Vitamin D, Food Allergy, and Food-induced Anaphylaxis

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Presentation
1. Food allergy / anaphylaxis
2. Vitamin D
3. Observational studies
4. Potential mechanisms
5. Summary

Food Allergy / Anaphylaxis
- Surveillance complicated by false-positives (proxy measure: Rx epinephrine autoinjector)
- Prevalence of food allergy rising in many developed nations. Likewise, frequency of food-induced anaphylaxis also rising – though unpublished data suggest plateau or decline
- Causes of food allergy epidemic are unclear
  - Hygiene hypothesis?
  - Early exposure to food allergens?

Vitamin D Synthesis & Metabolism
- Vitamin D
  - 7-dehydro cholesterol
  - Sun
  - Liver 25-hydroxylase (CYP27A1)
  - Kidney 1α-hydroxylase (CYP27B1)
  - 25(OH)D
  - 25(OH)D
  - 1,25(OH)2D
  - Kidney 24-hydroxylase
  - Diet & Suppl.
  - Vitamin D
  - 24,25(OH)2D

Severe Vitamin D Deficiency → Rickets
- Severe Vitamin D Deficiency
- Rickets

Vitamin D Receptor (VDR)
- VDR present in most tissues and cells of body
- Growing recognition that many different cells have the enzymatic machinery to convert 25(OH)D to the active hormone, 1,25(OH)2D
- >2,700 binding sites for VDR along genome
- Significant effects on activity of 229 genes

A. Norman, 2006; Ramagopalan, Genom Res 2010
Non-Calcemic Functions of Vitamin D

Figure 1. Global climatology (1979-1992) of noon daily erythemal (i.e., “sunburning”) UV dose (from the NCAR web site http://www.acd.ucar.edu/TUV/).

Serum 25(OH)D (cut-points controversial)

- Conversion factor: 1 ng/ml = 2.496 nmol/L
- US average: ~25 ng/ml

- "Inadequate" vitamin D
  - <10 ng/ml (everyone)
  - <20 ng/ml (AAP, IOM)
  - <30 ng/ml (many researchers)
  - <40 ng/ml (few researchers)

Table 1. Optimal level also controversial...

- ≥30 ng/ml
- 40 ng/ml
- 40-60 ng/ml
- 60-80 ng/ml

Bischoff-Ferrari, Osteopor Int 2010; Canadian Paediatric Society 2007; Wagner, Pediatrics 2008; Institute of Medicine 2011; www.grassrootshealth.net

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EpiPen Prescriptions per 1,000 State Residents

Camargo, JACI 2007

Dna Spectral Exposure (W/m2) for July 1992

Holick, J Clin Invest 2006
EpiPen Rx in Australia

Hypoallergenic Formula Rx in Australia

Season of Birth and Food Allergy in Boston

Maternal Vitamin D Intake During Pregnancy and Food Allergen IgE in Offspring at Age 5y
Immunologic Effects of Vitamin D


Vitamin D Deficiency

Vassallo & Camargo, JACI 2010

Curvilinear Association with IgE?

- UK (Hyponnen, Allergy 2009):
  - Cross-sectional study, n=9377 adults, age 45y
  - Low & high 25(OH)D associated with higher levels of total IgE

- Arizona (Rothers, JACI 2011):
  - Birth cohort study, n=219 newborns → age 5 years
  - Low & high 25(OH)D associated with higher risk of aeroallergen sensitization

Summary & Clinical Implications

- For unclear reasons, the prevalence of food allergy is rising in many developed nations
- Definition of vitamin D deficiency is controversial but most experts agree that population levels are low
- ↓ UVB exposure, and possibly ↓ 25(OH)D, are associated with ↑ prevalence of food allergy/anaphylaxis
- Observational data and mechanisms remain unclear ...
  - Further research needed
- My best guess for target 25(OH)D?
  - Age 1 year and older: ~40 ng/ml ~100 nmol/L