Nutrient Intake Levels

- **RDAs:** maintain known functions in health
- **Optimal:** maximize functions, both known and potential
- **Nutriceutical:** 2-10 x RDA / specific therapy
- **Pharmaceutical:** higher intakes / chemical action
**Therapeutic Strategies in IDDM**

WHO Study Group, 1994

**Primary:** prevent onset
- genetic background
- environmental trigger

**Secondary:** early detection & management
- tight glycemic control

**Tertiary:** attenuate complications
- adjunct therapies
Niacinamide vs Onset of IDDM

Elliott et al, Ann. NY Acad Sci

- **very high risk pediatric (ICA >80; age ≤ 16)**
  - incidence @ 2 yrs: 0% vs 90%
  - 4 yrs: 40% vs 90%

- **moderate risk pediatric (ICA ≥ 10; age ≤ 10**
  - incidence @ 3 yrs: 15% vs 20%
  - 5 yrs: 20% vs 80%

- **all ages (ICA > 20)**
  - incidence @ 5 yrs: 15% vs 40%
Nicotinamide Intervention Studies

- **meta-analysis:** no clinical effect; improved B-cell function
  
  (Diab Care 19:1357, 1996)

- **positive outcome:** 50% decrease in incidence
  
  (J Ped Endo Metab 9:501, 1996)

- **negative outcome:** progression to IDDM
  
  (J Autoimmun 2:733, 1989)
Deutsche Nicotinamide Intervention Study
Lampeter et al, Diabetes 47:980-84, 1998

- **participants:** siblings; ages 3-12; ICA>20
- **treatments:** B₃ (n=25) @ 2 x 0.6 g/m²
  placebo (n=30)
- **expectation:** 6% vs 30% IDDM @ 3yrs
- **outcomes:** adverse effect on FPIR
  (vs + effect Br J Clin Pract 46:177-79, 1997);
  NSD incidence (@ 22%);
  termination
ENDIT / CanENDIT Trials

Enroll individuals at high risk for IDDM:

5 - 40 years of age;  ICA + ( GAD +)
normal GTT / first phase Insulin variable

To prolong “prediabetic” state:

1200 mg niacinamide (B3) per m2 daily dosage
predict 50% reduction in incidence over 4 years
Hyperglycemia

Glycosylation or Aldose reductase action

Aminoguanidine ARIs

Vitamin E Vitamin C!

? Vitamin C ?

Cross linking of Proteins Sorbitol Accumulation

Chronic Complications of Diabetes
# Vitamin C Status in IDDM

*Cunningham et al., Metabolism 1991 & JACN 1994*

## Mononuclear Leukocyte Concentrations

<table>
<thead>
<tr>
<th></th>
<th>mg Asc / gram prot</th>
<th></th>
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</thead>
<tbody>
<tr>
<td><strong>Nondiabetics</strong> (n = 24)</td>
<td>2.6</td>
<td>(75% ≥ 1.8)</td>
</tr>
<tr>
<td><strong>IDDMs</strong> (n = 20)</td>
<td>1.8</td>
<td>(15% ≥ 2.6)</td>
</tr>
</tbody>
</table>
Ascorbic acid: an ARI *in vitro*

*Cunningham, JACN 1998*

inhibition of AR activity in semi-purified brain, glyceraldehyde substrate & NADPH assay
Ascorbic Acid: an ARI in vivo

Cunningham et al., JACN 1994

vit C supplements (100 mg or 600 mg daily)

Erythro sorbitol nmol/ gHb

Day 0 Day 30 Day 58

Nondiabetic

IDDM
Vitamin E: a Nutriceutical in Diabetes

**NIDDM (pharmacologic)**

600 or 1200 mg / 2 months; 900 mg / 4 months
improved insulin action & increased glucose disposal
protects against LDL oxidation
(see also Sharma et al Ann. Nutr. Metab. 44:11, 2000)

**IDDM (pharmacologic)**  
Bursell et al, Diab Care 22:1245, 1999
1800 IU / d for 4 months
normalization of retinal blood flow; NSD glycHb

**IDDM (nutriceutical)**  
Jain et al, JACN 15:458, 1996
100mg / 3 months significantly reduced glycHb
Vitamin E Prevents Hb Glycation

Jain et al, JACN 1996

100 IU daily for 3 months; plasma E doubled

% GlycHb (affinity)

Baseline-P  Placebo n = 16  Baseline-vit E  Vit E n = 13

p < 0.05
Vitamin C & Glycosylation

- **Documented lowering of glycHb:**
  - 2,000 mg x days
  - 2 x 500 mg x 12 weeks

- **Failure at lowering of glycHb:**
  - 750 or 1500 mg x 12 weeks / nondiabetics