

**VITAMIN D DEFICIENCY**

**EPIDEMIC**

**CONSEQUENCES FOR HEALTH**

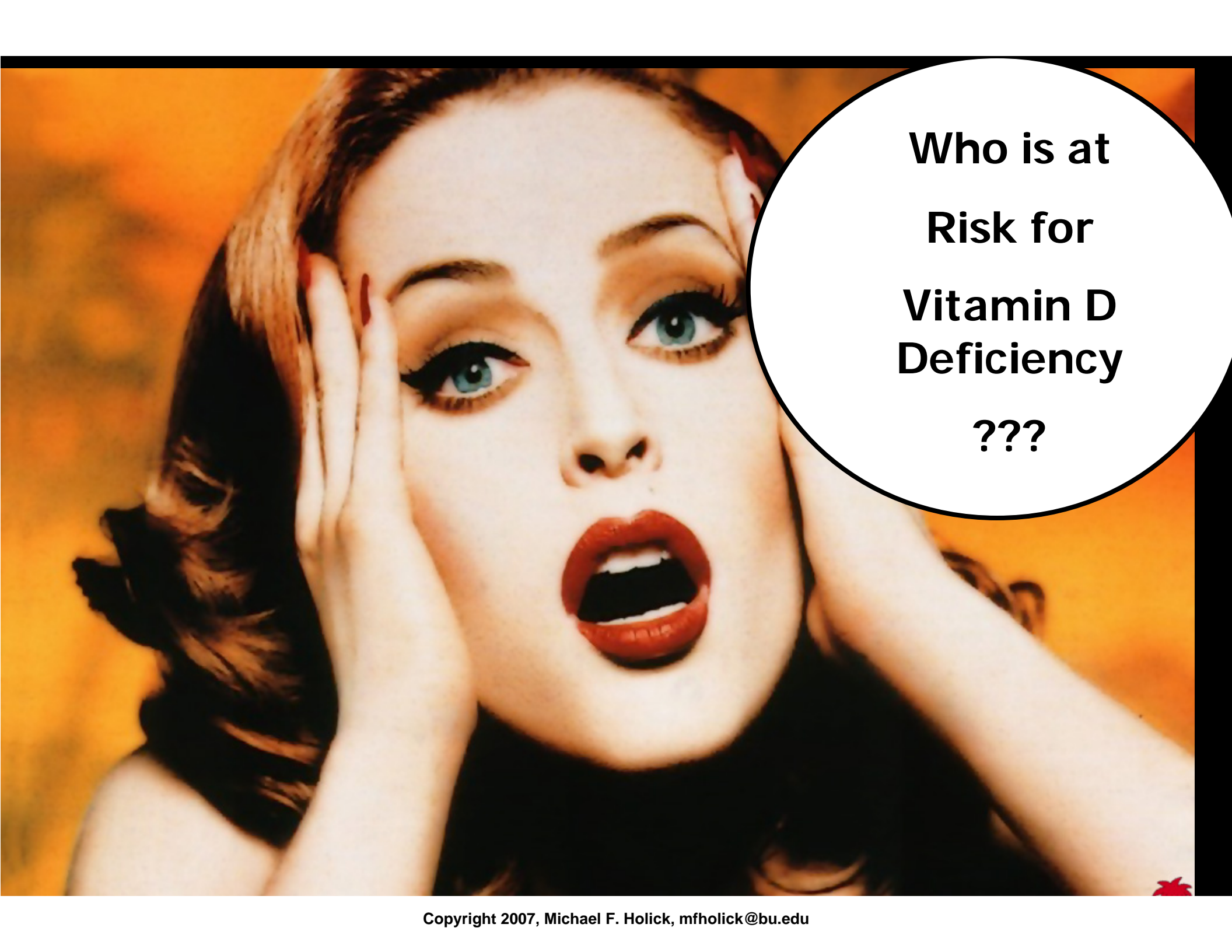
**M F HOLICK BUMC**



**Dr Holick  
Receives support  
From NIH  
&  
UV Foundation**




AND SUPPORT  
FROM THE  
SUN



**Who is at  
Risk for  
Vitamin D  
Deficiency  
???**



EVERYONE

A close-up photograph of a man with dark hair, looking thoughtful with his hand to his chin. A large yellow speech bubble is overlaid on the left side of his face, containing text. At the bottom of the image, a red banner with white text spans across the width.

**WHAT'S  
THE BIG DEAL ABOUT  
VITAMIN D  
DEFICIENCY  
???????**

**GLOBAL WARMING !!!!!!!**

An aerial photograph of a snow-capped mountain peak, likely Mount Ricketts, with the word "RICKETS" overlaid in large, bold, black capital letters.

# RICKETS

**VITAMIN D**  
**SUNSHINE**  
**VITAMIN**







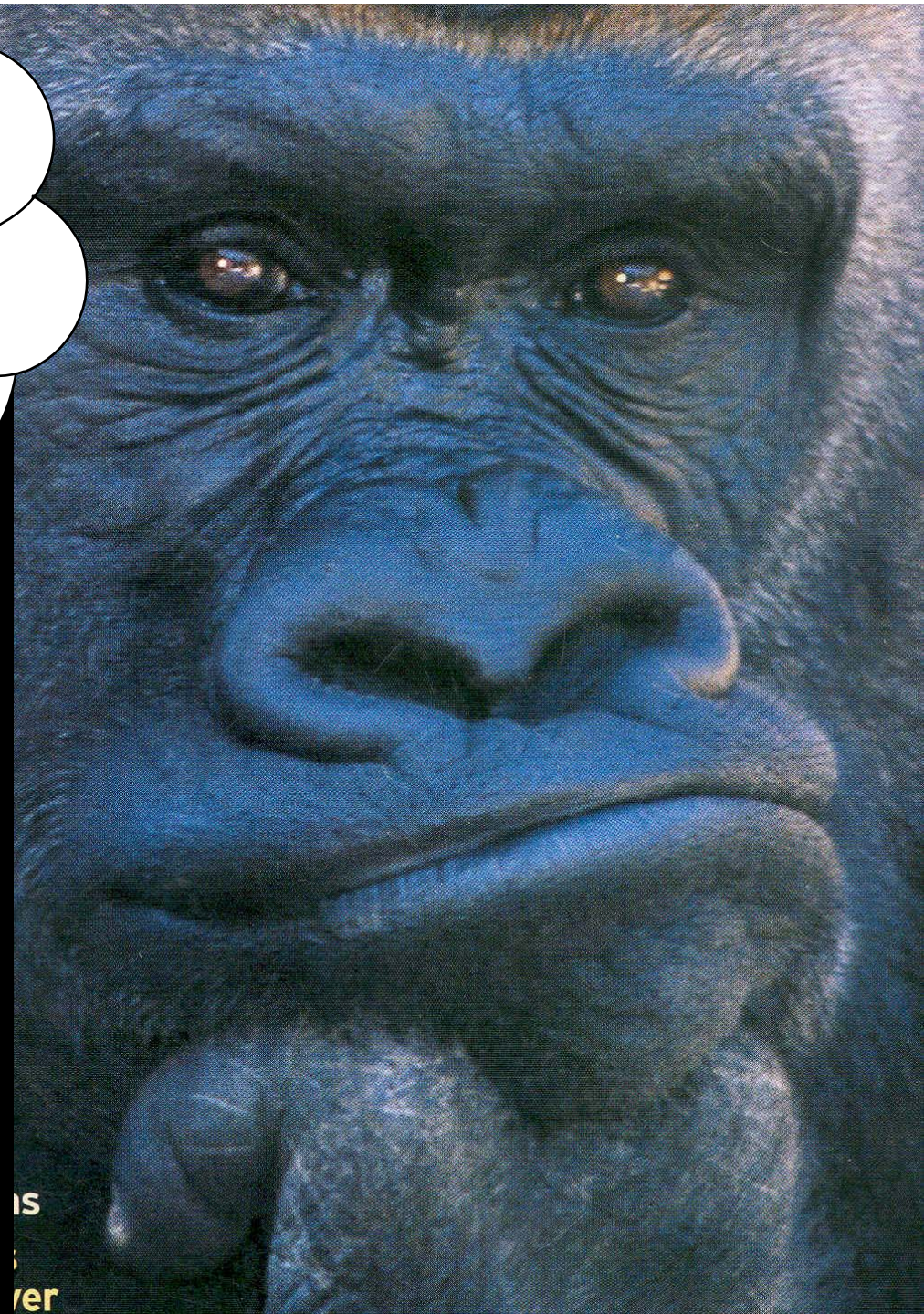


©2003 Bill Pruitt





**OUR SKIN  
WAS DESIGNED  
TO MAKE  
VITAMIN D**



**HESS & UNGER**

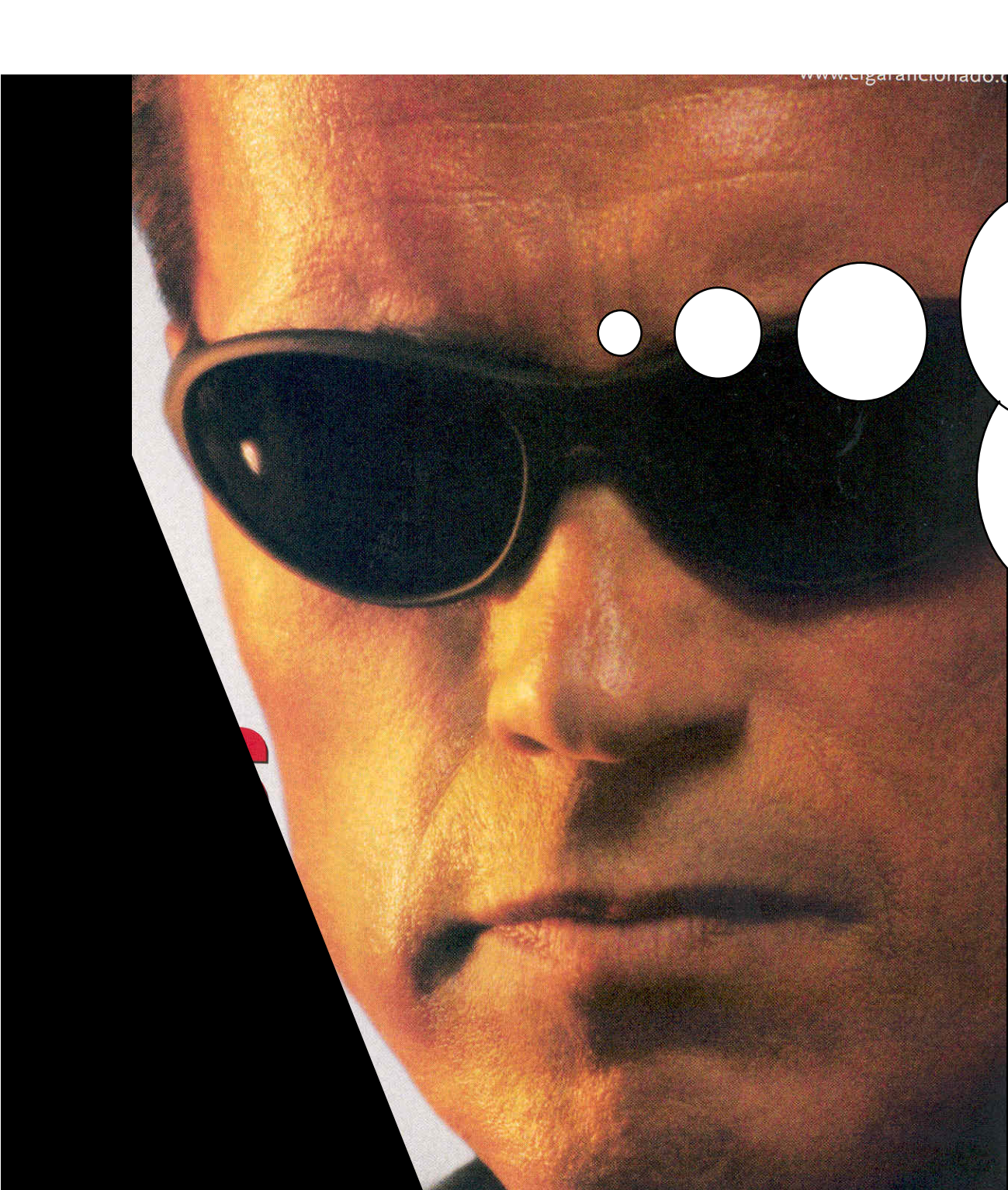
**1921**

***SUN CURED RICKETS***



**1931 US GOVERNMENT  
PROVIDED RECOMMENDATIONS  
FOR SUN EXPOSURE**





**Dermatology  
Societies  
FOR 40 YEARS  
ARE YOU  
SURE  
??????**



WHAT WILL  
HAPPEN IF MY  
CHILDREN GO  
OUT WITHOUT  
SUNSCREEN ?



# CHILD ABUSE

VITAMIN D

is

ESSENTIAL

FOR

BONE HEALTH

# Case #1

- **7 month Old Female**
- **Muscle Weakness**
- **Tetanic seizures**
- **Serum calcium 4.2mg%**



KIRMANI

KIKI

Franklin ZOO



**MY  
BONES  
HURT!!!!**



MY DAUGHTER  
NEEDS HELP  
IMMEDIATELY  
!!!!





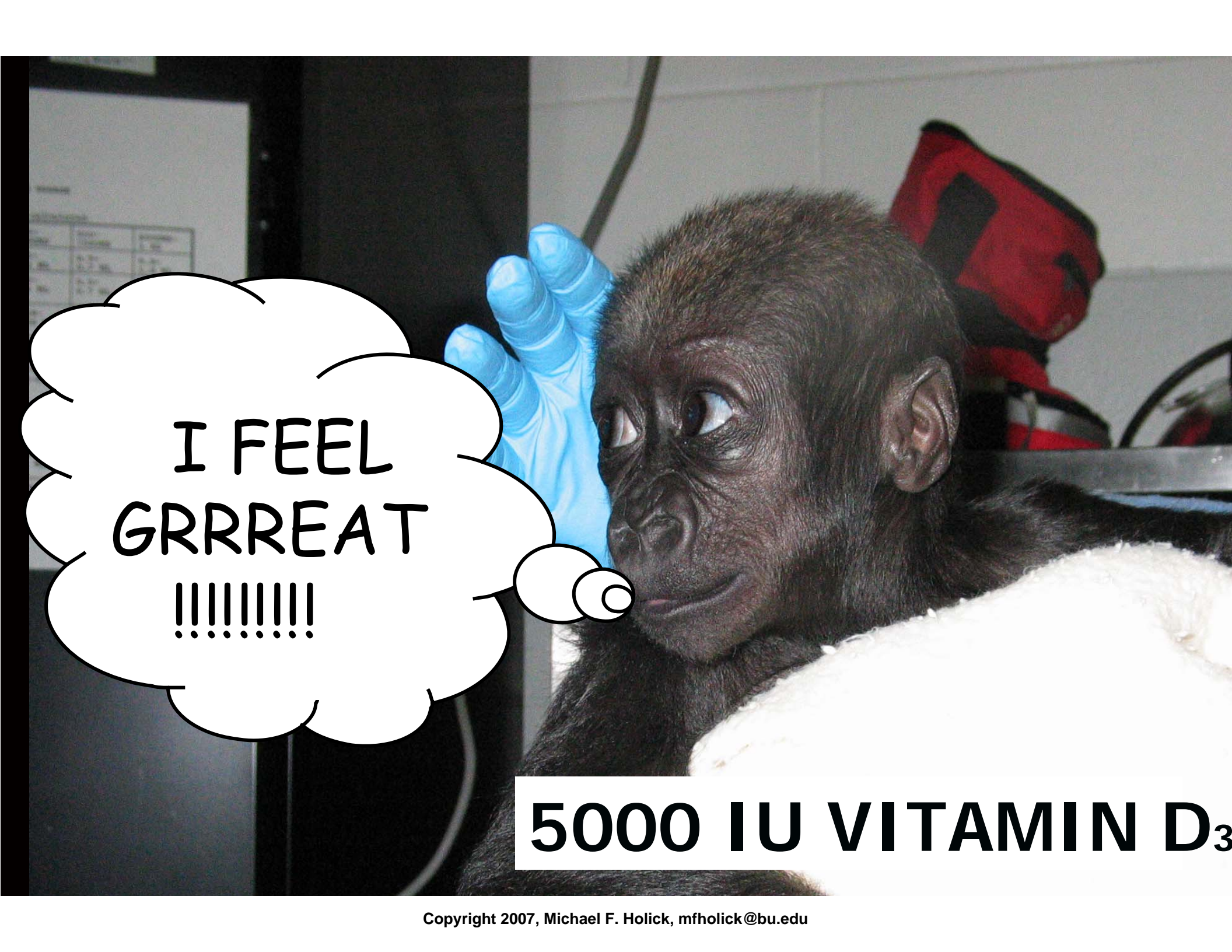
**WE NEED  
Dr. HOLICK  
!!!!!!!!!!!!!!!**



FINALLY  
THEY GOT  
Dr. Holick  
!!!!!!!!!!



D-ficient



I FEEL  
GRRREAT  
!!!!!!!!!!

**5000 IU VITAMIN D<sub>3</sub>**



1<sup>st</sup> BIRTHDAY



**1889**

**BOSTON**

**80% INFANTS**

***RICKETS***

**BUT IS RICKETS**

**A PROBLEM**

**20000 ???? ?**

**YES!!!**



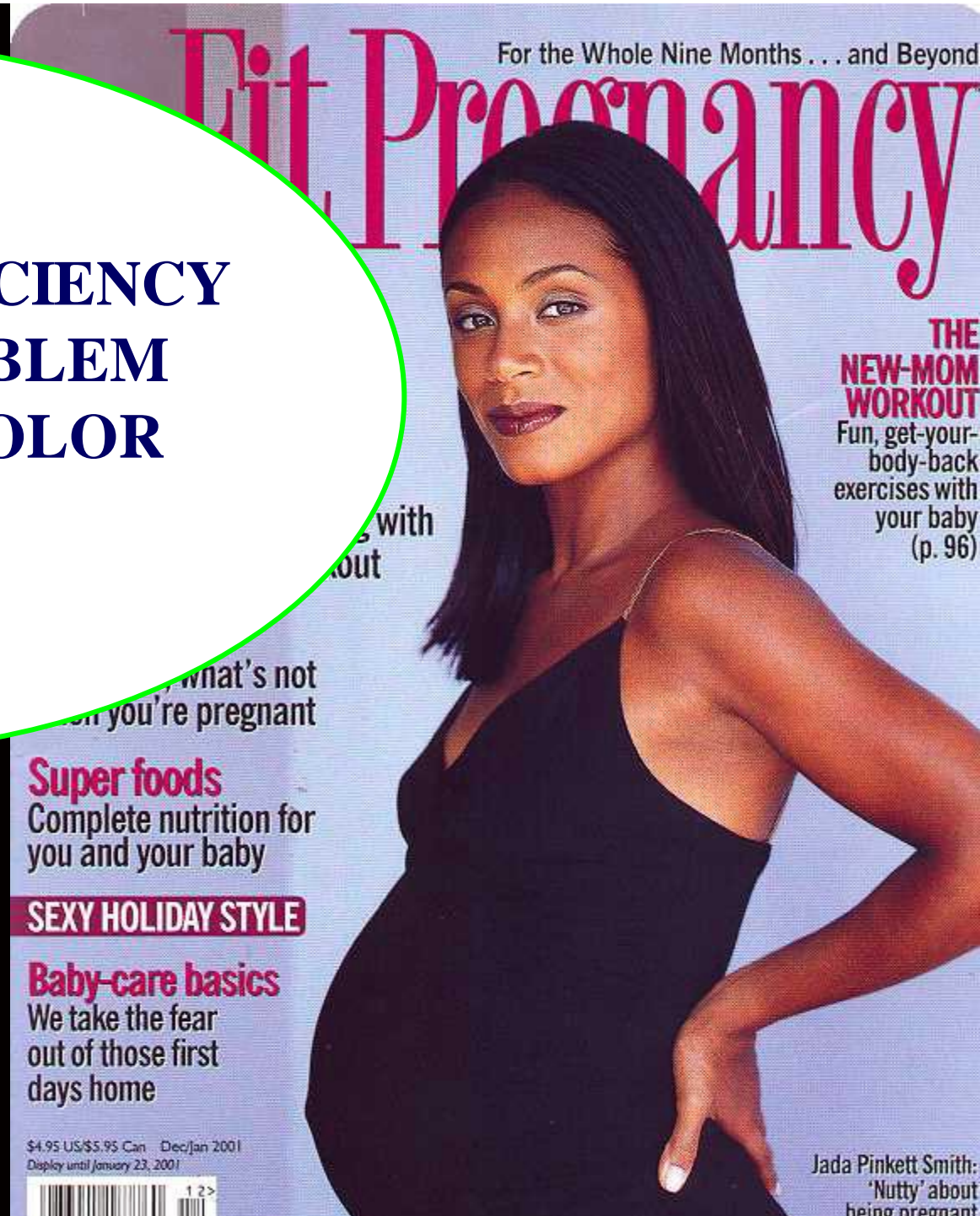


**BOSTON MEDICAL CENTER**



THERE IS  
LITTLE VITAMIN D  
BREAST MILK  
~ 25 IU/L

**IS VITAMIN D DEFICIENCY  
A COMMON PROBLEM  
IN WOMEN OF COLOR  
??????**



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

Joyce M. Lee, MD, MPH<sup>1</sup>, Jessica R. Smith, MD<sup>2</sup>,  
Barbara L. Philipp, MD<sup>3</sup>, Tai C. Chen, PhD<sup>4</sup>,  
Jeffrey Mathieu, MS<sup>4</sup>, Michael F. Holick, MD, PhD<sup>4</sup>

**BOSTON MEDICAL CENTER**

**40 MOTHERS AND THEIR INFANTS  
AT BIRTH**

**MEASURED VITAMIN D STATUS  
25-HYDROXYVITAMIN D**

**Maternal Demographics (n=40)**

|                          | <b>N(%)</b> |
|--------------------------|-------------|
| <b>Race</b>              |             |
| Black                    | 25 (62.5%)  |
| Caucasian                | 10 (25%)    |
| Asian                    | 3 (7.5%)    |
| More than 1 race         | 2 (5%)      |
| <b>Ethnicity</b>         |             |
| Not Hispanic             | 28 (70%)    |
| Hispanic                 | 10 (25%)    |
| Unknown                  | 2 (5%)      |
| <b>Drinks milk</b>       | 37 (92.5%)  |
| <b>Eats fish</b>         | 44(89.7%)   |
| <b>MVI(400 IU Vit D)</b> | 28(70%)     |
| <b>Ca supplement</b>     | 4(10%)      |
| <b>Vit D supplement</b>  | 0 (0%)      |

**Mean Values**

|   |            |
|---|------------|
| <b>Age (years)</b>                              | 28.8 ± 6.5 |
| <b>Milk Consumption<br/>(8 oz. glasses/day)</b> | 2.3±2.4    |
| <b>Fish Consumption<br/>(servings a month)</b>  | 6.2±5      |

**70% MTV**

**DRANK 2.3  
GLASSES  
MILK/D**

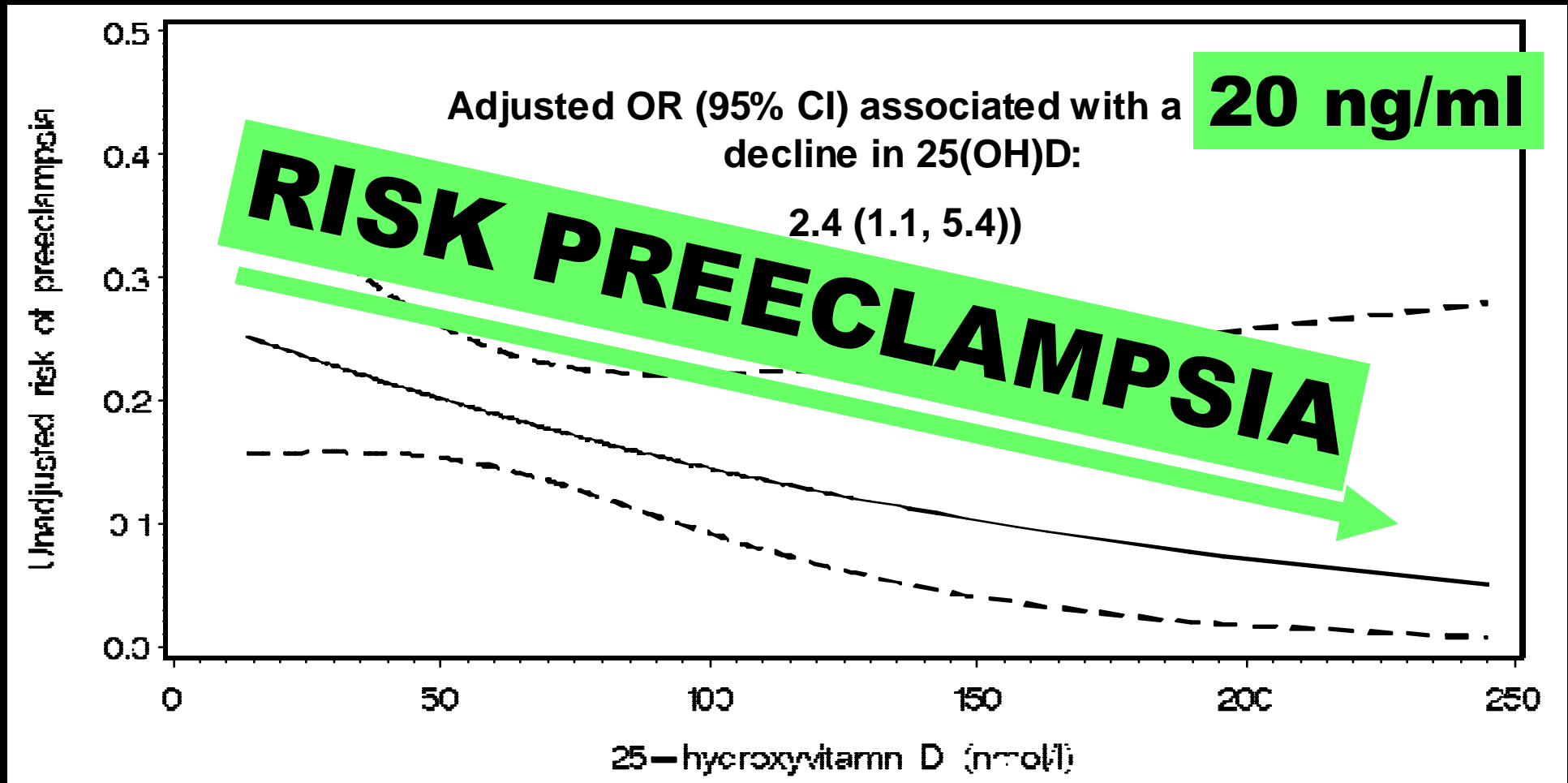
**76% MOTHERS**

**81% NEWBORNS**

**25(OH)D < 20NG/ML**

**VITAMIN D DEFICIENT**

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



# PROBABILITY C-SECTION



0

20

40

60

80

**MOTHER'S 25(OH)D NG/ML**



# JURASSIC SYNDROME

JURASSIC PARK™

750,000 young at risk

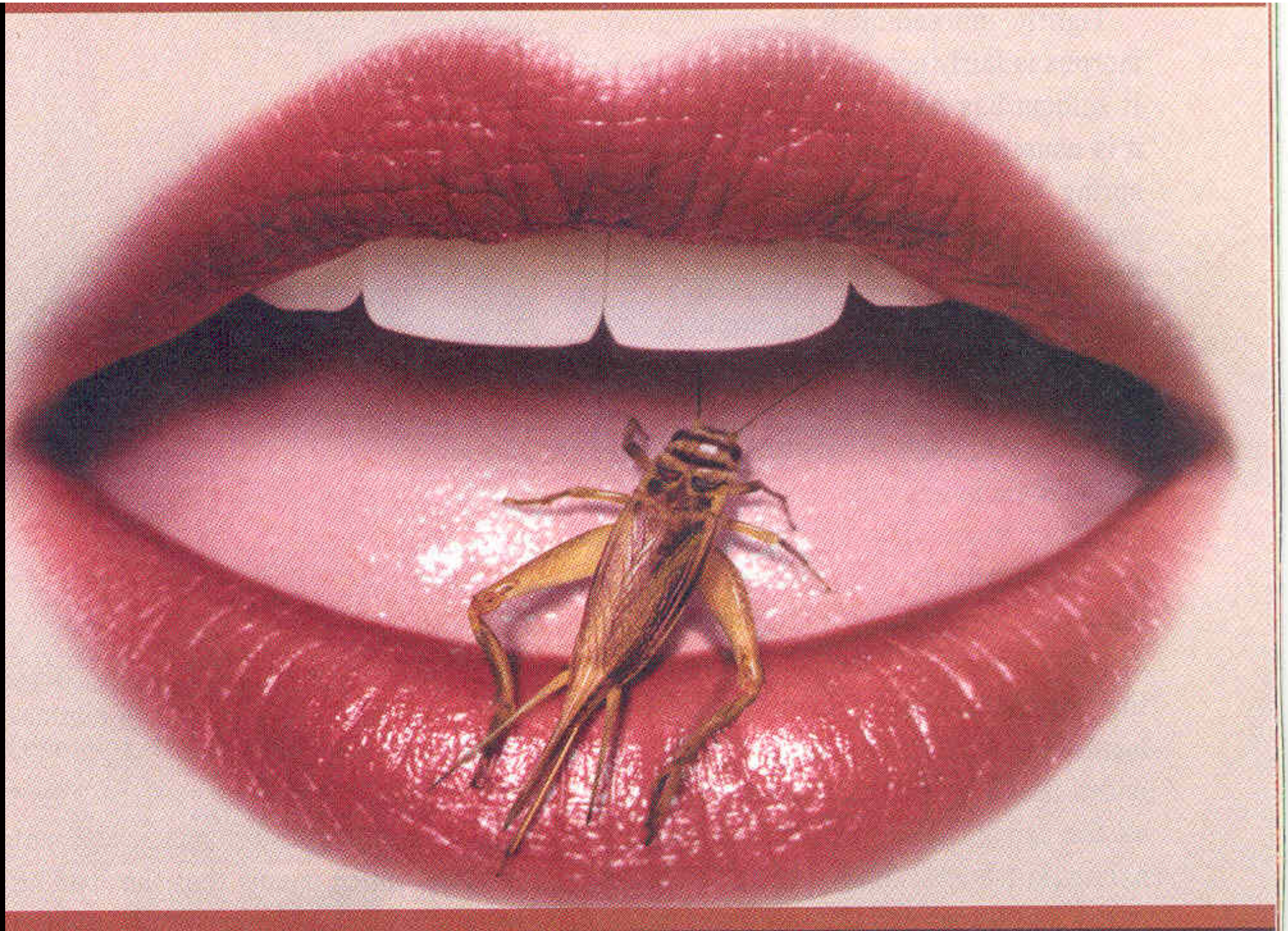
# Case #2

- **1 Year Old Female**
- **Muscle Weakness**
- **Boney Deformities**
- **Failure to Thrive**

# Diet

- Lettuce
- Crickets

Dx ?

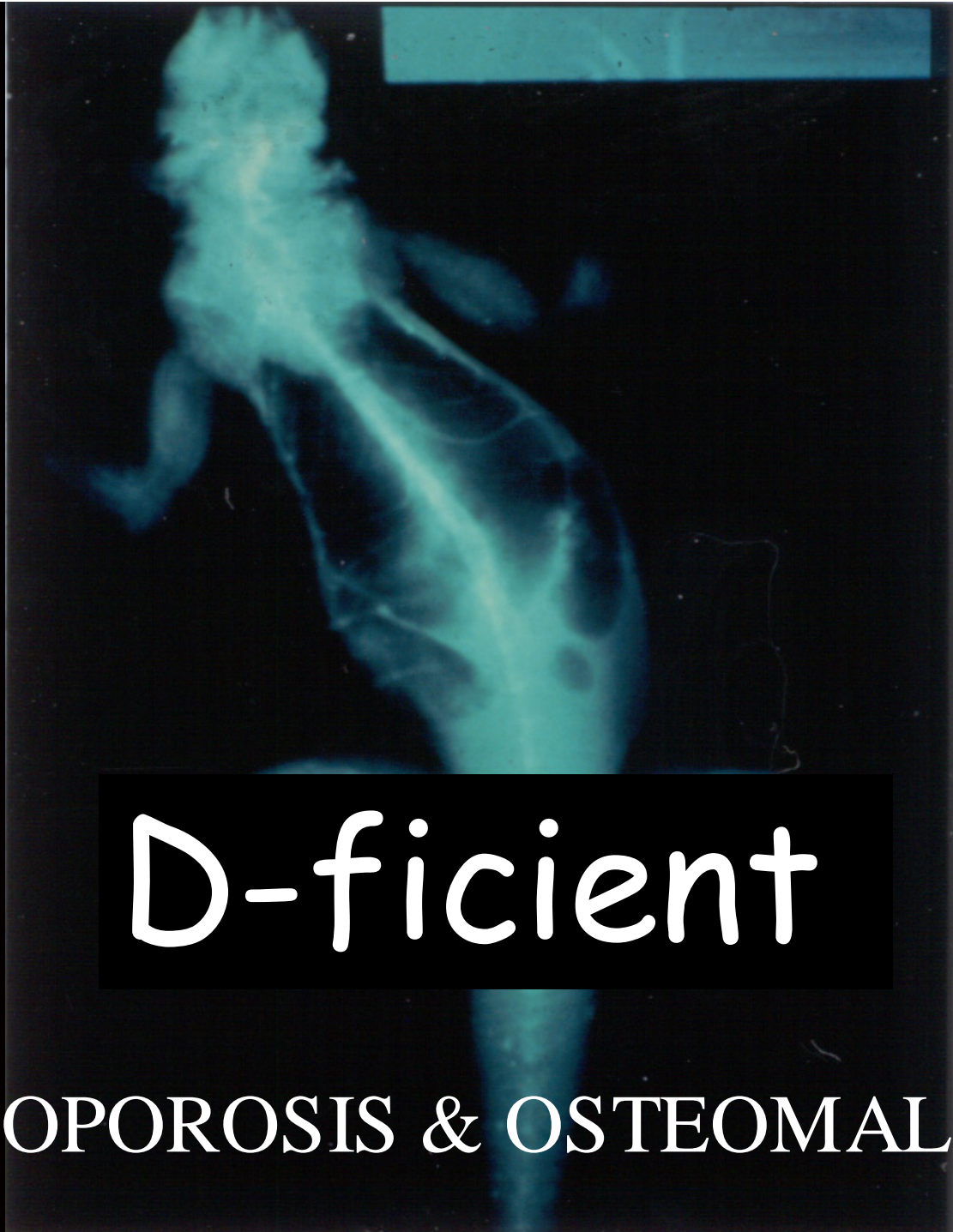


# Dinner is Served.



**750,000 IMPORTED/YEAR**





D-ficient

OSTEOPOROSIS & OSTEOMALACIA



Pancake Tortoise • Vegas-Vicinity Herping

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August 1997

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Spiny-Tailed Iguanas • Fiji Island Iguanas

STRIPED FOREST PIT VIPERS

# Metabolic Bone Disease

**MBD encompasses a wide range of reptile and amphibian ailments. Learn how to avoid the most common.**

**A** beginning herper purchases a baby green iguana, proudly brings it home and sets it up in its new cage. The new owner didn't receive much information when he purchased the new lizard, and he feeds it the diet he was instructed to: a variety of greens, vegetables and fruits. He neglected to purchase a thermometer for the cage, nor did he acquire a full-spectrum light or proper equipment to heat the cage. The iguana has a bowl for water, but rarely, if ever, is allowed to swim in a tub or pool.

Although the young iguana has a good appetite, the owner notices that its limbs are beginning to look muscle-bound and the lizard doesn't seem to be able to lift up its trunk normally. During one cage cleaning, as the iguana is jumping around the cage, the owner notices that a front leg appears to be broken.



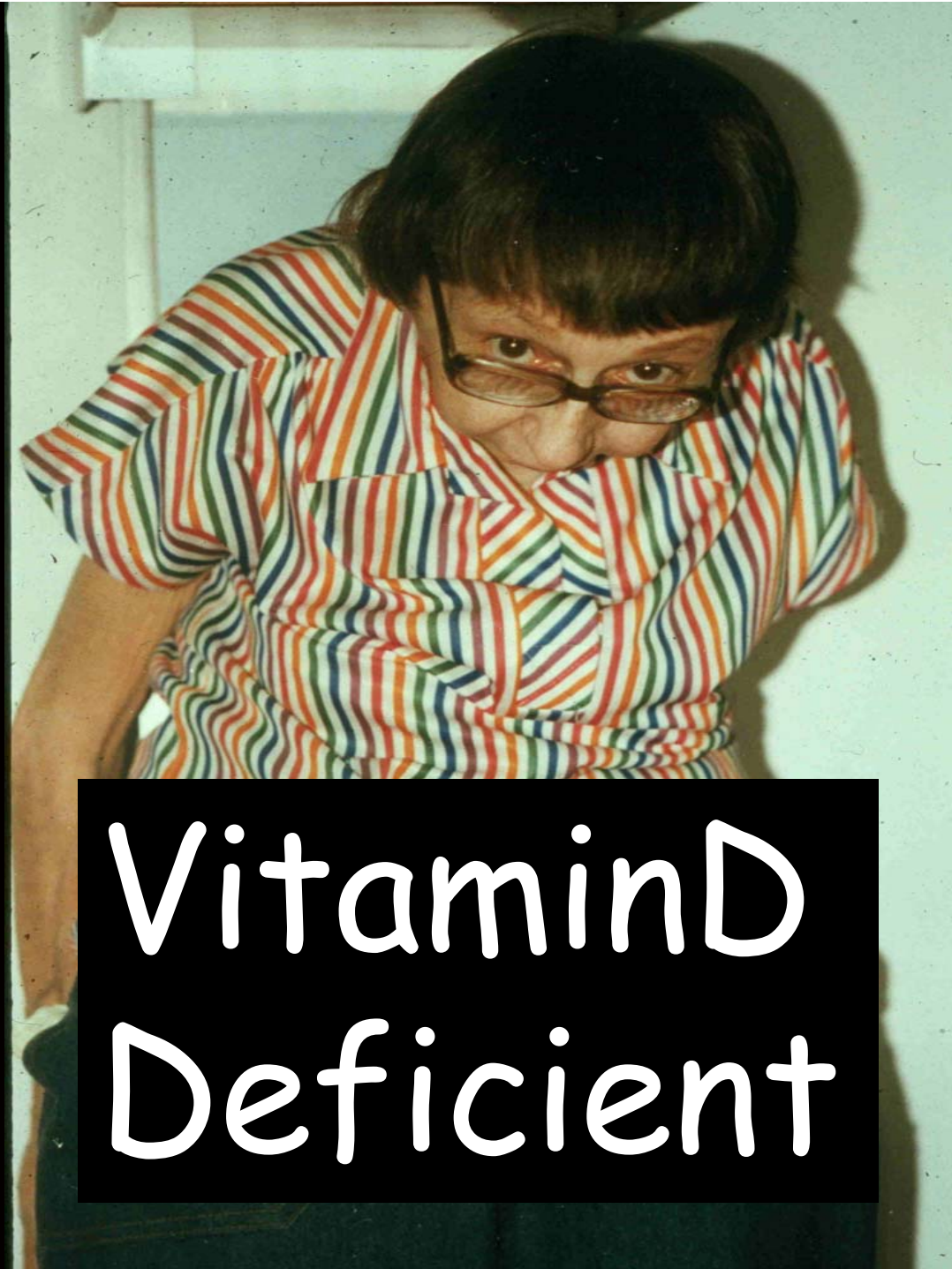
article by  
margaret  
a. wissman,  
dvm, dabvp

photos by  
douglas mader  
dvm, dabvp

Metabolic bone disease (MBD) may result in various deformities in a herp. This iguana is suffering from scoliosis.



# **VITAMIN D DEFICIENCY**



# Vitamin D Deficient



# VITAMIN D DEFICIENCY



# VITAMIN D DEFICIENCY

RX



Rickets

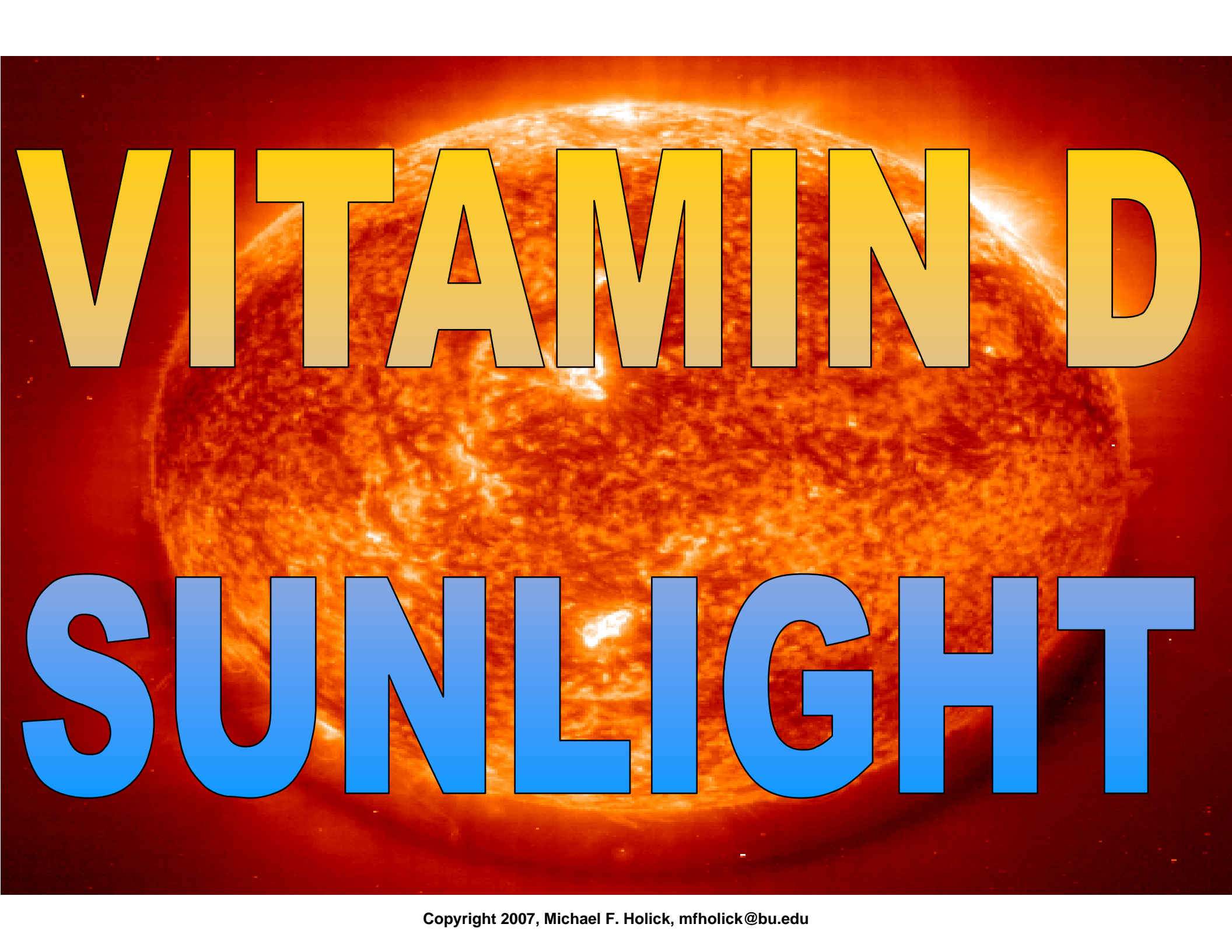
Osteomalacia



**CALCIUM**

# LOW FAT CREAM CHEESE





VITAMIN D

SUNLIGHT

**Even reptiles  
need sunlight for  
their Vitamin D**



# REPTA-SUN™

LONG LIFE FULL SPECTRUM LIGHTING

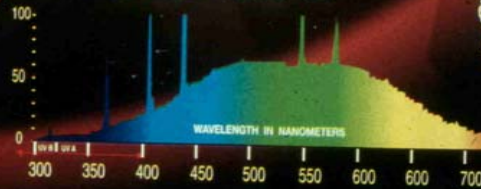
## FULL SPECTRUM

Full spectrum lighting closely simulates natural sunlight. Reptiles and all other animals requiring sunlight often feel better and see better, with food colors and skin tones appearing as they do in natural sunlight.

## HIGH COLOR RENDERING

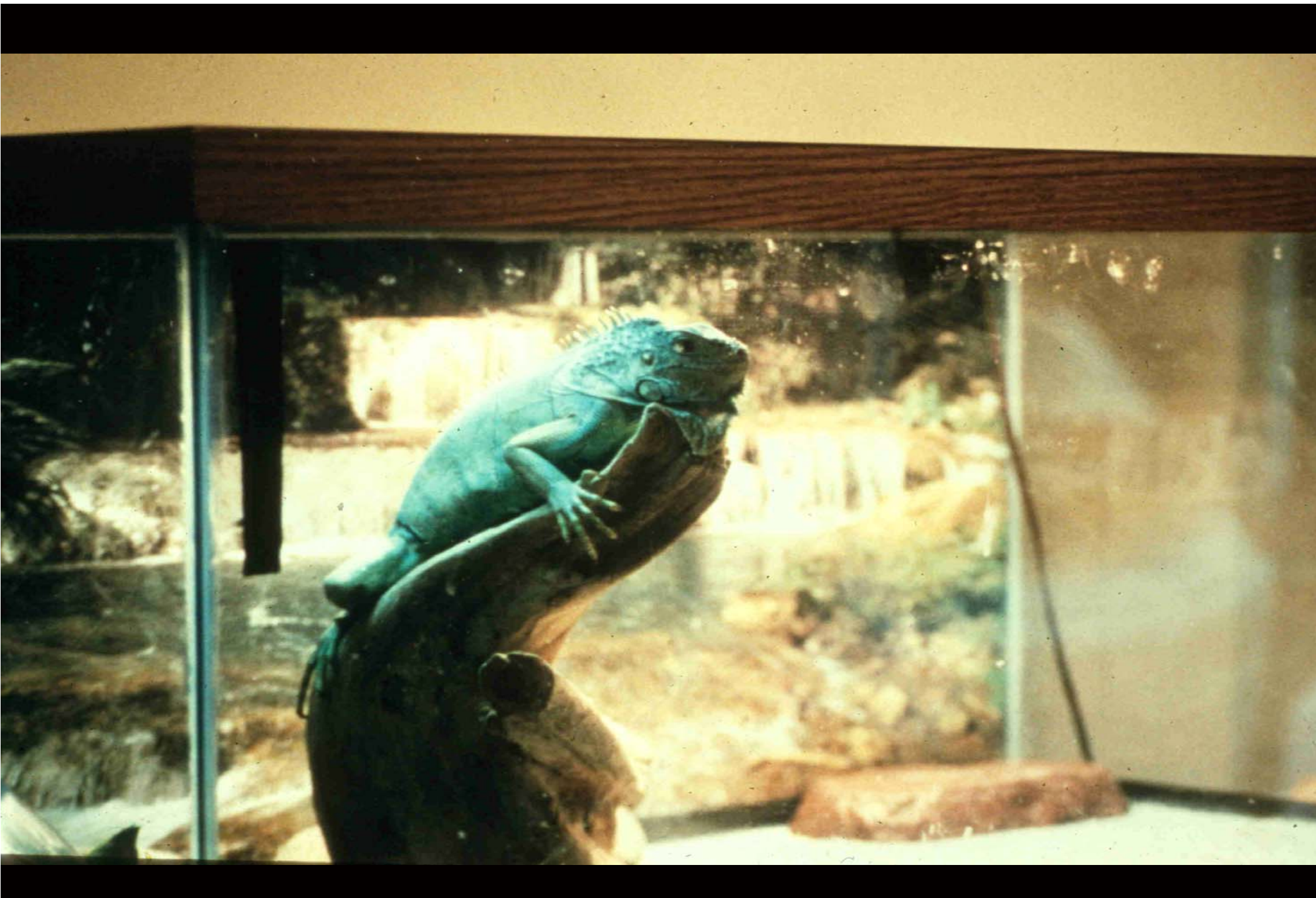
Providing a natural environment for your reptile is an important factor in your animals health. REPTA SUN has a high Color Rendering Index of 91. The CRI Scale refers to how closely a light source simulates the color rendering properties of natural sunlight. Natural sunlight has a CRI of 100.

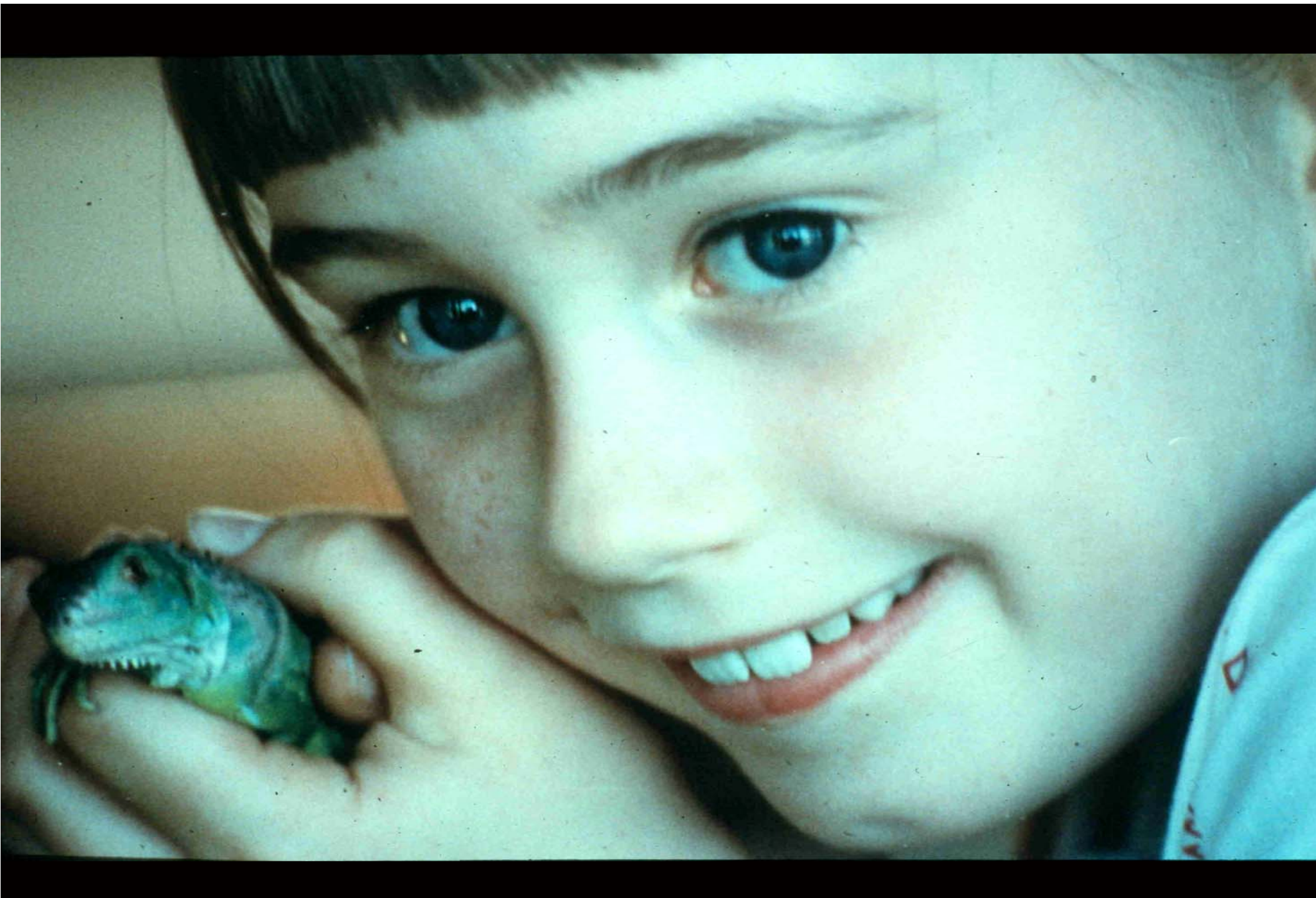
SPECTRAL GRAPH  
CRI-91 5600 K



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**We need Calcium  
& Vitamin D for  
Strong Bones &  
Teeth**









# Vitamin D is Rare in Foods

**UM, UM GOOD**

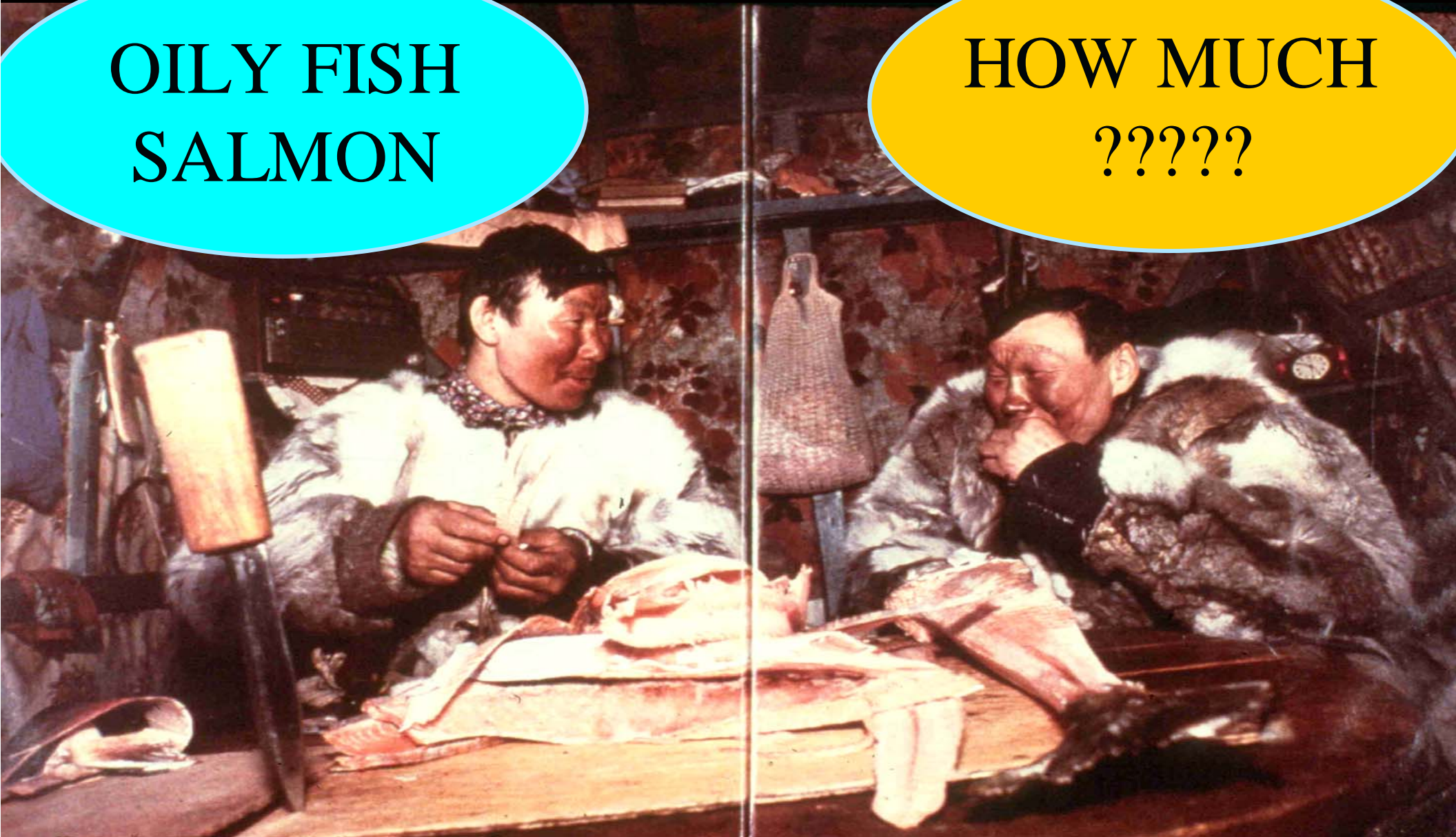




**BUT I EAT  
FISH**

OILY FISH  
SALMON

HOW MUCH  
??????





500-1000 IU/3.5 oz

5-7 TIMES/WEEK



**BUT**

**YOU DRINK  
MILK**



Got Vitamin D?



**100 IU/ 8 OZ**

# NOW + VITAMIN D



# 100 IU / 8 OZ



Copyright 2007, Michael F. Holick, [mfholick@bu.edu](mailto:mfholick@bu.edu)



**Sunlight makes  
us feel good !**

IS VITAMIN  $D_3$  MADE  
IN SKIN  
DURING THE WINTER?

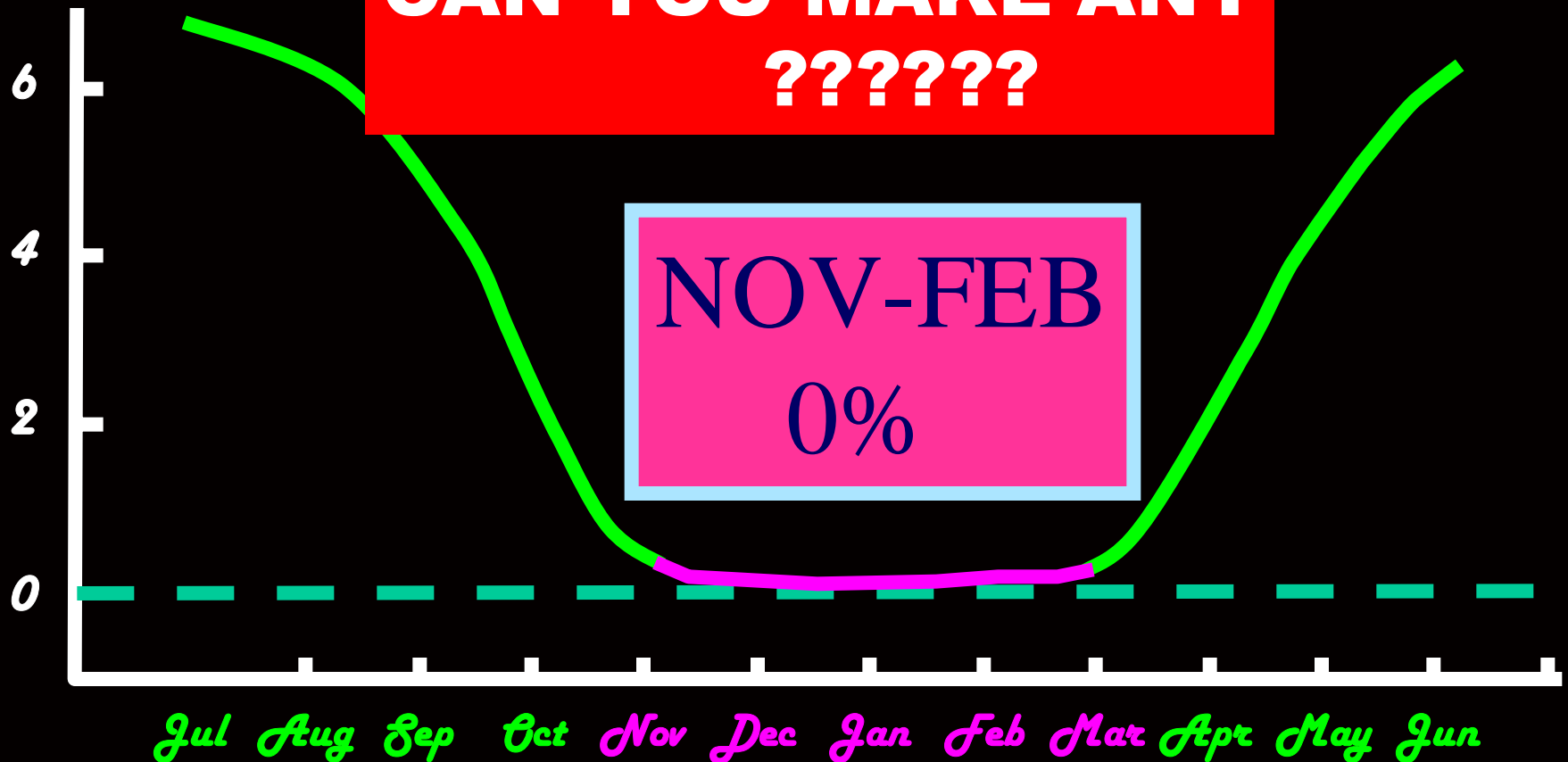




# Seasonal Effect on Cutaneous Vitamin D Synthesis in Boston

**CAN YOU MAKE ANY  
???????**

*Vitamin D Synthesis %*



**NOV-FEB  
0%**

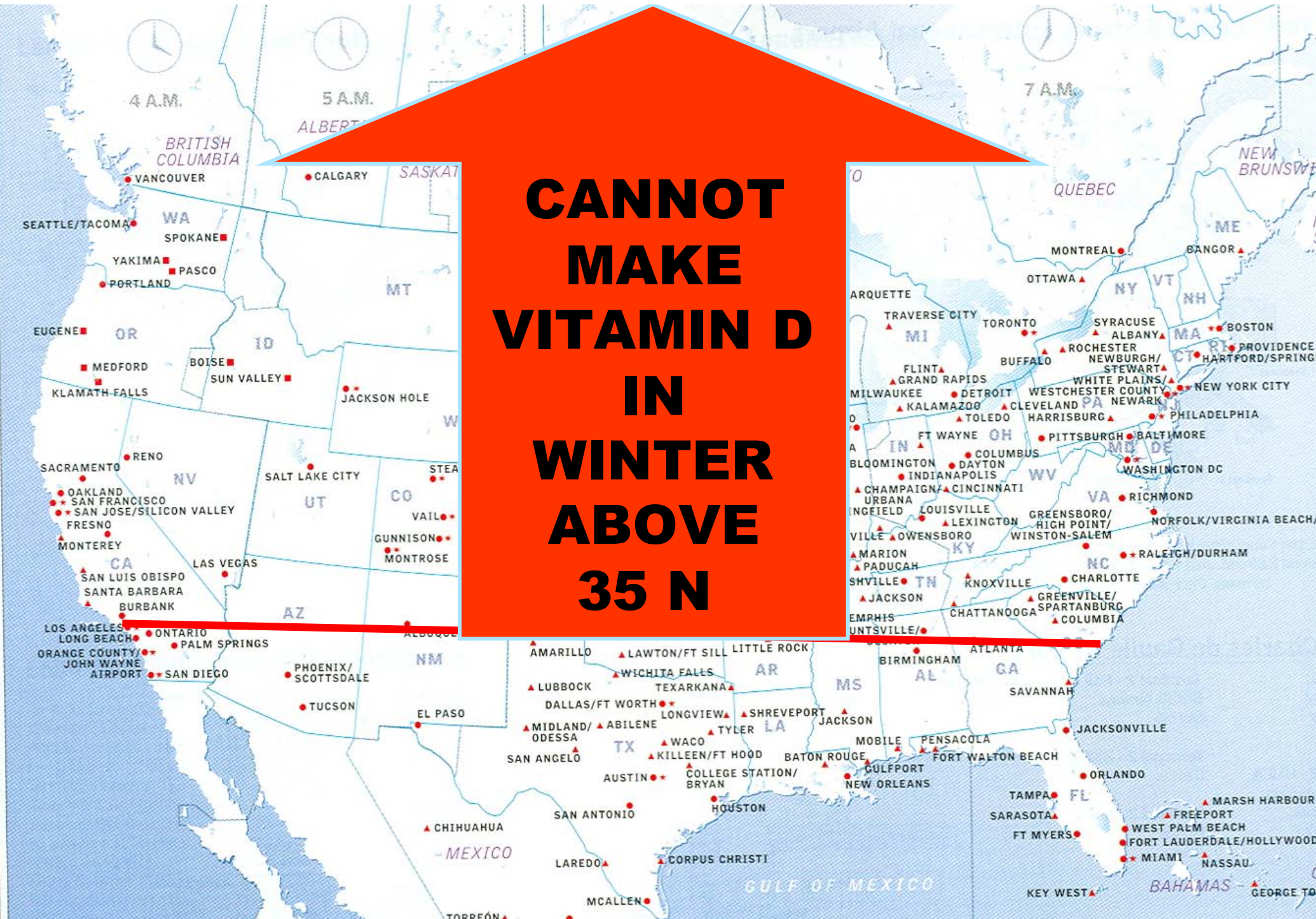
Webb et al

**NOT IN THE  
WINTER**





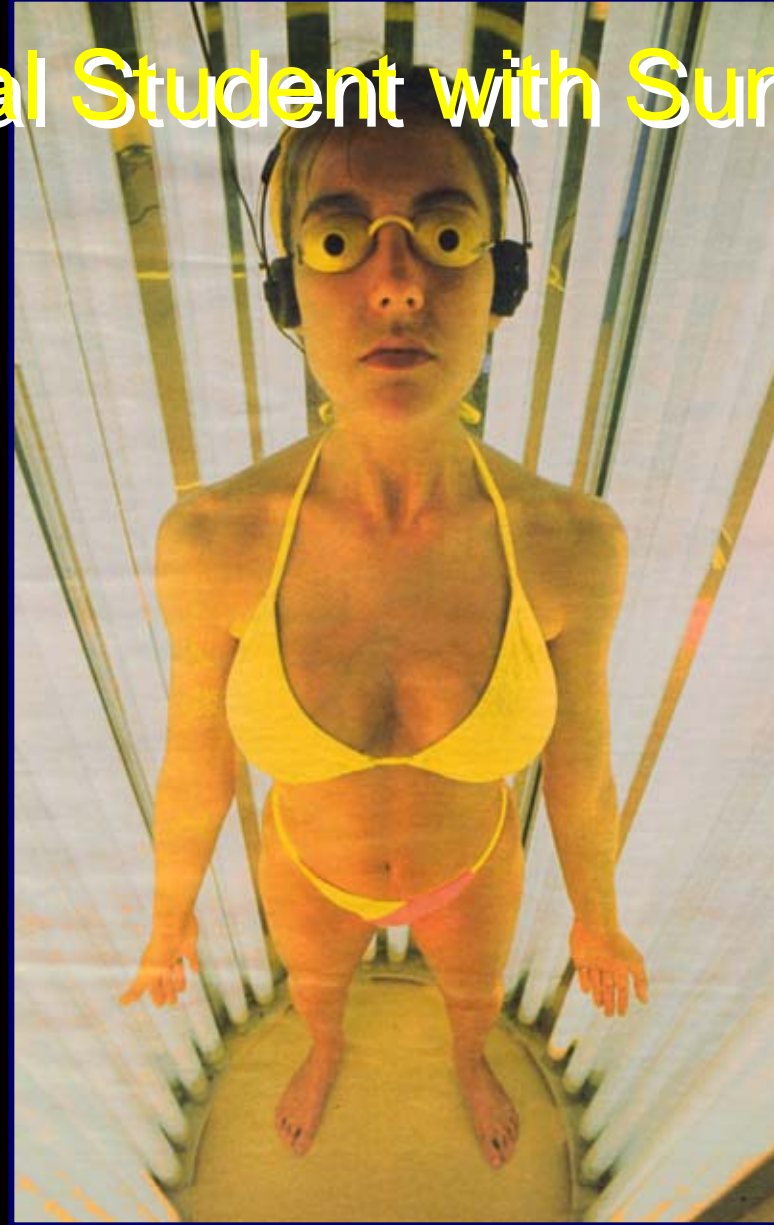
**CANNOT  
MAKE  
VITAMIN D  
IN  
WINTER  
ABOVE  
35 N**







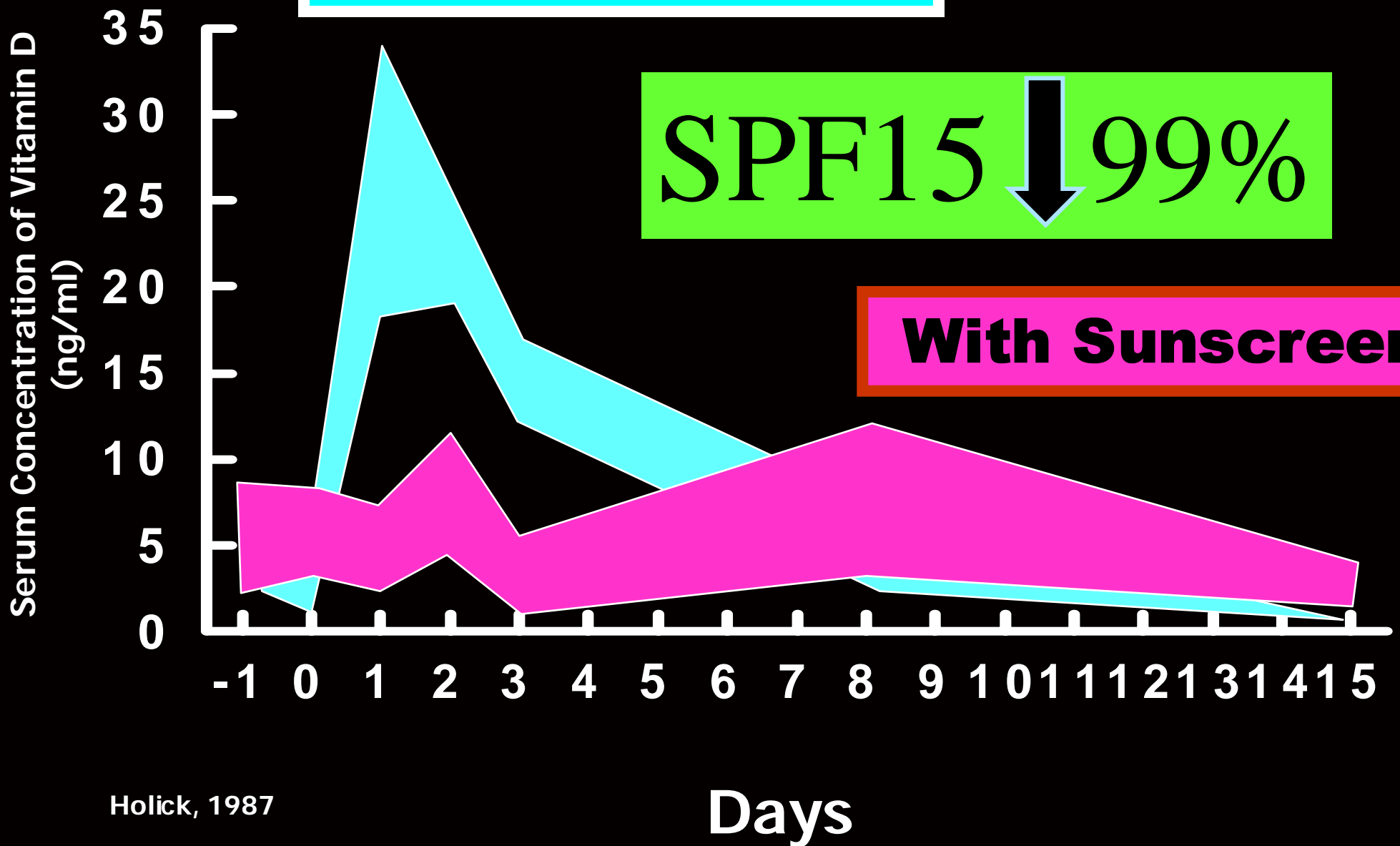
# Medical Student with Sunscreen



**Without Sunscreen**

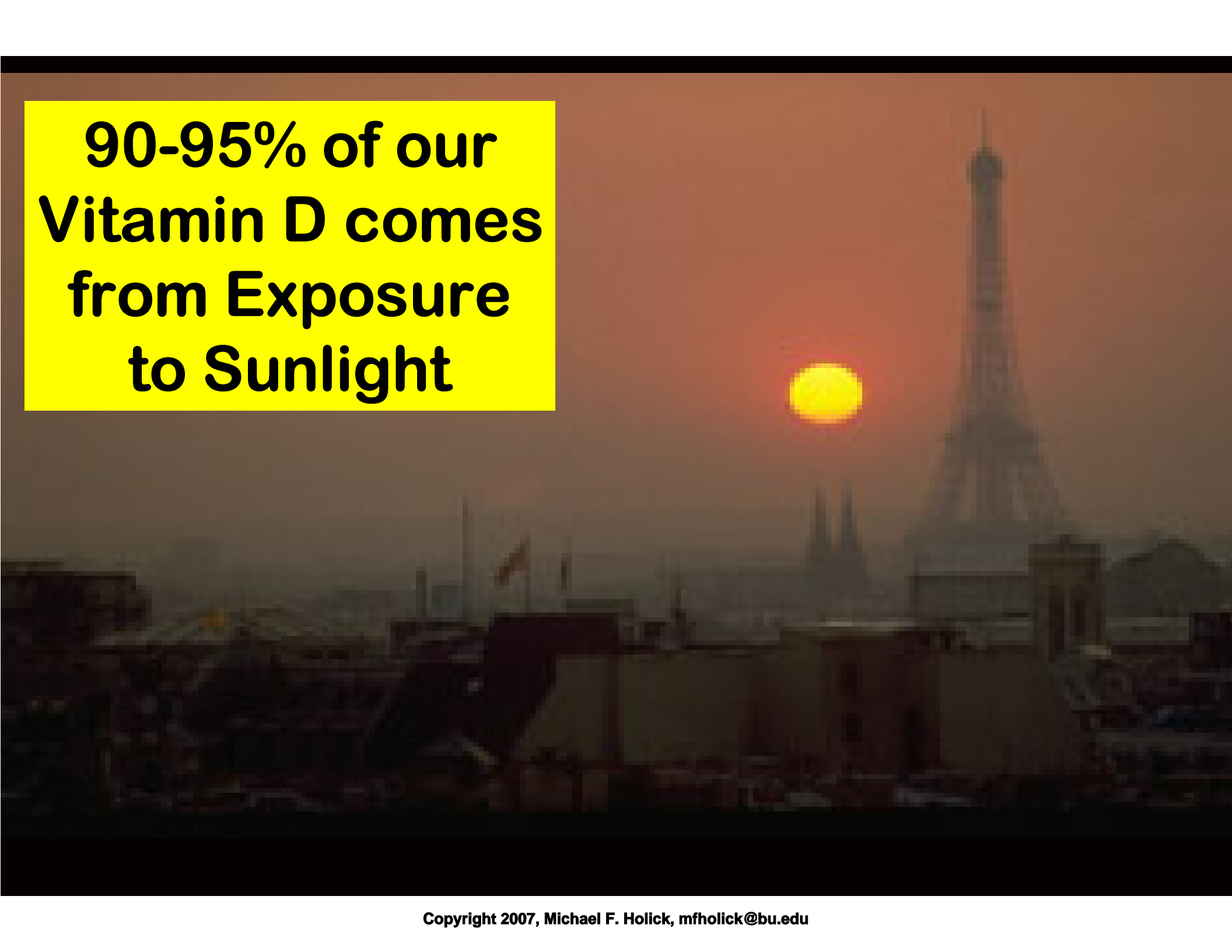
**SPF15 ↓ 99%**

**With Sunscreen**



Holick, 1987

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



HOW MUCH

SUN

EXPOSURE

????????????

**NEVER**

***BURRNV***





NEVER BURN



# Total Body



Exposure to  
1 Minimum Erythema  
Dose

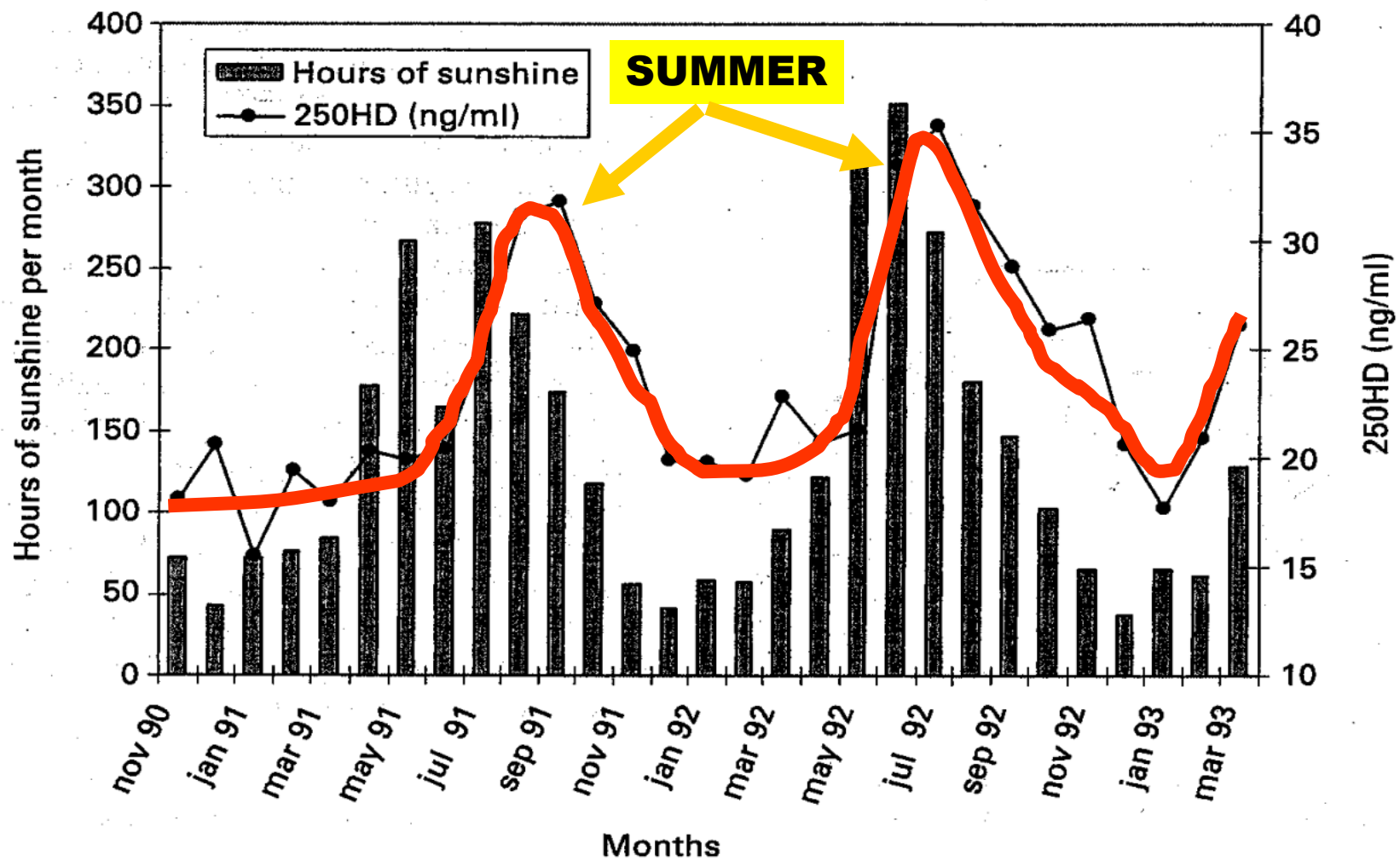
~20,000 IU Vitamin D<sub>3</sub>

(AI = 200-600 IU)

Does Sunlight Really  
Provide us with Vitamin D

??????

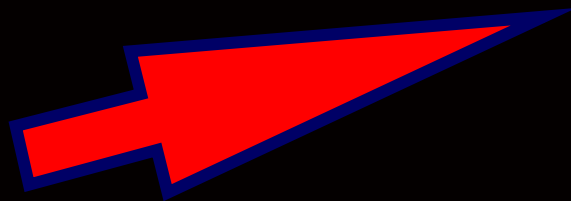




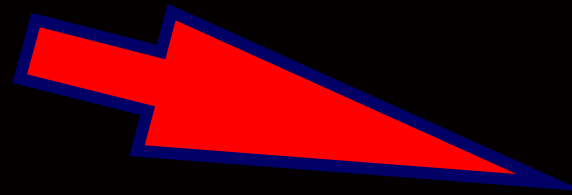
Brot *et al*, Brit J Nutr (2001), 86, Suppl. 1, S97-S103

# Recommendation in Boston

5 to 15  
Minutes  
Sunlight  
2-3X/wk



ARMS



LEGS







To get  
vitamin D,  
*brief*  
exposure  
to sunlight  
without  
sunscreen  
is okay.

Does skin pigment affect  
vitamin D synthesis ?



**Am I at risk for  
Vitamin D  
deficiency ??**



30-50%

AFRICAN AMERICANS

VITAMIN D DEFICIENT

**VITAMIN D DEFICIENCY**

**IS OFTEN A**

**MISDIAGNOSED**

WHY???

HOW DO YOU KNOW  
WHAT YOUR VITAMIN D  
STATUS IS ????????????



# 25(OH)D ASSAY

USED TO DETERMINE

VITAMIN D STATUS

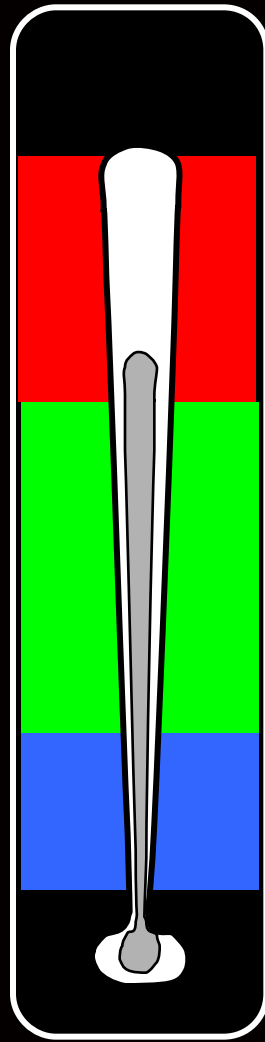
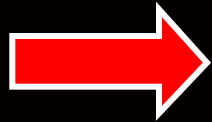
*NOT*

1,25(OH)<sub>2</sub>D

# 25(OH)D

**H**

**55 ng/ml**

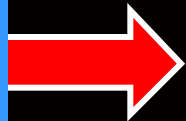


**Excess**

**N**

**Normal**

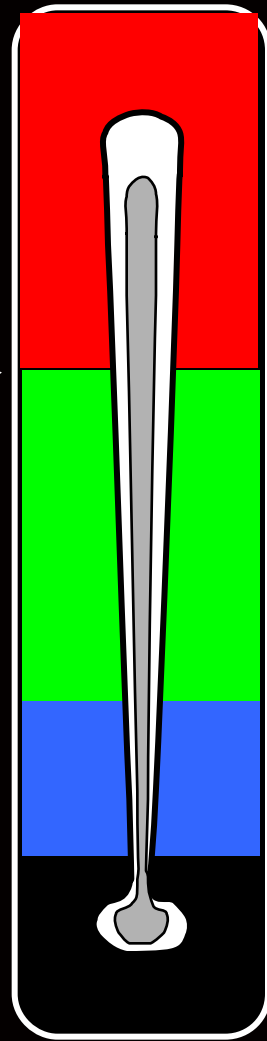
**10 ng/ml**



**Deficient**

**L**

# 25(OH)D in Lifeguards



60 ng/ml

55 ng/ml

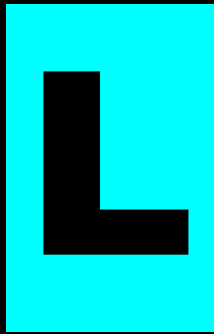
100  
ng/ml



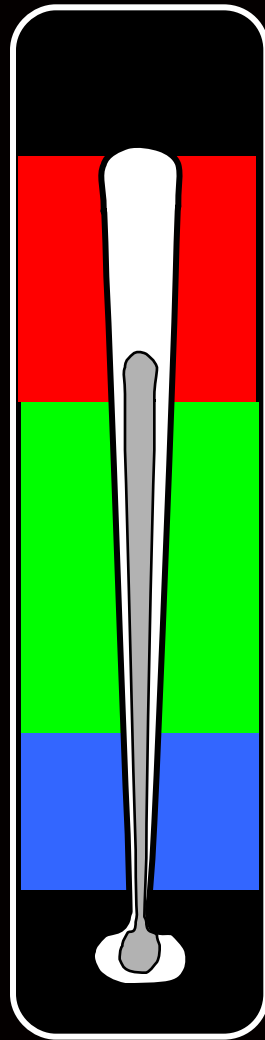
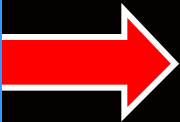
# VITAMIN D INTOXICATION

**25(OH)D > 150 NG/ML**

# 25(OH)D



**10 ng/ml**

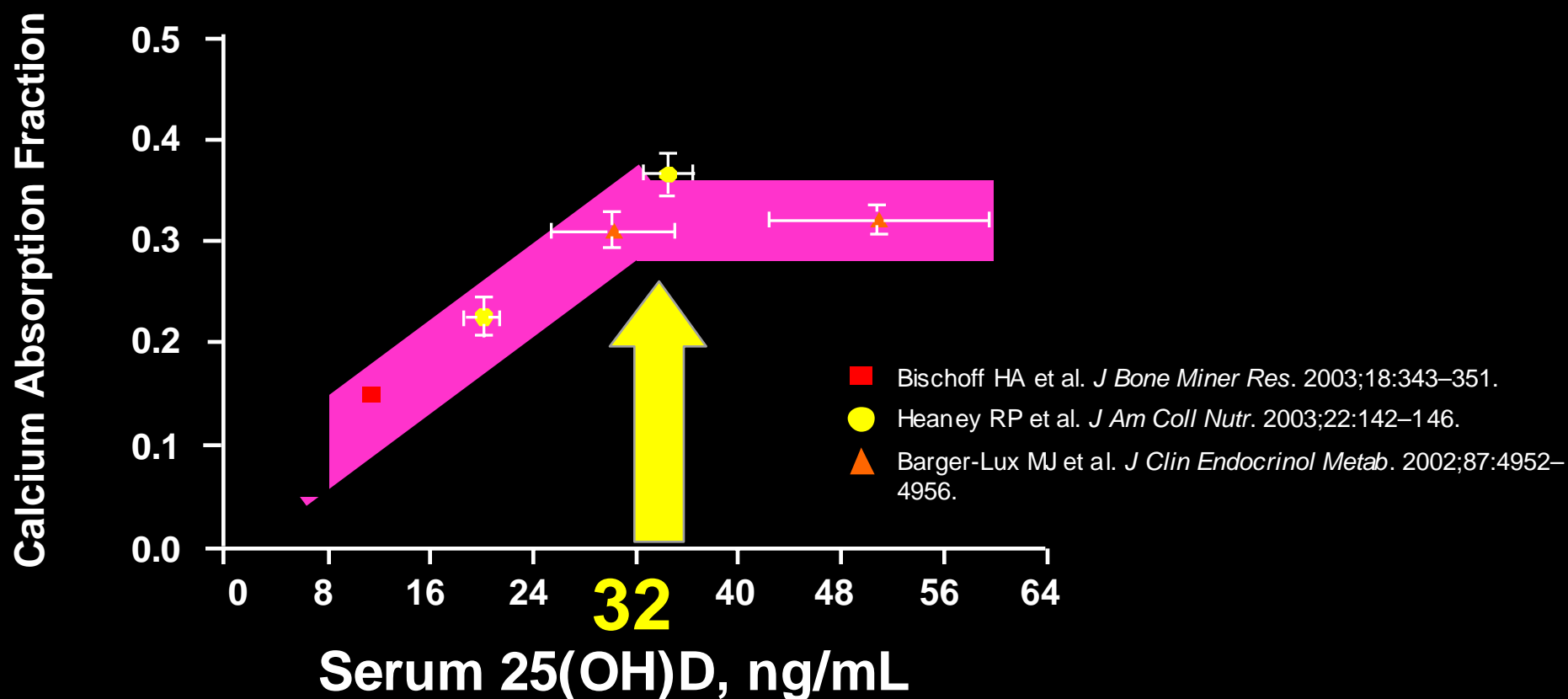


**Normal**

**Deficient**

# 25(OH)D Is Essential for Calcium Absorption

Calcium Absorption Plateaus at Serum 25(OH)D Levels  $\geq 32$  ng/mL



Adapted from Heaney RP. *Am J Clin Nutr.* 2004;80(suppl):1706S–1709S. Reproduced with permission from *The American Journal of Clinical Nutrition.*

# 25(OH)D

**>100 ng/ml**

**Excess**

**Normal**

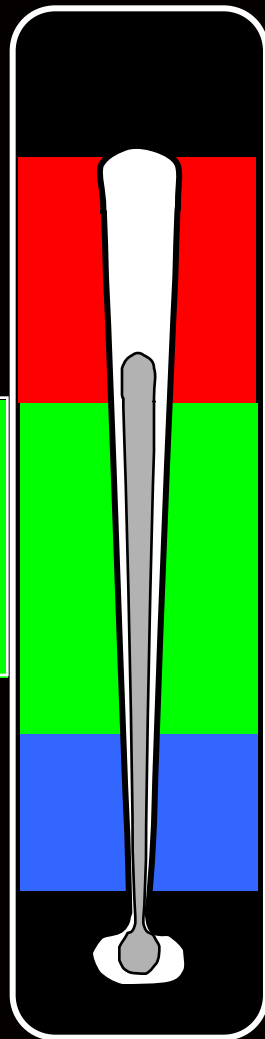
Ideal

**20-100 ng/ml**

30-60 ng/ml

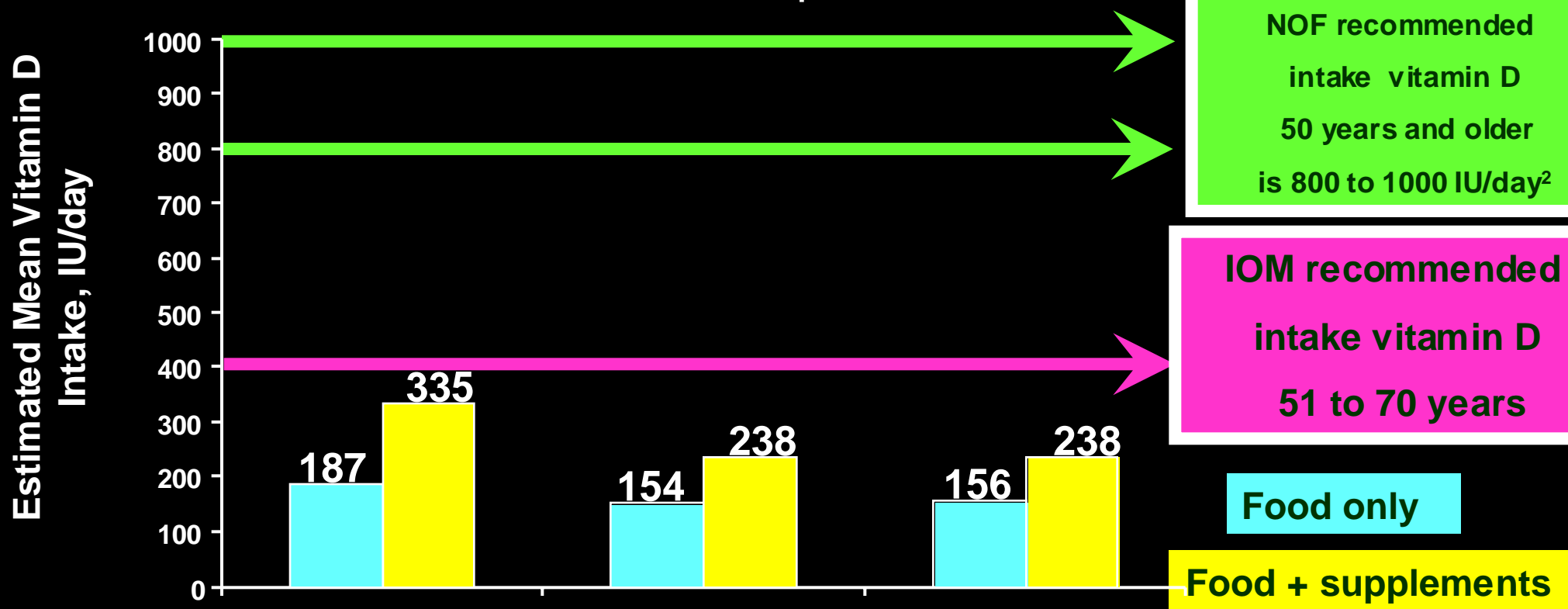
**<20 ng/ml**

**Deficient**



# Vitamin D Intake Did Not Reach 400 IU/day for Women 50 Years and Older, Even With Supplementation

NHANES III Population<sup>1</sup>



NHANES = National Health and Nutrition Examination Survey.

1. Calvo MS et al. *Am J Clin Nutr.* 2004;80(suppl):1710S–1716S.

2. National Osteoporosis Foundation. National Osteoporosis Foundation's Updated Recommendations for Calcium and Vitamin D<sub>3</sub> Intake. Available at: [http://www.nof.org/prevention/calcium\\_and\\_VitaminD.htm](http://www.nof.org/prevention/calcium_and_VitaminD.htm). Accessed April 24, 2007.

3. Institute of Medicine of the National Academies. Dietary reference intakes (DRIs): recommended intakes for individuals. Available at: <http://www.iom.edu/?id=21381>. Accessed April 24, 2007.

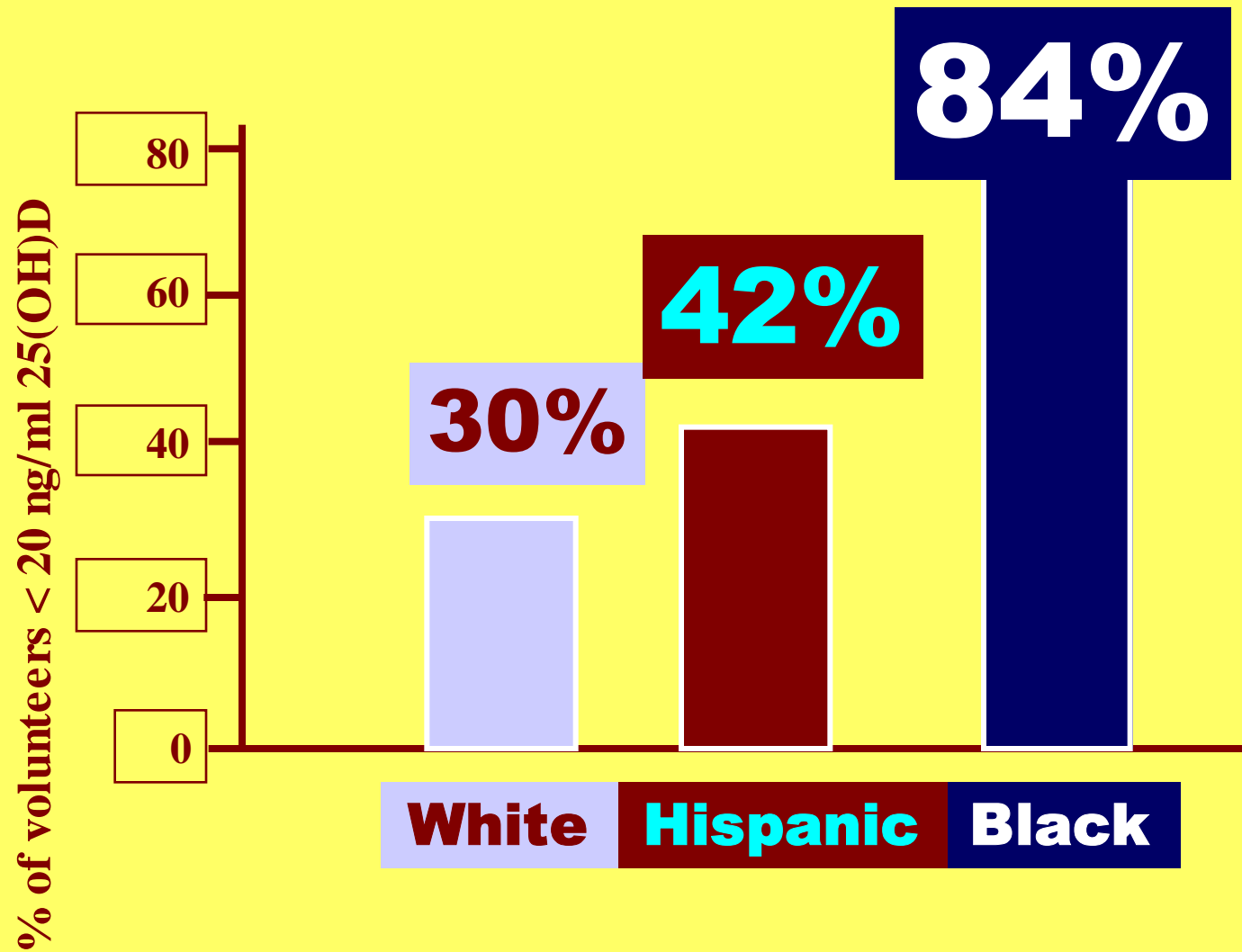


# AI for Vitamin D

**TOTALLY INADEQUATE  
NEED 1000 IU/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**

*Gloth et al JAMA, 1995*

**Vitamin D Deficiency**

**Is an**

**unrecognized**

**epidemic**

**in**

**adults 50+ yrs**

WHAT ABOUT

YOUNG ADULTS

????????????

CDC

42%

AFRICAN AMERICAN WOMEN  
IN US AGES 15-49Y <15NG/ML

VITAMIN D DEFICIENT

# BMC MEDICAL STUDENTS AND RESIDENTS 18-29 y

??

## VITAMIN D INSUFFICIENT

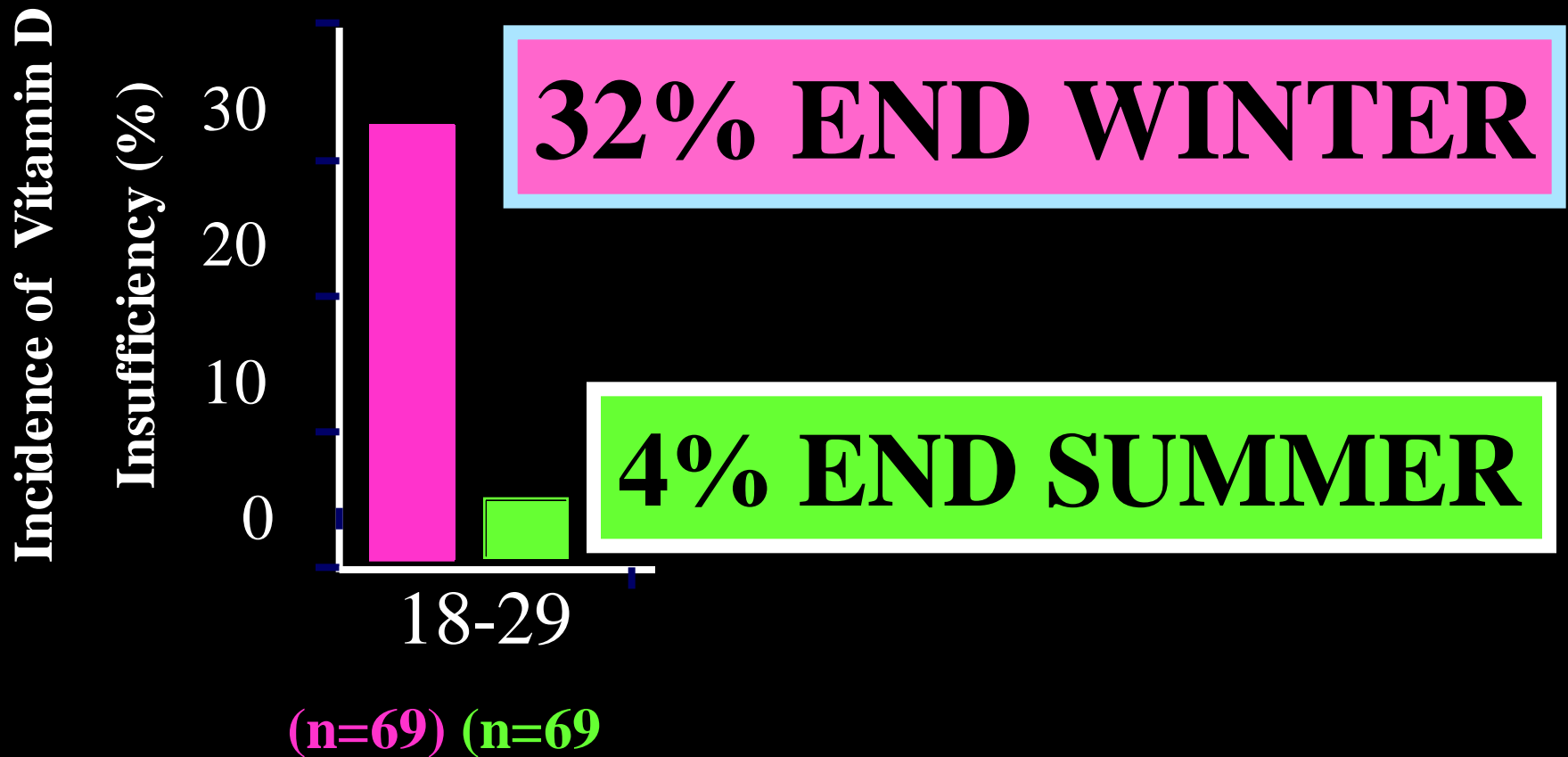
?????%

## VITAMIN D INSUFFICIENT





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



Tangpricha et al Am J Med 2002

# ARE WE AT RISK FOR VITAMIN D DEFICIENCY ???

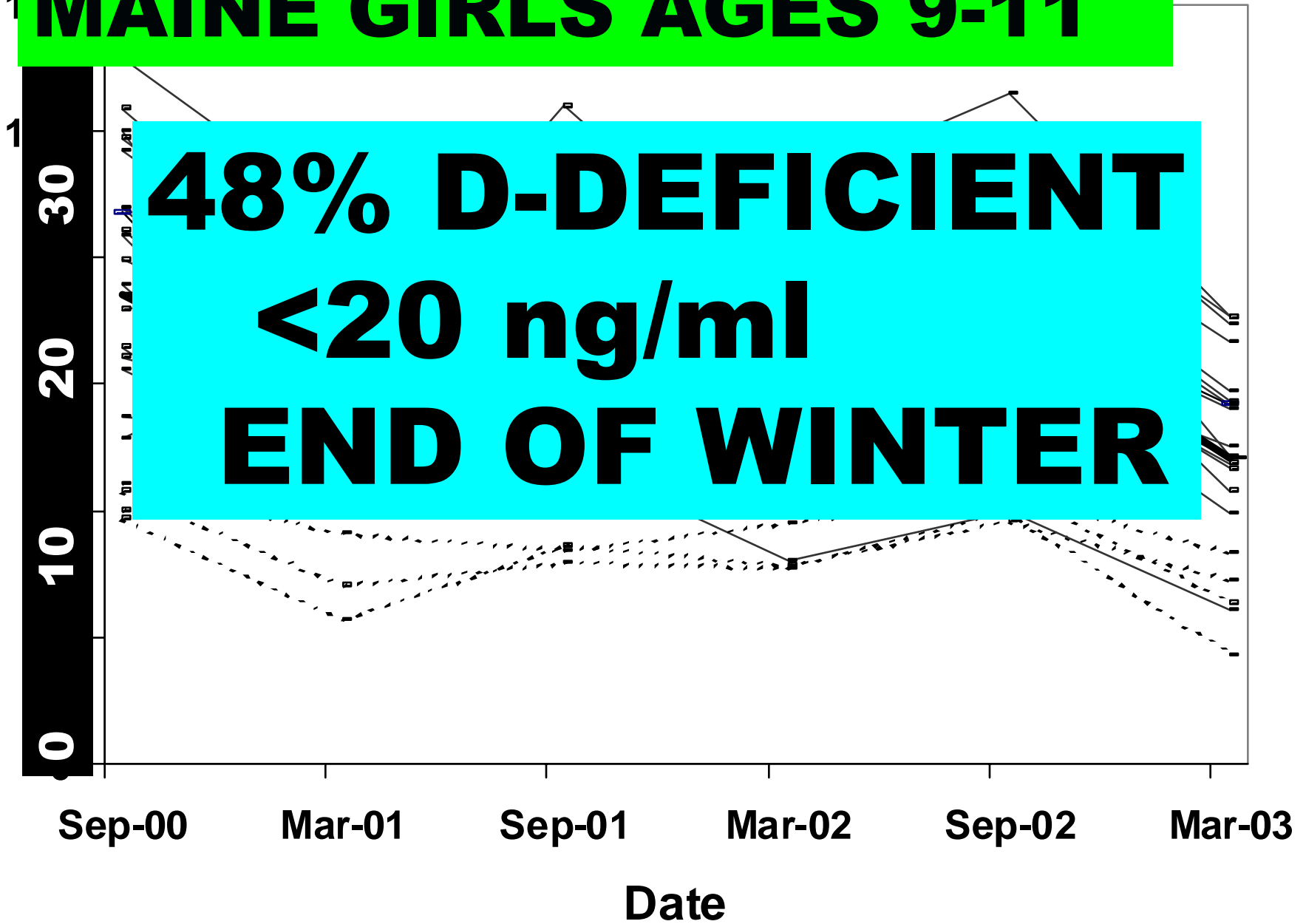


**BANGOR MAINE**

**25(OH)D NG/ML**

**MAINE GIRLS AGES 9-11**

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



**SULLIVAN, ROSEN, HOLICK**

**WHAT ABOUT  
END OF SUMMER  
?????????**

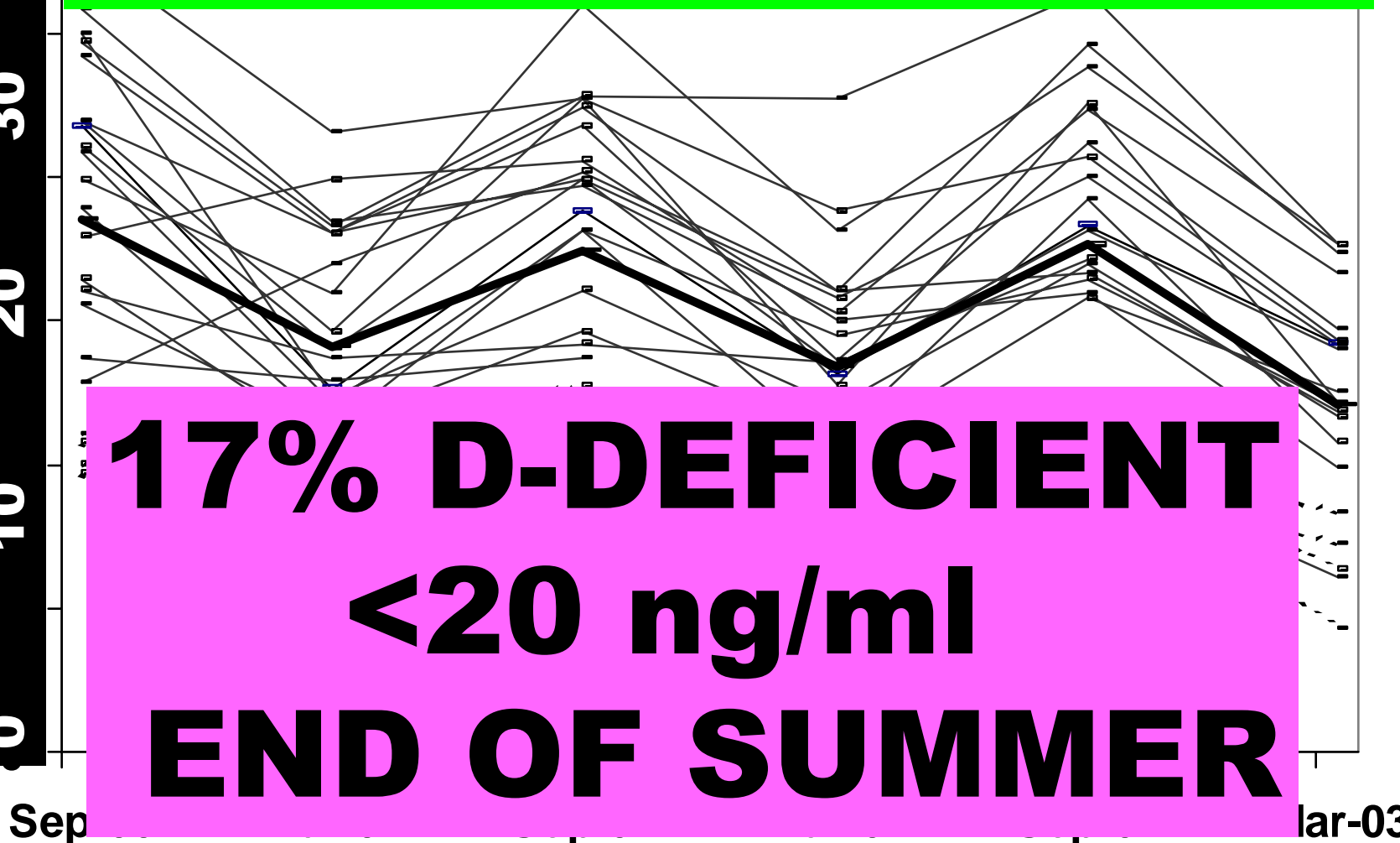


**I ALWAYS  
WEAR  
SUNSCREEN  
?????????**

25(OH)D NG/ML

40  
30  
20  
10  
0

**MAINE GIRLS AGES 9-11**



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

SULLIVAN,ROSEN,HOLICK

# BOSTON Herald

MONDAY, SEPTEMBER 1, 2003 ■ 50 CENTS (75 CENTS 30 MILES OUTSIDE BOSTON)

## Millions of children may be affected by vitamin D deficiency

By **LINDSEY TANNER**  
ASSOCIATED PRESS

CHICAGO — In some ways, Leon Jordan is a pretty typical teenager — he doesn't get much outdoor exercise, prefers movies and video games, and won't drink milk.

Those habits contributed to a vitamin D deficiency that has helped weaken the 18-year-old's bones and left him prone to fractures.

Doctors say it's an often overlooked problem that may affect millions of U.S. adolescents. Often undetected and untreated, vitamin D deficiency puts them at risk for stunted growth and debilitating osteoporosis later in life.

There's even evidence that chronic deficiency may be linked with some cancers, diabetes and

sorb sunlight as easily as whites.

Ironically, so are kids who follow the advice of moms and doctors to slather on sunscreen to avoid skin cancer, because it can block the absorption of ultraviolet rays.

But while too much sunlight is bad, ultraviolet rays also interact with chemicals in the skin to produce vitamin D. Holick recommends kids spend about 10 minutes a few times a week in the sun without sunscreen.

"We get into lively debates with dermatologists because they say we should all have sunscreen on all the time," said Dr. Catherine Gordon, a Boston pediatric endocrinologist who has many patients with vitamin D deficiency.

Her recent research suggests as many as 20 percent of healthy children in Boston may be vitamin D

# Prevalence of Vitamin D Deficiency Among Healthy Adolescents

*Catherine M. Gordon, MD, MSc; Kerrin C. DePeter, BA; Henry A. Feldman, PhD;  
Estherann Grace, MD; S. Jean Emans, MD*

52% D-deficient

<20 ng/ml

**OSTEOPOROSIS**

**IS OFTEN A**

**SILENT DISEASE**



# **Subclinical**

## **Vitamin D Deficiency**

**CAUSES DEFECTS  
IN BONE  
MINERALIZATION  
OSTEOMALACIA**

**OSTEOMALACIA**

**IS NOT A**

**SILENT DISEASE**

# Symptoms

- Generalized bone pain
- Isolated bone pain
- Muscle aches



40-60% OSTEOMALACIA

***FIBROMYALGIA***

# *Mayo Clinic Proceedings*

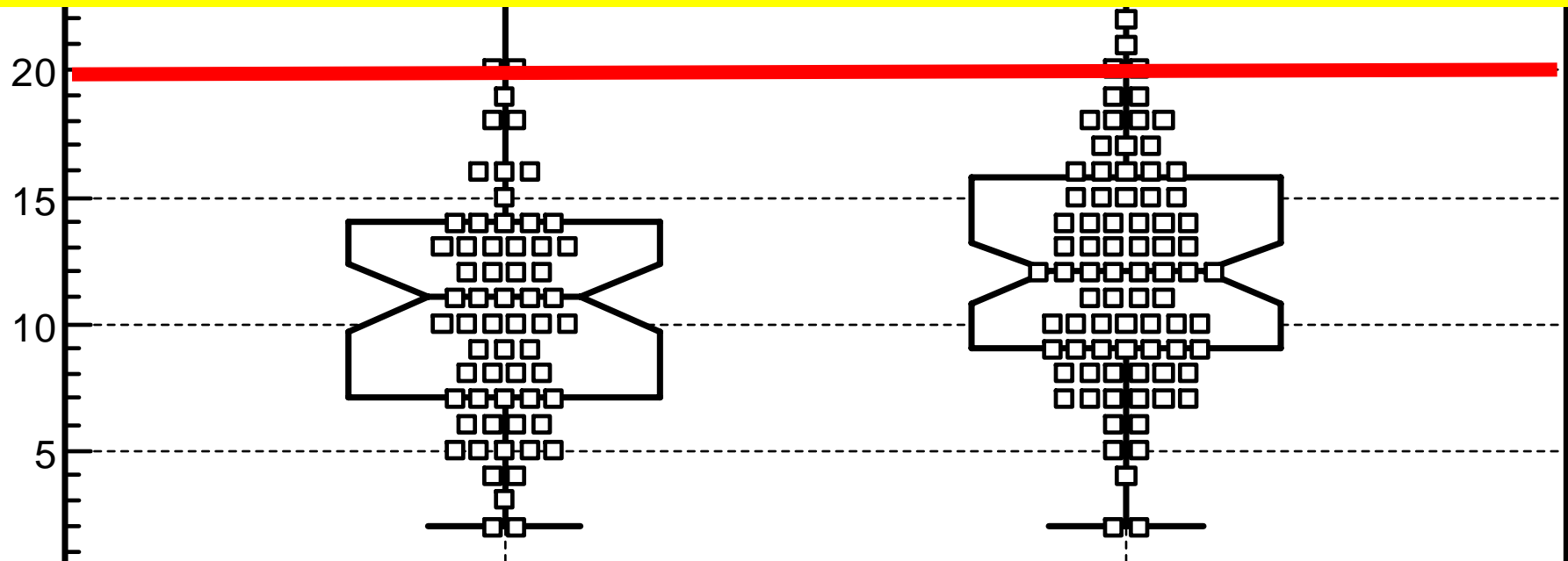
**Original Article**

## **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

# 150 aged 10-65 yrs Bone & Muscle Pains



**93% Vitamin D Deficient**

**Higher 25-hydroxyvitamin D concentrations are associated with better lower-extremity function in both active and inactive persons aged  $\geq 60$  y<sup>1,2,3</sup>**

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

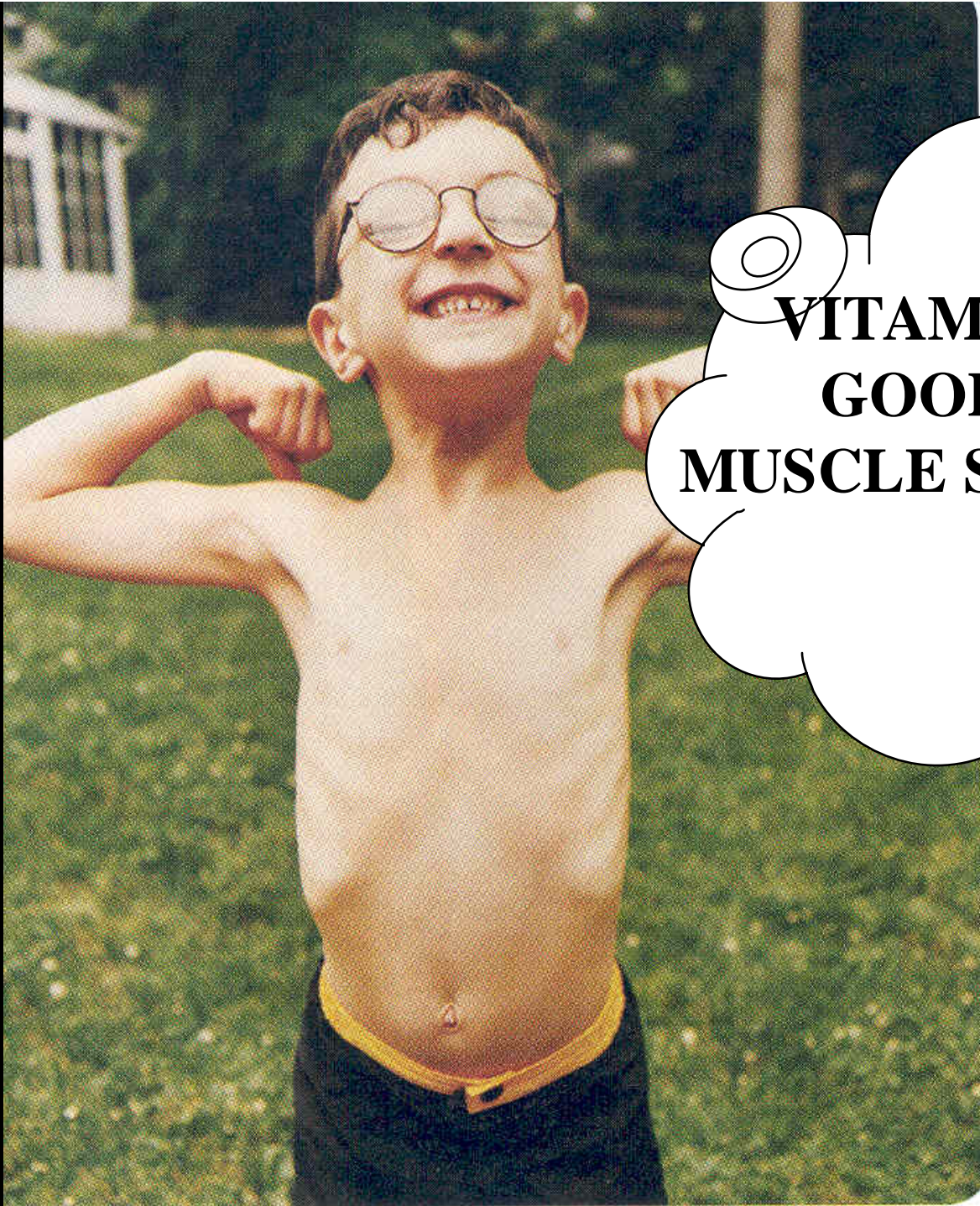
# Rickets







**DID YOU KNOW  
VDR IS IN  
SKELETAL MUSCLE  
!!!**

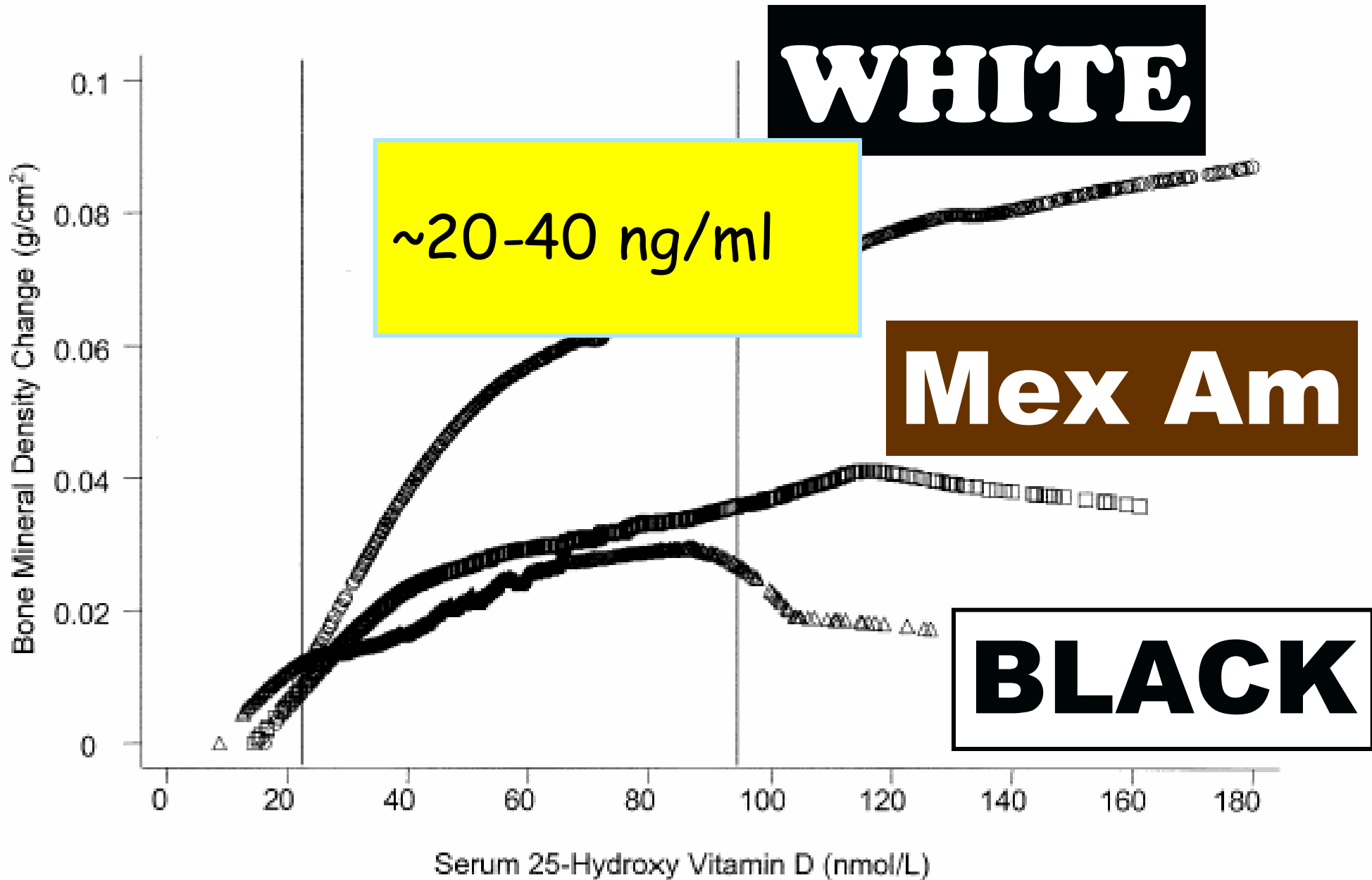


**VITAMIN D IS  
GOOD FOR  
MUSCLE STRENGTH**

# **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

*25-Hydroxy Vitamin D Levels and Bone Mineral Density/Bischoff-Ferrari et al*



**HOW DO YOU TREAT**

**VITAMIN D DEFICIENCY ?????**

# HOW MANY???

400 IU

TOO MUCH  
VITAMIN A

1,2,4,10,20??????????

**DO YOU PURCHASE  
GALLON OF GAS ???**



**TREAT VITAMIN D DEFICIENCY**

**50,000 IU VITAMIN D<sub>2</sub>**

**ONCE/WEEK**

**8 WEEKS**

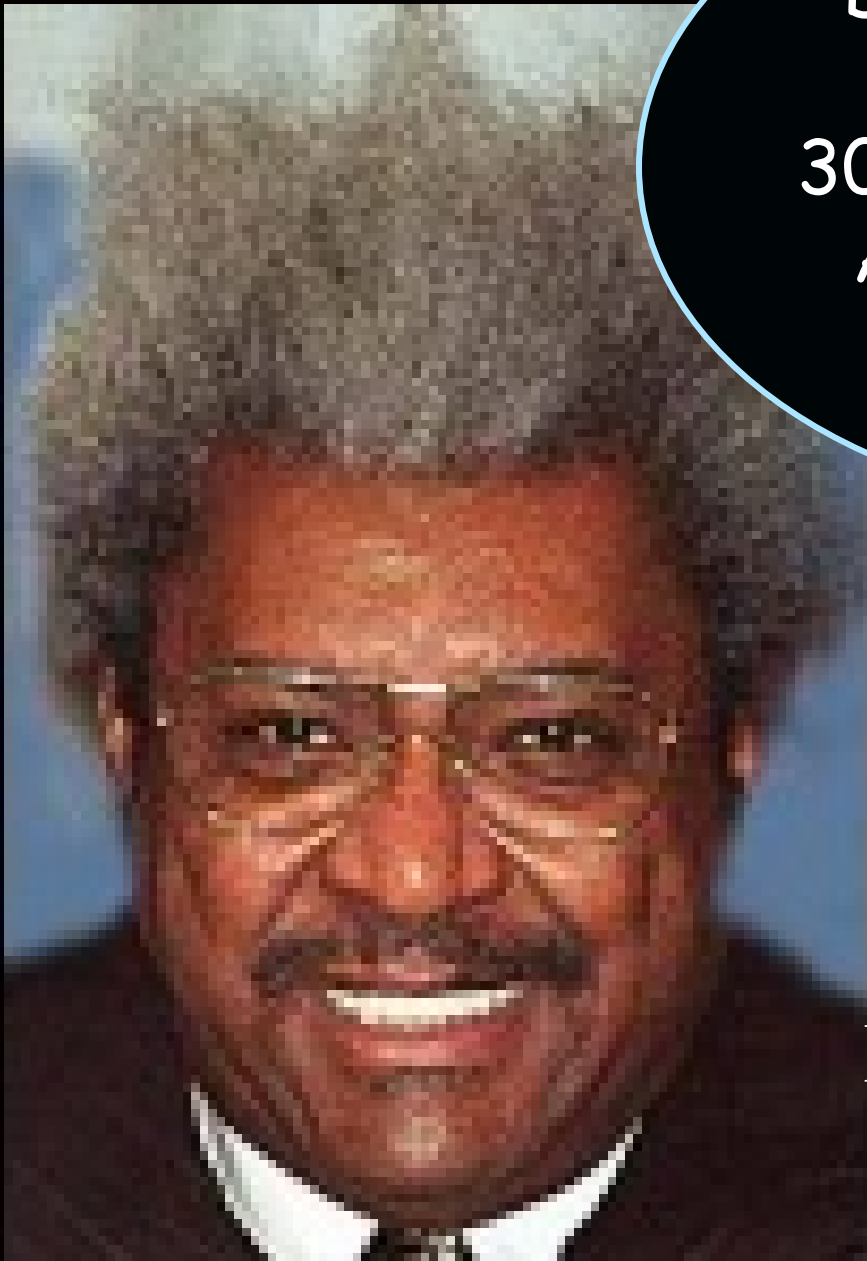




**MAINTAIN VITAMIN D SUFFICIENCY**

**50,000 IU VITAMIN D**

**ONCE/ 2WEEKS**



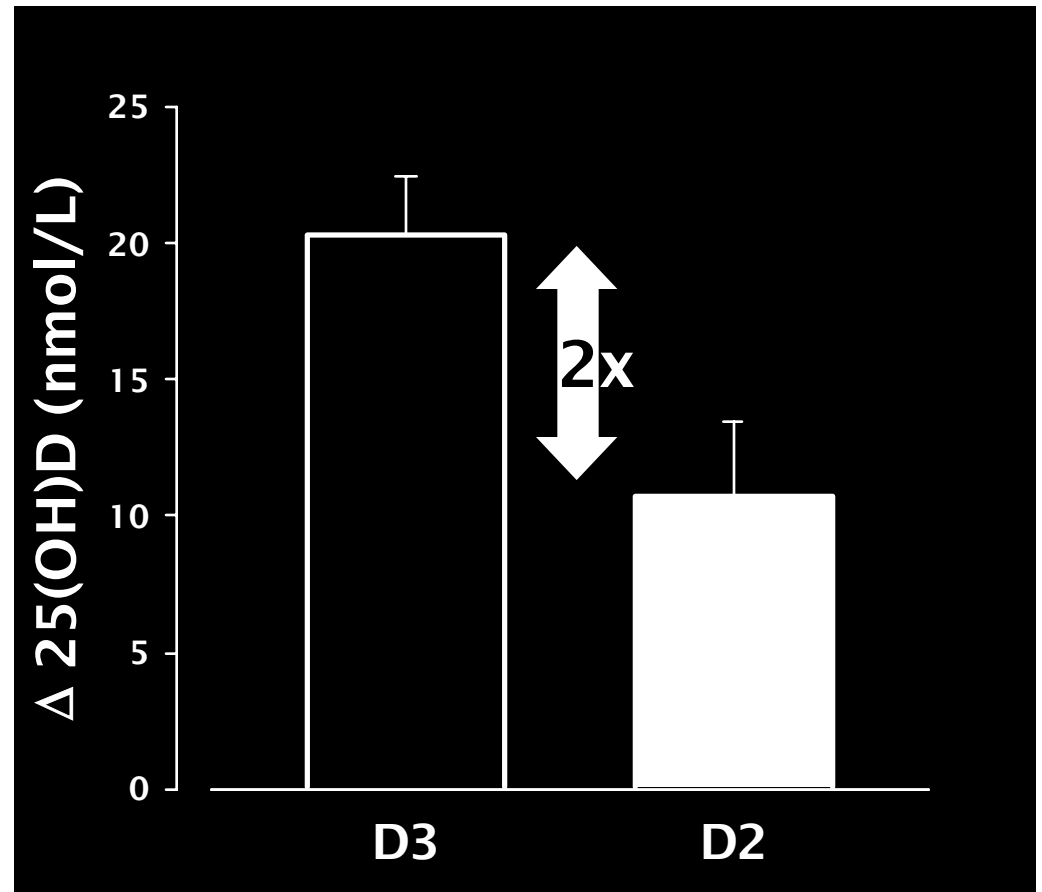
DID YOU KNOW  
VITAMIN D2 is  
30% as EFFECTIVE  
As VITAMIN D3

!!!!!!!

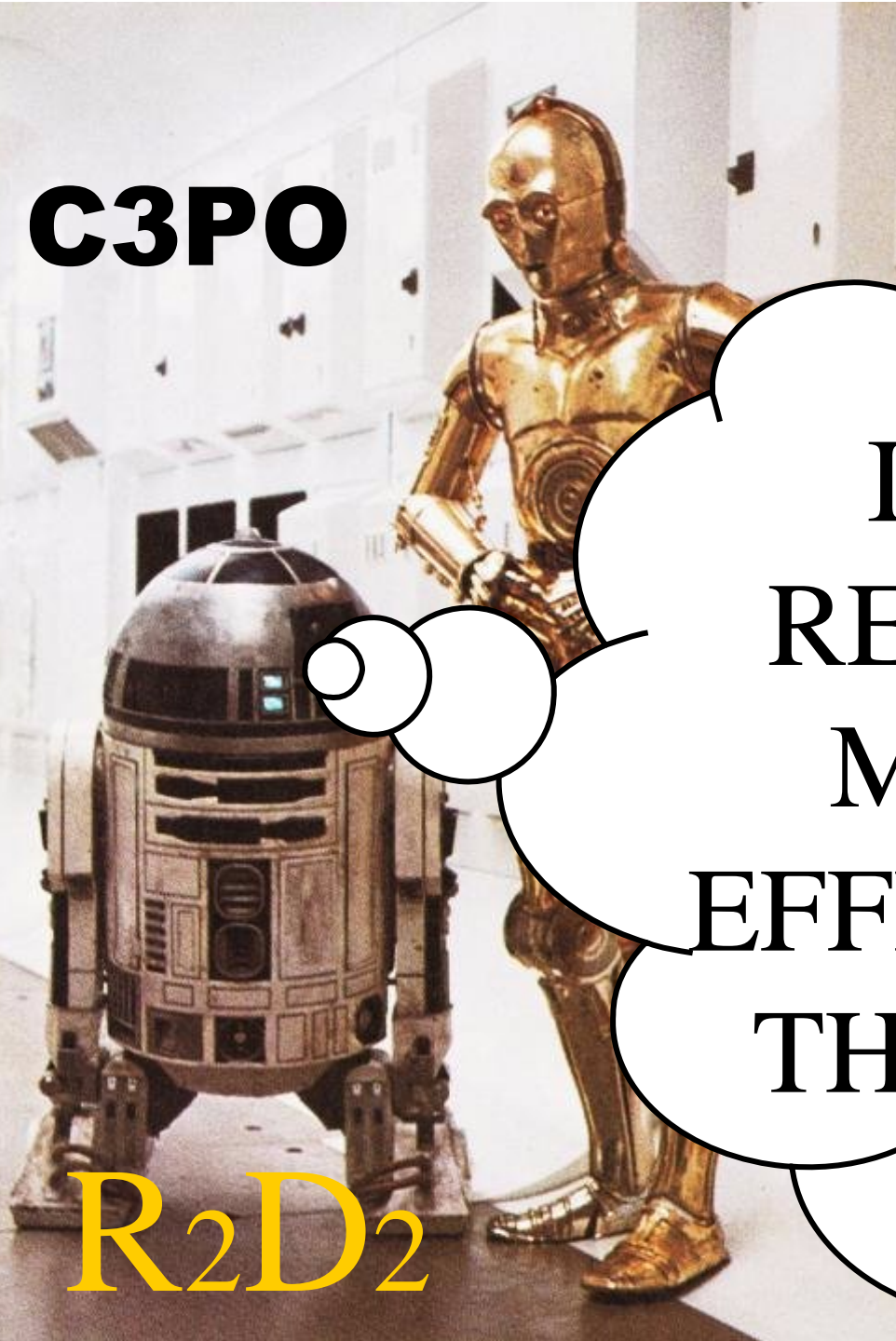
Heaney et al 2005

# VITAMIN D<sub>2</sub> vs. VITAMIN D<sub>3</sub>

- 4,000 IU/d either D<sub>2</sub> or D<sub>3</sub> **IN ETOH**
- 14 days
- values adjusted for change in untreated group
- [after Trang et al. *AJCN*; 68:854-8 (1998)]



**C3PO**

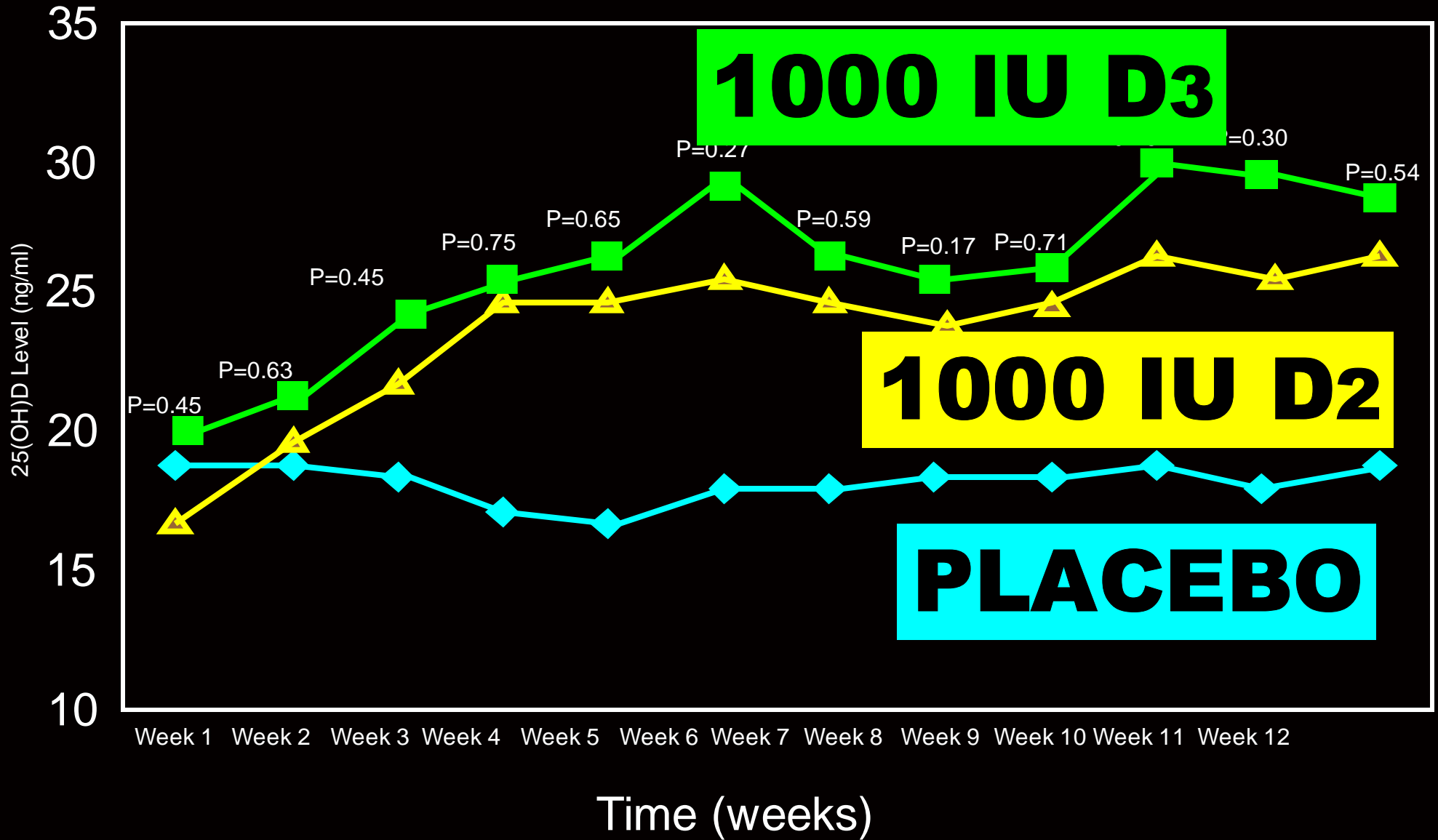


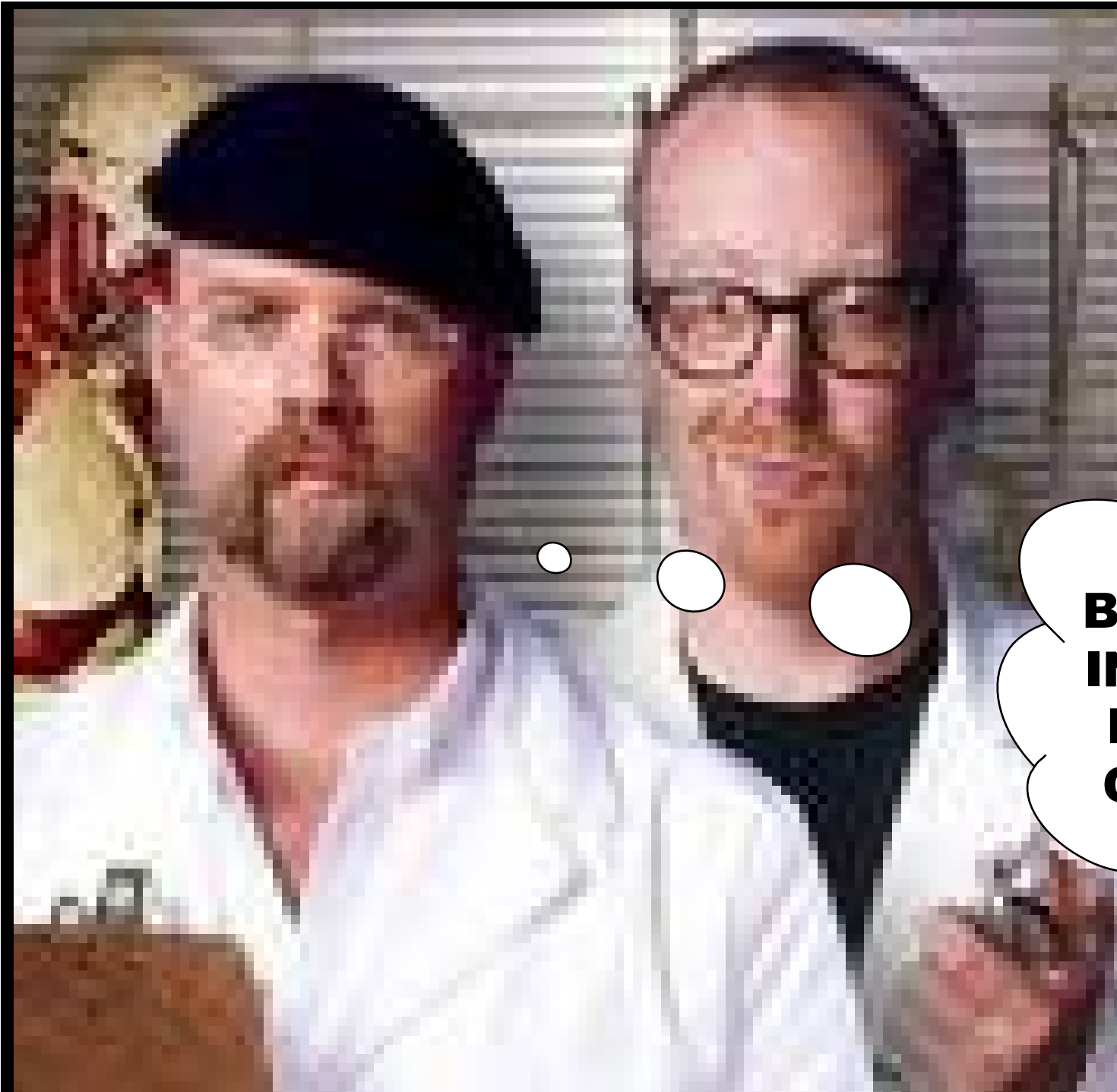
**R2D2**

IS D3  
REALLY  
MORE  
EFFECTIVE  
THAN D2  
????



# Mean Serum Total 25(OH)D Levels

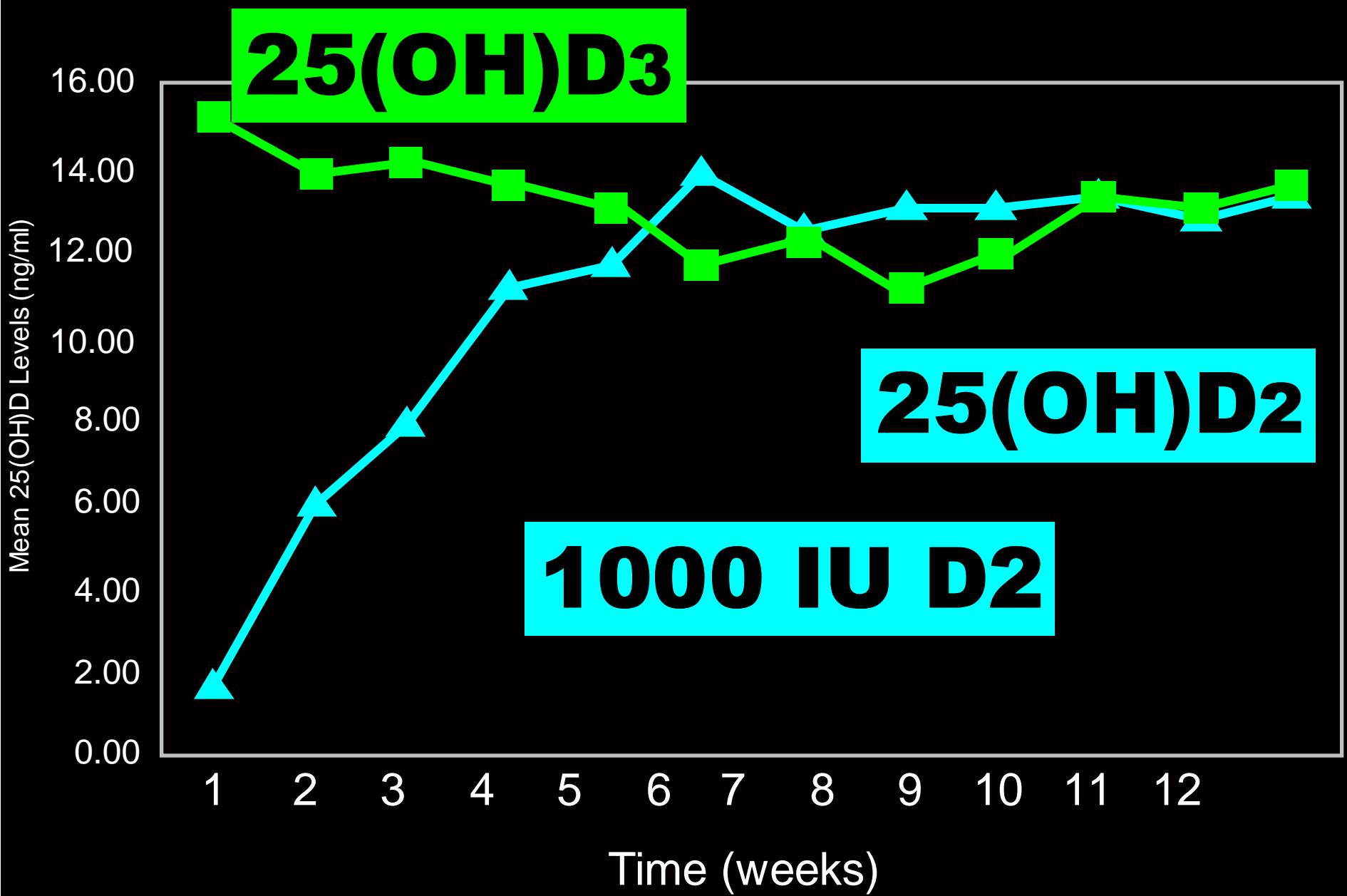





**BUT VITAMIN D<sub>2</sub>  
INCREASES THE  
DESTRUCTION  
OF VITAMIN D<sub>3</sub>  
!!!!!!!**




**Mean Serum 25(OH)D<sub>2</sub> and 25(OH)D<sub>3</sub> in Subjects receiving Vitamin D<sub>2</sub>**





**VITAMIN D3  
REALLY IS NO BETTER  
THAN VITAMIN D2  
???????**

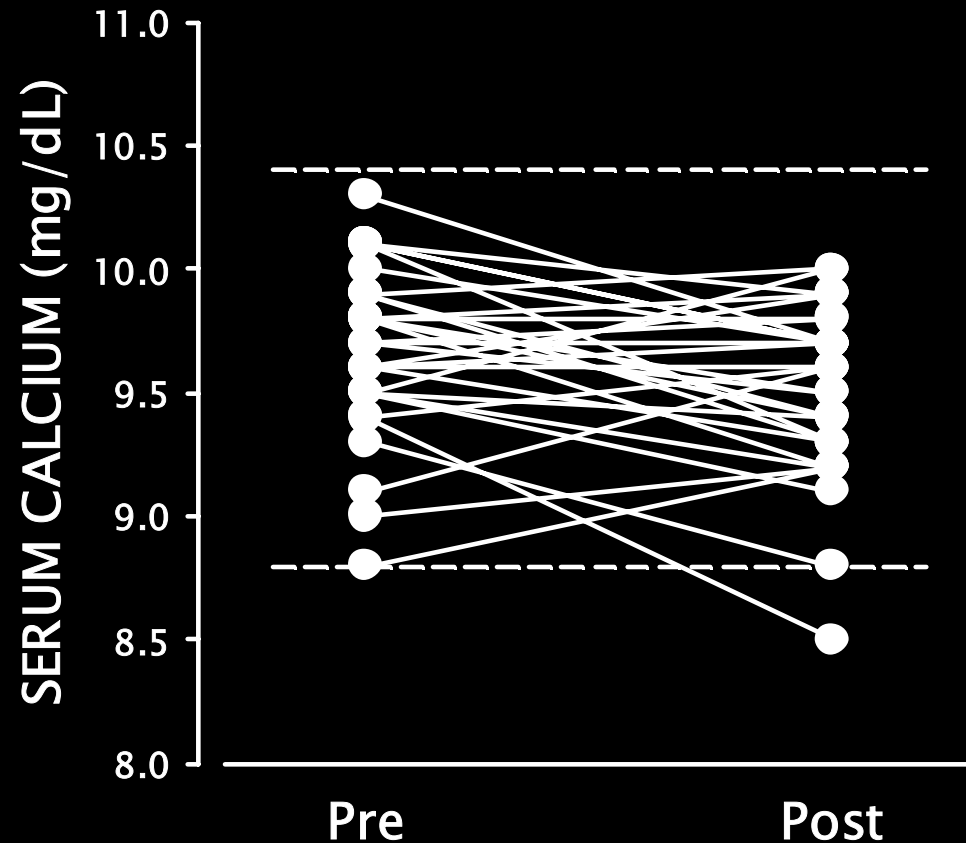
**BUSTED**



**WILL YOU BECOME  
VITAMIN D  
INTOXICATED  
????**

# SAFETY AT HIGH DOSES

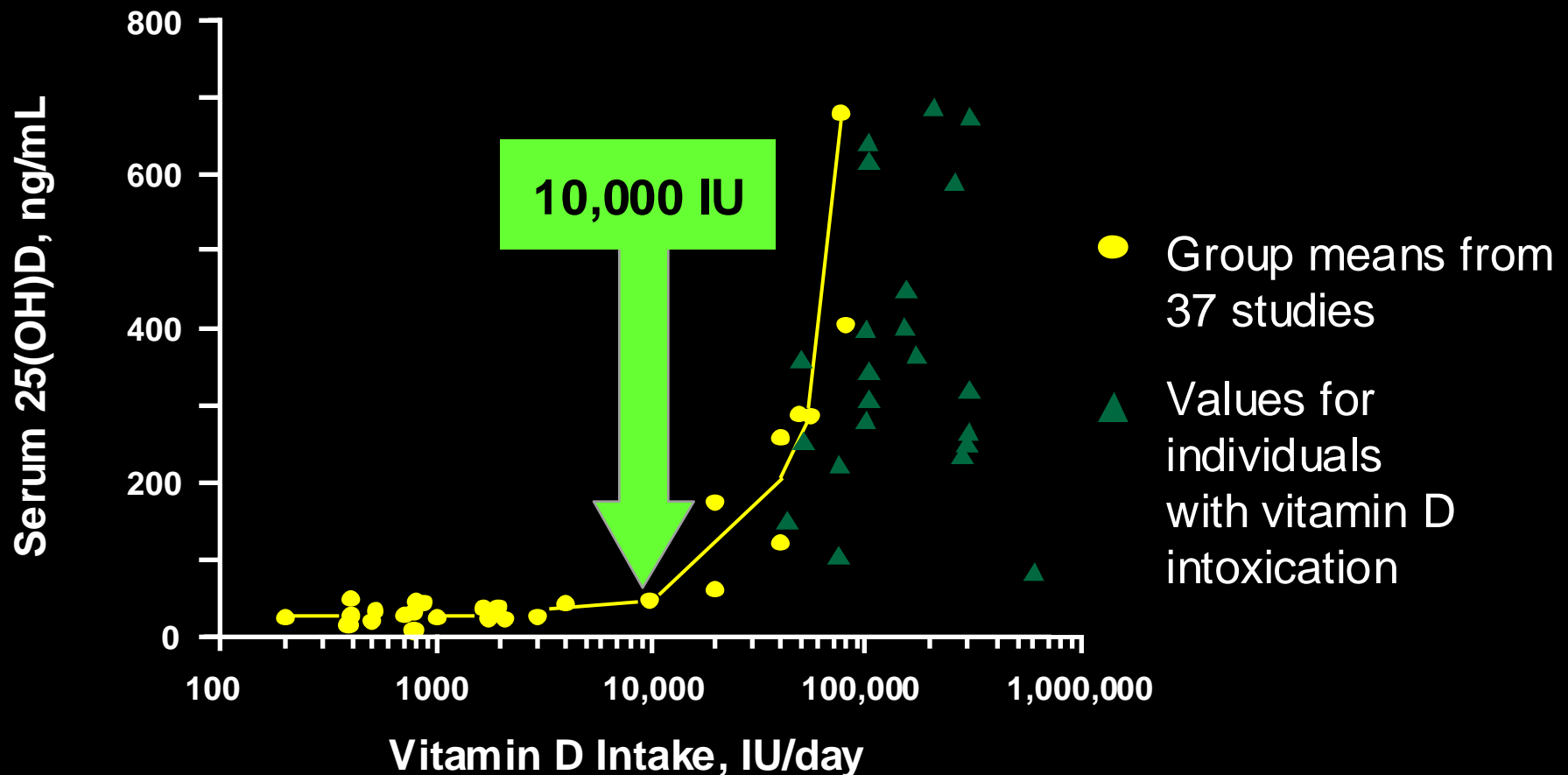
- 33 males
- aged 38.7 yr ( $\pm 11.2$ )
- dosed with vit D<sub>3</sub> from October thru February
- 5,000 & 10,000 IU/d




Vieth et al 1998


# Vitamin D Intoxication Occurred at Doses Over 10,000 IU Daily: Survey of 37 Clinical Studies

Serum 25(OH)D levels were maintained between 30 and 88 ng/mL at vitamin D intakes from 800 to 10,000 IU/day





**IT IS  
DIFFICULT  
TO BECOME  
VITAMIN D  
INTOXICATED**

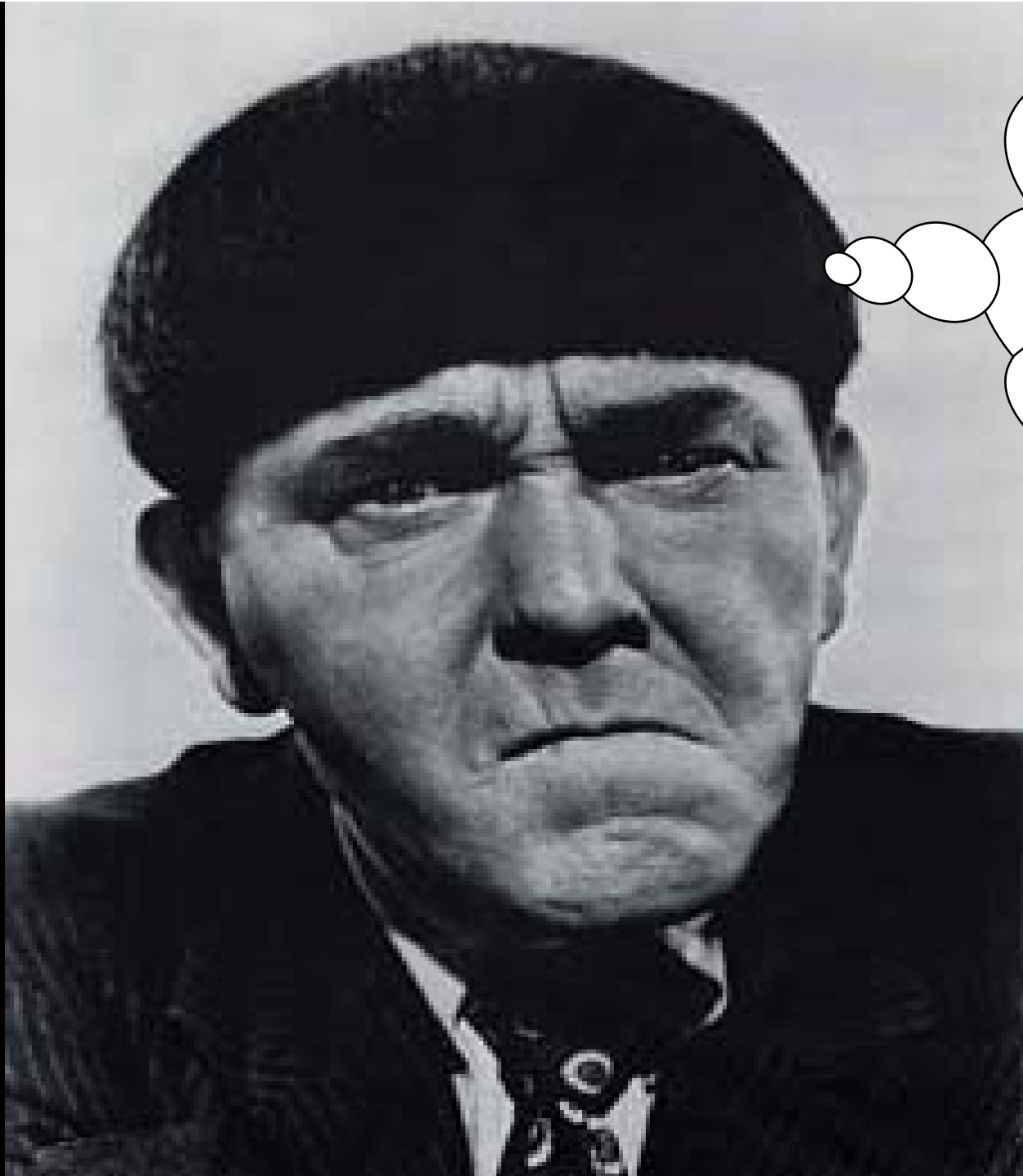
A man with short, dark hair, wearing a dark suit jacket, a white shirt, and a dark tie. He has a thoughtful expression. A large, white, cloud-shaped thought bubble is positioned to the left of his face, containing text. Three smaller circles lead from the bottom of the thought bubble to his chin.

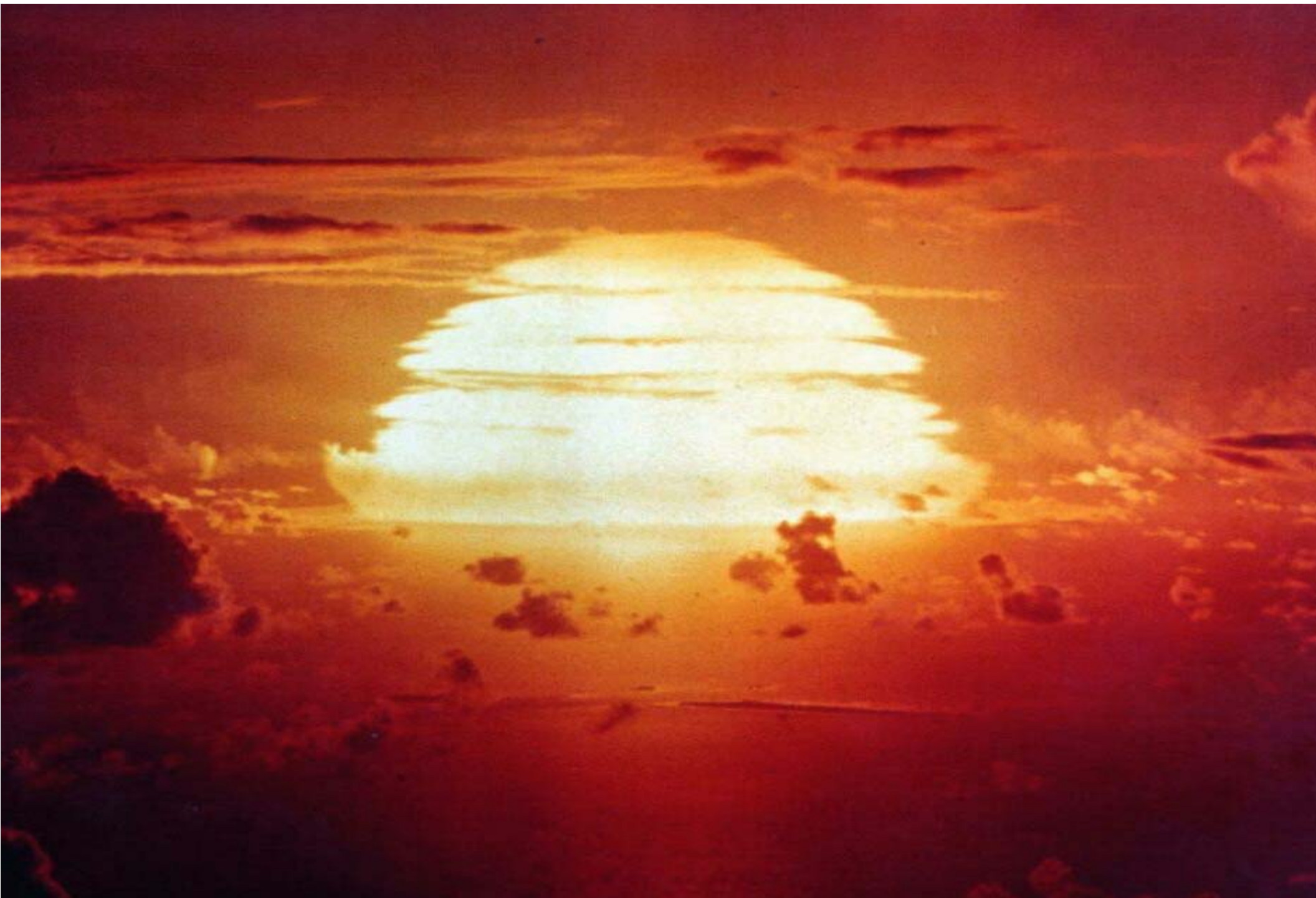
**WHO IS AT  
RISK FOR  
VITAMIN D  
DEFICIENCY  
?????????**

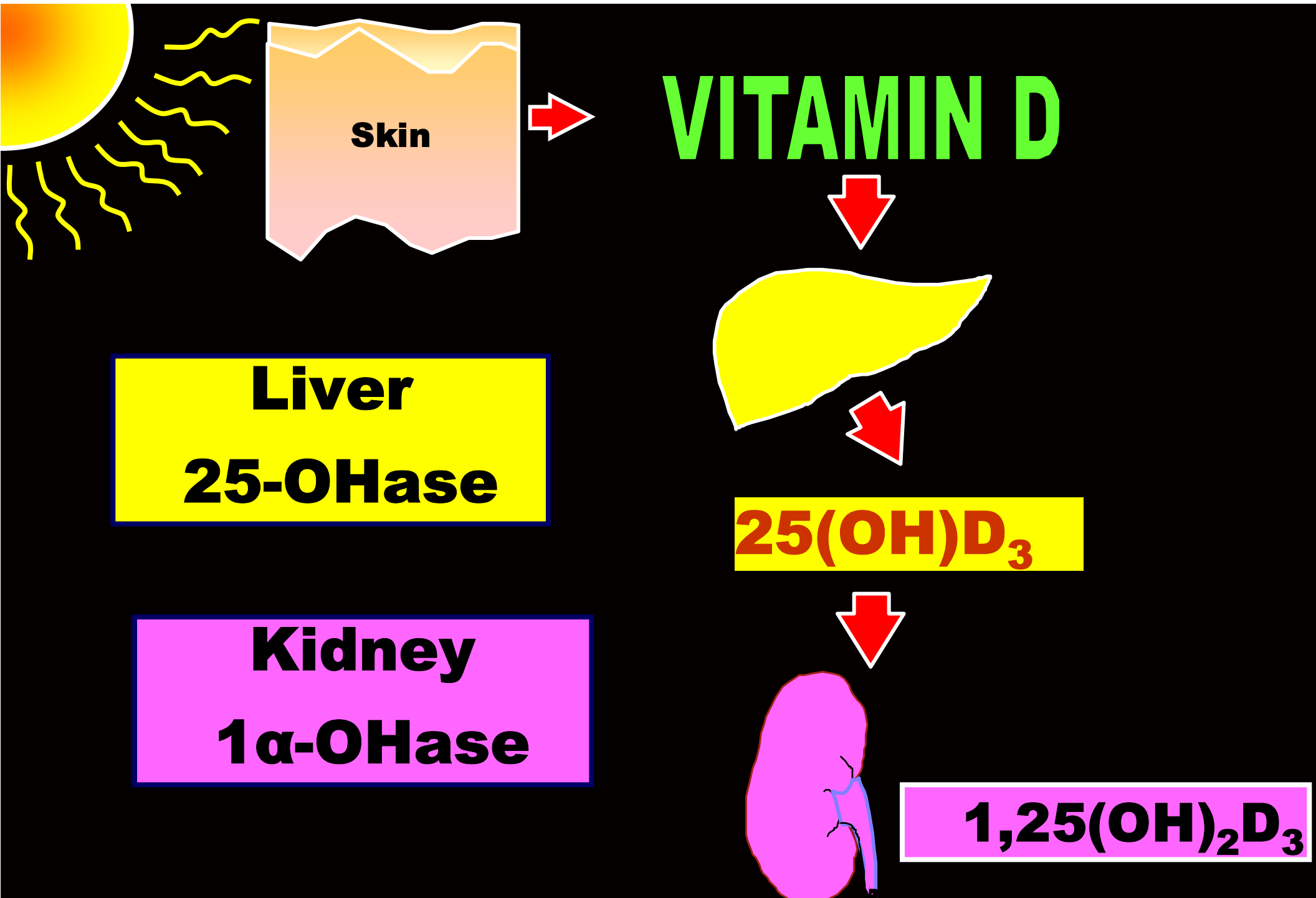


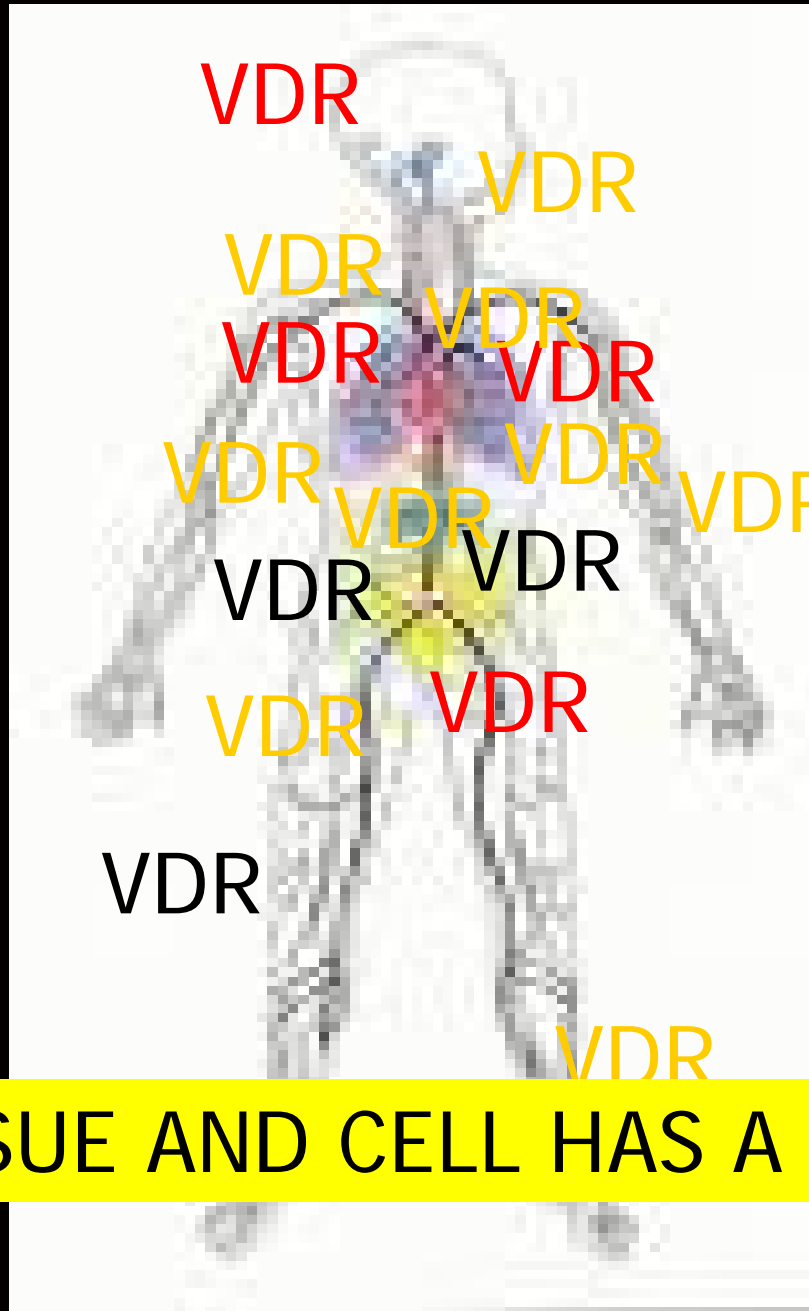
**EVERYONE**  
**!!!!!!!!!!!!!!**











**EVERY TISSUE AND CELL HAS A VDR**

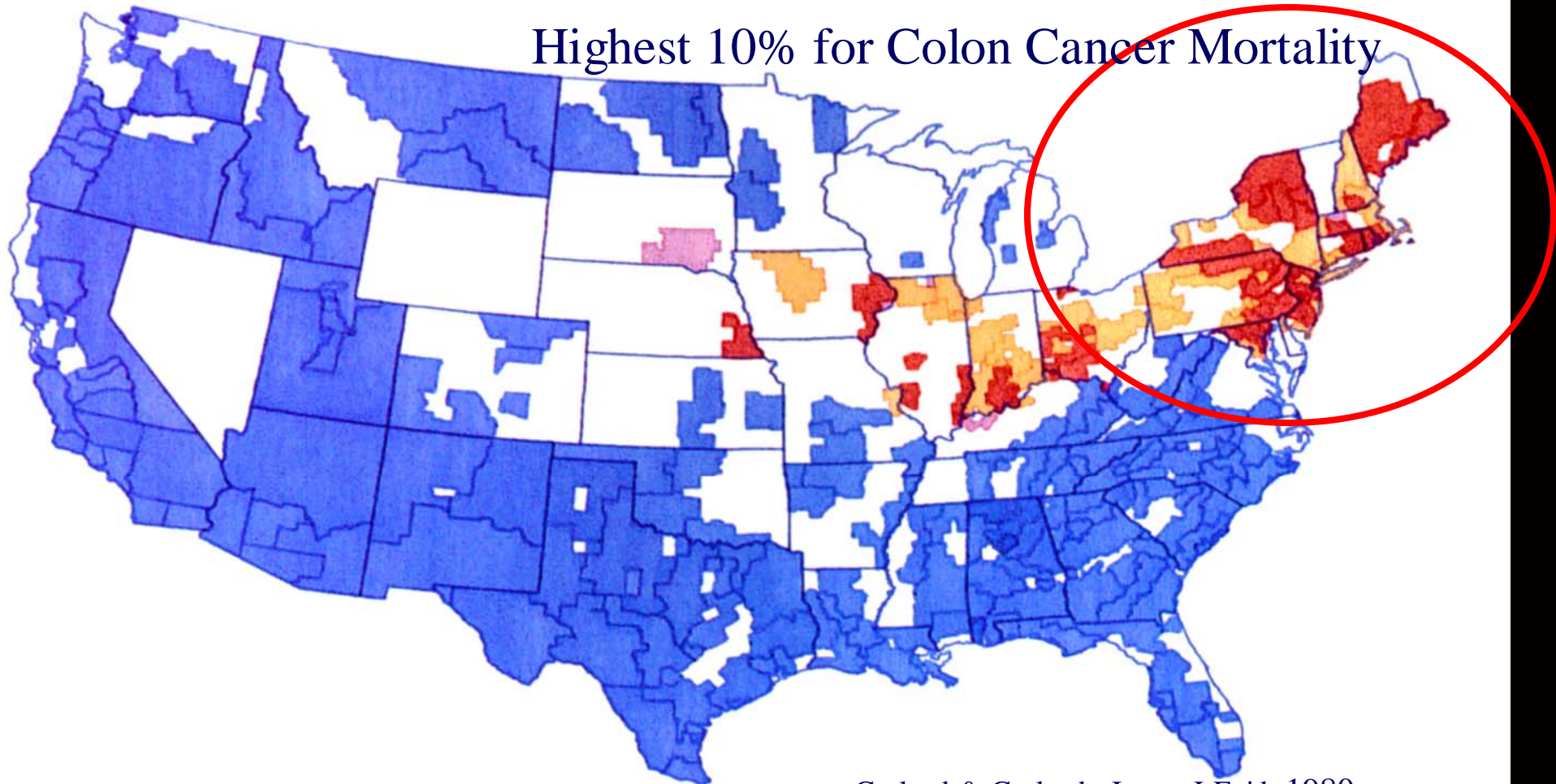
VITAMIN D

&

CANCER

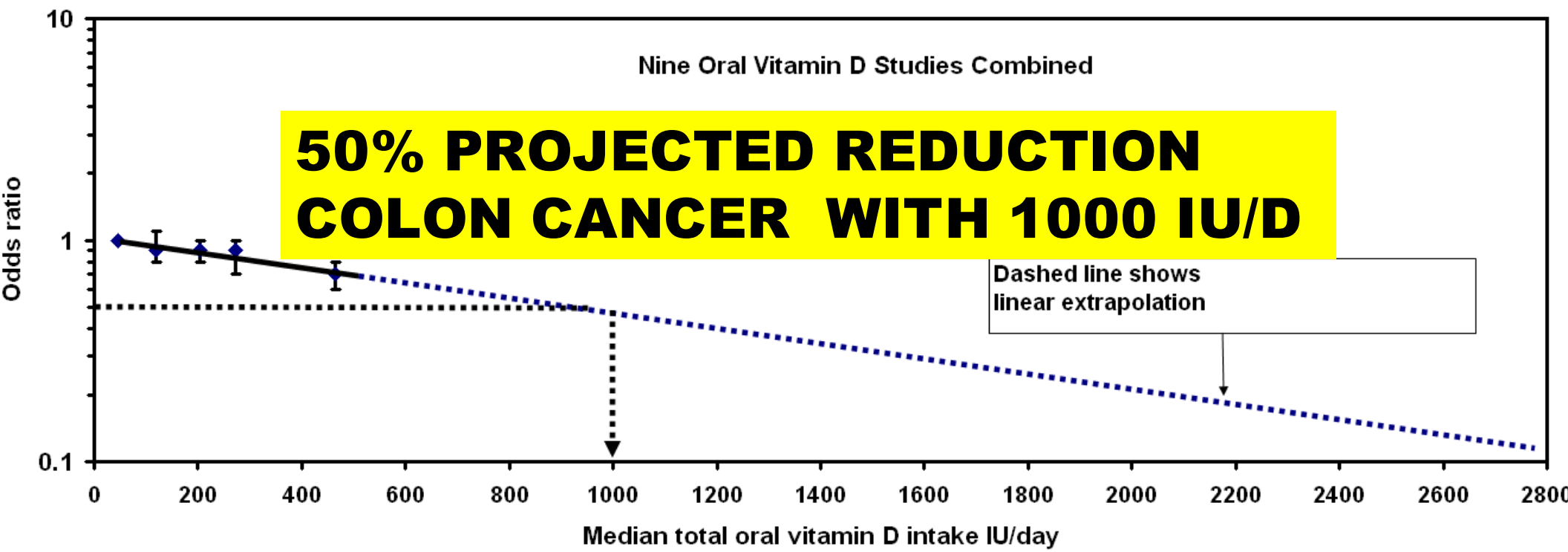
# Colon Cancer Mortality Rates 1970-80 in White Females

Highest 10% for Colon Cancer Mortality



Garland & Garland. Intern J Epid. 1980

**DIE WITH COLON CANCER**



# COLON CANCER

25(OH)D

>20ng/ml

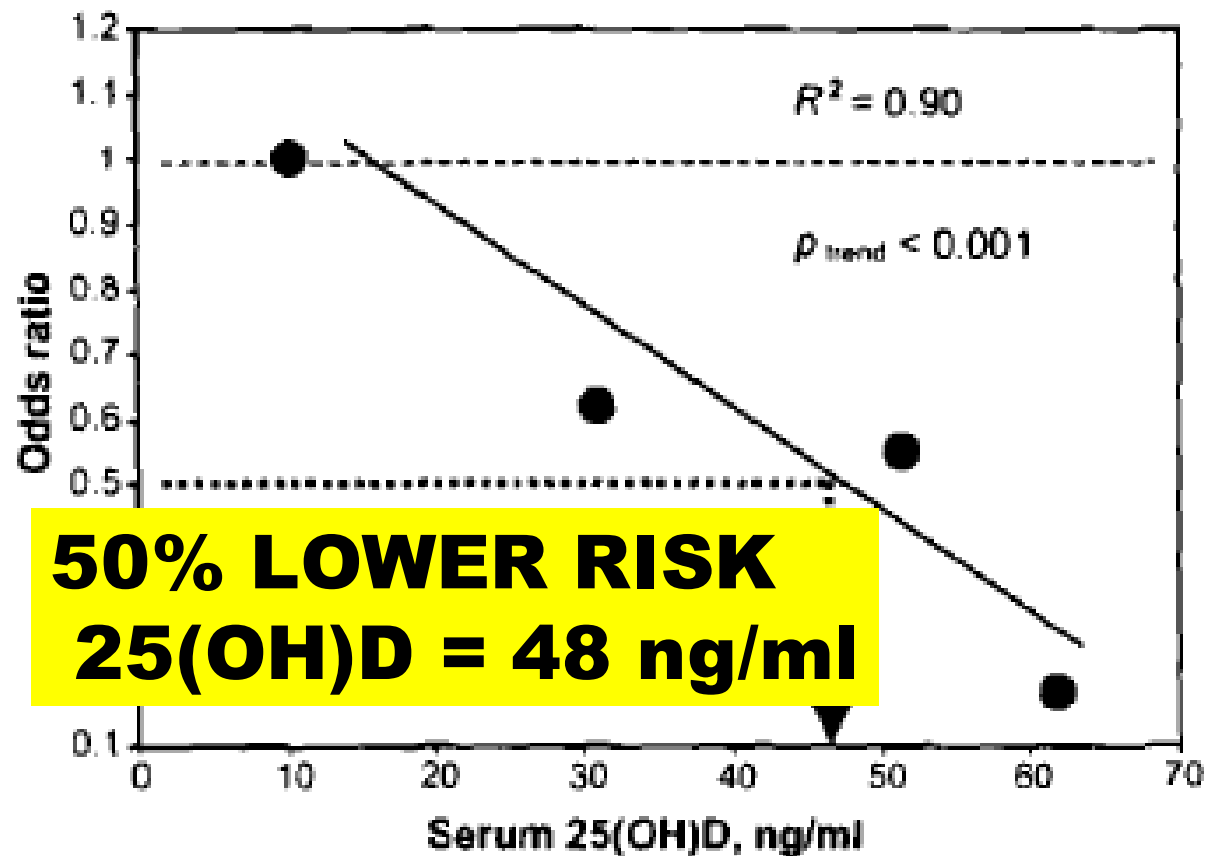
R  
I  
S  
K

50%



# Vitamin D and prevention of breast cancer: Pooled analysis

Cedric F. Garland<sup>a,\*</sup>, Edward D. Gorham<sup>a</sup>, Sharif B. Mohr<sup>a</sup>, William B. Grant<sup>b</sup>,  
Edward L. Giovannucci<sup>c</sup>, Martin Lipkin<sup>d</sup>, Harold Newmark<sup>e,f</sup>,  
Michael F. Holick<sup>g</sup>, Frank C. Garland<sup>a</sup>



ORIGINAL ARTICLE

# Calcium plus Vitamin D Supplementation and the Risk of Colorectal Cancer

▶ Top Worldwide

▼ Regions

└ Asia

└ Australia & New Zealand

└ Canada

└ Europe

└ Germany

└ Japan

└ Latin America

└ U.K.

└ **U.S.**

▶ Markets

▶ Economy/Politics

▶ Commentary

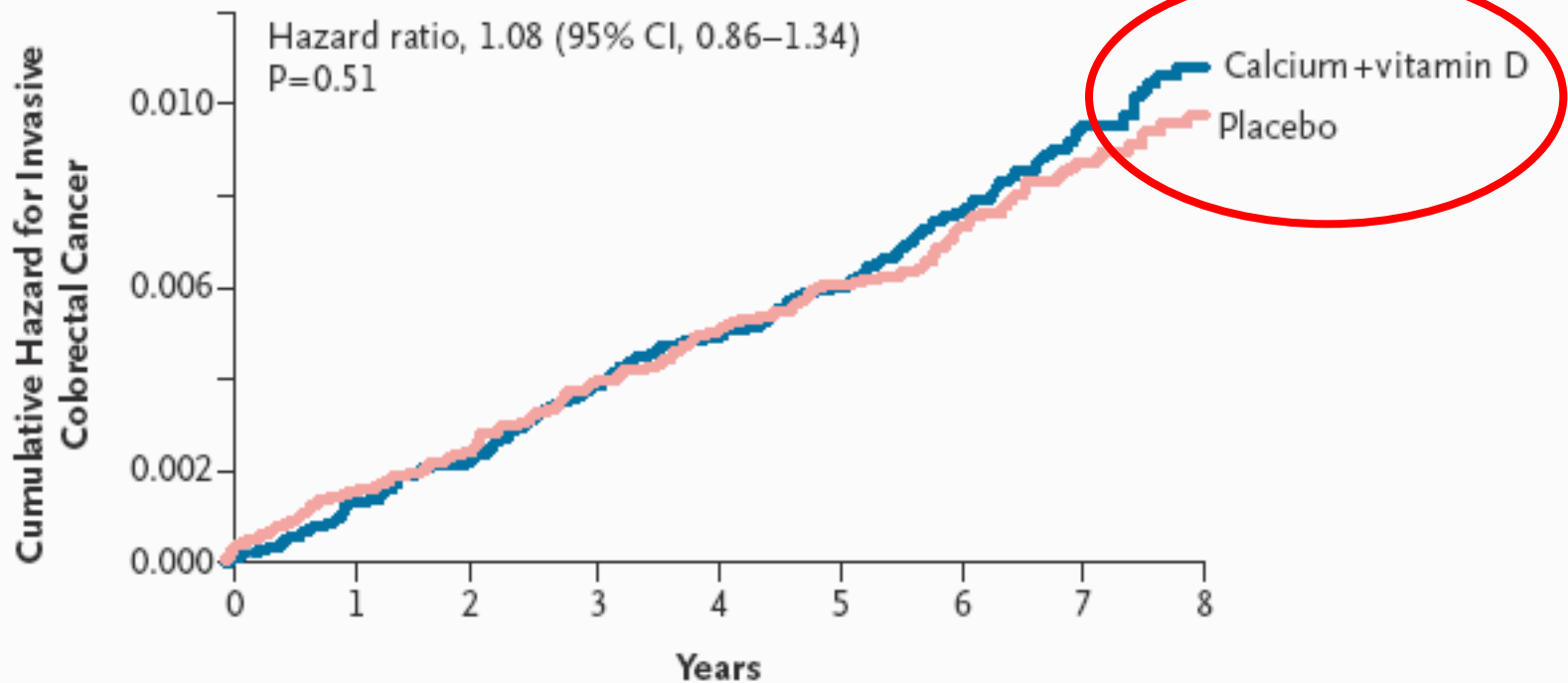
**U.S.**

▶ ✉ E-Mail This Story ▶ 🖨️ Printer-Friendly Fo

## Calcium, Vitamin D Supplements Don't Cut Fracture, Cancer Risk

Feb. 15 (Bloomberg) -- Calcium and vitamin D supplements failed to prevent fractures in older women in a large U.S.-funded study that casts doubt on a bedrock therapy for women whose bones weaken after menopause.

The results from the \$725 million Women's Health Initiative, published in the New England Journal of Medicine, show supplements boost bone density and kidney stone risk without substantially cutting fracture rates. A related study found the supplements didn't prevent colorectal cancer,



#### Calcium+vitamin D

|               |        |        |        |        |        |        |        |      |      |
|---------------|--------|--------|--------|--------|--------|--------|--------|------|------|
| No. of events | 0      | 23     | 17     | 28     | 20     | 19     | 27     | 23   | 9    |
| No. at risk   | 18,176 | 18,048 | 17,936 | 17,780 | 17,605 | 17,248 | 14,680 | 9138 | 4403 |

#### Placebo

|               |        |        |        |        |        |        |        |      |      |
|---------------|--------|--------|--------|--------|--------|--------|--------|------|------|
| No. of events | 0      | 27     | 16     | 27     | 20     | 18     | 20     | 17   | 7    |
| No. at risk   | 18,106 | 17,967 | 17,832 | 17,663 | 17,471 | 17,093 | 14,530 | 9041 | 4351 |

**Figure 3.** Kaplan–Meier Estimates of the Cumulative Hazard for Invasive Colorectal Cancer with Supplemental Calcium plus Vitamin D, as Compared with Placebo.

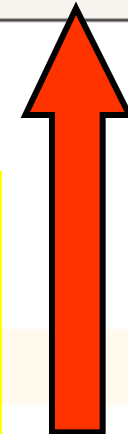
CI denotes confidence interval. Two events in each group that occurred after year 8 are not shown.

**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 Nested Case–Control Study.\*

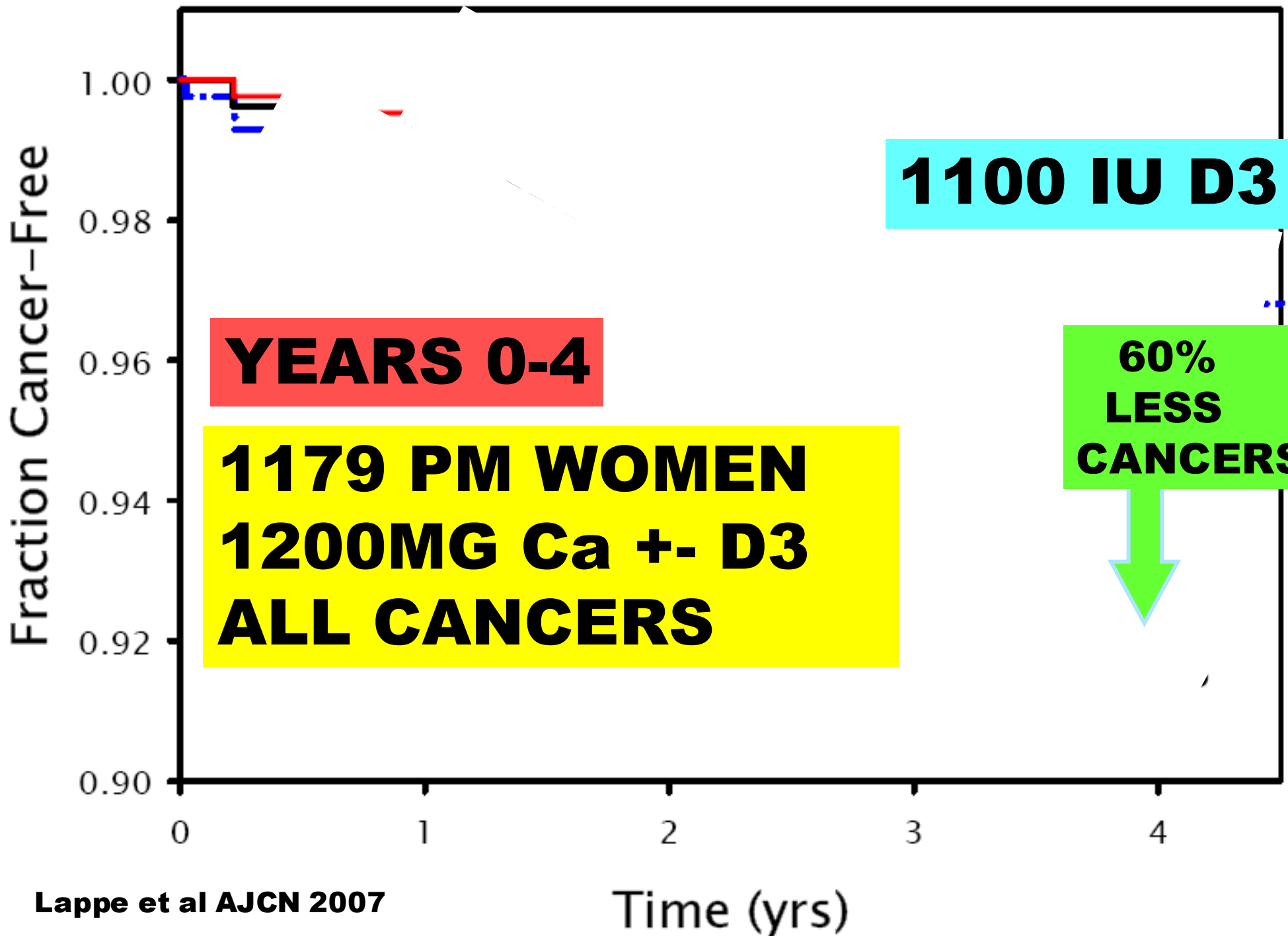
| Baseline Serum 25-Hydroxyvitamin D | Main-Effect Odds Ratio (95% CI) <sup>†</sup> | Calcium+ Vitamin D | Placebo |
|------------------------------------|--|--------------------|---------|
| ≥58.4 nmol/liter                   | 1.00   |                    |         |
| 42.4–58.3 nmol/liter               | 1.96 (1.18–3.24)                             |                    |         |
| 31.0–42.3 nmol/liter               | 1.95 (1.18–3.24)                             | 35/32              | 45/41   |
| <31.0 nmol/liter                   | 2.53 (1.49–4.32)                             |                    | 42/28   |

**253%**

**<12 ng/ml**

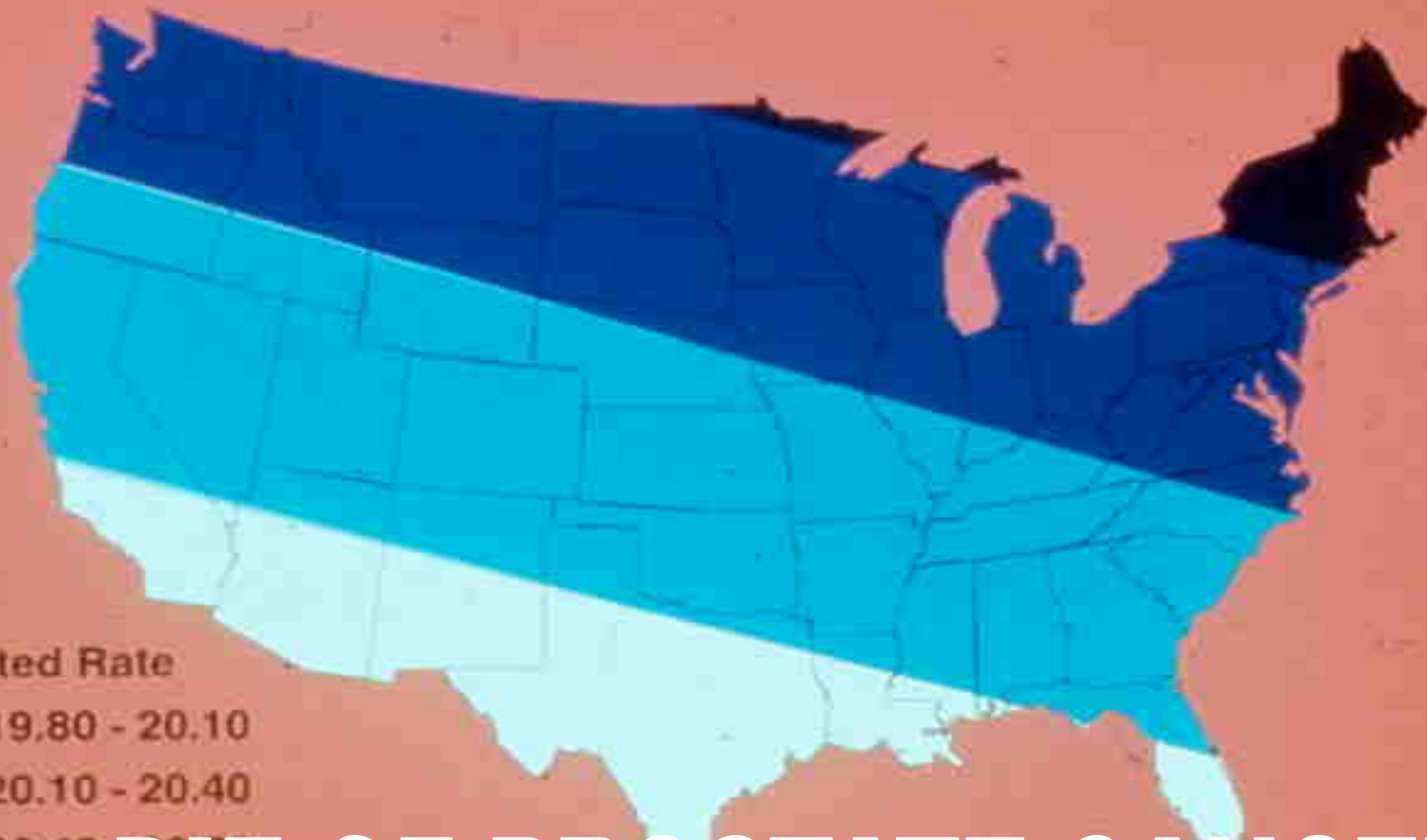


**INVASIVE COLORECTAL  
CANCER**



Lappe et al AJCN 2007

Linear trend surface map of prostate cancer mortality among white men, 1970 - 1979



**DIE OF PROSTATE CANCER**

Hanchette CL, Schwartz GG. Cancer 1992;70:2861-9.

# PROSTATE CANCER

25(OH)D

>20ng/ml

R  
I  
S  
K

50%



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

# Autocrine Regulation of Cell Growth

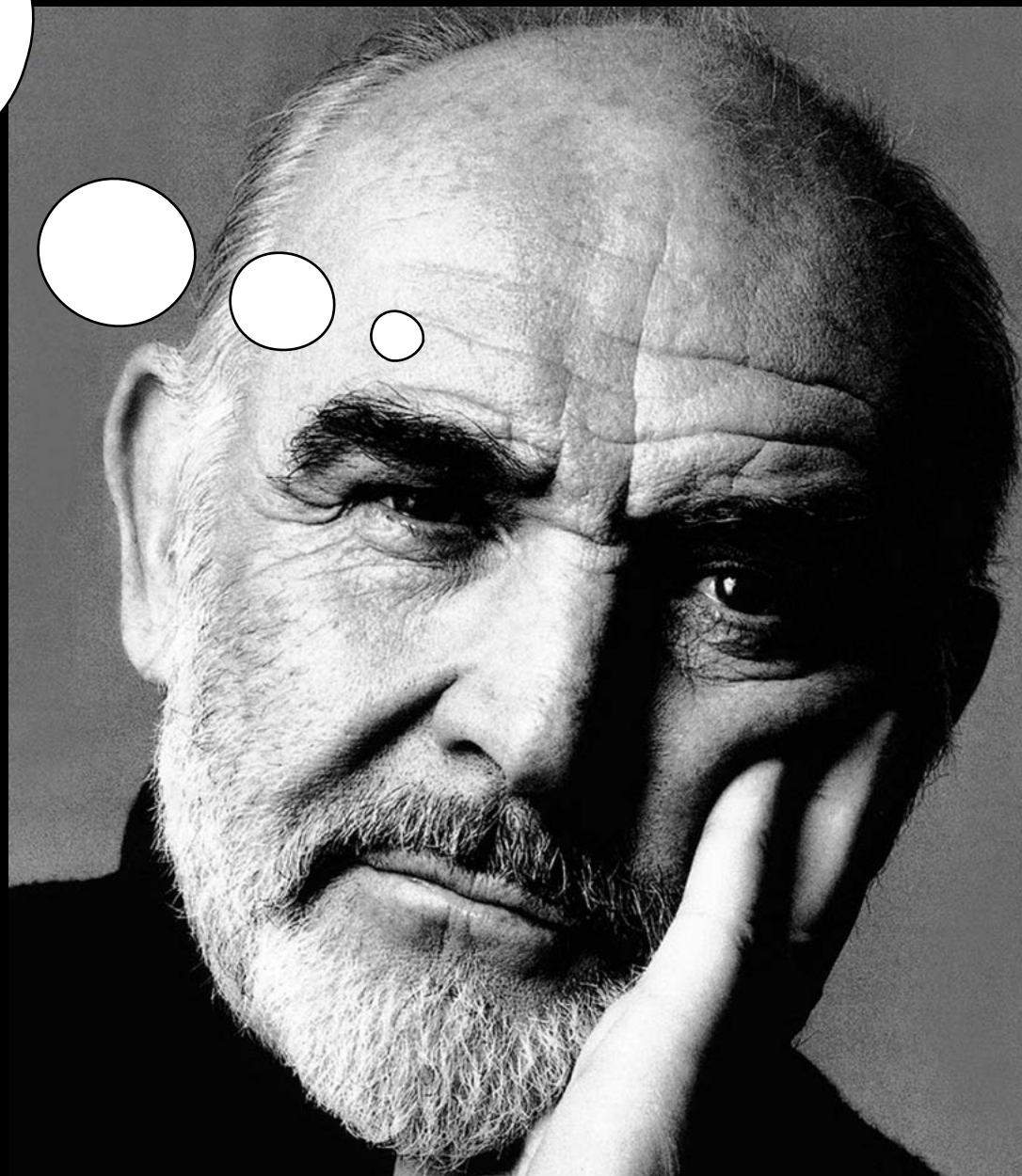
~ 200 GENES  
AFFECTED  
BY 1,25(OH)<sub>2</sub>D

25(OH)D

CALCITRIOL  
ACID  
INACTIVE

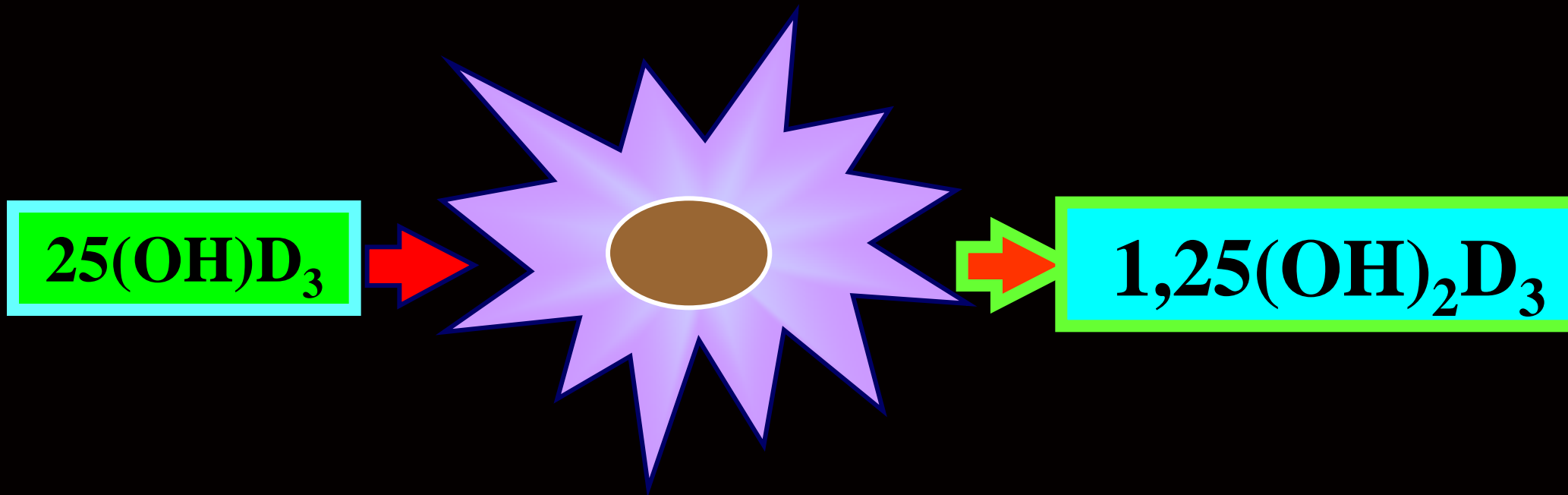
Control of cell growth

**WHAT IS  
THE EFFECT OF  
VITAMIN D ON  
THE  
IMMUNE SYSTEM  
?????????**



# ACTIVATED MACROPHAGES

Metabolize  $25(\text{OH})\text{D}_3$  to  $1,25(\text{OH})_2\text{D}_3$



*Adams et al JCEM 1987*

# Vitamin D Protects Against Tuberculosis

02.23.06, 12:00 AM ET

Published Online February 23, 2006  
Science DOI: 10.1126/science.1123933

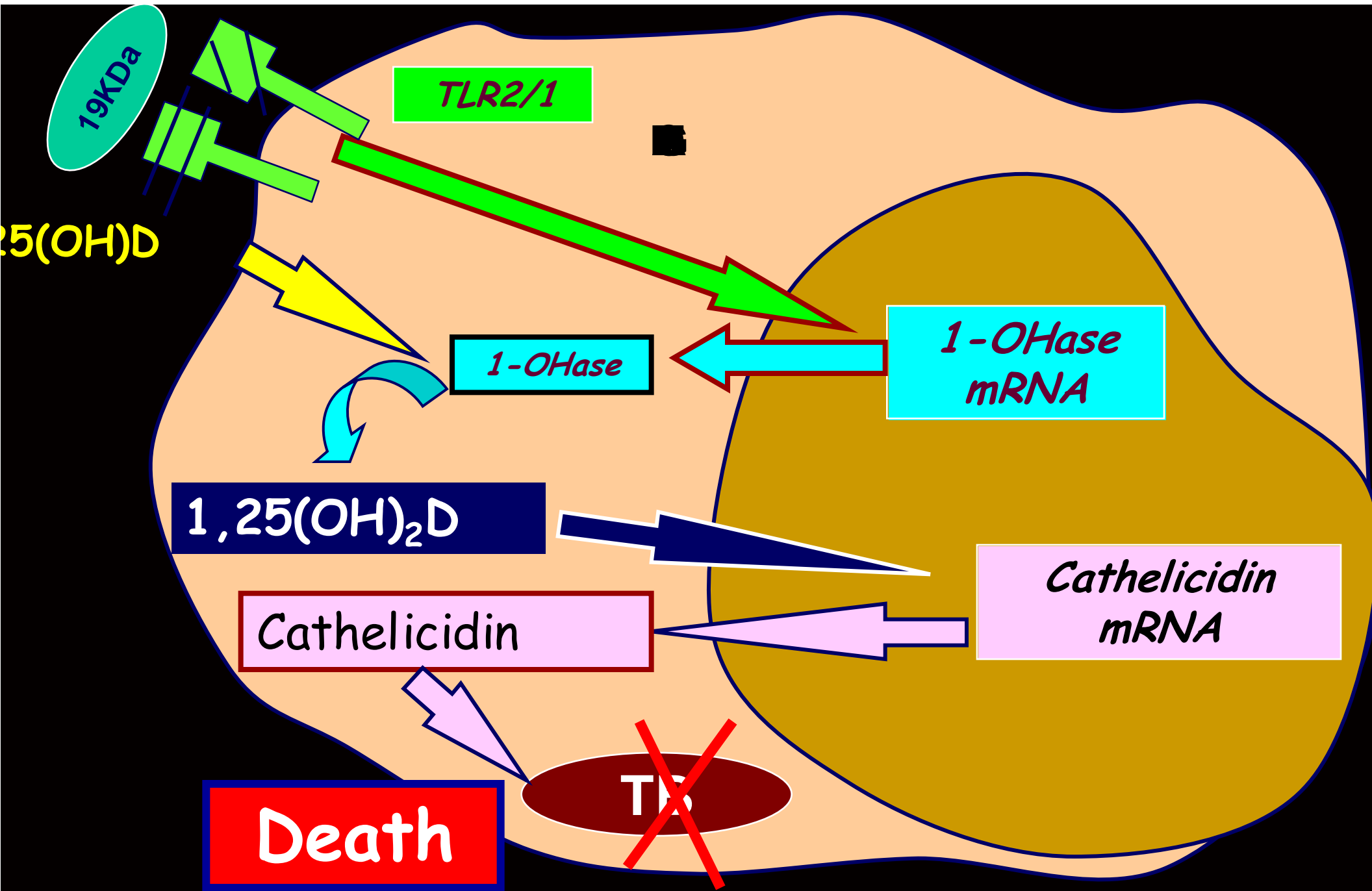
## REPORTS



Submitted on December 16, 2005  
Accepted on February 8, 2006

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

Philip T. Liu <sup>1</sup>, Steffen Stenger <sup>2</sup>, Huiying Li <sup>3</sup>, Linda Wenzel <sup>2</sup>, Belinda H. Tan <sup>1</sup>,  
Stephan Krutzik <sup>4</sup>, Maria Teresa Ochoa <sup>4</sup>, Jürgen Schaubert <sup>5</sup>, Kent Wu <sup>6</sup>,  
Christoph Meinken <sup>2</sup>, Diane L. Kamen <sup>7</sup>, Manfred Wagner <sup>8</sup>, Robert Bals <sup>9</sup>,  
Andreas Steinmeyer <sup>10</sup>, Ulrich Zügel <sup>11</sup>, Richard L. Gallo <sup>5</sup>, David Eisenberg <sup>3</sup>,  
Martin Hewison <sup>12</sup>, Bruce W. Hollis <sup>13</sup>, John S. Adams <sup>12</sup>, Barry R. Bloom <sup>14</sup>,  
Robert L. Modlin <sup>1\*</sup>



The finding also helps explain why blacks are more vulnerable than whites to tuberculosis and why they develop more severe cases when infected, according to a study in the Feb. 23 online issue of *Science*.





**Local production  
1,25(OH)<sub>2</sub>D  
Initiates  
INNATE IMMUNITY  
Against TB and  
other INFECTIVES**



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

*A. Giulietti · C. Gysemans · K. Stoffels · E. van Etten · B. Decallonne · L. Overbergh · R. Bouillon · C. Mathie*

*Laboratory for Experimental Medicine and Endocrinology (LEGENDO), Catholic University of Leuven, UZ Gasthuisberg, Onderwijs en Navorsing, Leuven, Belgium*

**10,366 CHILDREN IN FINLAND  
WHO RECEIVED 2000IU/D**

**VITAMIN D**

**RISK TYPE 1 DIABETES AFTER 31 YEARS**

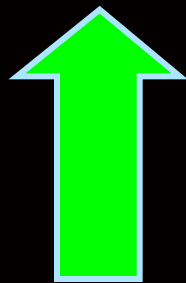
 **78%**

Hypponen et al. Lancet 2001

**CHILDREN IN FINLAND**

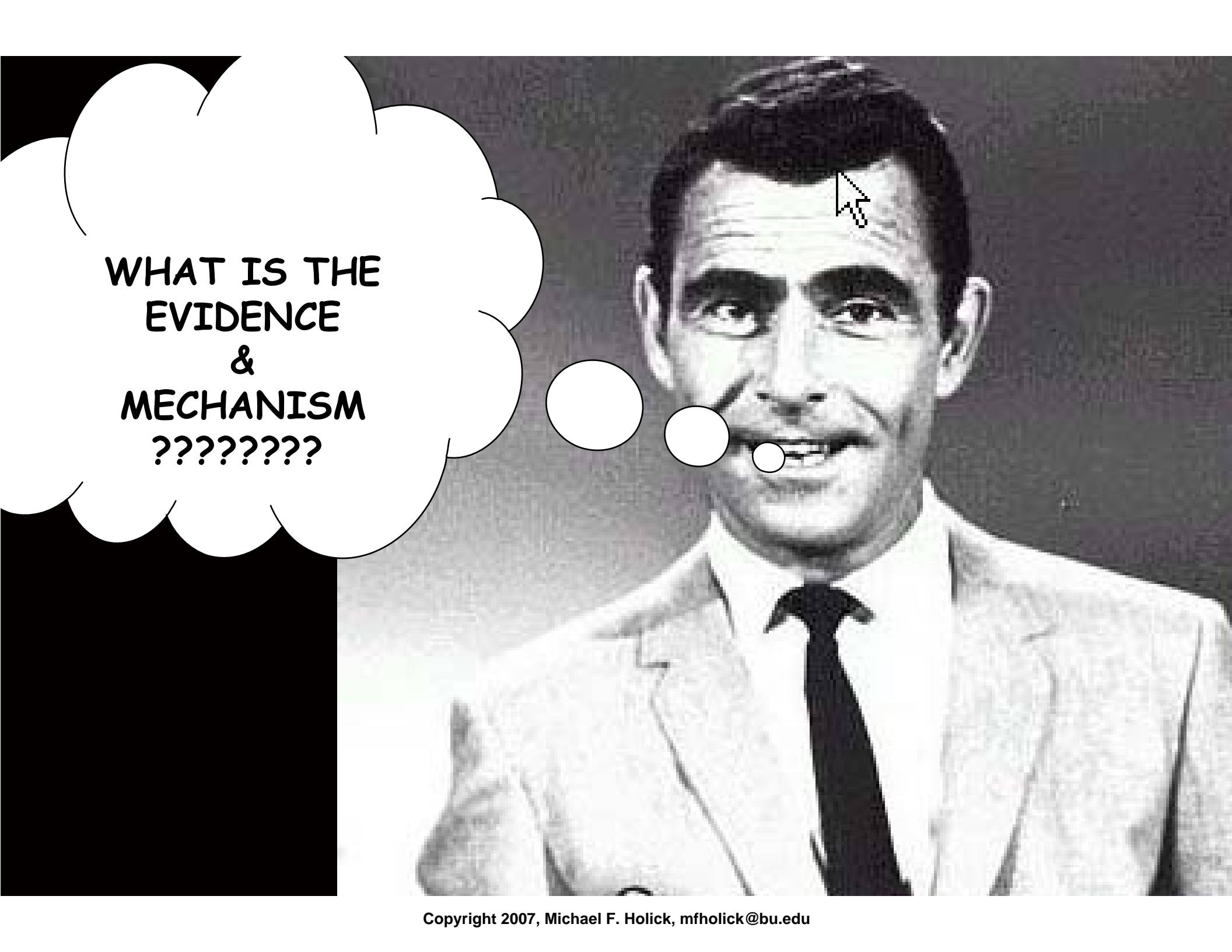
**WITH RICKETS**

**RISK TYPE 1 DIABETES**



**2.4 FOLD**

Hypponen et al. Lancet 2001



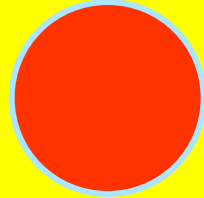
**WHAT IS THE  
EVIDENCE  
&  
MECHANISM  
????????**

Beta-ISLET CELL

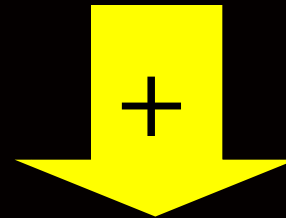
1,25(OH)D<sub>3</sub>



VDR +



VDR +



INSULIN

**METABOLIC SYNDROME  
& TYPE 2 DIABETES**

# REVIEW: The Role of Vitamin D and Calcium in Type 2 Diabetes. A Systematic Review and Meta-Analysis

Anastassios G. Pittas, Joseph Lau, Frank B. Hu, and Bess Dawson-Hughes

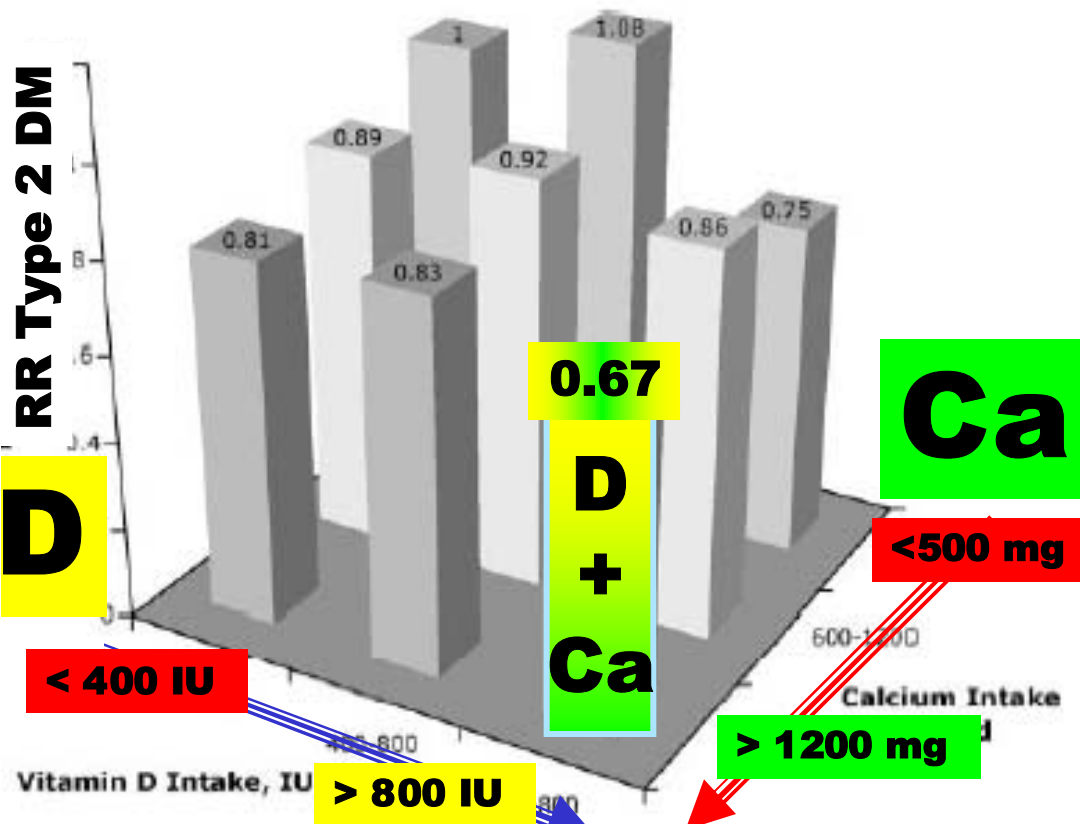


FIG. 1. Adjusted relative risk of incident type 2 DM in the Nurses Health Study by calcium and vitamin D intake (52).

**RR**

**33%**

**Ca > 1200 MG**

**+**

**VIT D > 800 IU**

Pittas et al JCEM 07

# Vitamin D Supplementation and Total Mortality

*A Meta-analysis of Randomized Controlled Trials*

*Philippe Autier, MD; Sara Gandini, PhD*



**ALL CAUSE MORTALITY  
DECREASED 7%  
ON 528 IU VITAMIN D**





# Vitamin D intake and incidence of multiple sclerosis

K.L. Munger, MSc; S.M. Zhang, MD, ScD; E. O'Reilly, MSc; M.A. Hernán, MD, DrPH; M.J. Olek, DO; W.C. Willett, MD, DrPH; and A. Ascherio, MD, DrPH

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. Merlino,<sup>1</sup> Jeffrey Curtis,<sup>2</sup> Ted R. Mikuls,<sup>3</sup> James R. Cerhan,<sup>4</sup> Lindsey A. Criswell,<sup>5</sup>  
and Kenneth G. Saag<sup>2</sup>

VITAMIN D INTAKE (>400IU/D)  
INVERSELY RELATED TO RA  
IN WOMEN

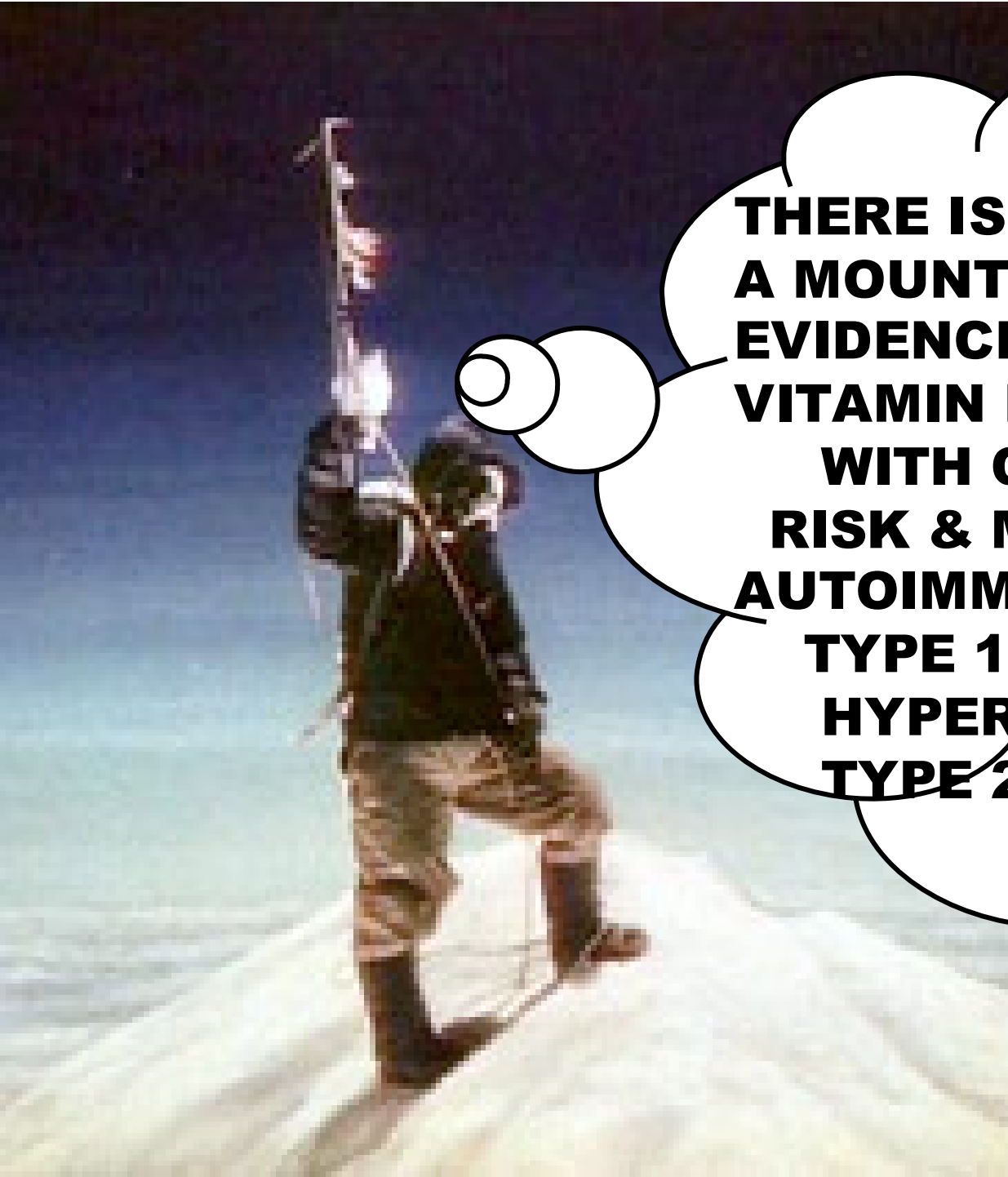


**44%**

VITAMIN D

***DEFICIENCY***

IS A DISEASE OF NEGLECT

A photograph of a person climbing a rope on a ship's mast. The person is wearing a dark jacket and shorts, and is positioned against a blue sky and a light blue sea. The image is partially obscured by a large white thought bubble on the right side.

**THERE IS NOW  
A MOUNTAIN OF  
EVIDENCE LINKING  
VITAMIN D DEFICIENCY  
WITH CANCER  
RISK & MORTALITY  
AUTOIMMUNE DISEASES  
TYPE 1 DIABETES  
HYPERTENSION  
TYPE 2 DIABETES**

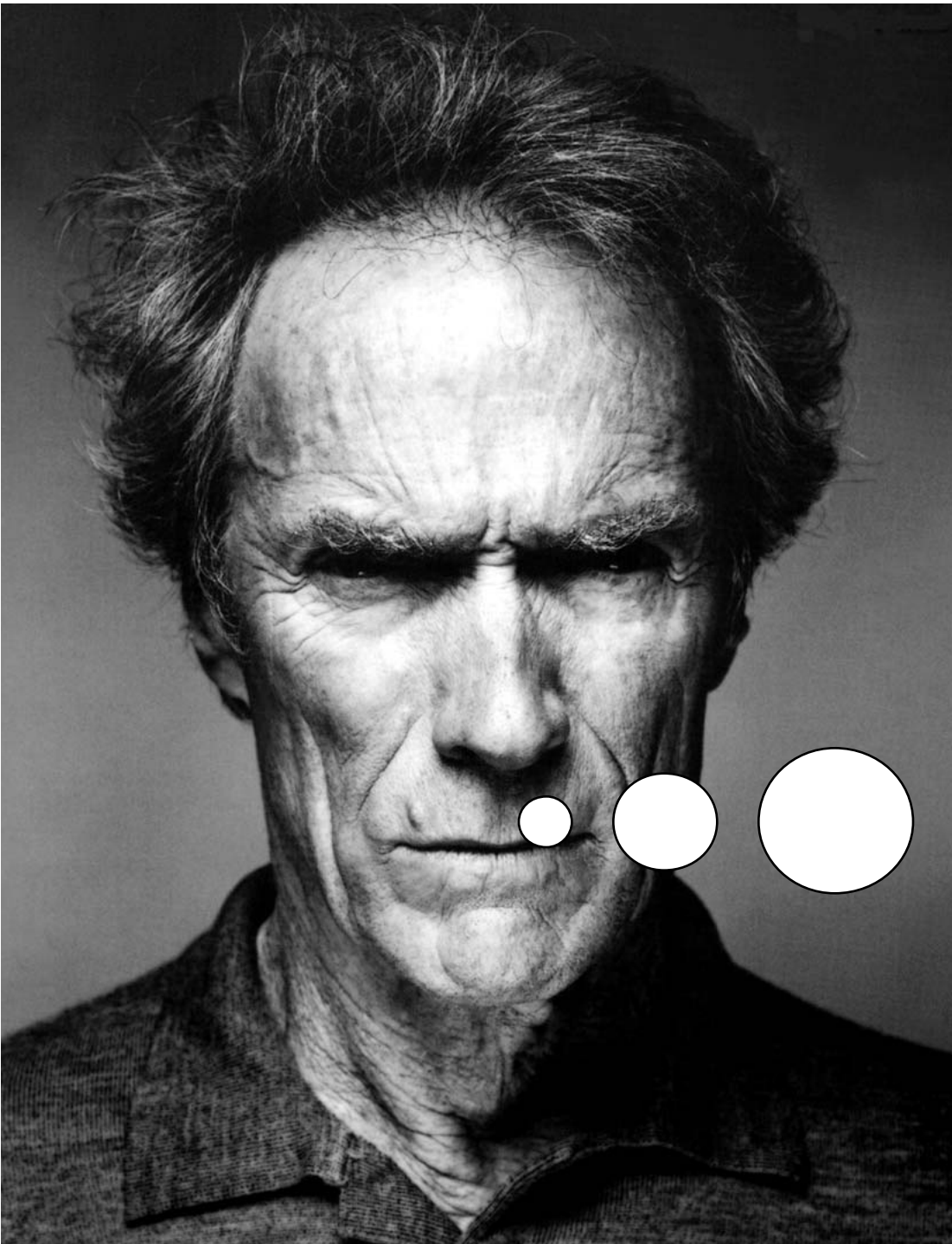
**!!!!**

WHAT IS A  
**NORMAL**  
VERSUS  
**HEALTHY**  
25(OH)D LEVEL  
????????

**GOAL**

**25(OH)D**

**> 30 ng/ml**




**HOW MUCH  
VITAMIN D  
DO WE  
NEED  
????????**





**100 IU VITAMIN D3  
RAISES 25(OH)D  
BY ONLY**

**1NG/ML**



**CHILDREN & ADULTS  
HAVE  
25(OH)D ~18 -25 ng/ml**

**ADULTS & CHILDREN**

**SHOULD RECEIVE**

**1000IU VITAMIN D3/D**

**WITHOUT SUN EXPOSURE**



**YOU CAN  
GET IT FROM  
DIET !!!**

SUN

SUN

SUN

SUN

FREE

FREE


FREE

FREE

ARE YOU ALWAYS  
INDOORS WORKING  
And  
WEAR SUNSCREEN  
ALL THE TIME  
???????

ARE YOU VITAMIN D  
DEFICIENT  
??????????





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

**THE PUBLIC NEEDS TO BE  
AWARE OF THE INSIDIOUS  
CONSEQUENCES OF  
VITAMIN D DEFICIENCY**

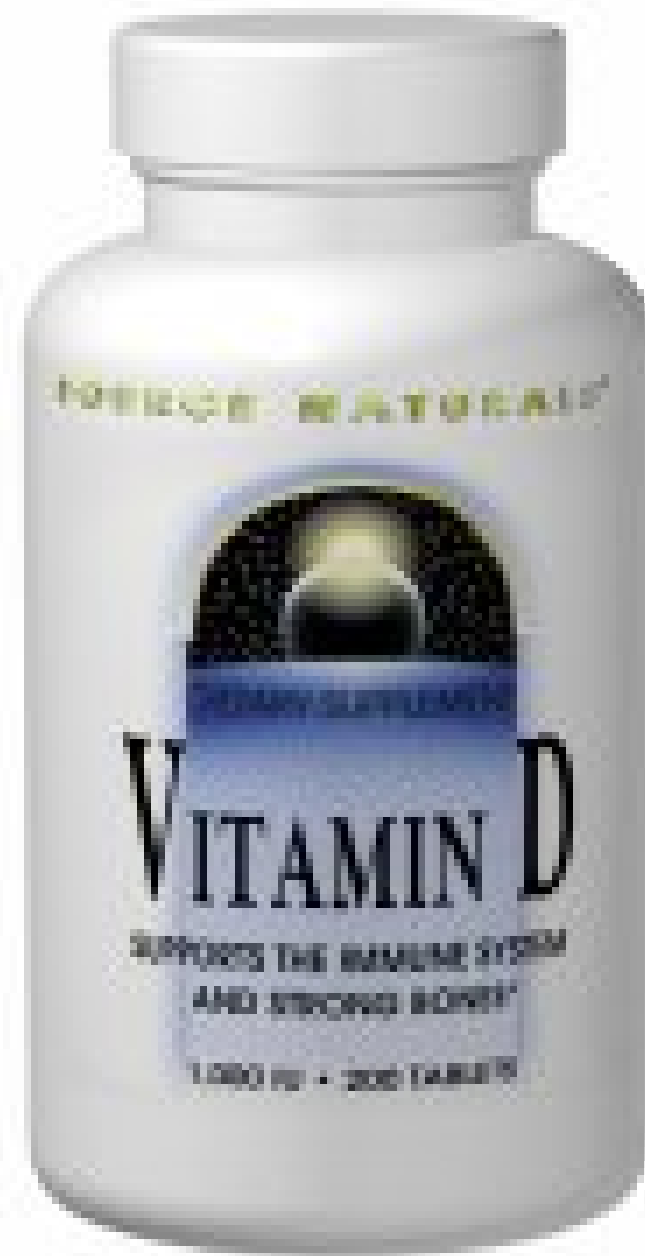
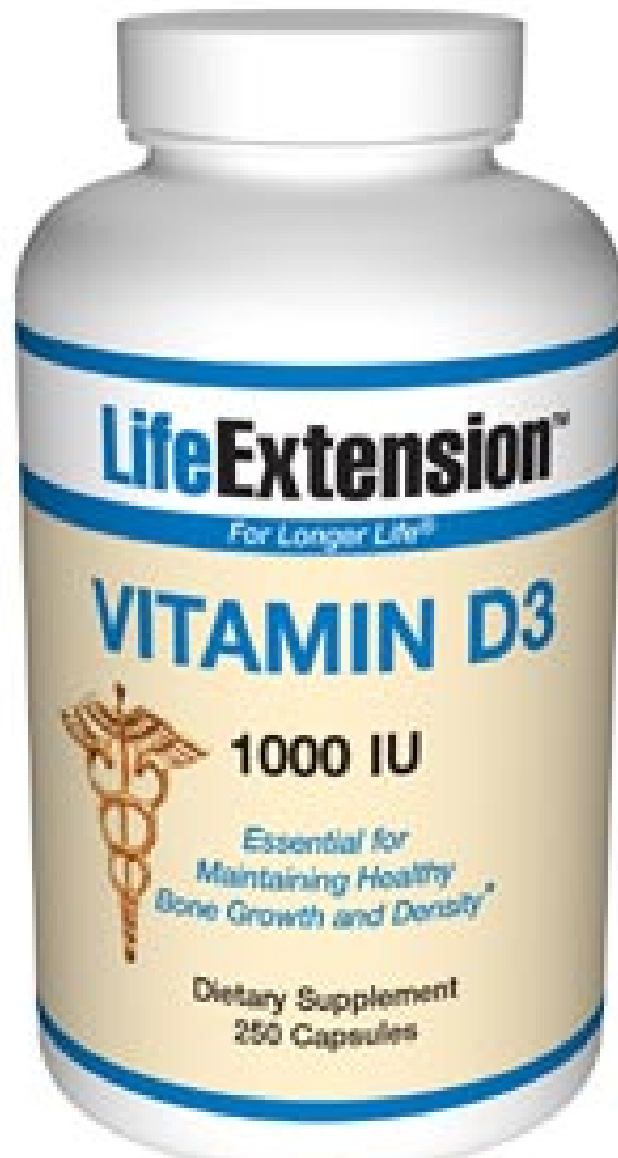
**What do I DO???????**







Copyright 2007, Michael F. Holick, [mfolick@bu.edu](mailto:mfolick@bu.edu)



**VITAMIN D  
DEFICIENCY  
IS THE  
MOST COMMON  
MEDICAL  
CONDITION**



**CAUSES**

***VITAMIN D DEFICIENCY***

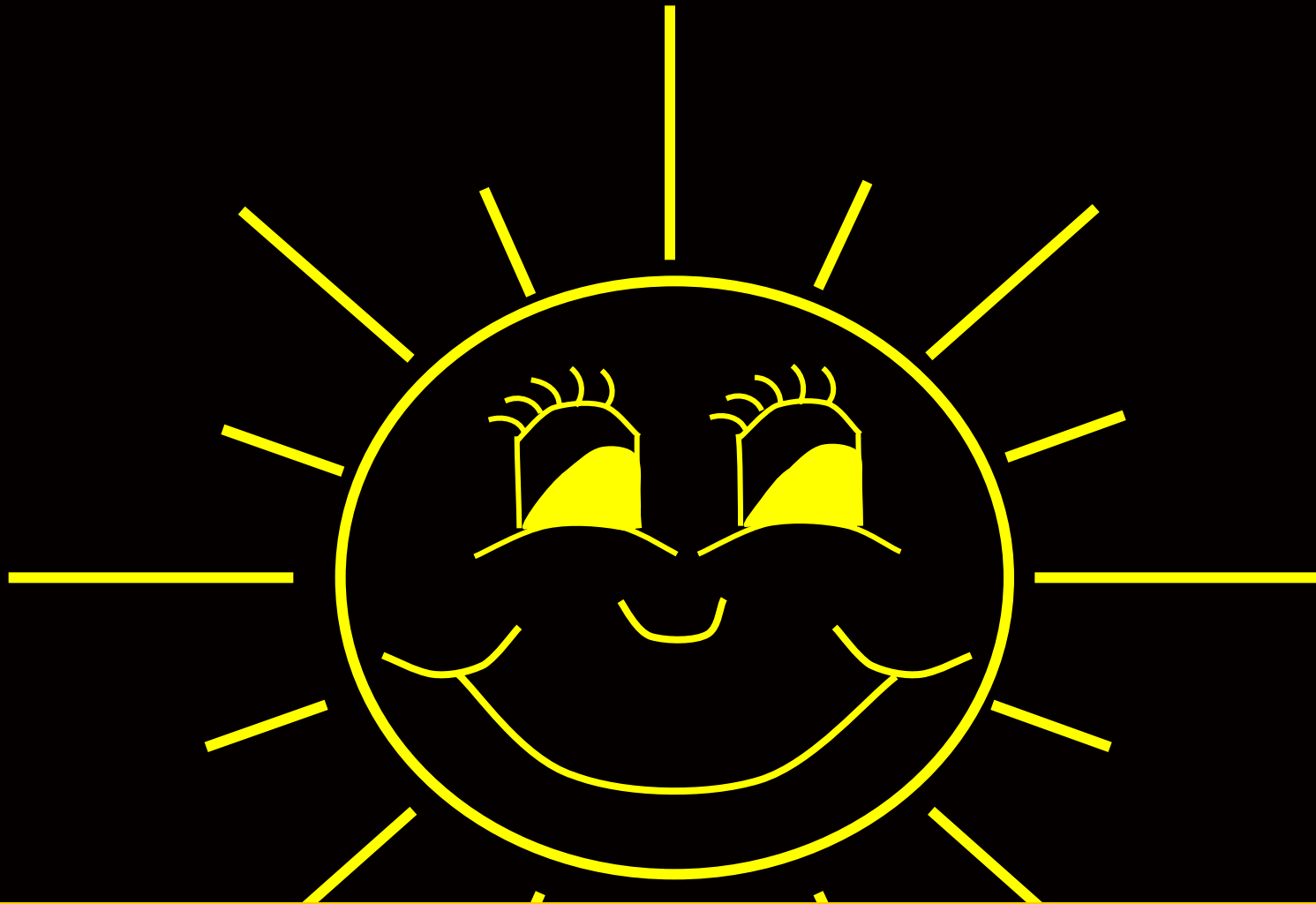
**CONSEQUENCES**

**Holick NEJM July 07**



**WE NEED  
SENSIBLE  
SUN  
&  
VITAMIN D  
SUPPLEMENTATION  
RECOMMENDATIONS  
!!!!!!!**

**YOU DO NOT NEED TO  
BE A GENIUS TO KNOW**



UVADVANTAGE.ORG