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New Horizons in the Prevention of Type 1 and Type 2

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Web Clinic Details

- To hear presentation, turn on your computer speaker or listen via your phone
- Questions? Type in question box or Please email us after program.
- Thank you for joining us!

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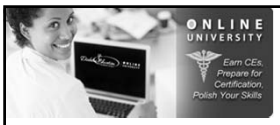

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Topics

- New findings in diabetes prevention and treatment
- Type 3 Diabetes? The relationship between diabetes and the brain
- Keeping your Mind Fit
- Answer the question.. What do Michael Jackson and diabetes have in common?

CDC Announces

1 in 3 Americans may have Diabetes by 2050

Boyle, Thompson, Barker, Williamson
2010, Oct 22:8(1)29
www.pophealthmetrics.com

Type 2 Diabetes in US

- 26 > **28** million or 8% > **8.3%**
- **79 million have pre diabetes**
- New cases increased **90%** in past 10 years.
  - 4.8 per 1,000 people during 1995-1997 to
  - 9.1 per 1,000 in 2005-2007 in 33 states.

CDC 2011

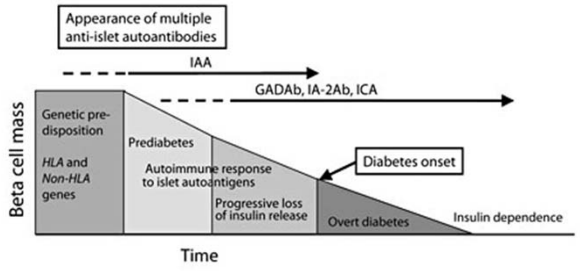
Get Involved
Action Item – Medicare Prevention Act 2013
Contact your Reps

Type 1 Diabetes Facts

- As many as **3 million Americans** may have type 1 diabetes.
- Each year, approximately **80 people per day** are diagnosed with type 1 diabetes in the U.S.
- Approximately **85 percent** of people living with type 1 diabetes are adults, and **15 percent** are children.
- The rate of type 1 diabetes incidence among children under age 14 is estimated to **increase by 3 percent annually** worldwide.
- Type 1 diabetes accounts for **$14.9 billion** in healthcare costs in the U.S. each year.

Source: JDRF

Natural History of Type 1



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

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)
- **Rate of beta cell loss is correlated with age**
- **Younger pts tend to have shorter honeymoons**

Medalist Study – Harvard Joslin Diabetes Center

- After 50 years with diabetes
  - Many still produced some insulin
  - Many had no eye disease

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

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

The Miracle of Insulin

Patient J.L., December 15, 1922

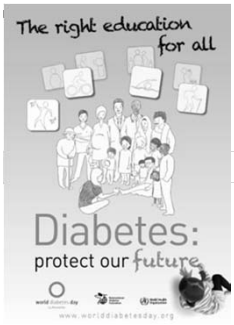
February 15, 1923

The Nobel Prize in Physiology or Medicine 1923

Frederick G. Banting

Born: 14 November 1891, Alliston, Canada
Died: 21 February 1941, Newfoundland, Canada
Affiliation at the time of the award: University of Toronto, Toronto, Canada
Prize motivation: "for the discovery of insulin"
Field: endocrinology, metabolism

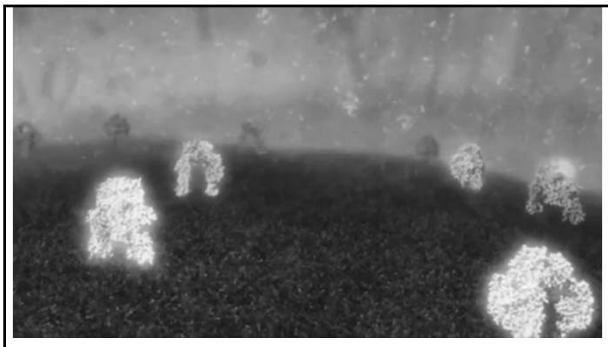
World diabetes day- November 14



2013 Nobel Prize for Medicine

"for their discoveries of machinery regulating vesicle traffic, a major transport system in our cells".

Awarded jointly to James E. Rothman, Randy W. Schekman and Thomas C. Südhof



Images showing insulin (blue) molecules binding with insulin receptors (yellow) could help in the development of new diabetes treatments – Jan 2013

The international research team was led by scientists from the Walter and Eliza Hall Institute (WEHI) in Melbourne, with collaborators from La Trobe University, the University of Melbourne, Case Western Reserve University, the University of Chicago, the University of York and the Institute of Organic Chemistry and Biochemistry in Prague.

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
- 1 million currently at risk

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TEDDY

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.

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

Outi Vaarala, MD, DMSc; Jorma Ilonen, MD, DMSc; Terhi Ruohtula, MA; Jouni Pesola, MD; Suvi M. Virtanen, MD, DMSc; Taina Härkönen, PhD; Matti Koski, MA; Harri Kallioinen, MSc (Tech); Olli Tossavainen, DSc (Tech); Tuija Poussa, MSc; Anna-Liisa Järvenpää, MD, DMSc; Jorma Komulainen, MD, DMSc; Raisa Lounamaa, 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: NCT01055080

TEDDY Update

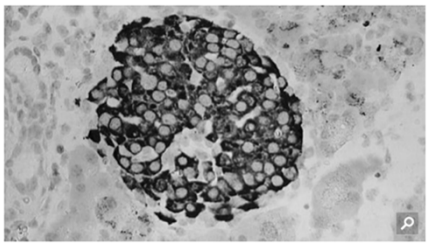
- No news yet on causes yet, but researchers have developed a reliable system of identifying who is at risk for type 1 diabetes based on autoimmune markers.
- TEDDY approach offers “appropriate and effective public health model for screening for type 1 diabetes in the general population”,
  William Hagopian, MD, PhD,

News 21.10.2013 18:56 | updated 22.10.2013 15:43

Finnish team makes diabetes vaccine breakthrough

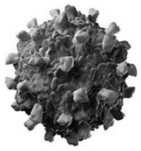
Researchers in Finland could be close to a breakthrough in the search for a vaccine against Type 1 diabetes. Clinical trials could start soon.

Recommend 10,395 people recommend this.



Coxsackie Virus Vaccine?

- Opens up novel possibilities for future research aimed at developing vaccines against these viruses to prevent type 1 diabetes.
- Since the group B coxsackieviruses includes only six enterovirus types it may be possible to include all of them in the same vaccine.



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
- •Daycare, other early exposures, lower risk for DM

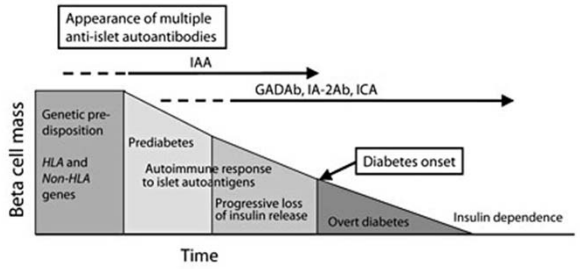
Take Home Message

- 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
- Keep an eye on new research results

Type 1 –Intervention Studies

- Trial Net – Oral insulin, delay onset 4 yrs
- Vaccine (glutamic acid decarboxylase)- Start earlier
- START Trial – Thymoglobulin – still enrolling
- CD3 Monoclonal Antibodies
- Stem Cell

Natural History of Type 1



CD3 – Teplizumab
Stops Autoimmune Destruction

- 52 participants
- Most less than14 years old, with “new-onset type 1 diabetes” within 8 wks of trial’s start.
- All 52 were treated with the experimental drug for two weeks at diagnosis and again one year later,
- About ½ of the participants on Teplizumab maintained insulin production

The clinical trial was led by Kevan Herold, MD, PhD, a professor of immunobiology and deputy director for translational science at Yale University.

University of Missouri scientist Habib Zaghouani, PhD, is developing a potential cure for type 1 diabetes by combining adult stem cells with a promising new drug he developed at MU. (Credit: Image courtesy of University of Missouri School of Medicine)

Stem Cells Research in Mice

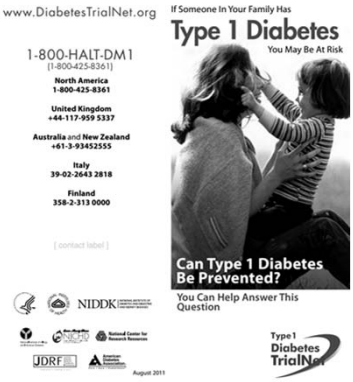
"The combination of Ig-GAD2 and bone marrow cells did result in production of new beta cells, but not in the way we expected,"

"We thought the bone marrow cells would evolve directly into beta cells. Instead, the bone marrow cells led to growth of new blood vessels, the blood vessels facilitated reproduction of new beta cells.

In other words, we discovered that to cure type 1 diabetes, we need to repair the blood vessels that allow the subject's beta cells to grow and distribute insulin throughout the body."

Get Involved – Get Screened

DiabetesTrialNet.org

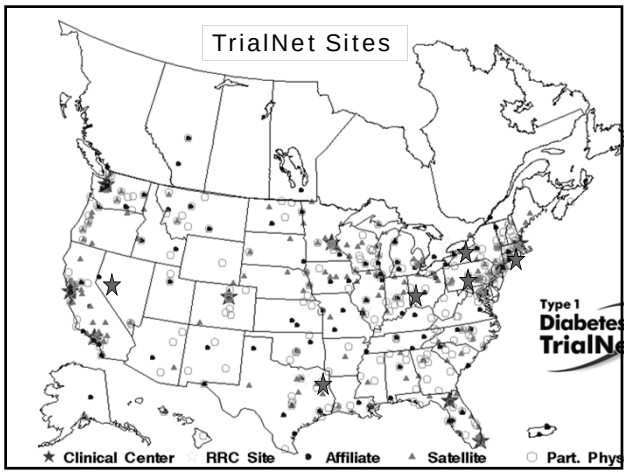


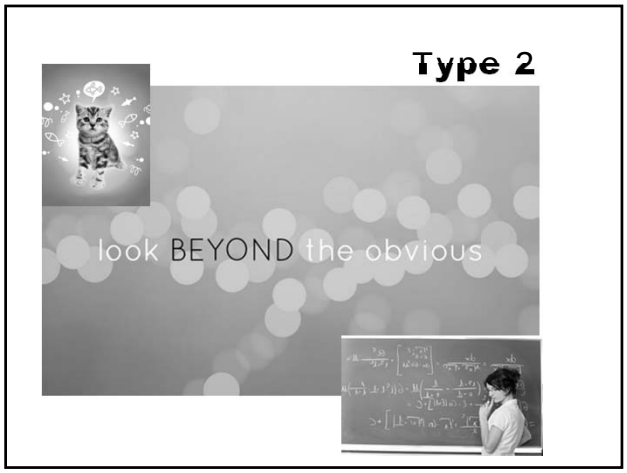
Why participate in Screening?

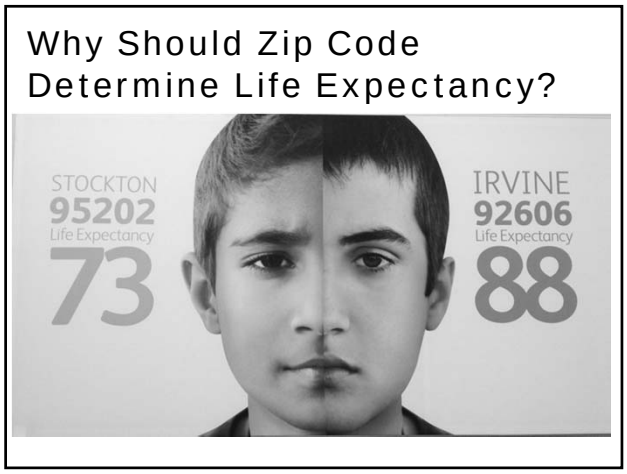
- Contribute to understanding
- Prevent DKA – Earlier diagnosis safer
- Start insulin sooner, may prolong honeymoon
- Early education and transitions
- Eligible for intervention studies

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


TrialNet Sites
Type 1
Diabetes
TrialNe
Clinical Center
RRC Site
Affiliate
Satellite
Part. Phys


Type 2
look BEYOND the obvious


Why Should Zip Code
Determine Life Expectancy?
STOCKTON
95202
Life Expectancy
73
IRVINE
92606
Life Expectancy
88

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



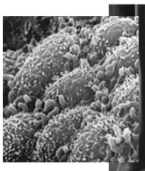
Newsweek, Fat Canaries in a Coal Mine, Dec 10, 2010.. Begley

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 habitants in green.

Obesity and Gut Flora, Nature 2006

Normal Gut Bacteria

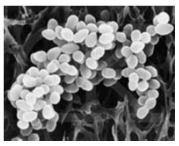
- Diverse
- Collected over a life time through
  - Environmental exposure
  - Types of foods consumed
    - Breast or bottle fed?
  - Parents
  - Vaginal delivery or C-Section
- Help us
  - utilize energy
  - fight off invaders

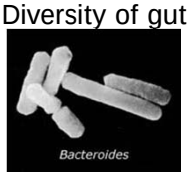
Intestinal Health – A Balancing Act

- Major Groups
  - Firmicutes
  - Bacteroidetes

  Plus thousands of others

  Diversity of gut bacteria more protective



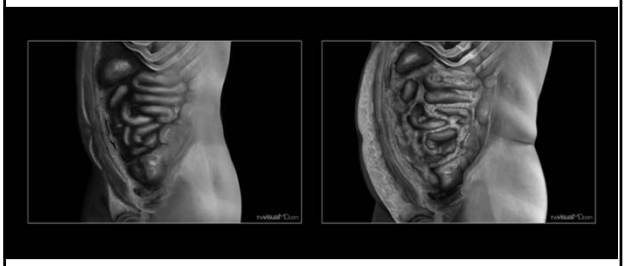


Weight and Gut Bacteria New and Early Research

- 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

Visceral Fat – "Endocrine Organ"



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. Plyori 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

Get Active and Keep Mind and Body Healthy

- Exercise –
  - Walking or weights 3 times a week
  - Dancing
  - Yoga and Mindfulness
- Engage – Get Social
- Lose weight: 5-10%

Flash Mob – World Diabetes Day to "Beat It"

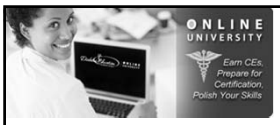
- March R/C/R
- Fred Astaire
- Point R/L
- Arms up, down
- Shoulder Walk
- Punch down/up
- Scoot Rt/Left
- Reach up R/L
- Shoulder Walk
- Open door
- Ride Horse
- Scoot Rt/Left
- Turn R & Clap, then L
- Shoulder Walk
- Punch down/up

Moving to a Happier Life ActionforHappiness.org

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



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- After you hit the green button to purchase enter the coupon code ***"almond"*** and you will see your $30 discount applied.

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

Thank You!