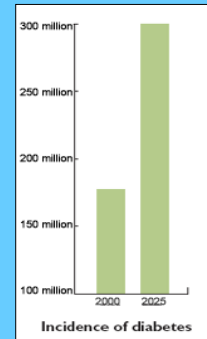




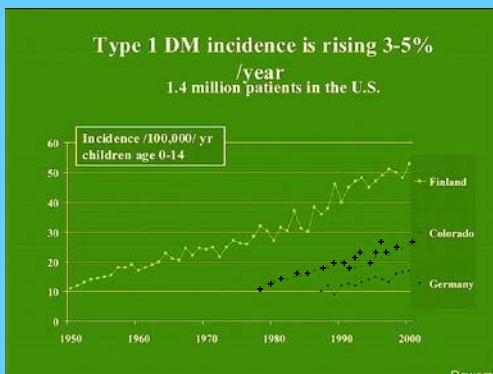
## Turning the tide: preventing type 1 and type 2 diabetes

## Projected worldwide incidence of diabetes



World Health Organization

It's not only the incidence of type 2 DM that is rising...



## Teddy trial: 2004-2023

“The Environmental Determinants  
of Diabetes in the Young”

- Ⓢ Pregnancy
- Ⓢ Diet in infancy
- Ⓢ Immunizations
- Ⓢ Drinking water
- Ⓢ Pets/allergens
- Ⓢ Psychosocial stress



## Possible causes of type 1 diabetes

- Ⓢ Genetic susceptibility
  - 1/300 general population have multiple anti-islet antibodies
- Ⓢ Environmental factors
  - Infections: e.g. Coxsackie virus
  - chemical toxins: nitrates, nitrites
  - neonatal nutrition: breast feeding, cows milk, vitamin D, gluten exposure < 3mo
- Ⓢ Immune mechanisms → beta cell destruction



Concordance rate ~ 20-35%

## Modifiable factors associated with an increased risk of type 1 diabetes

- Ⓢ Vitamin D
- Ⓢ Cow's milk
- Ⓢ Gluten
- Ⓢ Nitrates



## Vitamin D 25(OH)D

- Ⓢ Deficiency is common throughout the US
- Ⓢ Vitamin D has many roles:
  - Calcium balance
  - Cell growth & differentiation
  - Immune function
  - Anti-oxidant/anti-inflammatory activity
- Ⓢ Vitamin D is essential for normal  $\beta$ -cell insulin secretion



## Vitamin D and type 1 diabetes (T1D)

- Ⓢ Lancet 2001
  - Children given 2000 IU/d vitamin D were 80% less likely to develop T1D
- Ⓢ J Pediatrics 2009:
  - 84% of T1D patients had low vitamin D (25OHD < 75 nmol/l)
  - 51% of healthy adolescents 25OHD < 75nmol/l
- Ⓢ Diabetologia 2008
  - Worldwide incidence of T1D is inversely associated with UVB exposure



## Optimum level of 25(OH)D for prevention of chronic disease

- ~100 nmol/L
- Vitamin D3 is the best choice, taken with meals
- Most adults need at least 1000 IU/day



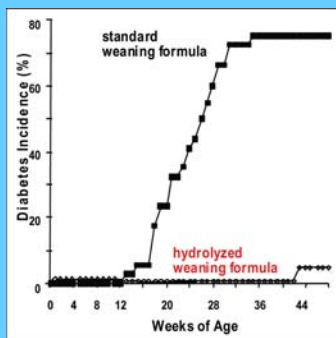
## Cows milk and type 1 diabetes



Animal studies and some recent human studies support an association between early introduction of cows milk protein and increased risk of T1D

Incidence of diabetes in non-obese diabetes prone mice is significantly influenced by weaning formula

- Hydrolyzed casein-based formula: 4.6%
- Formula with intact cows milk proteins: 59%



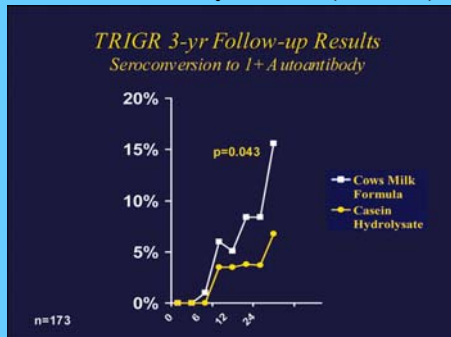
Caicedo, R. A. et al. Neoreviews 2005;6:e220-e226

## TRIGR (Trial to Reduce IDDM in the Genetically at Risk)

- 2,032 newborns at increased risk of T1DM
- Runs from 2002- 2017
- Infants will be weaned to:
  - casein hydrolysate formula
  - conventional cows milk formula
- Children will be followed for 10 years



## Trial to Reduce Insulin-Dependent Diabetes in the Genetically at Risk (TRIGR)



## TRIGR trial at 7 year follow up

- ⊙ Pediatric Diabetes 2008: study of 94 children in the cow's milk formula group
- ⊙ Children who developed T1D showed enhanced immune response to a variety of cow's milk proteins as compared with other children in cows milk group
- ⊙ Conclusion: "...a dysregulated immune response to oral antigens is an early event in the pathogenesis of T1D."



## Gluten

- ⊙ JAMA 2003 - dietary factors in the first year of life and development of islet auto antibodies (IA)
- ⊙ Introducing gluten containing foods < 3 months ⇒ 24% risk of developing IA
- ⊙ 7% risk of IA was found in infants who received breast milk only
- ⊙ Gluten introduced after age 6 months did not show increased IA

## Nitrates

- ⊙ We ingest nitrates from contaminated water & foods
- ⊙ Nitrates → formation of N-nitroso compounds (NOC)
- ⊙ NOC
  - genotoxic compounds
  - toxic to pancreatic β cells in animal studies
- ⊙ Several human studies have shown a increased risk of T1D with higher nitrate exposures



## Reducing the risk of type 1 diabetes

- Ⓢ Adequate vitamin D
- Ⓢ Avoid early cows milk exposure
- Ⓢ Avoid introduction of gluten grains < 6mo
- Ⓢ Reduce nitrate exposure



## Type 2 diabetes



## Diabetes has been called a “global pandemic” by the Canadian Diabetes Association

- Ⓢ The numbers of people with diabetes have jumped from 30 million in 1980, to 250 million in 2008. (A 700% increase)
- Ⓢ 350 million people are projected to have diabetes by 2030.



## Causes of type 2 diabetes

- Ⓢ Genetic susceptibility
- Ⓢ Obesity
- Ⓢ Dietary factors
  - Glycemic index/load
  - Fiber
  - Fruits/vegetables
  - Calcium/magnesium
  - Vitamin D
  - Nuts
  - Fats
- Ⓢ Environmental toxins
- Ⓢ Sedentary lifestyle

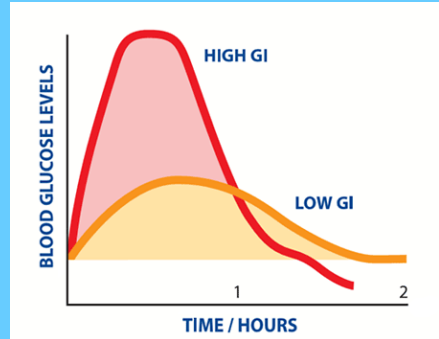


Concordance rate ~70% in identical twins

## Carbohydrates and obesity



## The glycemic index (GI)



low  $\leq 55$  medium 56-69 high  $\geq 70$

## The glycemic load (GL)

- ⊕ Glycemic load =  $\text{GI} \times \text{carbohydrate (gm per serving)} \div 100$
- ⊕ Low 0-10 low medium 11-19 high  $>20$



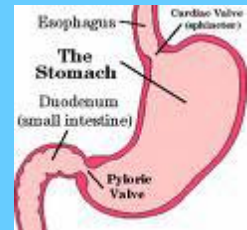
GI 80 GL 7.8  
1 cup watermelon



GI 72 GL 25.6  
 $\frac{1}{2}$  bagel

## 1. Factors that influence the GI: rate of stomach emptying

- ⊕ Slowing the rate of stomach emptying:
  - soluble fiber
  - acids
  - protein
  - fat



## 2. Factors that influence the GI: amylose vs amylopectin

Ⓜ Foods high in amylose starch: Basmati rice, kidney beans, lentils



Ⓜ Foods high in amylopectin starch: potatoes, wheat flour, sticky rice



Amylose starch molecules take longer to be acted upon by digestive enzymes than amylopectin starches

## 3. Factors that influence the GI: starch gelatinization

Ⓜ Gelatinization of starch increases the rate of digestion

- Sticky rice, Jasmine rice
- Pasta cooked 20 minutes



## 4. Factors that influence the GI: physical barriers

Ⓜ Physical barriers to digestion: whole grains are more resistant to action by digestive enzymes than finely pulverized flours



Bulgur 46



Whole wheat bread 69



Baguette 95

## Physiologic response to a high glycemic index food (part 1)

Ⓜ rapid rise in blood glucose → spike in insulin output → promotes glucose uptake by muscle & adipose tissue and fat storage

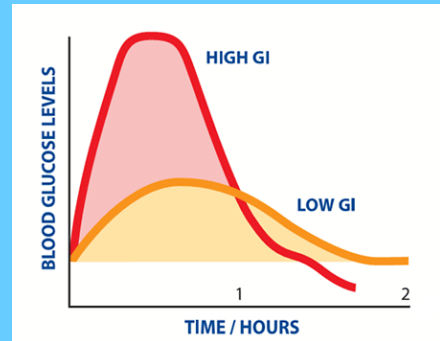


## Physiologic response to a high glycemic index meal (part 2)

- Ⓜ As blood glucose falls, counter-regulatory hormones are released: catecholamines, glucagon, cortisol, growth hormone



## The glycemic index



low <55 medium 55-70 high >70

## Physiologic response to a high glycemic index meal (part 3)

- Ⓜ Increased appetite is stimulated by declining blood glucose and counter-regulatory hormones

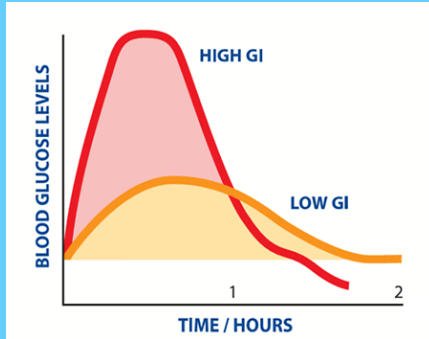


## Physiologic response to a low glycemic index meal

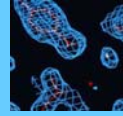
- Ⓜ Slower rise in blood glucose
- Ⓜ Moderate release of insulin
- Ⓜ Longer period of satiety
- Ⓜ No reactive hypoglycemia



## The glycemic index



low <55 medium 55-70 high >70

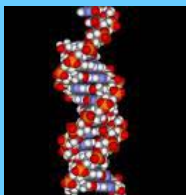


## High insulin secretors vs low

- Ⓢ People who are high insulin secretors lose more weight (than low insulin secretors) when they eat low glycemic load diets
- Ⓢ Weight loss: 5.8 kg vs 1.2 kg
- Ⓢ Lipids: Low glycemic load diet also has beneficial effects on lipids, raising beneficial HDL cholesterol and lowering triglycerides

## Nutrigenomics

Diet influences gene expression!



## Glycemic index and gene expression

- Ⓢ Low glycemic index diets have been found to down regulate 71 different genes, resulting in:
  - lower insulin levels and increased resistance to obesity
  - lower risk of type 2 diabetes
- Ⓢ High glycemic index diets have been found to up regulate 62 different genes, resulting in increased inflammation and oxidative stress

## GI/GL and weight loss

- Ⓢ Overweight and obese people have been shown to lose the most weight on low GI/GL diets compared to other diets
- Ⓢ This is thought to be because of a longer period of satiety after meals



## The aftereffects of breakfast and lunch...

- Ⓢ A study of obese teenage boys found that a high GI breakfast and lunch led to excessive hunger and overeating for the rest of the day
- Ⓢ The boys who ate a low GI breakfast and lunch were less hungry and spontaneously ate less for the rest of the day



## Type 2 Diabetes



High glycemic index diets can increase the risk of developing type 2 diabetes by 40%

## Whole grains/ high fiber diet

- Ⓢ A diet high in cereal grain fiber is associated with a lower risk of type 2 DM
- Ⓢ Combination of low fiber diet and high GI foods more than doubles the risk of type 2 DM





## Low GI carbohydrates

- ☉ Breads: 100% whole grain breads, pita bread, sourdough breads
- ☉ Rice: Basmati rice, Uncle Ben's™ converted rice
- ☉ Pasta: al dente
- ☉ Cooked grains: quinoa, bulgur, steel cut oats, large flake oats
- ☉ Cereals: All Bran™

## Higher GI carbohydrates

- ☉ Most breads, bagels and other flour products
- ☉ Puffed grains
- ☉ Most cold breakfast cereals
- ☉ Potatoes
- ☉ Goopy starches



## Advice to patients re: glycemic index

- ☉ Use it to choose the types of starchy foods you eat [www.glycemicindex.com](http://www.glycemicindex.com)
- ☉ Ignore the GI of proteins, fats, nuts and (most) fruits and vegetables
- ☉ Combine high GI foods with low GI foods
- ☉ Eat smaller portions of high GI foods
- ☉ Add lemon juice or vinegar to the meal
- ☉ Include healthy fats and lean proteins with every meal

## Nutrient density/quality



Apple  
GI 37



High fat ice cream  
GI 37

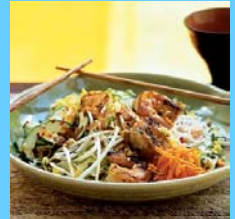


## The Bottom Line

- Ⓢ Large excursions in postprandial glucose levels are harmful to health
- Ⓢ Low GI/GL, nutrient dense carbohydrates from whole foods are recommended
- Ⓢ Overweight or obese people should be especially careful to choose low glycemic index/load carbohydrates

## What else influences the risk of developing type 2 diabetes?

- Ⓢ Vitamin D
- Ⓢ Magnesium
- Ⓢ Nuts
- Ⓢ Fats
- Ⓢ Endocrine disrupting chemicals



## Vitamin D

- Ⓢ Vitamin D is necessary for  $\beta$ -cell insulin secretion
- Ⓢ Low vitamin D is associated with  $\uparrow$ insulin resistance and  $\downarrow$ insulin secretion
- Ⓢ Nurses Health Study: 800 IU/d  $\Rightarrow$  23% lower risk of developing type II diabetes
- Ⓢ People in the highest quartile of vitamin D have been found to have a 30% reduction in their risk of developing type 2 diabetes



## Vitamin C

- Ⓢ Archives of Internal Medicine 2008:
  - Odds ratio for T2D in top quintile of plasma vitamin C 0.38 (62% lower risk)
  - Odds ratio for T2D in top quintile of fruit and vegetable consumption 0.78 (22% lower risk)
- Ⓢ Epidemiology 2004: risk of gestational DM 3x higher in women in the lowest quartile of plasma ascorbic acid
- Ⓢ NHANES: Newly diagnosed type 2 diabetics have significantly lower serum vitamin C levels



## Calcium and Vitamin D

- Ⓢ Some evidence that an intake of 700 IU vitamin D and 500mg calcium slows the rise of fasting blood glucose (>age 65)
- Ⓢ NIH trial currently recruiting: Vitamin D and Calcium Homeostasis for Prevention of Type 2 Diabetes
- Ⓢ Intervention: Vitamin D3 2000 IU/day and calcium carbonate 400 mg bid



## Magnesium

- Ⓢ Women's Heart Study found a significant inverse relationship between dietary magnesium and risk of developing diabetes
- Ⓢ Diabetes Care Jan 2004: Relative risk of type 2 diabetes was 0.66 in women and 0.67 in men who were in the highest quintile of magnesium intake (33%-34% lower risk)



## Peanut butter and nuts

- Ⓢ Nurses health study (JAMA 2002)
  - Women who ate nuts  $\geq$  to 5 times per week showed a 27% reduction in risk of type 2 diabetes
  - Women who ate 5 tbsp of peanut butter per week showed a 20% reduction in risk of developing type 2 diabetes
  - Results were independent of other known risk factors for type 2 diabetes

Epidemiological studies of Greenland Inuit, indigenous Alaskans and Finnish and Dutch populations have shown an association between higher n-3 PUFA intake and lower incidence of type 2 DM



## Saturated fat, trans fat and PUFA's

- Ⓢ High saturated fat (18%) ↓ insulin sensitivity and ↑ risk of DM
- Ⓢ Trans fats RR 1.31 for highest quintile
- Ⓢ Processed meats (5x/wk) RR 1.46
- Ⓢ PUFA's are protective RR 0.75 for highest quintile



## The role of stress

- Ⓢ SNS causes ↑HR, ↑BG, ↑BP, ↓HRV (heart rate variability)
- Ⓢ Autonomic dysfunction is associated with an increased risk of diabetes
- Ⓢ Lower resting HR and increased HRV are associated with ↓ DM



## Mind body medicine

- Ⓢ Meditation
- Ⓢ Guided Imagery
- Ⓢ Self Hypnosis
- Ⓢ Breath work
- Ⓢ Yoga
- Ⓢ Biofeedback



## Endocrine disrupting chemicals

- Ⓢ Bisphenol A
  - Found in canned foods, food storage containers, polycarbonate bottles (#7)
  - Mimics 17β-estradiol
  - Induces hyperinsulinemia and insulin resistance in mice
  - Epidemiological evidence of similar effects in humans





## Doing everything...

- Ⓢ NEJM 2002 >84,000 nurses 1980-1996
- Ⓢ “Low risk group”:
  - BMI < 25
  - High cereal fiber & polyunsaturated fat
  - Low trans-fat and glycemic load
  - Moderate-vigorous exercise 30 min/day
  - No current smoking
  - Average of ½ alcoholic drinks per day
- Ⓢ Lowest risk group had a RR = 0.09 for DM
- Ⓢ This is a 90% reduction in risk.

## Prevention strategies for type 2 DM

- Ⓢ Maintain a normal body weight or achieve a sustained weight loss
- Ⓢ Low GI/GL carbohydrates
- Ⓢ High fiber diet (especially cereal fiber)
- Ⓢ Vitamin D, calcium & magnesium
- Ⓢ Nuts, fatty fish
- Ⓢ Regular exercise
- Ⓢ Reduce exposure to environmental toxins
- Ⓢ Reduce stress with a daily mind body practice

