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15 years

*Advancing Your Career in Diabetes Education*

# New Horizons in the Prevention of Type 1 and Type 2

DiabetesedEd.net

DiabetesEducationUniversity.com



## New Horizons Topics

- New findings in diabetes prevention and treatment
  - Focus on Type 2
  - Focus on Type 1
- Double Diabetes

## Taking the CDE Exam in Future?


## CDC Announces

35% of Americans will have Diabetes by 2050

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

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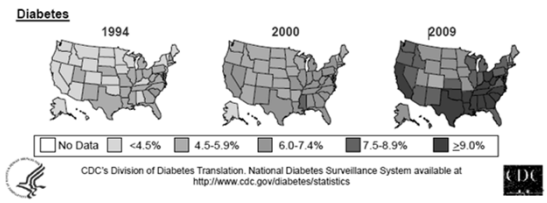
## Diabetes in America 2015

- 29 million or > 9.3%
- 27% don't know they have it
- 1 in 3 of US adults have pre diabetes (86 mil)

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## Type 2 in Kids


- 7 fold increase 1990
- 1 in 6 overwt kids (age 12- 19) have prediabetes.
- ~2,500 to 3,700 new cases in U.S. annually.
- Highest risk: very obese, minority, female, low socioeconomic status, limited education
- In age range 12-19, less than 1% have Type 2 – NHANES
- Environmental changes to urgently needed

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## Why Should Zip Code Determine Life Expectancy?


**California Endowment – look up your zip code at www.measureofamerica.org**

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## 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

- We live in an "Obesogenic" environment

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## Public Health Issue?

- 66% of our people are obese/overweight
- Rates of gestational diabetes on rise
- 30% of kids are obese/overweight


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## Average American Consumes 22 teaspoons of sugar a day

- Warning label on sodas proposed
- One soda has 12 teaspoons sugar
- On avg, 1 person consumes 40 gallons of soda each year
- ADA guidelines "limit sodas and beverages with sugar, High Fructose Corn Syrup, (HFCS)

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## WHO limits on Sodas

- According to Harvard researchers, drinking 1-2 sugary beverages per day increases a person's risk of developing Type 2 by 26%.
- Mexico's soda tax took effect Jan. 1 2014, and sales of sugar-sweetened drinks fell 10% in the next 3 months and people drank more water and milk
- Drinking a 20 ounce soda a day was equivalent to an average of 4.6 years of telomere shortening UCSF 2014
- World Health Organization
  - Reduce daily free sugar intake to 10% ~around 12tsps.
  - Ideally < 5% of total energy intake for additional health benefits
- ADA - Sugary beverages associated with possibly visceral adiposity

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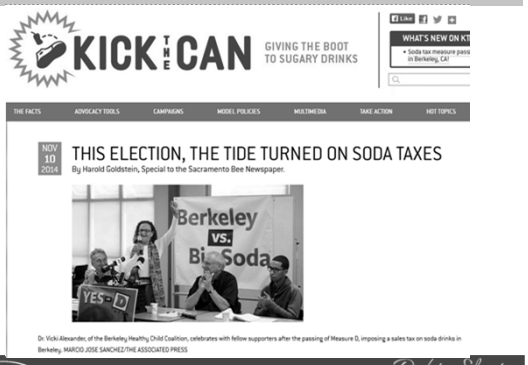
## Berkeley Passes Sugar Tax

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## Weight loss and Prevention

- For every 2.2 pounds of weight loss, risk of type 2 diabetes was reduced by 13%.

NATIONAL Diabetes PREVENTION PROGRAM

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## Type 2

look BEYOND the obvious

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## 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

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## Double Diabetes – An Increasing Problem

- Defined as a person who presents w/ features of both type 1 and type 2 diabetes.
- Someone with type 1 diabetes gains significant weight and manifests the clinical features of insulin resistance and type 2
- or in those with type 2 who develop autoantibodies to beta cells and manifest type 1 (esp in kids)

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## Double Diabetes in Adults – Type 1 then add on Type 2

- Seem to be especially susceptible if both parents had type 2 diabetes
- Treatment?
  - **REMOVAL** study (Reducing with Metformin Vascular Adverse Lesions) - adding metformin to insulin
  - GLP-1 Agonists – Victoza use early in type 1 may help preserve beta cells. Also helps with wt loss, lower insulin dose and improved A1c
  - SGLT-2 Inhibitors – add on to insulin in Type 1 also improve A1c and leads to wt loss

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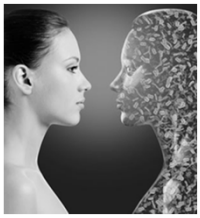
## Bacterial Cells Outnumber Human Cells 10 to 1

- 30 trillion human cells
- Host 100 trillion bacterial and fungal cells

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## Getting to the Gut

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

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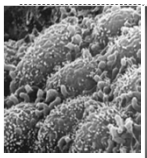
## Gut Bacteria – 10,000 species, 6 lbs



Electron micrograph of small intestine and bacterial habitants in green.
Obesity and Gut Flora, Nature 2006

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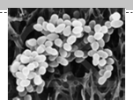
## Intestinal Health – A Balancing Act



- 2 Major Phyla:
  - Bacteroidetes- protein and carb breakdown
  - Firmicutes –absorption of fat (ratio has increased over time)
    - Plus thousands of others
    - Diversity of gut bacteria more protective



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## Gut Microbiome

- Part of endocrine axis
- Stabilized by 3 years of age
- Influenced by:
  - Birth method
  - Antibiotics
  - Environment
  - Breast fed?
  - Travel
- Help us
  - utilize energy
  - fight off invaders


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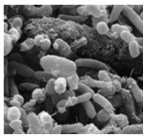
## 6 pounds of microbes in our Gut

- This community of bacteria can be thought of as an extra 'organ' which we call our "microbiome".
- We have evolved together with our microbiome over millions of years.
- Ratios of these communities has changed over the past 30 years
- Mirrors global spikes in obesity, diabetes, allergic and inflammatory diseases
- What are we doing to change these bacteria?
  - Antibiotic therapy?
  - Especially in early life can change fat metabolism for life?
  - Diets?



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## Type 1 Diabetes Prediction and Prevention Program (DIPP)

- Launched in 1994 to search for means to prevent or delay type 1 diabetes
- Follows a cohort of children at genetic risk for type 1
- Data consistently shows that those who develop type 1
  - Have less bacterial diversity
  - Increase in certain species of bacteroides associated with 20 fold increased risk of autoimmunity
  - Association is not causation

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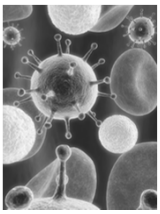
## Weight and Gut Bacteria New and Early Research



- Fecal samples in humans have distinct microbial signatures:
  - Obese
  - Type 1
  - Type 2

Pathobionts – at low levels in healthy people but can bloom under certain dietary conditions

Lipopolysaccharide Endotoxins – stimulated with high fat diets

Endocrine Today 10/2014

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## Obesity associated with

- Higher levels of:
  - Firmicutes
  - *Staphylococcus aureus*
- *Depletion of:*
  - *Bifidobacterium*
  - *Lactobacillus*
- Microbes might strategically generate cravings for food
- High fat diet, lower fiber diet decreases microbial diversity

*Endocrine Today, Oct 2014*
*Meghan Jardine*

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## McDonalds Study

**After eating for Fast Food for 10 Days**

McDonald's and the Microbiome: What Effect Does Junk Food Have on Gut Bacteria?

**Dramatic Changes**

- Gut microbiome diversity devastated
- Firmicutes replaced by Bacteroidetes
- Bifidobacteria decreased by over 50%
- Pt felt bad- took over 2 weeks to get gut back to health
- BritishGut.org – turn in your stool sample

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## 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
- Contributing to insulin resistance

- 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*

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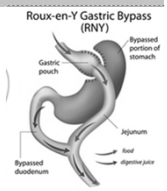
## Gastric Bypass effects on Blood Glucose




- Increases gut hormones but…
- Physical manipulation of the gut alters bacterial communities
- Levels of the Firmicute *Roseburia Intestinalis* increase
  - *Roseburia Intestinalis are lacking in people with type 2*
  - Maybe this increase lowers BG levels?
- Endocrine Today – April 2015

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## 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*

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## Getting to Better Gut Bacterial Health

**Eat more PREbiotics**

- Foods with indigestible fibers that nourish the good bacteria:
  - High fiber foods
  - Fruits, veggies
  - Jerusalem artichokes, onions, kale, Brussels sprouts, banana, berries, nuts

**PRObiotics**

- These foods contain healthy bacteria like bifodobacteria and lactobacillus.
  - Yogurt, Kefir – look for "live or active cultures"
  - Fermented foods like: Sauerkraut, Kimchee, Miso soup

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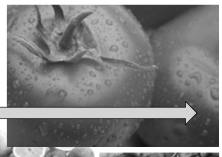
## 10 SuperFoods to Enjoy

- Beans
- Dark Green Leafy Vegs
- Citrus Fruit
- Sweet Potatoes
- Berries

- Tomatoes
- Fish High in Omega-3 Fatty Acids
- Whole Grains
- Nuts
- Fat-Free Milk and Yogurt

## Move toward the Tomato

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## What Does Type 1 Look Like?


**Mary Tyler Moore**

Justice Sonia Sotomayor

**Nick Jonas**


**Bret Michaels**

From Debbie Nagata's slide collection

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## Ms. Idaho and Ms America – Pumpin' It

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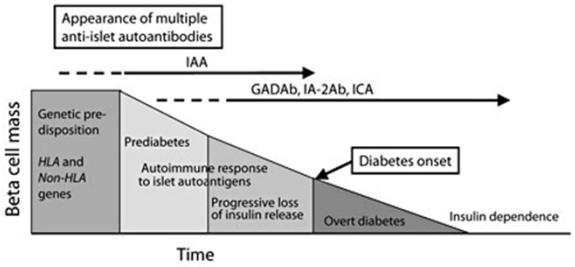
## Natural History of Type 1

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## Autoantibodies Assoc w/ Type 1

Panel of autoantibodies –

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



## Bedside Diagnosis of Type 1?

**A new microchip developed at Stanford University School of Medicine,** hopes to make diagnosis of type 1 easy and reliable.

Brian Feldman is one of the inventors of a microchip-based test for diagnosing type 1 diabetes. Norbert von der Groeben

The Stanford team has developed a cheap and portable microchip that instantly measures autoantibodies in the blood to differentiate between types of diabetes.

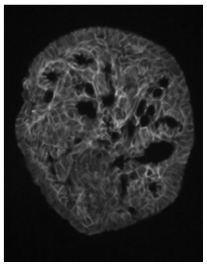
**IGI Stat**, a company started by the Stanford researchers, hopes to see the device in hospitals in less than two years, pending Food and Drug Administration (FDA) clearance.



## 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**

## Remaining Beta Cells



- **Can serve one well while it lasts…even if on supplemental insulin.**
- **Better overall glucose control lower A1C, less glycemic excursion, lower risk for severe hypoglycemia**

## Medalist Study – Harvard Joslin Diabetes Center

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


## 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

## 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.

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## 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

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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,

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## 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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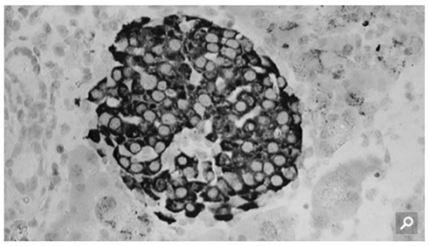
News 21.10.2013 18:56 | updated 22.10.2013 15:43

## 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.



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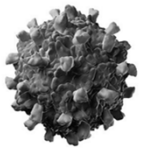
## Coxsackie Virus Vaccine?

- 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.



SCIENCEphotoLIBRARY

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Get Involved – Get Screened
**DiabetesTrialNet.org**

www.DiabetesTrialNet.org

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(1-800-425-8361)

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Finland
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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

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## 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.

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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

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

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## Taking the CDE Exam in Future?



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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

- Questions?
- Email bev@diabetesed.net
- Web www.diabetesed.net

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