Can Diabetes be Prevented with Vitamin D?

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Presenter Disclosure

Dr. Frank Garland

The following personal financial relationships with commercial interests relevant to this presentation existed during the past 12 months:

No relationships to disclose.
Can Diabetes be Prevented by Vitamin D

Learning Objectives

1. Add a disease to the list of ten vitamin D sensitive diseases

2. Quantify potential benefits of solving the vitamin D deficiency

3. Identify and quantify any risk categories for vitamin D treatment
Annual age-adjusted incidence rates of type 1 diabetes, children ≤ 14 years old, per 100,000 population, Finland, 1965-2005

Year
Incidence rate
The Scene of the Crime

The Islet Cells of the Pancreas
The Scene of the Crime

The Islet Cells of the Pancreas
Round up the usual suspects

Disease Causation Triad

Environment

Agent

Host
Annual age-adjusted incidence rates of type 1 diabetes, children ≤ 14 years old, per 100,000 population, Finland, 1965-2005.
Round up the usual suspects

Disease Causation Triad

Environment

Agent

Host
Virus theory

Increase in incidence rate of type I diabetes during picornavirus outbreak

Picornavirus outbreak (Cox B)

![Graph showing incidence rate of type I diabetes over years](Image)

**Figure 1**: Mean annual incidence rate of type 1 (insulin-dependent) diabetes mellitus in Swedish children 0–14 years
Round up the usual suspects

Environment

Agent

Host

Disease Causation Triad
Annual age-adjusted incidence rates of type 1 diabetes, children ≤ 14 years old, per 100,000 population, Finland, 1965-2005
The EURODIAB Study

- Goal was to study the epidemiology of type 1 diabetes in Europe (43 registries in most countries and Israel)
- Started in 1988
- Prospective establishment of registries
- 16,330 cases in children under 15 years of age
- Rates of increase per year: 6.2% children 0-4; 3.1% children 4-9; and 2.4% children 10-14 years
- Important sub-studies in Norway and Finland
Trends in Type 1 diabetes, Europe, girls, 1989-1994


Age 10-14
Age 5-9
Age 0-4
When you should consider that you may be dealing with a Vitamin D-Sensitive Disease.

- Varies by latitude
- Varies more by ultraviolet irradiance
- Varies by season
- Varies by race, BMI, physical activity
Type I diabetes, San Diego and Rochester MN, annual incidence rates per 100,000 children
Correlation between age-adjusted IDDM incidence in children under 15 and average yearly temperature

R = -0.55, \( p < 0.005 \)

Incidence Rates of Type I Diabetes in 51 Regions
World Health Organization

$R^2 = 0.25$
$p < 0.001$
Odds Ratios of 25-hydroxyvitamin D deficiency below 17.8 ng/ml (lowest quartile) by Season of blood draw, National Health and Nutrition Examination Survey III, N=13,331 Participants

- Winter (Jan-Mar) - 1.0
- Fall (Oct-Dec) - 0.63
- Summer (Jul-Sep) - 0.31
- Spring (Apr-Jun) - 0.67

*p < 0.01*
Diabetes in the DoD, Seasonality

Figure 2. Number of incident cases of Type 1 diabetes by month and year, active duty service members, Department of Defense, 2000-2004
Odds Ratios of 25-hydroxyvitamin D deficiency below 17.8 ng/ml (lowest quartile) by Race, NHANES III, N=13,331
<table>
<thead>
<tr>
<th>Plasma 25-hydroxyvitamin D quartiles ng/ml</th>
<th>Mean Body Mass Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;17.8 ng/ml (N=3,388)</td>
<td>28.1</td>
</tr>
<tr>
<td>17.8-24.3 ng/ml (N=3,344)</td>
<td>27.6</td>
</tr>
<tr>
<td>24.4 - 32.1 ng/ml (N=3,242)</td>
<td>26.4</td>
</tr>
<tr>
<td>&gt; 32.1 ng/ml (N=3,359)</td>
<td>25.3</td>
</tr>
</tbody>
</table>

Mean Body Mass Index by Plasma 25-hydroxyvitamin D Concentration Quartiles, National Health and Nutrition Examination Survey III, N=13,331 Participants

$p < 0.0001$
Odds Ratios of 25-hydroxyvitamin D deficiency below 17.8 ng/ml (lowest quartile) by Physical Activity, National Health and Nutrition Examination Survey III, N=13,331 Participants

Odds Ratio for Vitamin D Deficiency (<17.8 ng/ml)

- Low (Referent): 1.0
- Moderate: 0.65
- High: 0.44

\[ p < 0.001 \]
Person
Odds ratio and 95% confidence limits for developing diabetes before the age of 15 when exposed to vitamin D supplements in early infancy relative to children who were not exposed.

- Luxemborg
- Northern Ireland
- Romania
- Lithuania
- Latvia
- Bulgaria
- Austria

Pooled odds ratio = 0.67
95% CI 0.53-0.86, \( p < 0.01 \)

Heterogeneity \( p = 0.14 \)

Graphic by S. B. Mohr, MPH
Table 2 Clinical characteristics and plasma 25OHD at diagnosis in young adults with type 1 diabetes vs control subjects (mean±SEM)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patients</th>
<th>Control subjects</th>
<th>Test of difference between patients and controls ($p$ value)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>($n=459$)</td>
<td>($n=208$)</td>
<td></td>
</tr>
<tr>
<td>Males/females</td>
<td>1.6</td>
<td>1.1</td>
<td>0.016</td>
</tr>
<tr>
<td>Age (years)</td>
<td>24.4±0.3</td>
<td>25.6±0.5</td>
<td>0.027</td>
</tr>
<tr>
<td>25OHD (nmol/l)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>82.5±1.3</td>
<td>96.7±2.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Males</td>
<td>77.9±1.4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>93.9±2.7&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Females</td>
<td>90.1±2.4</td>
<td>99.7±2.9</td>
<td>0.014</td>
</tr>
</tbody>
</table>

Test of difference by sex: <sup>a</sup>$p<0.0001$; <sup>b</sup>$p=0.15$

Odds Ratio and 95% confidence intervals for diabetes by mothers use of cod liver oil, Norway, N=545 cases and 1,668 controls, 1997-2000

Infants’ Supplementation with Cod Liver Oil during First Year and Type I Diabetes in Children in Norway

Odds Ratio and 95% confidence intervals for diabetes by supplementation with cod liver oil, Norway, N=545 cases and 1,668 controls, 1997-2000

Finland study

• Hypponen and colleagues

• Intake of vitamin D and risk of type 1 diabetes: a birth cohort Study (Lancet 2001)

• 12,055 pregnant women who were to give birth in 1966 were followed for outcome until 1997.
Relative Risk* and 95% confidence intervals for diabetes by vitamin D supplementation, Birth Cohort study, N=12,055 pregnant women

*adjusted for gender, gestational age, birth weight, growth rate; maternal parity, age, education, ses
Infants’ Vitamin D Supplementation Dose and Incidence of Type I Diabetes in Children in Northern Finland

Relative Risk and 95% confidence intervals for diabetes by vitamin D supplementation dose, Birth Cohort study, N=12,055 pregnant women

Types of Intercellular Junctions

- **Tight Junction**
  - E-cadherin, calcium- and pH-dependent, labile, depends on vit D and calcium
  - Requires contact or very close proximity

- **Desmosome**

Proposed Mechanism
Capillary Endothelium

Normal situation with all types of junctions intact
Breakdown of junctions and breakdown of barrier function due to inadequate vitamin D immune system attacks Islet Cells
Annual age-adjusted incidence rates of type 1 diabetes, children ≤ 14 years old, per 100,000 population, Finland, 1965-2005.

Incidence rate: 15 25 35 45 55 65
Annual age-adjusted incidence rates of type 1 diabetes, children < 14 years old, per 100,000 population, and dates of changes in recommended daily intake of vitamin D in infants, Finland, 1965-2005

- **1964**: Recommended vitamin D intake reduced from 4500 IU to 2000 IU
- **1975**: Recommended vitamin D intake reduced to 1000 IU (1975)
- **1992**: Recommended vitamin D intake reduced to 400 IU
Infants’ Supplementation with Vitamin D and Incidence of Type I Diabetes in Children in Northern Finland

Relative Risk* and 95% confidence intervals for diabetes by vitamin D supplementation, Birth Cohort study, N=12,055 pregnant women

*adjusted for infant’s gender, gestational age, birth weight, growth rate; maternal parity, age, education, social status

Finland study Conclusion

- Hypponen et al 2001 Lancet

- The authors concluded:

  We suggest that, before any changes are made, health workers ensure that all infants are receiving at least the amount of vitamin D indicated in the current recommendation.” The current recommendation is 400 IU per day.
Annual age-adjusted incidence rates of type 1 diabetes, children ≤ 14 years old, per 100,000 population, and dates of changes in recommended daily intake of vitamin D in infants, Finland, 1965-2005

- 1964: Recommended vitamin D intake reduced from 4500 IU to 2000 IU
- 1975: Recommended vitamin D intake reduced to 1000 IU (1975)
- 1992: Recommended vitamin D intake reduced to 400 IU
What to do to reduce burden of Type I Diabetes in the World

Minimum oral intake of vitamin D3 at 30 degrees or higher, in general:

Infants: NAS UL 1,000 IU-1,800 IU (NAS NOAEL)

Adults: 2,000 (NAS UL)- 2,400 IU (NAS NOAEL)

Children 1-12 years: 2,000 IU

Serum target, all ages: 40-60 ng/ml

Risk/Benefit ratio is infinite since these are within established no adverse affects levels
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Learning Objectives Accomplished:

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