

Vitamin D and type 1 diabetes mellitus

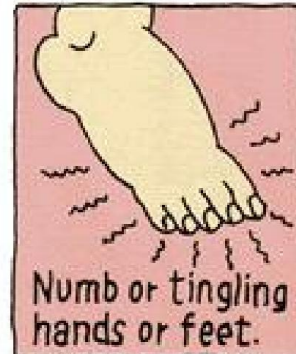
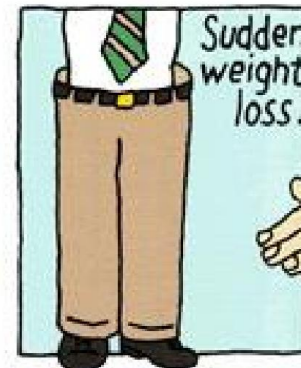
Definition

- ▶ Diabetes mellitus (or diabetes) is a chronic, lifelong condition that affects your body's ability to use the energy found in food. There are three major types of diabetes: type 1 diabetes, type 2 diabetes, and gestational diabetes.

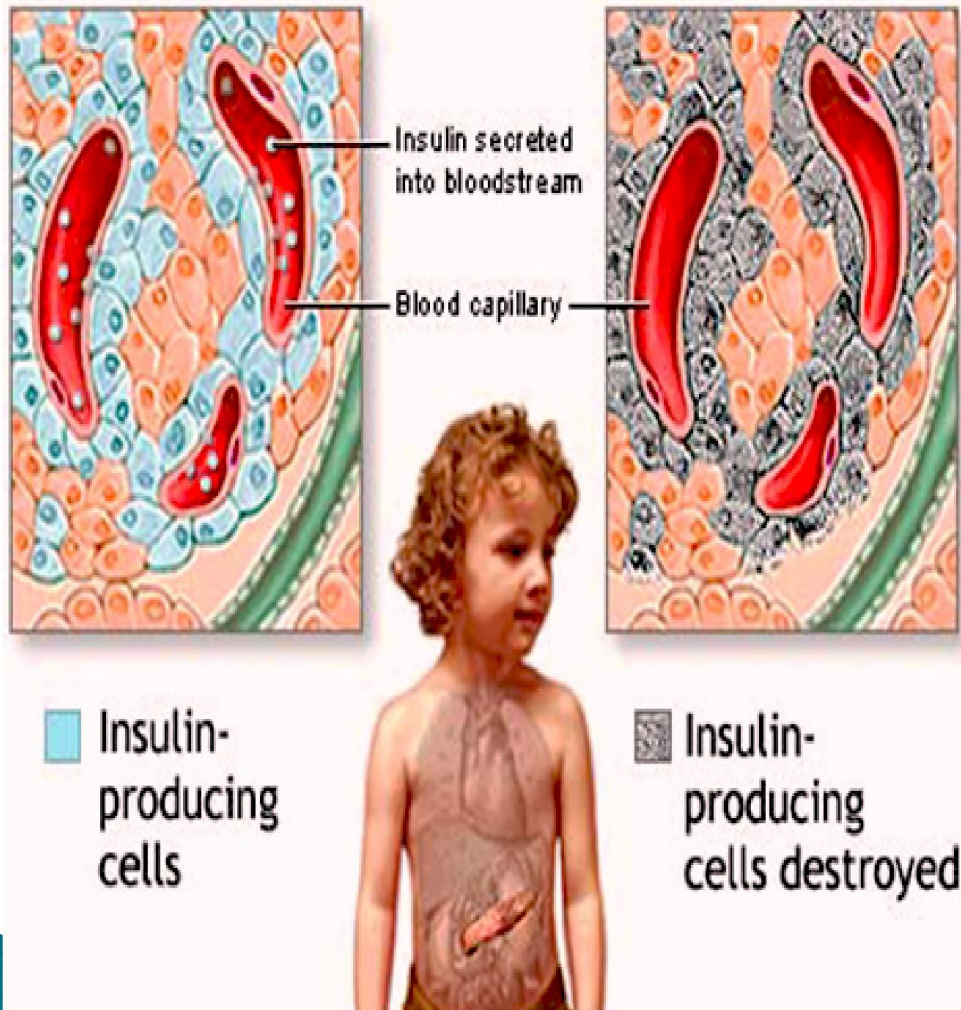
Symptoms of DIABETES



SYMPTOMS OF DIABETES



Diabetes mellitus type 1



Type 1 Diabetes Mellitus

- Less common than type 2
- Etiology (3 theories, simultaneously?)
 - **Viral** infection (e.g., mumps, rubella, CMV, mono) may lead to destruction of β cells
 - **Genetic** predisposition - (HLA-DR [3,4] genotype; HLA-DQ point mutation)
 - **Autoimmune** inflammation - Islet-cell antibodies found
- Pathogenesis
 - Marked, absolute insulin deficiency resulting from diminished β -cell mass - - - > low serum insulin levels

Diabetes mellitus type 2

Main symptoms of Diabetes

blue = more common in Type 1

Central

- Polydipsia
- Polyphagia
- Lethargy
- Stupor

Eyes

- Blurred vision

Breath

- Smell of acetone

Systemic

- Weight loss

Respiratory

- Kussmaul breathing (hyperventilation)

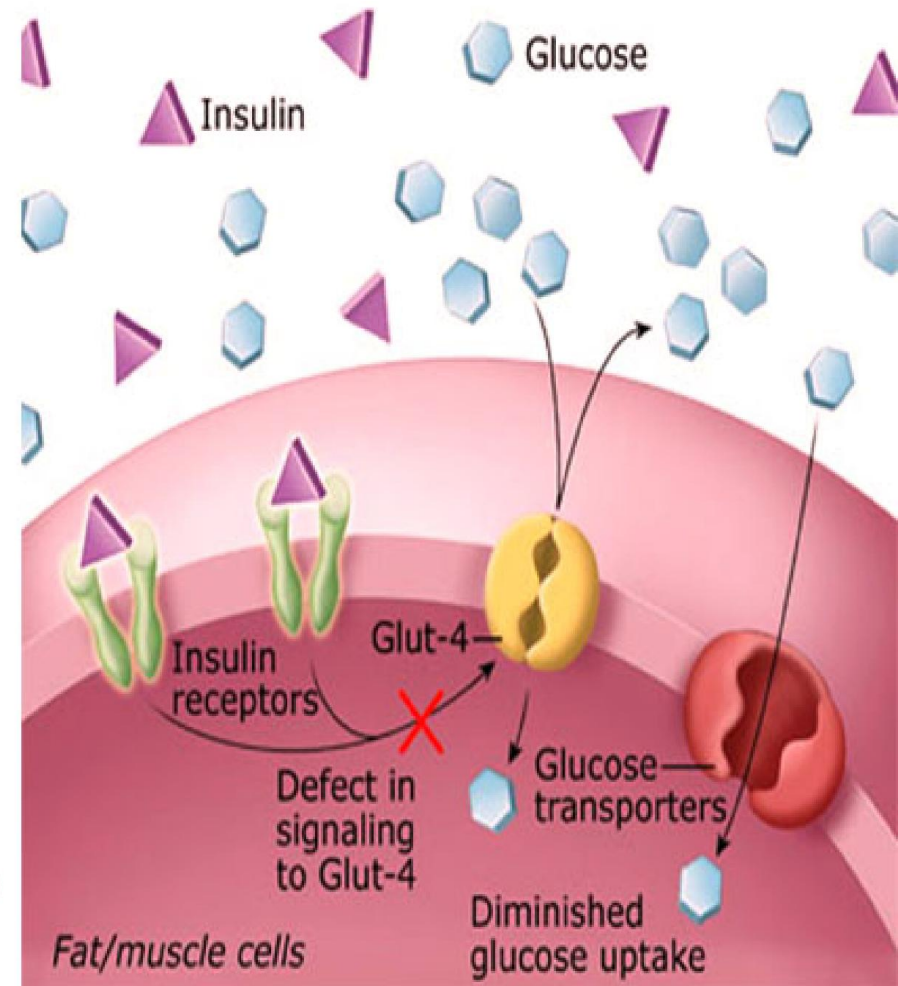
Gastric

- Nausea
- Vomiting
- Abdominal pain

Urinary

- Polyuria
- Glycosuria

Type 2 Diabetes: Insulin Resistance



Gestational diabetes

Gestational Diabetes



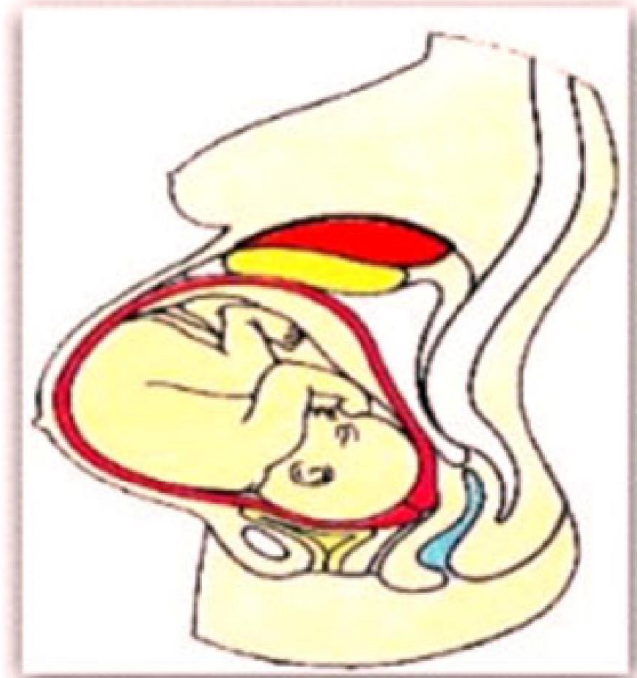
High blood
glucose level
in mother



Brings extra glucose
to baby



Causes baby to put
on extra weight



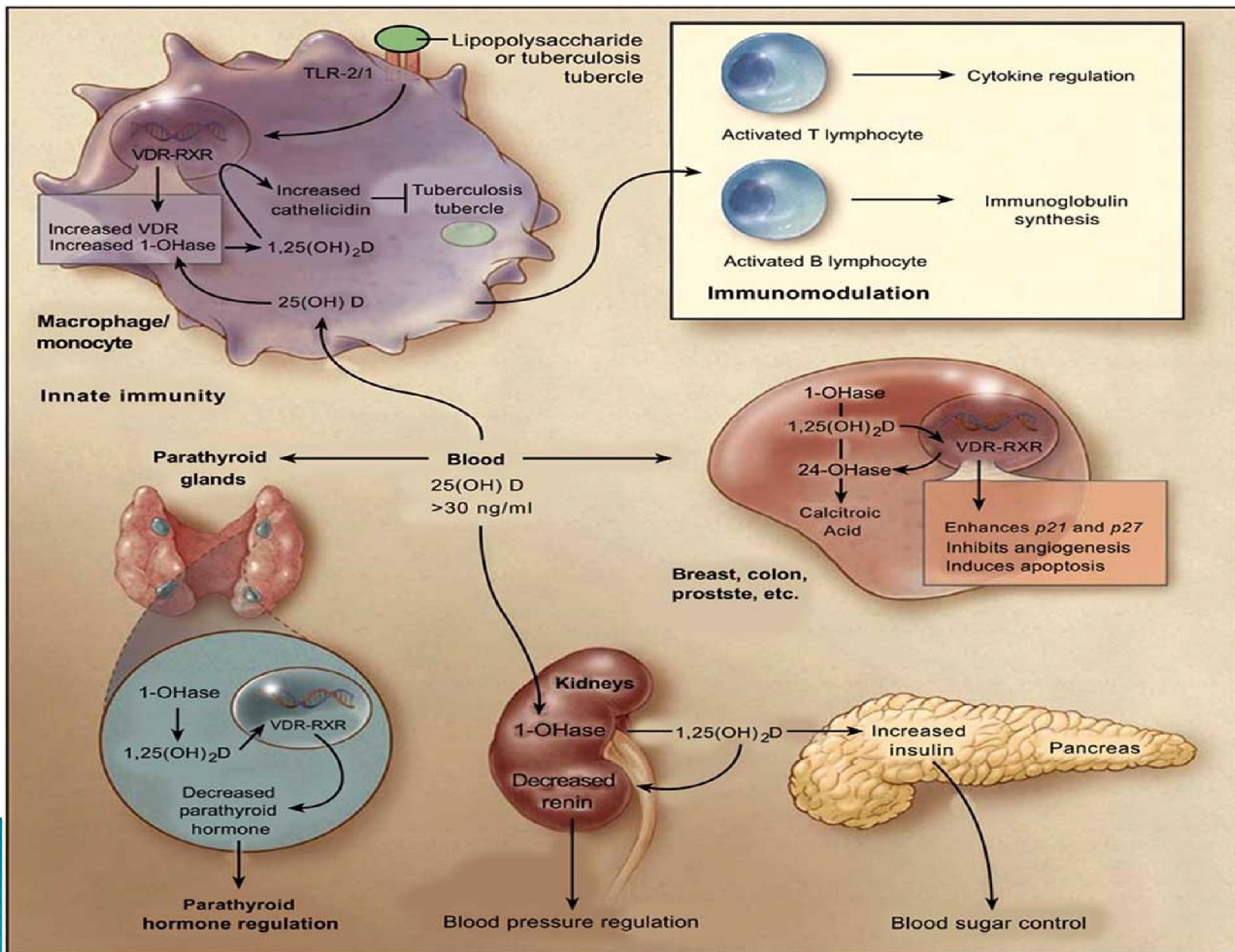
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Gestational Diabetes Mellitus, GDM) is a condition in which women without previously diagnosed diabetes exhibit high blood glucose levels during pregnancy.

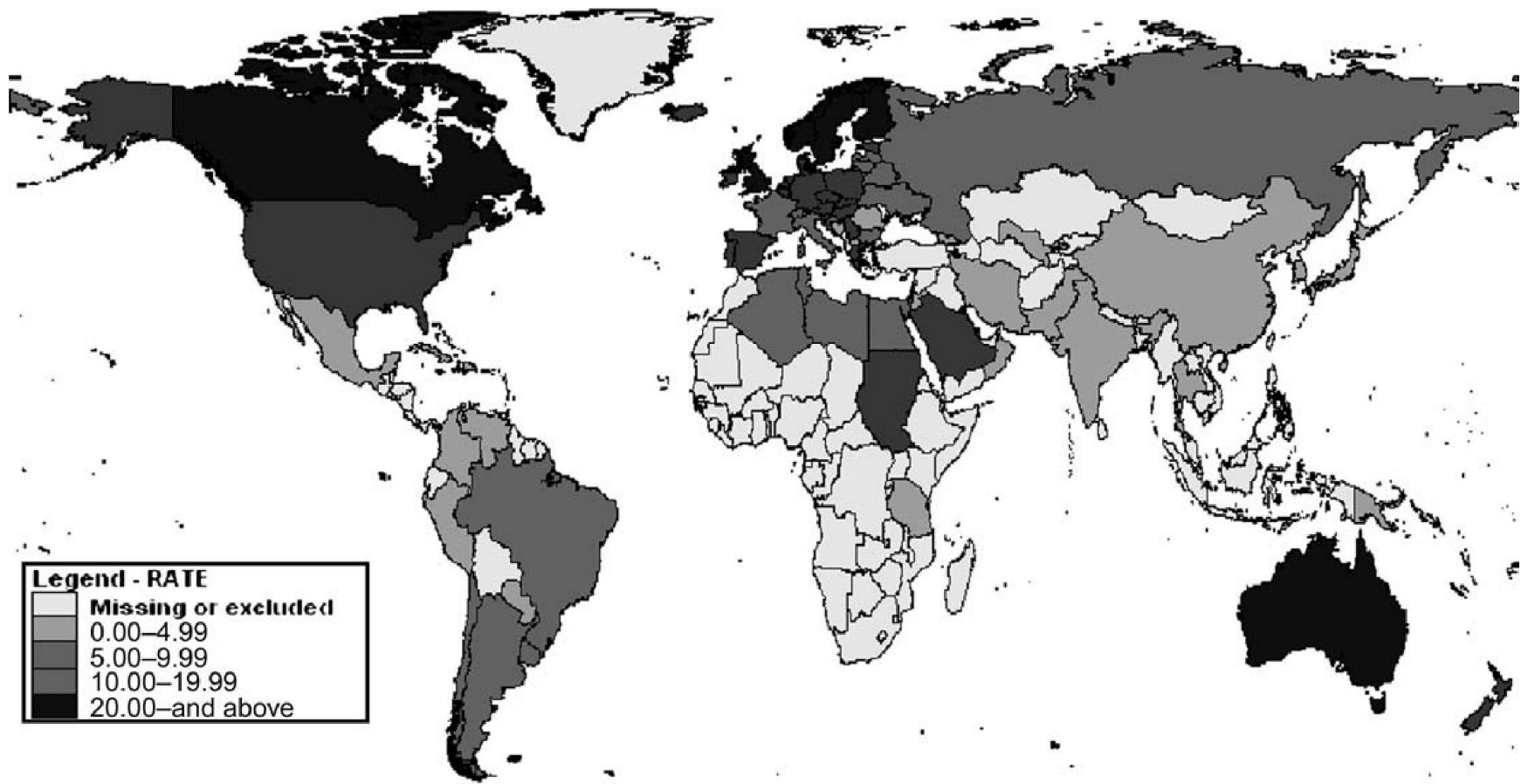
VITAMIN D

- ▶ Vitamin D is taken up from food (vitamin D2 and D3) or synthesized in the skin. In the circulation, all vitamin D metabolites are bound to vitamin D-binding protein (DBP). To become active, vitamin D3 is hydroxylated first in the liver (25-hydroxylases) and successively in the kidney (1 α -hydroxylase) to its final form 1 α ,25(OH) $_2$ D $_3$.

Showing an outline of the non skeletal functions of calcitriol (1,25-dihydroxyvitamin D), including innate immune, antiinflammatory and metabolic effects. (From 'Holick MF, Vitamin D deficiency. *NEJM* 2007; 357:266-81' with permission).



Map of published incidence rates (per 100 000) of type 1 diabetes in children. Source: Solte'sz et al. (2007)



Vitamin D intake and type 1 diabetes prevention

- ▶ Hypponen et al. found a significantly reduced risk of 0.22 for type 1 diabetes in a birth-cohort study when high-dose vitamin D supplementation (>50 microgam/day, 2000 U/day) was given regularly or irregularly.

Lancet. 2001 Nov

Intake of vitamin D and risk of type 1 diabetes: a birth-cohort study.

Hyppönen E¹, Läärä E, Reunanen A, Järvelin MR, Virtanen SM.

BACKGROUND:

- ▶ Dietary vitamin D supplementation is associated with reduced risk of type 1 diabetes in animals. Our aim was to ascertain whether or not vitamin D supplementation or deficiency in infancy could affect development of type 1 diabetes.

METHODS:

- ▶ A birth-cohort study was done, in which all pregnant women (n=12055) in Oulu and Lapland, northern Finland, who were due to give birth in **1966** were enrolled. Data was collected in the first year of life about frequency and dose of vitamin D supplementation and presence of suspected rickets. Our primary outcome measure was diagnosis of type 1 diabetes by end of December, **1997**.

INTERPRETATION:

- ▶ **Dietary vitamin D supplementation is associated with reduced risk of type 1 diabetes.** Ensuring adequate vitamin D supplementation for infants could help to reverse the increasing trend in the incidence of type 1 diabetes.

Vitamin D intake and type 1 diabetes prevention

- ▶ Those children with suspected rickets during the first year of life had a threefold increased risk of developing type 1 diabetes during later life.
- ▶ Similarly, increased vitamin D intake during pregnancy significantly reduced b-cell autoimmunity in children.

In Utero Dietary Exposures and Risk of Islet Autoimmunity in Children

OBJECTIVE— The goal of this study was to examine whether maternal dietary intake of vitamin D, omega-3 fatty acids, and omega-6 fatty acids during pregnancy is associated with the appearance of islet autoimmunity (IA) in offspring.

RESEARCH DESIGN AND METHODS— The Diabetes Autoimmunity Study in the Young (DAISY) is recruiting at birth and following children at increased risk for type 1 diabetes, as determined by HLA-DR genotype or by family history of type 1 diabetes. A total of 233 mothers of newly recruited DAISY subjects were asked to recall their intake of food and nutritional supplements during the third trimester of pregnancy. Children were followed for an average of 4 years (range 0.8–7.3 years) for the appearance of insulin, GAD65, and IA-2 autoantibodies. Sixteen children developed at least one autoantibody during this period. Unadjusted and adjusted hazard ratios (HRs) for the development of IA were estimated with survival analysis using a Weibull distribution.

RESULTS— Maternal intake of vitamin D via food was significantly associated with a decreased risk of IA appearance in offspring, independent of HLA genotype, family history of type 1 diabetes, presence of gestational diabetes mellitus, and ethnicity (adjusted HR 0.37; 95% CI 0.17–0.78). Vitamin D intake via supplements, -3 fatty acids, and -6 fatty acids intake during pregnancy were not associated with appearance of IA in offspring.

CONCLUSIONS— Our findings suggest that maternal intake of vitamin D through food during pregnancy may have a protective effect on the appearance of IA in offspring.

Fronczak, C.M. et al. (2003) Diabetes Care

Vitamin D intake and type 1 diabetes prevention

- ▶ In a Norwegian study, the use of cod liver oil either during pregnancy or in the first year of life was associated with a lower incidence of type 1 diabetes.
- ▶ Whether this was the result of the content of vitamin D or long-chain n-3 fatty acids (or a combination) merits further investigation.

Use of cod liver oil during the first year of life is associated with lower risk of childhood-onset type 1 diabetes: a large, population-based, case-control study.

Stene LC¹, Joner G; Norwegian Childhood Diabetes Study Group.

BACKGROUND:

- ▶ In Norway, cod liver oil is an important source of dietary vitamin D and the long-chain n-3 fatty acids eicosapentaenoic acid and docosahexaenoic acid, all of which have biological properties of potential relevance for the prevention of type 1 diabetes.

DESIGN:

- ▶ We designed a nationwide case-control study in Norway with 545 cases of childhood-onset type 1 diabetes and 1668 population control subjects. Families were contacted by mail, and they completed a questionnaire on the frequency of use of cod liver oil and other vitamin D supplements and other relevant factors.

RESULTS:

- ▶ Use of cod liver oil in the first year of life was associated with a significantly lower risk of type 1 diabetes (adjusted odds ratio: 0.74; 95% CI: 0.56, 0.99). Use of other vitamin D supplements during the first year of life and maternal use of cod liver oil or other vitamin D supplements during pregnancy were not associated with type 1 diabetes.

CONCLUSION:

- ▶ Cod liver oil may reduce the risk of type 1 diabetes, perhaps through the antiinflammatory effects of long-chain n-3 fatty acids

Vitamin D intake and type 1 diabetes prevention

- ▶ A EURODIAB (European Community Concerted Action Programme in Diabetes) subgroup multicentre study of cases and controls found that the risk for type 1 diabetes was significantly reduced in countries with vitamin D supplementation during childhood.

Diabetologia. 1999 Jan

Vitamin D supplement in early childhood and risk for Type I (insulin-dependent) diabetes mellitus. The EURODIAB Substudy 2 Study Group.

Abstract

- ▶ The initiation of the immunopathogenetic process that can lead to Type I (insulin-dependent) diabetes mellitus in childhood probably occurs early in life. Studies in vitro have shown that vitamin D3 is immunosuppressive or immunomodulating and studies in experimental models of autoimmunity, including one for autoimmune diabetes, have shown vitamin D to be protective. **Seven centers in Europe** with access to population-based and validated case registers of insulin-dependent diabetes patients participated in a case-control study focusing on early exposures and risk of Type I diabetes. **Altogether data from 820 patients and 2335 control subjects** corresponding to 85% of eligible patients and 76% of eligible control subjects were analysed. Vitamin D supplementation was associated with a decreased risk of Type I diabetes without indication of heterogeneity

In conclusion, this large multicentre trial covering many different European settings consistently showed a protective effect of vitamin D supplementation in infancy. The findings indicate that activated vitamin D might contribute to immune modulation and thereby protect or arrest an ongoing immune process initiated in susceptible people by early environmental exposures.

The Journal of Pediatrics 2010 Mar; Epub 2009 Nov 18.

Relationships between 25-hydroxyvitamin D levels and plasma glucose and lipid levels in pediatric outpatients.

[Johnson MD¹](#), [Nader NS](#), [Weaver AL](#), [Singh R](#), [Kumar S](#).

OBJECTIVE:

- ▶ To study the relationships between serum vitamin D levels and plasma glucose or lipid levels in children and adolescents.

RESULTS:

- ▶ 25(OH) D levels were inversely correlated with fasting plasma glucose levels ($r = -0.20$, $P < .001$). Lower 25(OH) D levels were also associated with lower serum high-density lipoprotein cholesterol (HDL) concentrations ($r = 0.41$; $P < \text{or} = .001$). The relationship between 25(OH) D levels and fasting glucose and HDL levels did not vary significantly with sex, age, body mass index z-score, or season. Children who were vitamin D insufficient (25[OH] D ≤ 30 ng/mL) had higher fasting plasma glucose ($P = .002$) and lower HDL levels ($P < .001$) than children who were vitamin D sufficient (25[OH] D > 30 ng/mL).

CONCLUSIONS:

- ▶ Low 25(OH) D levels in children and adolescents are associated with higher plasma glucose and lower HDL concentrations.

Diabetologia (2012) 55:3224–3227

Lower prediagnostic serum 25-hydroxyvitamin D concentration is associated with higher risk of insulin-requiring diabetes: a nested case-control study

E. D. Gorham & C. F. Garland & A. A. Burgi & S. B. Mohr & K. Zeng & H. Hofflich & J. J. Kim & C. Ricordi

Aims/hypothesis Low serum 25-hydroxyvitamin D [25 (OH)D] concentration may increase risk of insulin requiring diabetes.

Methods A nested case-control study was performed using serum collected during 2002–2008 from military service members. One thousand subjects subsequently developed insulin-requiring diabetes. A healthy control was individually matched to each case on blood-draw date (± 2 days), age (± 3 months), length of service (± 30 days) and sex. The median elapsed time between serum collection and first diagnosis of diabetes was 1 year (range 1 month to 10 years). Statistical analysis used matched pairs and conditional logistic regression.

Results ORs for insulin-requiring diabetes by quintile of serum 25(OH)D, from lowest to highest, were 3.5 (95% CI 2.0, 6.0), 2.5 (1.5, 4.2), 0.8 (0.4, 1.4), 1.1 (0.6, 2.8) and 1.0 (reference) (ptrend < 0.001). The quintiles (based on fifths using serum 25(OH)D concentration in the controls) of serum 25(OH)D in nmol/l, were < 43 (median 28), 43–59 (median 52), 60–77 (median 70), 78–99 (median 88) and ≥ 100 (median 128).

Conclusions/interpretation Individuals with lower serum 25(OH)D concentrations had higher risk of insulin requiring diabetes than those with higher concentrations. A 3.5-fold lower risk was associated with a serum 25 (OH)D concentration ≥ 60 nmol/l.

CONCLUSIONS

We are still without a definitive answer as to whether avoidance of hypovitaminosis D by appropriate supplementation will reduce the risks of T1DM. It is, therefore, to be hoped that the completion of adequate RCTs will lead to the eradication of vitamin D deficiency as a medical problem.



Large study to examine if vitamin D prevents diabetes

- ▶ Researchers have begun the first definitive, large-scale clinical trial to investigate if a vitamin D supplement helps prevent or delay type 2 diabetes in adults who have prediabetes, who are at high risk for developing type 2. Funded by the National Institutes of Health, the study is taking place at about 20 study sites across the United States.

THANK YOU FOR YOUR ATTENTION

