

# Family History and Diabetes



Practical Genomics for the Public  
Health Professional

# Outline

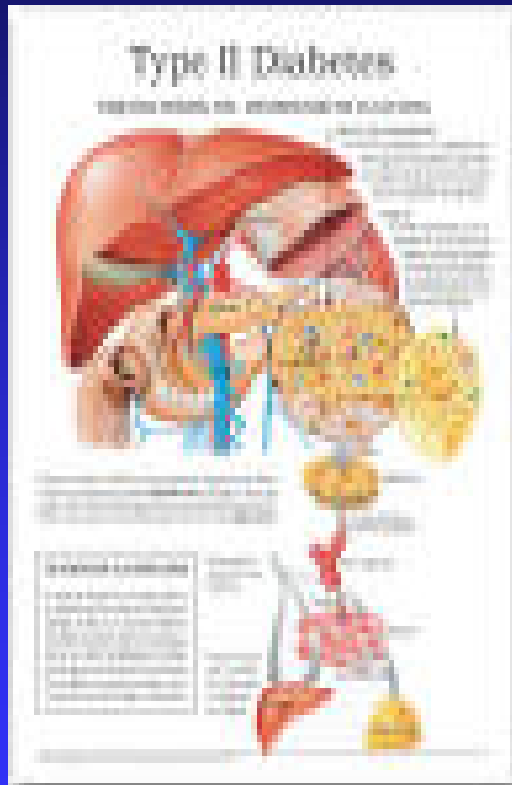
- Overview of Type 2 Diabetes/Gestational Diabetes
- Familial/Genetic Nature of Diabetes
- Interaction of Genes and “Environment” in Diabetes
- Diabetes Prevention and Screening
- Assessing Familial Risk and Developing Personal Plan

# Diabetes Statistics

- 17 million people in the U.S. (5.9 million undiagnosed)
- 6<sup>th</sup> leading cause of death
- Major cause of kidney failure, blindness, amputations

# Type 2 Diabetes

(*pka: Type II, NIDDM, AODM*)



- Multi-factorial and heterogeneous disorder
- Abnormalities in insulin secretion or action (insulin resistance) → elevated blood glucose → microvascular damage

# Type 2 Diabetes (cont)

- Primarily impacts adults
- Increasing problem in children/adolescents
- Associated with “Western” lifestyle (high energy food, sedentary behavior)
- Many cases are preventable!!!

# Gestational Diabetes (GDM)



- Glucose intolerance (elevated glucose) during pregnancy → increased risk of congenital anomalies, large infants
- 20-50% women with GDM eventually develop Type 2 diabetes

# Familial Risk for Developing Type 2 Diabetes

One parent with T2D < age 50	1 in 7
One parent with T2D > age 50	1 in 13
Both parents with T2D	1 in 2
Identical twin with diabetes	3 in 4

*\*Data from American Diabetes Assoc patient education information*

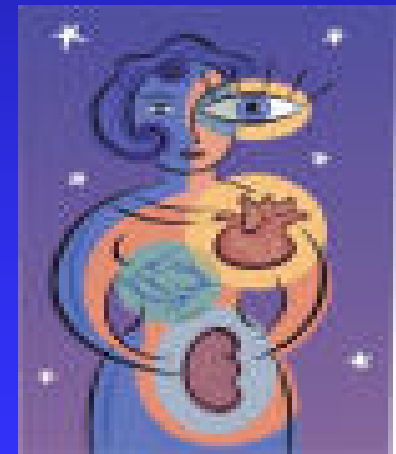
# Family History and Gestational Diabetes

- First degree relative with Type 2 diabetes → increased risk of gestational diabetes
- Level of risk depends on age of mother
  - < 30 y/o with + fam hx = general pregnant population risk
  - >30 y/o + fam hx = 3 x increased risk over general population



# Family History and Diabetic Complications

- Complications appear to cluster in families
- Likely shared genetic factors that contribute to development of complications in presence of hyperglycemia
- Examples:
  - ◆ Nephropathy (kidney)
  - ◆ Retinopathy (eyes)



# Ethnic Background and Type 2 Diabetes

- Greatest lifetime risk in Hispanic population (45% in males, 52 % in females)
- Other high risk groups → African-Americans, Native Americans, Southeast Asians
- Genetic factors + shared environment/ lifestyle factors (diet, exercise, obesity)= increased risk



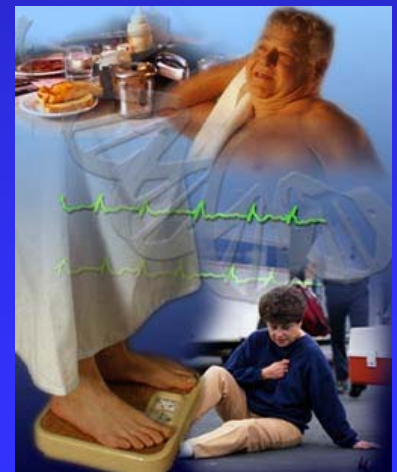


# Genes and Type 2 Diabetes

- Genes and gene variants + their products or functions + the environment = individual's risk of developing diabetes
- Risk gene variants are common in population
- Each gene variant contributes only small degree of added risk (or protection)

# Thrifty Genotype Hypothesis

- Proposed by Neel in 1960's
- General concept: certain **gene variants** promote fat storage and lower metabolic rates
- Historically: Food scarcity + high energy requirements + **gene variants** → survival
- Modern society: Over-nutrition + sedentary lifestyle + **gene variants** → predispose to illness

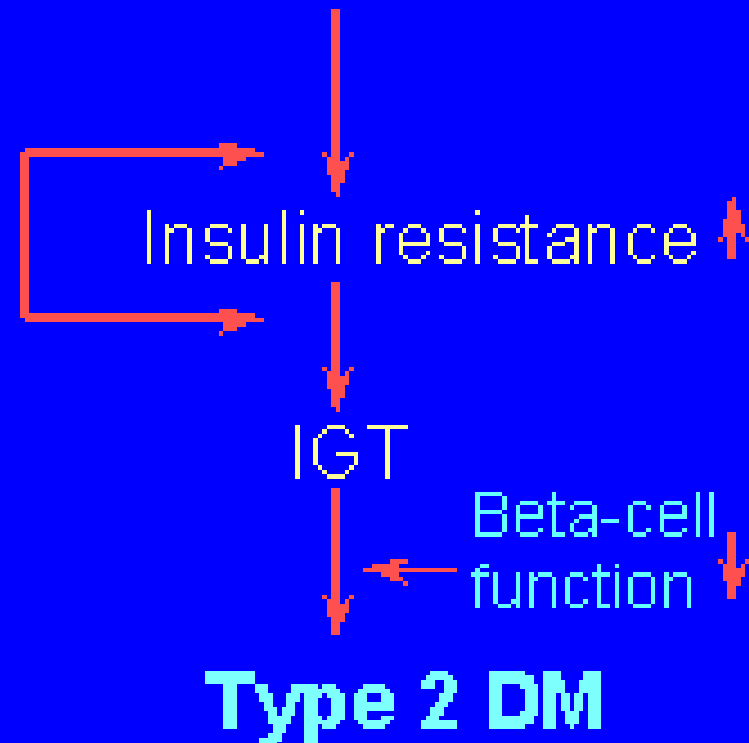


# Genetic Susceptibility

## ◆ *Step 1*

Obesity  
Physical inactivity  
Age

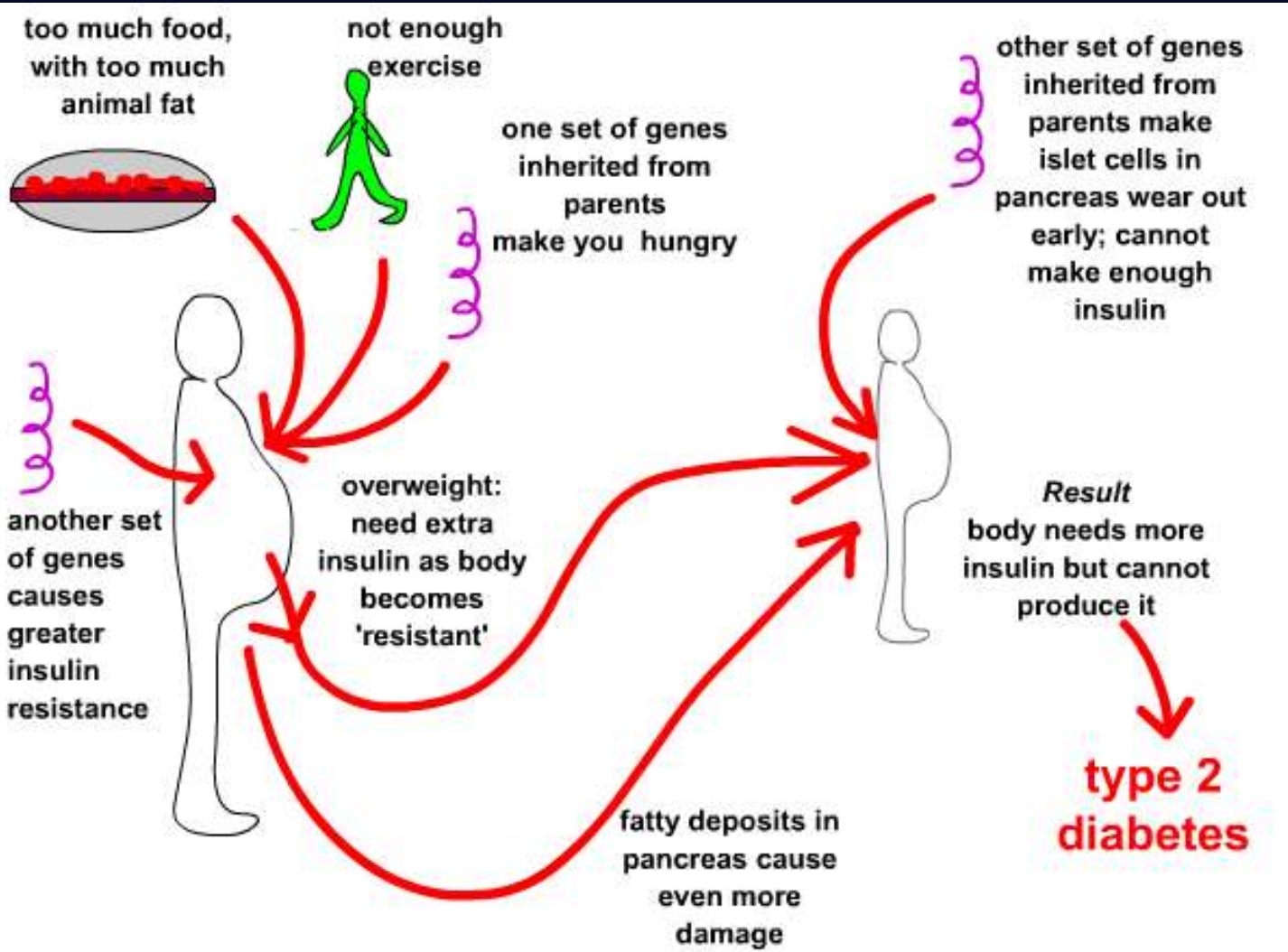
## ◆ *Step 2*



# Diabetes and Obesity

- 70% of Type 2 diabetics are obese
- 30% of obese individuals have Type 2 diabetes
- 38% of excess risk associated with family history could be avoided if BMI not allowed to exceed 30 kg/m<sup>2</sup> (Sargaent et al, *Int J Obes Relat Metabol Disord*, 2000)





# Obesity and Family Hx of Diabetes

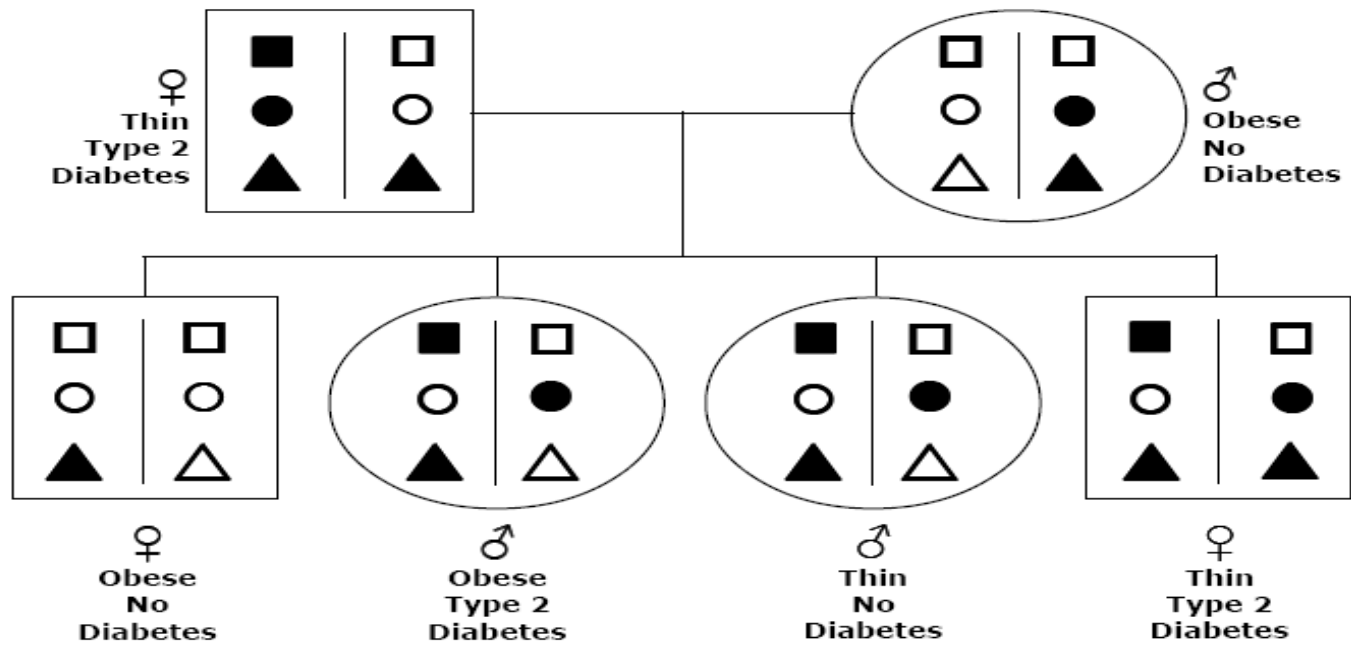
- Children of non-obese Type 2 diabetics more likely to develop diabetes than children of obese diabetics
- Hypothesis= greater “load” of risk genes in thin diabetics



# Obesity and Family Hx of Diabetes

	- Family History	+ Family History
- Obesity	1.6*	8.8*
+ Obesity	1.8*	16.7*

\*Age-adjusted incidence rate for development of diabetes per 1000 person-years (*Goldfine et al, PNAS, 2003*)



Diabetes Risk Gene Variants	No Diabetes Risk Gene Variants
■ ● ▲	□ ○ △
<hr/>	
> 4 Risk Genes	= Diabetes
3 Risk Genes + Obesity	= Diabetes
< 3 Genes - Obesity	= No Diabetes

# Type 2 Diabetes Prevention

- Progressive disorder
- Pre-diabetes stage (impaired glucose tolerance)
- Lifestyle and/or medication → prevent or delay progression  
*(Diabetes Prevention Program, Finnish Trial)*



# Type 2 Diabetes Prevention

- Identify individuals at risk of pre-diabetes/diabetes
  - ◆ Age >45 and overweight
  - ◆ Family history
  - ◆ Hx of GDM
  - ◆ Inactive lifestyle
  - ◆ High blood pressure
  - ◆ High cholesterol

# Type 2 Diabetes Screening: Adults\*

- Consider glucose screening every 3 years after age 45 years, esp if BMI  $>25$  kg/m<sup>2</sup>
- Screen before 45 years if positive family history and one other risk factor (obesity, hypertension, high cholesterol, sedentary lifestyle, ethnic group)
- Consider screening at age 30 in high-risk ethnic groups with additional risk factors

\* *USPTF recommends diabetes screening in adults with high blood pressure or high cholesterol (insufficient evidence for other adults)*

# Type 2 Diabetes Screening: Children\*

- Who to screen:
  - ◆ Overweight youth (BMI>85%) with two additional risk factors (family history, ethnic group or signs of insulin resistance)
- When to start:
  - ◆ Age 10 (or onset of puberty)
- How often:
  - ◆ Every 2 years



\* *ADA Consensus Statement*

# GDM Screening\*

- If 1<sup>st</sup> degree relative with Type 2 diabetes (and pt >30 yrs?) → screen at first prenatal visit, repeat at 24 weeks
- If average risk (including more distant relatives) → screen at 24-28 weeks
- If low risk (<25 y/o, no family hx, low risk ethnic group, nl weight) → consider no screening

\* *Modified from ADA position statement 2002 (Insufficient evidence for USPTF recommendation 2003)*

# Prevention Strategies

- Incorporate diabetes into family history assessment (and vice versa)
- Identify high risk individuals based on family history + environmental factors
- For high and moderate risk → Encourage lifestyle modifications (weight loss + physical activity)
- For high risk → conduct lab screening
  - ◆ Fasting blood glucose or oral glucose tolerance test



# “Genomic” Interventions for Individuals with Diabetes

- ◆ Monitor literature for advances in pharmacogenetics (individualized tx based on genetic make-up)
- ◆ Encourage sharing of diabetes risk information/prevention messages with at-risk family members





# Assessing Familial Risk

- Did/do you or a parent, sibling, child have Type 2 diabetes or GDM?
- How many relatives were/are affected?
- How old were the relatives when diagnosed (may be several years after onset of condition)?
- Were there associated factors (e.g. obesity, sedentary lifestyle)?
- What were complications (if known)?

# Assessing Familial Risk for Developing Type 2 Diabetes

## ■ Highest risk

- ◆ Multiple first degree relatives
- ◆ Young age of onset in relatives
- ◆ Diabetes in non-obese relatives



## ■ Moderate risk

- ◆ One first degree relative (or several distant relatives)
- ◆ Diabetes in family members associated with obesity/sedentary lifestyle

## ■ Lowest risk

- ◆ No personal or family history of Type 2 or GDM

# Adding Familial and Environmental Risks

- Consider simple tools
  - ◆ American Diabetic Association
  - ◆ Diabetes Detection Initiative

# **“Diabetes Risk Test”**

*(questions are from the American Diabetes Association's on-line)*

**Answer Each Question: Yes (score) No (0)**

Are you a woman who has had a baby weighing more than 9 pounds at birth? Yes=1, No=0

Do you have a sister or brother with diabetes? Yes=1, No=0

Do you have a parent with diabetes? Yes=1, No=0

Find your height on the chart. Do you weigh as much as or more than

the weight listed for your height? *(See chart on back)* Yes=5, No=0

Are you under 65 years old and get little or no exercise in a typical day? Yes=5, No=0

Are you between 45 and 64 years old? Yes=5, No=0

Are you 65 years old or older? Yes=9, No=0

**Add Your Score=\_\_\_\_\_**

# At Risk Weight for Height Chart

4'10	129	5'8	177
4'11	133	5'9	182
5'0	138	5'10	188
5'1	143	5'11	193
5'2	147	6'0	199
5'3	152	6'1	204
5'4	157	6'2	210
5'5	162	6'3	216
5'6	167	6'4	221
5'7	172		

# Diabetes Risk Scores

## ■ If you scored . . . then your risk is . . .

- ◆ 10 or more points → High for having diabetes now.
  - ◆ Talk with your **health care provider soon**.
- ◆ 3 to 9 points → Probably low for having diabetes now. Keep your risk low.
  - ◆ If you're overweight, lose weight.
  - ◆ Be active most days, and don't use tobacco.
  - ◆ Eat low-fat meals with fruits, vegetables, and whole-grain foods.
  - ◆ If you have high cholesterol or high blood pressure, talk to your healthcare provider about your risk for diabetes.

# Making a Personal Plan

- Based on your family history and other health information:
  - ◆ Are you a candidate for blood glucose screening?
  - ◆ Do you need to modify your lifestyle to reduce your risk of diabetes?
  - ◆ Is there an elevated risk in the family? Do other family members need information to help make decisions?