Vitamin Interventions to Prevent the Onset or Complications of Diabetes: promising data.

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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:** B_3 (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

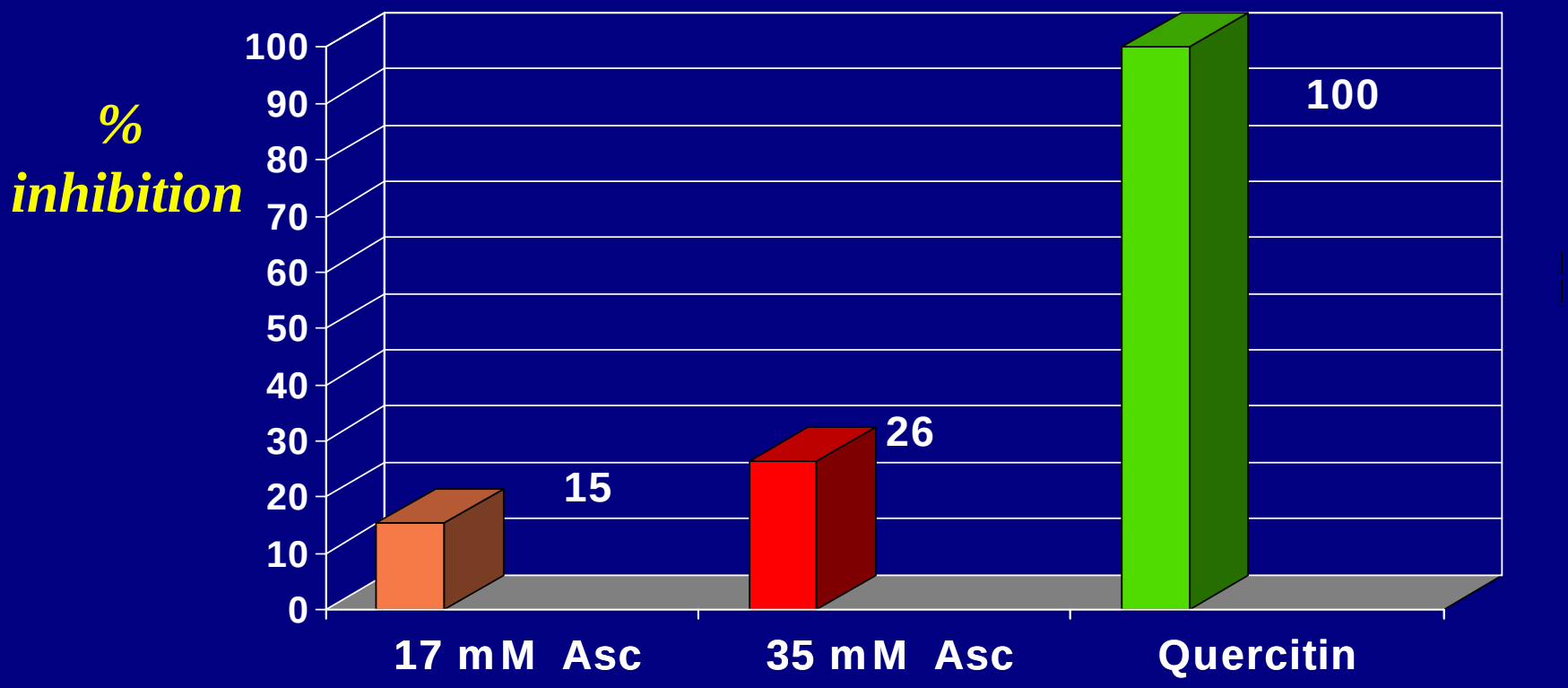
Cunningham et al., Metabolism 1991 & JACN 1994

Mononuclear Leukocyte Concentrations

		mg Asc / gram prot
Nondiabetics	**(n =24)**	**2.6**
		(75% ≥ 1.8)
IDDMs	**(n=20)**	**1.8**
		(15% ≥ 2.6)

Ascorbic acid: an ARI *in vitro*

Cunningham, JACN 1998



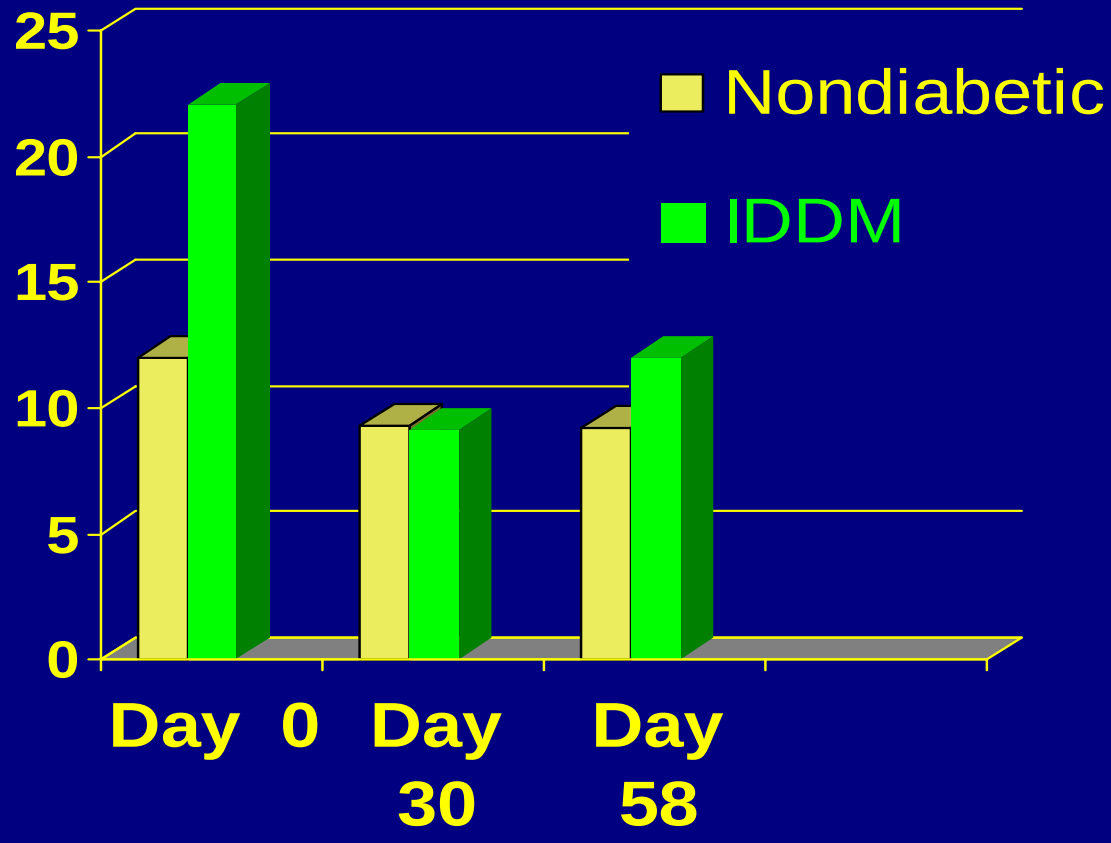
inhibition of AR activity in semi-purified brain, glyceraldehyde substrate & NADPH assay

Ascorbic Acid: an ARI *in vivo*

Cunningham et al., JACN 1994

vit C supplements (100 mg or 600 mg daily)

Erythro sorbitol nmol/ gHb



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 (nutriceutic)

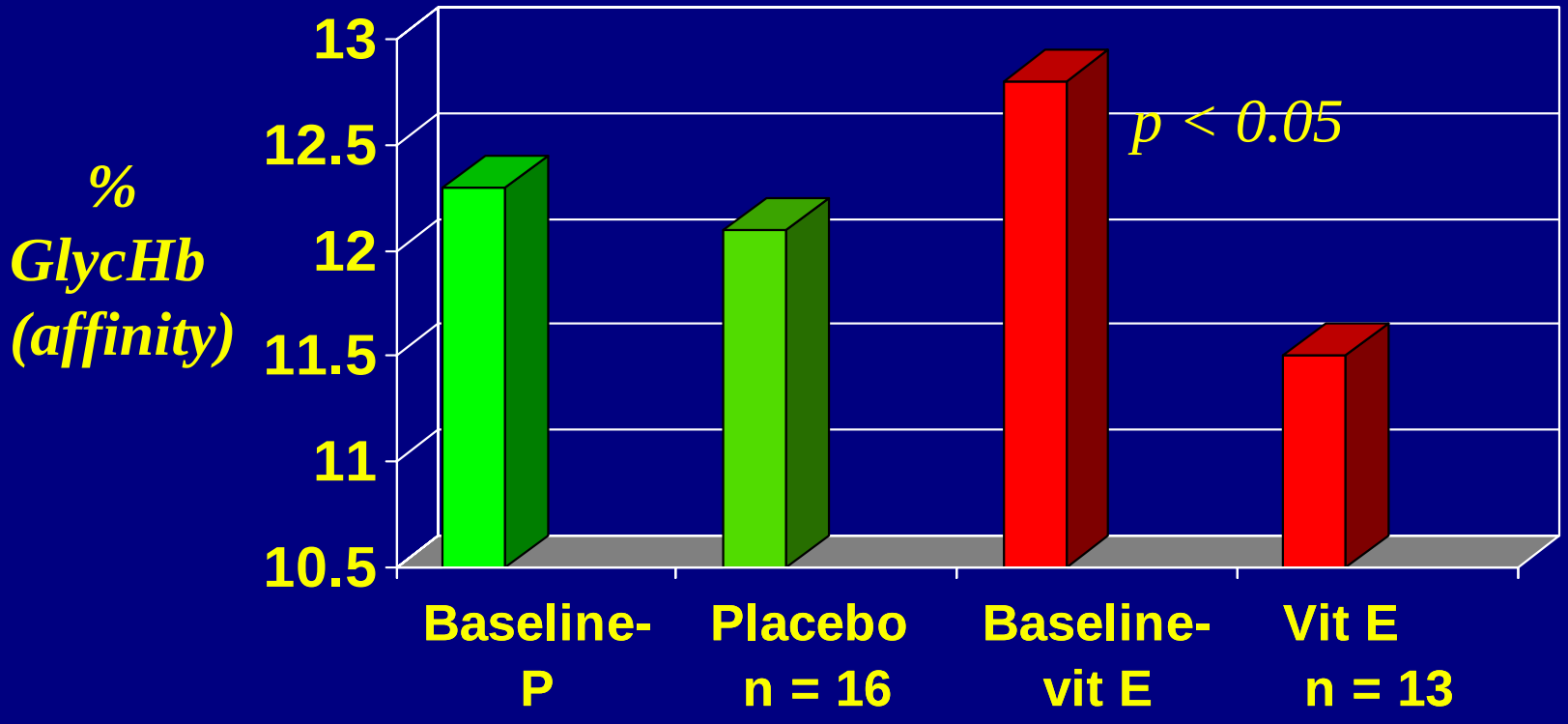
Jain et al, JACN 15:458, 1996

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



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