EXPOSURE TO ULTRAVIOLET (UV) LIGHT

An Introduction To The Health Effects of Radiation

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ULTRAVIOLET RADIATION

- Most significant source of U.V. is the sun.
- 1801, Johann Wilhelm Ritter
- Electromagnetic radiation
- Wavelength 400nm to below 290nm.
- Divided into three bands, A, B and C band.
- A and B bands reach the earth, whereas C band is filtered by the ozone layer. U.V.A penetrate farthest.
- Produce physiological effect by non-thermal mechanism.
- Deepest penetration with high intensity, long wavelength and lower frequency.
1. **Ultraviolet C** (UVC, 100-290 nm) are the shortest and most energetic portion of the UV spectrum. These highly energetic wavelengths The important wavelengths in the UVC are removed within the atmosphere, mainly by absorption in the ozone layer and not reach the earth's surface in any quantity.

2. **Ultraviolet B** (UVB, 290-320nm) is the most damaging part of UVR that we encounter. UVB are wavelengths mostly blocked by dense clouds, closely woven clothing and glass window panes. Significant amounts are transmitted from blue sky in the middle of the day in summer. It is less dangerous when the sun is low in the sky, at high latitude in winter, and in early mornings and late evenings in summer.

3. **Ultraviolet A** (UVA, 320-400nm) is about 1000 times less damaging to the skin than UVB as measured by sunburn (Erythema) or damage to cell DNA. On the other hand, 20 times more UVA than UVB reaches the earth in the middle of a summer's day. It is not greatly affected by absorption and scattering in the atmosphere when the sun is low in the sky, and is now known to contribute significantly to the total exposure at moderate levels throughout the whole day and year. UVA penetrates deeper into the skin and leads to deeper damage than UVB does. It penetrates cloud cover, light clothing and untinted glass relatively easily, and may induce a degree of continuing skin damage over long periods, even when UVR exposure is not obvious.

American Cancer Society 2006
PHYSIOLOGICAL EFFECTS OF U.V.R

1- Erythema production:
- Generalized response to UVR exposure culminates in development of an acute inflammatory reaction
- Depends on the amount of U.V.
- High dose $\rightarrow$ destructive.
- Suberythematous dose SED
  - No change in 24h after exposure.
- Minimal erythema dose MED
  - Smallest dose that produces erythema within 1-6 hr
  - Disappears within 24 hours
- 1st to 3rd-degree erythema
THE INVISIBLE HEALTH RISK


• Human exposure to UVR from natural sunlight and artificial sources is increasing substantially.
• UVR in sunlight is critical for vitamin D synthesis in the skin. However, it produces a variety of pathologic effects, including sunburn, pigmentary change, immunologic alterations, and neoplasia and photodamage.


The first evidence of the impact of UVR on the immune system in a rodent model was reported in 1977 by Fisher et al., who noticed that antigenic tumor cells, which are rejected by the immune system of non-irradiated mice, are not rejected when the animal has undergone a period of UVR prior to transplantation of the tumor cells.
Animal data

Immunity to herpes simplex virus type 2. Suppression of virus-induced immune responses in ultraviolet B-irradiated mice.
Yasumoto S¹, Hayashi Y, Aurelian L

A rat cytomegalovirus infection model as a tool for immunotoxicity testing.
Garssen J, Van der Vliet H, De Klerk A, Goetsch W, Dormans JA, Bruggeman CA, Osterhaus AD, Van Loveren H

A review of studies on the effects of ultraviolet irradiation on the resistance to infections: evidence from rodent infection models and verification by experimental and observational human studies.
Termorshuizen F¹, Garssen J, Norval M, Koulu L, Laihia J, Leino L, Jansen CT, De Grujil F, Gibbs NK, De Simone C, Van Loveren H
Ultraviolet Light (UVR) Effects Immunity

- Sub-erythemal doses of UVR (x5) increased polymorphonuclear chemotaxis in healthy volunteers. Csato M et al., British Journal of Dermatology 1984;111: 567-570.

- 410 athletes who received sub-erythemal doses of UVR (twice a year for three years) had more salivary IgA, IgG and IgM; 50% less respiratory viral infections, 300% fewer absence days and 30% shorter illness than did 446 non-irradiated control athletes. Gigineishvili GR, et al. Voprosy Kurortologii, Fizioterapii, i Lechebnoi Fizicheskoi Kultury 1990 May-Jun;(3):30-3.

HIV

Solar ultraviolet radiation exposure does not appear to exacerbate HIV infection in homosexual men. The Multicenter AIDS Cohort Study.


Maas J¹, Termorshuizen F, Geskus RB, Goettsch W, Coutinho RA, Miedema F, Van Loveren H


Termorshuizen F¹, Geskus RB, Roos MT, Coutinho RA, Van Loveren H
HERPES SIMPLEX

Prevention of ultraviolet-light-induced herpes labialis by sunscreen.
Rooney JF¹, Bryson Y, Mannix ML, Dillon M, Wohlenberg CR, Banks S,
Wallington CJ, Notkins AL, Straus SE

Sunlight is an important causative factor of recurrent herpes simplex.
Ichihashi M¹, Nagai H, Matsunaga K

The Effect of Ultraviolet Radiation on Human Viral Infections
Norval, Mary
Photochemistry and Photobiology; Nov/Dec 2006: 82, 6; ProQuest Nursing & Allied Health Source pg. 1495

The epidemiology of infectious mononucleosis in Northern Scotland: a decreasing incidence and winter peak
Elizabeth Ysset, Denis Milne, Ian Collacott, David McLemon, Carl Counsell and Mark Vickers
IMMUNE SUPPRESSION BY UV RAYS

- direct
  - pyrimidin dimers formation – mostly thymin

- indirect
  - ROS formation (following excitation of „chromophores“ – molecules containing conjugated double bonds and/or aromatic circles)
  - retinoid depletion in skin

- folate degradation – systemic effects

- UCA urocanic acid

Natural sunscreen
Cis-UCA immunosupression

An Action Spectrum for the Production of cis-Urocanic Acid in Human Skin In Vivo

Pauline McLoone,*† Eniko Simics,†‡ Alan Barton,† Mary Norval,* and Neil K. Gibbs§

The effect of clinical UVA/B exposures on urinary urocanic acid isomer individuals with caucasian type (II/III) skin types
Chandan M Sastry¹, Susan E Whitmore², Patrick N Breysse¹, Warwick T Strickland¹ Dermatology Online Journal 11 (3): 1 2005
Common Links among the Pathways Leading to UV-Induced Immunosuppression
Gary M. Halliday
UV-induced mechanisms of immunomodulation

Modulation of the immune system by UV radiation: more than just the effects of vitamin D?
Prue H. Hart, Shelley Gorman & John J. Finlay-Jones

UV radiation causes dysregulation of antigen-presenting cells such as Langerhans cells and dermal dendritic cells, which in turn can activate regulatory T cells to suppress the immune system. UV radiation can also induce keratiocytes produce immunospressive cytokines that inhibit the production of a number of “repair cytokines” that fix UV induced DNA damage.

Cellular traffic to the draining lymph nodes via lymphatic vessels increases and includes Langerhans cells, dermal DCs and mast cells. In the draining lymph nodes, cell–cell interactions stimulate the production of regulatory cells and soluble mediators that are responsible for UV-induced systemic immunoregulation.

UVR disrupts the corneal layer, which enables the penetration of bacteria and contact allergens (Jiang et al., 2006).

UVR stimulates keratiocytes to release antimicrobial peptides (AMPs), which attack the invading microbes (Gläser et al., 2009). UVR alters the capacity of Langerhans cells (LC) to present antigens including contact allergens. This finally does not result in sensitization but in the induction of regulatory T cells (Treg cells), which suppress the contact hypersensitivity response against these antigens (Schwarz, 2008).
The Primary Source Of Vitamin D Is UVB Radiation From Sunlight

The conversion of 7-dehydrocholesterol to previtamin D3 by 282–310 nm UV light and the temperature-dependent equilibrium between previtamin D3 and vitamin D3.

SEASONAL VARIATION OF 25(OH)D LEVELS

Serum vitamin D concentrations after a whole-body exposure to 1 MED (of simulated sunlight in a tanning bed and after a single oral dose of either 10,000 or 25,000 IU vitamin D-2.


VITD AND INFLAMMATION

- Vit D injections averaging 547iu/day x 2-5 years – 23% decrease in CRP. Timms et al. QJM. 2002;95:787.
- Vit D supp in pts w/ prolonged clinical illness saw decreases in IL-6 and CRP. Van den Berghe et al. J Clin Endocrinol Metab. 2003;88(10):4623
- 1,25(OH)2D3 has opposing effects: it can mimic immunosuppressive effects caused by UV irradiation in some models, or reverse UV-induced DNA damage and immunosuppression in other models.
- 1,25(OH)2D3 exerts effects on Langerhans cells that are characteristic of those associated with UV radiation (UVR)-induced suppression of contact hypersensitivity.
- 1,25(OH)2D3 as either a mediator of UVR-induced immune suppression or as a photoprotective molecule against UVR-induced DNA damage and immune suppression.

1,25(OH)2D3 mediates photoprotection in both mouse and human skin. It reduces DNA damage and skin-cell apoptosis after UVR irradiation of human skin cells in vitro,4,5 and in mouse skin in vivo.5–7

Treatment with 1,25(OH)2D3 or a cis-locked vitamin D analogue of cultured human fibroblasts, keratinocytes and melanocytes protects these cells from UVR-induced apoptosis.4

In both mouse skin in vivo and human skin cells cultured in vitro, 1,25(OH)2D3 is photoprotective, in that it decreases cell death and DNA damage, and also reverses immunosuppression caused by UVR in a murine CHS model.


Vitamin D promotes macrophage production of specific surface antigens, the lysosomal enzyme acid phosphatase, and the secretion of H₂O₂ (which is antimicrobial), but vitamin D deficiency decreases these functions. Abu-Amer Y, Bar-Shavit Z. Cellular Immunology 1993; 151: 356-368. Cohen MS, et al. Journal of Immunology 1986; 136: 1049-1053.

Acne
Acute lower respiratory infection
Alzheimer’s disease
Amyotrophic lateral sclerosis
Anaphylaxis
Anemia
Ankylosing spondylitis
Anxiety
Asthma
Athersclerosis
Autism
Bones – osteoporosis
Bones – Paget’s disease
Bones – rickets
Brain injury, traumatic
Bronchitis
Cardiovascular disease
Celiac disease
Cerebrovascular disease
Chronic kidney disease
Chronic liver disease
Cognitive impairment
Common cold
Epilepsy
Premature birth and low birth weight
Psoriatic arthritis
Renal failure
Renal osteodystrophy
Rheumatoid arthritis
Respiratory syncytial virus
Schizophrenia
Sepsis/Septicemia
Sickle cell disease
Systemic sclerosis
Tonsillitis
Tuberculosis
Thrombosis
Uterine leiomyomas (fibroids)
Vascular dementia
Vitiligo vulgaris

Research associates vitamin D with:

- Acne
- Acute lower respiratory infection
- Alzheimer’s disease
- Amyotrophic lateral sclerosis
- Anaphylaxis
- Anemia
- Ankylosing spondylitis
- Anxiety
- Asthma
- Athersclerosis
- Autism
- Bacterial vaginosis
- Biliary cirrhosis, primary (PBC)
- Birth defects
- Bones – fractures
- Bones – osteopenia
- Fertility, regular menses
- Fibromyalgia
- Hashimoto’s thyroiditis (HT)
- Headache
- Hearing loss
- Hepatitis
- HIV/AIDS
- Hypercalcemia
- Hyperparathyroidism
- Hypertension
- Inflammatory bowel disease
- Influenza, type A
- Insulin resistance
- Ischemic cardiac arrhythmias
- Kidney stones
- Bones – osteoporosis
- Bones – Paget’s disease
- Bones – rickets
- Brain injury, traumatic
- Bronchitis
- Cardiovascular disease
- Celiac disease
- Cerebrovascular disease
- Chronic kidney disease
- Chronic liver disease
- Lupus
- Macular degeneration
- Meningitis
- Metabolic disease
- Mononucleosis
- Multiple sclerosis
- Muscle strength
- Osteoarthritis
- Pancreatitis
- Parkinson’s disease
- Pelvic floor status
- Periodontal disease
- Peripheral artery disease
- Pneumonia
- Polycystic ovary syndrome
- Post herpetic neuralgia
- Preeclampsia
- Chronic, non-specific muscle pain
- Cognitive impairment
- Common cold
- Epstein-Barr virus
- Congestive heart failure
- Chronic obstructive pulmonary disease
- Coronary heart disease
- Craniotabes
- Cystic fibrosis
- Dental caries
- Depression
- Diabetes, type 1
- Diabetes, type 2
- Epilepsy
- Premature birth and low birth weight
- Psoriatic arthritis
- Renal failure
- Renal osteodystrophy
- Rheumatoid arthritis
- Respiratory syncytial virus
- Schizophrenia
- Sepsis/Septicemia
- Sickle cell disease
- Systemic sclerosis
- Tonsillitis
- Tuberculosis
- Thrombosis
- Uterine leiomyomas (fibroids)
- Vascular dementia
- Vitiligo vulgaris
VITAMIN D FROM SUNLIGHT AFFECTS TB

- The 1903 Nobel prize was awarded for the discovery that vitamin D from sunlight could cure cutaneous TB.

- The Nobel Prize in Physiology or Medicine 1903
- Niels Ryberg Finsen
- "in recognition of his contribution to the treatment of diseases, especially lupus vulgaris, with concentrated light radiation, whereby he has opened a new avenue for medical science"
- He has himself given the following short description of his work. «My disease has played a very great role for my whole development... The disease was responsible for my starting investigations on light
Vitamin D(3) downregulates proinflammatory cytokine response to Mycobacterium tuberculosis through pattern-recognition receptors while inducing protective cathelicidin production.

Cytokine. 2011 Aug;55(2):294-300

Khoo AL, Chai LY, Koenen HL, Oosting M, Steinmeyer A, Zuegel U, Joosten I, Netea MG, van der Ven AD

Cutting edge: Vitamin D regulates lipid metabolism in Mycobacterium tuberculosis infection.


Innate immunity to mycobacteria: vitamin D and autophagy.


Vitamin D, vitamin D receptor, and macroautophagy in inflammation and infection.


Vitamin D and tuberculosis.


The seasonality of tuberculosis, sunlight, vitamin D, and household crowding.

Grey A, Bolland M. J Infect Dis. 2014 Sep 1;210(5):774-83

Immunomodulation by vitamin D: implications for TB.

In the 1930’s, Vitamin A was investigated for its anti-infective properties using Cod liver oil, (which is also abundant in Vitamin D)

Five studies using cod liver oil, (involving over 7,000 subjects), showed that cod liver oil reduced respiratory infections

Cod liver oil given to 185 adults for four months reduced colds by 50%; Holmes AD, et al. Journal of Industrial and Engineering Chemistry 1932; 24; 1058-1060.

In a five year study, cod liver reduced industrial absenteeism caused by colds and respiratory illness; days of missed work was reduced by 30%. (n=3031) Homes AD, et al. Industrial Medicine 1936; 5: 359-361.
EPIDEMIC INFLUENZA

- Edgar Hope-Simpson pointed out that influenza outbreaks were inversely correlated with solar UV.

THE SEASONAL AND LATITUDINAL DISTRIBUTION OF OUTBREAKS OF TYPE A INFLUENZA IN THE WORLD, 1964-1975


- Zykov MP, Sosunov AV. Vaccination activity of live influenza vaccine in different seasons of the year. Journal of Hygiene, Epidemiology, Microbiology, and Immunology 1987; 31: 453–459.

(WHO Data)
RCT with Vitamin D for Type A Influenza

Urashima et al., Am J Clin

70%
VITAMIN D<sub>3</sub> SUPPLEMENTS ELIMINATE THE WINTER EXCESS INCIDENCE OF COLD / FLU

JOHN F. ALOIA AND MELISSA LI-NG, 2007, Epidemiology and Infection

RSV bronchiolitis

**Vitamin D receptor (VDR) polymorphisms and severe RSV bronchiolitis: a systematic review and meta-analysis.**

**McNally JD, Sampson M, Matheson LA, Hutton B, Little J.**

**J Pathol.** 2014 Jan;232(1):57-64.

Defective control of vitamin D receptor-mediated epithelial STAT1 signalling predisposes to severe respiratory syncytial virus bronchiolitis.

**Stoppelenburg AJ<sup>1</sup>, von Hegedus JH, Huis in't Veld R, Bont L, Boes M.**
Vitamin D: a new anti-infective agent?

Elisabetta Borella, Gideon Nesher, Eitan Israeli, and Yehuda Shoenfeld

<table>
<thead>
<tr>
<th>Population studied</th>
<th>Vitamin D dose and duration</th>
<th>Outcome</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>67 patients with TB</td>
<td>0.25 mg/day of vitamin D or placebo during TB treatment</td>
<td>Significantly higher rate of sputum conversion in the vitamin D group (100% vs. 77%, ( P = 0.002 ))</td>
<td>32</td>
</tr>
<tr>
<td>Children 1–5 years old with recurrent episodes of otitis media and 25(OH) vitamin D deficiency</td>
<td>5000 IU/day in addition to conventional therapy</td>
<td>Decreased number of otitis media episodes</td>
<td>40</td>
</tr>
<tr>
<td>140 patients with Ig deficiencies or frequent RTIs</td>
<td>4000 IU/day of vitamin D3 or placebo for 1 year</td>
<td>Significantly fewer infections in the vitamin D group (( P = 0.04 ))</td>
<td>68</td>
</tr>
<tr>
<td>247 children with vitamin D deficiency</td>
<td>Milk fortified with 300 IU of vitamin D3 (( n = 143 )), or regular milk for 3 months</td>
<td>Vitamin D significantly reduced the risk of RTIs in winter among children with vitamin D deficiency</td>
<td>49</td>
</tr>
<tr>
<td>569 subjects</td>
<td>1111–6800 IU/day of vitamin D (( n = 289 )) or placebo (( n = 280 ))</td>
<td>No significant difference in the number of RTIs between the two groups</td>
<td>50</td>
</tr>
<tr>
<td>164 young men (18–28 years old)</td>
<td>400 IU/day of vitamin D3 ( (n = 80) ) or placebo for 6 months</td>
<td>Subjects who received vitamin D had fewer days of absence due to RTI during the first 6 weeks of follow-up</td>
<td>71</td>
</tr>
<tr>
<td>334 school children</td>
<td>1200 IU vitamin D3/day ( (n = 167) ) or placebo for 4 months</td>
<td>Influenza A occurred in 11% of children in the vitamin D group compared with 19% in the placebo group (( P = 0.04 ))</td>
<td>72</td>
</tr>
<tr>
<td>162 adults</td>
<td>Vitamin D3 2000 IU/day or placebo for 12 weeks</td>
<td>No difference in incidence of RTIs or duration and severity of symptoms between the two groups</td>
<td>73</td>
</tr>
<tr>
<td>3046 children aged 1–11 months</td>
<td>100,000 IU of vitamin D3 once every 3 months for 18 months ( (n = 1524) ) or placebo</td>
<td>No significant difference in the incidence of pneumonia between the two groups</td>
<td>74</td>
</tr>
<tr>
<td>453 children aged 1–36 months with pneumonia</td>
<td>A single dose of 100,000 IU of vitamin D3 ( (n = 224) ) or placebo, along with antibiotics</td>
<td>No difference in mean number of days to recovery; risk of recurrent pneumonia within 90 days was lower in the vitamin D group (45% vs. 58%, ( P = 0.01 ))</td>
<td>75</td>
</tr>
<tr>
<td>322 healthy adults</td>
<td>200,000 IU vitamin D3 then 100,000 IU monthly ( (n = 161) ) or placebo, for 18 months</td>
<td>No reduction in incidence or severity of RTIs</td>
<td>76</td>
</tr>
</tbody>
</table>

Ig, immunoglobulin; RTI, respiratory tract infection; TB, tuberculosis.
Overall, 12 original studies were included in the review and meta-analysis comprising 32,142 mainly elderly study participants with measured 25(OH)D of whom 6921 died during follow-up. An inverse association between 25(OH)D levels and all-cause mortality was found in all but two studies that was statistically significant in several of the individual studies. In meta-analysis, 25(OH)D levels were significantly inversely associated with all-cause mortality with a pooled HR of 0.92 (95% confidence interval: 0.89-0.95) for a 20 nmol/l increase in 25(OH)D levels.


- HIV- immunological status, outcome, morbidity and mortality as well as the antiretroviral treatment
- Hepatitis B and C infection
- Colonic bacterial load and colitis, enteric infections, clostridium infections
- Bacterial vaginosis
- UTIs
- Sepsis
- Dengue fever
VITAMIN D AND INNATE AND ADAPTIVE IMMUNITY.
“to minimize the health risks associated with UVB radiation exposure while maximizing the potential benefits of optimum vitamin D status, {dietary} supplementation and small amounts of sun exposure are the preferred methods of obtaining vitamin D.”

Consensus statement, 2006
Estimating the global disease burden due to ultraviolet radiation exposure

Robyn M Lucas,1* Anthony J McMichael,1 Bruce K Armstrong2 and Wayne T Smith3

1.6 million Disability Adjusted Life Yrs due to UVR over exposure
3.3 billion Disability Adjusted Life Yrs due to UVR under exposure x 2000

Conclusions Sun protection messages are important to prevent diseases of UVR exposure. However, without high dietary (or supplemental) intake of vitamin D, some sun exposure is essential to avoid diseases of vitamin D insufficiency.

Lucas RM
Int J Epidemiology 2008
Effects of ultraviolet radiation reaching the biosphere

• Assess new understanding of relationship between ultraviolet wavelength and key “target processes”, e.g. vitamin D synthesis, suppression of the immune system.

Relationship between UV wavelength and immune suppression

Damian et al 2011
Both UVA and UVB interact to enhance UV induced immunosuppression, and this can occur even at doses that do not cause erythema.

UV radiation is not always the same; it changes based on:

- Time of day
- Time of year
- Location
- Altitude
- Weather
- Reflection
- Ozone Layer

Armas L. et al. 2007
XXIII/13.3 a) Effects of ultraviolet radiation reaching the biosphere and how those effects relate to physical, biological and environmental processes.

Changes in solar UV predicted for this century.

MINIMAL ERYTHEMAL DOSE (MED) DEPENDS ON

- Skin type and thickness
- Amount of melanin and ability to produce melanin after exposure
- Intensity of the radiation
- Six sun-reactive skin types
  - People with dark skin require significantly more sun exposure

Holick, 2004
Human pigmentation—the main skin types: African-American, Asian, Caucasian, and Hispanic (left to right).

Change in serum concentrations of vitamin D-3 in 2 lightly pigmented white (skin type II) (A) and 3 heavily pigmented African American subjects (skin type V) (B) after total-body exposure.
TANNING

- **Protective response to sun exposure**
  - **UV radiation**
    - Stimulates melanin (dark pigment) that absorbs UV protecting cells
  - **melanin** (pigment responsible for darkening) within skin causes tan
    - Functions as a biologic filter of UVR
      - By scattering radiation
      - By absorbing UVR
      - By dissipating absorbed energy as heat

- **Immediate tanning**: Induced by UV-A, no new melanin

- **Delayed tanning**: Induced by UV-B, begins at 2-3 days, peaks at 7-10 days, new melanin formed
  - * Increase production and upward migration of melanin granules
  - * Oxidation of premelanin in the skin
  - * Protective response of the body
Figure 5. Mechanisms involved in the (hyper)pigmentation induced by UV-R.

- UV
- ROS
- NO
- α-MSH
- ACTH
- PGE₂
- cGMP
- PKG
- DAG
- cAMP
- PKC
- PKA
- MELANOCYTES
- NUCLEUS
- CPD
- (6-4) photoproduct


Vitamin D and sun-screen

- SPF 8 reduces Vitamin D production by 95%
- SPF 15 reduces Vitamin D production by 99%

Matsuoka JCEM 1987


The current state of play of rodent models to study the role of vitamin D in UV-induced immunomodulation

Shelley Gorman* and Prue H. Hart

INFANTS

- Infants and toddlers are at higher risk of uv damage, as structurally, children’s skin is thinner- a thinner stratum corneum- than that of adults and has lower melanin concentrations. Thus, UV penetrates more deeply into skin that is less able to absorb UV radiation.


- Development of solar UVR-related **pigmentation** begins as early as the first summer of life. **Mack** MC, Tierney NK, Ruvolo E Jr, Stamatas GN, Martin KM, Kollias N.J Invest Dermatol. 2010 Sep;130(9):2335-
**Vitamin D Receptor Gene – Chr 12q13**

- Vitamin D receptors (VDRs) are activated by 1,25(OH)$_2$D and affect expression of over 200 genes, upregulating about two-thirds, downregulating one-third.

- VDRs come in different alleles, with different effects.

9 exons, alternatively spliced promoter region

**Binding domains:**
- DNA binding domain – binds VDRE
- Ligand binding domain – 1,25(OH)$_2$ Vit D

Human VDR >470 reported SNPs
Many have low allele frequency
E VOLUTION OF LOW AFFINITY FORMS OF DBP ENHANCES MONOCYTE RESPONSES TO VITAMIN D.
Confirmation of an Association Between Single Nucleotide Polymorphisms in the VDR Gene With Respiratory Syncytial Virus Related Disease in South African Children

T.L. Kresfelder, R. Janssen, L. Bont, and M. Venter

Vitamin D receptor gene polymorphism in children with urinary tract infection

Sule Aslan · Ipek Akil · Gulcin Aslan · Huseyin Onay · Beyhan Cengiz Ozyurt · Ferda Ozkinay

Tumour necrosis factor-alpha, interleukin-10, interferon-gamma and vitamin D receptor gene polymorphisms in patients with chronic hepatitis delta

**Erythemal UVR does not increase 1,25(OH)2D3 in the skin and serum of vitamin D3-deficient mice.**

**UVR suppresses immune responses in female and male.**

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**Acute Erythemal Ultraviolet Radiation Causes Systemic Immunosuppression in the Absence of Increased 25-Hydroxyvitamin D3 Levels in Male Mice**

Shelley Gorman¹*, Naomi M. Scott³, Daryl H. W. Tan¹, Clare E. Weeden¹, Robert C. Tuckey², Jacqueline L. Bisley¹, Michele A. Grimaldeston³, Prue H. Hart¹

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**UV radiation suppresses experimental autoimmune encephalomyelitis independent of vitamin D production**

Bryan R. Becklund, Kyle S. Severson, Souriya V. Vang, and Hector F. DeLuca³
Randomized controlled trial of oral omega-3 PUFA in solar-simulated radiation-induced suppression of human cutaneous immune responses


Photodermatology, Photoimmunology & Photomedicine

REVIEW ARTICLE

Nutritional abrogation of photoimmunosuppression: in vivo investigations

Suzanne M. Pilkington¹, Neil K. Gibbs¹, Peter S. Friedmann² & Lesley E. Rhodes¹

Photodermatol Photoimmunol Photomed 2014; 30: 112–127
WHAT ABOUT VACCINES?
WHAT ABOUT VACCINES?

**Polio**


**Tetanus**

**BCG**
INFLUENZA


• Vaccination activity of live influenza vaccine in different seasons of the year. Zykov MP¹, Sosunov AV


• Vitamin D and influenza vaccination. Principi N, Esposito S. Hum Vaccin Immunother. 2013 May;9(5):97


• Immuneogenicity of inactivated seasonal influenza vaccine in adult and pediatric liver transplant recipients over two seasons. Suzuki M¹, Torii Y, Kawada J, Kimura H, Kamei H, Onishi Y, Kaneko K, Ando H, Kiuchi T, Ito Y

• Vitamin D is not associated with serologic response to influenza vaccine in adults over 50 years old. Sundaram ME, Talbot HK, Zhu Y, Griffin MR, Spencer S, Shay DK, Coleman LA. Vaccine. 2013 Apr 12;31(16):2057-61
**HEPATITIS B**


Measles


Rubella


WHAT ABOUT VACCINES?


ACTIVE IMMUNIZATION

The administration of all/part of an agent (live-attenuated/killed/engineered) or a modified product of the agent (e.g., toxoid) to evoke the production of a long-lasting immunologic response ("antibodies").


- Immunization is a great success of preventive medicine. In the United States, most vaccine-preventable diseases of childhood are at or near record lows while the number of diseases preventable by vaccination has increased. These successes result from a comprehensive system that includes basic research; developing and testing vaccine candidates; a manufacturing base; a regulatory authority; development of immunization policies; implementation of immunization recommendations; and a compensation system for the few people unavoidably injured by vaccines.
POLICIE- time to change?

Vaccination Is Not Immunization

Tim O’Shea

THANK YOU FOR YOUR ATTENTION