SUNLIGHT-INDUCED VITAMIN D SYNTHESIS

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Skin-sunlight interface

Solar UVR reaching Earth’s surface is ~95% UVA, 5% UVB

Penetration depth into skin

- Epidermis
- Dermis

Action spectrum

Skin-sunlight interface

Health outcomes

- Sunburn
- Immunosuppression
- Skin cancers
- Photoageing

Photosensitivity

Vitamin D synthesis
• VITAMIN D SYNTHESIS
Vitamin D synthesis

UVB → SKIN
7-dehydrocholesterol (Pro-vitamin D) → Previtamin D₃ → Vitamin D₃ → Bloodstream

*Vitamin D₃ *Vitamin D₂

DIET

Liver 25-Hydroxylase (CYP27A1, CYP2R1, CYP3A4)

LIVER

25 – Hydroxyvitamin D

Kidney 1-Hydroxylase (CYP27B1)

KIDNEY

1,25 dihydroxyvitamin D₃

Calcium absorption

1,25 dihydroxyvitamin D₃

Calcium resorption

Cellular Functions
- Differentiation
- Proliferation

Inhibition of PTH production
Vitamin D synthesis

• Most of the 7-DHC is present in the epidermis although there is a little in the dermis

• Within the epidermis, the cells in the lower layers (basal and stratum spinosum) are believed to contain most of the 7-DHC

Holick et al (1980) Science
MacLaughlin & Holick (1985) J Clin Invest
Biosynthetic pathway

Vitamin D hormone synthetic pathway

7DHC

Pre-vitamin D₃

Lumisterol

Tachysterol

5,6 Transvitamin D₃

Suprasterol I

Suprasterol II

Vitamin D₃

25(OH)D

1,25(OH)₂D₃

Webb et al (1989) J Clin Endocrinol Metab
# Cut-off Levels for Vitamin D status

<table>
<thead>
<tr>
<th>Circulating 25(OH)D</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 5 -10 ng/ml (12.5 -25 nmol/L)</td>
<td>Deficient&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>&lt; 20 ng/ml (50 nmol/L)</td>
<td>Insufficient</td>
</tr>
<tr>
<td>≥ 20 ng/ml (50 nmol/L)</td>
<td>Sufficient&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>&lt; 32 ng/ml (80 nmol/L)</td>
<td>“Suboptimal”</td>
</tr>
<tr>
<td>≥ 32 ng/ml (80 nmol/L)</td>
<td>“Optimal”&lt;sup&gt;3,4&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

2. Institute of Medicine (2011) Washington, DC.
• MODIFIERS OF VITAMIN D STATUS
Solar source of vitamin D: external factors - predictable

Factors influencing solar zenith angle, UVR path-length:

- Latitude (low)
- Season (summer)
- Time of day (solar noon)

[UK latitudes (50-60°N) – insufficient ambient UVB in winter]
Solar source of vitamin D: external factors – more variable

Atmospheric conditions affecting UVR transmission:

– **Ozone** (*stronger absorber in UVB than UVA*)
– **Clouds** (*generally reduce all wavelengths*)
– **Aerosol pollutants** (*generally reduce all wavelengths*)

*Earth’s surface conditions - reflectivity*
Solar source of vitamin D: personal factors - physiological

Skin pigmentation:

- Melanin is a broad UV-visible radiation absorber

- Melanin competes with the chromophore 7-DHC for absorption of UVB, thus making less available to 7-DHC.

- Darker skin reported to have same capacity for vitamin D synthesis but higher absolute UVR doses required.

- Experimental data conflicting. Situational.

Solar source of vitamin D: personal factors - physiological

**Age:**
- 7-DHC content in skin ↓ with age
- accompanied by ↓ ability to photosynthesise pre-vitamin D₃ (ex vivo study of skin samples)

**Tissue sink/storage:**
- Fat, BMI
- Muscle

**Genetic factors**

Solar source of vitamin D: personal factors - behavioural

**Lifestyle:**

- Time spent outdoors
- Time of day when outdoors
- Sunny holidays abroad

Solar source of vitamin D: personal factors - behavioural

Photoprotective measures:

- **Use of shade**
- **Clothing**
  - Usually confers high level of protection, though dependent on weave, colour, tight/loose fit
  - Surface area exposed: Reportedly important at low UVR doses (0.75 SED and 6 to 24% SA; without effect at 1.5 and 3 SED)

*Bogh et al* (2011) *Br J Dermatol*
Solar source of vitamin D: personal factors - behavioural

Photoprotective measures:

- **Sunscreens**
  - Increase in 25(OH)D occurred after UVR, except at sunscreen thickness of 2 mg/cm²
  - Due to imperfect application methods, less impact in real life

• SUN EXPOSURE & PUBLIC HEALTH MESSAGES
National guidance on sun protection

• **Aimed at reducing excessive exposure** in summer - particularly evidenced by sunburn (also “sunbaking”)

• **Focuses on those at higher risk of skin cancer** particularly skin types I & II, multiple moles, freckles, h/o skin cancer

• **Vitamin D**: increasingly aware of need for messages allowing some “safe” exposure, and for more specific information for population sectors, incl. skin types V & VI.
Vitamin D from casual sun exposure at northerly (UK) latitudes

- Has been stated that brief, casual exposures to summer sunlight, several times per week, are sufficient for fulfilling vitamin D requirements in a light-skinned person. NRPB Handbook (2002)

- However:
  - Previously based on estimates from very limited experiments
  - May not be appropriate based on re-evaluation of 25(OH)D cut-off levels for vitamin D sufficiency
• RESEARCH EXAMINING SUNLIGHT EXPOSURE GUIDANCE & VITAMIN D
Studies in Manchester UK

245 white Caucasian adults

(A) Intervention study:
Course of simulated summer sunlight
– mimicking casual exposures

(B) Field study: Measure personal natural sunlight exposure levels throughout the year

Relate resultant vitamin D to levels for deficiency, insufficiency & proposed “optimum”

Define amount & patterns of sun exposure sufficient to avoid low vitamin D in winter

Public health guidance on sunlight exposure

DH guidance on vitamin D supplements

Simulated summer sunlight exposures

- N=120 white Cauc, 20-60y, phototypes I-IV, Manchester, UK
- 6-wk course UVR - length of school summer holiday period
- Jan - Feb when ambient UVB is negligible at UK latitudes
- Low dose (1.3 SED, ~1.1 SED in sunlight) UVR x 3 weekly
- Wearing T-shirts & knee-length shorts - ~35% skin SA
- 95% UVA: 5% UVB (Philips HB598 horizontal cabinet, irradiation of dorsal and ventral surfaces simultaneously, tubes replaced by Arimed B & Cleo Natural tubes).

Pre-Vitamin D irradiance

Majority moved from insufficiency to sufficiency (IOM) after a simulated summer’s casual sunlight exposures

Equivalent to 13 mins exposures, to 35% surface area, on a clear June midday in Manchester (53.5°N)
Approximate guide: how much time in the sun?

Lying flat:
Cabinet irradiates dorsal & ventral surfaces simultaneously. In sunlight, this would be sequential
= ~13 mins x 6/week

Standing up:
Radiative transfer modelling,
Model SMARTS 2.95. Standing vertical with body sites randomly orientated to the sun
= ~17 mins x 6/week

## Manchester, UK & other locations

<table>
<thead>
<tr>
<th>Latitude</th>
<th>Solar elevation, midsummer, noon</th>
<th>Horizontal: ventral/dorsal sequentially (mins)*</th>
<th>Random vertical (mins)</th>
<th>Dates with noon solar elev &gt; 45º</th>
</tr>
</thead>
<tbody>
<tr>
<td>53.5 ° N Manchester</td>
<td>60º</td>
<td>13</td>
<td>17</td>
<td>11 Apr – 31 Aug</td>
</tr>
<tr>
<td>30° N (Cairo, Austin)</td>
<td>83º</td>
<td>8</td>
<td>13</td>
<td>9 Feb – 2 Nov</td>
</tr>
<tr>
<td>40° N (Beijing, Philadelphia)</td>
<td>73º</td>
<td>10</td>
<td>14</td>
<td>8 Mar – 5 Oct</td>
</tr>
<tr>
<td>50° N (Frankfurt, Winnipeg,)</td>
<td>63º</td>
<td>12</td>
<td>15</td>
<td>2 Apr – 10 Sept</td>
</tr>
<tr>
<td>60° N (Oslo, Anchorage)</td>
<td>53º</td>
<td>16</td>
<td>19</td>
<td>1 May–1 Aug</td>
</tr>
<tr>
<td>Anywhere</td>
<td>solar elevation 45º</td>
<td>22</td>
<td>24</td>
<td></td>
</tr>
</tbody>
</table>

*Approximate times based on 6 x weekly exposure. Other locations derived from UVR action spectra & local sunlight emission spectra. *Webb et al (2011) Photochem Photobiol*
Manchester white Caucasian field study

Median solar exposures >3 SED/week in spring/summer vs 0.1 SED in winter
Clear seasonal pattern with late summer (Sep) peak and winter (Feb) trough
Mean noontime (11-00 to 13-00) mins outdoors = 9 mins (weekdays) & 18 mins (weekend days)

Retaining sufficiency in winter?

- Regression analysis in the field study indicates those (~25%) subjects reaching a summer-peak level of ~32 ng/mL, (80 nmol/l) retain >20 ng/mL (50 nmol/l) at winter trough (62% variance, p<0.001) Webb et al (2010) Br J Dermatol

- If a year-round level of 20 ng/mL (50 nmol/l) is required, then current UK recommendations on sunlight exposure and oral vitamin D intake achieve this in a minority

- Further evaluation currently ongoing in larger data set with assessment against UK climate conditions
Darker skin types: field study

Complex of contributory factors in the field:

- **Behavioural:**
  - lower dietary vitamin D
  - virtually absent vitamin D supplement use
  - reduced skin exposure to when outdoors (diary cards vs UV badge data)

- **Physiological:**
  - darker skin

Darker skin types: UVR intervention study (simulated summer)

Identical UVR protocol
Commonly exposed skin sites; 35% SA

White square: white Cauc, n=120
Black square: S. Asians, n=15

***P<0.001

Darker skin types: 
S. Asian UVR-25(OH)D dose-response

n=10 per dose group. Those receiving ≥1.95 SED achieved >10 ng/ml (mean 25(OH)D 15.7ng/ml, ~40nmol/l)

Risk in photosensitivity conditions

• Large group of disorders where people show abnormal reactions to low doses of UV &/or visible radiation

• Aetiology: genetic, biochemical, immune, drug-induced

• Skin symptoms on sun exposure →
  – They avoid sunlight
  – Employ vigorous photoprotective measures
  – BUT: are no more likely to take vitamin D supplements

Vitamin D status in photosensitive patients

Red: Photosensitive individuals, n=59
Black: Healthy, n=109

Peak <20ng/ml (<10 ng/ml): 47% (9%) photosensitive vs 17% healthy subjects
Trough <20ng/ml: 73% (32%) photosensitive vs 54% healthy subjects

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