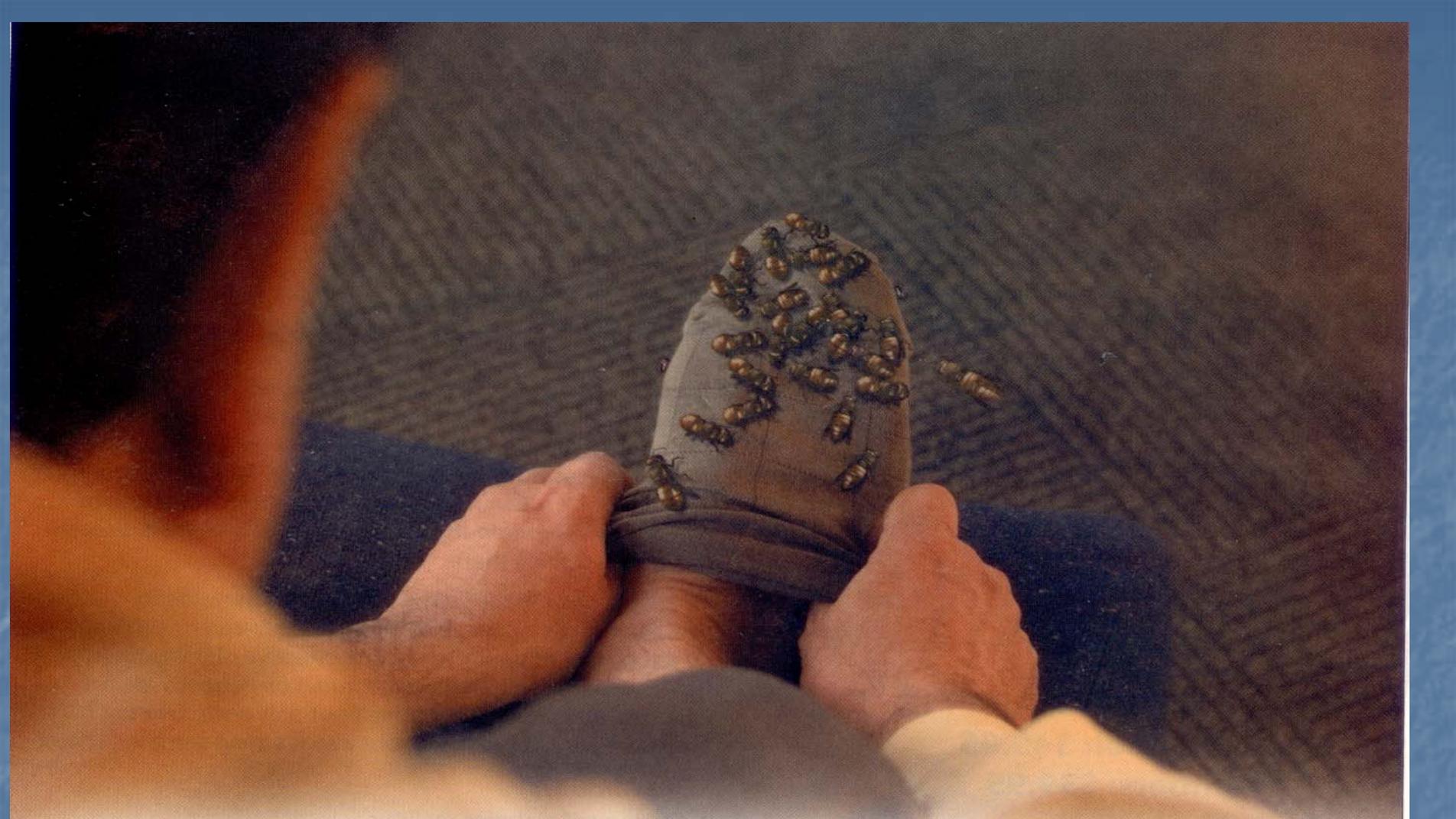


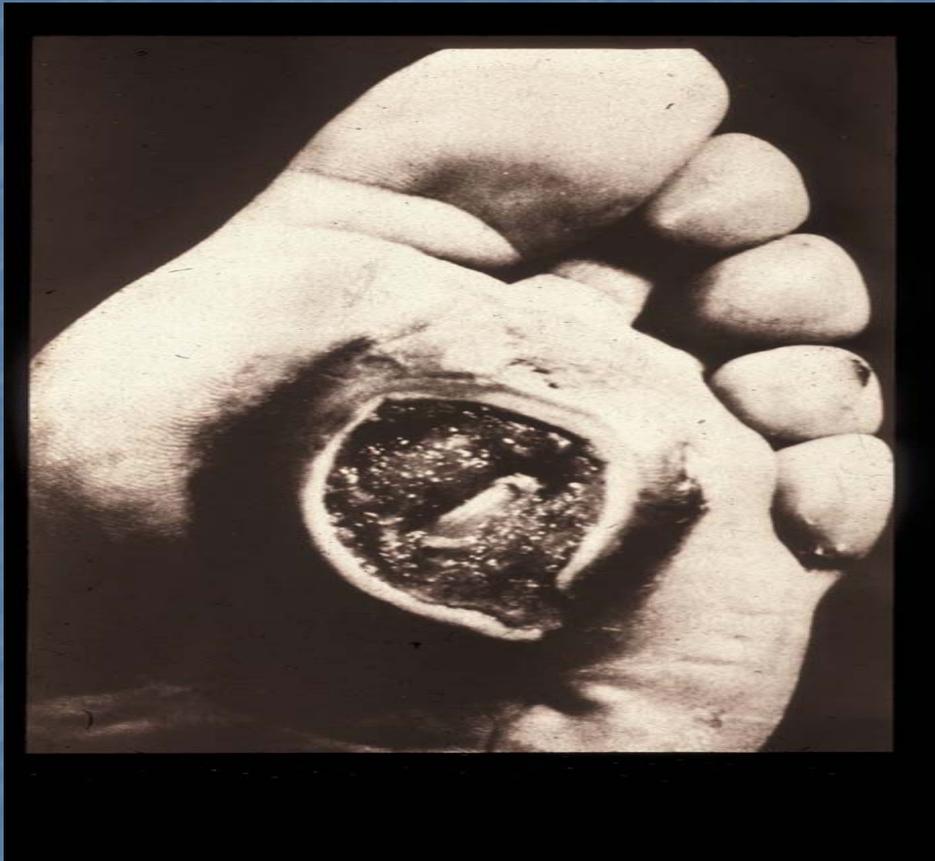
Fig.1. The prevalence of peripheral neuropathy in Type 1 (□) and Type 2 (+) diabetic patients by duration of diabetes

Diabetologia 36:150-154, 1993



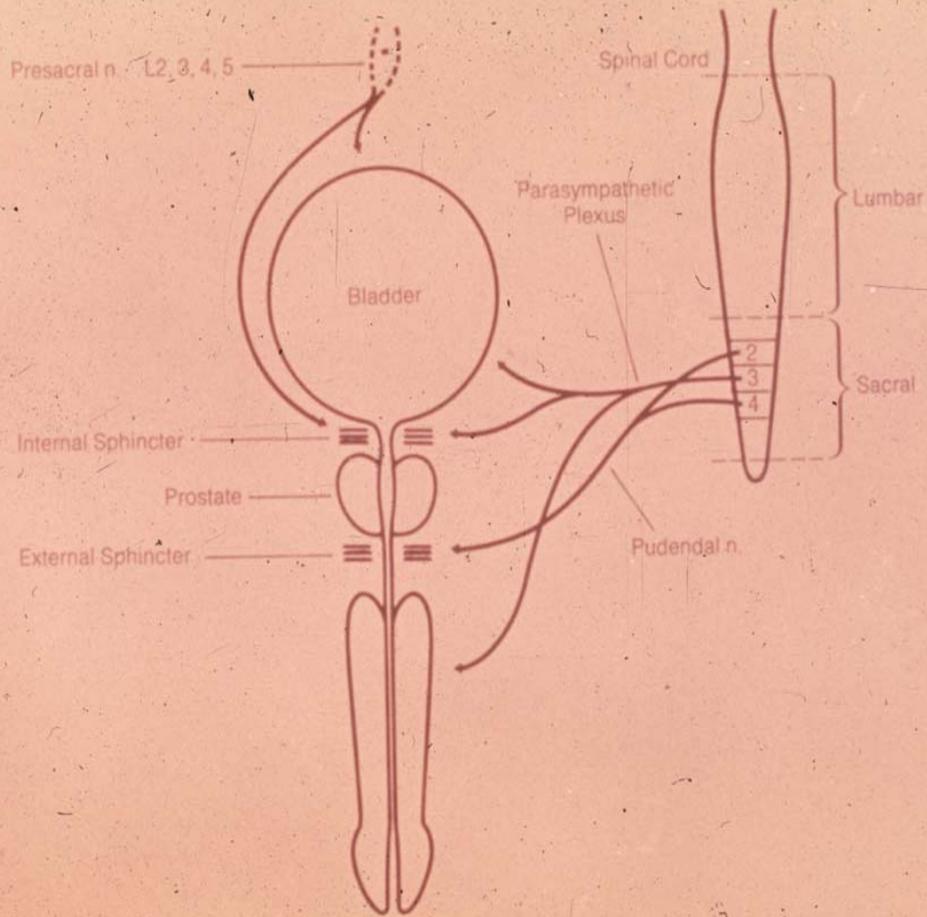
For millions with diabetes,  
this feeling is all too real.

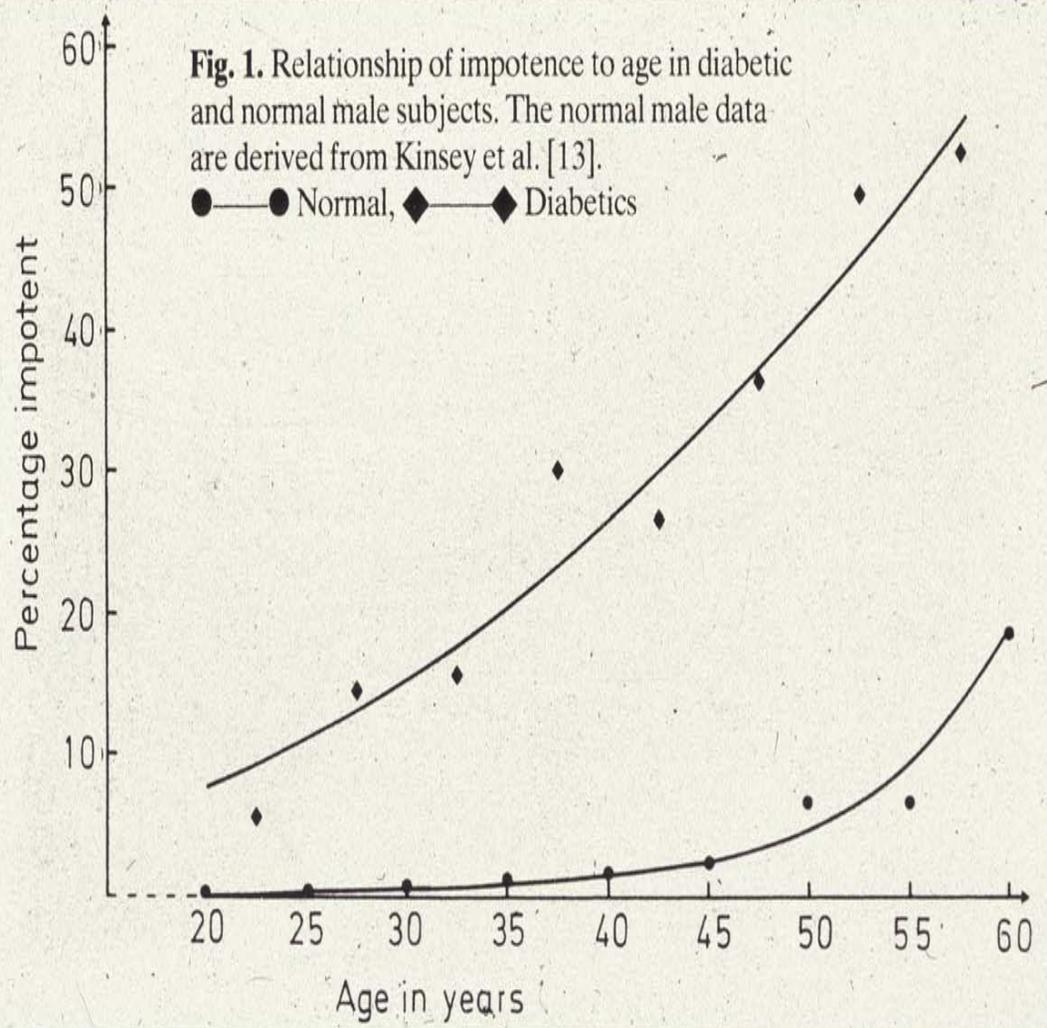












# LARGE BLOOD VESSEL COMPLICATIONS

Heart attacks – twice as common in men and four times more common in women with diabetes; 75% of people with type 2 diabetes will die from a heart attack

Strokes – twice as common in people with diabetes

Leg arteries – 2 ½ times as common in people with diabetes, especially smokers (can lead to gangrene)

# CLASSIFICATION OF DIABETES MELLITUS

Type 1 – 5 % (Autoimmune)

Type 2 – 90% (Insulin resistance and  
decreased insulin secretion)

Other Types – 5%

- Specific genetic lesions

- Certain drugs (e.g., steroids)

- Diseases of the pancreas

- Certain endocrine diseases

# INHERITANCE OF DIABETES

## Identical twins

- \_ Type 1 diabetes - ~35% concordance
- Type 2 diabetes - ~95% concordance

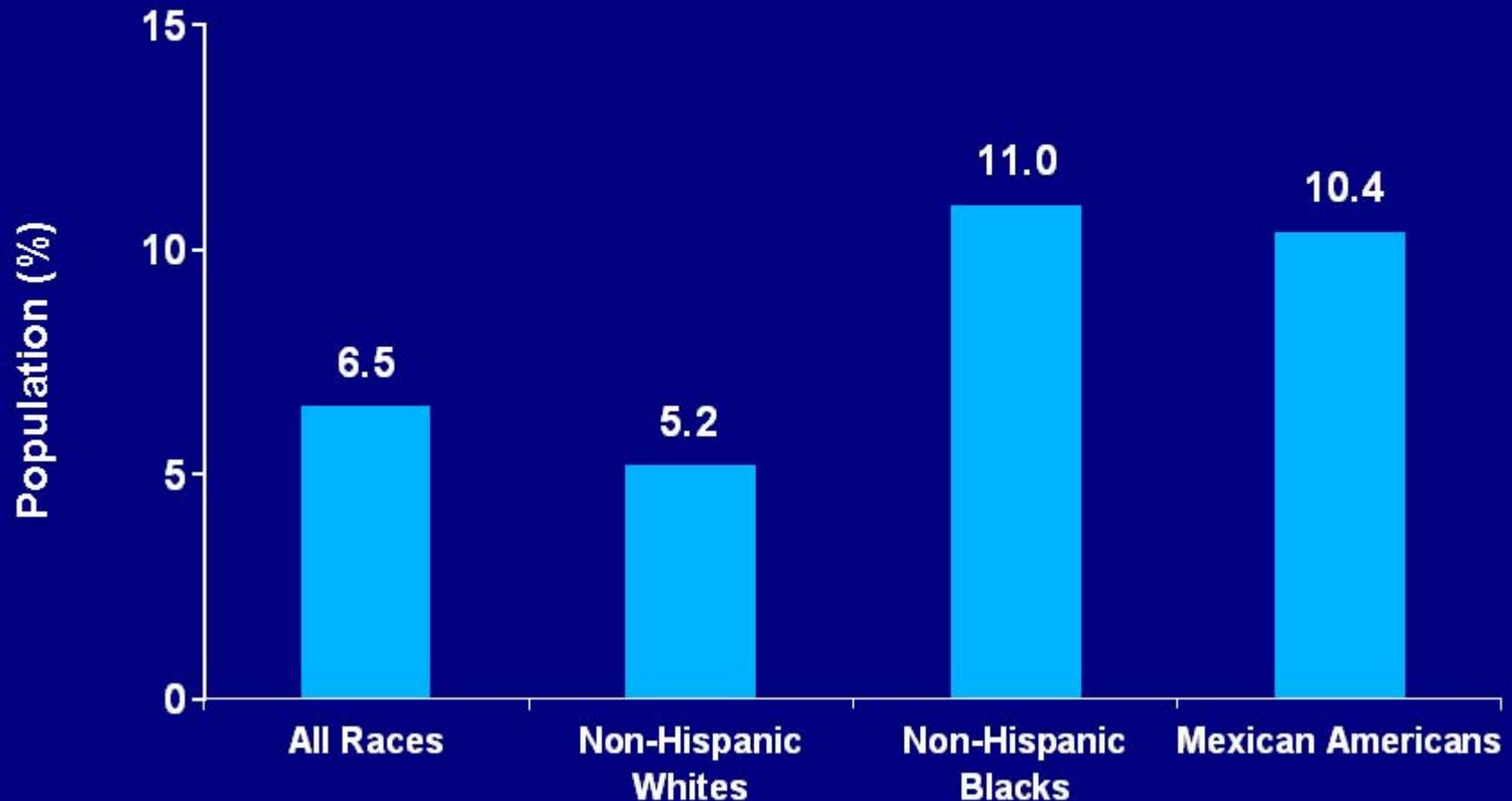
## First degree relatives (siblings, parents)

Type 1 diabetes - ~10%

Type 2 Diabetes - ~40% (more if both parents have diabetes)

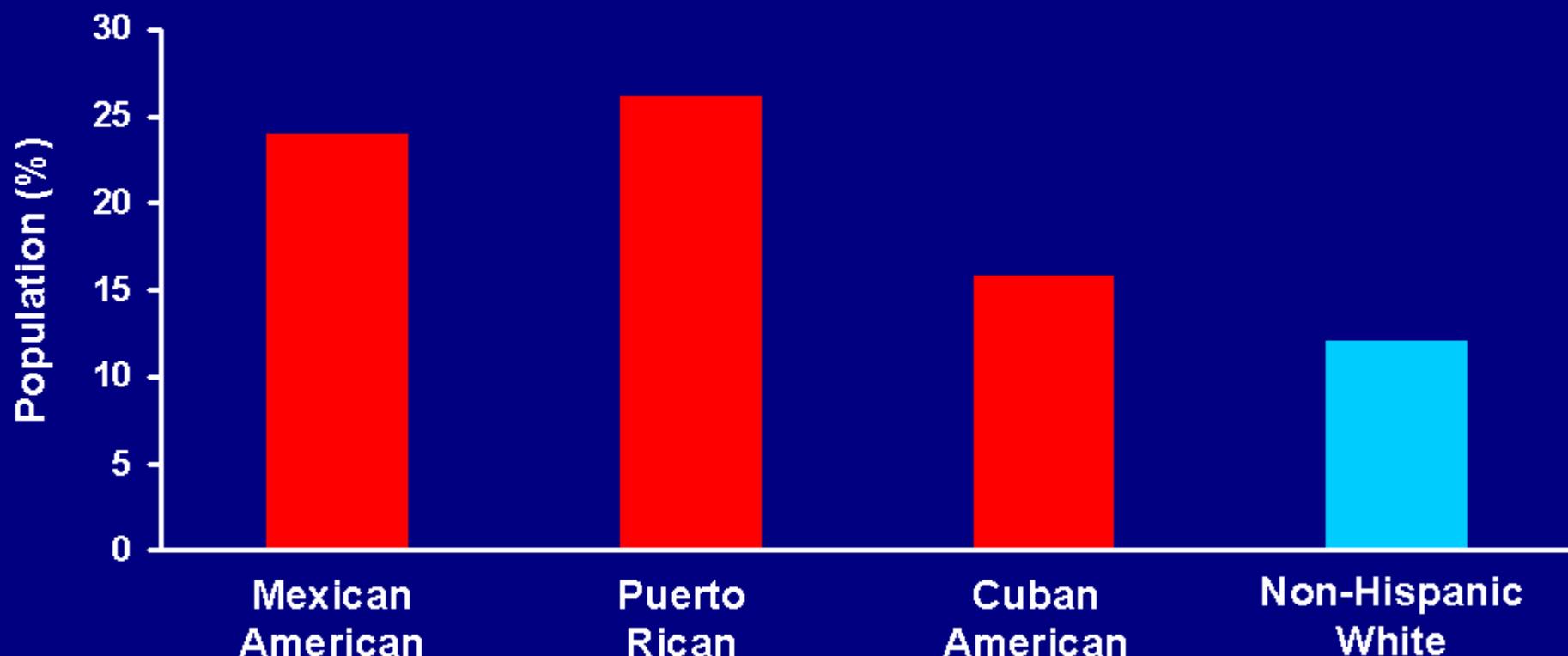


# Prevalence of Diagnosed Diabetes by Race





# Prevalence of Diabetes at Age 45 to 74 Years



# **DIABETES MELLITUS:**

**WHAT IT IS  
(METABOLICALLY)**

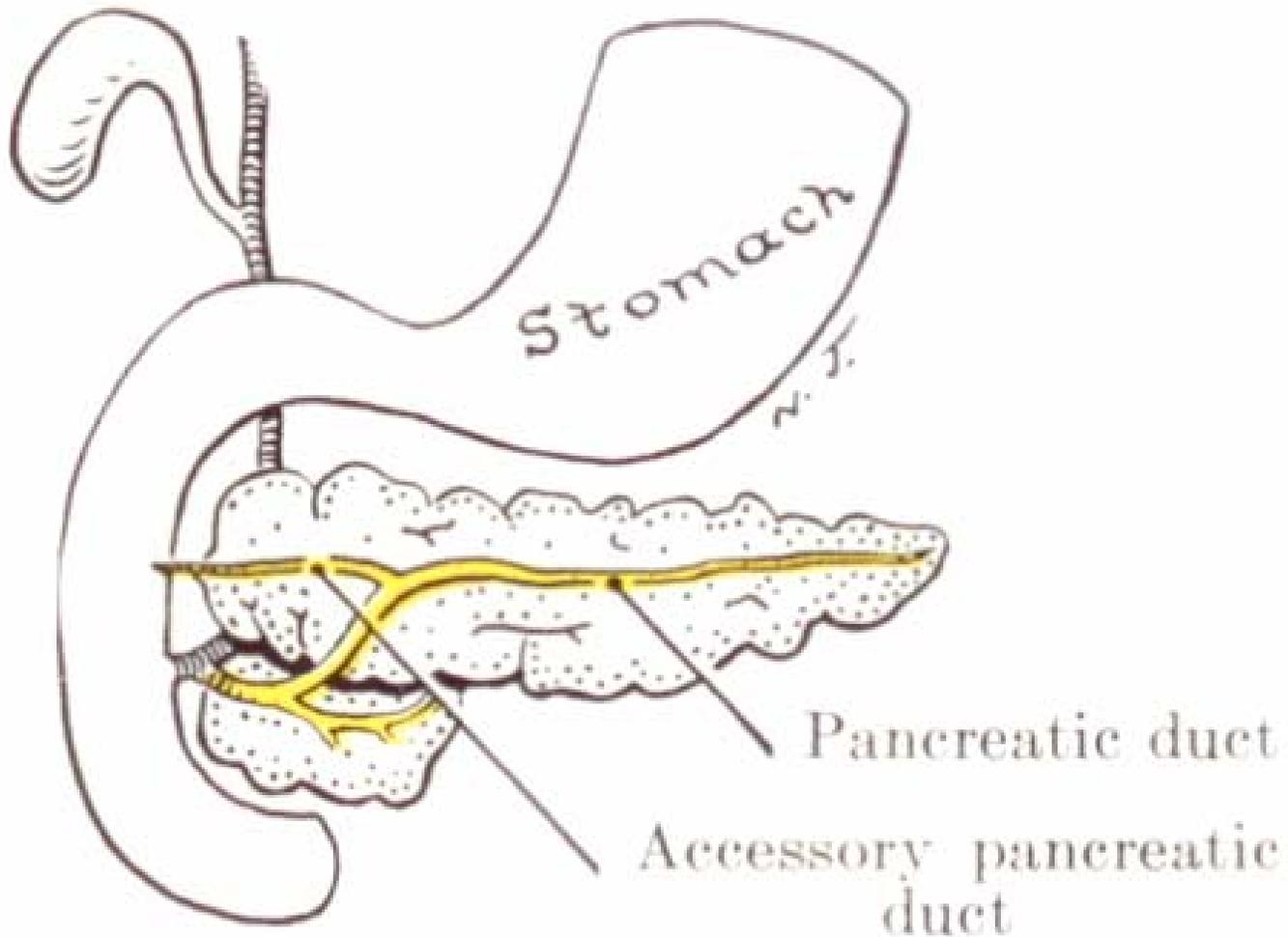
# DIETARY CONSTITUENTS

Proteins: AA-AA-AA-AA-AA-AA-AA-AA-AA-AA-AA-AA-AA-AA-AA

Carbohydrates: G-G

Fats (Triglycerides): C - FA  
|  
C - FA  
|  
C - FA

AA = amino acids; G = glucose; C = carbon; FA = fatty acids



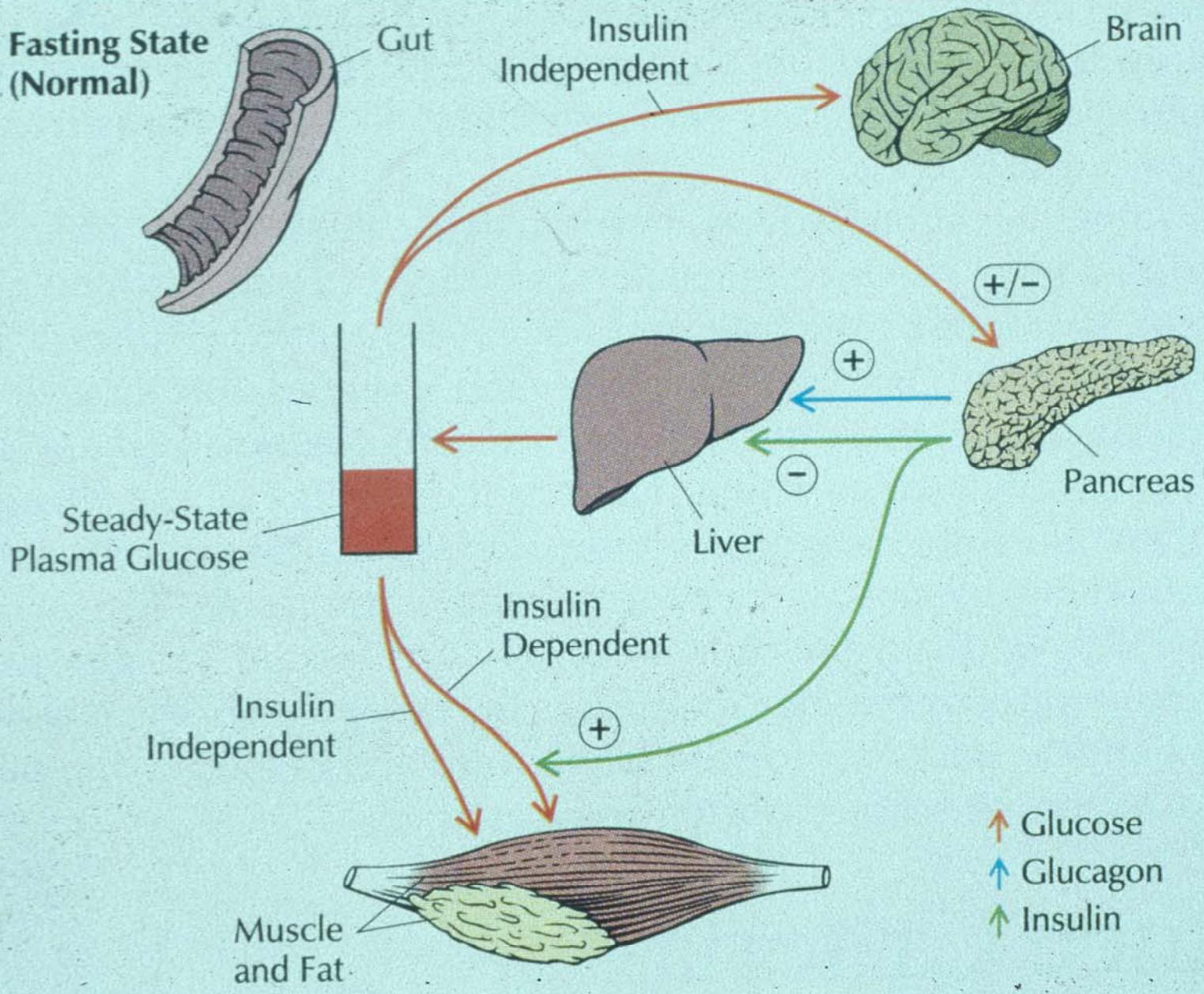
# $\beta$ - and $\alpha$ -Cells in the Pancreas of Normal Individuals

$\beta$ -Cells	$\alpha$ -Cells
<ul style="list-style-type: none"><li>■ Comprise about 70%–80% of the endocrine mass of the pancreas<sup>1,2</sup></li></ul>	<ul style="list-style-type: none"><li>■ Comprise about 15% of the endocrine mass of the pancreas<sup>1</sup></li></ul>
<ul style="list-style-type: none"><li>■ Located in the central portion of the islet<sup>1,2</sup></li></ul>	<ul style="list-style-type: none"><li>■ Located in the periphery of the islet<sup>1</sup></li></ul>
<ul style="list-style-type: none"><li>■ Produce insulin and amylin<sup>3</sup></li></ul>	<ul style="list-style-type: none"><li>■ Produce glucagon<sup>1</sup></li></ul>
<ul style="list-style-type: none"><li>■ Insulin released in response to elevated blood glucose levels<sup>1</sup></li></ul>	<ul style="list-style-type: none"><li>■ Glucagon released in response to low blood glucose levels<sup>1</sup></li></ul>

1. Cleaver O et al. In: *Joslin's Diabetes Mellitus*. Lippincott Williams & Wilkins; 2005:21–39.

2. Rhodes CJ. *Science*. 2005;307:380–384.

3. Kahn SE et al. *Diabetes*. 1998;47:640–645.

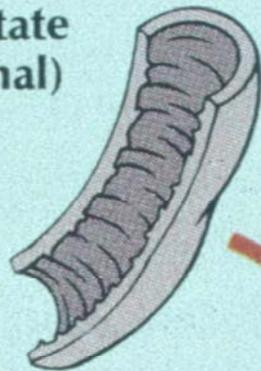


Fed State  
(Normal)

Insulin  
Independent

Dietary  
Intake

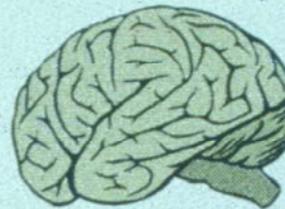
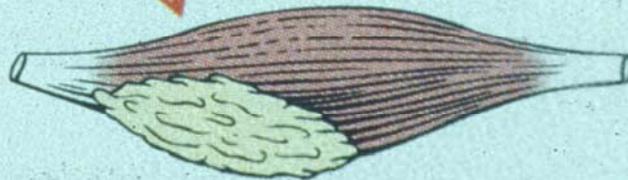
Steady-State  
Plasma  
Glucose



Insulin  
Dependent

Insulin  
Independent

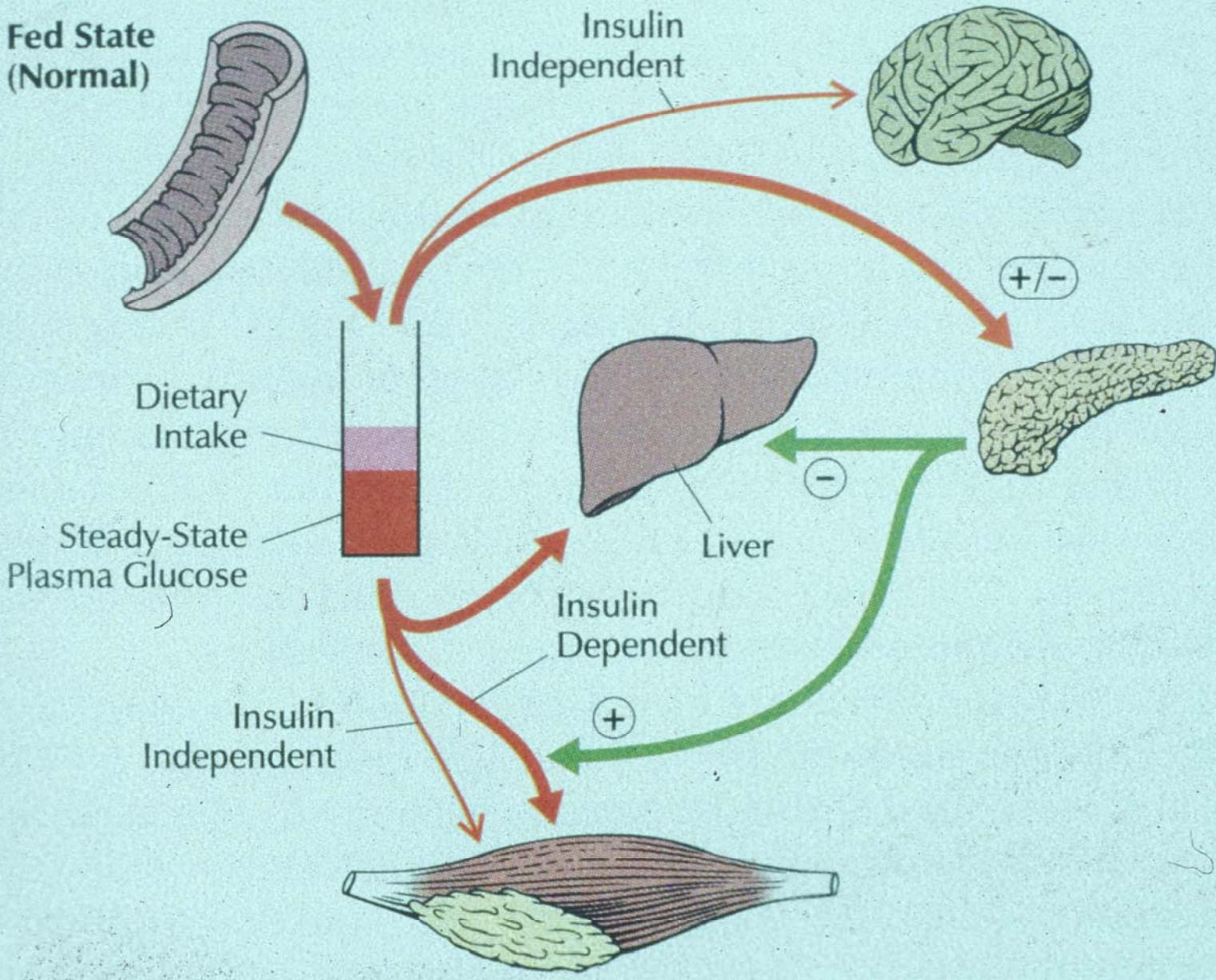
Liver



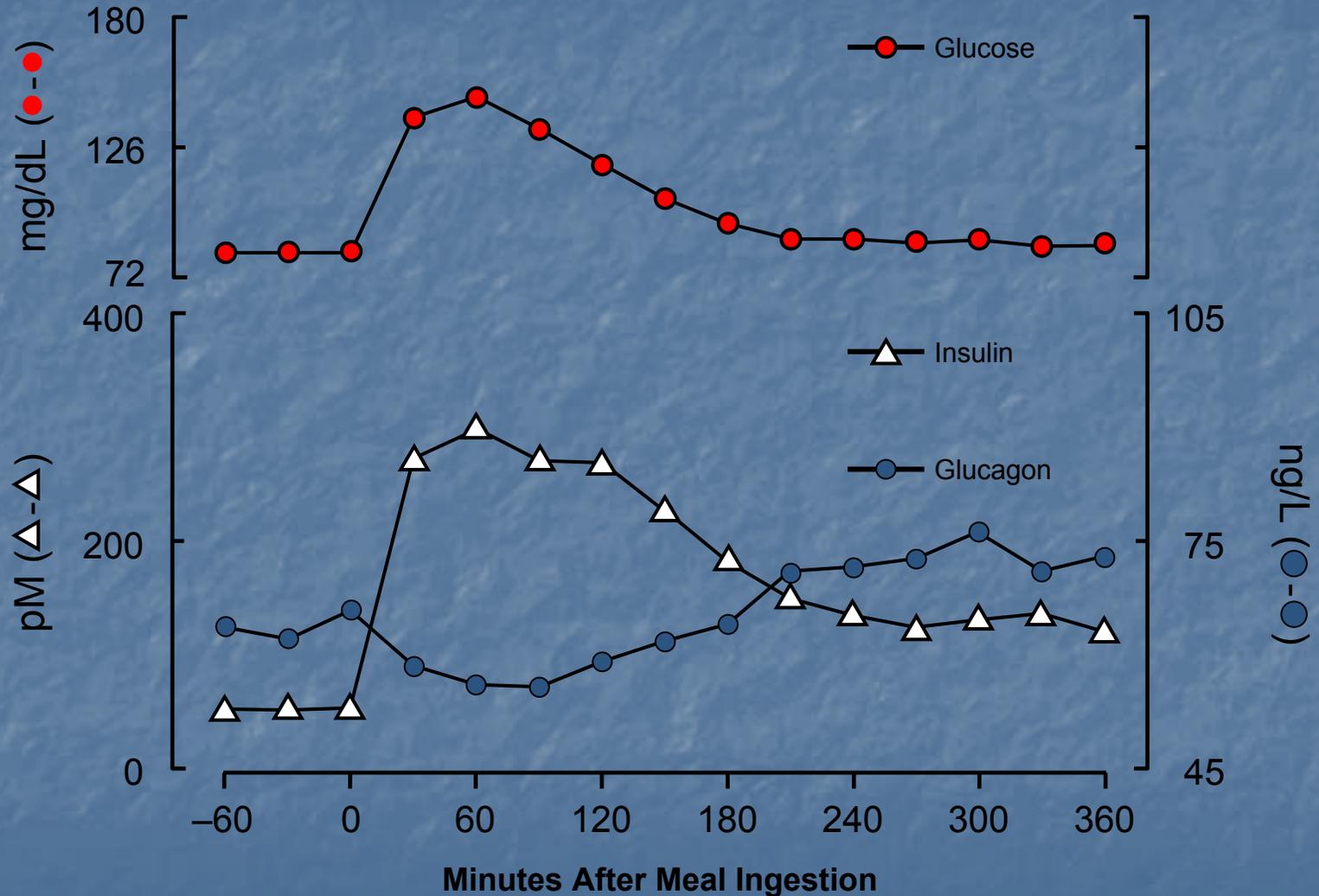
+/-

-

+



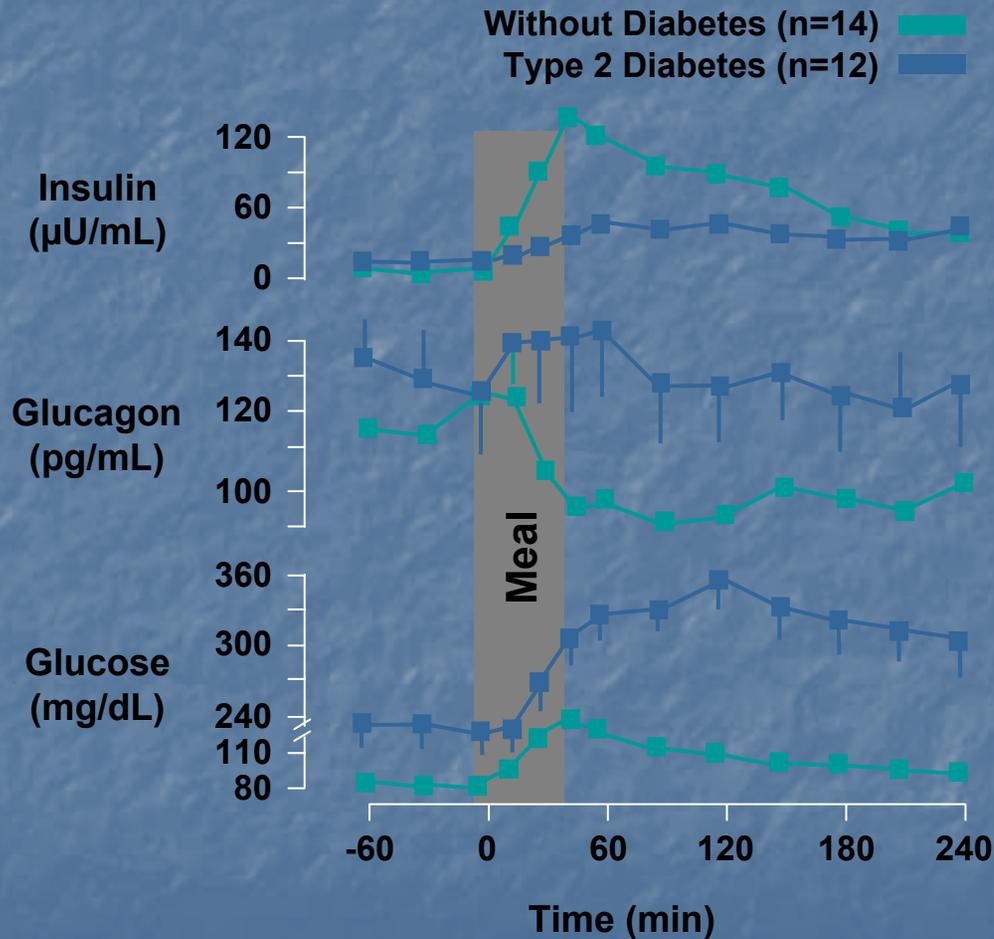
# Insulin Increases and Glucagon Falls in Response to Meals in Normal Subjects



N=11.

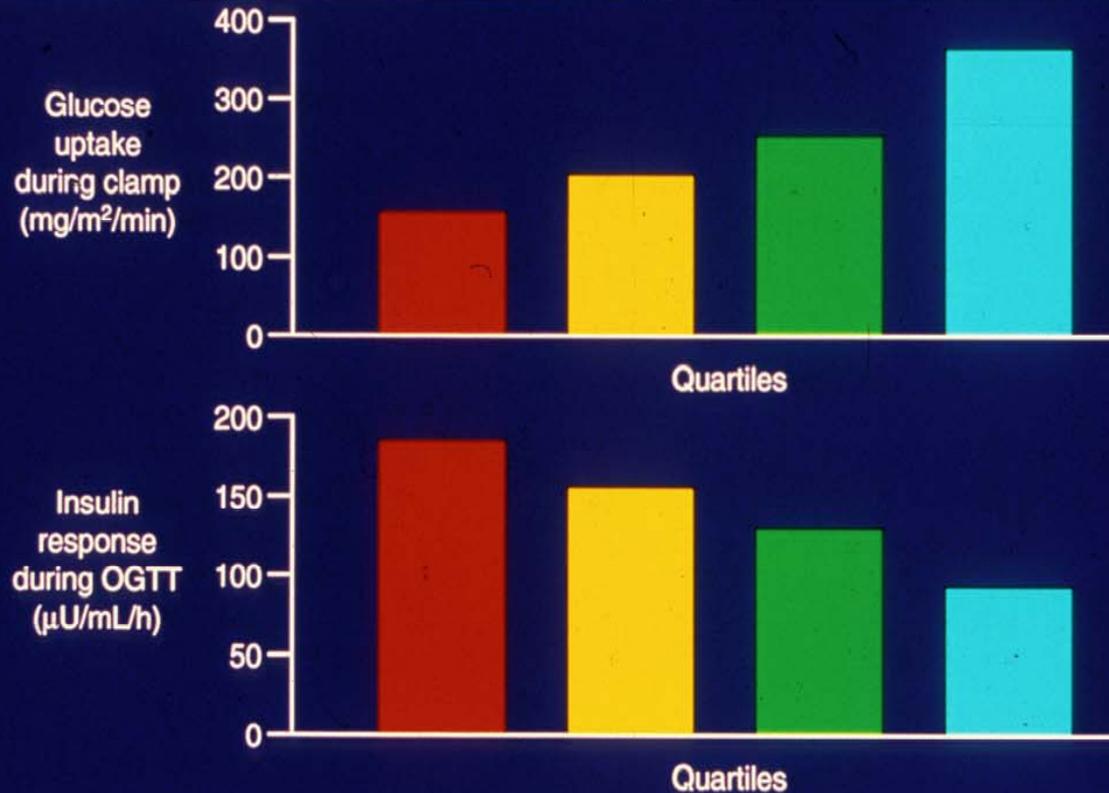
Adapted with permission from Woerle HJ et al. *Am J Physiol Endocrinol Metab.* 2003;284:E716–E725.

# Deficient Insulin: Hypersecreted Glucagon TYPE 2 DIABETES



- Defects in diabetes:
- Deficient insulin release
- Glucagon not suppressed (postprandially)
- Hyperglycemia

# Insulin Resistance and Insulin Secretion in Healthy Subjects

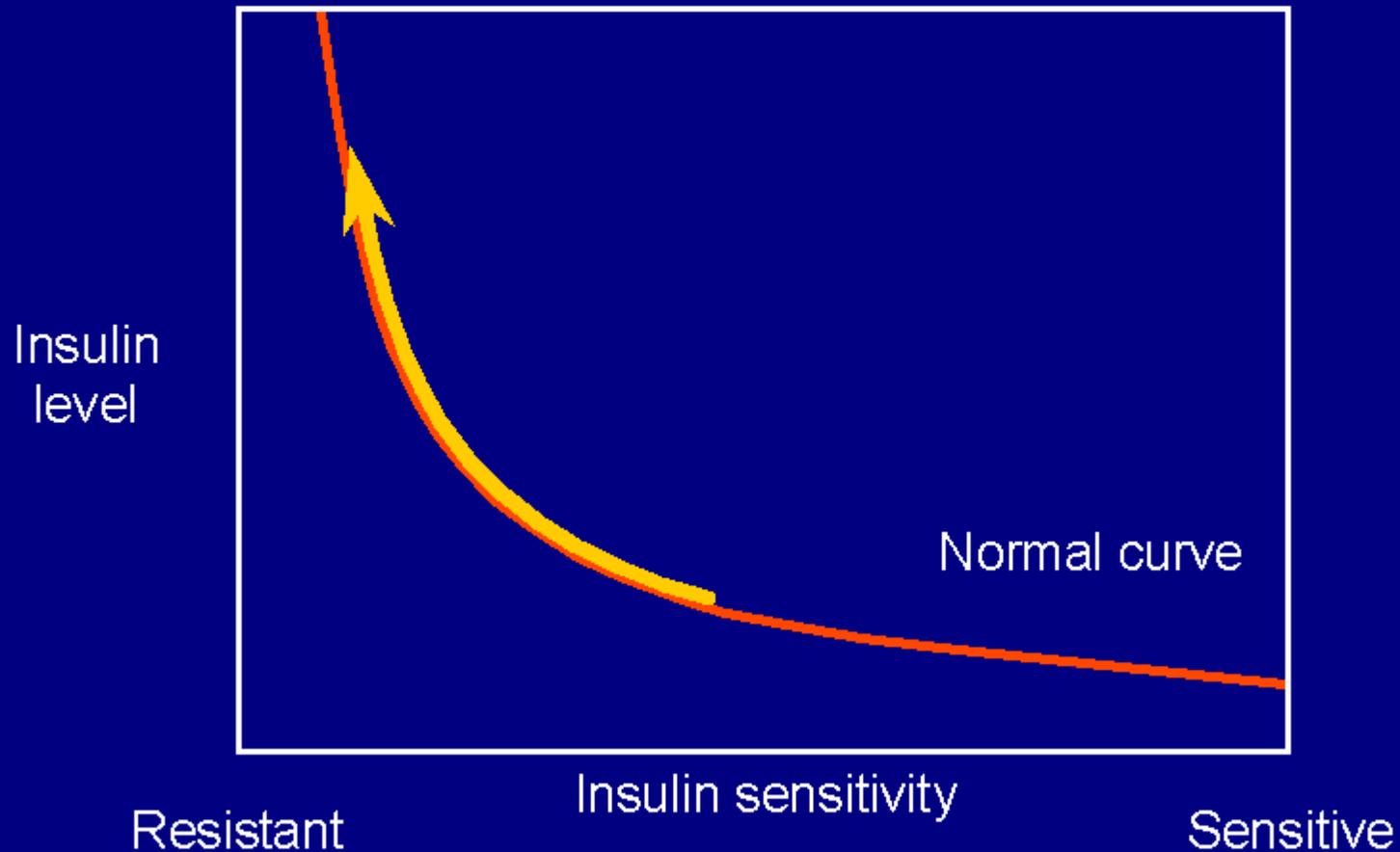


Hollenbeck and Reaven. J Clin Endocrinol Metab. 1987;64:1169-1173.



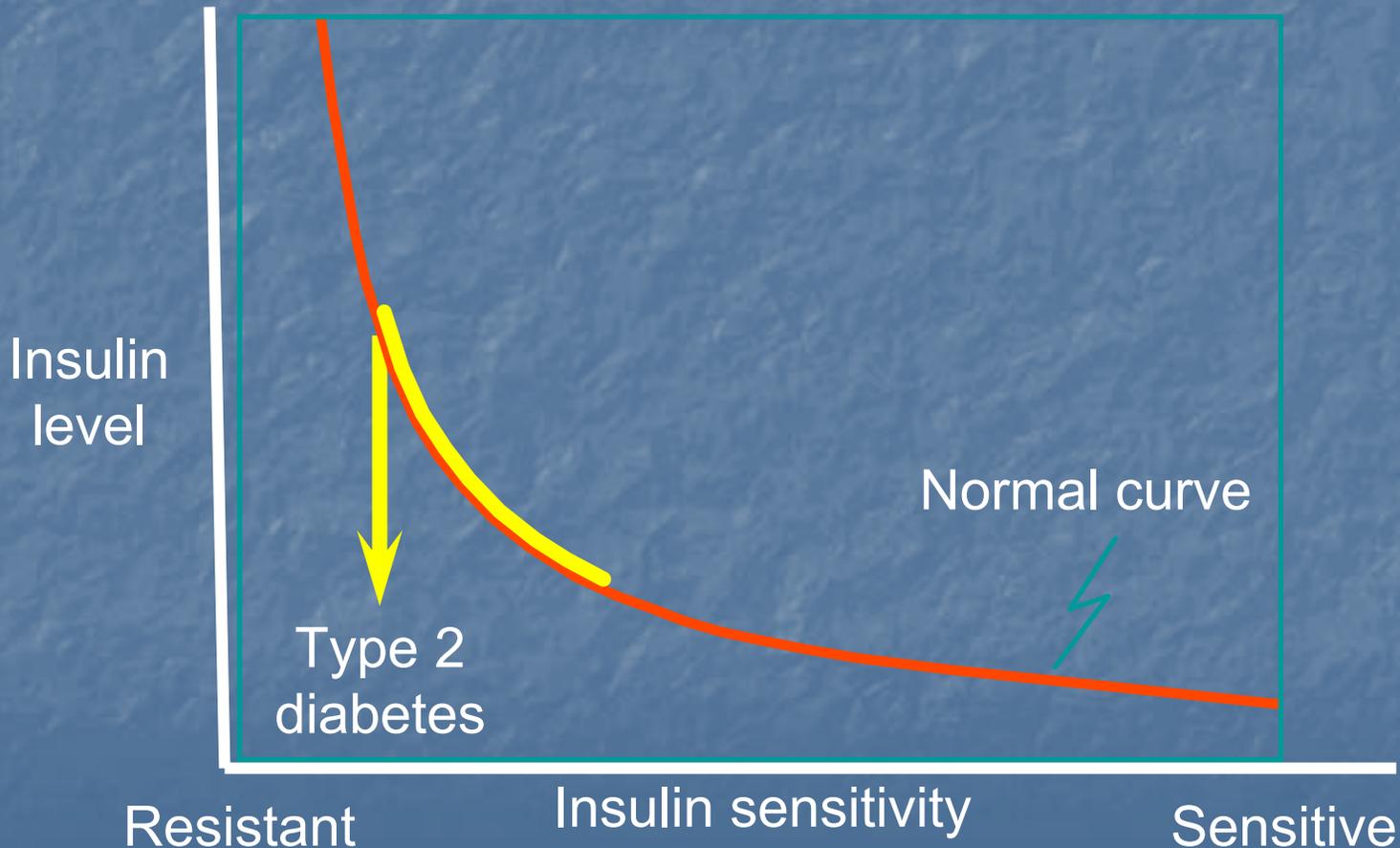
# Insulin Resistance With Normal $\beta$ Cells

## 'Climbing the Curve'

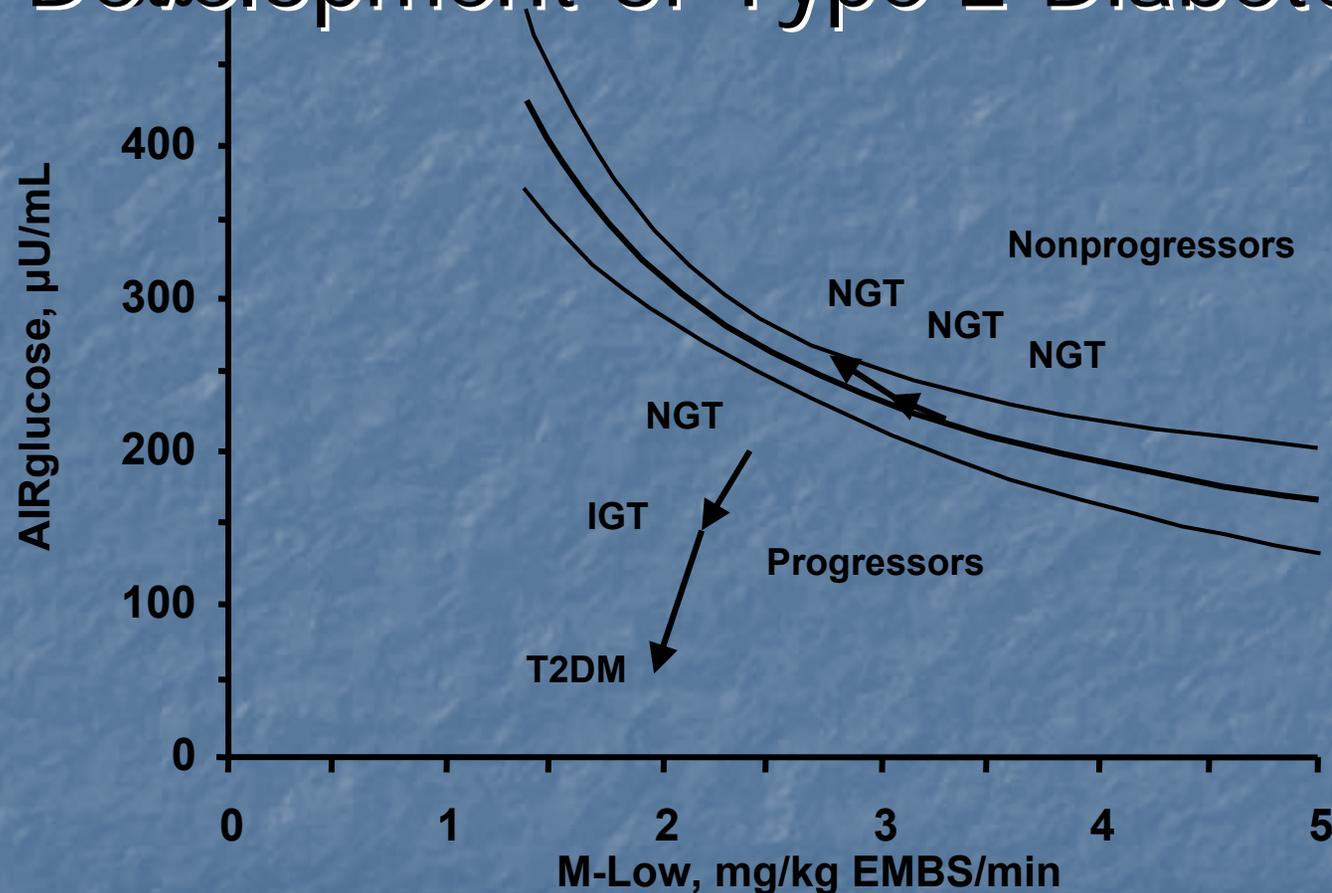


# Pathogenesis of Type 2 Diabetes

## 'Falling off the Curve'



# The Relationship Between Insulin Secretion and Insulin Action During the Development of Type 2 Diabetes



N=277 Pima Indians; NGT=normal glucose tolerance; IGT=impaired glucose tolerance; T2DM=type 2 diabetes; EMBS=estimated metabolic body size.

Changes in  $\beta$ -cell function, measured as acute insulin response to glucose (AIR glucose) relative to changes in insulin sensitivity, measured by clamp technique at a low insulin concentration (M-low).

Adapted with permission from Weyer C et al. *J Clin Invest.* 1999;104;787-794.



# Insulin Resistance: Inherited and Acquired Influences

## Inherited

### Rare Mutations

- Insulin receptor
- Glucose transporter
- Signaling proteins

### Common Forms

- Largely unidentified

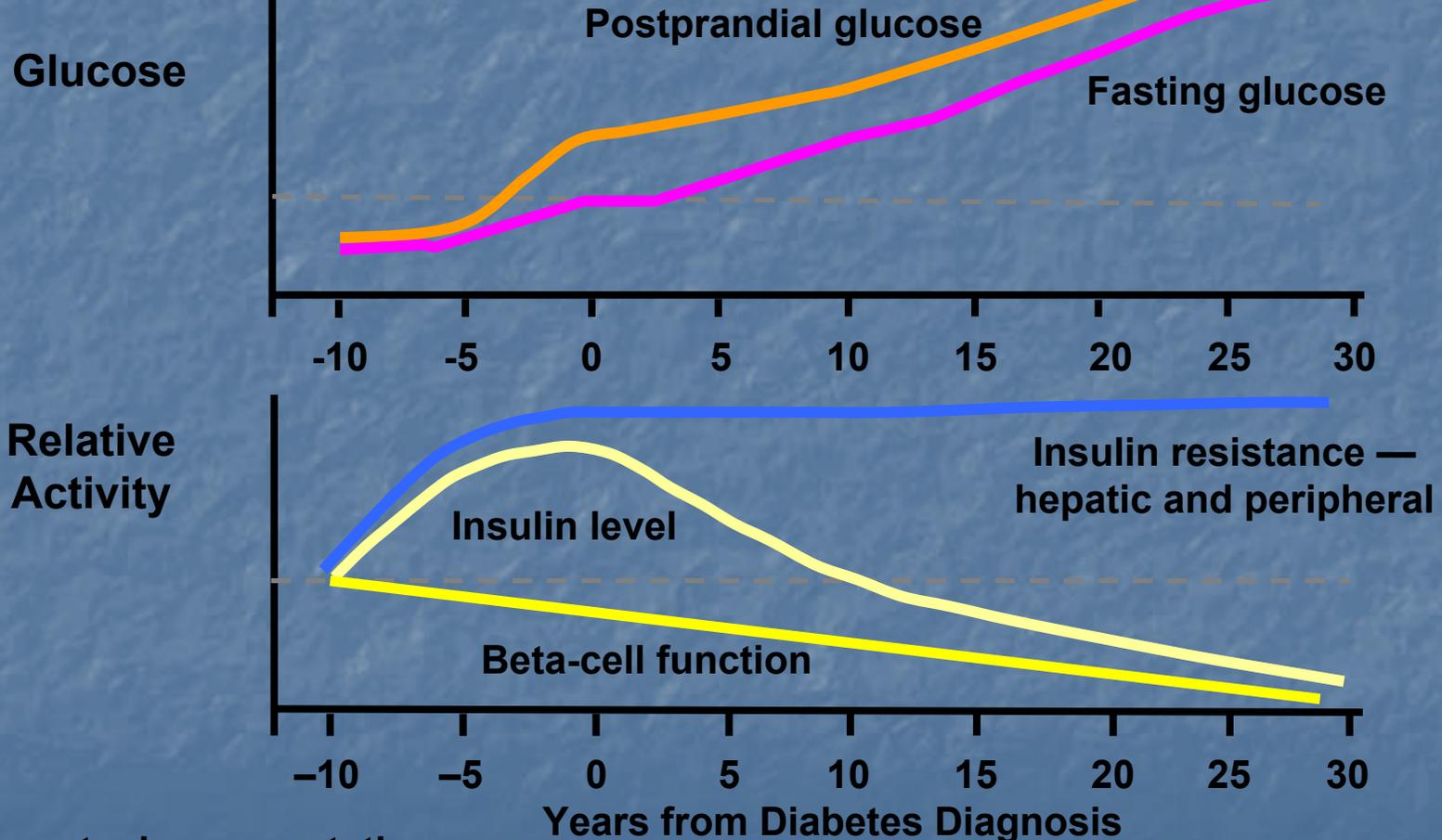
## Acquired

- Inactivity
- Overeating
- Aging
- Medications
- Hyperglycemia
- Elevated FFAs

**INSULIN RESISTANCE**

# Development and Progression of Type 2 Diabetes\*

NGT → Insulin Resistance → IGT/ IFG → Type 2 Diabetes



\*Conceptual representation.

NGT=normal glucose tolerance; IGT=impaired glucose tolerance; IFG=impaired fasting glucose.

Adapted from Ferrannini E. Presentation at 65th ADA in Washington, DC, 2006.; and Ramlo-Halsted et al. *Prim Care*.

1999;26:771–789. Permission pending.

**DIABETES MELLITUS:**

**WHAT CAN BE DONE  
ABOUT IT**

**PREVENT THE  
DISEASE**

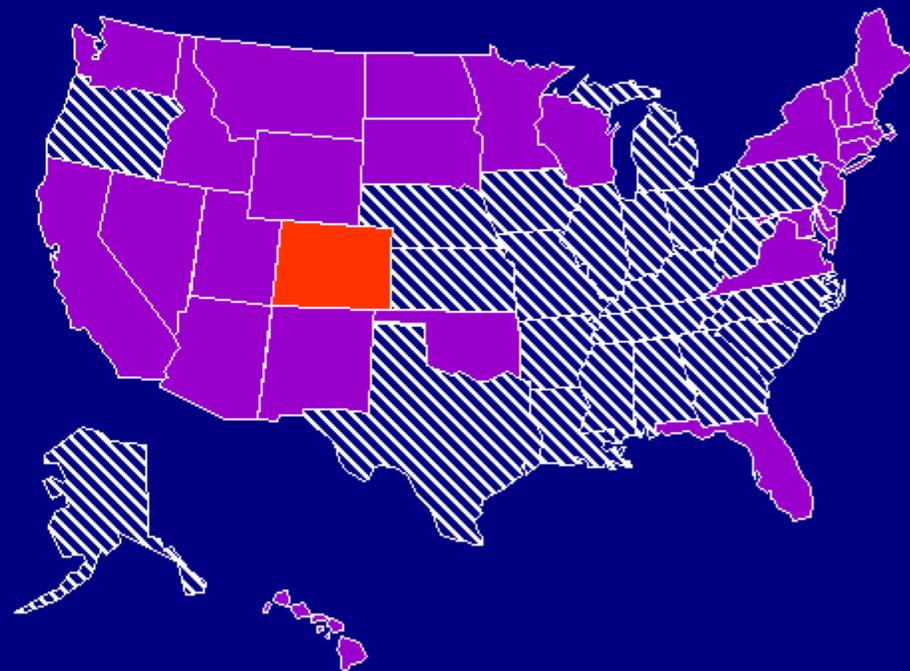
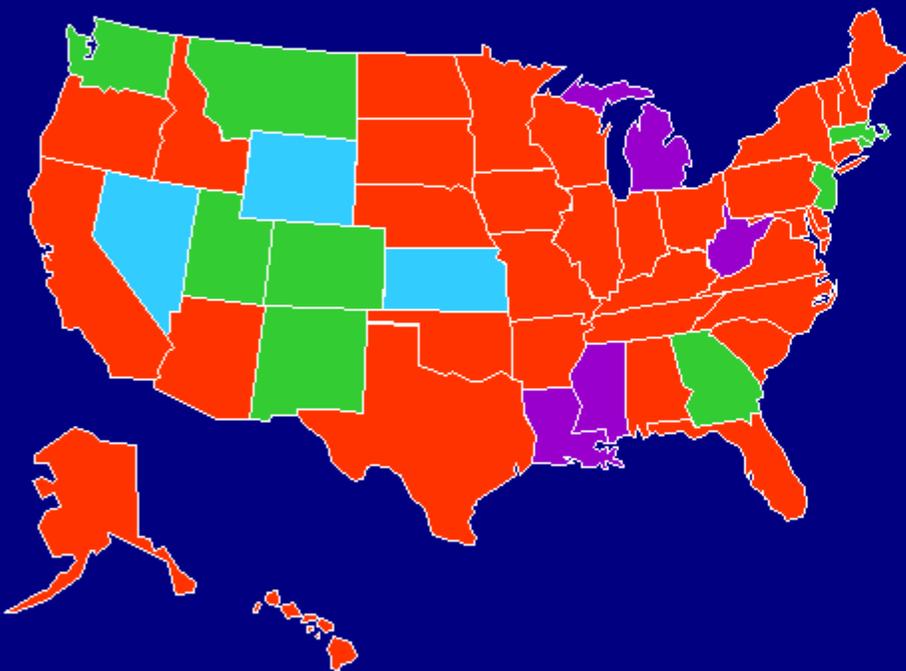


# Prevalence of Obesity in the United States



1991

2000



■ No Data

■ <10%

■ 10%–14%

■ 15%–19%

■ ≥20%

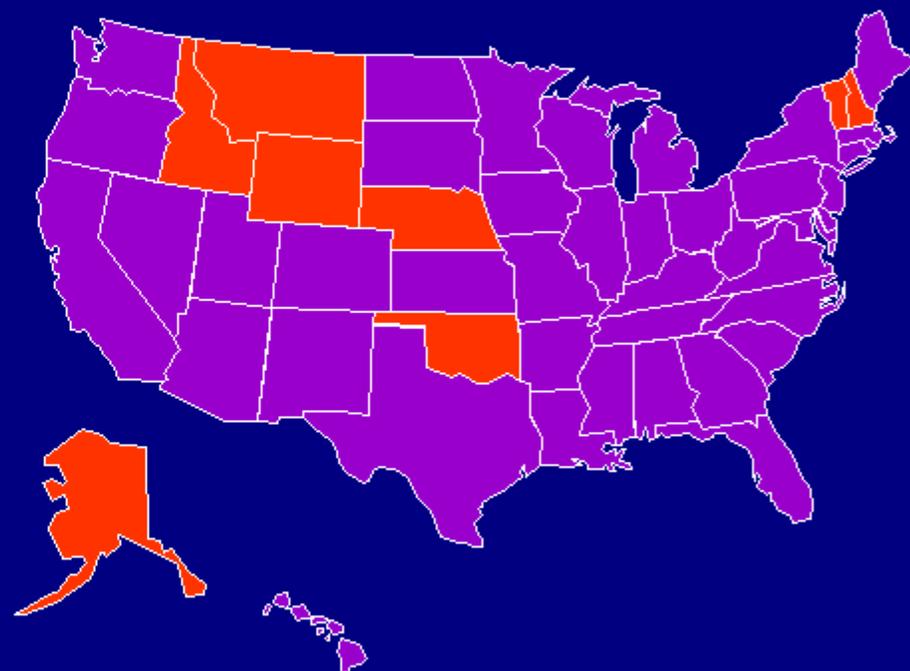
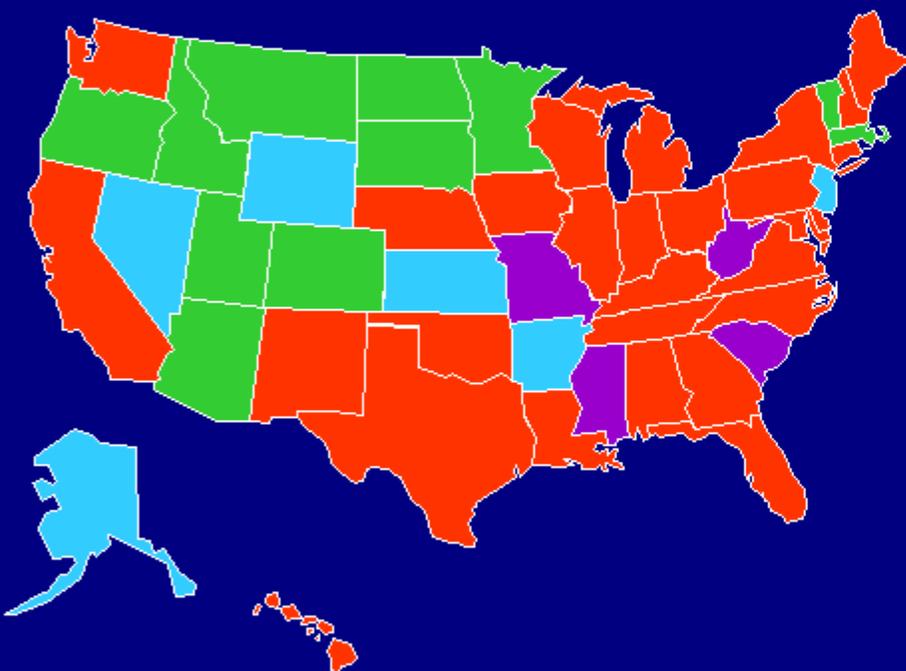


# Prevalence of Diabetes in the United States



1990

2000



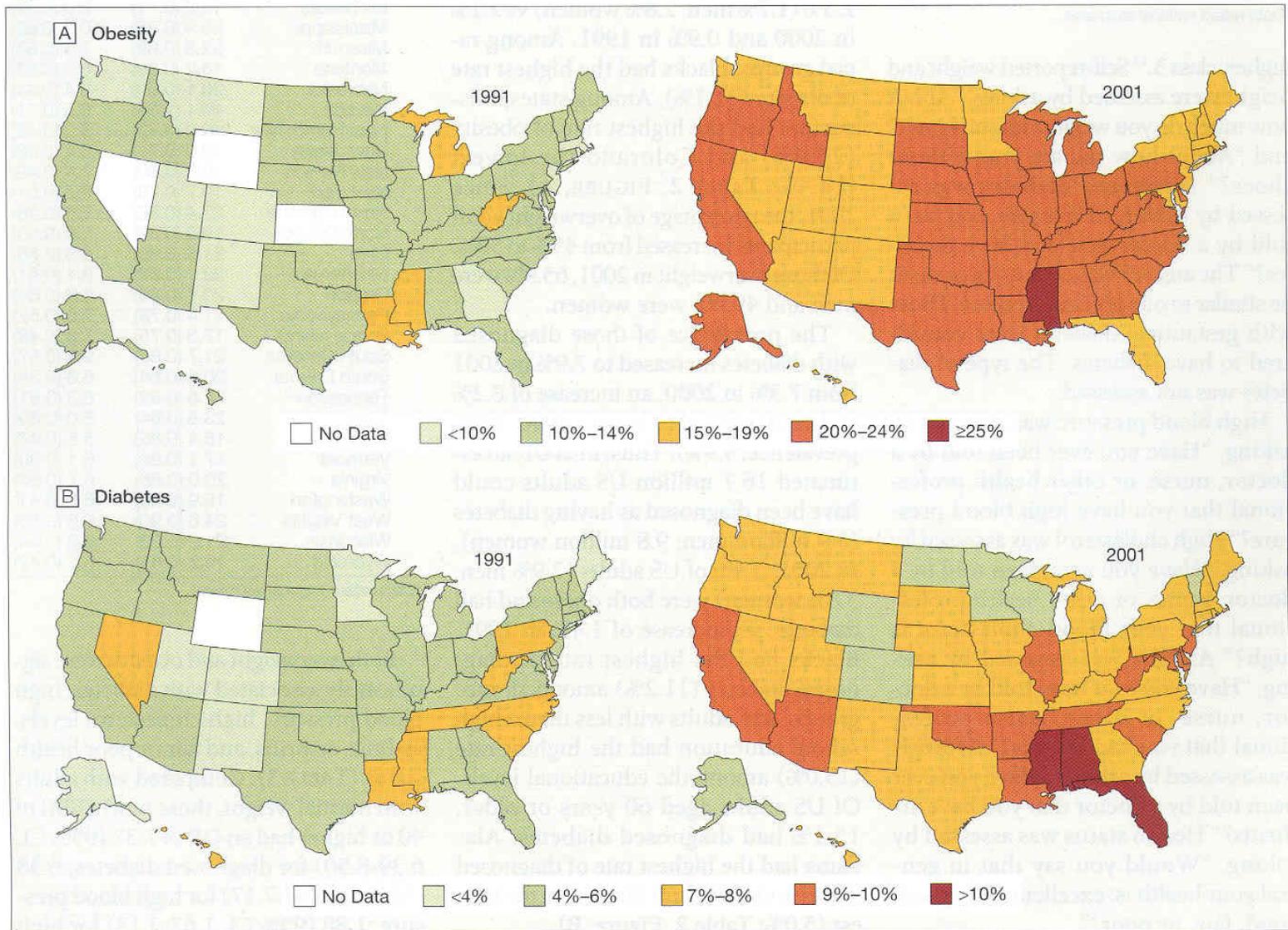
■ No Data

■ <4%

■ 4%–6%

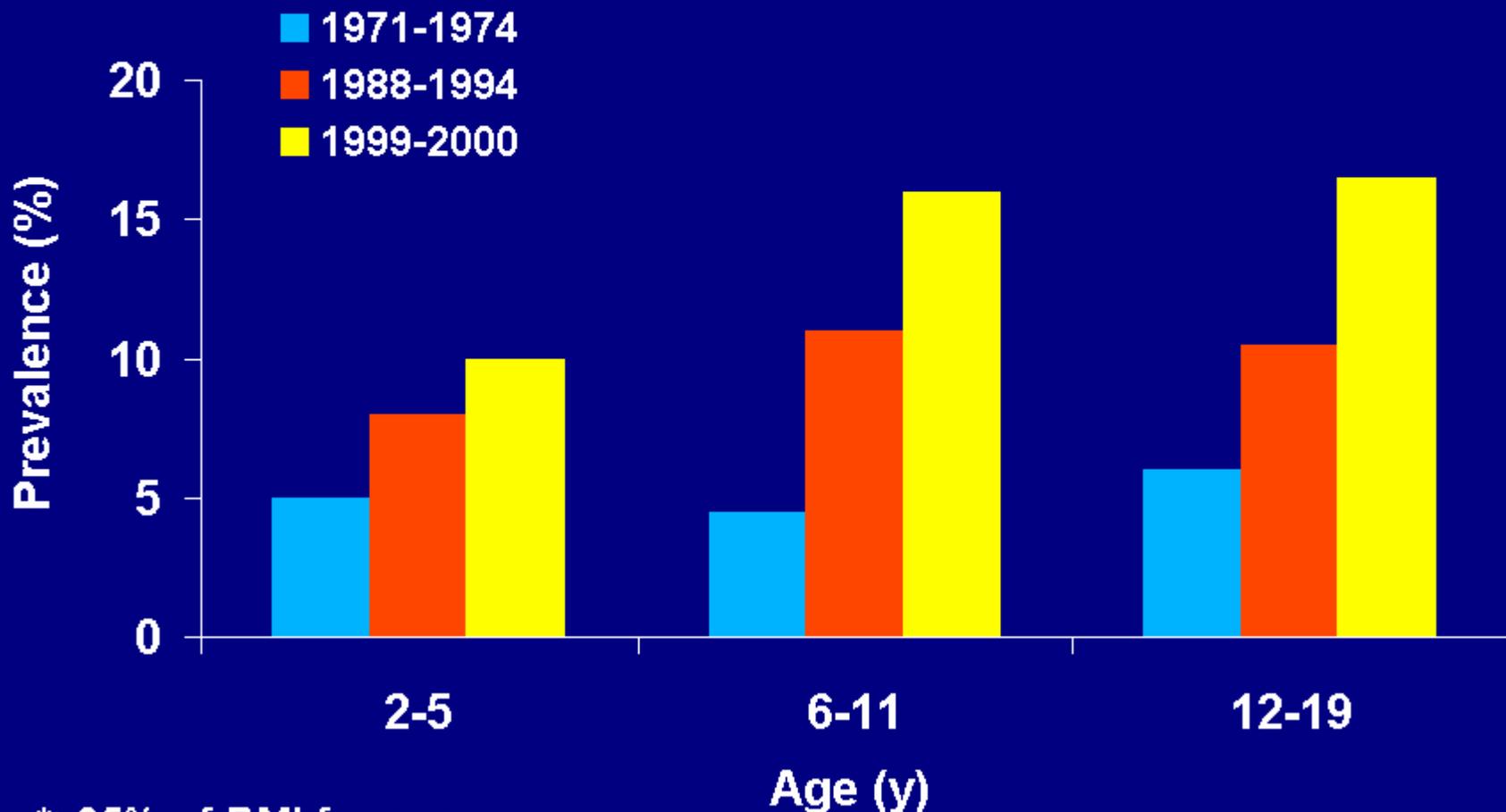
■ >6%

**Figure.** Prevalence of Obesity and Diagnosed Diabetes Among US Adults, 1991 and 2001





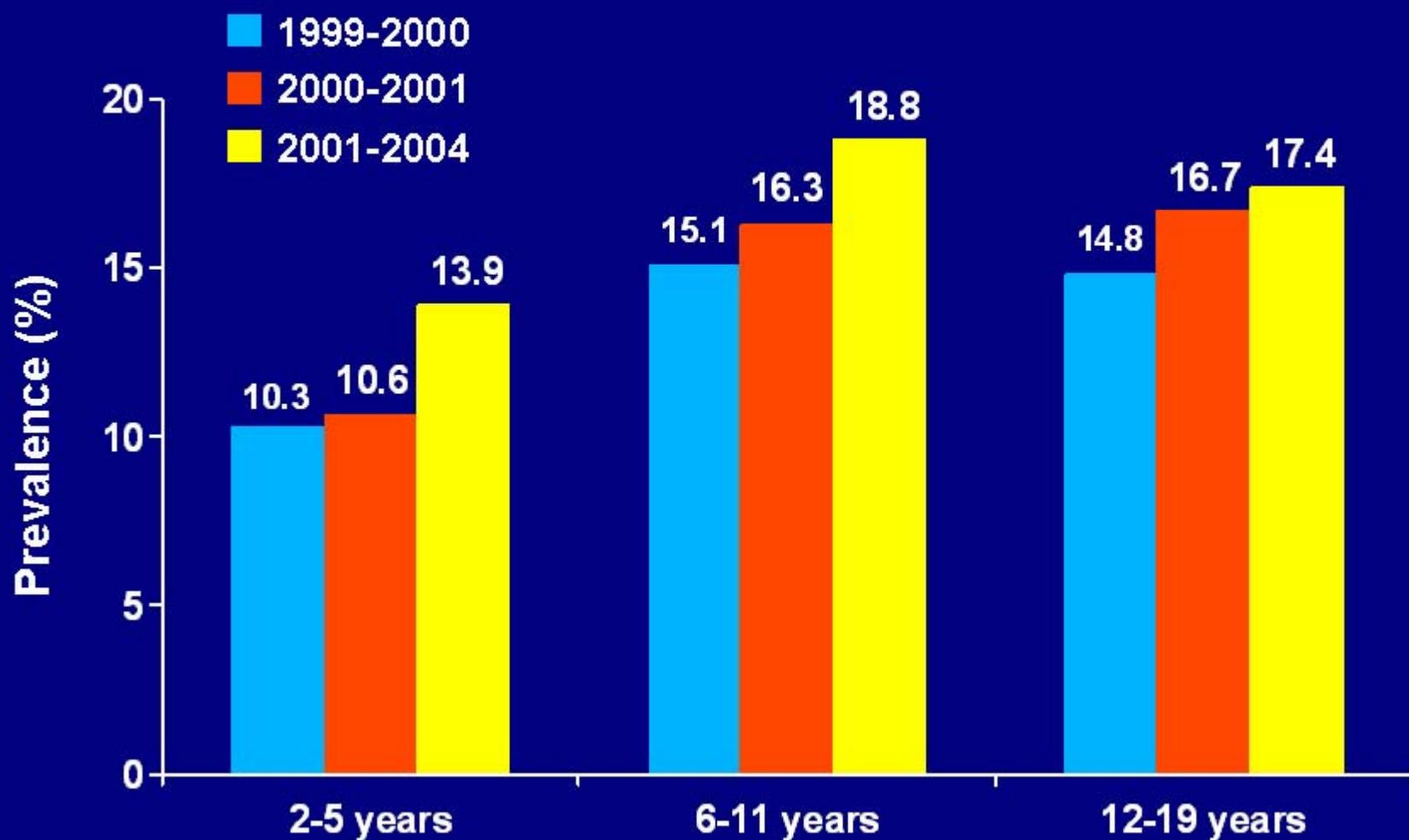
# Prevalence of Overweight\* Among US Children and Adolescents



\* $\geq 95\%$  of BMI for age.



# Prevalence of Overweight\* Among US Children and Adolescents



\*BMI for age  $\geq$ 95th percentile.

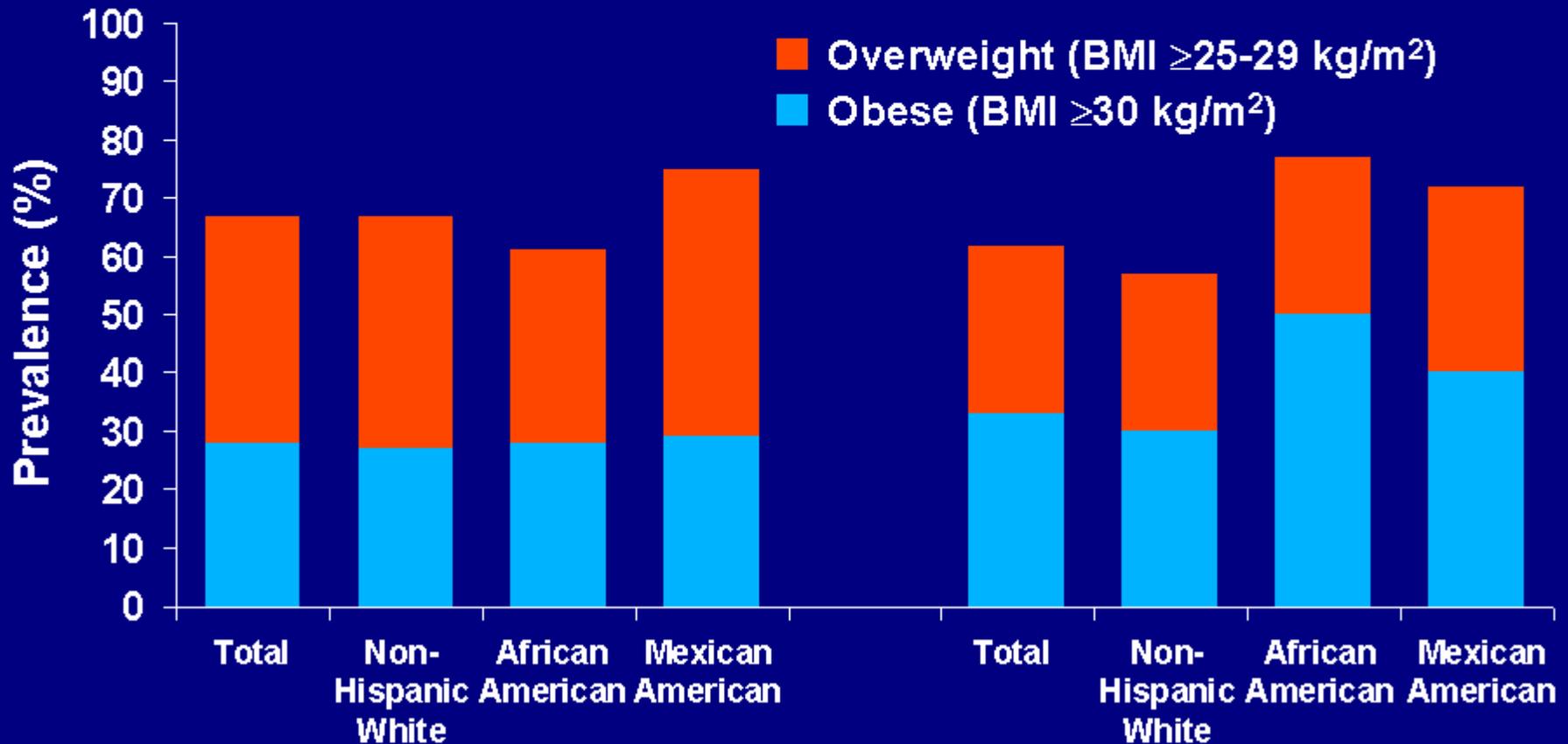
Data from Ogden CL et al. *JAMA*. 2006;295:1549-1555.



# Prevalence of Overweight and Obesity Among US Adults by Sex and Ethnicity

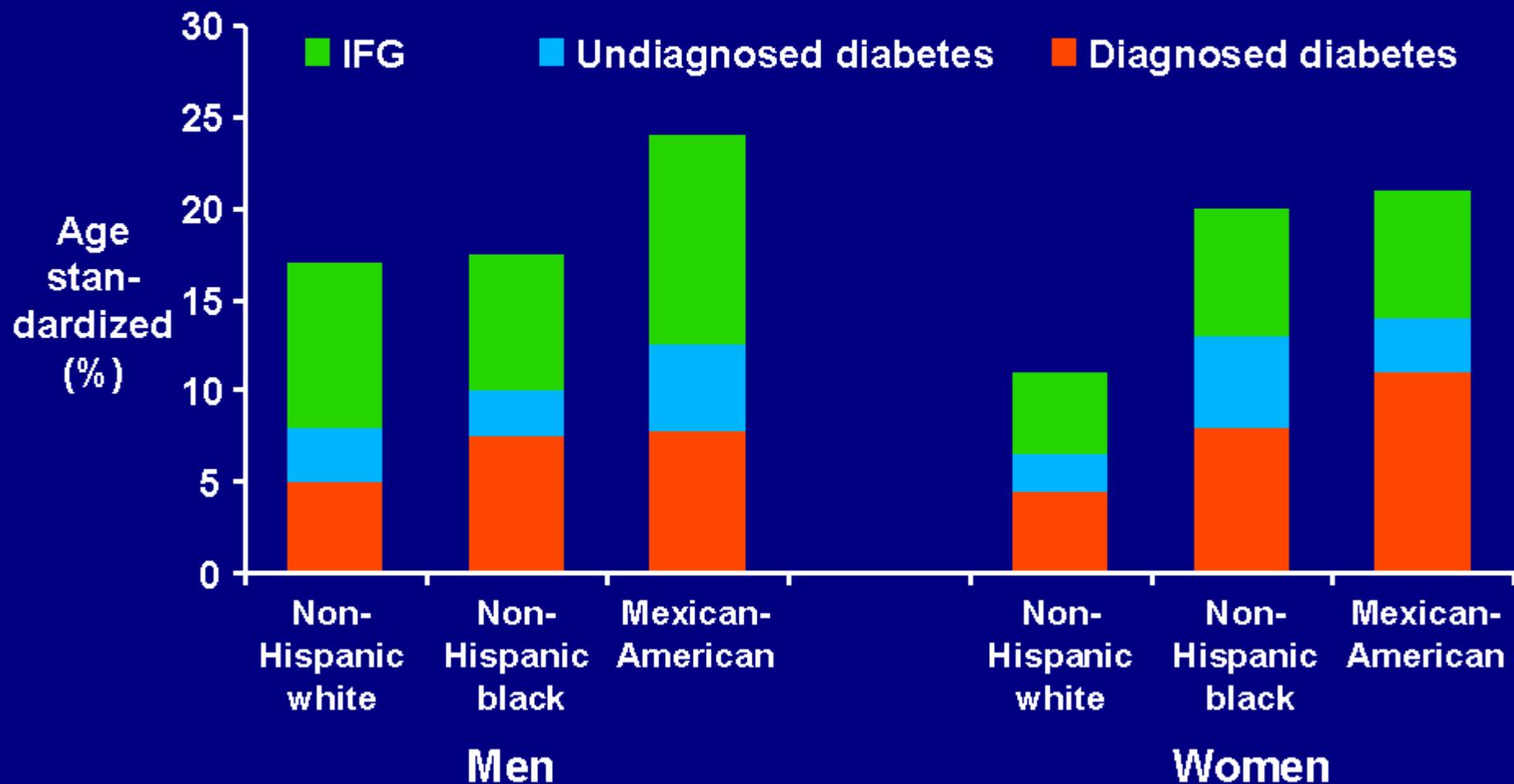
Men  $\geq 20$  years of age

Women  $\geq 20$  years of age



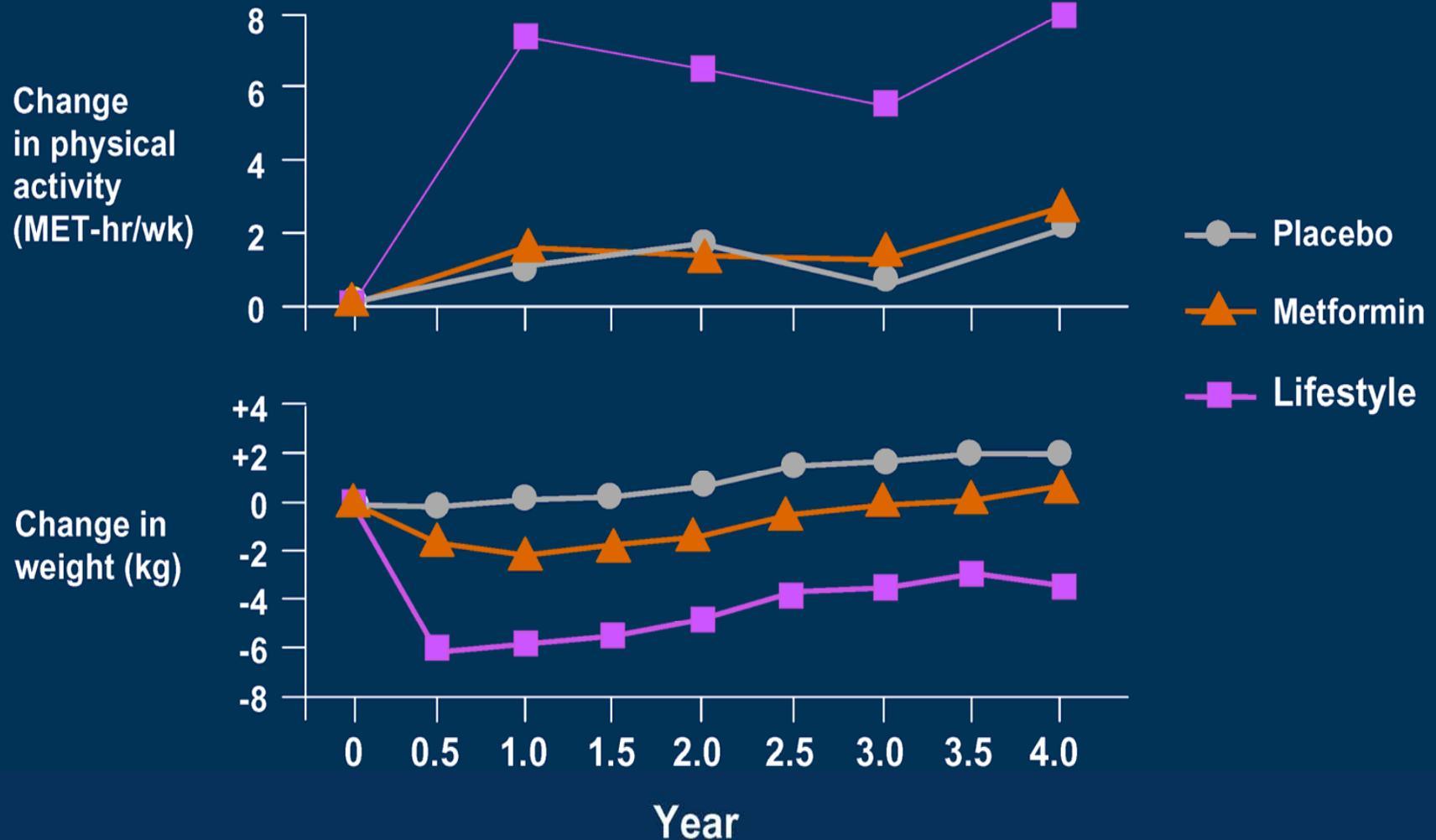


# Prevalence of Diagnosed and Undiagnosed Diabetes and IFG in US Population $\geq 20$ Years by Sex and Racial/Ethnic Group <sup>©</sup>



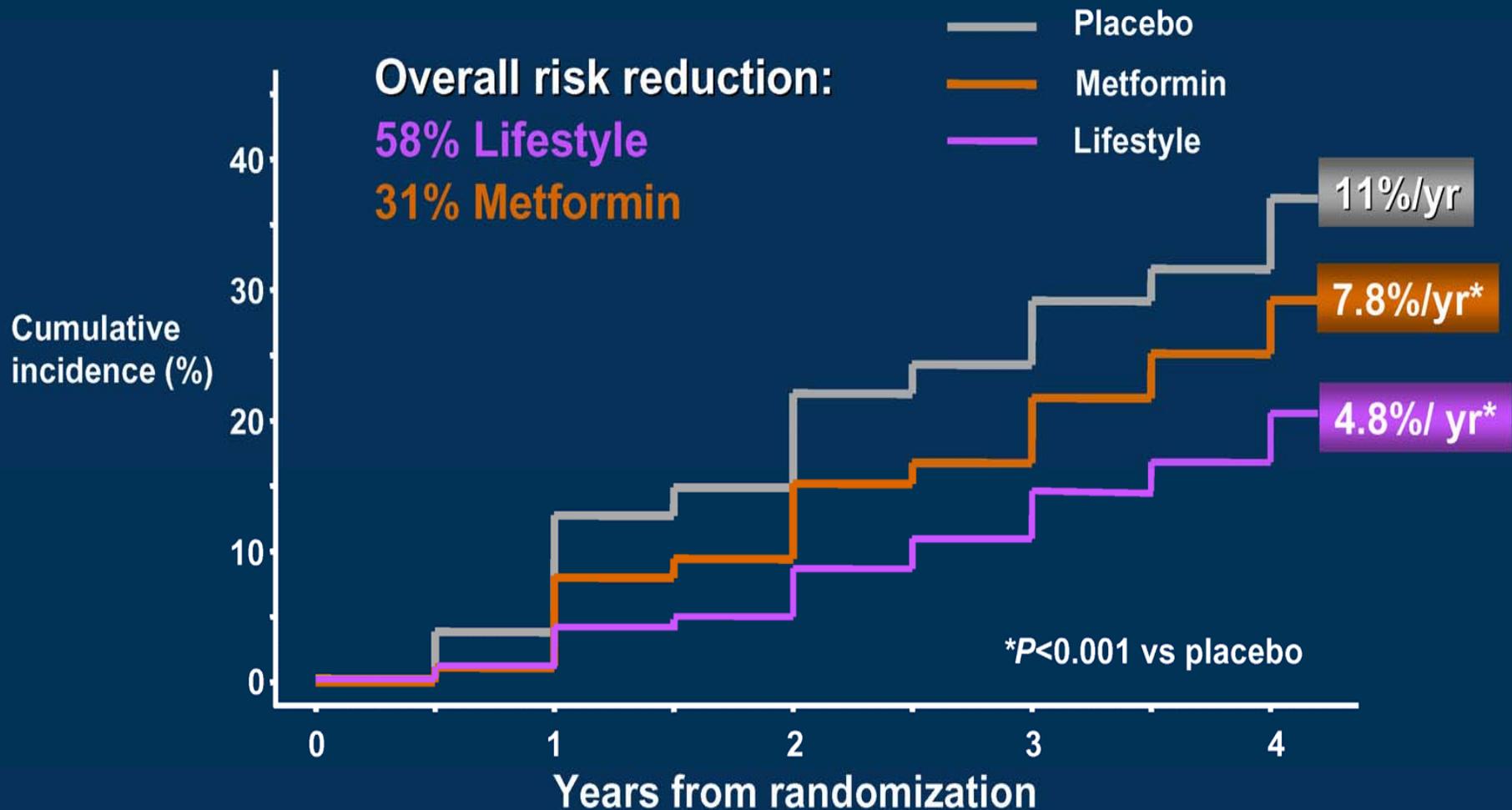
# DPP: Diabetes Prevention Program

## Physical Activity and Weight Loss by Study Group



# DPP: Diabetes Prevention Program

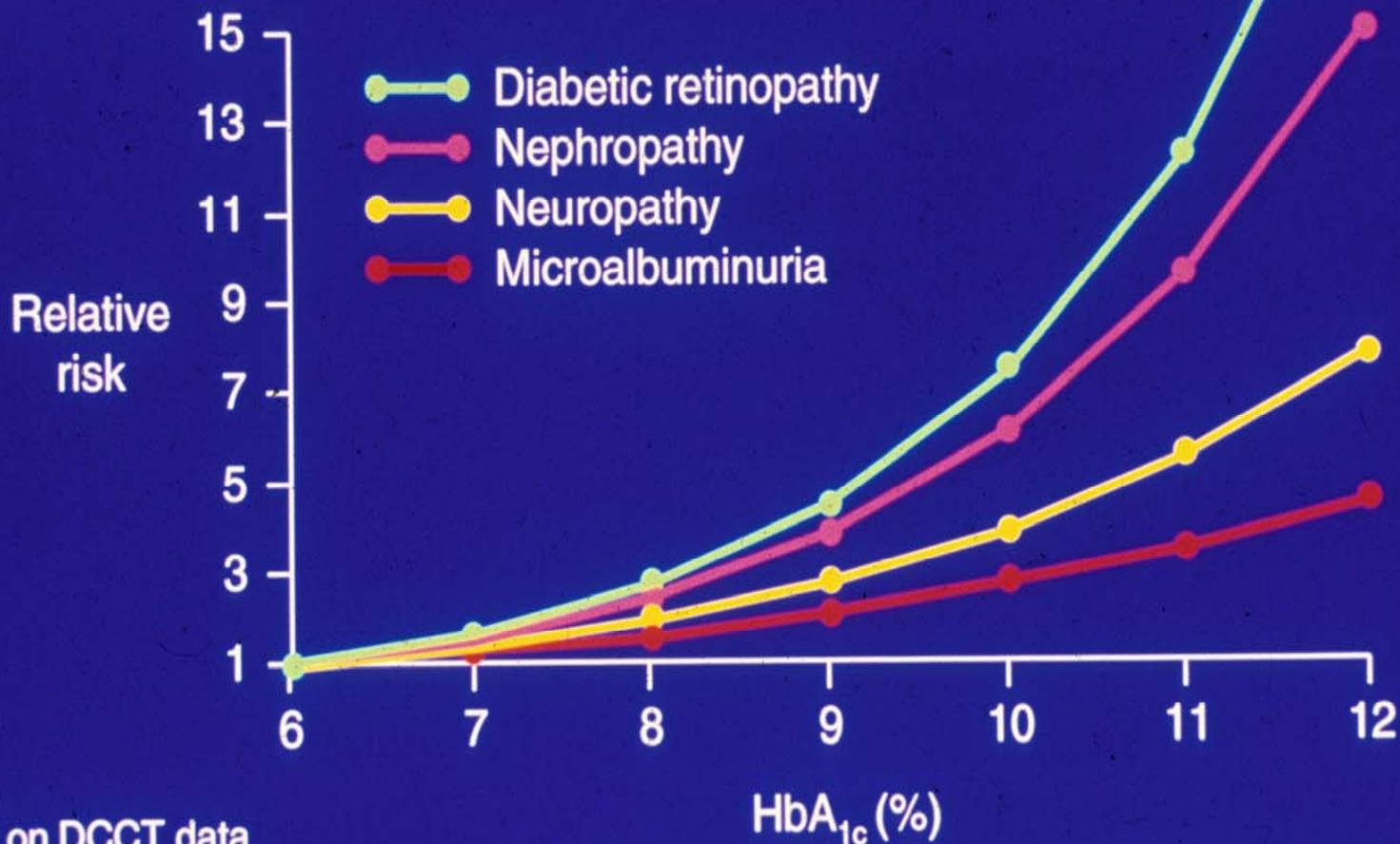
## Incidence of Diabetes



**PREVENT THE  
COMPLICATIONS**

# DCCT

## Relative risk of progression of diabetic complications by mean HbA<sub>1c</sub>\*



\*Based on DCCT data

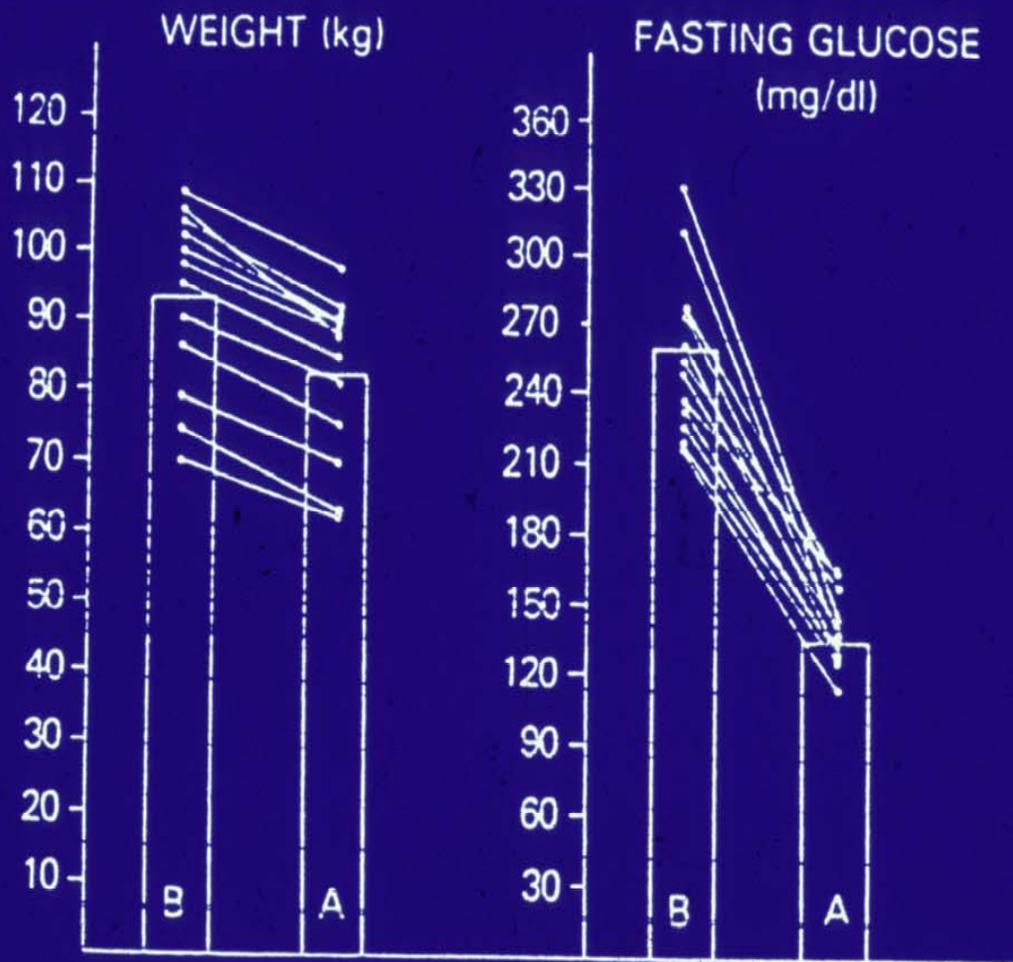
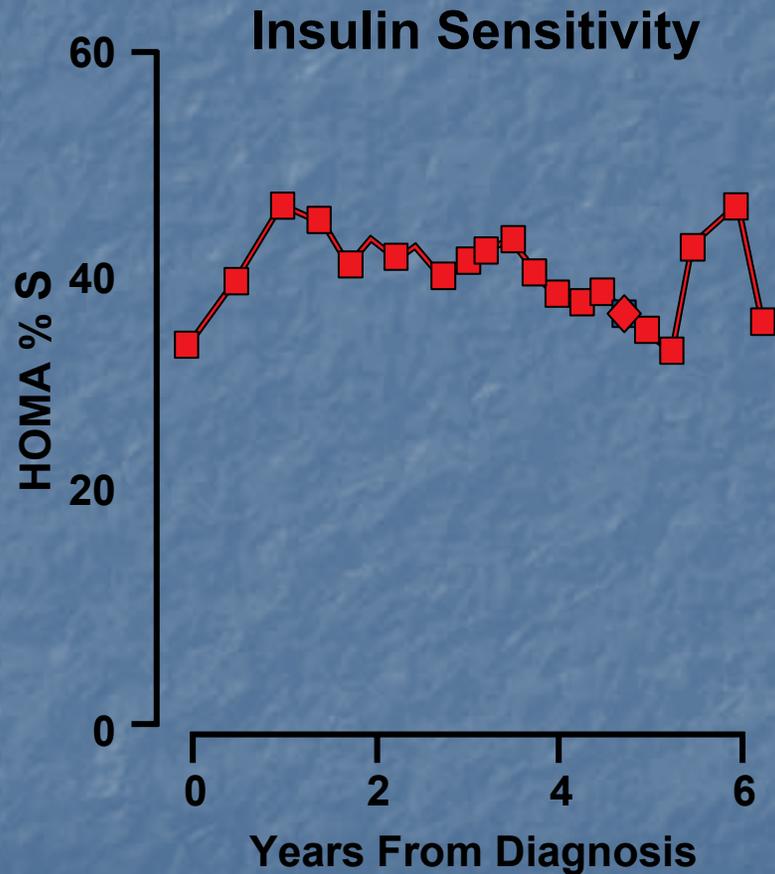
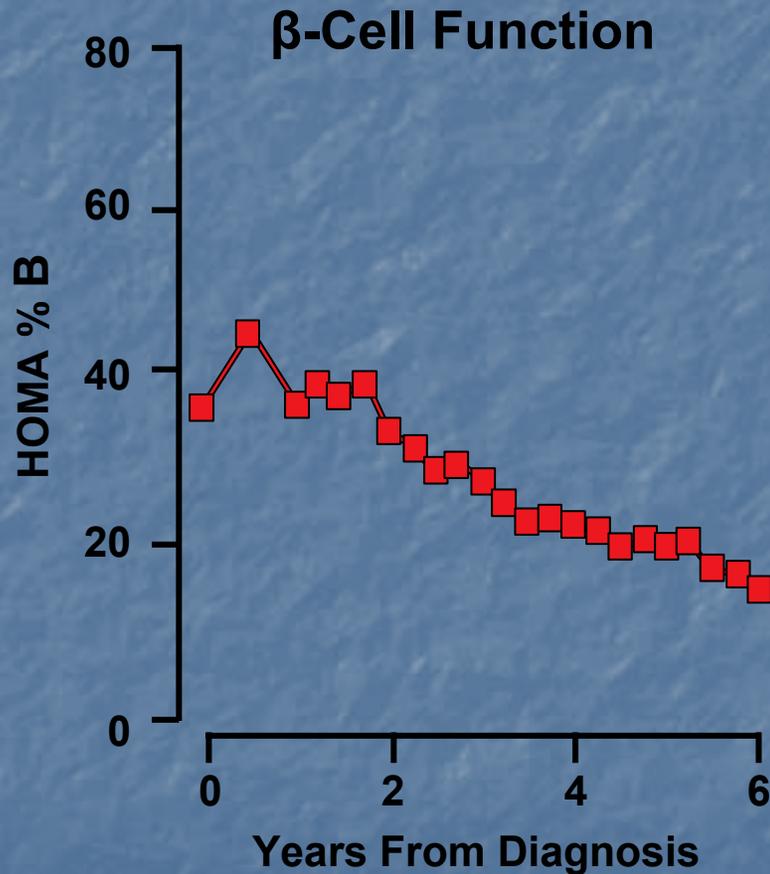


FIGURE 1. Body weights and fasting glucose concentrations of the 12 patients who completed the weight loss program, before (B) and after (A) the weight loss period. The data for each patient (means  $\pm$  SEM) are connected by lines, and the heights of the bars represent the means of the groups.

# $\beta$ -Cell Function Declines After Diagnosis, Whereas Insulin Sensitivity Remains Relatively Stable



HOMA=Homeostasis Model Assessment; HOMA % B= $\beta$ -cell function; HOMA % S=Insulin sensitivity.  
N=432. 10-year follow-up of the Belfast Diet Study. Data from Group 2 shown: newly diagnosed T2DM subjects who required additional treatment (due to secondary failure to diet therapy) at 5–7 years.  
Reproduced with permission from Levy J et al. *Diabet Med.* 1998;15:290–296. © 1998 Blackwell Publishing.

# TREATMENTS

Diet (weight loss)

Exercise

Oral drugs

sulfonylureas      thiazolidinediones

glinides              alpha-glucosidase inhibitors

biguanides          DPP-IV inhibitors

Injectables

insulin (also inhaled)

GLP-1 analogues

IT IS ESTIMATED THAT  
ONE IN THREE CHILDREN  
BORN IN THE UNITED  
STATES TODAY WILL  
DEVELOP DIABETES IN  
THEIR LIFETIME !!!

African-Americans – 1 in 2

Latinos - ????? (probably  
similar)

# **FINAL MESSAGE**

**SO – GOOD LUCK IN DOING  
WHAT YOU NOW KNOW WHAT  
YOU HAVE TO DO TO  
PREVENT YOURSELF FROM  
GETTING DIABETES!**

**SPREAD THE WORD!**

**THANK YOU**