



New Horizons in the Prevention of Type 1 and Type 2

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Happy Birthday Dr. Banting





The Miracle of Insulin



Patient J.L., December 15, 1922



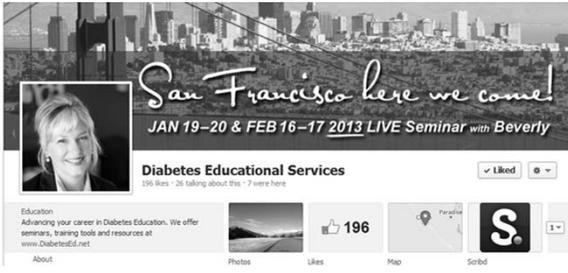
February 15, 1923

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Celebrating World Diabetes Day and 200 Facebook LIKES

(almost)  196

We are providing 1.0 CE FREE.



How to Earn Your CE

● It's Easy

- After the Webinar, we will email you a 3 question quiz.
- Reply to the email and just type in the correct answers.
- Email answers by **end of day tomorrow (11/15/2012)** to earn your FREE CE.
- We will email your certificate of completion by Friday.
- Thank you!

Objectives

1. Describe the role of gut Bacteria and gut hormones in type 1 and type 2 diabetes.
2. Discuss current research on the prevention and cure for type 1 diabetes
3. State strategies that promote healthy communities and decrease risk of type 2 diabetes.

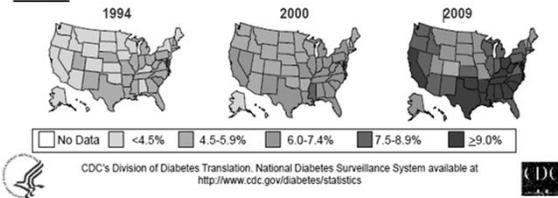


Diabetes in America 2012

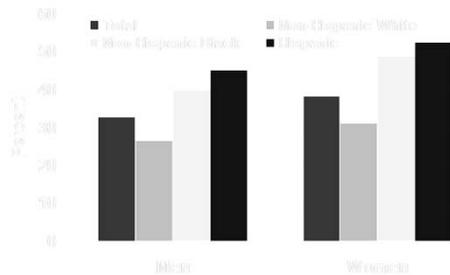
- 28 million or 8.3%
- 79 million have pre diabetes

CDC 2012

Diabetes



Estimated lifetime risk of developing diabetes for individuals born in U.S. in year 2000



Narayan et al, JAMA, 2003

Type 1 Rates Increasing Globally



- 23% rise in type 1 diabetes incidence from 2001-2009
- Why?
 - Autoimmune disease rates increasing over all
 - Changes in environmental exposure and gut bacteria?
 - Hygiene hypothesis
 - Obesity?

Risk Of Developing Type 1 Diabetes

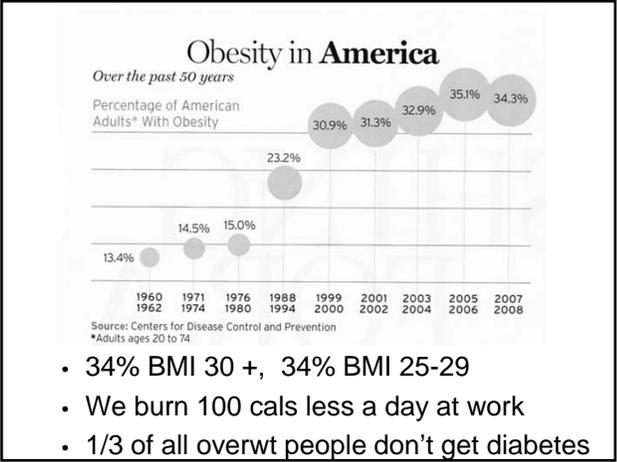
- General Pop 0.3%
- Sibling 4%
- Mother 2-3%
- Father 6-8%



Type 1 Diabetes Associated with other immune conditions

- Celiac disease (gluten intolerance)
- Thyroid disease
- Addison's Disease
- Rheumatoid arthritis
- Crohn's
- Multiple Sclerosis





Obesity - other factors?

- Not only humans are gaining weight globally
- Animals are getting heavier too (and not just the domestic kind).
- Factors – sleep deprivation, AC, other?
 - Marmosets to macaques





Newsweek, Fat Canaries in a Coal Mine, Dec 10, 2010.. Begley



Bacterial Cells Outnumber Human Cells 10 to 1

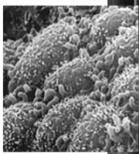


Getting to the Gut

- Gut bacteria and body weight
- Gut bacteria health influence on expression of type 1 and type 2
- Gut hormones



The Work of Gut Flora



Electron micrograph of small intestine and bacterial inhabitants in green.

Obesity and Gut Flora, Nature 2006



Normal Gut Bacteria

- Diverse
- Collected over a life time through
 - Environmental exposure
 - Types of foods consumed
 - Breast or bottle fed?
 - Parents
 - Vaginal delivery or C-Section
- Help us
 - utilize energy
 - fight off invaders



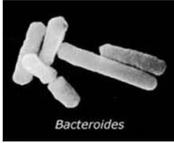
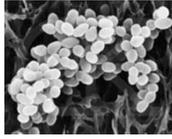
Intestinal Health – A Balancing Act

● Major Groups

- Firmicutes
- Bacteroidetes

Plus thousands of others

Diversity of gut bacteria more protective



Weight and Gut Bacteria New and Early Research

- Leaner people
 - more bacterial diversity
 - More **bacteroidetes**
 - Gut bacteria less efficient at converting food to calories
- Obese people
 - More **firmicutes**
 - Gut bacteria very efficient at calorie extraction
- Bacteria tend to run in families

Newsweek, July 6 2010

Fatty Foods Trigger Leaky Gut?



With diabetes, a high fat meal appears to trigger:

- Passage of bacterial endotoxins through intestinal wall
- Increase levels of inflammatory cytokines and triglycerides
- Seems to be worse if eat frequent fatty meals throughout the day – increases presence of lipopolysaccharide endotoxins

Research by Alison Harte, PhD - Clinical Endocrinology News- Nov 11, 2011

H. Pylori a Gut Culprit?



- *Helicobacter pylori* infection doubled risk of DM among Latinos 60 yrs +
- Study details:
 - 1,789 Latino men, women in Sacramento Area Latino Study on Aging (SALSA)
 - During 10 yr study, 18% developed diabetes
 - 2.7 times more likely to develop diabetes if seropositive for *H. pylori* (also assoc w/ higher BMI)
 - Why? Inflammation?

Reported at Annual Meeting of Infectious Disease Society of America –
Research led by Dr. Christine Y. Jeon of Columbia University - Clinical
Endocrinology News- Nov 11, 2011

Type 1 Diabetes & Gut Bacteria

- Exciting research in Finland
 - 8 children with same risk of getting type 1 diabetes based on family history and HLA DQ genotype
 - In the 4 children with ATB conversion, w/in 6 months before, the levels of firmicutes decreased and bacteroidetes increased.
 - The bio diversity also decreased
 - Hope that can id kids early on and halt progression to type 1.

DIPP – Diabetes Prediction and Prevention Study

Gut Bacteria Shift Prior to Diagnosis

Type 1 Diabetes

- ↓ Firmicutes
- ↑ Bacteroidetes
- Less diverse
- Less stable

No Type 1

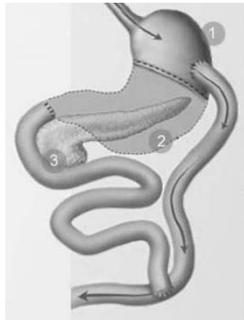
- ↑ Firmicutes
- ↓ Bacteroides
- Healthy Microbiome, diversity increased

Gut Hormones and Bacteria



Post Gastric Bypass

- the diversity of gut bacteria increase
 - ↓ Firmicutes
 - ↑ Bacteroidetes
- availability of gut hormones also increase



Gut Hormone Replacement in Type 1? Liraglutide Study

- 14 type 1 pts, 24 wks received liraglutide daily w/ insulin therapy
 - Lowered wt – 68 kg to 63kg
 - Lowered A1c – 6.5 to 6.1
 - Basal insulin dropped by 48%
 - Bolus insulin lowered by 42%
 - Less glucose fluctuations



Annual meeting of Endocrine Society -8/11
Dr Anjay Varanasi investigator

Prevention to Cure of Type 1

- Determining who is at risk
- Environmental triggers
- Pharmacologic interventions to halt autoimmune destruction
- Transplantation
- Artificial Pancreas



How do we know someone has Type 1 vs Type 2

- Type 1
 - Positive antibodies
 - GAD
 - ICA
 - IAA and others
- Younger the person is, the more quickly it develops
- Older people take longer to develop



Autoantibodies Assoc w/ Type 1

Panel of autoantibodies –

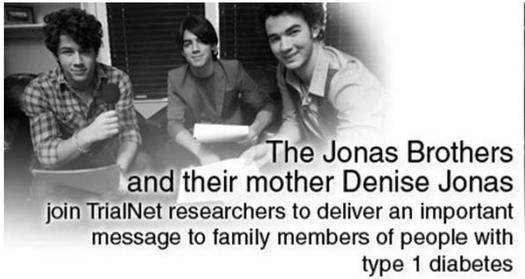
- GAD65 - Glutamic acid decarboxylase –
- ZnT8 - Zinc Co-Transporter 8
- ICA - Islet Cell Cytoplasmic Autoantibodies
- IA-2A - Insulinoma-Associated-2 Autoantibodies
- IAA - Insulin Autoantibodies



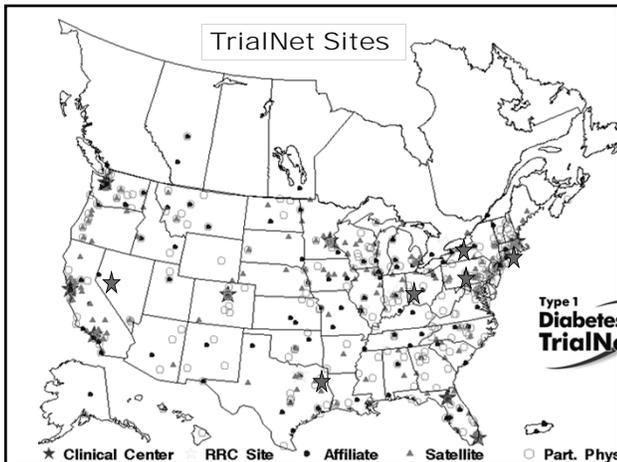
Screening for Type 1 – ADA 2012 Standards of Med Care

- Evidence from type 1 prevention studies suggest that measurement of islet autoantibodies identifies individuals at risk for developing type 1 diabetes.
- Such testing may be appropriate in high-risk individuals ... in the context of clinical research studies - see, for example, <http://www2.diabetestrialnet.org>

Type 1 Diabetes Trial Net Natural History and Prevention www.DiabetesTrialnet.org



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TrialNet Natural History Study

- Who is eligible for screening?
 - Ages 1-45 & immediate family member w/ DM
 - Ages 1-20 for extended family
- What is the screening test?
 - Single blood test for panel of autoantibodies
 - Those < 18 & Ab neg rescreened yearly
- What happens if they have 1 or > Abs?
 - Monitoring and on-going surveillance Genetic screen: HLA class II
 - Metabolic screen: Oral glucose tolerance test

Type 1 Prevention - Stages

- Primary Prevention
 - Genetic susceptibility
- Secondary Prevention
 - Islet Autoimmunity
- Tertiary Prevention
 - Expressing Type 1 Diabetes



Primary Prevention of Type 1

- Strategy – Find those at highest risk of Type 1 diabetes and see if early intervention to protect beta cells prevents or delays onset.
- Identify through genetic testing
 - HLA DQ and HLA DR alleles are the major determinant of type 1
 - 1 million currently at risk



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The Honeymoon

- By diagnosis, 15-40% of beta cell function remains
- Length of honeymoon varies
 - 10-15% of teens and adults still have clinically significant insulin production > 5 yrs after DM onset (DCCT, NEJM 1993)
- Medalist study: 2/3's with measurable insulin > 50 yrs after dx (King, Diabetes, YEAR)
 - Rate of beta cell loss is correlated with age
Younger pts tend to have shorter honeymoons

Remaining Beta Cells

- Can serve one well while it lasts...even if on supplemental insulin.
- Better overall glucose control lower HbA1C, less glycemic excursion, lower risk for severe hypoglycemia



Research on Type 1

- Primary Prevention – what triggers type 1?
 - Viruses
 - Hygiene (too much?)
 - Lack of breastfeeding
 - Early exposure to foods?
- Intervention – Secondary and Tertiary
- Cure



The Hygiene Hypothesis

- In studies, mouse raised in clean environment is higher risk for DM than one raised in dirty one
- “Clean living” may increase risk for autoimmune diseases
- Risk is higher in urban than rural settings
- Inverse correlation with immunizations, antibiotic use
- Daycare, other early exposures, lower risk for DM





The Environmental Determinants of Diabetes in the Young

Funded by NIDDK, the National Institute of Allergy and Infectious Diseases (NIAID), the National Institute of Child Health and Human Development (NICHD), the National Institute of Environmental Health Sciences, the CDC, the JDRF, and the ADA.

The Environmental Determinants of Diabetes in the Young (TEDDY) Consortium

- The main mission of the TEDDY consortium, an international group of clinical centers, is to identify infectious agents, dietary factors, or other environmental factors—including psychosocial events—that trigger type 1 diabetes in those who are genetically susceptible.

TEDDY – to determine if...

- Can reduce the risk of type 1 diabetes w/
 - Avoid early cows milk exposure
 - Avoid introduction of gluten grains < 6mo
 - Adequate vitamin D
 - Reduce nitrate exposure
 - Others



JOURNAL CLUB

Removal of Bovine Insulin From Cow's Milk Formula and Early Initiation of Beta-Cell Autoimmunity in the FINDIA Pilot Study

Otti Vaarala, MD, DMSc; Jorma Ilonen, MD, DMSc; Terhi Ruushtala, MA; Jonni Pesola, MD; Savi M. Virtanen, MD, DMSc; Taina Härkönen, PhD; Matti Koski, MA; Harri Kallioinen, MS; (Tech); Olli Tossavainen, DSc; (Tech); Tuula Poussa, MS; Anni-Liisa Järvenpää, MD, DMSc; Jorma Komulainen, MD, DMSc; Raija Lounamäe, MD, DMSc; Hans K. Åkerblom, MD, DMSc; Mikael Knip, MD, DMSc

Objective: To test whether weaning to a bovine insulin-free cow's milk formula (CMF) reduces type 1 diabetes mellitus-associated autoantibodies in children at genetic risk.

Design: Randomized, double-blind pilot trial (Finnish Dietary Intervention Trial for the Prevention of Type 1 Diabetes [FINDIA]).

Setting: Three pediatric hospitals in Finland from May 15, 2002, to November 22, 2005.

Participants: A total of 1113 infants with HLA-conferred susceptibility to type 1 diabetes were randomly assigned to receive study infant formulas; 908 children provided at least 1 follow-up blood sample (last follow-up, June 2009).

Intervention: The CMF (n=389), whey-based hydrolyzed formula (WHF) (n=350), or whey-based FINDIA formula essentially free of bovine insulin (n=365) during the first 6 months of life whenever breast milk was not available.

insulin, the 65-kDa isoform of glutamic acid decarboxylase, and the tyrosine phosphatase-related IA-2 molecule were screened, and islet cell autoantibodies and autoantibodies to zinc transporter 8 were analyzed in infants whose primary screening test results were positive.

Results: In the intention-to-treat analysis, 6.3% of children in the CMF group, 4.9% of those in the WHF group, and 2.6% of children in the FINDIA group were positive for at least 1 autoantibody by age 3 years. The odds ratios were 0.75 (95% CI, 0.37-1.54) in the WHF group and 0.39 (0.17-0.91) in the FINDIA group when compared with the CMF group. In the treatment-received analysis, the corresponding odds ratios were 0.81 (95% CI, 0.37-1.76) and 0.23 (0.08-0.69).

Conclusion: In comparison with ordinary CMF, weaning to an insulin-free CMF reduced the cumulative incidence of autoantibodies by age 3 years in children at genetic risk of type 1 diabetes mellitus.

Trial Registration: clinicaltrials.gov Identifier: NCT01099388

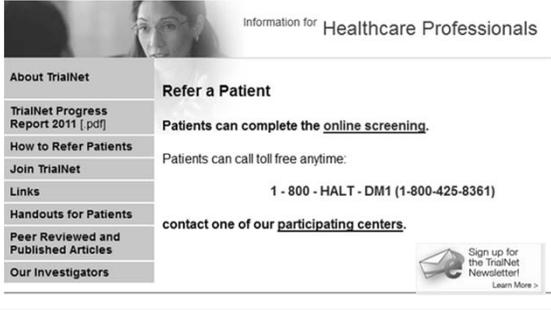
Take Home Message

- Get Dirty
- Breastfeed if possible.
- Avoid early exposure to cows milk and cows milk based formula and gluten? – year of life for those at high risk



How to Get Screened? www.DiabetesTrialNet.org

- How to get families linked to screening?



Information for Healthcare Professionals

About TrialNet

Refer a Patient

TrialNet Progress Report 2011 [pdf]

Patients can complete the [online screening](#).

How to Refer Patients

Patients can call toll free anytime:

Join TrialNet

1 - 800 - HALT - DM1 (1-800-425-8361)

Links

Handouts for Patients

contact one of our [participating centers](#).

Peer Reviewed and Published Articles

Our Investigators

Sign up for the TrialNet Newsletter! [Learn More >](#)

Why participate in Screening?

- Contribute to understanding
- Prevent DKA – Earlier diagnosis safer
- Start insulin sooner, may prolong honeymoon
- Early education and transitions
- Eligible for intervention studies



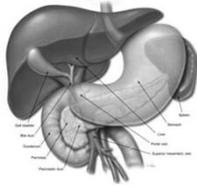
Type 1 –Intervention Studies

- Trial Net – Oral insulin
- GAD Vaccine (glutamic acid decarboxylase)
- START Trial – Thymoglobulin
- CD3 Monoclonal Antibodies
- Stem Cell



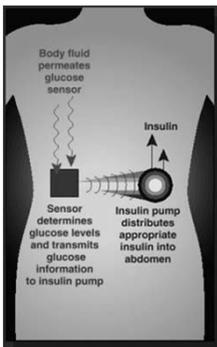
3 Types of Pancreas Transplants

- A **combined pancreas and kidney transplant** – most common – 75%
- A **solitary pancreas transplant** - less common – usually done after kidney transplant –
- An **islet transplant** — beta cells isolated from 2 pancreases, injected into portal vein of liver (lowers BG for a period of time)



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Other “Cures”? www.JDRF.org



Closed loop system
“artificial pancreas”

Prevention Strategies Type 2



Getting to Health



- Promoting healthy communities to decrease type 2
 - National Initiatives
 - Legislation in communities and states
 - Diabetes Educator's emerging role in health promotion





Thoughts on Diabetes, Weight, Social Change

- "The only way on a societal basis to reduce the prevalence of obesity is through community action" –
Dr. Frieden, CDC
- Poverty, Obesity, Diabetes inter-related

Will Legislation/ Policy/ Community Action Halt the Epidemic?

- Restaurant Calorie labeling
- Sugar tax – no Big Gulps
- Healthy foods in schools
- No Happy Meal toy unless make healthy choice (San Francisco, CA)
- Salt restriction
- Blue Zone (smaller plates, sidewalks)
- Let's move

Cookie Dough Incident





Pepsi Machine Incident

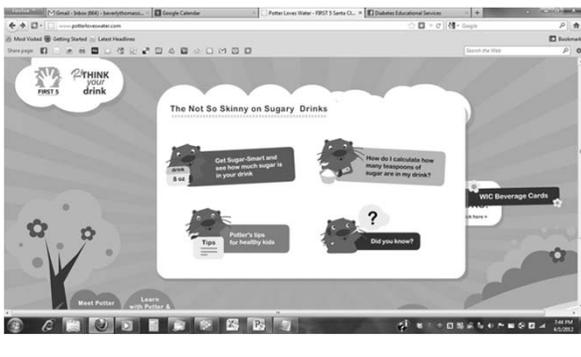


Soda Tax?



- Penny an ounce for every soda, sugar sweetened beverage sold.
- Initial projections estimate that tax on beverage distributors would raise \$1.7 billion a year
- Funds for CA cities/schools to pay for childhood obesity prevention programs in state.
- www.publichealthadvocacy.org.

Water Making a Come Back? PotterLovesWater.com





Let'sMove.Gov

1. Help Parents Make Healthy Family Choices
2. Create Healthy Schools
3. Provide Access to Healthy and Affordable Food
4. Promote Physical Activity

America's Move to Raise a Healthier Generation of Kids



National Salt Reduction Initiative

- 80% of salt intake from prepared foods
- Only 11% comes from own saltshakers
- Coalition of local and state health authorities and orgs working with food manufacturers and restaurants to **voluntarily** reduce the amount of salt
- The goal - reduce Americans' salt intake by 20% over 5 years.



Diabetes Prevention Programs

- Delay or Prevent Type 2 Diabetes
 - Save \$5.7 billion over 25 years
 - Programs
 - Partnering with 
 - CDC now recognizes Diabetes Prevention Programs
- www.cdc.gov/diabetes/prevention

Health Affairs 31, No 1 2012 p50-60

In Conclusion

“Never doubt that a small group of thoughtful, committed citizens can change the world. Indeed, it is the only thing that ever has.”

—Margaret Mead



We would love an Invitation to Present in Your Town –
DiabetesEd.net



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