SUNLIGHT
UVR
FOR HEALTH
Michael F. Holick
Boston University Medical Center
Publics’ View of the Sun
EDUCATION
EDUCATION
EDUCATION
EDUCATION
Dependence of wavelength and skin penetration

- Str. corneum
- Epidermis
- Dermis
- Subcutaneous adipose tissue

ENERGY NANOMETERS
HOW DOES THE SKIN RESPOND TO THE SUN ????
nature

Suntanned hammerheads
Protective Effects of Melanin

![Diagram showing the protective effects of melanin against DNA damage caused by UVA & B and heat.](Image)
NEVER
BURN
Does sunlight & UVR have any beneficial effects?
HOW DO YOU MAKE VITAMIN D ????
Solar UV Radiation

7-DHC $\leftrightarrow$ PreD$_3$

Vitamin D$_3$

Sunlight radiation responsible for making vitamin D

290-315 nm
HOW MUCH
SUN
EXPOSURE
?????????????????????????
1 minimal erythematous dose
Exposure to 1 Minimum Erythemal Dose

\(~20,000\) IU Vitamin D\(_3\)

(RDA 600-800 IU)
Adults age 18 – 65 exposed to 0.5 MED UVB radiation Once a week for three months or receiving 1000 IU of vitamin D2 or vitamin D3 daily
Is Tanning good for Vitamin D and your bones???????
SERUM 25(OH)D LEVELS IN TANNERS AND NONTANNERS END OF WINTER IN BOSTON

What are the Other Beneficial Consequences Of Being Exposed To UVR ???????
Why do People Feel Good in Sunlight
Do Human Skin Cells produce a Happy Substance in response to sunlight?
Does Human Skin Produce β-Endorphin?
Simulated Sunlight

measure β-endorphin
β-Endorphin Induced by UVB in Cultured Human Keratinocytes

Does Human Skin Produced β-Endorphin enter the bloodstream to make you Feel Good ?????
Sunlight - β-endorphin – Skin Connection

Keratinocyte

β-endorphin ?

β-endorphin

in blood ?

feeling of well-being

Sunlight Exposure May Elevate Serum β-endorphin Levels in Humans

Simulated Sunlight

- Endorphin (pg/ml) vs. Time (min)

0 10 20 30 40 50

β-Endorphin

+44%
I can make β–endorphin in my skin!
β-endorphin: opioid peptide

β-endorphins responsible for:
- Pain relief
- Feeling of well-being
- Relaxation

β-endorphin has approximately 33 times the analgesic potency of morphine.
UV may have some potential in reducing chronic pain and improving mood in persons with Fibromyalgia syndrome.
Ultraviolet radiation and cardiovascular disease (CVD)

Beneficial effects of UV radiation on diseases other than cancer
Asta Juzeniene
Seasonal variations in mortality caused by CVDs

The seasonal variation in CVDs mortality, with an excess in winter, has been documented in many studies.


Mean monthly CVD mortality ratio (ICD 9: 390–459) in Norway and Ireland for men (left) and women (right) in the age group 60 years and older for the 10-year period 1985–1994. The figures beside the arrows indicate the percentage difference between the lowest summer mortality and the highest winter mortality.
There is a tendency for both systolic (S) and diastolic (D) blood pressure (BP) to rise in winter.

Will UVB irradiation help my hypertension?
Hypertension

18 patients (ages 26-66y)

6 Weeks, measure BP

Serum 25(OH)D

Krause et al. 1998

Graph showing the increase in serum 25(OH)D levels from UVA to UVB with a 180% increase.
Effect of UVA on Blood Pressure

![Graph showing the effect of UVA on blood pressure.

Change in BP (mmHg)

- Diastolic
- Systolic

UVA Krause et al 1998
Effect of UVB & UVA on Blood Pressure

Change in BP (mmHg)

UVA

Krause et al 1998
UV radiation and CVD

Vitamin D effects on the cardiovascular system

Effects on the myocardium
- Anti hypertrophic effects
- Modulation of calcium flux and contractility
- Renin suppression
- Modulation of extracellular matrix turnover

Effects on the vessels
- Anti atherosclerotic effects
- Inhibition of vascular calcification
- Improvement of endothelial function

Effects on cardiovascular risk factors
- Renoprotective effects
- Antihypertensive effects
- Antidiabetic effects
- PTH suppression
- Anti inflammatory effects
- Antioxidative effects

Feelisch (2010) Eur Heart J
Nitric oxide (NO) and UV

Human skin is capable of releasing nitric oxide (NO) in an enzyme independent manner. This is due to photolysis of nitric oxide stores by UV radiation.


Figure 1 Sunlight-induced export of nitric oxide bioactivity from storage forms in the skin.

Feelisch (2010) *Eur Heart J*

Suschek (2010) *Nitric Oxide*
What is the role of nitric oxide (NO)?

- Vasodilatation
- UV-induced melanogenesis
- UV-induced immunosuppression
- Inflammation
- Apoptosis
- Wound healing
- Antimicrobial effects

**Bacteria** – *Staphylococcus aureus*

**Dermatophytes** – *Trichophyton rubrum, Trichophyton mentagrophytes*

**Yeasts** – *Candida albicans*

UVA liberates nitric oxide (NO) from the epidermis

Confocal fluorescence microscopy studies of human skin pre-labeled with the NO-imaging probe diaminofluorescein 2 diacetate revealed that **UVA-induced NO release** occurs in a NOS-independent, dose-dependent manner, with the majority of the light-sensitive NO pool in the upper epidermis.

Sunlight Has Cardiovascular Benefits Independently of Vitamin D

Richard B. Weller

Medical Research Council Centre for Inflammation Research, University of Edinburgh, Queen’s Medical Research Institute, Edinburgh, UK
Summary: Sunlight has beneficial effects on cardiovascular risk factors independently of vitamin D. Key Messages: All-cause mortality should be the primary determinant of public health messages. Sunlight is a risk factor for skin cancer, but sun avoidance may carry more of a cost than benefit for overall good health.
Carbon monoxide (CO) and UV

- Vasodilation
- Neurotransmitter
- Cell signaling
- Relaxation
- Antioxidant
- Anti-inflammation
- Anti-apoptosis

How Does UVR Effect my IMMUNE SYSTEM?
Multiple Sclerosis Prevalence
55 Global Regions

$R^2 = 0.46$

$p < 0.0001$

Continuous treatment with UVR dramatically suppresses clinical signs of experimental autoimmune encephalomyelitis (MS).

Multiple sclerosis

Down-regulation of T helper 1 activity involved in demyelination through T regulatory cells and/or B regulatory cells and/or immunosuppressive cytokines

Effect of UVR:
Protection against disease
Development and reduces symptoms of MS
Multiple sclerosis and adrenocorticotropic hormone (ACTH)

**H.P. Acthar® Gel**

- Highly purified preparation of adrenocorticotropic hormone (ACTH)
- Key approved indications:
  - Multiple sclerosis (MS) exacerbations
  - Nephrotic syndrome
- Significant off-label usage

A five-day course of intramuscular or subcutaneous ACTH gel improves symptoms associated with acute exacerbations of multiple sclerosis.

Slominski et al. (2012)
Embryology and Cell Biology

How about UV phototherapy for MS?
Ramune Jacobsen*, Peder Frederiksen and Berit L. Heitmann

Exposure to sunshine early in life prevented development of type 1 diabetes in Danish boys
Methods: The study population included 331,623 individuals born in Denmark from 1983 to 1988; 886 (0.26%) developed T1D by the age of 15 years. The values of sunshine hours were obtained from the Danish Meteorological Institute. The variable was linear and then was split into two categories separated by the median value.

Results and Conclusions: Cox regression models showed that more sunshine during the third gestational trimester was associated with lower hazards (HR) of T1D at age 5–9 years in males: HR (95% CI): 0.60 (0.43–0.84), p=0.003. Our results should be considered in the context of evidence-based recommendations to the public about skin protection from the sun.
„Der Zauberberg“ (Thomas Mann 1924)

Treat and Prevent TB
WHAT IS THE EFFECT OF VITAMIN D ON THE IMMUNE SYSTEM
Vitamin D Protects Against Tuberculosis
02.23.06, 12:00 AM ET
UV Effects on Other Diseases ($T_{\text{reg}}$ cells ↑)

**Beneficial effects of UV radiation on diseases other than cancer**

Asta Juzeniene

UV radiation increases the number of regulatory T cells and reduces immune responsiveness.

- Suppression of allergy and asthma
- Suppression of chronic inflammatory diseases
- Prevention of autoimmune diseases (Type 1 Diabetes, Multiple Sclerosis)

LC, Langerhans cells  
$T_{\text{reg}}$, regulatory T cells
Skin → Vitamin D → 25(OH)D3 → Liver 25-OHase → 25(OH)D3 → Kidney 1α-OHase → 1,25(OH)2D3
ESSENTIALLY EVERY TISSUE AND CELL HAS A VDR
VITAMIN D & CANCER
Vitamin D and Reduced Risk of Breast Cancer: A Population-Based Case-Control Study

Julia A. Knight, Maia Lesosky, Heidi Barnett, Janet M. Raboud, and Reinhold Vieth

Table 2. ORs and 95% CIs for an association between vitamin D–related exposure variables at ages 10 to 19 (sun exposure and dietary vitamin D) and breast cancer in cases and controls

<table>
<thead>
<tr>
<th></th>
<th>Cases (%)</th>
<th>Controls (%)</th>
<th>OR* (95% CI)</th>
<th>OR† (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Girls 10-19 yrs most sun</td>
<td>69%</td>
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</tbody>
</table>

Table 3. ORs and 95% CIs for an association between vitamin D–related exposure variables at ages 20 to 29 (sun exposure and dietary vitamin D) and breast cancer in cases and controls

<table>
<thead>
<tr>
<th></th>
<th>Cases (%)</th>
<th>Controls (%)</th>
<th>OR* (95% CI)</th>
<th>OR† (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women 20-29 yrs most sun</td>
<td>51%</td>
<td></td>
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</tbody>
</table>

Women 45-54 yrs most sun 0.0%
Colon Cell

~ 2000 Genes Affected By 1,25(OH)₂D

VITAMIN D DEFICIENCY IS A DISEASE OF NEGLECT
THERE IS NOW A MOUNTAIN OF EVIDENCE LINKING VITAMIN D DEFICIENCY WITH CANCER RISK & MORTALITY AUTOIMMUNE DISEASES TYPE 1 DIABETES HYPERTENSION TYPE 2 DIABETES !!!!!!
WHAT IS A NORMAL VERSUS HEALTHY 25(OH)D LEVEL ?????
OUR 25(OH)D
40-60 ng/ml

GOOD MUSCLE STRENGTH
LOW CANCER RISK
LOW RISK AUTOIMMUNE & HBP & CVD DISEASE

THE VITAMIN D SOLUTION
A 3-Step Strategy to Cure Our Most Common Health Problems
The Influence of Painful Sunburns and Lifetime Sun Exposure on the Risk of Actinic Keratoses, Seborrheic Warts, Melanocytic Nevi, Atypical Nevi, and Skin Cancer

Cornelis Kennedy, Chris D. Bajdik,* Rein Willemze, Frank R. de Gruijl, and Jan N. Bouwes Bavinck, for the members of the Leiden Skin Cancer Study
Departments of Dermatology, Leiden University Medical Center, Leiden, The Netherlands; *British Columbia Cancer Agency, Vancouver, British Columbia, Canada

Lifetime sun exposure was predominantly associated with an increased risk of squamous cell carcinoma (p-value for trend = 0.03) and actinic keratoses (p-value for trend <0.0001) and to a lesser degree with the two types of basal cell carcinoma. By contrast, lifetime sun exposure
I should Avoid ALL Sunlight to Prevent Melanoma !!!!
Did you Know
Most Melanomas Occur on the Least Sun Exposed Areas
????????
Occupational sun exposure Decreases risk of melanoma
The Influence of Painful Sunburns and Lifetime Sun Exposure on the Risk of Actinic Keratoses, Seborrheic Warts, Melanocytic Nevi, Atypical Nevi, and Skin Cancer

Cornelis Kennedy, Chris D. Bajdik, Rein Willemze, Frank R. de Gruijl, and Jan N. Bouwes Bavinck, for the members of the Leiden Skin Cancer Study
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By contrast, lifetime sun exposure appeared to be associated with a lower risk of malignant melanoma, despite the fact that lifetime sun exposure did not diminish the number of melanocytic nevi or atypical nevi. Neither painful sunburns nor lifetime sun exposure were associated with an increased risk of seborrheic warts. Key words: actinic keratoses/atypical nevi/melanocytic nevi/seborrheic warts/skin cancer/ultraviolet light. J Invest Dermatol 120:1087–1093, 2003
WHAT DID THE AUTHORS CONCLUDE?

INCREASES RISK MELANOMA

INCREASED # MOLES

BAD GENETICS

RED HAIR COLOR

# SUNBURNS as CHILD

YOUNG ADULT
"GOOD GRIEF!"

"ANOTHER NOTE!"

"ARE YOU SITTING IN THE SUN? I HOPE SO. FOR A LITTLE SUN IS GOOD AS LONG AS WE DON'T OVERDO IT. PERHAPS TEN MINUTES A DAY THIS TIME OF YEAR IS ABOUT RIGHT."

"CHARLIE BROWN"
What is the Best Source of SENSIBLE SUNLIGHT
WHEN CAN YOU MAKE VITAMIN D ????

How about an App???

http://dminder.info
Lack of Adequate Sunlight & Vitamin D Deficiency Has a Major Impact On Health

DrHollick.com
VITAMIN D DEFICIENCY

CAUSES
- Sunscreen
- Melanin
- Latitude
- Winter
- Malabsorption
- Crohn's
- Whipple's
- Cystic Fibrosis
- Celiac
- Liver disease
- Obesity
- Medications: Antiseizure, Glucocorticoids, Rifampin, HAART, St John’s Wart

CONSEQUENCES
- Schizophrenia
- Depression
- Infections: URI, TB
- HBP
- CHD
- FEV1
- Wheezing
- Autoimmune: Type 1 Diabetes, MS, Crohn’s, RA
- AODM
- Syndrome X
- Cancer: Colon, Breast, Prostate, etc.
- Infections: URI, TB
- Muscles: Weakness, Aches
- Osteoporosis
- Osteomalacia
- Rickets
- Musculoskeletal: Arthritis

There Is No Downside To Obtaining Sensible Sun Exposure !!!!

DrHollick.com
We Need Sensible Sun + UVR & Vitamin D Supplementation Recommendations

This is NOT HYPOTHESIS

You Do Not Need To Be A Genius To Know
Sunlight radiation responsible for making vitamin D

POMC
ACTH
B-Endorphin
NO & CO

Immune Modulation

Wound healing

Holick et al Science 1980; MacLaughlin et al Science 1982
Knowing how to limit exposure to UV radiation is the key to a healthy and fun sun experience.

- Limit your UV risk when you are working outdoors!
- Enjoy your holiday without getting burnt by the Sun!

Through INTERSUN, WHO provides scientific information and practical advice on the health impact and environmental effects of exposure to UV radiation.

INTERSUN collaborators:

- UNEP: United Nations Environmental Programme
- WMO: World Meteorological Organization
- IARC: International Agency for Research on Cancer
- ICNIRP: International Commission on Non-Ionizing Radiation Protection.

Several WHO collaborating centres are also actively involved in INTERSUN.

More information on WHO INTERSUN can be found at: www.who.int/uv/intersunprogramme
WHO Recommendations

The known health effects of UV

Are there beneficial effects of UV radiation?

The sun's rays provide warmth and light that enhance your general feeling of well-being and stimulate blood circulation. Some UV radiation is essential to the body as it stimulates the production of vitamin D. Vitamin D has an important function in increasing calcium and phosphorus absorption from food and plays a crucial role in skeletal development, immune function and blood cell formation. There is no doubt that a little sunlight is good for you! But 5 to 15 minutes of casual sun exposure of hands, face and arms two to three times a week during the summer months is sufficient to keep your vitamin D levels high. Closer to the equator, where UV levels are higher, even shorter periods of exposure suffice.