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DIABETES MELLITUS

M2 - Endocrine Sequence

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Winter 2009



DIABETES MELLITUS

Diabetes (fr. Ionian Greek): “To pass through”

“Diabetes is a dreadful affliction, the melting down of flesh and limbs into urine. The patients never stop making water, and the flow is incessant, like the opening of aqueducts. Life is short, unpleasant, and painful, and thirst, unquenchable, drinking excessive, and disproportionate to the large quantity of urine, for yet more urine is passed.”

**Areteus of Capadocia
2nd Century A.D.**

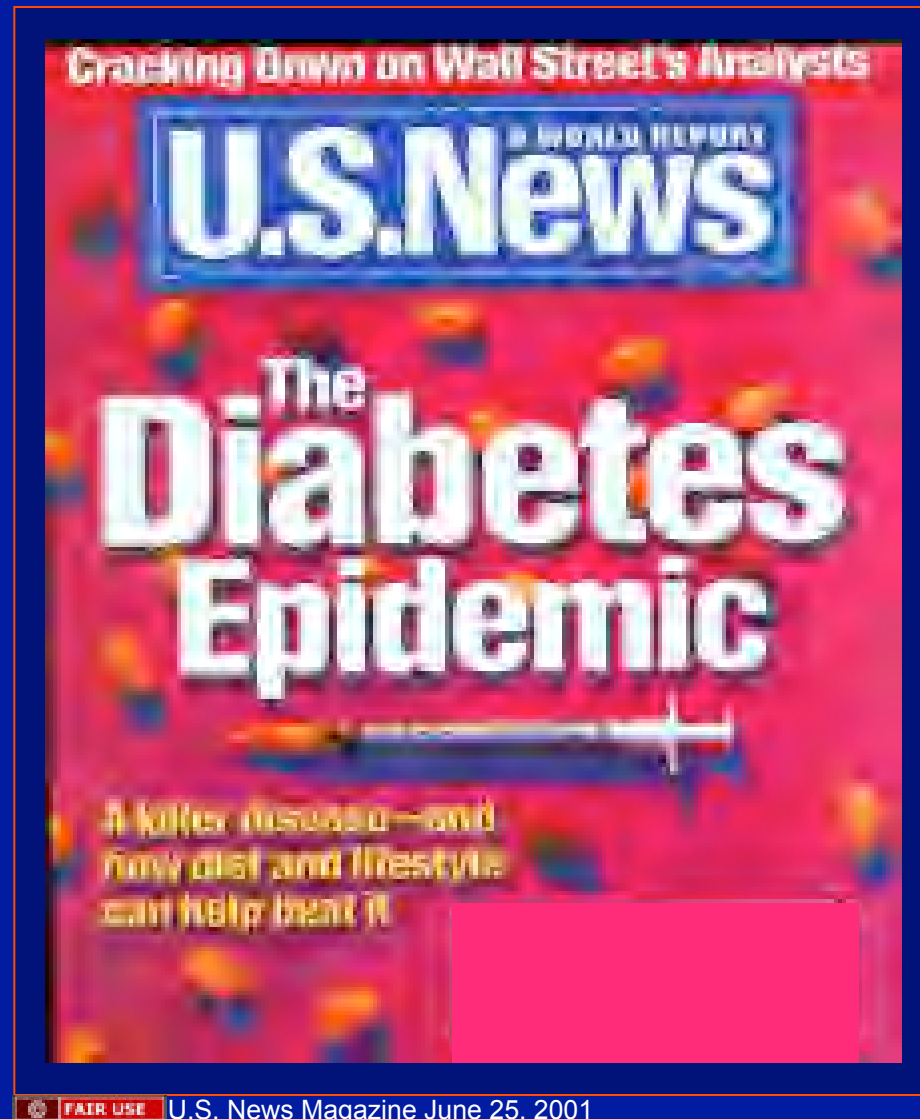
DIABETES MELLITUS

Mellitus (fr. Latin) = “Sweet” or “Honey-like”

4th Cent. A.D. India: Susruta and Charaka

- Urine from polyuric patients tasted like honey, was sticky to the touch and attracted ants.
- Two types of people with this disorder: old, obese people and young, thin people who did not survive very long.
- “Madhumeḥ” = “honey disease”
- Renaissance England: “The Pissing Evile”
- 17th Cent. England. Thomas Willis: Diabetic urine contains sugar. Diabetes due to “sadnesse and longe griefe.”
- 18th Cent. England. Matthew Dobson: Diabetic serum contains sugar.

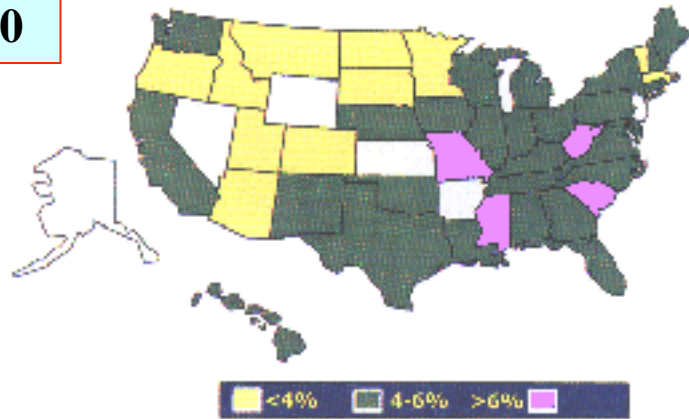
DIABETES: THE GROWING EPIDEMIC



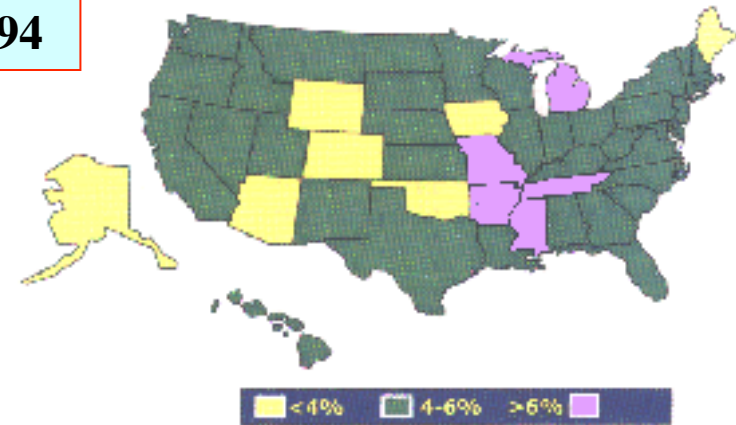
Diabetes Mellitus: The Growing Epidemic

CDC Study of Diabetes in the United States: 1990-1998

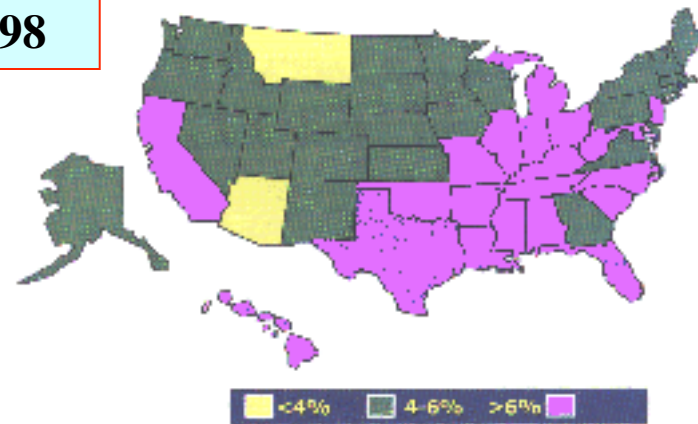
1990



1994



1998



**Pink >6%DM
by self-report**

DIABETES MELLITUS

Approximately 8% of the U.S. population, some 18 million individuals, have diabetes.

BUT,

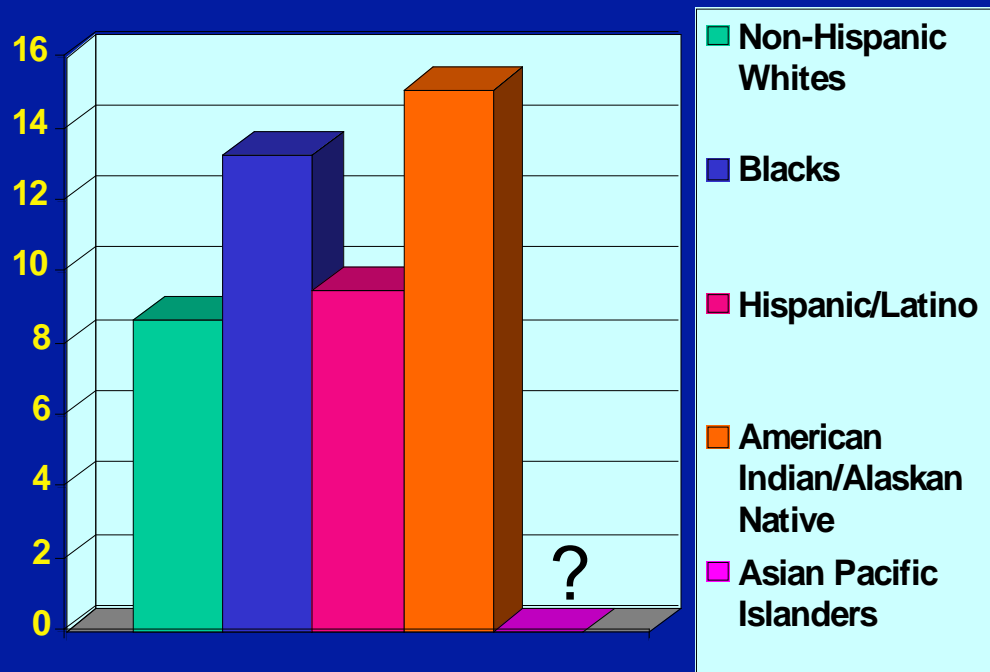
ONE THIRD of the people who have diabetes are unaware that they have the disease.

Approximately 1.5 million people are diagnosed with diabetes mellitus each year in the US alone.

DIABETES MELLITUS

Diabetes disproportionately affects ethnic minorities in the United States.

% in
Adults > 21
yo



Currently, there are no nationwide prevalence data for Asian Americans. Based on regional studies, risk appears to be between 1.5-2 times higher than that for White Americans.

DIABETES MELLITUS

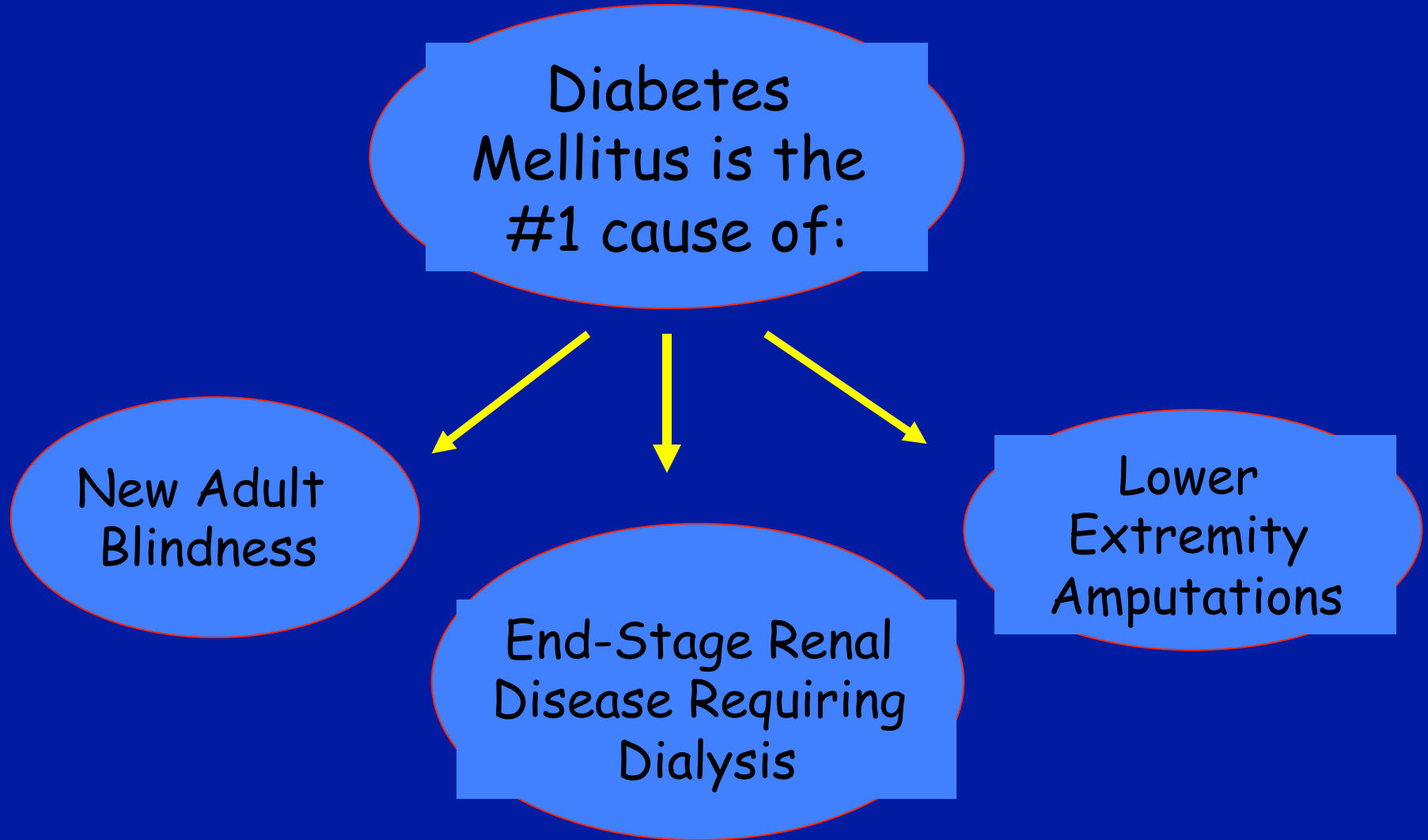
Annually, 34,000 deaths are attributable to diabetes, making it the 6th leading cause of death.

BUT,

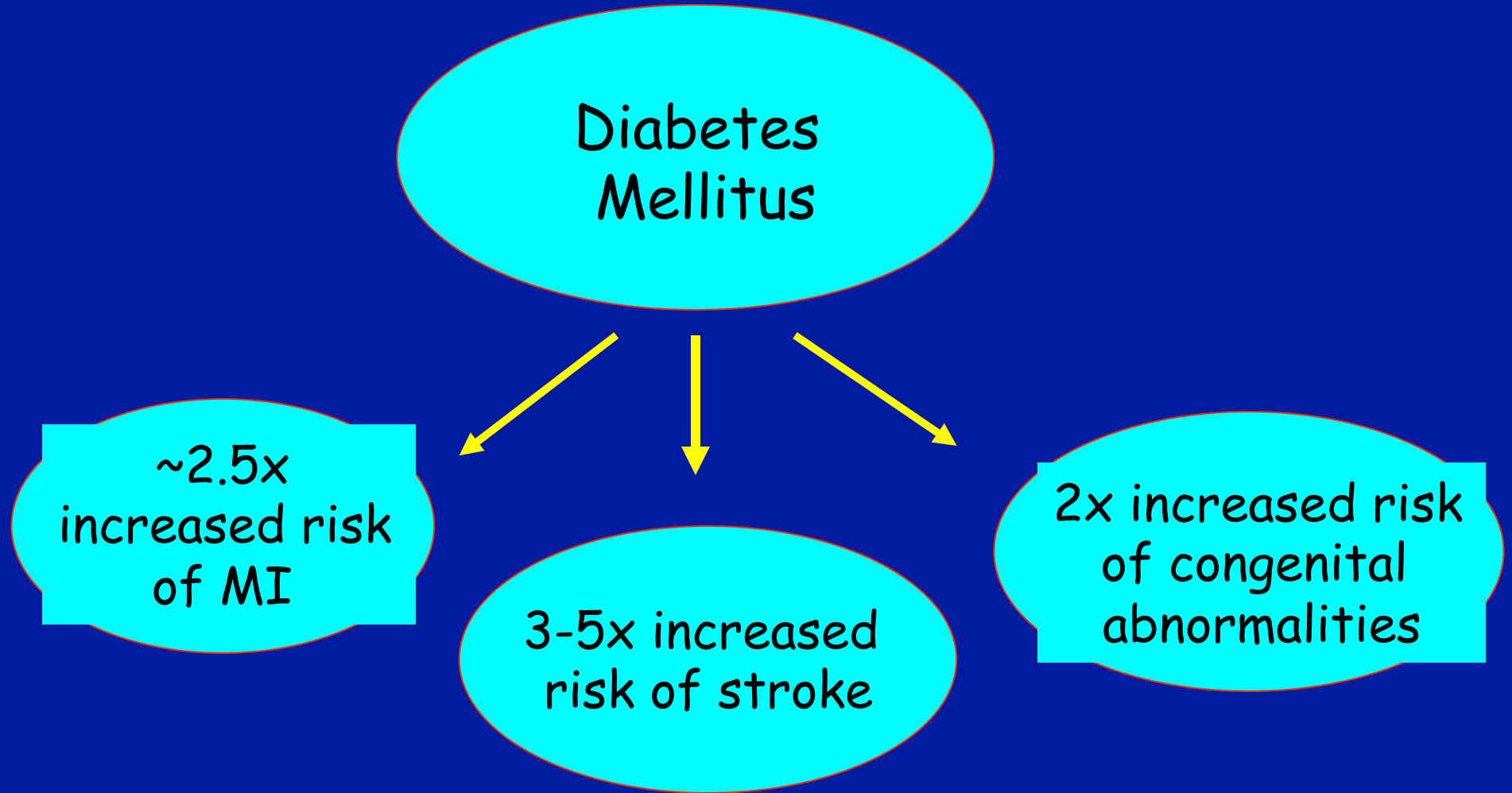
Diabetes is a significant contributing factor in the deaths of 320,000 Americans each year.

Approximately 65% of individuals with diabetes die of cardiovascular disease (MI and stroke).

DIABETES MELLITUS



DIABETES MELLITUS



DIABETES MELLITUS: The Socioeconomic Impact



**HEALTH CARE
RESOURCES**

DIABETES MELLITUS: The Socioeconomic Impact



**\$92 BILLION (direct) and
\$39 BILLION (indirect)
annually is spent on
diabetes and its related
problems***

**\$13,243 spent annually per
capita for those with diabetes
versus \$2,560 for those
without**

*** 2002 costs
(American Diabetes Association)**

DIABETES MELLITUS: Psychosocial Issues

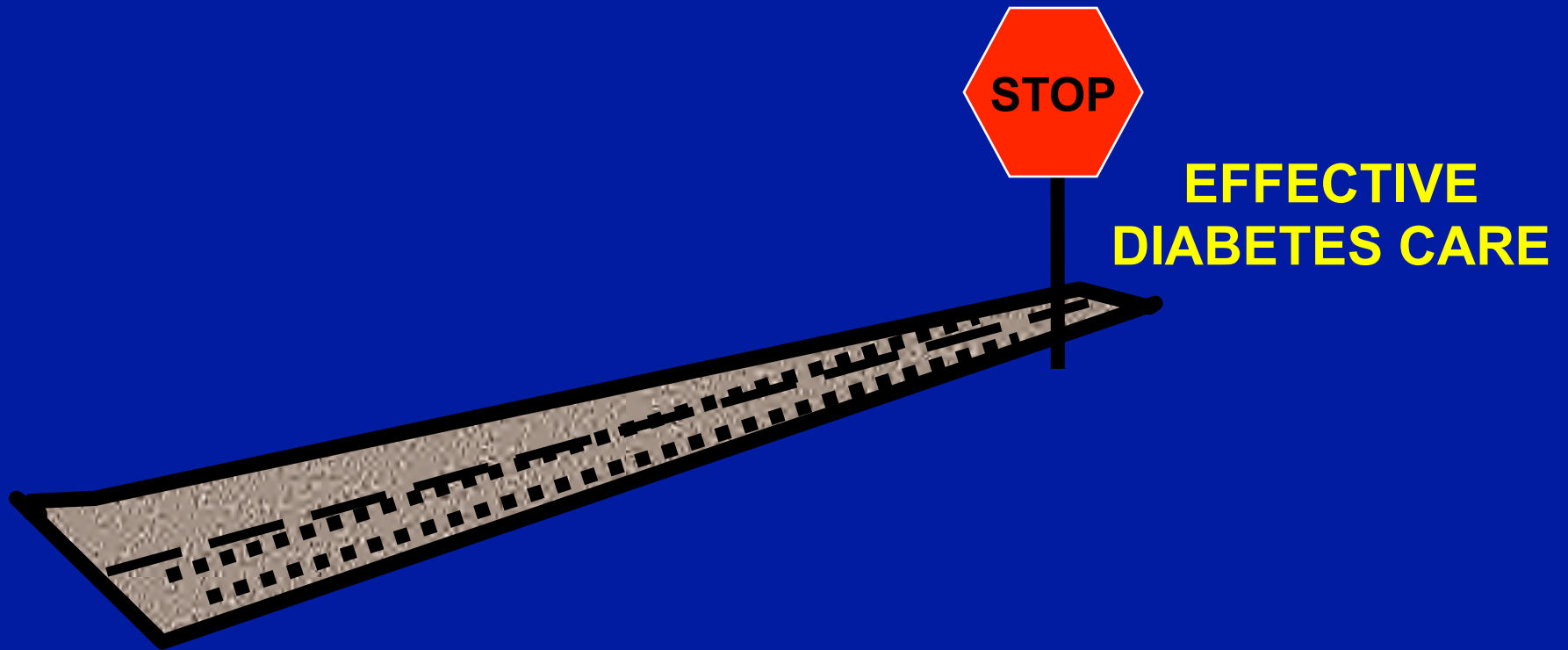


Les Pauvres by Picasso, 1903

 PD-EXP Pablo Picasso

Once the diagnosis of diabetes is made, the individual with diabetes and his or her family may be plagued by feelings of anxiety, guilt, shame, fear and a sense of loss of control over his/her life.

DIABETES MELLITUS: Societal Issues



Factors such as socioeconomic status and cultural and linguistic differences may present obstacles to quality care.

Diabetes Mellitus: Definition

IMPORTANT!

Diabetes mellitus is a chronic disorder of carbohydrate metabolism that is characterized by:

- Chronic hyperglycemia
- A RELATIVE or ABSOLUTE deficiency of insulin.
- “The Three P’ s”: Polyuria, Polydipsia and Polyphagia.
- The development of chronic microvascular and macrovascular complications.

Diabetes Mellitus

IMPORTANT!

TYPE 1 or Insulin-Dependent Diabetes Mellitus (IDDM)

- Represents ~5-10% of individuals with diabetes in U.S.
- Absolute deficiency of endogenous insulin production and dependence on exogenous insulin for survival.
- Ketosis-prone.
- Onset generally at young age (<20-years-old). Older name is “Juvenile Diabetes.”
- Result of autoimmune destruction of pancreatic beta cells.
- Often appears in association with other autoimmune diseases, e.g, autoimmune thyroiditis, Addison’s disease, etc.

Diabetes Mellitus

IMPORTANT!

Type 2 or Non-Insulin-Dependent Diabetes Mellitus (NIDDM):

- Represents 90-95% of diabetes in U.S.
- Presence of endogenous insulin; however, not effective.
- Not ketosis-prone under basal conditions.
- Onset usually older (>40-years-old) and MAY GO UNDETECTED FOR YEARS OR DECADES.
- High (>85%) correlation with obesity in most ethnic groups.
- Hereditary/genetic factors very strong.

Diabetes Mellitus

Gestational Diabetes

- Occurs only in the setting of pregnancy
- Affects ~7% of all pregnancies in US.
- Higher risk: certain ethnic groups (African Americans, Hispanic/Latino, and Native Americans), obesity, and positive family history of diabetes.
- There is a 30-50% risk of developing type 2 diabetes within 5-10 years.

Diabetes Mellitus

Diabetes Associated with Other Medical Disorders

- Pancreatic Damage or Destruction: chronic pancreatitis, hemachromatosis, cystic fibrosis.
- Endocrine Diseases: Acromegaly, Cushing's Syndrome.
- States of extreme physiological stress: e.g., infections, burns.
- Drugs: GLUCOCORTICOIDS, thiazide diuretics, niacin.

Pink = important to remember

Diabetes Mellitus

Atypical or Genetic Forms of Diabetes

Atypical or Non-Autoimmune Diabetes

- Most cases seen in African Americans and Hispanic/Latinos.
- Almost always associated with obesity.
- May present with diabetic ketoacidosis.
- Do not need insulin for survival.

Genetic Syndromes. Example: MODY = Maturity Onset Diabetes of Youth

- Autosomal dominant inheritance pattern
- Non-insulin dependent diabetes occurs at very young age.
- Deletions or mutations in genes found to play role in regulating glucose metabolism.

Diabetes Mellitus: DIAGNOSIS--New Criteria (1997)

Normal blood glucose: 80-100 mg/dL

Diabetes is present with either:

Two fasting blood glucose values of ≥ 126 mg/dL.

or

A random blood glucose of >200 mg/dL + symptoms.

The Oral Glucose Tolerance Test (GTT): measurement of blood glucose values in a timed manner after ingestion of a standard amount of glucose. Used clinically on a regular basis only to detect diabetes developing during pregnancy.

Diabetes Mellitus: DIAGNOSIS

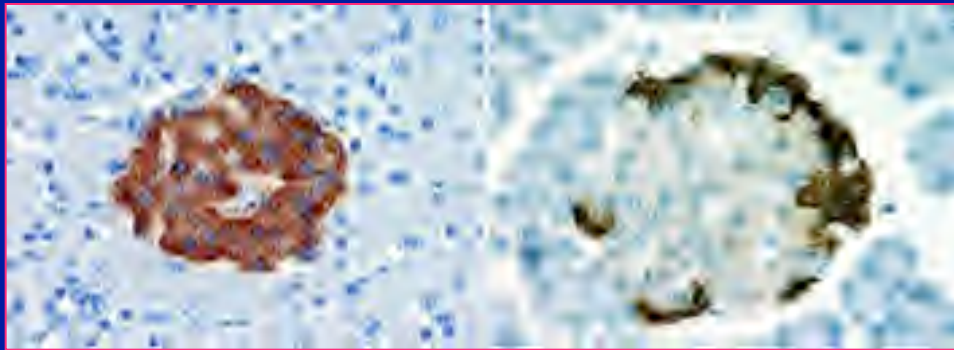
Remember:

**Most of the time, diabetes is
ASYMPTOMATIC, or its symptoms are
subtle and nonspecific.**

Diabetes Mellitus

Pathogenesis

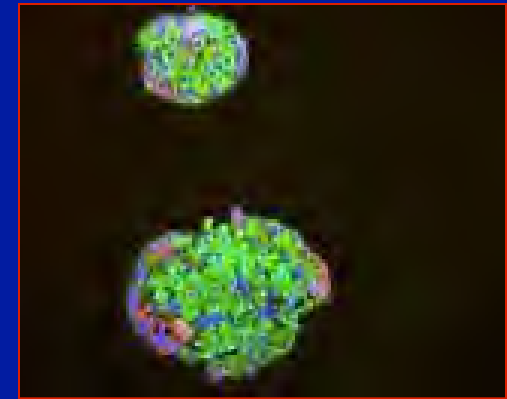
Type 1 Diabetes



Alpha Cells:
GLUCAGON

Beta Cells:
INSULIN

 [Dr. Thomas Caceci](#)

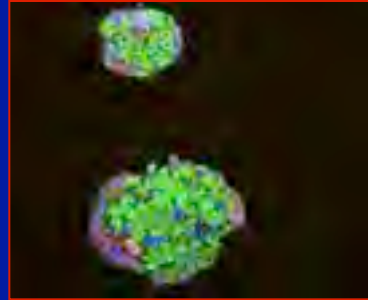


Isolated islets stained for insulin (green) and caspase-3 (pink).

 W. Moritz, Ph.D., Univ. of Zurich

Type 1 diabetes involves selective autoimmune destruction of the insulin-secreting beta cells of the pancreatic islets.

Type 1 Diabetes: Pathogenesis

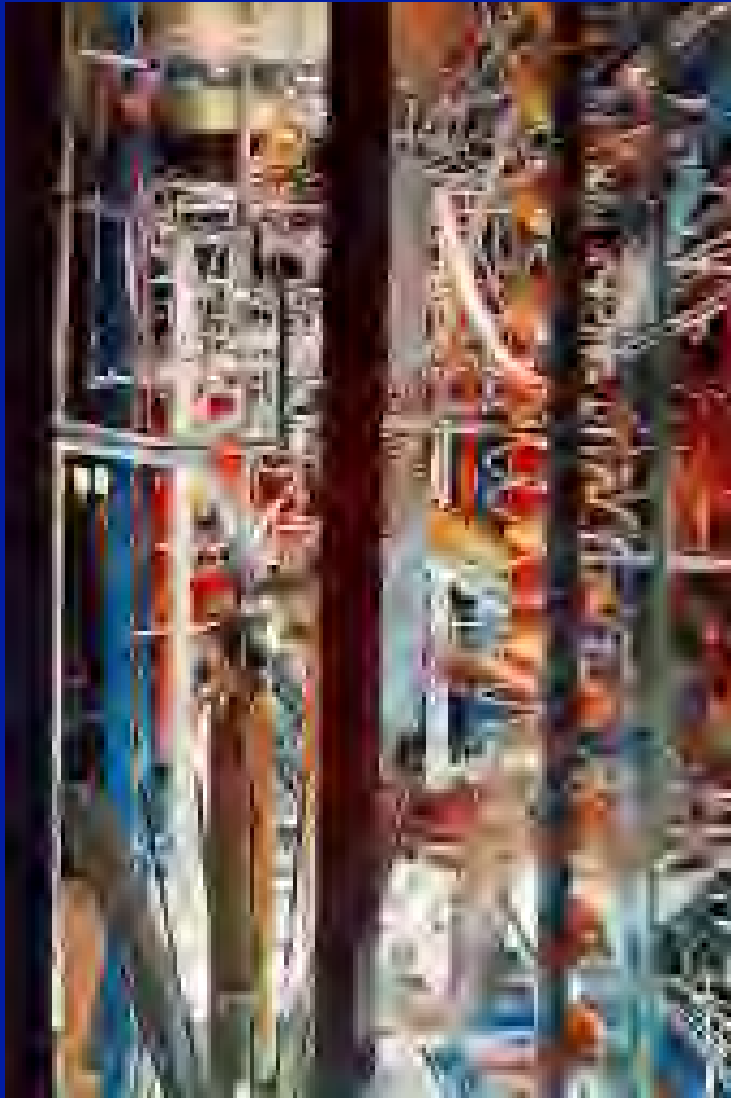


Isolated islets stained for insulin (green) and caspase-3 (pink).

PD-INEL W. Moritz, Ph.D., Univ. of Zurich

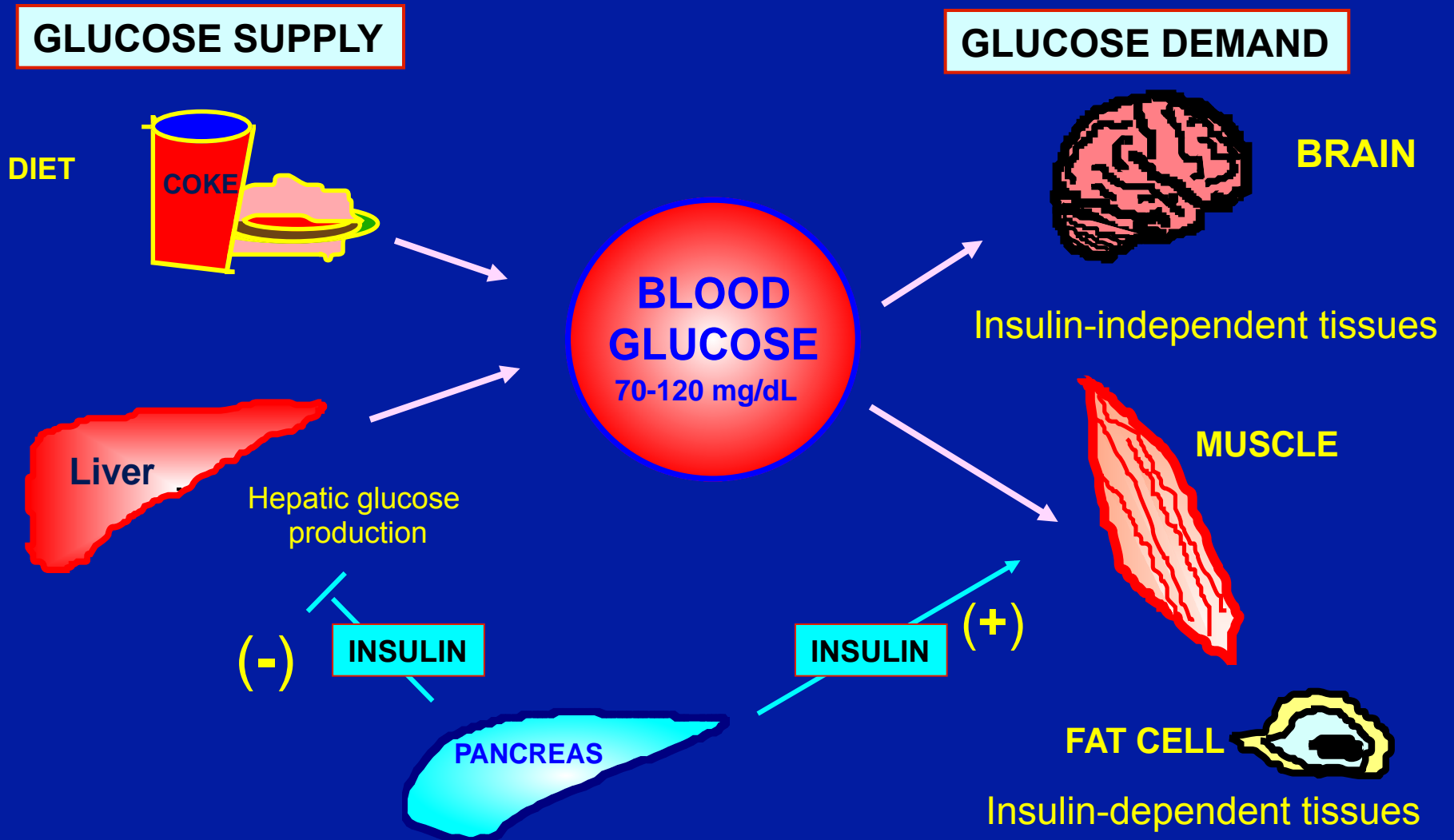
- A T cell-mediated autoimmune process causing inflammation and destruction of the β cells of the pancreas.
- Associated with the presence of autoimmune antibodies, including antibodies against islet cells, insulin and the 65 kDa form of glutamic acid decarboxylase (GAD65).
- Autoimmune antibodies play no apparent role in development of diabetes but serve as useful markers for those at high risk.
- Genetic factors play a role: association with specific HLA haplotypes.
- Concordance among identical twins: 30-50%.

Type 2 Diabetes: Pathogenesis



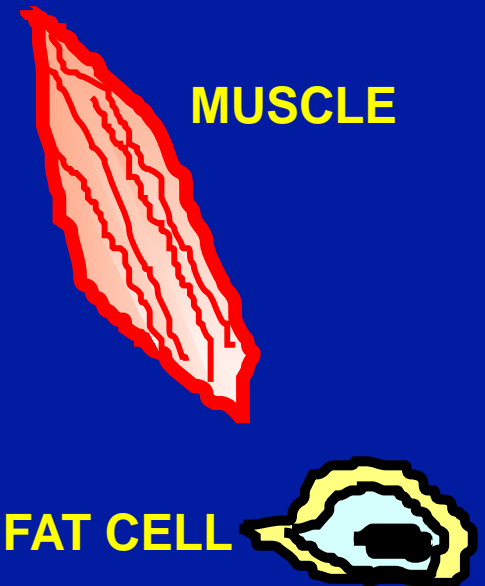
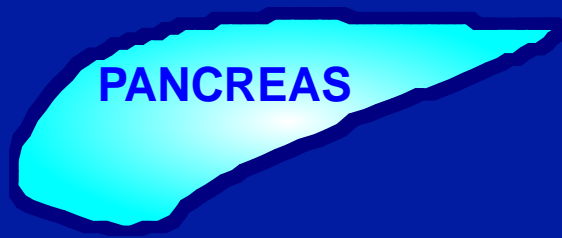
The pathogenesis of type 2 diabetes is slightly more complex...

DIABETES MELLITUS: Normal Glucose Metabolism

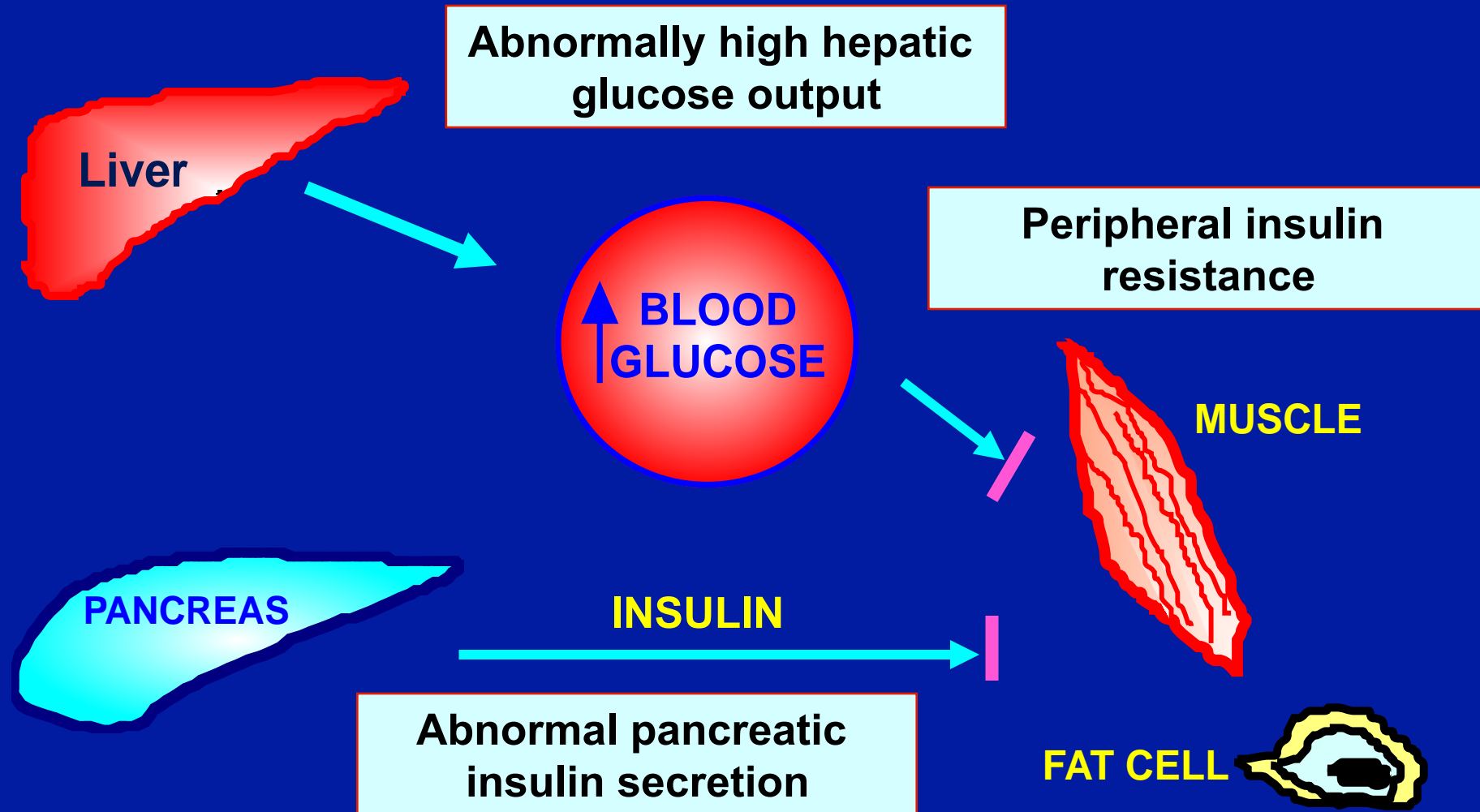


Type 2 Diabetes: Pathophysiology

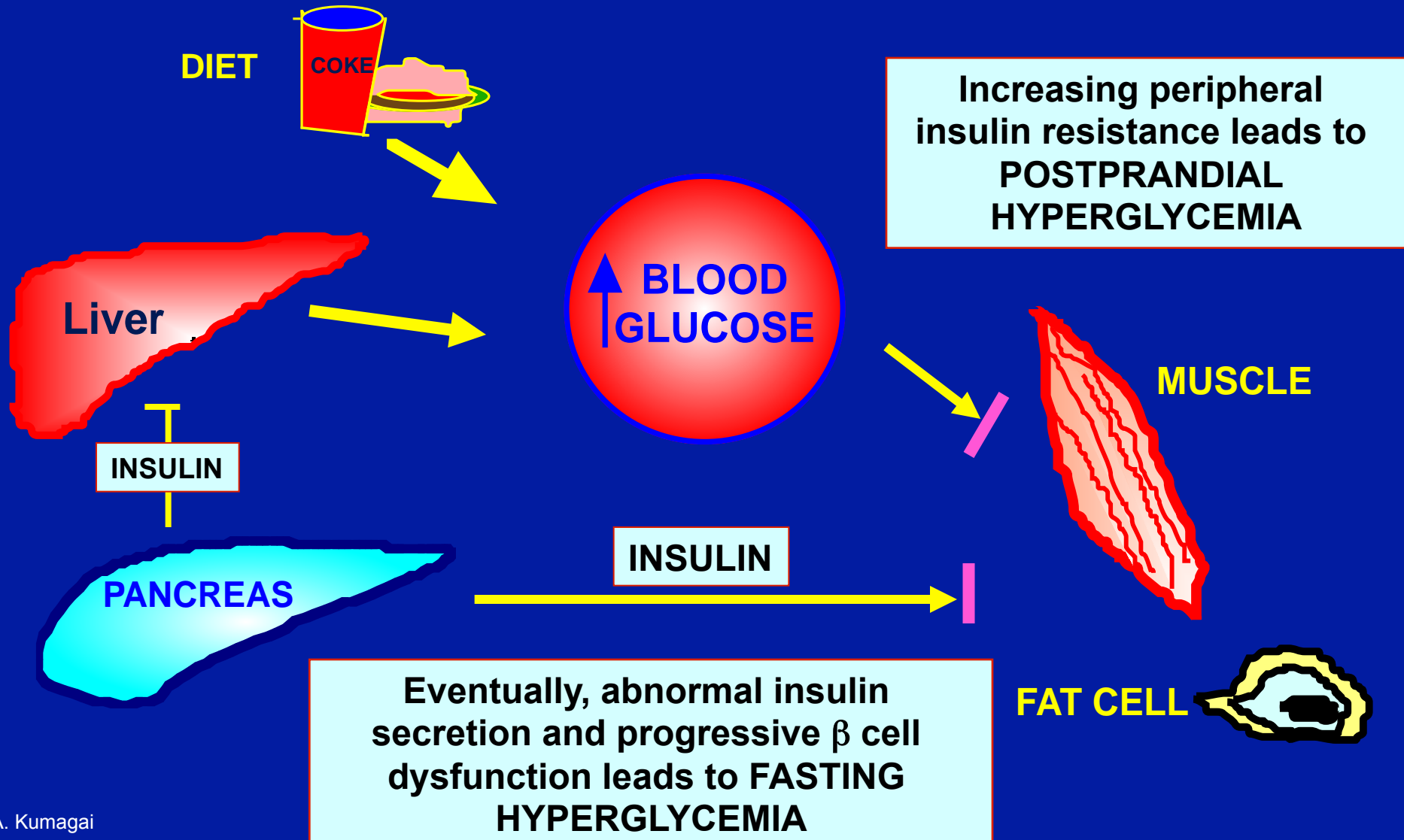
Introducing the Players in Type 2 Diabetes....



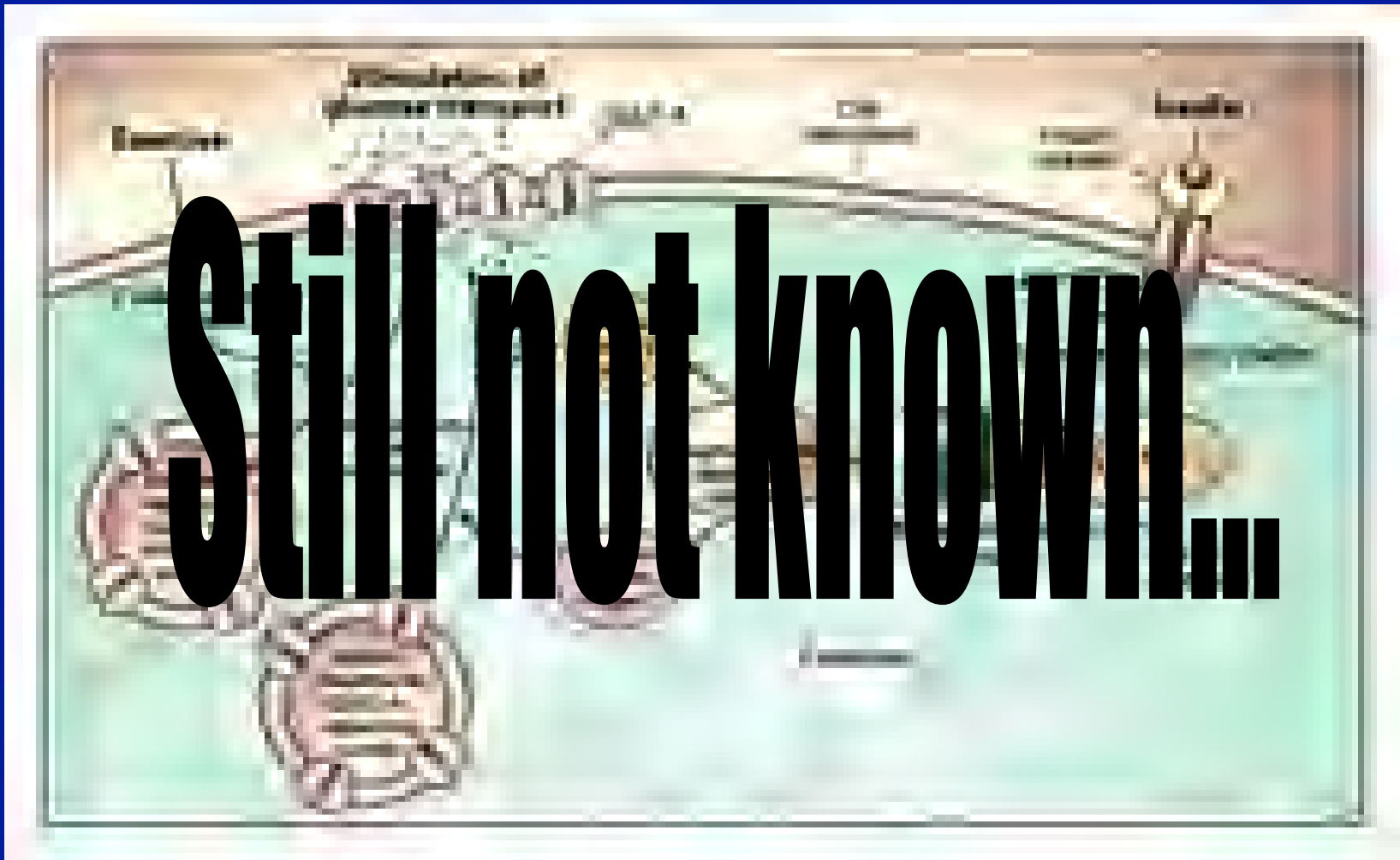
Type 2 Diabetes: Pathophysiology



Type 2 Diabetes: Development and Progression



Pathogenesis of Type 2 Diabetes: the Molecular Level



Diabetes Mellitus: Points to Remember

Understand:

1. The epidemiology of diabetes: the current “epidemic,” high prevalence in minority populations, effects on individuals and society.
2. The differences between type 1 and type 2 diabetes.
3. The pathogenesis of type 1 and type 2 diabetes.

Additional Source Information

for more information see: <http://open.umich.edu/wiki/CitationPolicy>

Slide 6: U.S. News Magazine June 25, 2001

Slide 7: CDC Diabetes Care, 23:1278, 2000. (All Images)

Slide 9: NIDDK National Institutes of Health

Slide 11: Arno Kumagai

Slide 12: Arno Kumagai

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Slide 14: Arno Kumagai

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Slide 16: Arno Kumagai

Slide 26: Dr. Thomas Caceci, Image from <http://education.vetmed.vt.edu/Curriculum/VM8054/Labs/labtoc.htm>; W. Moritz, Ph.D., Univ. of Zurich

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Slide 33: www.hanall.co.kr