THE D-LIGHTFUL VITAMIN FOR HEALTH
Michael F. Holick
Boston University Medical Center

Teaching Goals
1. How to Dx Vitamin D Deficiency
   A. Which Vitamin D metabolite should be ordered?

2. How to Tx Vitamin D Deficiency
   A. Vitamin D2 vs Vitamin D3

3. What are the non-calcemic Benefits of Vitamin D?

Institute of Medicine
IOM
Dietary Reference Intakes for Calcium and Vitamin D

Agency for Healthcare Research
AHRQ
Depended on Randomized Controlled Trials
Ignored Association Studies

AI for Vitamin D
1997
Need at Least 1000 - 2000 IU/d

IOM RDA
0-0.5 YEARS 400 IU/D
0.5-1 YEARS 600 IU/D
1-8 YEARS 600 IU/D
9-12 YEARS 600 IU/D
13-70 YEARS 800 IU/D
70+ YEARS 800 IU/D
How much calcium do we need?

Who is at Risk for Vitamin D Deficiency??

RICKETS

VITAMIN D DEFICIENCY

DM, MS, RA, INFECTIONS

HBP, CHD, CANCER

Super Vitamin to the Rescue!

Can sunlight, supplements, and milk be the simple solutions to an increasingly common teen-health concern?
OUR SKIN WAS DESIGNED TO MAKE VITAMIN D

Do you know why I became hypopigmented ???????

Ancient DNA Reveals Neandertals

Normal Female Pelvis

Rachitic Pelvis
HOW DO YOU MAKE VITAMIN D ????

Solar UV Radiation

Can I make Too much Vitamin D ????

YOU CANNOT BECOME VITAMIN D TOXIC FROM SUN EXPOSURE
OCTOBER 1, 1918

NOVEMBER 12, 1918

UVR 1 Hr
2/WK FOR
6 WEEKS

1931 US GOVERNMENT
PROVIDED RECOMMENDATIONS
FOR SUN EXPOSURE

HESS & UNGER
1921
SUN CURED RICKETS

Dermatology
Societies
FOR 40 YEARS.
ARE YOU
SURE
?????
WHAT WILL HAPPEN IF MY CHILDREN GO OUT WITHOUT SUNSCREEN?

VITAMIN D is ESSENTIAL FOR BONE HEALTH

Case #1
• 7 month Old Female
• Muscle Weakness
• Tetanic seizures
• Serum calcium 4.2mg%
MY DOCTOR SAID BREAST MILK PROVIDES ALL THE NUTRITION MY INFANT NEEDS.

BOSTON MEDICAL CENTER

BUT IS RICKETS A PROBLEM 2000 ?????
IS VITAMIN D DEFICIENCY A COMMON PROBLEM FOR PREGNANT WOMEN?

BOSTON MEDICAL CENTER

40 MOTHERS AND THEIR INFANTS AT BIRTH

MEASURED VITAMIN D STATUS

25-HYDROXYVITAMIN D

Vitamin D Deficiency in a Healthy Group of Mothers and Newborn Infants

Joyce M. Lee, MD, MPH, Jessica R. Smith, MD, Barbara L. Phillips, MD, Tai C. Chen, PhD,
Jeffrey Mathieu, MS, Michael F. Holick, MD, PhD

Daily Intake Vitamin D ~600 IU

70% MTV DRANK 2.3 GLASSES MILK/D

IOM 81,600 IU/d

Vitamin D Deficient

25(OH)D < 20NG/ML

Strong, inverse relation between maternal 25(OH)D at <22 weeks and risk of preeclampsia

Adjusted OR (95% CI) associated with a decline in 25(OH)D:

20 ng/ml

2.4 (1.1, 5.4)

RISK PREECLAMPSIA

Bodnar et al 07
Association Between Severe Vitamin D Deficiency and Primary Caesarean Section

Anne Merewood MPH, IBCLC**, Supriya D. Mehta PhD, MHS**, Tai C. Chen PhD***, Michael F. Holick PhD, MD****, Howard Bauchner MD*****

Poster title: Maternal Vitamin D Status and Cesarean Birth: Is There a Connection? Session time: 4276.0: Tuesday, November 06, 2007: 4:30 PM-5:30 PM

Mother's 25(OH)D ng/ml

Probability C-Section

Risk C-section 400 %

0 20 40 60 80

Mother's 25(OH)D ng/ml

I NEED 1000 IU VITAMIN D/DAY TO PROVIDE ENOUGH VITAMIN D FOR ME & MY INFANT

How much vitamin D does my mom need to provide me with adequate vitamin D ?????

4000 IU/D

American Academy Pediatrics
Beginning at Birth
All INFANTS need
400 IU Vitamin D/d

Infants
400-800 IU/d

Pregnant & Lactating Women
2000 IU/d

Breast-fed infants need extra vitamin D

Total vitamin D intake from all sources during the first year should be 200 IU/day in the premature infant (recommendation grade A) and 400 IU/day in the full-term infant, with an increase to 600 IU/day for infants beginning solid foods (recommendation grade B). In addition to vitamin D in formula from solid foods, breast-fed infants need extra vitamin D. Infants need 400 IU/day of vitamin D to reach a sufficient level of 25(OH)D. Breast-fed infants require extra vitamin D to meet this need. Infants given vitamin D supplements should receive 400 IU/day of vitamin D to meet the needs of breast-fed infants. The American Academy of Pediatrics recommends a minimal daily intake of 400 IU/day.
What is a Common Symptom of Vitamin D Deficiency? Night Sweating!!! And VAGINITIS

<table>
<thead>
<tr>
<th>IOM</th>
<th>RDA</th>
<th>UL</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-70YEARS</td>
<td>600IU/D</td>
<td>4000</td>
</tr>
</tbody>
</table>

No Need To Increase Intake Pregnancy or Lactation

Case #2
- 1 Year Old Female
- Muscle Weakness
- Boney Deformities
- Failure to Thrive

RX
- Rickets
- Osteomalacia

VITAMIN D
CALCIUM
SUNLIGHT
We need Calcium & Vitamin D for Strong Bones & Teeth

IOM
You can get your Vitamin D from Diet

Vitamin D is Rare in Foods

Dairy Fortified with Vitamin D

100 IU/Serving

Did you Know Mushrooms Make Vitamin D ?????
Shrooms’ plant sterol - ergosterol - converts to vitamin D when exposed to light.

Growers can expose mushrooms to UV light to increase vitamin D levels.

UV-B Exposed Portabelas have 387 IU vitamin D per raw 84 gram serving.
BUT I EAT FISH

OILY FISH SALMON

HOW MUCH ?????

500-1000 IU/3.5 oz

5-7 Times/Week

100-250 IU/3.5 oz

10-25% VIT D in FARMED VS WILD CAUGHT SALMON
Seasonal Effect on Cutaneous Vitamin D Synthesis in Boston

Can You Make Any Vitamin D
Nov-Feb 0%

Webb et al

Seasonal Effect on Cutaneous Vitamin D Synthesis in EDMONTON

Cannot Make Vitamin D In Winter Above 32 N

Webb et al
Great for Romance  
Not for Vitamin D  
10am-3pm

**NO KIDDING?**

**THE PRICE OF A TAN**

Skin Cancer in the U.S.

1. Primary cause - sun in 90% of cases
2. New cases — 1,370 each day
3. 63 life-threatening cases each day
4. 1 in 7 will contact in a lifetime
5. Risk of life-threatening skin cancer in lifetime — 1 in 150 persons

Source: The Skin Cancer Foundation

**Without Sunscreen**

**With Sunscreen**

**SPF30**

99%

90-95% of our Vitamin D comes from Exposure to Sunlight

UVB

UVB

Vitamin D3

Vitamin D3

~1%

~1%

:1:.6& $gbvvs!

Wjb n j E tIp ft!

gspn Fygptvsvf!

up Tvomhiiu
Exposure to 1 Minimum Erythemal Dose
~20,000 IU Vitamin D₃

Does Sunlight Really Provide us with Vitamin D

Brot et al, Brit J Nutr (2001), 86, Suppl. 1, S97-S103
Did You Know

Obesity Causes Vitamin D Deficiency?

![Graph showing serum vitamin D levels after exposure]

- Normal Weight
- Obese BMI >30

**Serum Vitamin D Levels After Exposure Of Non-obese And Obese Adults To The Same Amount Of Ultraviolet Radiation**

- 55% difference

**Recommendation in Boston**

- 5 to 15 Minutes Sunlight 2-3X/wk
- ARMS
- LEGS

**Rx Obese pts need**

- 2-3 X vitamin D
- 50,000 IU vitamin D/wk

**Effect of UVB on Serum Vitamin D Levels in Caucasian and Black Subjects**

- CAUCASIAN: 60 ng/ml
- BLACK: 0 ng/ml
- 5-10X difference

**5-15 MINUTES THEN SUNPROTECTION**

- Both D2&D3

- Vitamin D

- 54 mJ/cm²
- 320 mJ/cm²
30-50% African Americans Vitamin D Deficient

How Do You Know What Your Vitamin D Status Is ???????

What Is The Most Sensitive Indicator Vitamin D Deficiency ?????????????

25(OH)D Assay Used To Determine Vitamin D Status Not 1,25(OH)₂D

Excess
Norm
Deficient

25(OH)D

H

55 ng/ml

10 ng/ml

Tfsvn 36)Pi*E j!
ui/fkbspn fufs gqs!
wjbn je E tibut
Vitamin D Intoxication

25(OH)D > 150 ng/ml

Normal

10 ng/ml

Deficient

25(OH)D & SERUM iPTH*

30-40 ng/ml

25(OH)D & SERUM iPTH*

30-40 ng/ml

VITAMIN D STATUS & THE Ca ECONOMY

- 31 women
- age: 63.2 ± 9.3

studied 2x – 1 yr apart in Spring
given 10 μg 25(OH)D/day (D+)
or no treatment (D–)

Chapuy et al

25(OH)D ng/ml

Heaney et al 2004

25(OH)D

>100 ng/ml

Excess

Normative

20-100 ng/ml

Preferred

30-60 ng/ml

<20 ng/ml

Deficient

Did you know

25(OH)D Assay Most ordered Assay In US
What does 25(OH)D2 & 25(OH)D3 mean? Should I just use the total?

Use Total 25(OH)D

Is Vitamin D Deficiency a Health Problem for adults 50+ yrs?

Percent ADULTS >50 YRS who were vitamin D Deficient <20 ng/ml in August

Sunlight Deprivation > 65 years

25(OH)D < 10 ng/ml

In 54% community dwellers
38% nursing home

Vitamin D Deficiency Is an unrecognized epidemic in adults 50+ yrs

WHAT ABOUT YOUNG ADULTS?
AFRICAN AMERICAN WOMEN IN US AGES 15-49Y <15NG/M VITAMIN D DEFICIENT

42%

BMC MEDICAL STUDENTS AND RESIDENTS 18-29 y VITAMIN D INSUFFICIENT

% VITAMIN D INSUFFICIENT <20ng/ml BMC RESIDENTS & STUDENTS

32% END WINTER

4% END SUMMER


MAINE GIRLS AGES 9-11

48% D-DEFICIENT <20 ng/ml END OF WINTER

SULLIVAN, ROSEN, HOLICK 2002

17% D-DEFICIENT <20 ng/ml END OF SUMMER

SULLIVAN, ROSEN, HOLICK 2002

evaluated using reports of time spent outdoors. The mean decrease in serum 25-OHD from September to March was 28%. Vitamin D insufficiency (at least one serum 25-OHD level <50 nmol/L) was observed in 11 of 23 (48%) subjects. Four of 23 subjects (17%) exhibited vitamin D insufficiency in both September and March. Mean parathyroid hormone levels increased 4 pg/mL (15%) from September to March. Vitamin D intakes need to be increased in winter at northern latitudes.

52% D-deficient
<20 ng/ml

Vitamin D Deficiency
• Osteomalacia
• 2º HPTH
• ↑ Osteoporosis

Subclinical Vitamin D Deficiency
PRECIPITATES & EXACERBATES OSTEOPOROSIS

OSTEOPOROSIS IS OFTEN A SILENT DISEASE
Symptoms

- Generalized bone pain
- Isolated bone pain
- Muscle aches

40-60% OSTEOMALACIA

25(OH)D < 5 ng/ml

25(OH)D = 35 ng/ml

Mayo Clinic Proceedings

Prevalence of Severe Hypovitaminosis D in Patients With Persistent, Nonspecific Musculoskeletal Pain

GREGORY A. PLOTNIKOFF, MD, MTS, AND JOANNA M. QUIGLEY, BA
Serum 25-Hydroxyvitamin D Levels (ng/ml) in Non-immigrant and Immigrant Subjects

<table>
<thead>
<tr>
<th>Race</th>
<th>Age (yrs)</th>
<th>Sex</th>
<th>Symptoms</th>
<th>Diagnoses</th>
<th>Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-immigrant</td>
<td>150</td>
<td>10-65</td>
<td>Bone &amp; Muscle Pains</td>
<td>Dysthymia, non-DJD low back pain</td>
<td>OTC NSAID, Rx NSAID</td>
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</tbody>
</table>

93% Vitamin D Deficient

Bone Mineralization Defects and Vitamin D Deficiency: Histomorphometric Analysis of Iliac Crest Bone Biopsies and Circulating 25-Hydroxyvitamin D in 675 Patients


Department of Radiology and Biostatistics, University Medical Center Hamburg-Eppendorf, Hamburg, Germany
Department of Trauma, Hand, and Reconstructive Surgery, University Medical Center Hamburg-Eppendorf, Hamburg, Germany
Department of Internal Medicine, University Medical Center Hamburg-Eppendorf, Hamburg, Germany
Department of Pathology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany
Department of Radiology and Biostatistics, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Defects were present in 25.5% of the patients. These were found independent of bone volume per trabecular volume (BTV) throughout all ages and affected both sexes equally. While we could not establish a minimum 25(OH)D level that was inversely associated with mineralization defects we did find pathologic accumulation of remodeling bone in patients with circulating 25(OH)D below 25 nmol/L (10 ng/ml) that pathologists misinterpret as pathological bone formation. Defects of bone mineralization were found in patients with a serum 25(OH)D level below 25 nmol/L (10 ng/ml) and strongly argue that in regulation such a deficient level may be used as a marker of bone mineralization. Bone mineralization defects or 25(OH)D levels below 25 nmol/L (10 ng/ml) may impact mental health. © 2019 American Society for Bone and Mineral Research.
Priemel et al.

100% > 30 ng/ml

There is TOO Much scatter FOR the PTH Plateau!!!

Serum 25(OH)D (ng/mL)

20 25 30 35 40 45 50 55

OV/BV (%)

0

1

2

3

4

5

6

IOM

25(OH)D > 20 ng/ml

97.5 % no evidence

OSTEOMALACIA

Bone Mineralization Defects and Vitamin D Deficiency: Histomorphometric Analysis of Iliac Crest Bone Biopsies and Circulating 25-Hydroxyvitamin D in 675 Patients

Matthias Priemel,1,2 Christoph von Domarus,1 Till Orla-Klepp1,2 Steffen Kessler,1 Julia Schlue,1 Simon Meier,1 Nils Proksch,1 Frederic Pattee,1 Clemens Netter,1 Thomas Steinhart,6 Klaus Fuchs,6 and Michael Ameling2

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unmineralized matrix

normal

osteomalacia

IOM

25(OH)D > 30 ng/ml= no Osteomalacia!

IOM

25(OH)D > 20 ng/ml

97.5 % no evidence

OSTEOMALACIA

Bone Mineralization Defects and Vitamin D Deficiency: Histomorphometric Analysis of Iliac Crest Bone Biopsies and Circulating 25-Hydroxyvitamin D in 675 Patients

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unmineralized matrix

normal

osteomalacia

IOM

25(OH)D > 30 ng/ml= no Osteomalacia!
78 Y/O M  
MUSCLE WEAKNESS  
ATROPHY, DENERVATION

Muscle weakness. Results of the neurological examination were remarkable, showing diffuse limb weakness and atrophy, rare fasciculations, normal sensory examination, no bulbar weakness, and no upper motor neuron signs. Electromyography revealed mild chronic changes, denervation and re-innervation, without fibrillations or positive waves.

+EMG  
+NCS

ALS

Symptoms resolved  
Rx VITAMIN D

Progressive painless muscle weakness with muscle atrophy, which manifests like lower motor neuron disease and improves after vitamin D supplementation.

Time to Stand vs 25(OH)D Levels

Higher 25-hydroxyvitamin D concentrations are associated with better lower-extremity function in both active and inactive persons aged ≥60 y1,2,3

Heike A Bischoff-Ferrari, Thomas Dietrich, E John Orav, Frank B Hu, Yuqing Zhang, Elisabeth W Karlson and Hess Dawson-Hughes

DID YOU KNOW  
VDR IS IN SKELETAL MUSCLE !!!
VITAMIN D IS GOOD FOR MUSCLE STRENGTH

A Higher Dose of Vitamin D Reduces the Risk of Falls in Nursing Home Residents: A Randomized, Multiple-Dose Study

Lynn E. Rock, MPH,1* Eric Clark, PhD,2 Janice Weinberg, MS,1 Heike A. Bischoff-Ferrari, MD, MPH,3 Michael F. Holick, MD, PhD,4 and Douglas P. Kiel, MD, MPh1

DISCUSSION

72% Less Falls
800 IU/d 5 months

Vitamin D Status Predicts Physical Performance and Its Decline in Older Persons

JCEM 2007

JCEM 2007

Positive Association between 25-Hydroxy Vitamin D Levels and Bone Mineral Density: A Population-Based Study of Younger and Older Adults

Heike A. Bischoff-Ferrari, MD, MPH, Thomas Dietrich, MD, MPH, E. John Orav, PhD, Bess Dawson-Hughes, MD

Vitamin D3 and calcium to prevent hip fractures in the elderly women

MC Chinapen, ME Ario, P Debong, J Brunn, B Ooraik, S Arnaud, PO Dalmas, and NJ Mannon
Incidence of Non-Vertebral Fractures in Men & Women >65yrs

After Dawson-Hughes, NEJM 1997

Cumulative Incidence (%)

Month

Placebo

~58%

500 mg Ca 700 IU D

25(OH)D > 30 ng/ml

↓Muscle strength, ↓balance, ↓lower extremity function

↑BMD

↓Fall risk

↓FxS

 HOW DO YOU TREAT VITAMIN D DEFICIENCY ????

TREAT VITAMIN D DEFICIENCY

50,000 IU VITAMIN D\textsubscript{2} ONCE/WEEK

6000 IU/d 8 WEEKS

MAINTAIN VITAMIN D SUFFICIENCY

50,000 IU VITAMIN D ONCE/ZWEEKS

3000 IU/d

Cut in half
Add Milk etc

↑Muscle strength, ↑balance, ↑lower extremity function

↓BMD

↓Fall risk

↓FxS
MEAN 25(OH)D LEVELS IN PATIENTS RECEIVING 50,000 IU VITAMIN D2 EVERY 2 WEEKS FOR 6 YRS

Mean 25(OH)D (ng/dL)

- 20 ng/ml (DEFICIENT)
- 40 ng/ml (SUFFICIENT)
- 60 ng/ml (INSUFFICIENT)

Mean 25(OH)D Levels in Patients receiving 50,000 IU Vitamin D2 every 2 weeks for 6 yrs

Mean Serum Total 25(OH)D Levels

- 1000 IU D3
- 1000 IU D2
- PLACEBO

Mean Serum 25(OH)D2 and 25(OH)D3 in Subjects receiving Vitamin D3

Mean Serum 25(OH)D Levels (ng/ml)

- 0.00
- 2.00
- 4.00
- 6.00
- 8.00
- 10.00
- 12.00
- 14.00
- 16.00

Time (weeks)

Change in Serum 25(OH)D Levels (ng/ml)

- 1000 IU D2
- 500 IU D2 + 500 IU D3

1000 IU Vitamin D3/d

or

500 IU Vitamin D3 + 500 IU Vitamin D2/d
CA= 15.2 mg/dl

25(OH)D= 520 ng/ml

1 MILLION IU VITAMIN D/DAY

10,000 IU/d Is Safe

WILL YOU BECOME VITAMIN D INTOXICATED ?

IT IS DIFFICULT TO BECOME VITAMIN D INTOXICATED
WHO IS AT RISK FOR VITAMIN D DEFICIENCY ????????

EVERYONE

WHY SHOULD I CARE ??????

VITAMIN D

Liver
25-OHase

25(OH)D₃

Kidney
1α-OHase

1,25(OH)₃D₃

EVERY TISSUE AND CELL HAS A VDR

Suda et al 1979

RX -1,25(OH)₂D₃
1915 8X more likely to Die Worked Indoors

Colon Cancer Mortality Rates 1970-1994


Highest 10% for Colon Cancer Mortality — DIE WITH COLON CANCER

Source: Compiled from data of National Cancer Institute and Colorectal Disease and Prevention Administration data available at http://www.cancer.gov/dictionary (see above).
Inverse Relationship between 25(OH)D Levels & Risk of Colon Cancer

Garland et al. 1989

50% PROJECTED REDUCTION
25(OH)D = 40 ng/ml

50% PROJECTED REDUCTION
25(OH)D = 27 ng/ml

50% PROJECTED REDUCTION
25(OH)D = 38 ng/ml
Garland et al. 1995

50% PROJECTED REDUCTION
WITH 480 IU/D

Garland et al. 2005

50% PROJECTED REDUCTION
COLON CANCER WITH 1000 IU/D

Original Article

Calcium plus Vitamin D Supplementation and the Risk of Colorectal Cancer
I HATE TAKING CALCIUM & VITAMIN D EVERY DAY

60 %

Did not follow Protocol

25(OH)D = 48 ng/ml

50% LOWER RISK

INVASIVE COLORECTAL CANCER

Table 2. Odds Ratios for Invasive Colorectal Cancer According to the Quartile of Serum 25-Hydroxyvitamin D Level at Baseline and Treatment Groups in a Randomized Calcium-Control Study.

<table>
<thead>
<tr>
<th>Based on Serum 25(OH)D level</th>
<th>Main Effect</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;12 ng/ml &amp; &lt;12 nmol/l</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>12–29.99 &amp; 25–59.99</td>
<td>1.06 (1.01–1.12)</td>
<td></td>
</tr>
<tr>
<td>30–49.99 &amp; 60–99.99</td>
<td>1.95 (1.18–3.24)</td>
<td></td>
</tr>
<tr>
<td>100–149.99 &amp; 150–199.99</td>
<td>2.53 (1.49–4.32)</td>
<td></td>
</tr>
</tbody>
</table>

After Garland et al., Preventive Medicine, 1990

Vitamin D and prevention of breast cancer: Pooled analysis

25(OH)D = 48 ng/ml

50% LOWER RISK

Breast Cancer Mortality Inversely Correlates with Mean Solar Radiation

After Garland et al., Preventive Medicine, 1990

Solar radiation (calories per square centimeter)
By looking at the latitudinal variation of breast cancer mortality rates in Europe, and controlling for diet, Grant found that lack of UV-B from sunlight accounts for perhaps 25% of the breast cancer mortality rates in northern Europe.
The Association of Solar Ultraviolet B (UVB) with Reducing Risk of Cancer: Multifactorial Ecologic Analysis of Geographic Variation in Age-adjusted Cancer Mortality Rates

William B. Grant and C. Garland

MORTALITY INCREASE
SUN EXPOSURE
WHITE MALES & FEMALES

y = 0.2238x + 25.905
R² = 0.1888
r = 0.44

Latitude (Degrees N)
Rate (Cases per 100,000)
30 32 34 36 38 40 42
30 40 45 50 55 60 65

San Francisco
San Diego

COLON CANCER IN CALIFORNIA

 latitude versus the number of all individuals diagnosed with colon cancer independent of race in the state of California.

Premature cancer deaths in the U.S. The ecologic results presented here have been used to estimate that between 20,000 (6) and up to 50,000-60,000 cancer deaths annually in the U.S. can be considered premature due to insufficient UVB irradiance and vitamin D (94, 95). This represents about 10% of all U.S. cancer deaths. It was also estimated that between 1,000 and 3,000 I.U. (25-75 μg) of oral vitamin D intake per day in the absence of UVB irradiance would provide optimal protection against cancer.

Vitamin D 'aids lung cancer ops'

Lung cancer patients who have surgery in the winter are 40% more likely to die of the disease than those operated on in the summer, a US study suggests.

A study of 456 patients found high levels of vitamin D - from sun exposure and food supplements - had a positive impact on the success of surgery.

DIE OF PROSTATE CANCER

Linear trend surface map of prostate cancer mortality among white men, 1970 - 1979
Kaplan-Meier plot showing association of UVR exposure and age at diagnosis with prostate cancer

C. J. Luscombe et al., The Lancet Vol 358 Num 9282, 2001

Vitamin D and Reduced Risk of Breast Cancer: A Population-Based Case-Control Study

Julia A. Knight,1 Maia Lesosky,1 Heidi Ramott,1 Janet M. Raboud,1 and Reinhold Vieth

Table 2. ORs and 95% CIs for an association between vitamin D-related exposure variables at ages 50 to 90 (sun exposure and dietary vitamin D) and breast cancer in cases and controls.

Girls 10-19 yrs most sun 69%

Women 20-29 yrs most sun 51%

Women 45-54 yrs most sun 0.0%

Cancer Epi Biomarkers & Prev 07

WHAT IS THE POSSIBLE CONNECTION BETWEEN VITAMIN D & CANCER ?????????

ACTIVATED VITAMIN D INHIBITS CANCER CELL GROWTH
This is a REAL CONUNDRUM !!!!!!!!

Autocrine Regulation of Cell Growth

BREAST COLON PROSTATE ACTIVATE VITAMIN D

1-OHase

25(OH)D

1,25(OH)_{2}D_{3}

CALCITROIC ACID INACTIVE

Control of cell growth

25(OH)D

1,25(OH)_{2}D_{3}

IS IT POSSIBLE PROSTATE CELLS MAKE 1,25(OH)_{2}D_{3} TO REGULATE CELL GROWTH ???????

1,25(OH)_{2}D_{3}

25(OH)D

BUT VITAMIN D INTAKE OR SUNLIGHT DOES NOT INCREASE 1,25(OH)_{2}D_{3}
**25(OH)D>30 ng/ml** Colon Cell

- Mitochondria
- ~ 2000 Genes Affected By 1,25(OH)₂D
- Differentiation
  - CDK2, p21, p27, p53
  - Ki67, E-Cadherin

**This is the Likely Explanation for the Sun--Cancer Connection**

**ACTIVATED MACROPHAGES**

Metabolize 25(OH)D₃ to 1,25(OH)₂D₃

**1849**

Codliver oil - Rx Tuberculosis

Brompton Hospital Records, 38 1849

**Vitamin D Protects Against Tuberculosis**

02.23.08, 12:00 AM ET

- 25(OH)D₃
- 1,25(OH)₂D₃

Adams et al. JEM 1987

- 1,25(OH)₂D₃
- 25(OH)D₃

Toll-Like Receptor Triggering of a Vitamin D-Mediated Human Antimicrobial Response

- Philip T. Liu 1
- Steffen Sienger 2
- Hailing Li 3
- Linda Wenzel 2
- Belinda H. Tan 1
- Stephan Krutzik 4
- Maria Teresa Ochoa 4
- Jürgen Schaubert 5
- Kent Wu 6
- Christoph Meinken 7
- Diane L. Kamen 7
- Manfred Wagner 8
- Robert Bals 9
- Andreas Stemmeyer 10
- Ulrich Zügel 10
- Richard L. Gallis 5
- David Eisenberg 3
- Martin Hewison 5
- Bruce W. Hoilla 10
- John S. Adams 10
- Barry R. Bloom 11
- Robert L. Modlin 1

*Accepted on February 8, 2006*
Why is flu Season always In the WINTER ????

1981 Edgar Hope-Simpson Suggested a "SEASONAL STIMULUS"

Fig. 2. Weekly consultation rates for illnesses diagnosed clinically as influenza or influenza-like, calculated from res...


eason of reported cold-like symptoms according to season. The placebo group reported more cold-like symptoms in the winter. Only one subject had cold-like symptoms while taking high doses of Vitamin D (50 mcg/d).

2000 IU/D
90% ↓ URIs

Aloia et al 2007
Serum 25-Hydroxyvitamin D and the Incidence of Acute Respiratory Tract Infections in Healthy Adults

James R. Sabetta, Paolo DePetris, Ralph J. Caprino, Joanne Smerdon, Lillian A. Barn, Marie L. Leduc

In this prospective cohort study, serial monthly concentrations of 25-hydroxyvitamin D were measured over the fall and winter 2006-2007 in 108 healthy adults. Blinded to the results of the cytokine levels measured, the participants were evaluated for the development of any acute respiratory tract infections by investigators blinded to the 25-hydroxyvitamin D concentrations. The incidence of infection in participants with different concentrations of vitamin D was determined. One hundred ninety-eight (98.5%) of the enrolled participants completed the study. Light skin complexion, lean body mass, and supplementation with vitamin D were found to correlate with higher concentrations of 25-hydroxyvitamin D. Concentrations of 25-hydroxyvitamin D were associated with a significantly lower incidence of acute respiratory tract infections. A risk of developing acute respiratory tract infections was with a marked reduction in the percentage of participants infected with the flu.

25(OH)D=38 ng/ml  2X ↓

Vitamin D deficiency in early life accelerates Type 1 diabetes in non-obese diabetic mice

J. Gribble, C. Gysbers, K. Stoffe, E. van Eem, R. Deshaies, I. Overleigh, R. Baillie, C. Maties

Laboratory of Experimental Medicine and Radiobiology, U.E.R. di Medical, University of Leuven, T. C. University, Leuven, Belgium.

Type 1 Diabetes/100,000 Boys<14 yrs

Garland et al 2008

Annual age-adjusted incidence rates of type 1 diabetes, children <14 years old, per 100,000 population, Finland, 1965-2005

Garland et al. Lancet 2001

10,366 Children in Finland WHO RECEIVED 2000 IU/D

Vitamin D Risk Type 1 Diabetes After 31 Years  88%

Hyppenen et al. Lancet 2001

Randomized trial of vitamin D supplementation to prevent seasonal influenza A in schoolchildren

Influenza A + School Children

Placebo  18.6%

+1200 IU Vitamin D  10.8%

**Beta-ISLET CELL**

\[ 1,25(OH)D_3 \]

\[ \text{VDR +} \]

\[ \text{VDR +} \]

\[ + \]

**Insulin**

**Metabolic Syndrome & Type 2 Diabetes**

---

**Serum 25-Hydroxyvitamin D, Diabetes, and Ethnicity in the Third National Health and Nutrition Examination Survey**

Scragg et al Diabetes Care 27:2813;04

**DIABETES INVERSELY RELATED SERUM 25(OH)D**

**WHITES-NH**

75%

**MEXICAN-AM**

83%

**BLACKS NO EFFECT**

---

**North-South Gradient in Mortality from MS**

**100% MS**

35

---

**Vitamin D Intake (>400IU/D) Inversely Related To MS In Women**

41%

---

**Vitamin D Intake Is Inversely Associated With Rheumatoid Arthritis**

Results From the Iowa Women’s Health Study

Linda A. Metzner,1 Jeffrey Curtis,2 Ted R. Mihalko,1 James R. Cerkov,1 Lindsey A. Crowell,1 and Kenneth G. Saag2

**Vitamin D Intake (>400IU/D) Inversely Related To RA In Women**

44%
OSTEOARTHRITIS

Rostand 1979

Reported Inverse Relationship Between BP & Latitude

Hypertension 1997; 30:150-156

Vitamin D deficiency in humans is associated with heart failure.
Suppression of Renin Transcription by VDR Activation

> 200 Genes in Heart & Vessels

First MI >50% Increase Associated With Vitamin D Deficiency

Independent Association of Low Serum 25-Hydroxyvitamin D and 1,25-Dihydroxyvitamin D Levels With All-Cause and Cardiovascular Mortality

What are the consequences of Vitamin D Deficiency on Our health???

50 Million Teens Deficient/Insufficient

2.4 X HBP
2.5 X Elevated BS
4 X Metabolic Syndrome

adolescents with the lowest levels of vitamin D were:
- 2.38 times more likely to have high blood pressure.
- 2.54 times more likely to have high blood sugar.
- 3.99 times more likely to have metabolic syndrome.

49 NT Blacks 16 yrs
400 vs 2000 IU/d 4 Mos

25(OH)D 11 to 24 ng/ml 400 IU/d
25(OH)D 11 to 34 ng/ml 2000 IU/d

Significant Decrease in Arterial Wall Stiffness

Vitamin D Deficiency and Risk of Cardiovascular Disease


Circulation. 2009;119(18):2277-2284

What are the consequences of Vitamin D Deficiency on Our health???
All Cause Mortality Decreased 7% On 528 IU Vitamin D

25-Hydroxyvitamin D Levels and the Risk of Mortality in the General Population

Several authors have commented that the optimal levels of 25(OH)D should be greater than 30 ng/mL. In our observational study, we found that there was a lower risk of mortality at levels of 30 to 49 ng/mL, but that at levels greater than 50 ng/mL there was again a higher risk of mortality in women. This is similar to findings about antioxidant vitamins and vitamin E, which show that too much may be harmful.

VITAMIN D DEFICIENCY IS A DISEASE OF NEGLECT
**WHAT IS A NORMAL VERSUS HEALTHY 25(OH)D LEVEL??**

**GOAL**

25(OH)D $> 30$ ng/ml

---

**100 IU VITAMIN D3 RAISES 25(OH)D BY ONLY 1NG/ML**

---

**CHILDREN & ADULTS HAVE 25(OH)D $\sim 18-25$ ng/ml**

---

**Adults & Children SHOULD RECEIVE 2000/1000 IU Vitamin D/d**

---

**Sufficient**

1000 IU vitamin D/d

No one was sufficient

---

**Serum 25(OH)D Levels (ng/ml)**

<table>
<thead>
<tr>
<th>Time (weeks)</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
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<th>6</th>
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<td>1000 IU vitamin D/d</td>
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No one was sufficient.
Conquer Vitamin D Deficiency

What is the Best Source of Vitamin D?

![Image of Bond Bread](bond_bread.png)

![Image of Schlitz Beer](schlitz_beer.png)

![Image of Historical Scene](historical_scene.png)

![Image of Cartoon Character](cartoon_character.png)
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. Bajak, Ron Wellman, Frank R. de Groot, and Jan N. Bouterse Huisveld
Department of Dermatology, Leiden University Medical Center, Leiden, The Netherlands; National Cancer Agency, Vrije Universiteit, Amsterdam, The Netherlands

Lifetime sun exposure was predominantly associated with an increased risk of squamous cell carcinoma (p-value for trend < 0.05) 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 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.


I DO NOT ADVOCATE TANNING !!!!!!!!

The UV Advantage

MAY 04

HOLICK HOW DO YOU GET THE MESSAGE OUT ???????

ANCESTORS APPRECIATION OF THE SUN FOR ITS LIFE GIVING BENEFITS
UNENLIGHTENED DERMATOLOGISTS VIEW OF THE SUN'S EFFECT ON HEALTH

Inquisitors NEED Large RCTs
Galileo recanted IMPRISONED FOR THE REST OF HIS LIFE

Agency for Astronomical Research And Quality
AARQ

Need more Randomized Controlled Astronomical Trials
RCATs
Instituted Hand Washing Prevent Maternal & Infant Mortality

Committed himself Insane Asylum
Died Infection

Always wear a sunscreen
Dermatologist advising about sun exposure

Charles M. Schulz
1922 - 2000

Peanuts featuring "Good ol' Charlie Brown"

Cast any characters in the strip? Hope so.
Long time coming, but I think it's worth mentioning.

Charlie Brown and Linus:
Good grief!
Arrived here!
The vitamin D status of Australian dermatologists
2009 British Association of Dermatologists • Clinical and Experimental Dermatology

Australian dermatologist

87% < 20 ng/ml

87% Vitamin D Deficient
end of Summer

Vitamin D and Risk of Cognitive Decline in Elderly Persons

American Academy of Dermatology Association
Reconfirms Need to Boost Vitamin D Intake Through Diet and Nutritional Supplements Rather Than Ultraviolet Radiation
Consensus Conference Acknowledges Some Populations Most Vulnerable to Nutrient Deficiency
YOU CAN GET IT FROM DIET !!!

YOU CANNOT GET IT FROM DIET

If you and your family are not taking at least 1000-2000 IU/d
You are Vitamin D Insufficient

WHAT IS YOUR 25(OH)D LEVEL ????????

+ 2000 IU Vitamin D3
+ MTV=400 IU
+ 3 glasses milk += 300 IU
My Total Vitamin D= 2700 IU/d
My 25(OH)D = 52 ng/ml

Vitamin D Deficiency Is The Most COMMON Medical Condition

vitamindhealth.org
Vitamin D Deficiency

**CAUSES**
- Sunscreen
- Melanin
- Latitude
- Winter
- Malabsorption
  - Crohn's
  - Whipple's
  - Cystic Fibrosis
  - Celiac
  - Liver disease
- Hepatic Failure
- Renal Failure
- Nephrotic syndrome
- Obesity

**MEDICATIONS**
- Antiseizure
- Glucocorticoids
- Rifampin
- HAART
- St John's Wart

**Illnesses**
- Schizophrenia
- Depression
- Muscular weakness
- Muscle aches
- Osteoporosis
- Osteomalacia
- Rickets
- Autoimmune
  - Type 1 Diabetes
  - MS
  - Crohn's
  - RA

**AODM**
- Syndrome X

**CANCER**
- Colon
- Breast
- Prostate
- etc.

**INFECTIONS**
- URI
- TB

**Other**
- Osteoarthritis
- Sarcoidosis

---

**Holick NEJM July 07**

**vitamindhealth.org**

---

**We Need Sensible Sun & Vitamin D Supplementation Recommendations**

---

**There Is No Downside To Increasing Vitamin D Intake!!!**

---

**Do we need to Screen everyone For their 25(OH)D level?**

---

**No !!!!!!!**

---

**But Yes BMI>30**

---

**Malabsorption**
- Meds/AEs.
- Glc
- Sarcoidosis

---

**You Do Not Need To Be A Genius To Know**

---

**Ben quoi ?**

---

**THE VITAMIN D SOLUTION**

**April 1, 2010**

**Most Common Health Problems**

**DrHolick.com**
### IOM RDA

<table>
<thead>
<tr>
<th>Age Group</th>
<th>IOM</th>
<th>RDA</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-0.5 YEARS</td>
<td>400 IU/D</td>
<td></td>
</tr>
<tr>
<td>0.5-1 YEARS</td>
<td>600 IU/D</td>
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</tr>
<tr>
<td>1-8 YEARS</td>
<td>600 IU/D</td>
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</tr>
<tr>
<td>9-12 YEARS</td>
<td>600 IU/D</td>
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</tr>
<tr>
<td>13-70 YEARS</td>
<td>600 IU/D</td>
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</tr>
<tr>
<td>70+ YEARS</td>
<td>800 IU/D</td>
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### Adequate Intake

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Adequate Intake</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1 YEAR</td>
<td>600-1000 IU/D</td>
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<tr>
<td>1-12 YEAR</td>
<td>1000-2000 IU/D</td>
</tr>
<tr>
<td>13+ YEARS</td>
<td>1500-2000 IU/D</td>
</tr>
<tr>
<td>Obesity</td>
<td>2-3 Times more</td>
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### Safe Upper Limit

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Safe Upper Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1 YEAR</td>
<td>2000 IU/D</td>
</tr>
<tr>
<td>1-12 YEAR</td>
<td>5000 IU/D</td>
</tr>
<tr>
<td>13+ YEARS</td>
<td>10,000 IU/D</td>
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</tbody>
</table>

DrHolick.com