New Horizons in the Prevention of Type 1 and Type 2
Beverly Thomassian, RN, MPH, CDE, BC-ADM
President, Diabetes Educational Services
Diabetesed.net

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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.

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: IDF
Natural History of Type 1

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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

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
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
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.

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

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**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

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**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 than 14 years old, with “new-onset type 1 diabetes” within 8 weeks of trial’s start.
- All 52 were treated with the experimental drug for 2 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.

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
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


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*

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

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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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Thank You!