Diagnosis and Treatment of Vitamin D Deficiency Workshop

UV: The original Source! How to use it
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The following personal financial relationships with commercial interests relevant to this presentation existed during the past 12 months:

No relationships to disclose

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OBJECTIVES

Identify environmental, behavioral, and constitutive risk factors for vitamin D deficiency syndrome

Describe cutaneous evolutionary adaptations for use of UVB for vitamin D synthesis

Identify the portion of the UVB spectrum available and effective in Vitamin D Photosynthesis

Make recommendations for optimal serum levels of 25 (OH) D for any patient whether from sun exposure or oral intake
Vitamin D Deficiency as a Syndrome

Marfan’s Syndrome
Affects connective tissue leading to a myriad of disease consequences, including skeletal and coronary vascular disorders.

Vitamin D Deficiency Syndrome
Affects intercellular communications (tight junctions) and calcium regulation also with a myriad of health consequences.

These include skeletal and coronary heart disease effects and increased risk of:

- Cancers (17 sites*)
- Multiple sclerosis
- Seasonal influenza
- Diabetes (Types 1 & 2)
- Muscle pain and weakness
- Pregnancy complications
- Impaired wound healing

UVB Photons and Vitamin D Synthesis

The sun is the source of UVB photons used to make vitamin D.

Of all solar photons available at noon at ground level, fewer then 0.5% are useful in vitamin D synthesis (297-309 nm wavelength).
Photons Available for Vitamin D Photosynthesis: 297-309 nm

- Ultraviolet B
  - Range, 280-319 nm
- Ultraviolet A
  - Range, 320-399 nm

Photons available for vitamin D synthesis: 297-309 nm

Solar ultraviolet irradiance

Visible light
297-309 nm

7DHC
Provitamin D
7-dehydrocholesterol

preD3
Provitamin D3

Vitamin D3
cholecalciferol

kidney
calcitriol

in plasma

other cells
throughout
the body
calcitriol

25(OH)D3
calcidiol
25-hydroxy vitamin D3

Liver
At 23.4° N. latitude the optical path length of sunlight through the atmosphere is longer at the equator.
Erythemal UVB dose (kiloJoules/square meter) on a globally clear day at world-wide solar noon on the Summer Solstice, 21 June 2007

Erythemal UVB dose (kiloJoules/square meter) on a globally clear day at world-wide solar noon on the Winter Solstice, 21 December 2007.

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

Type 1 Diabetes Incidence Peaks Annually in the Winter-Spring Season (Odds Ratio = 1.46, \( p < 0.01 \))

Incidence of Type 1 diabetes by month and year, active-duty DoD, 2000-2004, \( N = 2,918 \) new cases, 18-44 years (median age 28 years)

Randomized Controlled Trial of Vitamin D and Bone Loss in Postmenopausal Women

Follow-up every 6 months for self-reported flu symptoms

Aloia JF, Li-Ng M. Re: epidemic influenza and vitamin D. Epidemiol Infect. 2007;135:1095-6
Season of Diagnosis

Prostate Cancer Survival by Season of Diagnosis,
N = 46,205 Cases, 1964-1992, Norway

25-Hydroxyvitamin D Serum Levels, 15,536 participants
National Health and Nutrition Examination Survey III, Seasonal Sampling

74% of NHANES sample below 32 ng/ml (Clinical vitamin D insufficiency)
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

Physical Activity and Cancer Incidence Among 5,138 men 25-74 years of age, 1982-84, NHANES 1

D Albanes, A Blair, and P R Taylor
Women are at Elevated Risk for Vitamin D Deficiency

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

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

Constitutive Pigmentation is a Risk Factor for Vitamin D Deficiency

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

Odds Ratios:
- White (non-Hispanic): 1.0
- Black (non-Hispanic): 10.2
- Hispanic: 2.5
- Other: 3.0

Human Photoprotective Response
Human Photoprotective Response

UV A
320-399 nm

UV B
297-309 nm

Dermis

Basal layer

Stratum spinosum

Stratum granulosum

Stratum corneum

Melanin

Melanocyte

Keratinocytes

Vit D
Thickened Stratum corneum
Thickened Stratum granulosum
Stratum spinosum
Basal layer
Dermis

Human Photoprotective Response
Thickened Stratum corneum
Thickened Stratum granulosum
Stratum spinosum
Basal layer
Dermis

Human Photoprotective Response
Human Photoprotective Response
Melanosome migration in response to UV
Melanosome migration in response to UV
Melanosome migration in response to UV
Melanosome migration in response to UV
Melanosome migration in response to UV

Melanosome

Keratinocytes

Melanosome migration in response to UV
Melanosome migration in response to UV
Melanosome migration in response to UV
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Melanosome migration in response to UV
Dates of introduction of suntan lotions and sunscreens

Homosalate and glyceryl-\(p\)-aminobenzoate (late 1940s)
Dates of introduction of suntan lotions and sunscreens

- Homosalate and glyceryl-\(p\)-aminobenzoate (late 1940s)
- PABA (early 1960s, ~ SPF 8)
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- PABA (early 1960s, ~ SPF 8)
- Higher Erythemal Blocks (1975, SPF 20-35)
Dates of introduction of suntan lotions and sunscreens and age-adjusted melanoma incidence rates per 100,000

Source: Connecticut Tumor Registry

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Solar ultraviolet irradiance and relative energy absorbance by para-aminobenzoic acid.
Relative absorption spectrum of PABA sunscreen agent and fish melanoma action spectrum

Absorption spectrum of octyl methoxycinnamate in toluene (−−−); ethyl acetate (−−); 1 propanol (−−−−); and methanol (−−)
Emission spectrum of octyl methoxycinnamate in toluene (---); ethyl acetate (- -); 1 propanol (---); and methanol (—)

Absorption spectrum of PABA in toluene (--.--); ethyl acetate (---); 1 propanol (--- ); and methanol (---)

Emission spectrum of PABA
in toluene (---); ethyl acetate (--); 1 propanol (---); and methanol (--)

Absorption spectrum of 5% Mexoryl SX and 5%2-EHMC

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Odds Ratio</th>
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<tr>
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<td>Holly, 1995</td>
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<tr>
<td>Espinosa, 1999</td>
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<td>Holman, 1986 (ns)</td>
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<td>Naldi, 2000 (ns)</td>
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<tr>
<td>Osterlin, 1988 (ns)</td>
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<tr>
<td>Youl, 2002 (ns)</td>
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<tr>
<td>Aufer, 1988</td>
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<td>Graham, 1985</td>
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<td>Whitman, 1997 (ns)</td>
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<td>Wolf, 1998</td>
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</table>

Odds Ratios for malignant melanoma associated with sunscreen use (4 lower, 5 not statistically significant, 7 elevated)
Studies at > 40° latitude
Beitner 1990, Sweden 62°
Westerdahl 2000, Sweden 62°
Westerdahl 1995, Sweden 62°
Osterlind 1988, Denmark 56°
Autier 1998, Belgium, France, Germany 49°
Wolf 1998, Austria 48°
Graham 1998, New York 43°
Naldi 2000, Italy 41°
Berwick, New York 41°

Studies at < 40° latitude
Espinosa Arranz 1999, Spain 40°
Holly 1995, San Francisco 38°
Rodenas 1996, Spain 37°
Bakos 2002, Brazil 25° S
Holman 1986, Australia 30° S

Pooled odds ratio = 1.41
Test for overall effect $p < 0.0001$

Pooled odds ratio = 0.59
Test for overall effect $p < 0.0001$

Pooled odds ratio, all studies = 1.14
Test for overall effect $p = 0.02$

$R^2 = 0.35$

Source: Connecticut Tumor Registry

Incidence per 100,000

Annual Sunscreen Sales (Millions $)
Sunscreens and Free Speech

• “Whether consumers are told that a product has an S.P.F. rating at a specific level above 30, or that a product containing sunscreen helps prevent skin aging,— it is difficult to see how the transmission of such information results in real harm…”

• Mr. John G. Roberts, Cosmetics Industry Lawyer in a letter to F.D.A., 2001
“Well, Donald – forgot your sun block, I see.”
Recommendations for Vitamin D Photosynthesis

Guiding Principal: Minimize UVA exposure while allowing beneficial UVB exposure

- If skin type allows, advise 10-15 minutes per day in the sun more for heavily pigmented individuals
- Expose ≥ 40% of skin area without application of chemical sunscreen
- Advise sun exposure between 10:00 AM and 2:00 PM on clear days
- Control SO₂ and particulate air pollution that blocks or scatters UVB photons

But when season, latitude, skin type or atmospheric conditions preclude sun exposure:
- Use oral supplementation with vitamin D₃ to achieve circulating levels of 25 (OH)D between 40-60 ng/ml or 100-150 nMols/L
What is the best serum 25 (OH) Vitamin D concentration?

People living in sunny places with minimal clothing that doesn’t limit vitamin D photosynthesis have serum 25(OH)D levels of 54 to 90 ng/ml (1).

A good target is:

40-60 ng/ml  good target

A useful rule of thumb is that for every 100 IU of vitamin D\(_3\) ingested, there is a gain of 1 ng/mL in serum 25 (OH)D (2).

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