Diabetes Mellitus糖 尿 病

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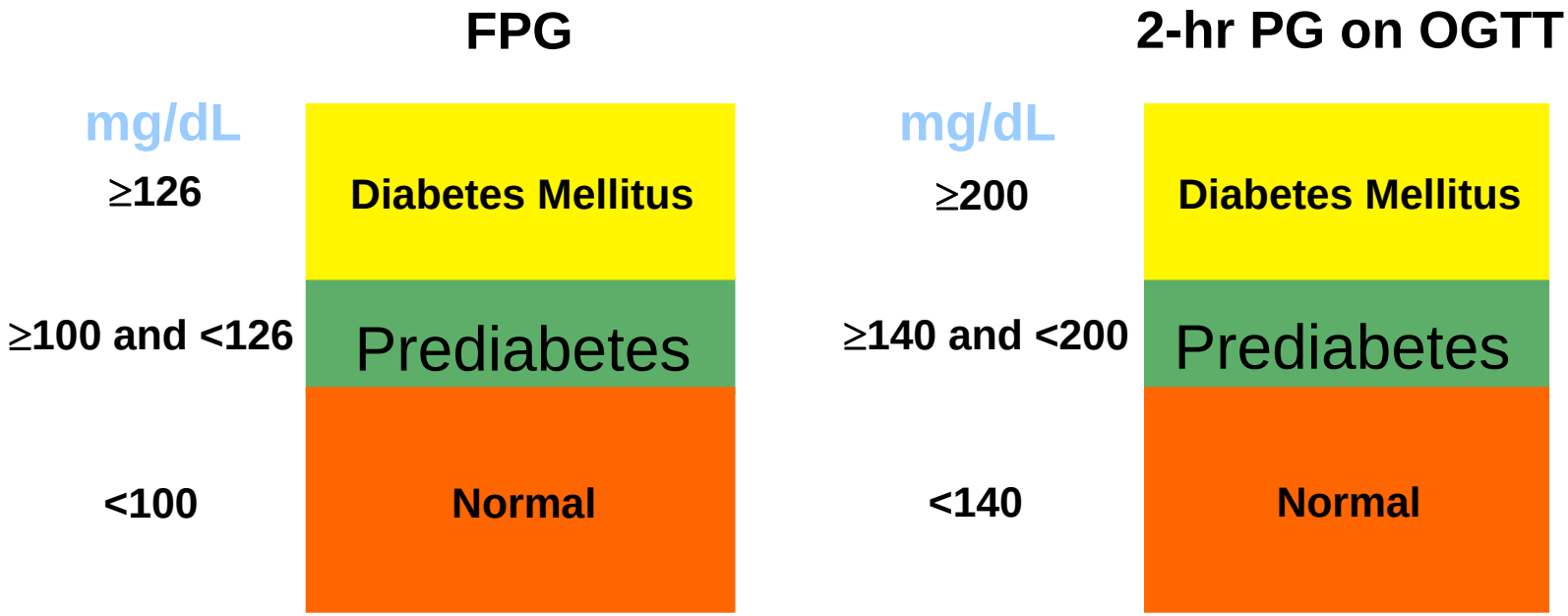
MD FRCP

Glucose Tolerance Categories



Etiologic Classification of Diabetes Mellitus

Type 1	β-cell destruction with lack of insulin
Type 2	Insulin resistance with insulin deficiency
Other specific	Genetic defects in β-cell Types exocrine pancreas diseases, drug- or chemical-induced, and other rare forms
Gestational	Insulin resistance with β-cell dysfunction

GLOBAL PROJECTIONS FOR THE DIABETES EPIDEMIC: 2003-2025 (millions)

World
2003 = 194 million
2025 = 333 million
Increase 72%

Diabetes Today: An Epidemic

- 20.8 million Americans have diabetes
- 1.5 million new cases in 2005 more than 3500 each day
- Complications of diabetes are a major cause of mortality and morbidity (2002 statistics)

90% of patients with diabetes are treated by primary care physicians

ADA National Diabetes Fact Sheet. Available at: http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2005.pdf. Accessed April 11, 2005; ADA Diabetes Statistics. Available at http://www.diabetes.org/utils/printthispage.jsp?PageID=STATISTICS_233181. December 29, 2005.

The Problem

Modern Life Has Both Conveniences and Costs

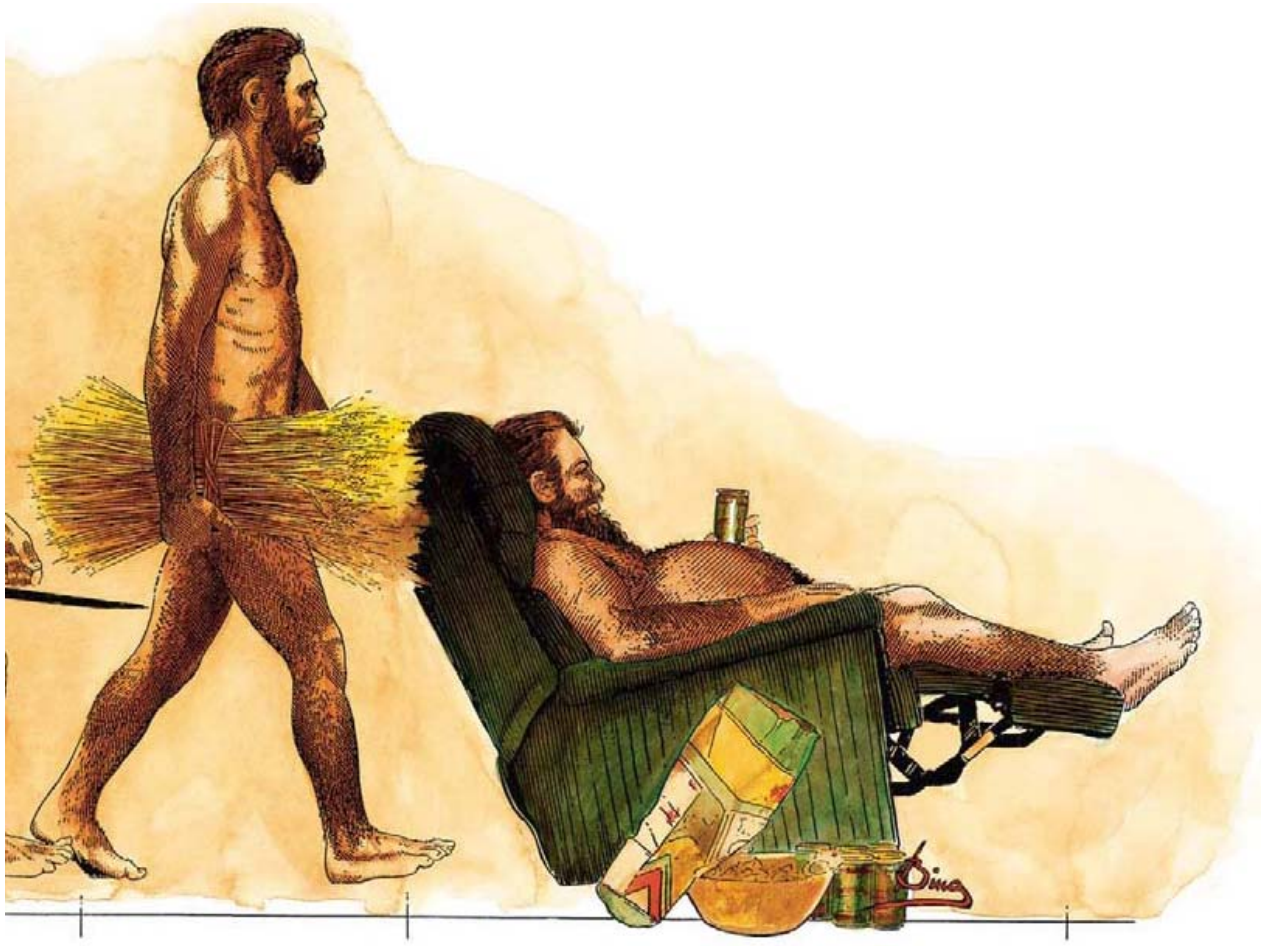
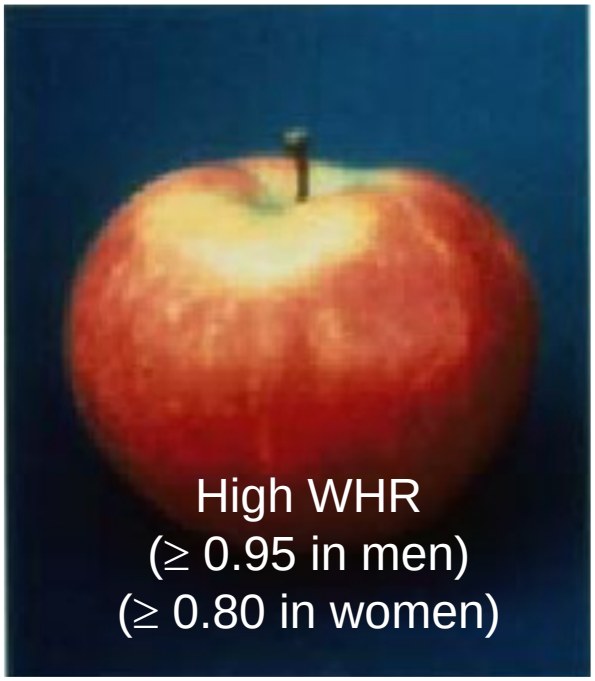


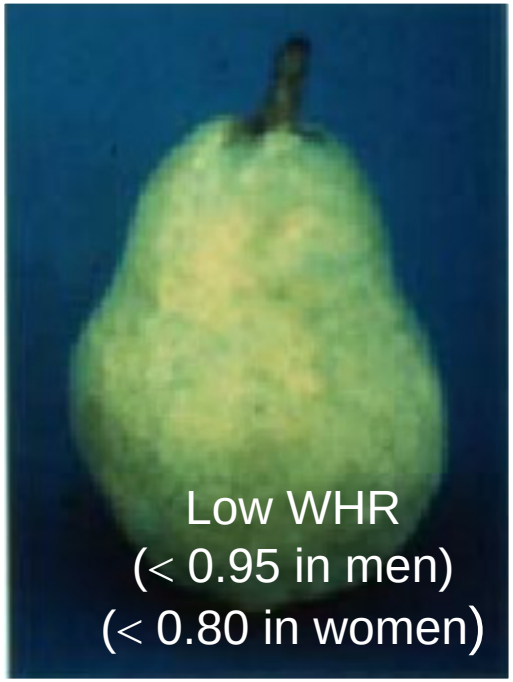
Illustration taken from: Lambert C, Bing C. The Way We Eat Now. *Harvard Magazine*. May-June, 2004;50.

METABOLIC SYNDROME

- Obesity- high waist to hip ratio
- Hyperlipidemia
- Hyperinsulinemia
- Hypertension
- Hyperglycemia
- Acanthosis Nigricans
- PCOS

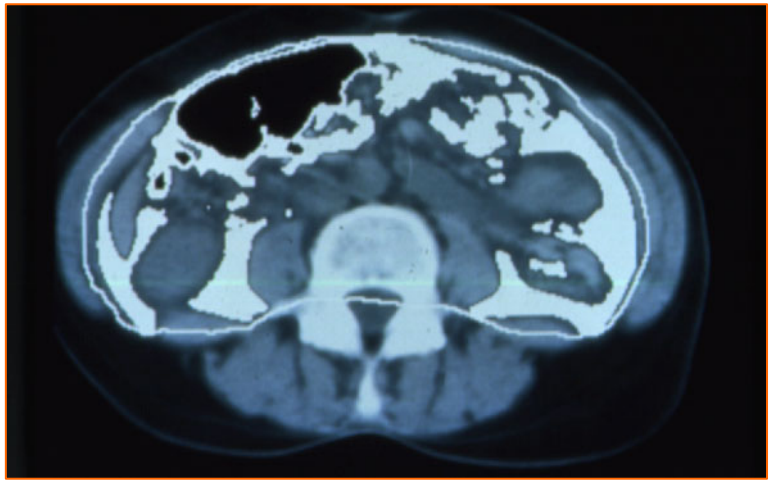
Waist/Hip Ratio
An Index of Abdominal Versus Peripheral Obesity

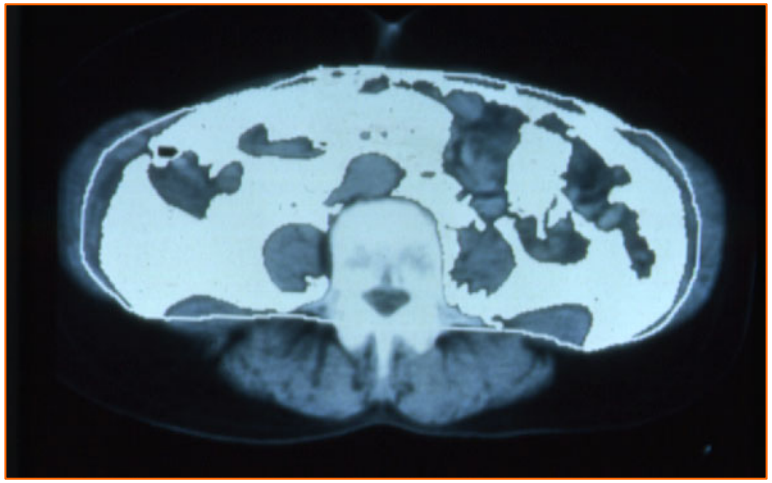




Visceral Fat Distribution

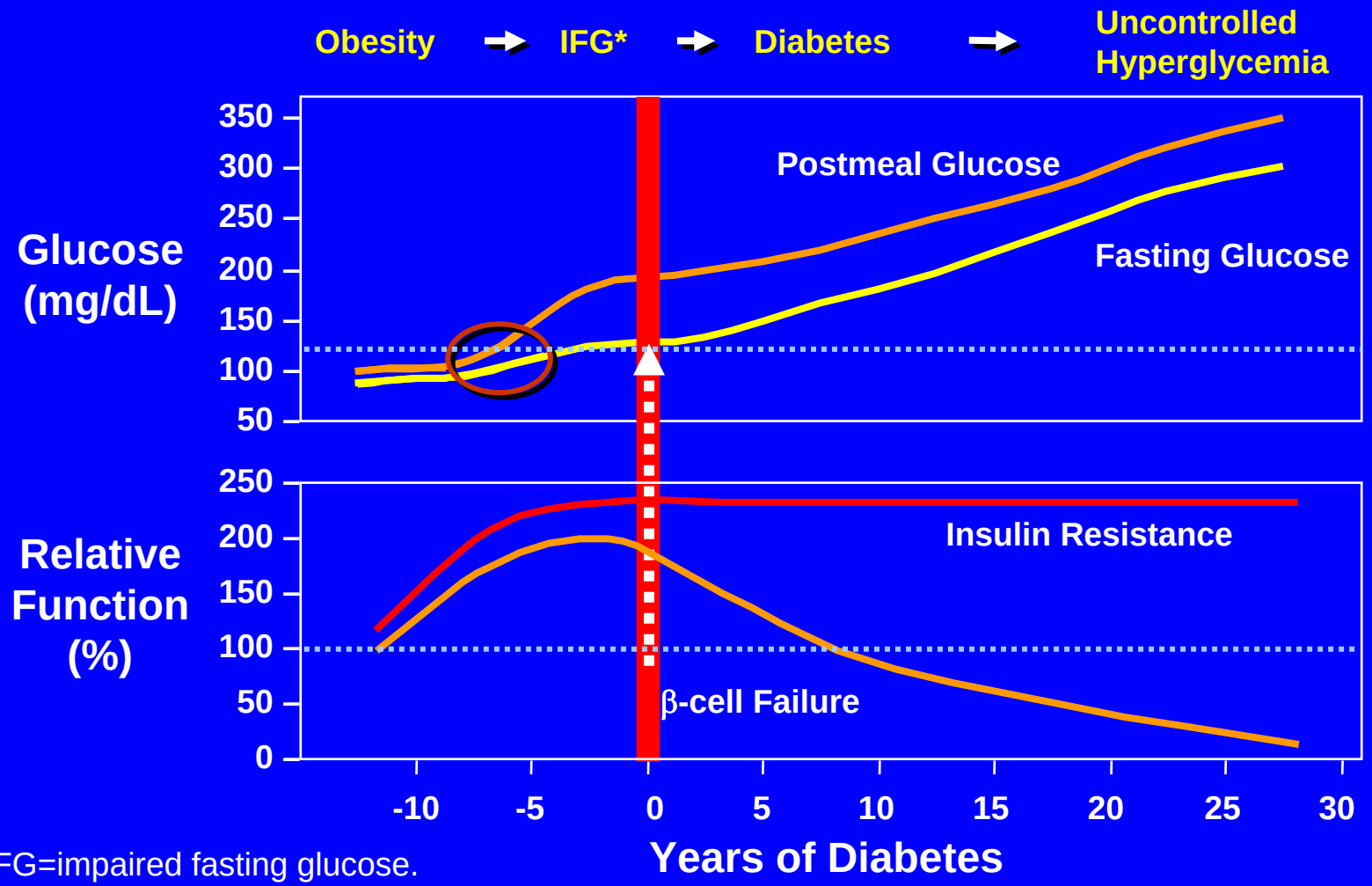
Normal vs Type 2 Diabetes





Courtesy of Wilfred Y. Fujimoto, MD.

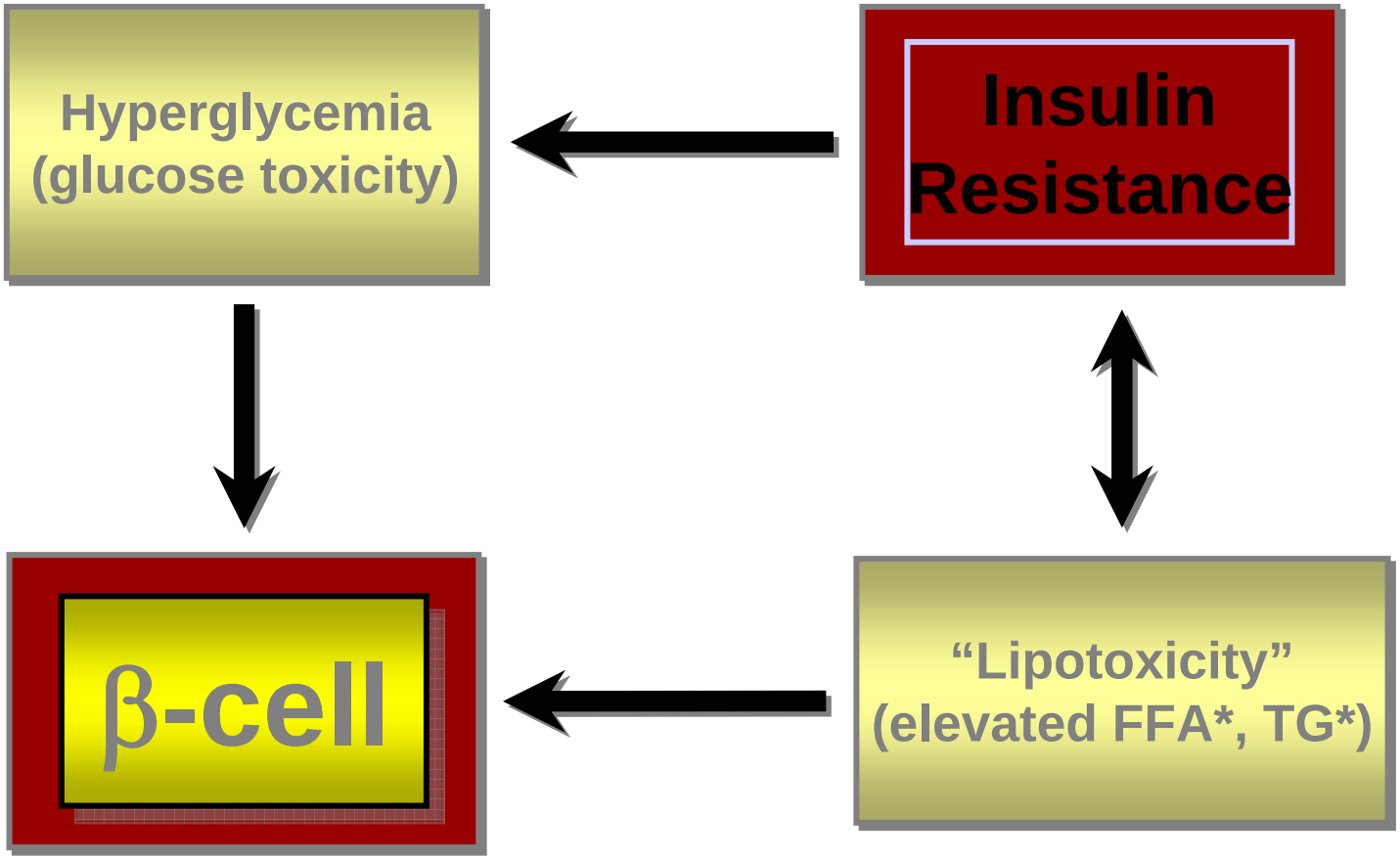
Course of Type 2 Diabetes



*IFG=impaired fasting glucose.

Burger HG, Loriaux DL, Marshall JC, Melmed S, Odell WD, Potts JT, Jr., Rubenstein AH. 2001. Diabetes Mellitus, Carbohydrate Metabolism, and Lipid Disorders. Chap. in *Endocrinology*. 4th ed. Edited by Leslie J. DeGroot and J. Larry Jameson. Vol. 1. Philadelphia: W.B. Saunders Co. Originally published in *Type 2 Diabetes BASICS*. (Minneapolis, International Diabetes Center, 2000).

Factors That May Drive the Progressive Decline of Beta-cell Function

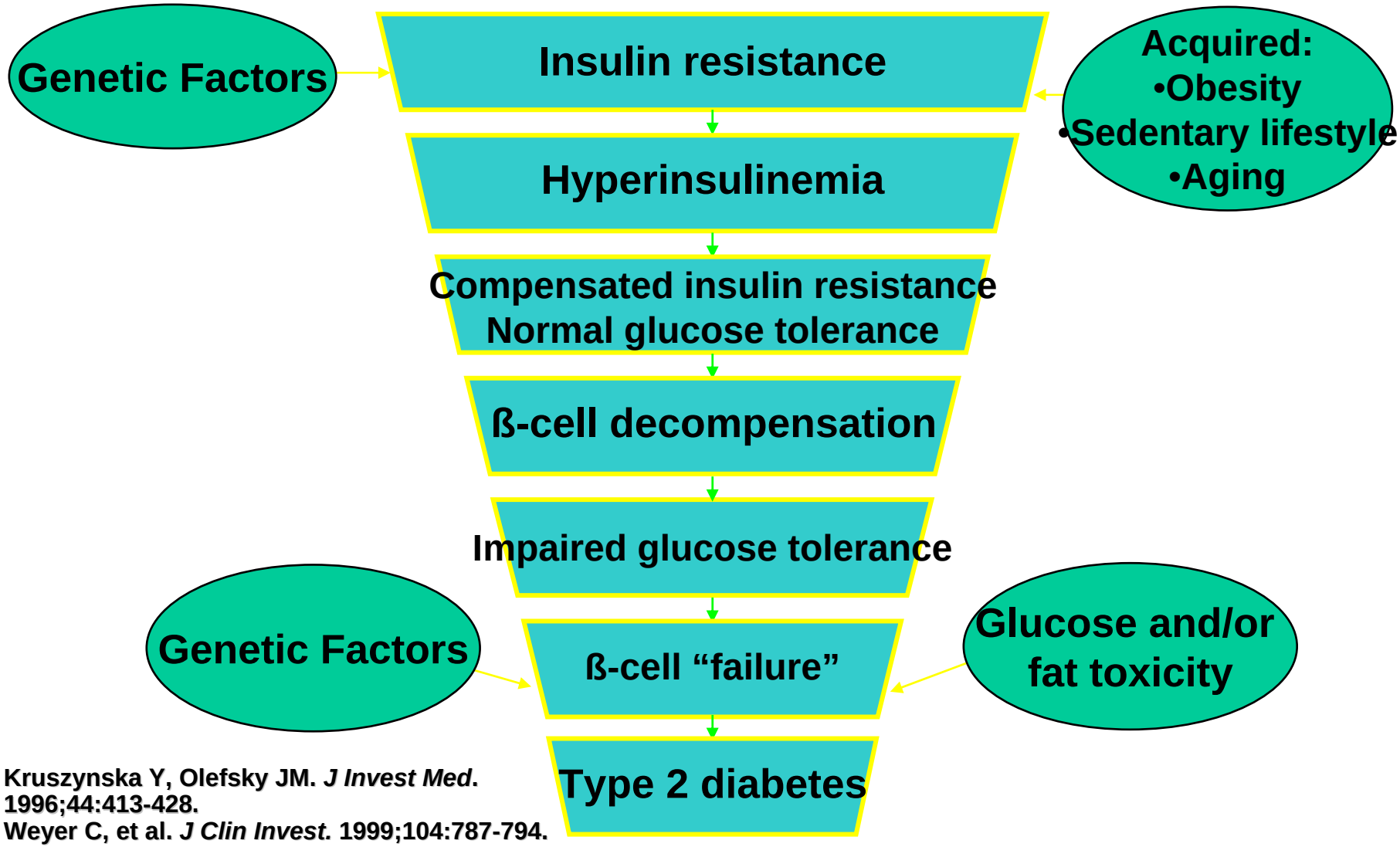


*FFA=free fatty acids; TG=triglycerides.

Adapted from: Kahn SE. *J Clin Endocrinol Metab*. 2001;86(9):4047-4058.

Adapted from: Ludwig DS. *JAMA*. 2002;287(18):2414-2423.

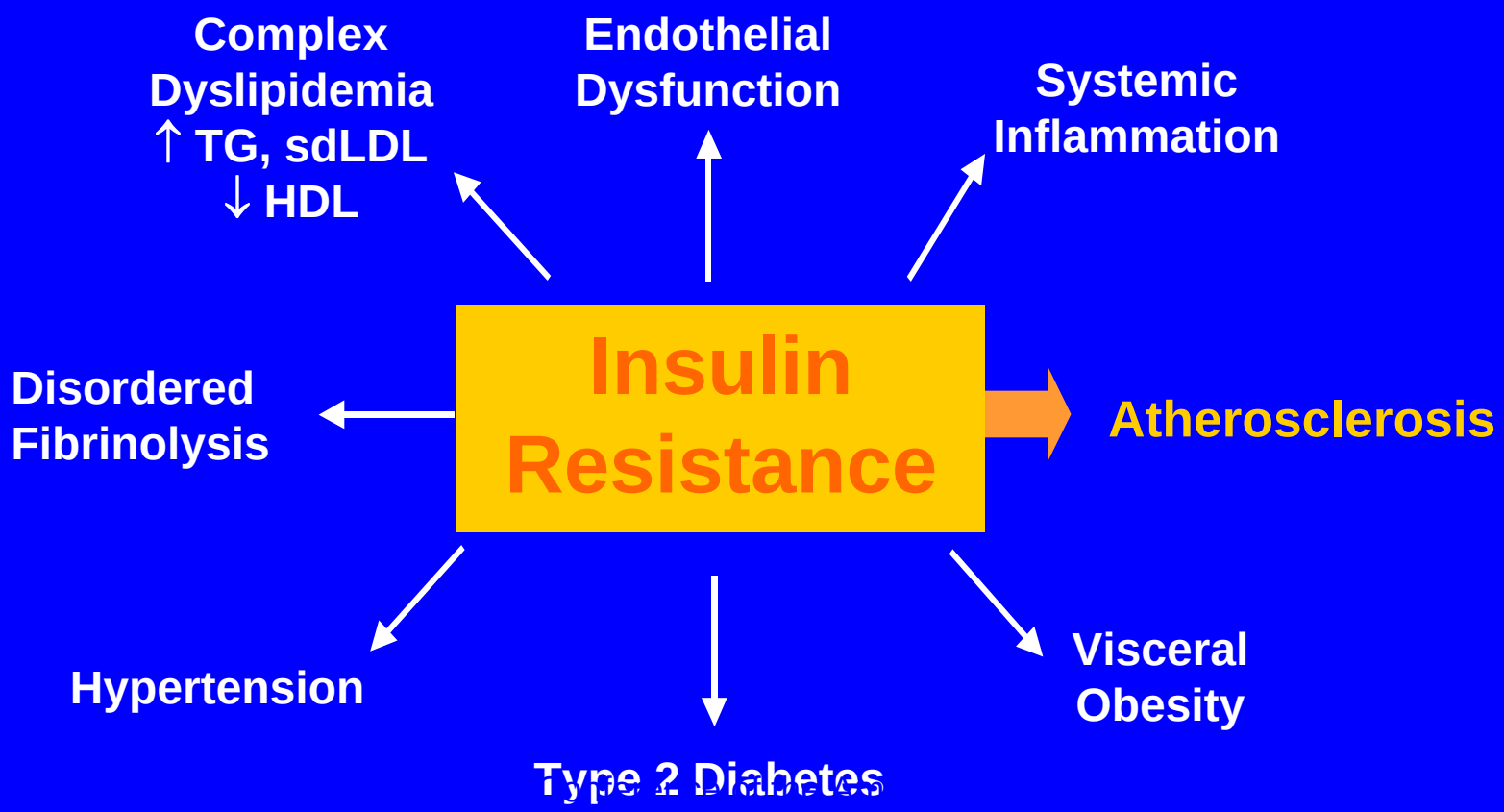
Progression to Type 2 Diabetes



Kruszynska Y, Olefsky JM. *J Invest Med*. 1996;44:413-428.
Weyer C, et al. *J Clin Invest*. 1999;104:787-794.

The Importance of Targeting Insulin Resistance

Over 90% of type 2 diabetics are Insulin Resistant



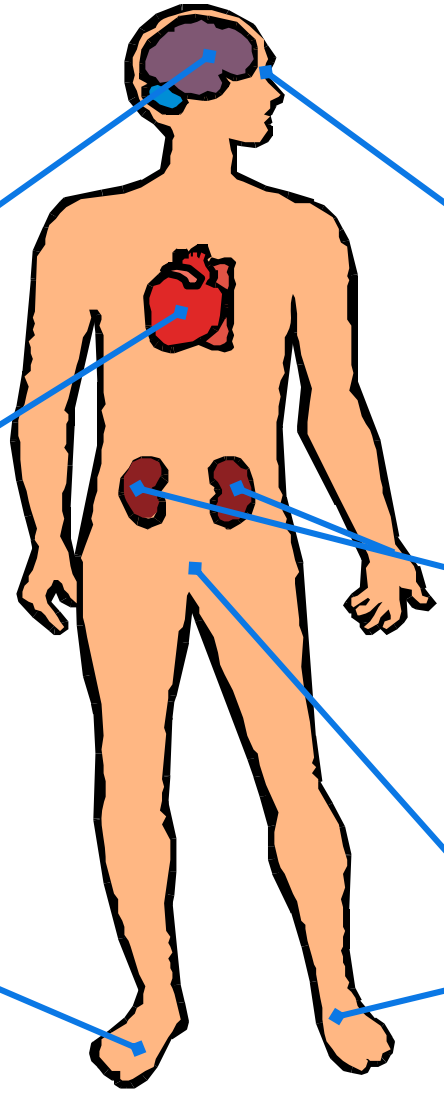
Complications of Diabetes

Macrovascular

Brain
Cerebrovascular disease
- Transient ischemic attack
- Cerebrovascular accident
- Cognitive impairment

Heart
Coronary artery disease
- Coronary syndrome
- Myocardial infarction
- Congestive heart failure

Extremities
Peripheral vascular disease
- Ulceration
- Gangrene
- Amputation



Microvascular

Eye
Retinopathy
Cataracts
Glaucoma

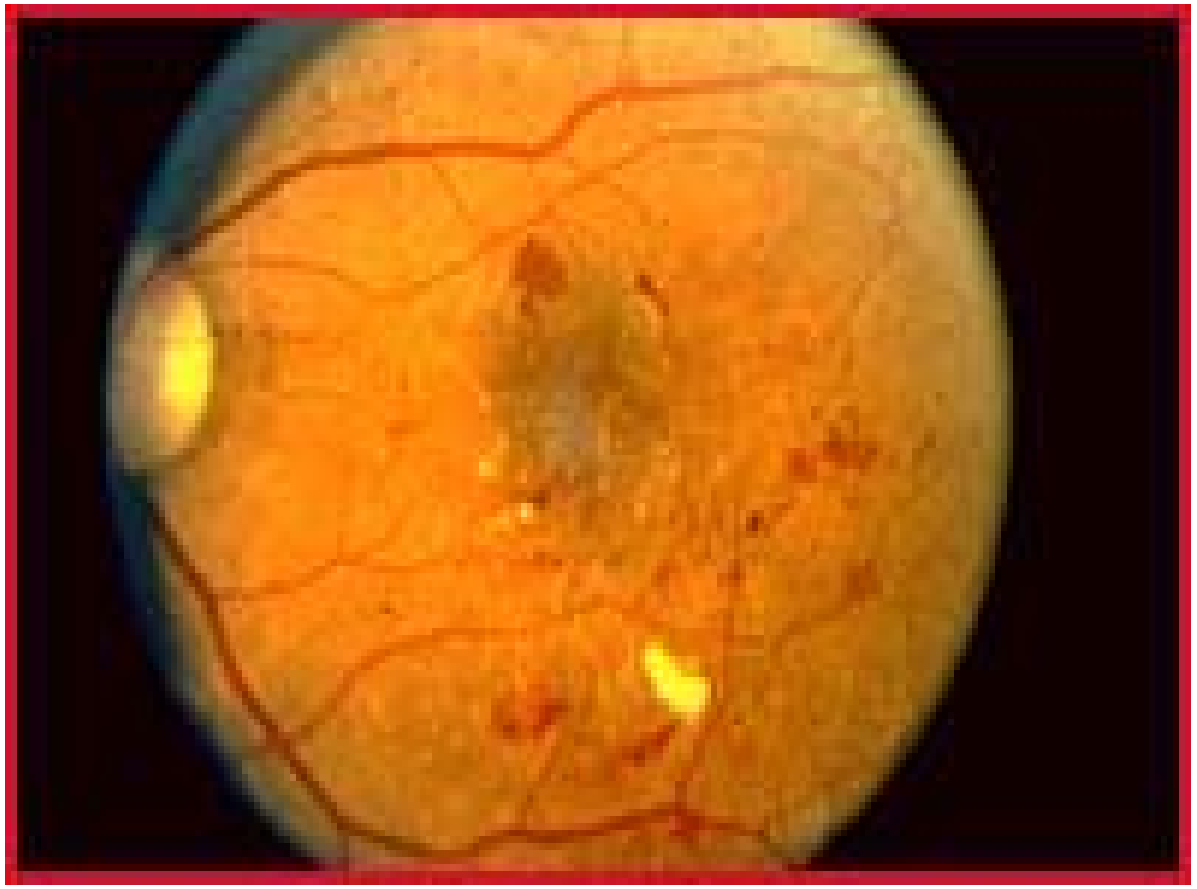
Kidney
Nephropathy
- Microalbuminuria
- Gross albuminuria
- Kidney failure

Nerves
Neuropathy
- Peripheral
- Autonomic

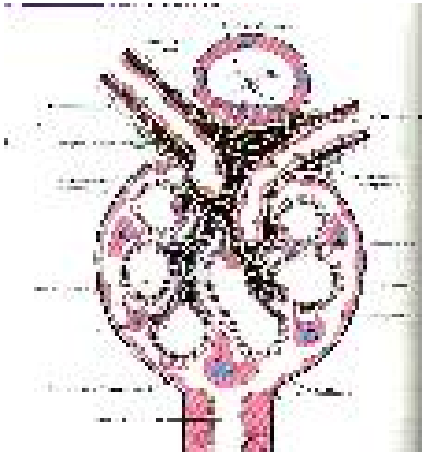
Diabetic foot

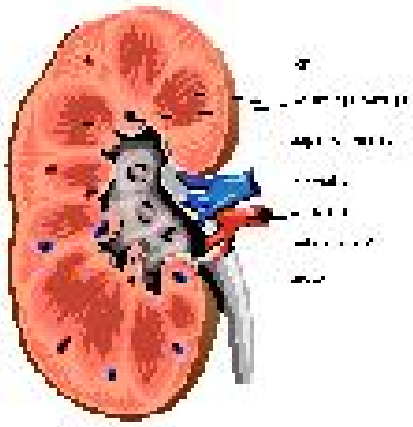
Diabetic foot

Non-proliferative Retinopathy



Nephropathy





Good Glycemic Control (Lower HbA1c) Reduces Incidence of Complications

HbA1c	DCCT 9 → 7%	Kumamoto 9 → 7%	UKPDS 8 → 7%
Retinopathy	63%	69%	17-21%
Nephropathy	54%	70%	24-33%
Neuropathy	60%	–	–
Macrovascular disease	41%*	–	16%*

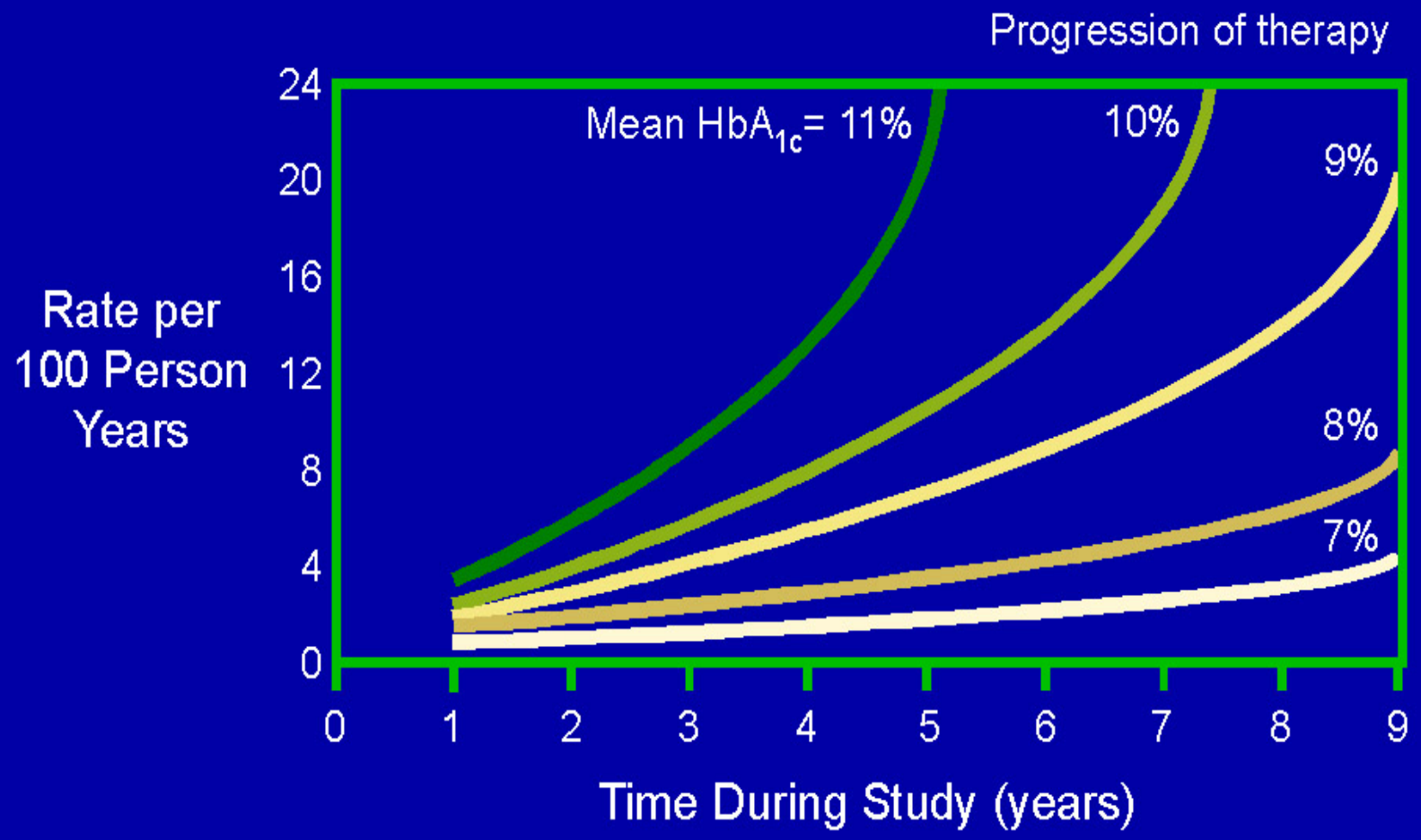
*** not statistically significant**

Diabetes Control and Complications Trial (DCCT) Research Group. *N Engl J Med*. 1993;329:977-986.

Ohkubo Y et al. *Diabetes Res Clin Pract*. 1995;28:103-117.

UK Prospective Diabetes Study Group (UKPDS) 33: *Lancet*. 1998;352:837-853.

HbA_{1c} as Predictor of Retinopathy
(Type 1 diabetes)

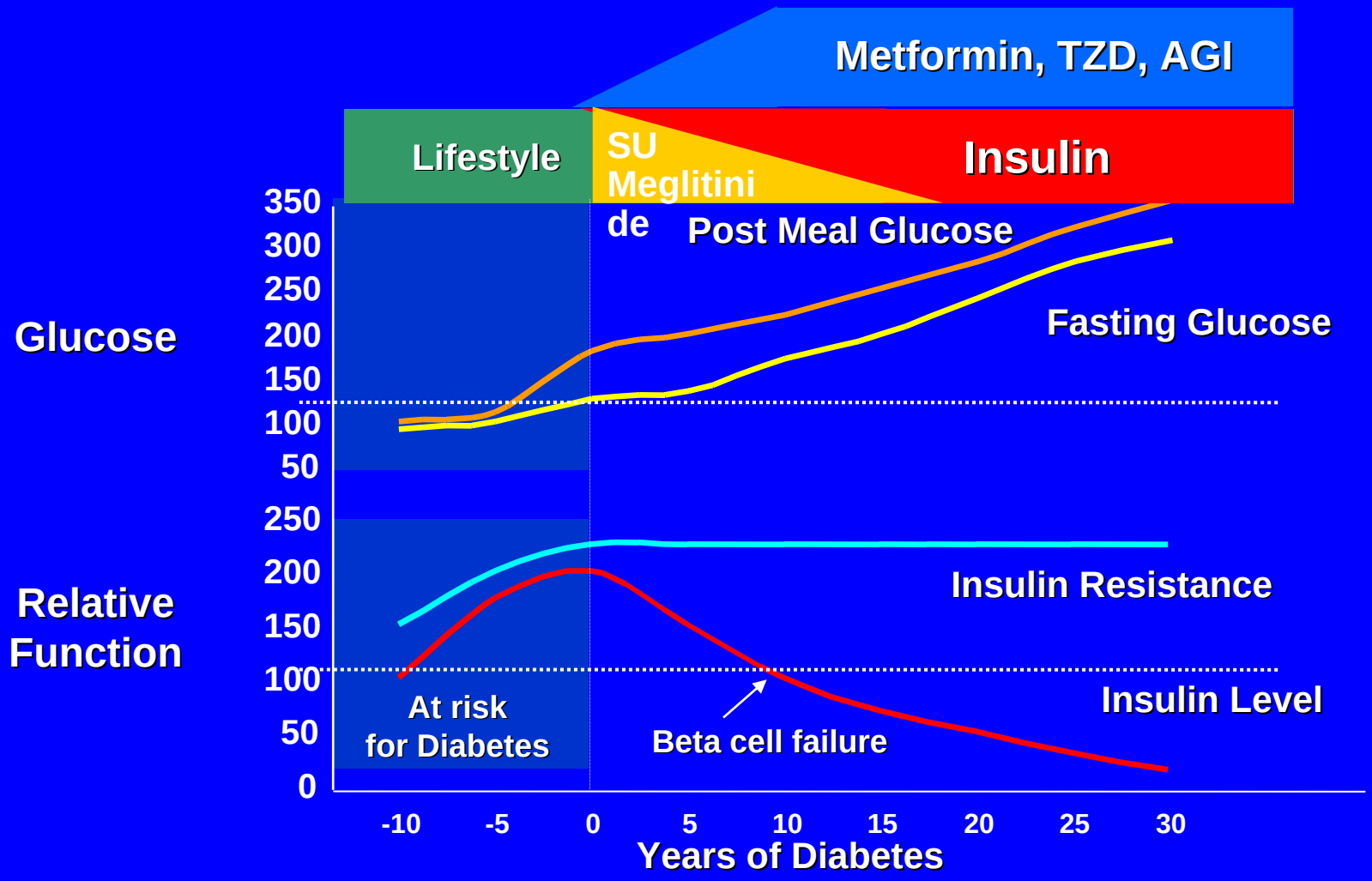


DCCT Research Group. Diabetes. 1995;44:968-983.

TREATMENT OF DIABETES

- IV INSULIN THERAPY
- ORAL HYPOGLYCMIC AGENTS
- INSULINS
- NEW AGENTS
  - SYMLIN
  - BYETTA
  - DPP-IV INHIBITORS
  - ALPHA-GAMMA TZD

Timeline for Utilization of Therapies

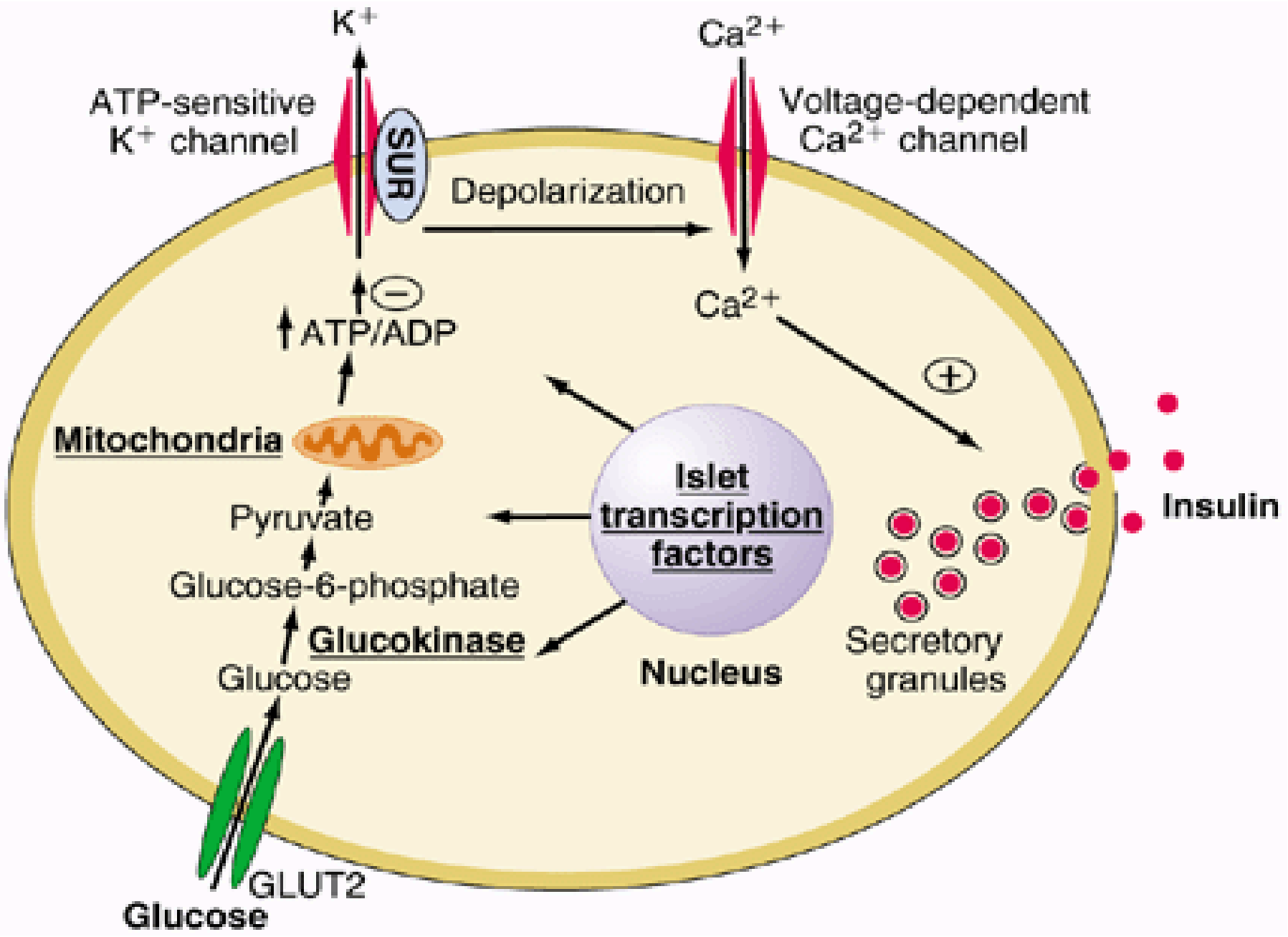


Oral Agents

Drug Class	Examples	Principal Mode of Action	Key Issues
Sulfonylureas	Glimepiride Glipizide Glyburide	Stimulate insulin secretion from pancreatic ß-cells	Hypoglycemia Weight gain
Meglitinides	Repaglinide Meglitol	Stimulate insulin secretion from pancreatic ß-cells	Hypoglycemia Weight gain

Oral Agents

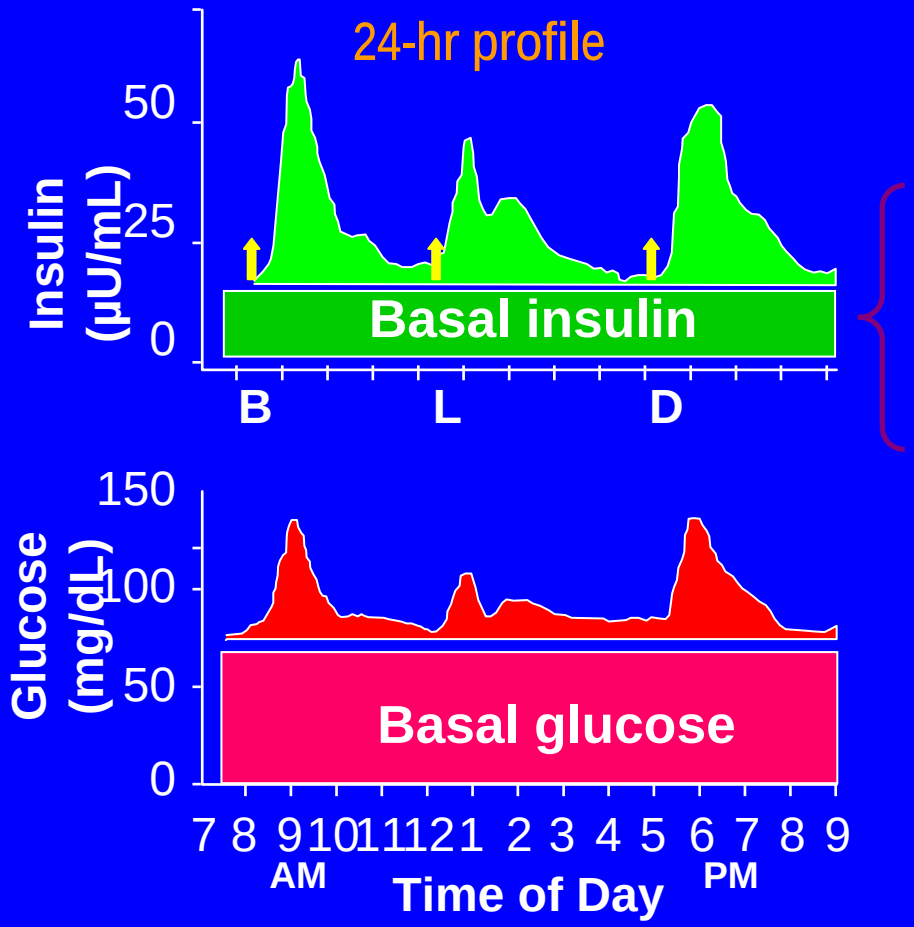
Drug Class	Examples	Principal Mode of Action	Key Issues
Biguanides	Metformin	Decreases hepatic glucose	GI upset Renal dis. Liver enzymes Weight gain
TZD	Rosiglitazone Pioglitazone	Improve peripheral insulin sensitivity	
Alpha-glucosidase inhibitors	Acarbose Miglitol	Delay carbohydrate absorption	Flatulence



Principles of Molecular Medicine. Totowa, NJ, Humana, 1998

Mimicking Nature With Insulin Basal/Bolus Concept

Physiologic Insulin Secretion



- **Suppresses glucose production between meals and overnight**
- **Nearly constant levels**
- **50% of daily needs**

Adapted with permission from Bergenstal RM et al. In: DeGroot LJ, Jameson JL, eds. *Endocrinology.* 4th ed. Philadelphia, Pa: WB Saunders Co.; 2001:821

EXUBERA INHALABLE INSULIN


D-TRON™plus
0831
0.5U/h
DISETRONIC
Deltec
Buddy
Basal:Pattern 1
Rate: 1.00 u/hr
<Stop
Menu>
BOLUS
SUSPEND
HISTORY
BASAL
SETUP
PRIME
STATUS
Animas
h
m
prime
reset
clock
basal
data
units
bolus
temp
17:01
STOP
315.0
H-TRONplus
DISETRONIC
MiniMed
ACT
Off
Prog
Return
Dahlidi
Bolus
Insulin Pump
On
Set
Enter
Insulin U/100
DANA
MiniMed 508
sel
12:43
act

Continuous Glucose Monitoring System (CGMS)
Physician Diagnostic System

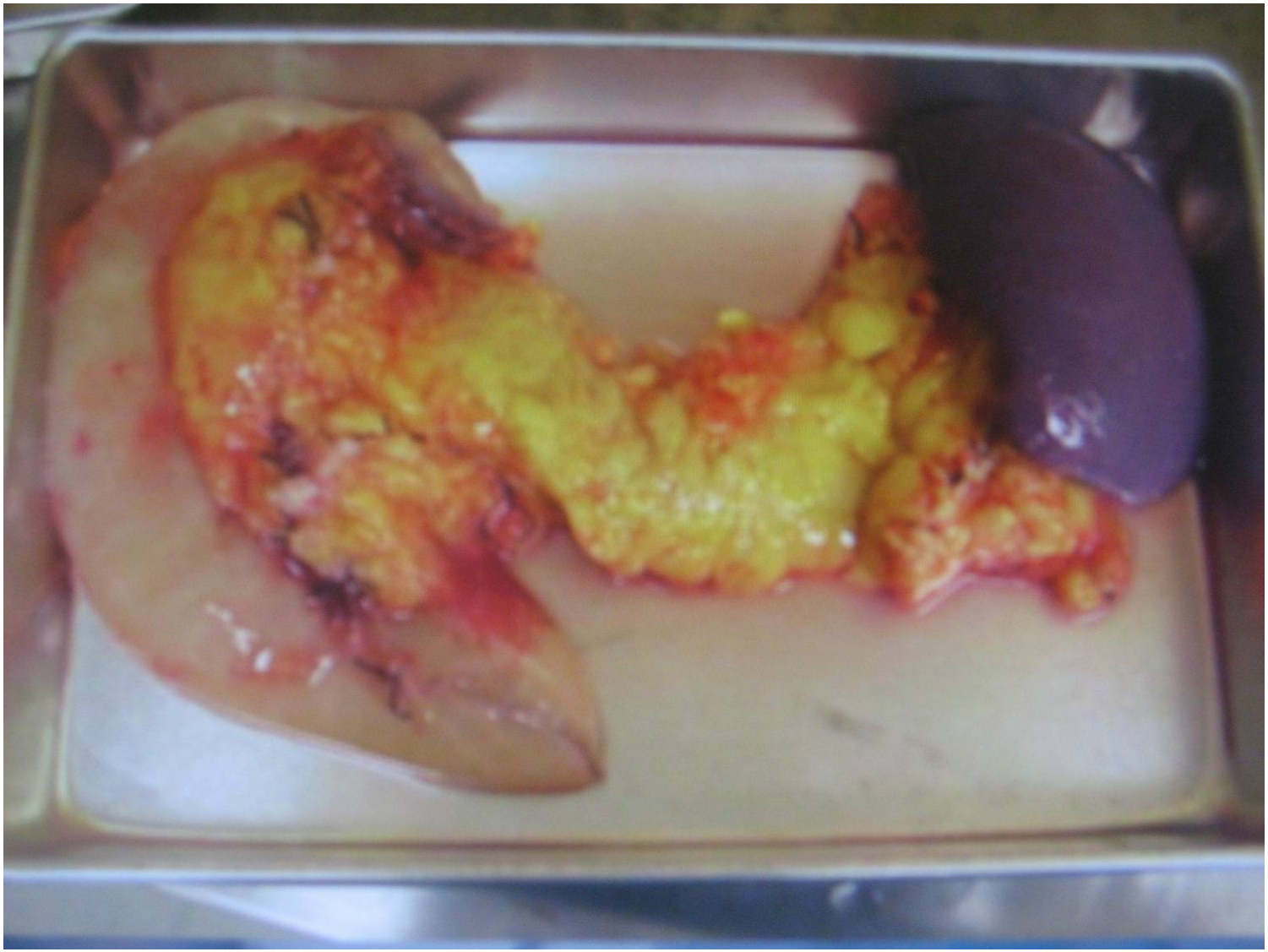
Insulin Pump

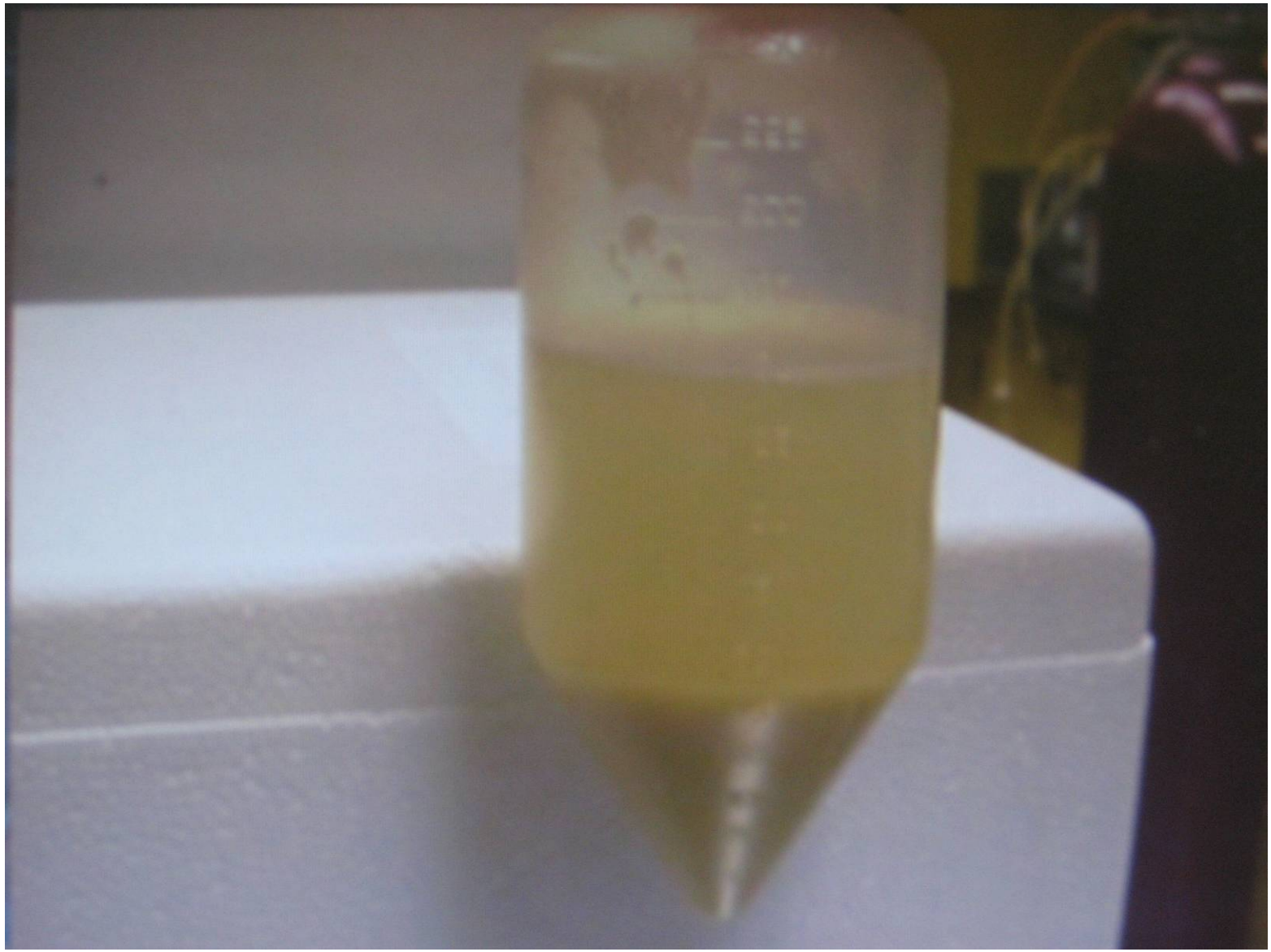
Internal Insulin Pump

Type 2 Diabetes
Treat to Target:

- Blood pressure <130/80 mmHg
- Lipids
  - LDL <2.6mmol/L (100mg/dl)
  - Triglycerdies <1.7mmol/L (150mg/dl)
  - HDL* >1.1mmol/L (40mg/dl)

* For women, target 10 mg/dl higher





Thiogamma 600 filmtablet

Composition

- Active ingredient
  - 600 mg tioctic acid/alfa-lipoic acid
- Other ingredients
  - simethicone, magnesium-stearate, microcristalline cellulose, lactose 1 H2O, silicium-dioxide highly dispersed, hipromellose, talc, carmellose-sodium, sodium-lauryl-sulphate, macrogol 6000

Alpha-lipoic acid

Historical summary

- **Discovery**
  - **1948 O´Kane and Gunsalus**
- **Isolation**
  - **1951 Reed** (liver of cow)
- **Construction of the structure**
  - **1952**
  - **Today**
    - **Causal therapy for diabetic neuropathies**

Alpha-lipoic acid

Pharmacodynamic properties

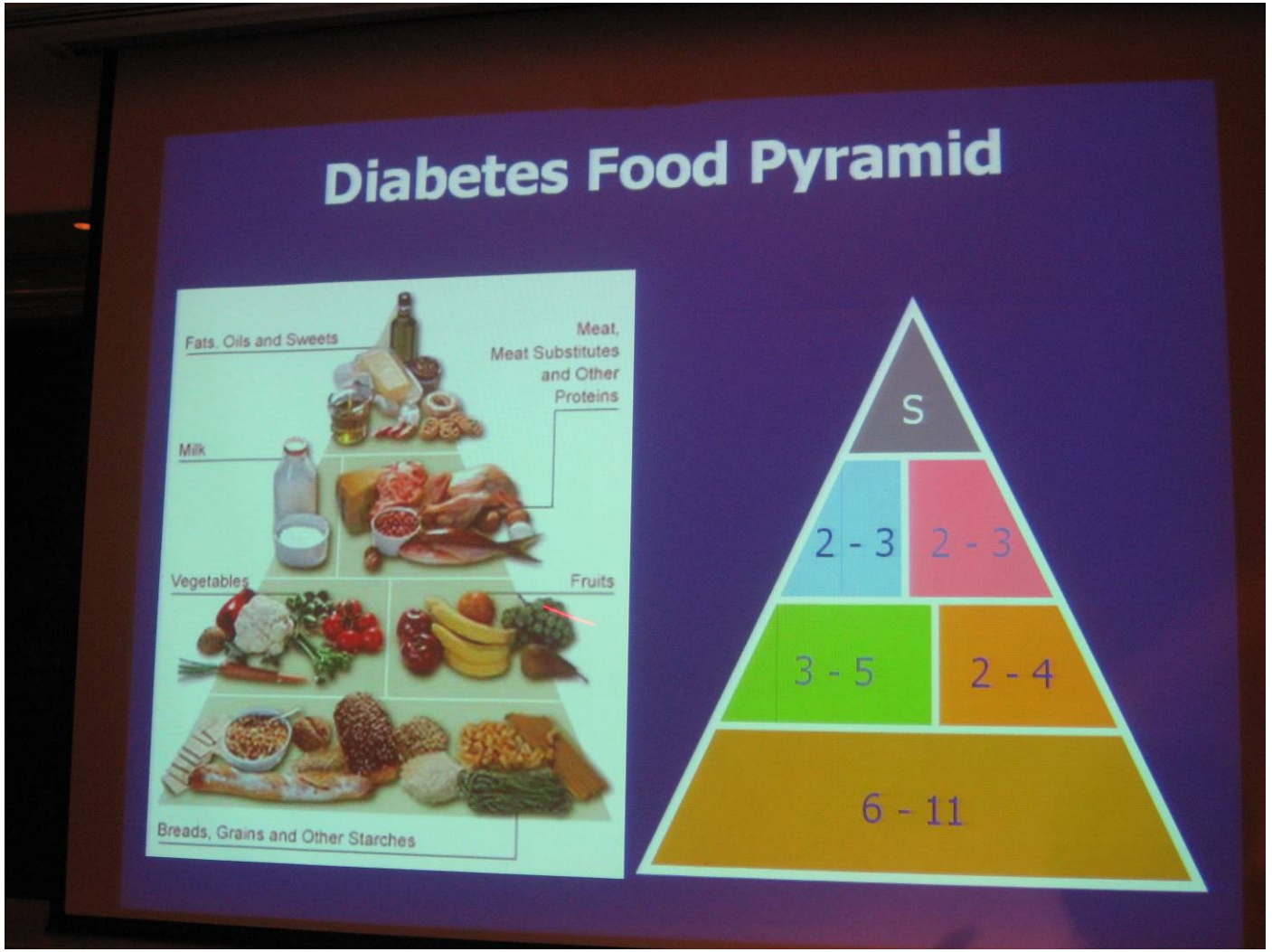
- Natural antioxidant compound
- Developes by endogenic way
- Coenzyme in oxidative metabolic processes
- Free radical scavenger
- Role in glucose utilisation

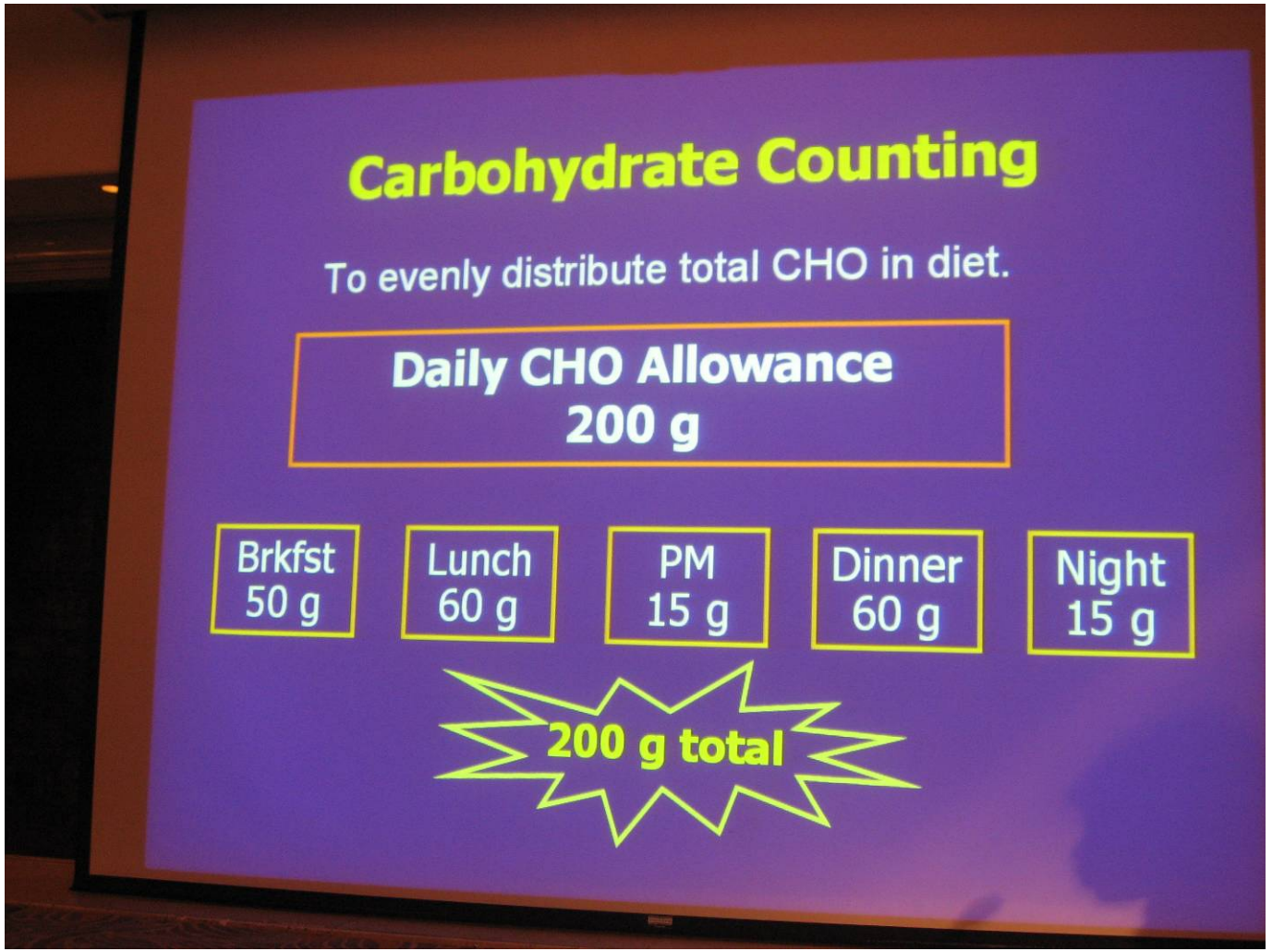
Alpha-lipoic acid

Physiology

- Plays a central role in oxidative catabolism of aliments

- Coenzymes dependent on lipoic acid
  - pyruvate-dehydrogenase
  - alpha-ketoglutarate-dehydrogenase
  - enzymes of amino acid-dehydrogenase with ramifying chains


Diabetes Food Pyramid
Fats, Oils and Sweets
Meat, Meat Substitutes and Other Proteins
Milk
Vegetables
Fruits
Breads, Grains and Other Starches
S
2 - 3
2 - 3
3 - 5
2 - 4
6 - 11


Carbohydrate Counting
To evenly distribute total CHO in diet.
Daily CHO Allowance
200 g
Brkfst
50 g
Lunch
60 g
PM
15 g
Dinner
60 g
Night
15 g
200 g total


中國食物的升糖指數
Chinese Foods Glycemic Index
饅頭 88.1
油條 79.6
白飯 83.2
糯米飯 87
黑米粥 42.3
蕎麥麵 59.3
粉絲 31.6
黃豆 18
豆腐 22.3
四季豆 27
綠豆 27
花生 14
南瓜 75
薯仔 60 – 85
胡蘿蔔 71
芋頭 47.7
魔芋 17
雪梨 36
柚子 25
蘋果汁 41
汽水 68
低脂乳酪 33
餃子 28
中國食物成份表2002

Summary

- The evidence is overwhelming that good control does count
- Morbidity and mortality can be reduced
- There is nothing inevitable about the complications of diabetes

Summary (cont)

- The cost of diabetes is in its complications
- Any expense paid up front in better management will pay off handsomely in the long run
- The tools for good diabetes care already exist
- No tool is more important than the services of a certified diabetes educator

Summary (cont)

- Assessment tools include Self Monitoring of Blood Glucose and HbA1C
- Targets should be established for each of these for each patients within the national guidelines
- When targets are not reached the help of a specialist should be sought

Summary

- Insulin administration should mimic nature
- Natures way is basal insulin 24 hrs. a day
- And bolus insulin with every feeding
- Insulin lispro, asparte or glulisine can supply bolus
- Insulin glargine or detemir can supply the basal with one injection per day
- Control of blood sugar will prevent the complications of diabetes