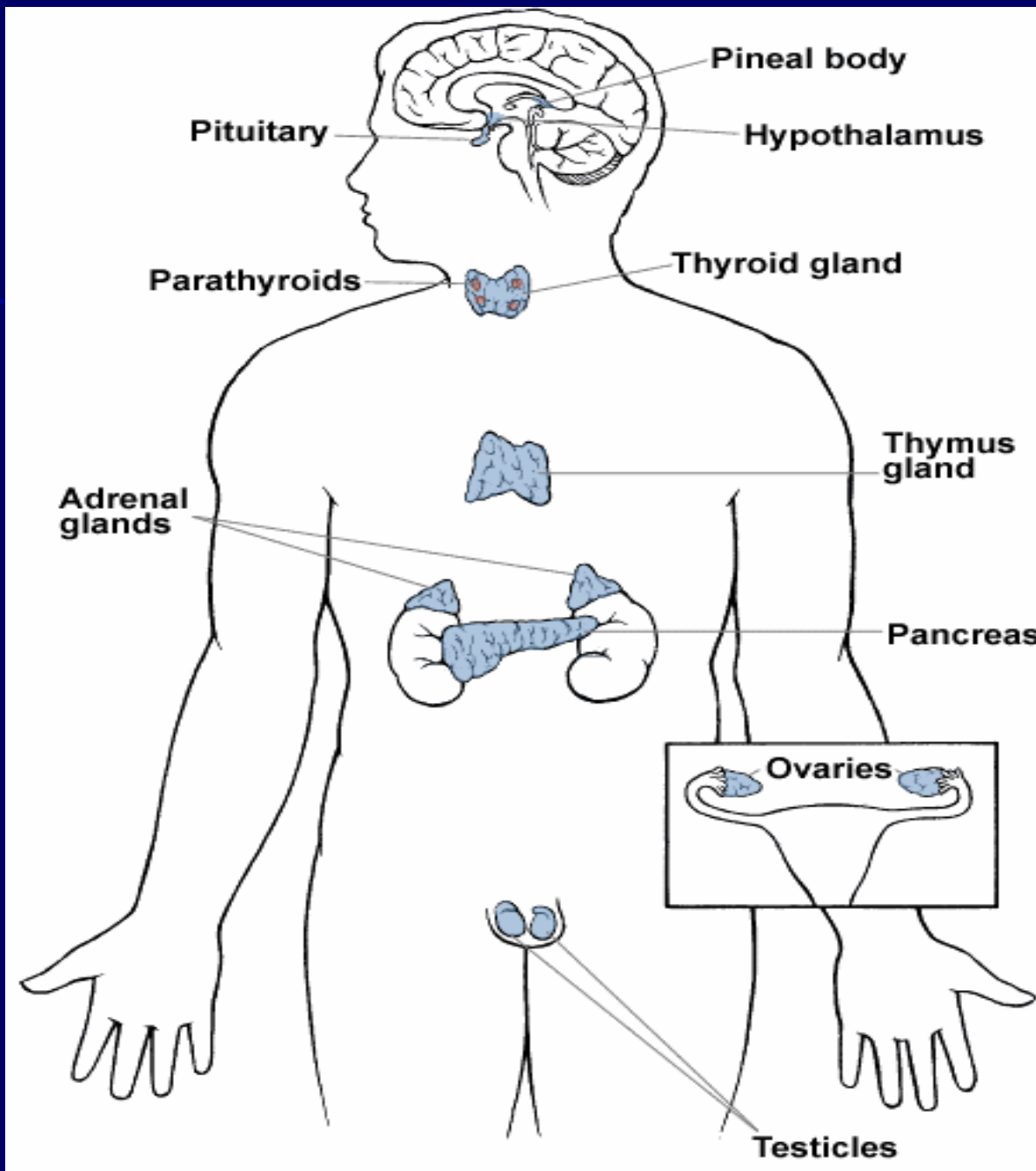
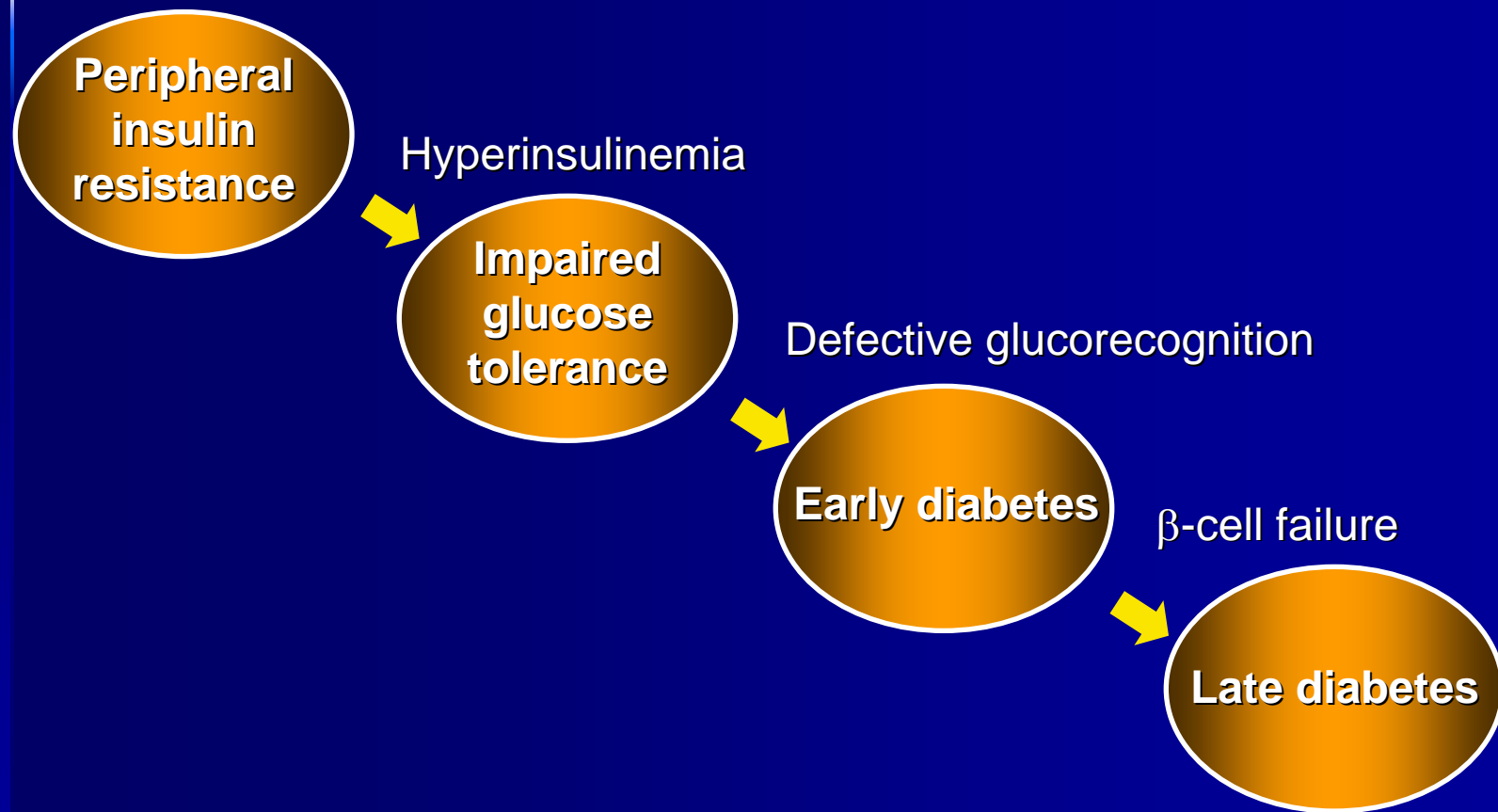


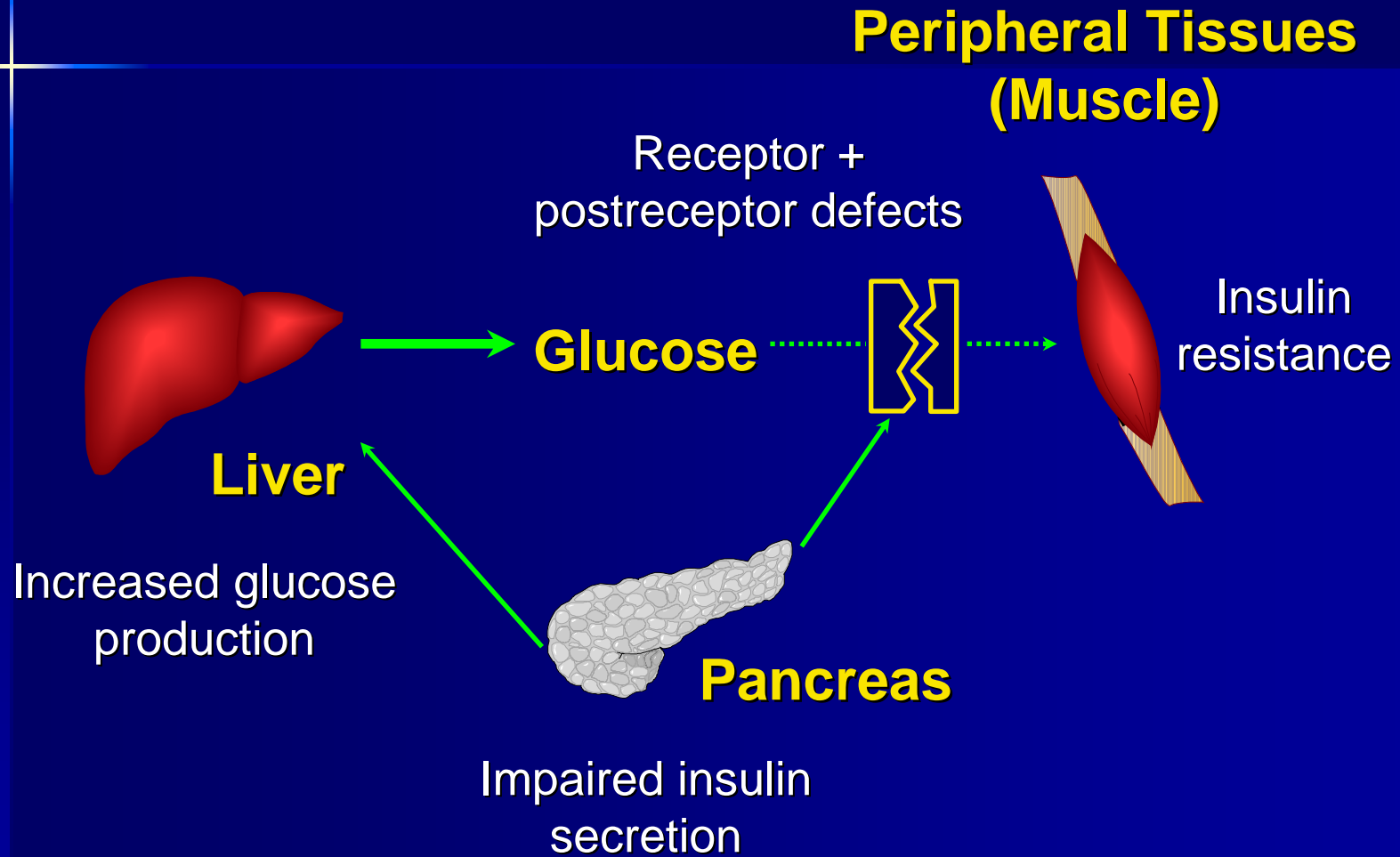
County of Riverside
Noontime Health Lecture
Diabetes type 2

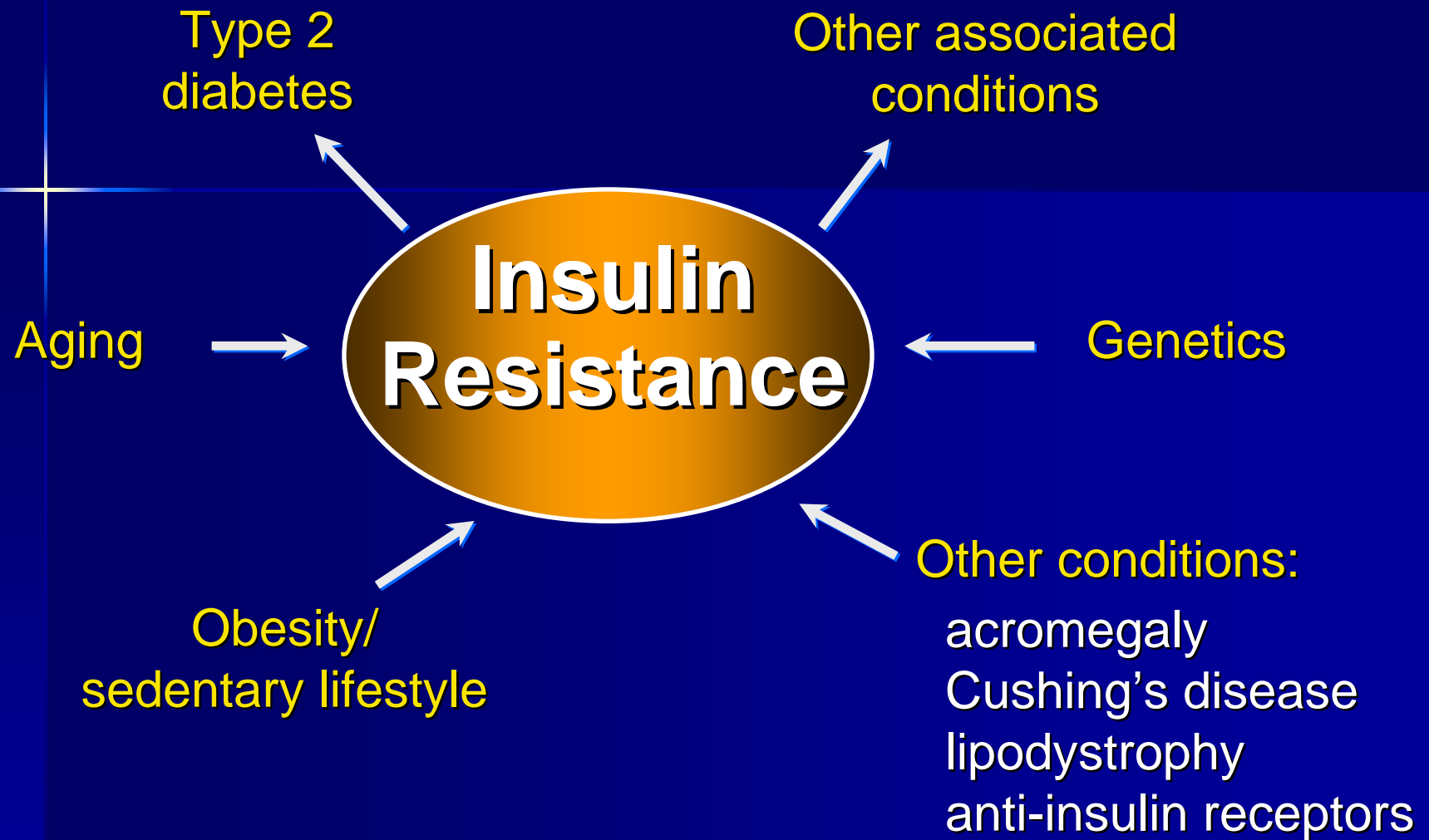


Metabolic Staging of Type 2 Diabetes



Pathophysiology of Type 2 Diabetes





Olefsky JM. In: *Endocrinology*. 2nd ed. 1989:1369-1388.
Reaven GM. *Clinical Diabetes*. 1994;12:32-36.
Seely BL, Olefsky JM. In: *Insulin Resistance*. 1993:187-252.

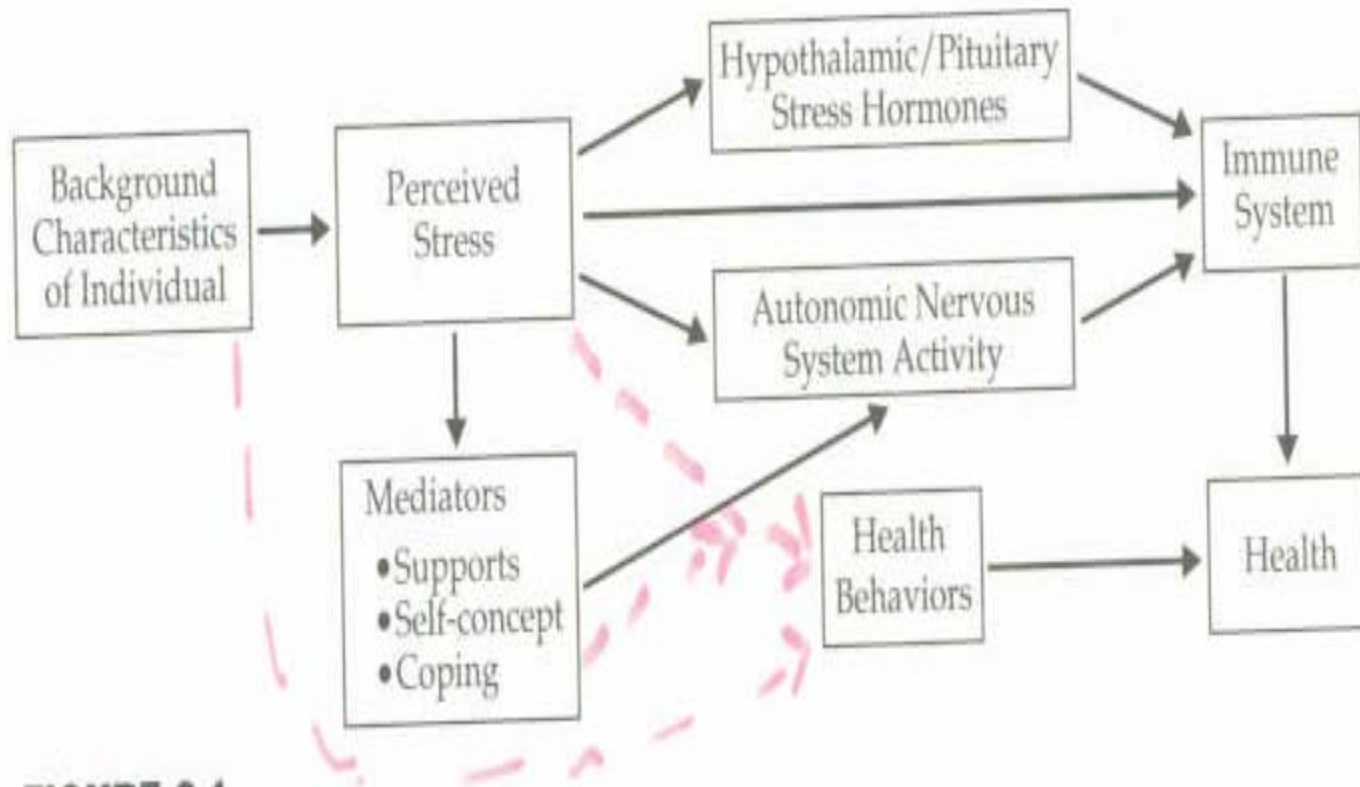


FIGURE 6-1
Biopsychosocial stress model.

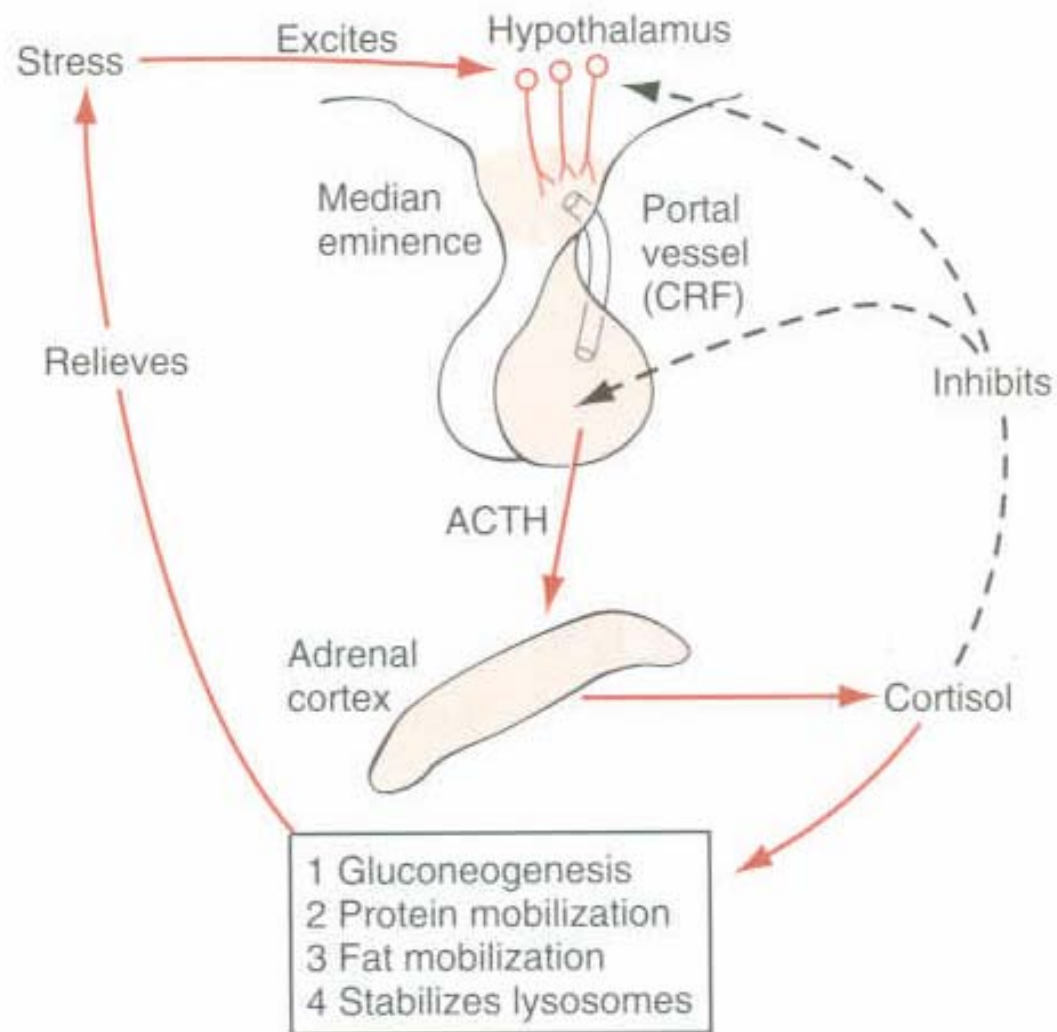


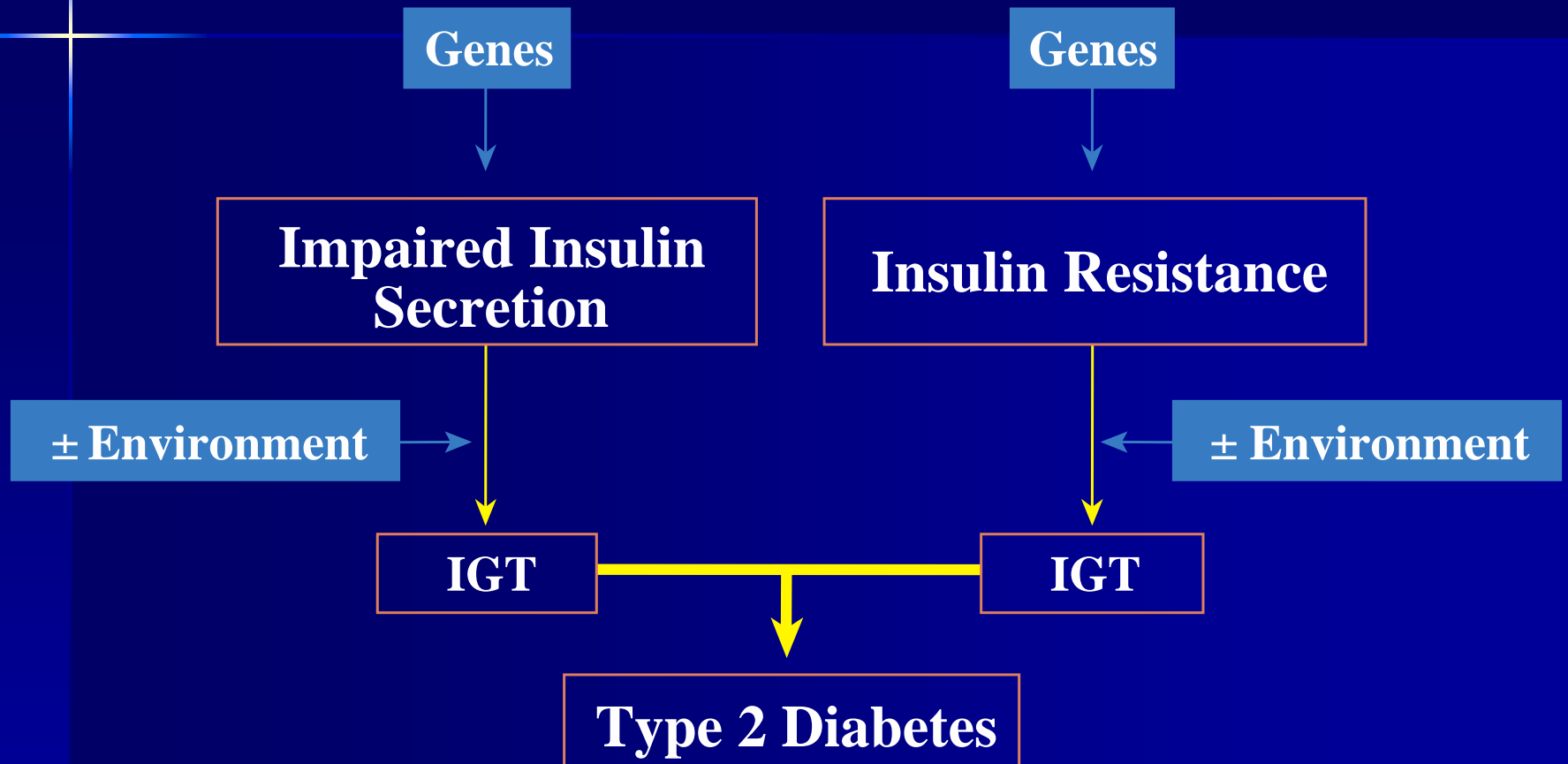
FIGURE 77-6

Mechanism for regulation of glucocorticoid secretion. ACTH, adrenocorticotropic hormone; CRF, corticotropin-releasing factor.

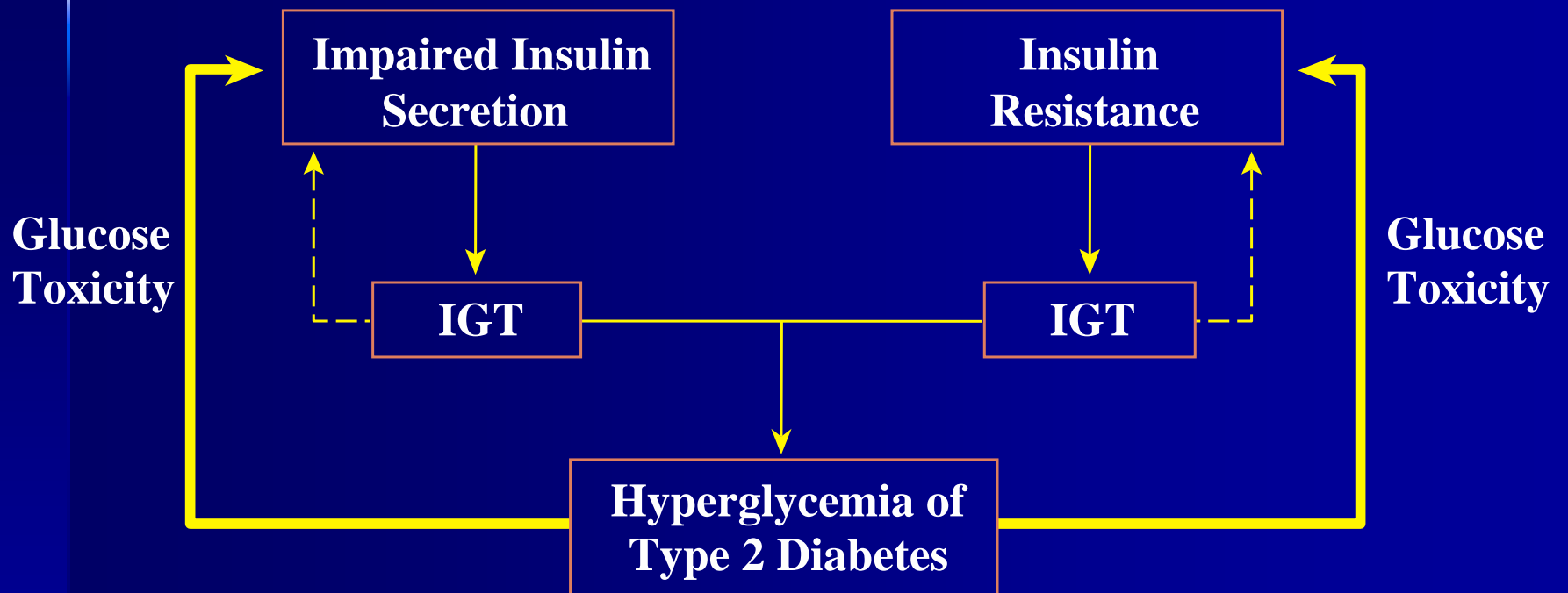
Insulin Resistance: Definition

- Condition in which greater than normal amounts of insulin are required to produce a normal biological response

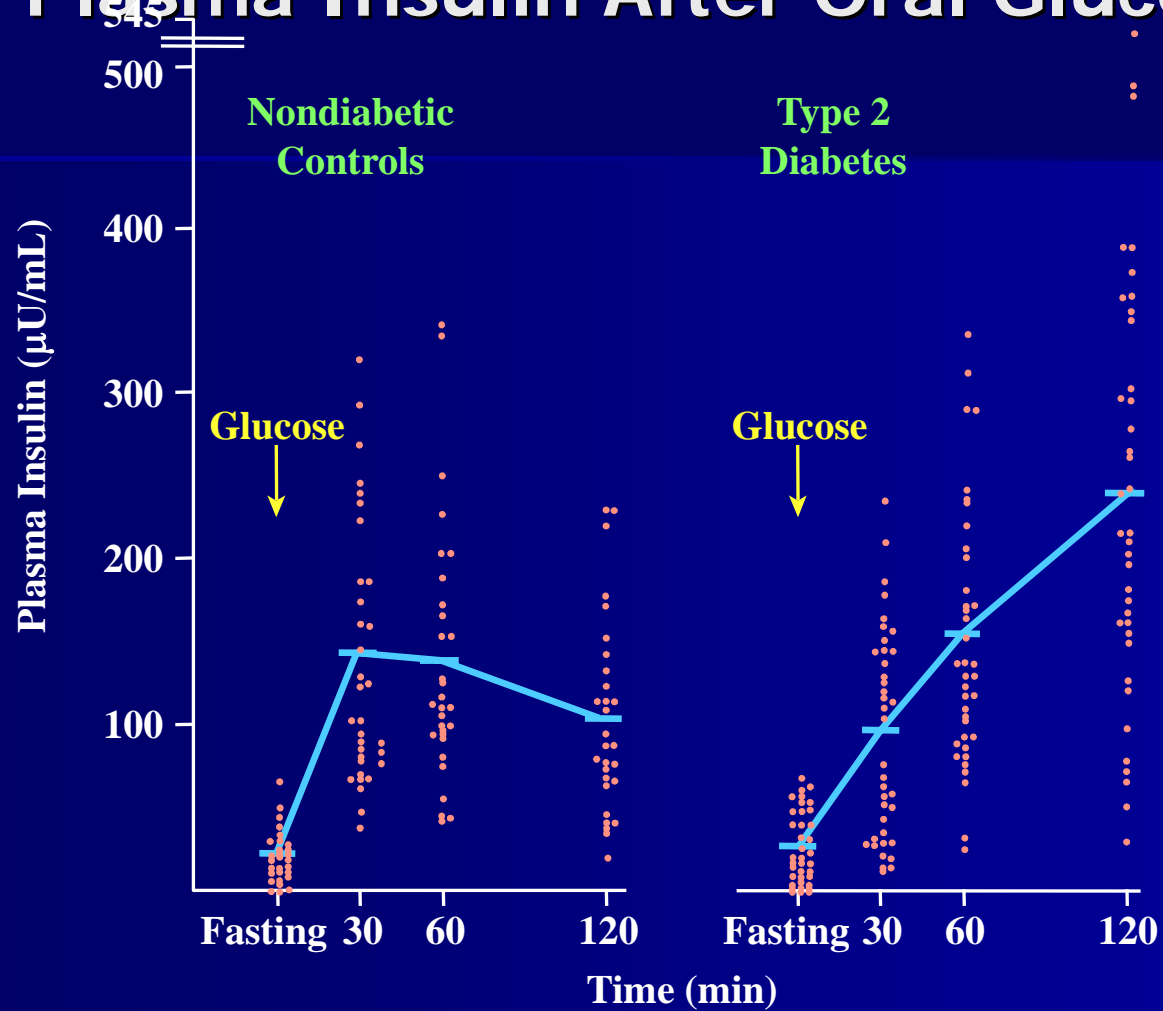
Type 2 Diabetes: Two Defects



Type 2 Diabetes: Role of Glucose Toxicity

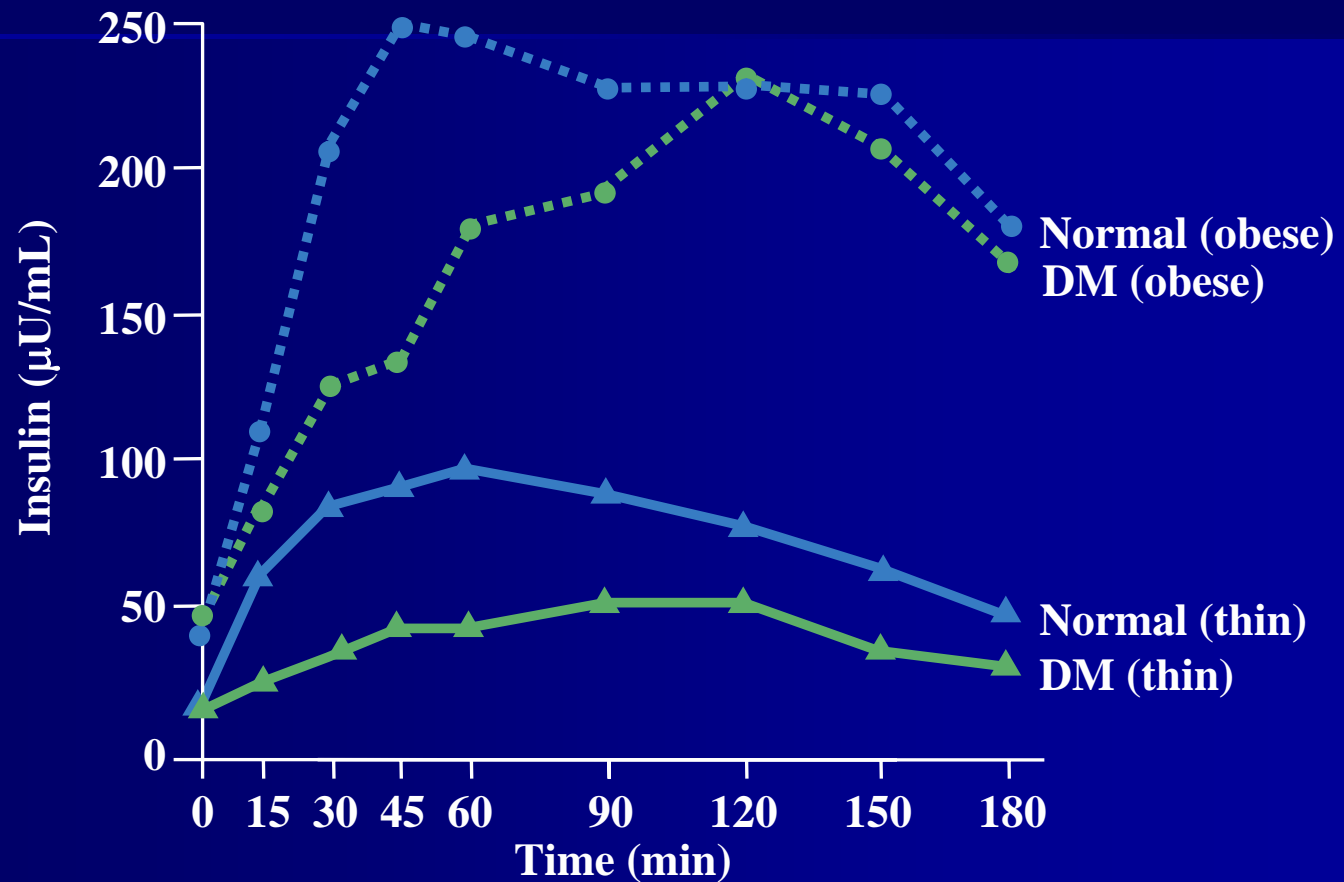


Plasma Insulin After Oral Glucose



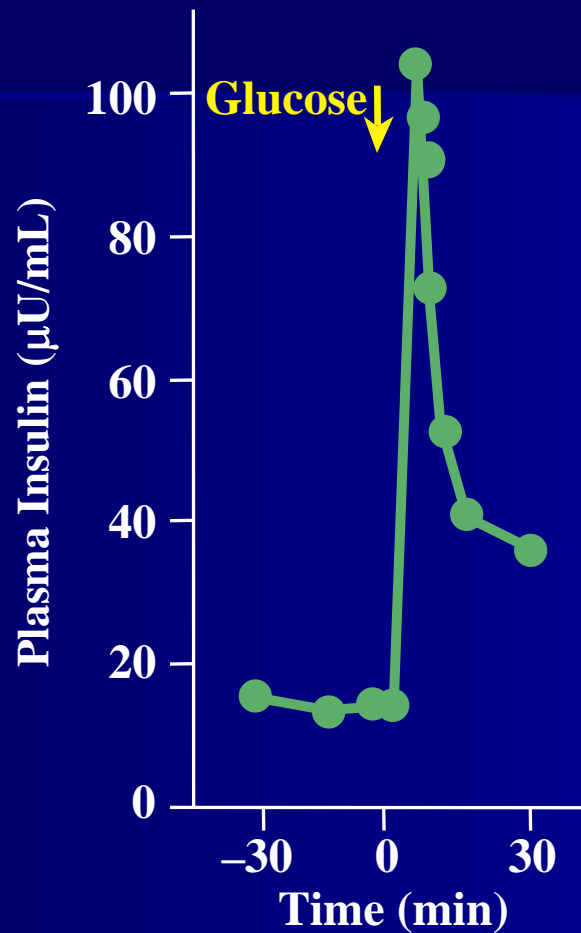
Adapted from Yalow & Berson. *J Clin Invest.* 1960;39:1157-1175, with permission.

Plasma Insulin After Glucose: Effects of Obesity and Diabetes



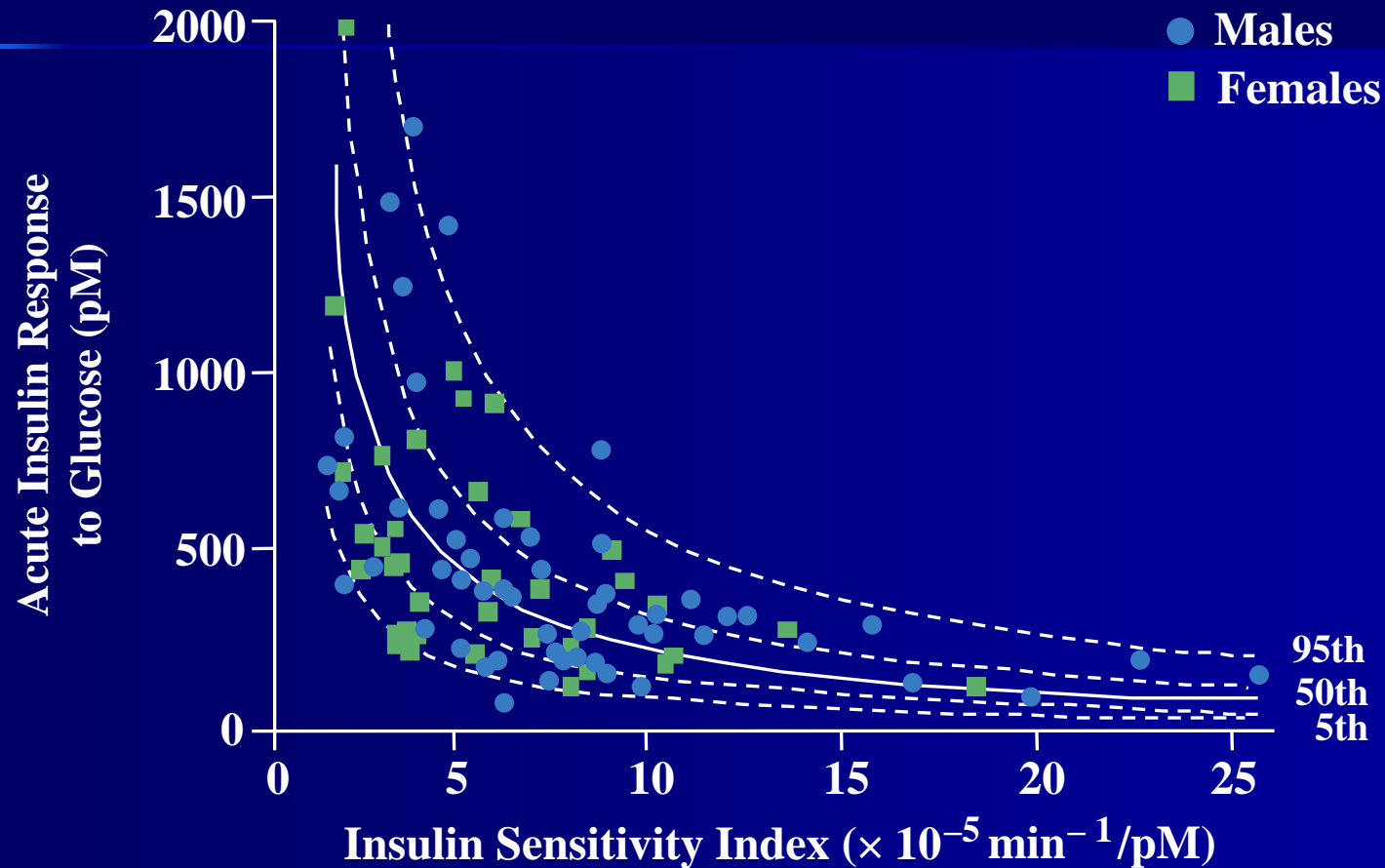
Bagdade, et al. *J Clin Invest.* 1967;46:1549-1557, with permission.

Acute Insulin Response to IV Glucose: Normal Subjects



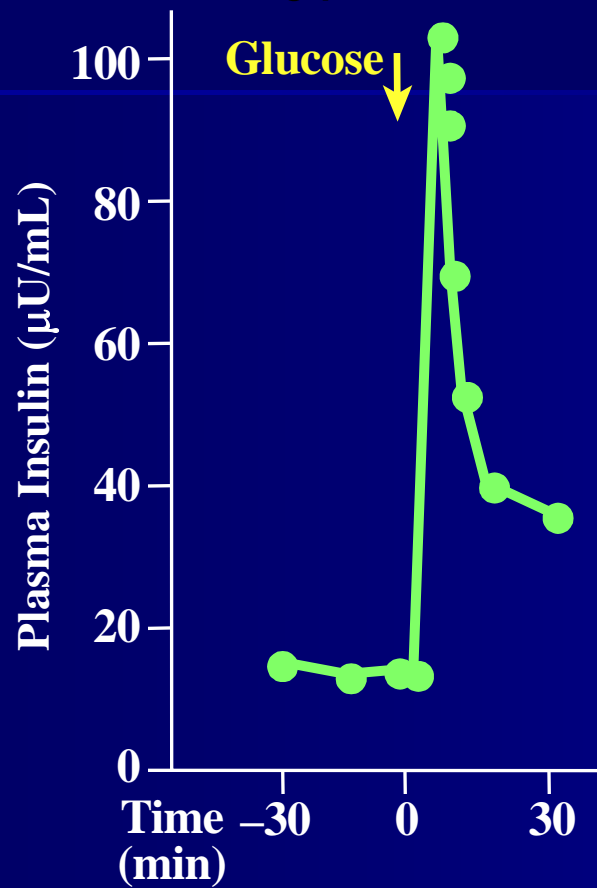
Adapted from Robertson & Porte. *J Clin Invest.* 1973;52:870-876, with permission.

Insulin Secretion: Modulation by Insulin Sensitivity

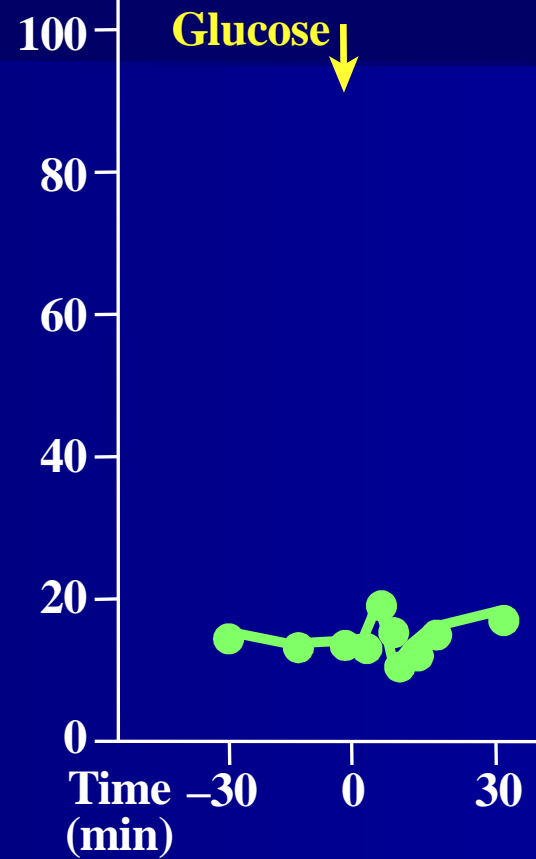


Adapted from Kahn, et al. *Diabetes*. 1993;42:1663-1672, with permission.

Acute Insulin Response to IV Glucose: Normal and Type 2 Diabetic Subjects



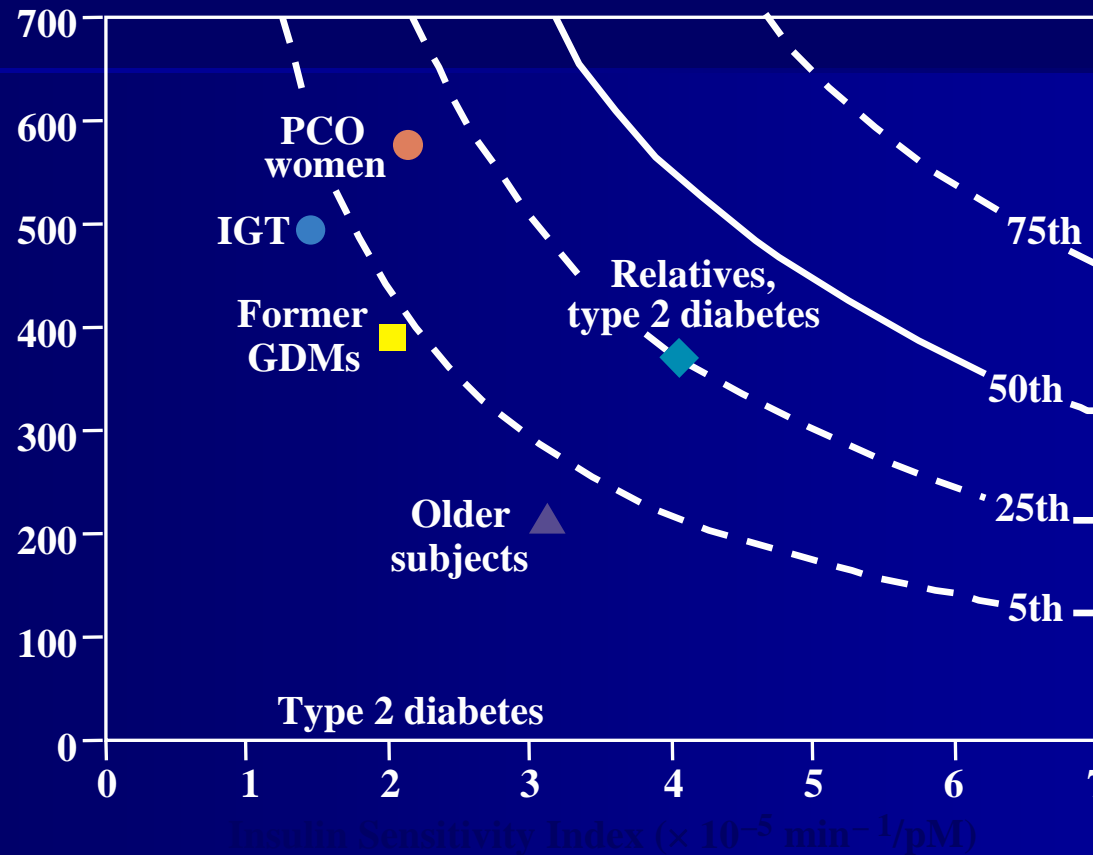
Normal



Type 2 Diabetes

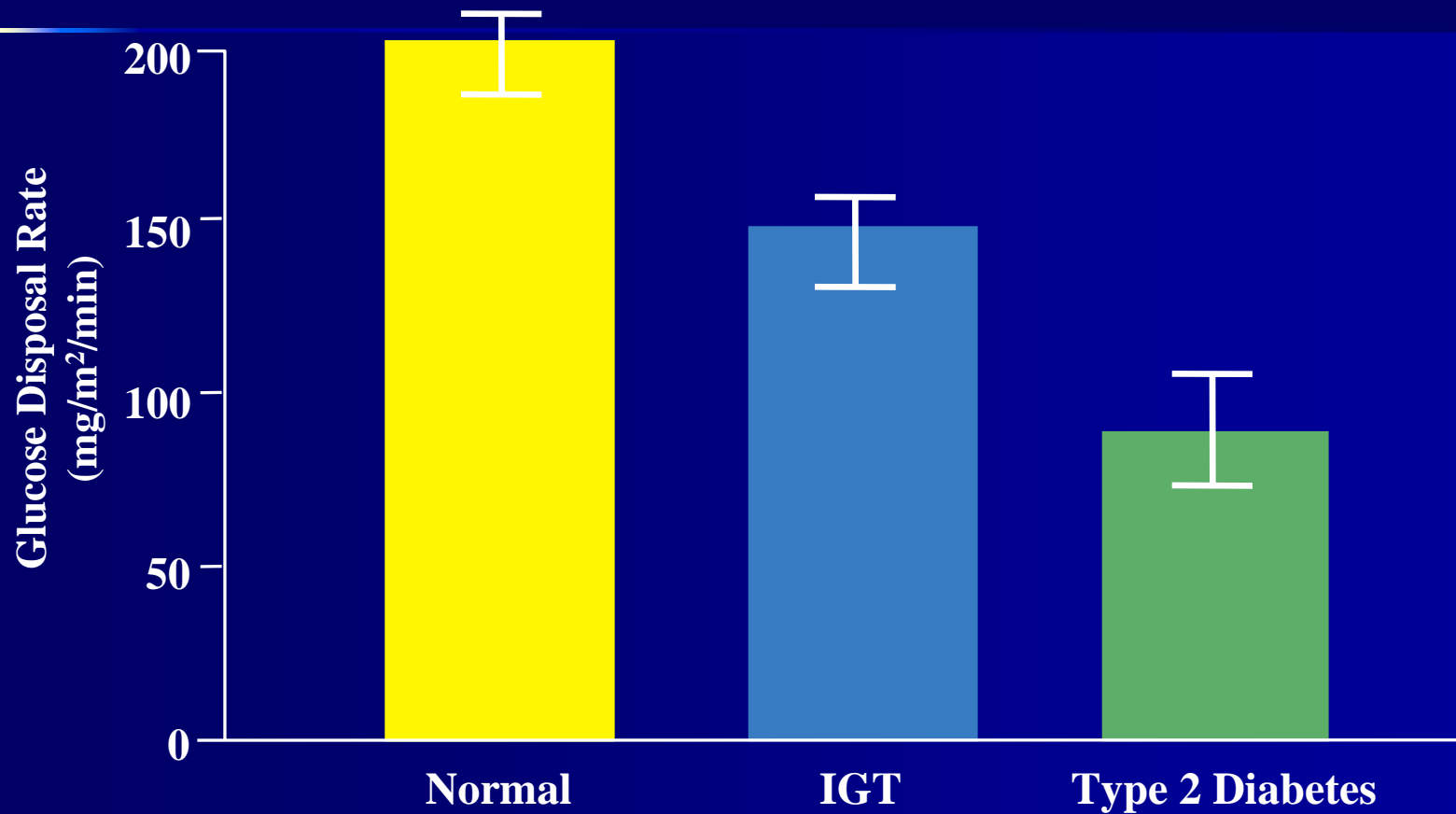
Adapted from Robertson & Porte. *J Clin Invest.* 1973;52:870-876, with permission.

Insulin Sensitivity & Insulin Secretion: Relationship in Type 2 Diabetes & Groups at High Risk



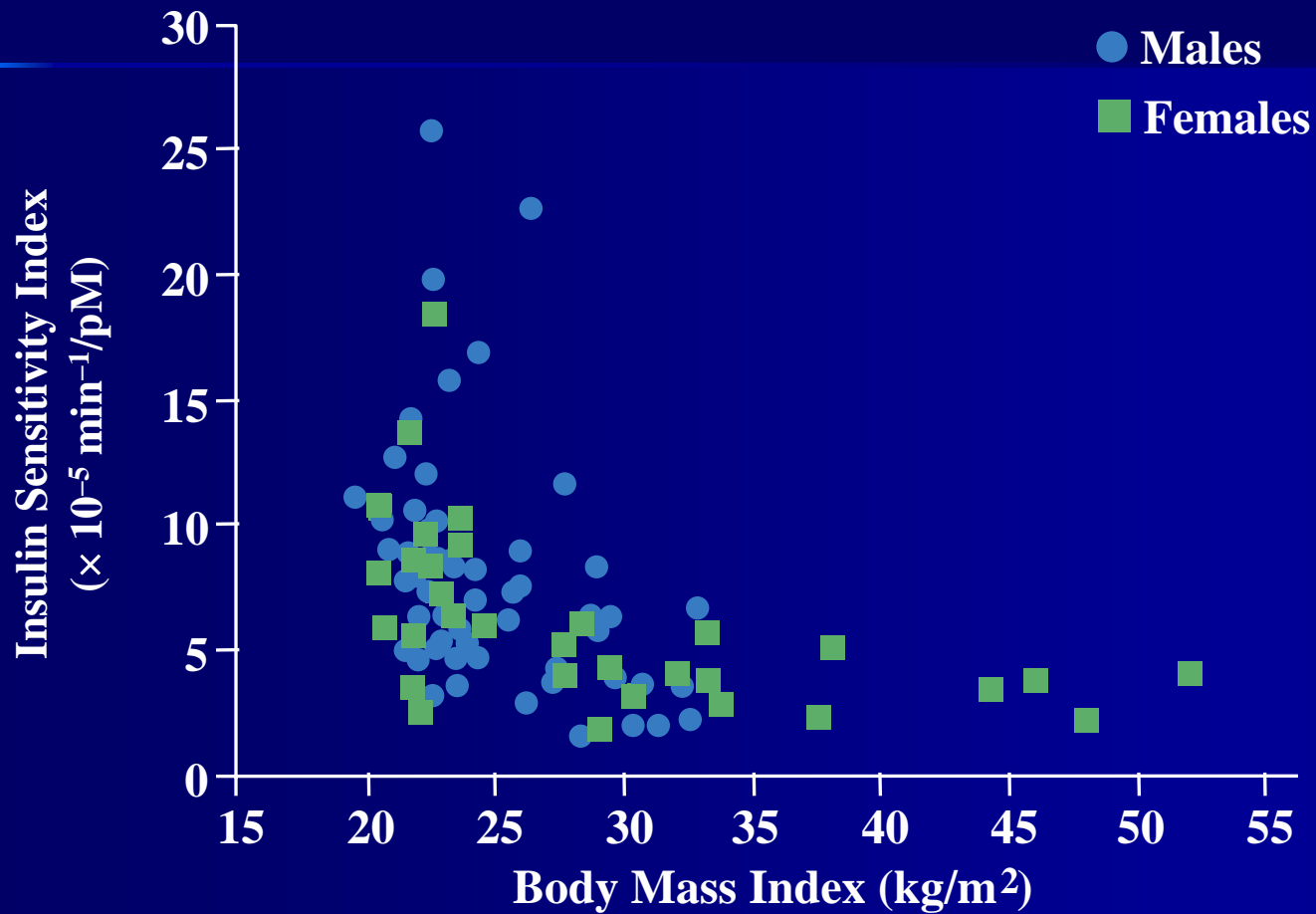
Adapted from Kahn, et al. *Diabetes*. 1993;42:1663-1672; Ward, et al. *Diabetes*. 1985;34:861-869; Kahn, et al. *Am J Physiol*. 1990; 258:E937-E943; Welch, et al. *J Clin Endocrinol Metab*. 1990;71:1508-1518; Ehrmann, et al. *J Clin Invest*. 1995;96:520-527; Cavaghan, et al. *J Clin Invest*. 1997;100:530-537.

Insulin Resistance in IGT & Diabetes: Glucose Disposal Rates at Identical Plasma Insulin Levels



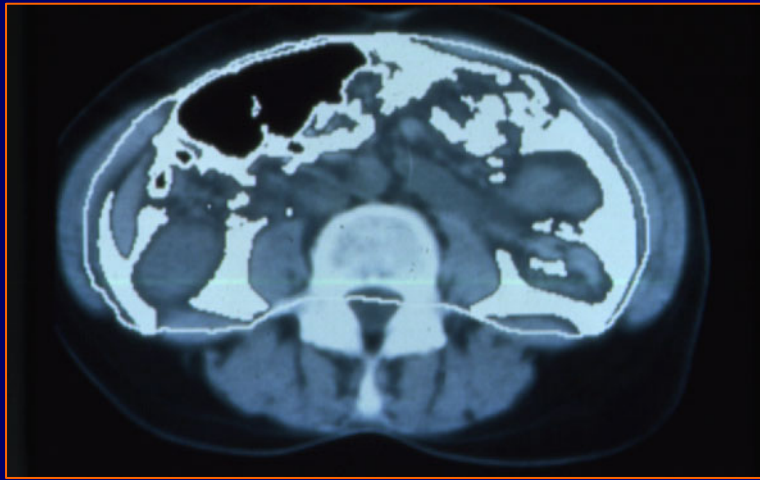
Kolterman, et al. *J Clin Invest.* 1981;68:957-969.

Body Size: Relationship to Insulin Sensitivity

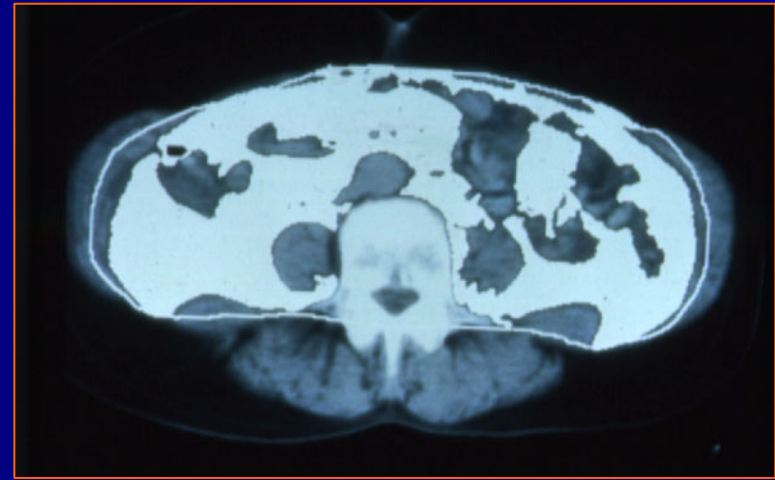


Adapted from Kahn, et al. *Diabetes*. 1993;42:1663-1672.

Visceral Fat Distribution: Normal vs Type 2 Diabetes

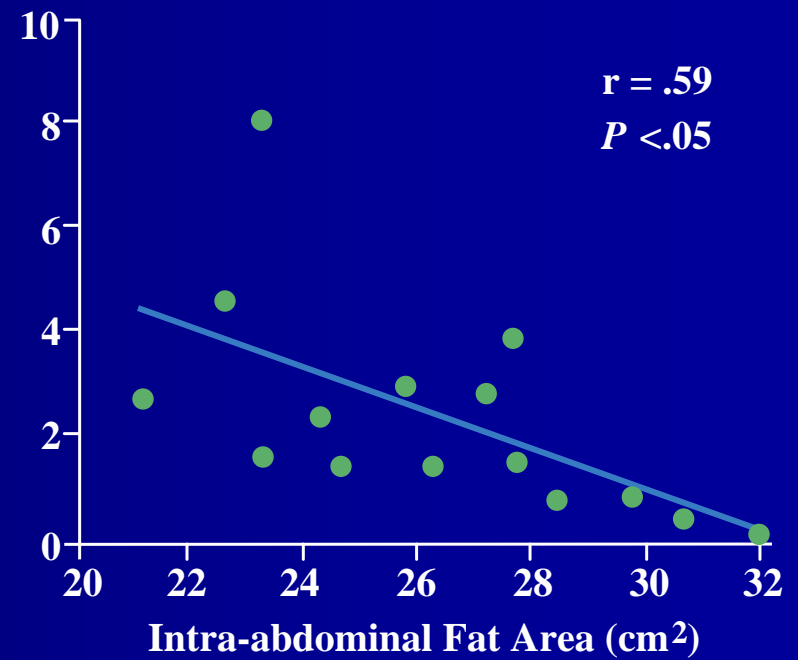
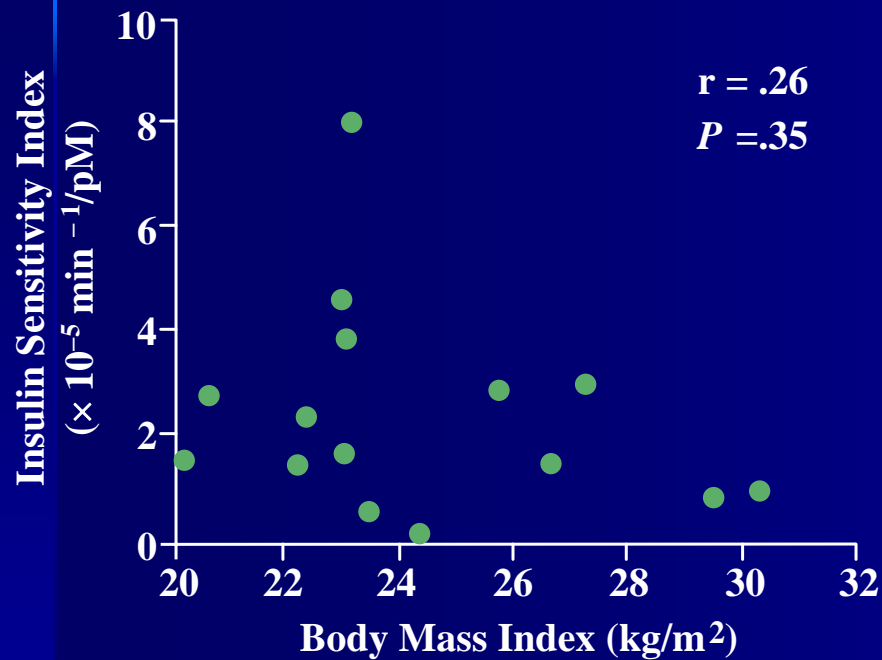


Normal



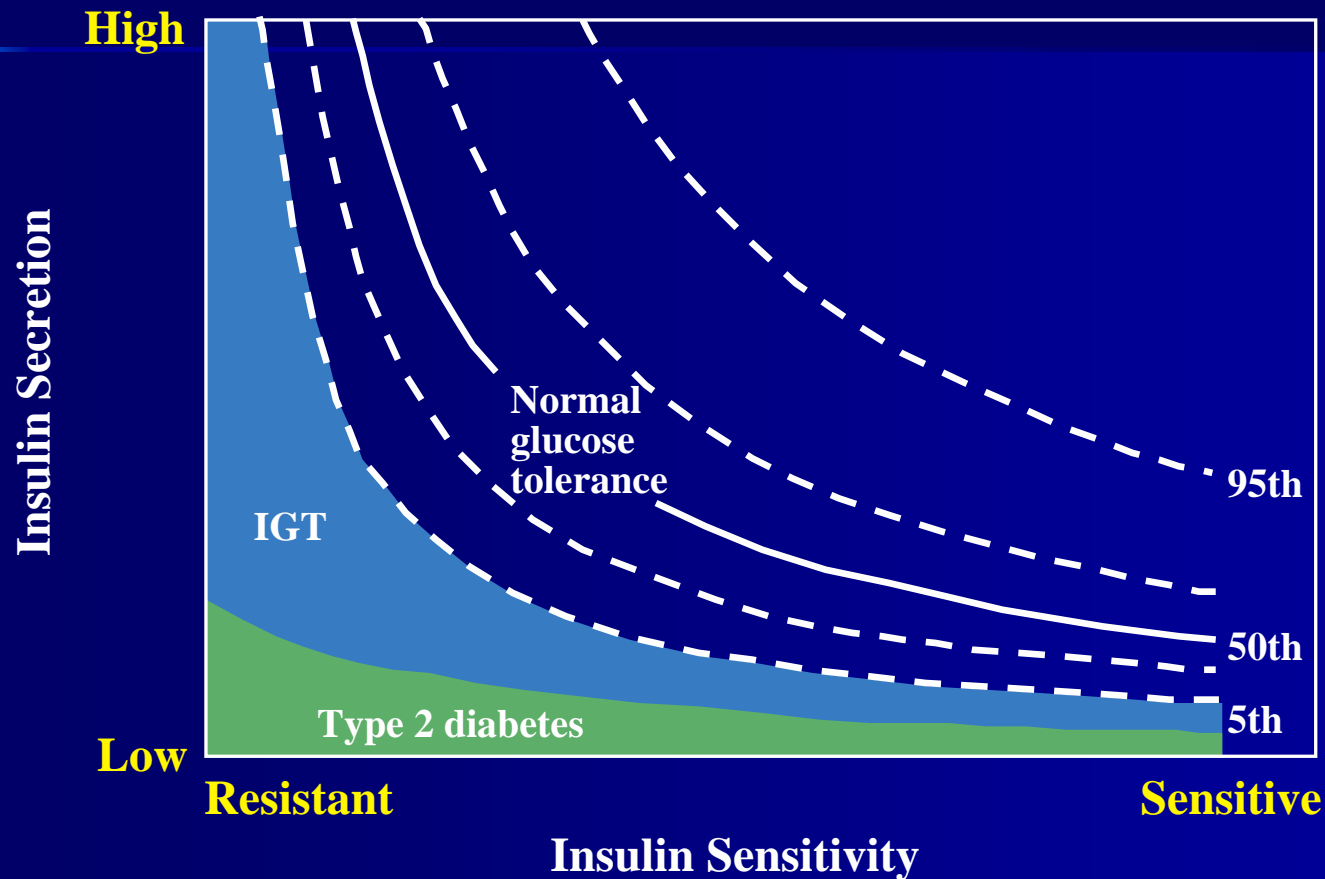
Type 2 Diabetes

Insulin Sensitivity: Relationship to Body Size and Intra-abdominal Fat



Data from Fujimoto, et al. *Obes Res.* 1994;2:364-371.

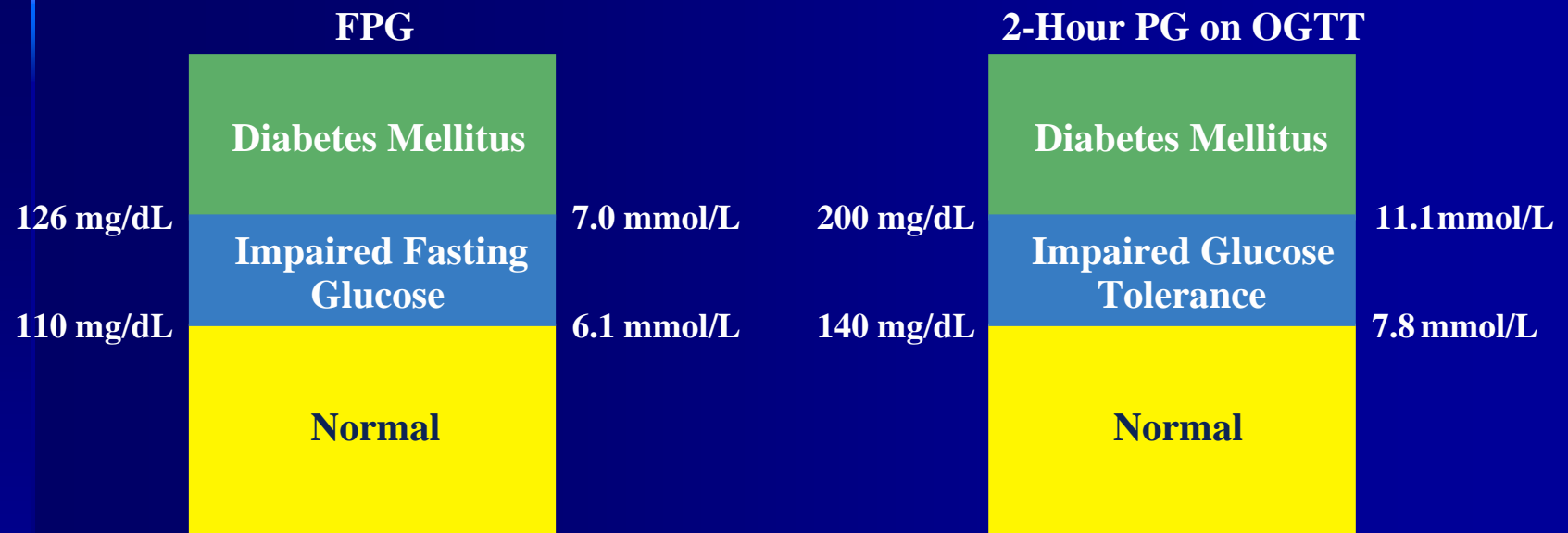
Glucose Tolerance Categories: Hypothetical Relationship Between Insulin Sensitivity & Insulin Secretion



Adapted from Kahn, et al. *Diabetes*. 1993;42:1663-1672, with permission.

Classification of Diabetes Mellitus

Glucose Tolerance Categories



Adapted from The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care*. 1997;20:1183-1197.

ADA Targets for Glycemic Control and Recommended Action Levels

■ Biochemical Index	Goal	Action Suggested
FPG (preprandial), mg/dL	80 – 120	>140
Bedtime glucose, mg/dL	100 – 140	>160
HbA _{1c} , %	<7	>8

Values are for nonpregnant individuals

ADA. *Diabetes Care*. 1997;20(suppl 1):S5-S13.

Complications of Diabetes Mellitus

Causes of Death Among People With Diabetes

Cause	% of Deaths
Ischemic heart disease	40
Other heart disease	15
Diabetes (acute complications)	13
Cancer	13
Cerebrovascular disease	10
Pneumonia/influenza	4
All other causes	5

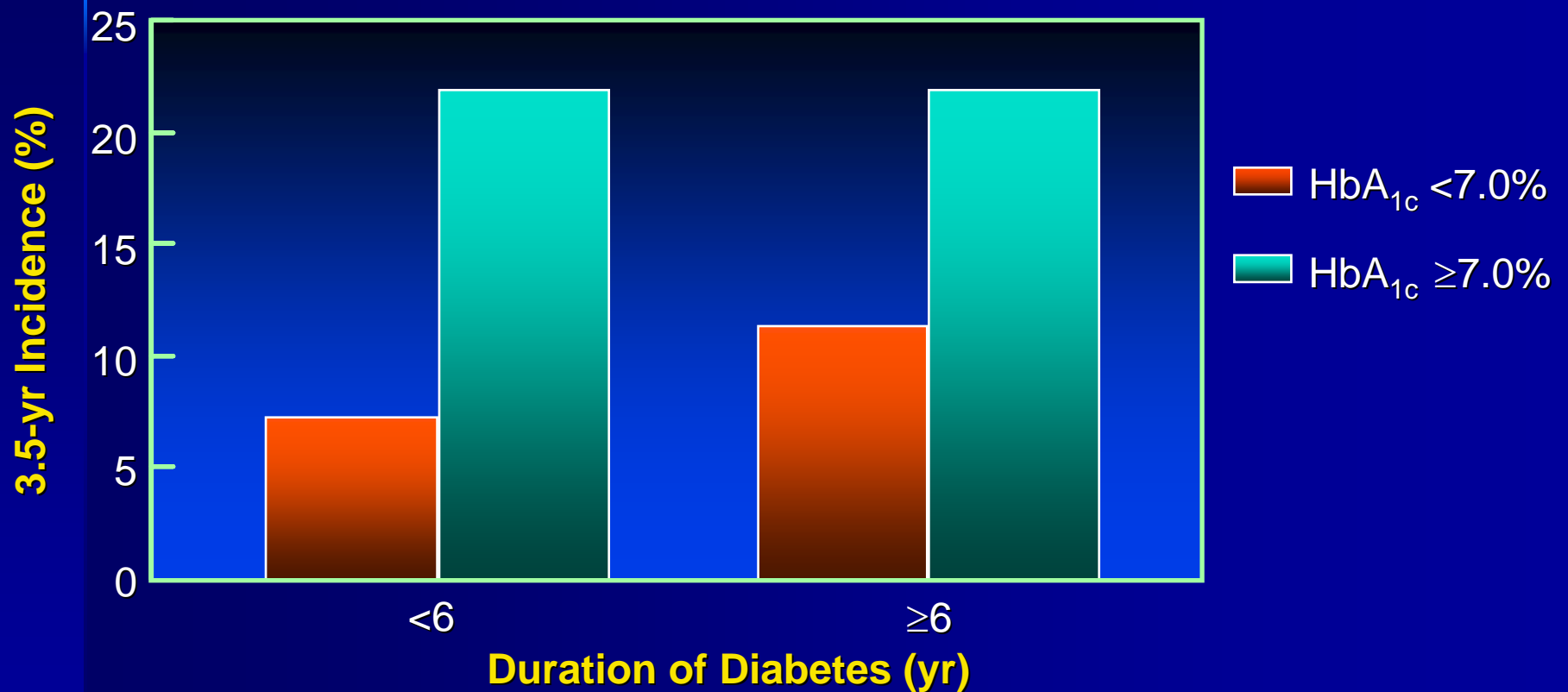
Geiss LS et al. In: *Diabetes in America*. 2nd ed. 1995:233-257.

Heart Disease and Stroke in Diabetes Patients

- Evidence of CHD in 7.5%–20% of diabetes patients >45 years old in the US
 - 55% of deaths in diabetes patients are caused by cardiovascular disease
- 5-year average cost of surviving acute MI: **>\$51,000**
- Stroke occurs 2X–4X more often in diabetes patients

Diabetes complications. In: *Diabetes 1996 Vital Statistics*. 1996:29-44.
National Diabetes Fact Sheet. November 1, 1997:1-8.
Wittels EH et al. *Am J Cardiol*. 1990;65:432-440.

Relationship Between Glycemic Control and Coronary Heart Disease Events in Type 2 Diabetes Patients (Ages 65 to 74)



Kuusisto J et al. *Diabetes*. 1994;43:960-967.

Kidney Disease in Diabetes Patients

- 27,851 new cases of ESRD in diabetes patients in 1995
 - 40% of all new cases in the US
- Nearly 99,000 diabetes patients required dialysis or kidney transplantation that year
- Annual cost of ESRD:
 - **\$45,000** in diabetic patients ages 45–64

Relationship Between Hyperglycemia and Nephropathy

- Diabetic nephropathy: persistent proteinuria (total excretion >500 mg/day), resulting in ESRD
 - 25% to 50% of diabetes cases
 - mortality from all causes in ESRD patients
20X to 40X higher than in those without renal dysfunction
- Preceded by microalbuminuria (protein excretion 30–300 mg/day)
 - 20X higher risk of nephropathy than in normoalbuminuric patients

Relationship Between Hyperglycemia and Neuropathy

- Slowly progressive disease preferentially affecting the long axons
- 30% to 40% of all diabetics are symptomatic
 - 60% have neuropathy (symptomatic or asymptomatic)
- Peripheral symptoms:
 - numbness/tingling in the feet, cramps, sensitivity/insensitivity to touch, loss of balance/coordination
- Autonomic symptoms:
 - urinary incontinence, loss of sexual response, gastric stasis, orthostatic hypotension
- Exact etiology unknown

Foot Ulcers and Amputations in Diabetes Patients

- >50% of lower limb amputations in the US
 - 67,000/yr (1993 –1995)
- Foot ulcers occur in 15% of diabetes patients over a lifetime
- Cost of diabetes-related amputation: **\$27,000**

Retinopathy and Blindness in Diabetes Patients

- It is estimated that retinopathy affects 80%–97% of patients with diabetes of ≥ 15 years' duration
- Diabetes is the leading cause of new cases of blindness in adults*
- Diabetic retinopathy accounts for the majority of these cases
- Minimum cost of blindness for working-age adult is estimated at \$12,769 per year

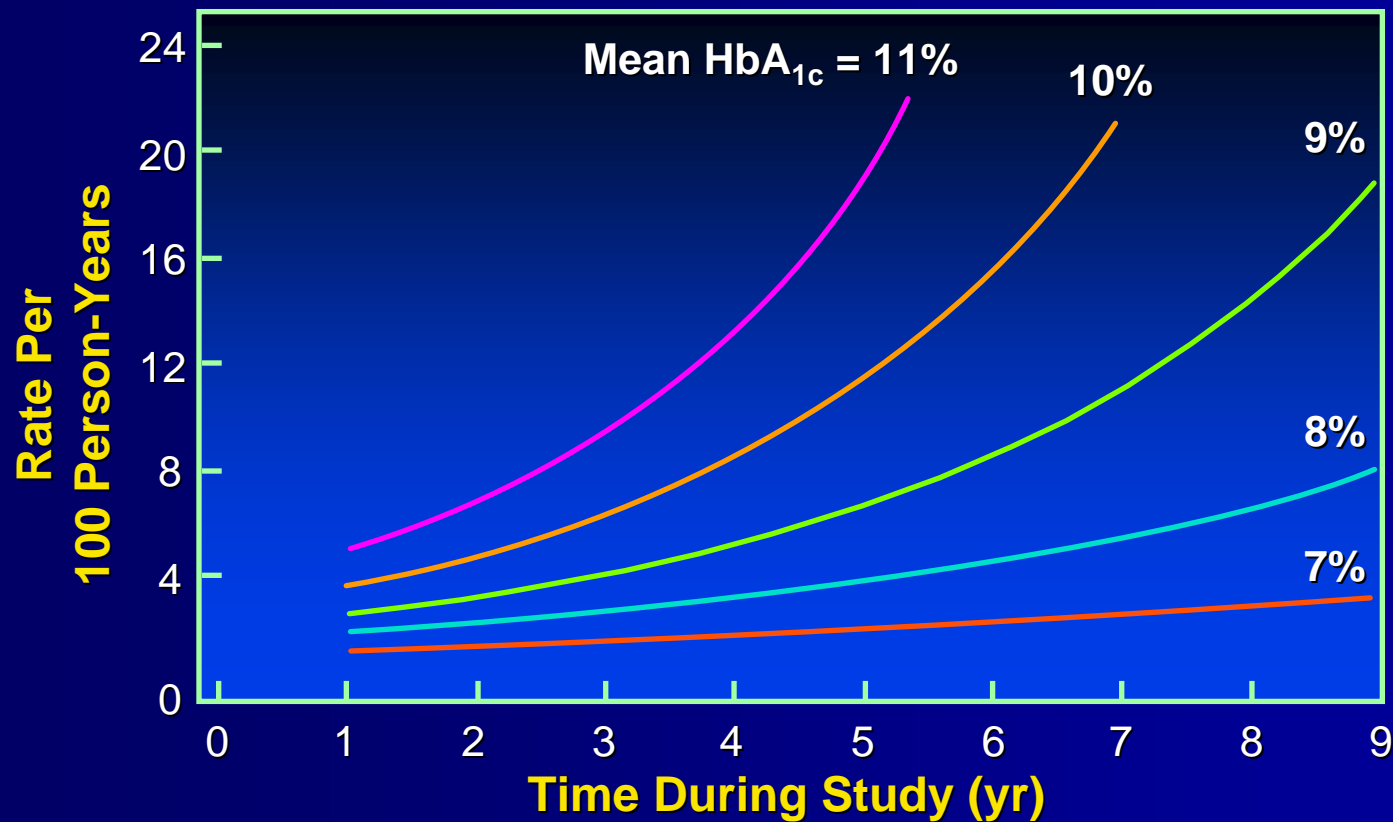
*Blindness is defined as visual acuity $\leq 20/200$

Klein R, Klein BEK. In: *Diabetes in America*. 2nd ed. 1995:293-338.

The Diabetes Control and Complications Trial (DCCT)

- Multicenter, randomized study of type 1 diabetes patients
- To assess effect of intensive glycemic control vs conventional therapy on:
 - development and progression of retinopathy and other long-term complications
- Results of this trial led to similar studies of type 2 diabetes patients

DCCT: Risk of Sustained Retinopathy Progression by HbA_{1c} Level and Years of Follow-up



DCCT Research Group. *Diabetes*. 1995;44:968-983.

Overall Results of the DCCT Trial

- Intensive control of blood glucose reduced risk of diabetic complications
 - retinopathy onset ↓76% in patients with no retinopathy at baseline ($P \leq 0.002$)
 - retinopathy progression ↓54% in patients with mild retinopathy at baseline ($P \leq 0.002$)
 - nephropathy ↓54% ($P < 0.04$)
 - neuropathy ↓60% ($P \leq 0.002$)
- There was, however, a 2- to 3-fold greater incidence of severe hypoglycemia