Population Screening for T1D and Celiac Disease

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I have no conflicts of interest to report
Opportunities for T1D Prevention

Primary

100%

Functional Beta Cell Mass

Increased Genetic Risk

T1D Stages:

1

2

3

Secondary

Increased Genetic Risk

High-affinity Single IA

30%/5y

Multiple IAs

50%/5y

Dysglycemia

Tertiary

>40% in DKA

>80% hospitalized

Symptomatic Type 1 Diabetes

Insel, R et al., Diabetes Care 2015
Increasing Prevalence of DKA among Children Diagnosed With T1D

Colorado 1998-2012,  N=3,439

Arieta Rewers et al. JAMA 2015
DKA at T1D onset can be prevented by screening for islet autoantibodies and education!

Colorado 1998-2012, N=3,439

1106 (83%) of DKAs could be prevented, had all children been screened for islet autoantibodies and given anticipatory diabetes education.

Prevalence of DKA

- Colorado community cases: n=3106
- DAISY, TEDDY, TrialNet: n=133

p < 0.0001

[Source: Arleta Rewers et al. JAMA 2015]
DKA at diagnosis predicts worse long-term A1c
3364 Colorado children followed for up to 15 yrs

- No DKA
- Mild/Moderate DKA HbA1c ↑ 0.9% p<0.0001
- Severe DKA HbA1c ↑ 1.4% p<0.0001

Duca L et al. Diabetes Care 2017
Autoimmunity Screening for Kids (ASK)

Goals:

1. Determine the prevalence of pre-symptomatic T1D and Celiac Disease in general population children.
2. Prevent DKA at diagnosis of diabetes in screening identified children through structured education and monitoring.
3. Evaluate interventions that may slow progression from stage 1 T1D to clinical diabetes.
4. Reduce morbidity in children with undiagnosed CD.
5. Increase community awareness of T1D and CD.
6. Analyze the cost and cost-effectiveness of the screening.
ASK Screening Inclusion Criteria

• Children ages 1.0-17.9

• Reside in Colorado, screened in Denver Metro

• Parent/legal guardian consent

• No current type 1 diabetes diagnosis

• Target – screen 50,000 children
ASK Population: children 1-17 y old

Denver Metro Area
7 counties

10,000 screened
Jan ’17- Jun ‘18

~31,000 approached for consent

50,000 to be screened
Screening N = 9511

Positive

Confirmation

Persistent Positive

Follow-up

Prevent:
• T1D
• DKA

Optional q6M
OGTT
CGM

Monitoring & Education
Home BG monitor
Symptoms
BG, A1c
Ht & Wt

Body composition
Blood draw
Questionnaires
Med Records

Negative

Not Confirmed HbA1c <5.7%

Data as of 6/20/18
Autoantibody Assays

2nd generation RBAs

3rd generation ECL
Electro Chemi Luminescence

Islet
IA-2A GADA mIAA ZnT8A

Celiac
IA-2A GADA IAA TGA IgA

TGA
Age distribution

- 1-5 y: 27.6%
- 6-9 y: 26.7%
- 10-13 y: 18.5%
- 14-17 y: 27.2%

Data as of 6/6/18
1\textsuperscript{st} degree relative with T1D or CD

- T1D: 90.9%
- T1D & CD: 3.7%
- CD: 0.5%
- None: 4.9%

Data as of 6/6/18
Race/ethnicity of ASK participants vs Denver Metro Area

- non-Hispanic white
- Hispanic (any race)
- African American
- Asian American
- Native American
- other/unknown

Data as of 6/6/18
Results: Islet Autoimmunity (IA)

8,812 Screened

317 Positive (3.6%)

Negative N=8,495 (96.4%)

317 Positive (3.6%)

Multiple +
42 (0.5%)

95%

Single+
RBA and ECL
50 (0.6%)

95%

Single+
RBA only: 202 (2.3%)
ECL only: 28 (0.3%)

78%

Confirmation (persistent positive)
Results: Celiac Disease Autoimmunity

8,812 Screened

238 Positive (2.7%)

Positive RBA and ECL: 177 (2%)

Positive RBA only: 4 (0.1%)
ECL only: 57 (0.6%)

99%

49%

Negative N=8,574 (97.3%)

Confirmation (persistent positive)

Data as of 6/6/18
Conclusions

Screening for pre-symptomatic T1D and Celiac Disease is:

• Feasible and well-accepted by parents and providers
• Novel step towards universal prevention of T1D
• 1.1% of children have pre-symptomatic T1D
• 2.0% have Celiac disease/Celiac Disease Autoimmunity
• Major ethnic differences in the prevalence of multiple IA+ and TGA+
  parallel the prevalence of T1D and CD
Future Directions

• Analyze the cost and cost-effectiveness of screening for pre-symptomatic T1D and CD

• Transition to provider-centered screening and locations outside Colorado

• Enroll eligible children into prevention trials
Work towards a safe prevention for T1D

Beta cell function

- oral insulin
- probiotics
- $\Omega-3$ FA
- vit. D

100 %

Islet autoantibodies

- oral insulin
- anti-CD3
- abatacept
- alefactept
- hydroxychloroquine
- methyldopa
- (anti-CD20+abatacept)
- $\uparrow$ carb intake

anti-CD3
anti-CD20
abatacept
alefactept
anti-IL-6R, T-reg lymphocytes
$\alpha$-1 antitrypsin
anti-TNF$\alpha$ or (anti-TNF$\alpha$+anti-IL-1$\beta$)
(ATG + GCSF)
IL-2
pleconaril+ribavirin; Coxsackie vaccine

Diagnosis of diabetes

Time

Peter Gottlieb
Andrea Steck
Practical take-home pearls

✧ 1 in 30 children have undiagnosed T1D or CD
✧ Screening for antibodies can prevent 80% of DKA
✧ Screening for antibodies shortens delay in diagnosis of CD (on average 10 years in the U.S.)
✧ Call us at 303-724-1275 or ASKhealth.org
Thank You!

• 10,000 ASK participants and their parents:

• Our sponsors:

• Our partners: