The Autoimmunity Screening for Kids (ASK) Study: Screening Expansion

303-724-1ASK | ASKhealth.org

A SIMPLE TEST TO DETECT
Childhood Diabetes + Celiac

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www.ASKhealth.org
Objectives

1. Highlight findings from the Autoimmunity Screening for Kids (ASK) study to date

2. Provide an update on screening for early-stage type 1 diabetes

3. Share information on future directions for general population screening
Autoimmunity Screening for Kids (ASK) Goals:

1. Determine frequency of pre-symptomatic T1D and celiac disease
2. Prevent diabetic ketoacidosis (DKA) at diagnosis of diabetes
3. Offer interventions to slow progression to diabetes
4. Reduce complications of undiagnosed celiac disease
5. Analyze cost-effectiveness of screening -> universal screening?
6. Increase community awareness
ASK Population:

- Children >1 to <18 y old 
  And now adults
- Reside in Colorado...
  And the US
- Parent/guardian consent
- Can have celiac disease, but not diabetes
- 1/2017-10/1/2023

33,229 children screened
In addition:
>1,700 re-screened
+1,256 adults screened

>100,000 approached for consent

623,000 eligible children in Denver metropolitan area
Diabetic Ketoacidosis (DKA) at Diagnosis of Type 1 Diabetes (T1D) is Increasing

Potential Outcomes:

- Brain edema
  - Acute neurological impact
  - Permanent neurological damage
- Risk of Mortality
- Cost of ED, hospitalization, PICU
- Trauma to the child and family
- Impact on long-term beta-cell capacity

Adapted from: Rewers A et al. JAMA 2015
Alonso T et al. Diabetes Care 2020
Colorado T1D Prospective and Screening Studies

Began 1992

General population cohort
Sibling/offspring cohort

DAISY

Colorado: 31,881 newborns screened
2,547 general population and first-degree relatives followed

Began 2004

Multinational:
424,000 newborns screened
8,677 high-risk children intensively followed ‘omics studies

Began 2004

Multinational:
> 220,000 relatives screened
Free screening for:
- family members of those with T1D (ages 2.5-45 years)
- anyone found Ab+ outside of TrialNet (2.5-45 years)
Monitoring for relatives with positive Abs
Participation in studies that may stop or slow the progression of T1D (both GP and relatives)

Type 1 Diabetes TrialNet

Began 2014

Colorado and the US:
33,000+ general population children ages 1-17 years screened
islet autoantibody positive individuals followed and monitored through ASK or Ask the Experts national monitoring program

ASK
**Autoantibody Assays in ASK**

**Radiobinding assays (RBA)**
- Detect both high-affinity (predictive) and low-affinity (non-predictive) autoantibodies
- Detects all isotypes IgG, IgA, IgM, IgD, IgE

**Electrochemiluminescence (ECL) assays**
- Detect only high-affinity autoantibodies
- Detects all isotypes IgG, IgA, IgM, IgD, IgE
- Multiplexed
- Multiplexed with SARS-CoV-2 antibodies

<table>
<thead>
<tr>
<th>Islet autoantibodies</th>
<th>Celiac</th>
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<tbody>
<tr>
<td>IA-2A, GADA, mIAA, ZnT8A</td>
<td>tTGA</td>
</tr>
<tr>
<td>IgG only</td>
<td>IgA only</td>
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</tbody>
</table>

**Celiac**
- Serum
- 44 µL

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<tr>
<th>IA-2A, GADA, IAA, ZnT8A, tTGA</th>
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<tr>
<th>IA-2A, GADA, IAA, ZnT8A, tTGA, SARS-CoV-2A</th>
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**Celiac**
- Serum
- 13 µL
ASK Protocol

Screening at multiple sites

CONFIRMATION
Islet autoantibodies:
- multiple
- single high-affinity

Celiac:
tTG Abs

Not confirmed and HbA1c <5.7%

Monitoring:
HbA1c, CGM, OGTT

Education:
symptoms
blood glucose monitoring
access to diabetes team

Prevent:
- DKA
- Diabetes

Low levels & no symptoms
PCP

High levels or symptoms
Specialist

www.ASKhealth.org
Age distribution

- 1-5 y: 35.7%
- 6-9 y: 4.6%
- 10-13 y: 0.8%
- 14-17 y: 1.9%
- 18%: 2.5%

Race/ethnicity

- non-Hispanic white: 50.4%
- Hispanic: 35.7%
- African American: 4.6%
- Asian American: 0.8%
- Native American: 1.9%
- Other or Unknown: 6.5%

1st degree relative

- T1D: 90.6%
- T1D & CD: 5.0%
- CD: 0.5%
- None: 3.8%
ASK Results: Islet Autoimmunity and Diabetes

Initial screening:
- Overall 1018 (3.1%) IAb+ (by both RBA and ECL)
- 176 multiple IAb+ (by both RBA and ECL)
- 181 single IAb+ (by both RBA and ECL)
- 661 single IAb+ (by one method only)

Confirmation:
- 189 (0.58%) multiple IAb+
  - 10-y risk of DM = 70%
- 163 (0.5%) single IAb+
  - by RBA and ECL
  - 10-y risk of DM = 25-50%
- 668 single IAb+ by one method only or not confirmed

Clinical T1D:
- 3 T1D before confirmation
- 52 T1D (3 DKA)
- 8 T1D (no DKA)
- 4 T1D (no DKA)

Data as of 10/01/2023

33,229 screened excluding parents & re-screens
ASK Results: Celiac Autoimmunity and Disease

- **33,229 Screened**

  - **996 Positive (3.0%)**
    - RBA+ (2.5%)
    - ECL+ (0.5%)

  - **83% Confirmed RBA Positive**

  - **Celiac disease N= 255**

  - **Data as of 10/1/2023**
Autoimmunity Screening for Kids (ASK), 2017-2023

- Screened >33,000 Colorado children 1-17 y old
- Prevalence of pre-symptomatic T1D - 1.0% (95%CI: 0.9- 1.1%)
- Prevalence of celiac disease/autoimmunity - 2.1% (1.9- 2.3%)
- DKA at diagnosis of diabetes <5% vs 62% in screened vs not screened
- Evidence of cost-effectiveness of the screening
- Increased community awareness of T1D and CD

Tips from ASK for general population screening

• The initial screening test has to be sensitive to avoid false negatives and disease-specific to avoid false-positives
• Confirmation at another time point is needed and using the most specific assay is essential
• Multiple IAbs confirmed in 90%; single high-affinity in 77%
• Single autoantibody positive children do progress to T1D and cannot be ignored
• Multiplex assays can overcome barriers to screening (specificity, sensitivity, cost, throughput)
Future Directions

- Further expansion nationally, including targeted efforts within hospital and provider networks
- Screening of adults and children to identify all who are at risk
- Develop and test sustainability plan utilizing electronic medical record systems and telehealth options to enhance reach
- Work towards adoption of universal screening at the state government, payor, and healthcare provider levels
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