

# **Agony and Ecstasy Of Translational Vitamin D Research**



**Science & Evidence Based  
Perspective**

**Michael F. Holick Boston University Medical Center**



**What can you tell**

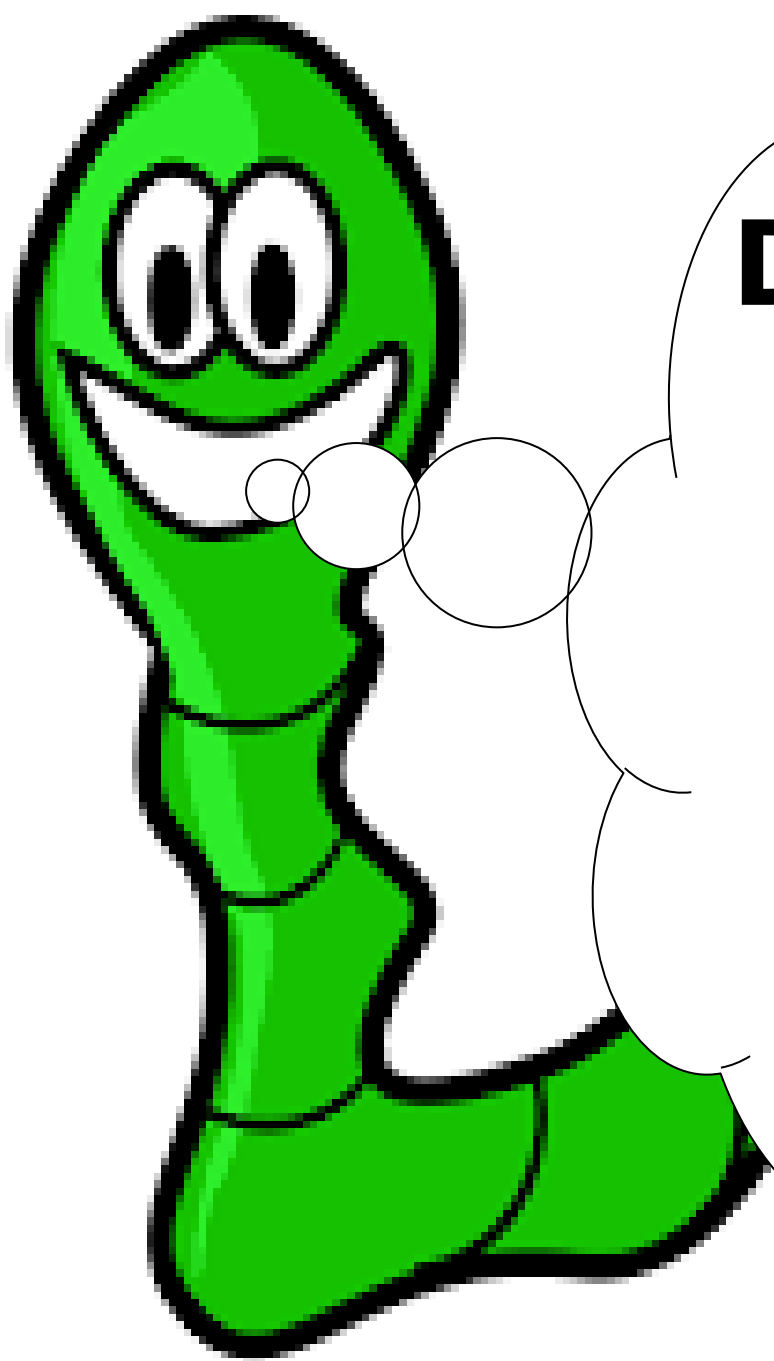
**Us about**

**vitamin D**

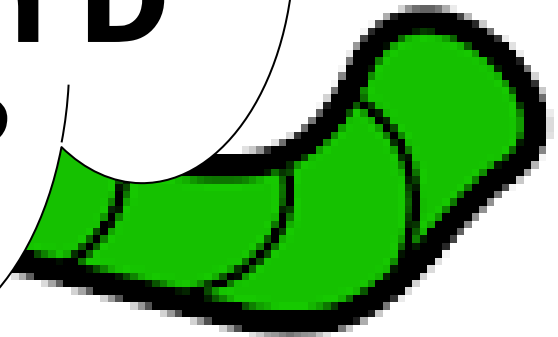
**That we**

**Don't know about**

**?????????**



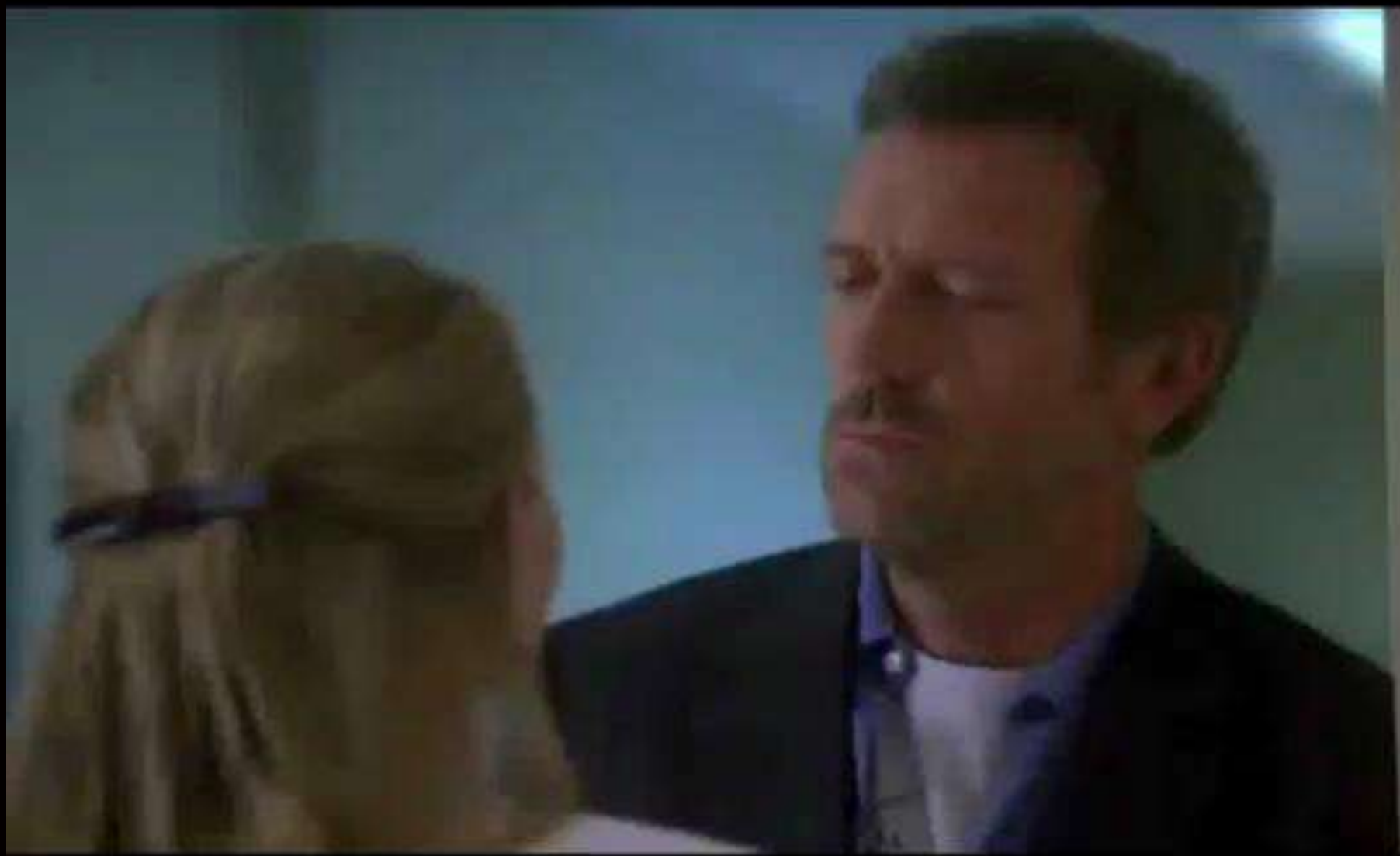
**Did you know  
That Worms  
Can  
Benefit  
From  
Vitamin D  
?????**




A man with a shaved head, wearing a dark suit, is shown from the chest up. He is pointing his right index finger towards the viewer. A large, semi-transparent grey letter 'D' is superimposed on his forehead. The background is a textured, light-colored wall.

**Holick  
You Need to  
Seek Council  
From a  
Higher Authority**

Premium



FOX  
5



*1 MAN. 1 YEAR.  
52 JOBS. THE  
ULTIMATE  
SEARCH FOR  
CAREER  
HAPPINESS*

*FIT TO BE  
TOYED  
WE TAKE  
ON THE  
WII FIT  
(AND LOSE)*

**Holick you are  
An Idiot !!!**

**What else can you say  
To this audience  
About vitamin D that  
They do not know  
From the  
**IOM REPORT**  
**????****

**Institute of Medicine**

**IOM**

**IOM 2010**

**Dietary Reference Intakes  
Intakes for Calcium  
and Vitamin D**

# IOM 2010

**RDA = 3X**

**200 IU to 600 IU/d**

**UL = 2X**

**2000 to 4000 IU/d**



**WOW!!!**



**But  
Did they get it  
Right  
??????**

**June 6, 2011**

**Endocrine Practice  
Guidelines Committee  
Recommendations**



**Neil Binkley**



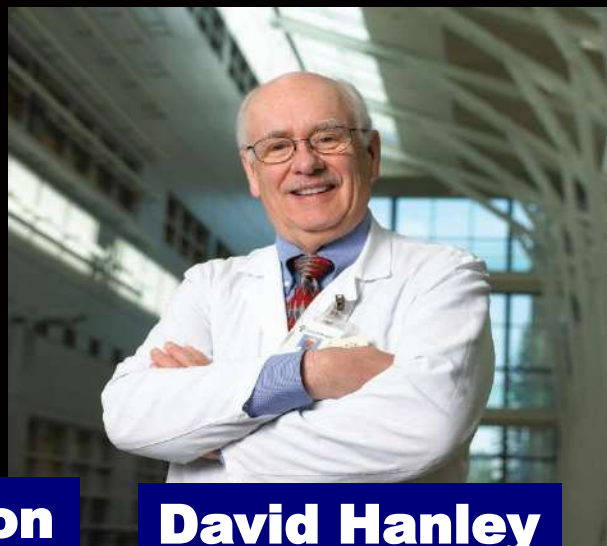
**Michael Holick**



**Heike Bishoff-Ferrari**



**Catherine Gordon**



**David Hanley**



**Robert Heaney**



**Connie Weaver**

# Objective:

The objective was to provide guidelines to clinicians for the evaluation, treatment, and prevention of vitamin D deficiency with an emphasis on the care of patients who are at risk for deficiency.

# IOM Guidelines

**“not intended to direct physicians on care of patients”**

**“it is up to professional associations to establish guidelines for care”**

**“used a population model, not a medical model”**

# Recommended Intake

**0-1 YEAR**

**400-1000 IU/D**

**1-18 YEAR**

**600-1000 IU/D**

**18+ YEARS**

**1500-2000 IU/D**

**Obesity**

**2-3 Times more**

A man with a mustache, wearing a grey suit and tie, is pointing his right index finger upwards. He has a speech bubble coming from his mouth. The background is slightly blurred, showing what appears to be a wall with some colorful letters or graphics.

**Consultant and Speaker**  
**Quest Diagnostics**  
**Shire**  
**Vital Choice**  
**Ontometrics**  
**Sanofi**  
**Hypermarcus**  
**Abbott**

**Dr Holick  
Receives support**

**From NIH**



A silhouette of a person holding a glowing orb against a sunset background. A large yellow oval is overlaid on the right side of the image, containing the text "And Support From The Sun".

And Support  
From The  
Sun

***DrHolick.com***



**Michael**

**There has been some  
controversy swirling around  
you**

**Give us an update**



RENT:  
\$4.5M

UNDER CONTRACT

Luxury Digs for  
MassHousing

# BRUTE FORCE



RAGING MICHAEL SNAPS  
TELEPHONE POLES, FLOODS  
STREETS IN FLORIDA

# Hurricane Michael

# *Vitamin D, the Sunshine Supplement, Has Shadowy Money Behind It*

The doctor most responsible for creating a billion-dollar juggernaut has received hundreds of thousands of dollars from the vitamin D industry.

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9/4/2018

Huh? The New York Times says vitamin D health benefits are a right-wing conspiracy theory – NaturalNews.com

# Huh? The New York Times says vitamin D health benefits are a right-wing conspiracy theory

Wednesday, August 22, 2018 by: Isabelle Z.

*Tags: badhealth, badmedicine, Big Pharma, conspiracy, Dr. Michael Holick, hypocrisy, left cult, Libtards, mainstream media, Michael Holick, natural cures, natural medicine, natural remedies, New York Times, nutrients, prevent disease, prevention, propaganda, stupid, sunshine, sunshine vitamin, vitamin D, vitamins*



The New York Times



**I wonder  
What Glen  
Thinks about this  
??????????**



**Dr. Holick**

**I do not think**

**You are being paid**

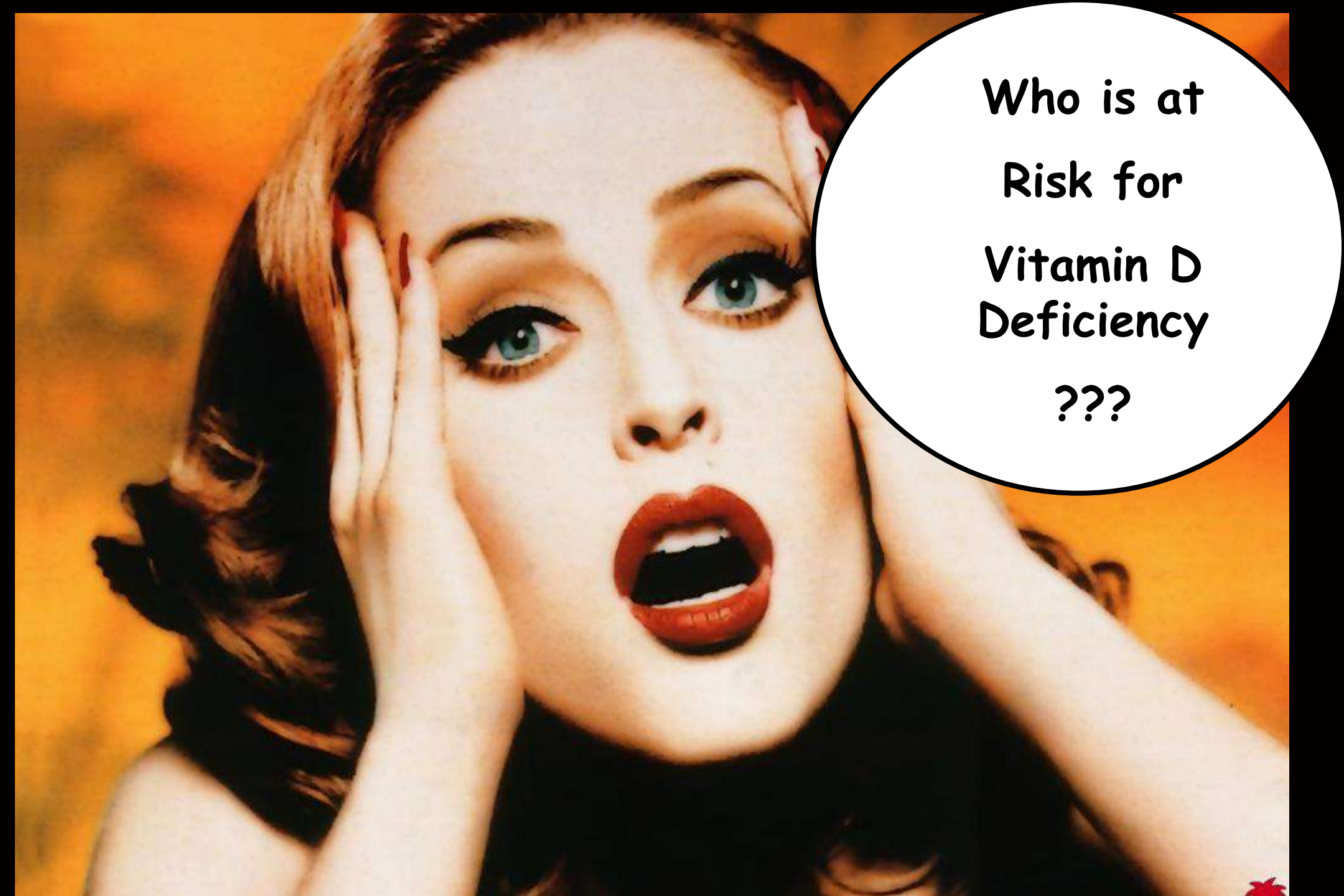
**ENOUGH !!!!!!!**

# Vitamin D

*Boring !!!*








**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 !!!!!!!!**

# **RIKETS**



found by Geha and Simon have such high concentrations of dark matter, it's likely that many other satellite galaxies could be 100 percent dark matter.

"We expect some to be undetectable, with no stars or gas," says Geha. "There are indirect ways of finding the dark matter satellites, but it will take more work."

Some astrophysicists believe that dark matter particles may occasionally annihilate each other, producing bursts of high-energy gamma rays. If the Milky Way has dark matter satellites, and if they do emit gamma rays, the Gamma-Ray Large Area Space Telescope, scheduled for launch in February, might detect them.

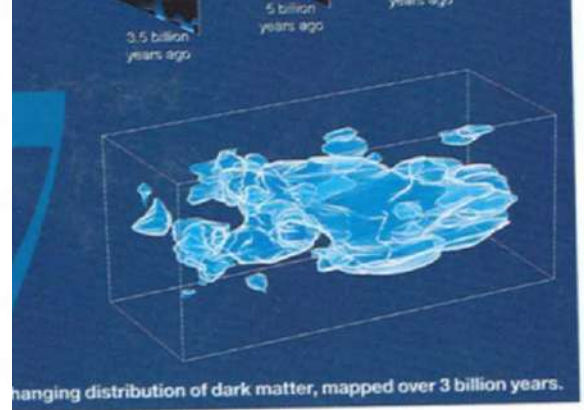
Dark matter may also be responsible for creating the most awesome objects in the universe: the enormous black holes believed

...but the most unexpected result of the model was that the filaments could catastrophically collapse, warping space-time to form a huge black hole.

"Even if only 1 percent of the mass in a filament takes part in the collapse, that's already 100,000 times the mass of the sun, a very good start to making one of these supermassive black holes," Theuns says. "We know that the formation of these supermassive black holes has to be very rapid because we can see very bright quasars very soon after the Big Bang, not much later than the epoch of the first star formation."

Is there any chance that astronomers could detect an echo of the primordial cataclysms that birthed these black holes?

"You would think it's such a violent process that something would be left over from that," Theuns says. "I don't have any predictions, but you would think there would be something." **Tim Folger**



Changing distribution of dark matter, mapped over 3 billion years.

Medicine

# Can Vitamin D Save Your Life?

paper in June. Vitamin D comes from three sources: the sun's ultraviolet (UVB) rays penetrating the skin, a few D-rich foods like fatty fish and some fortified foods, and supplements. The Canadian Paediatric Society has already recommended that pregnant or breast-feeding women get 2,000 IU of vitamin D daily. Some clinicians have suggested that increased vitamin D in-

take might help ward off multiple sclerosis (MS), believed to be a progressive autoimmune disease. Last December, a team of researchers at the Harvard School of Public Health and other institutions published results from the first large-scale prospective study of the relationship between vitamin D levels and MS. After analyzing stored blood samples taken from 7 million military personnel and identifying those individuals who developed MS during a 12-year period, the team determined that the risk of getting MS was 62 percent lower for those whose blood concentration of vitamin D put them in the top quintile than for those in the bottom quintile. The study did not make clear, however, whether low vitamin D levels were a cause of MS or a marker of MS risk.

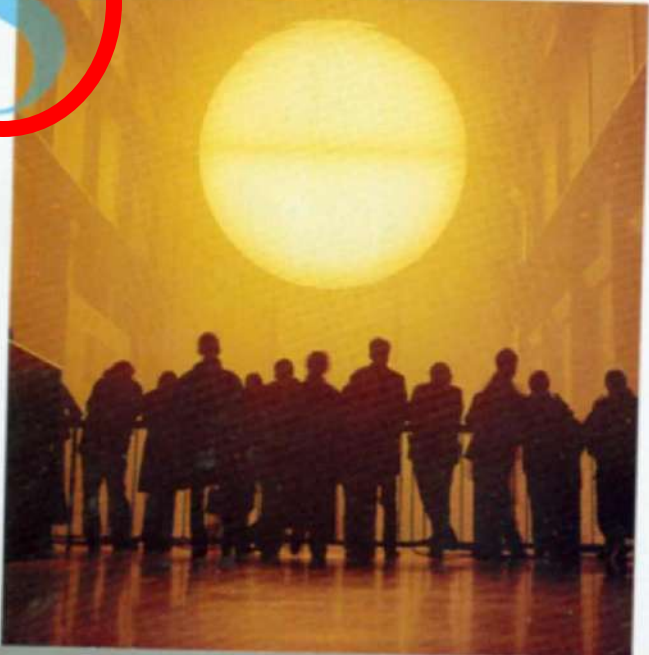
Vitamin D status may also affect vulnerability to infections. For example, African Americans need more sun exposure than Caucasians to make sufficient vitamin D; they also suffer from increased risk of tuberculosis. In a breakthrough study published in March, scientists from several institutions, including UCLA, discovered a possible link. On encountering the TB bacillus, receptors on immune-system scavenger cells known as macrophages stimulate the conversion of circulating vitamin D to its active form, which produces a peptide that destroys the bacillus. If circulating levels of D are low, macrophages can't activate the vitamin D to initiate this response. A similar scenario could be operating with other infectious agents, maybe even the influenza virus.

**Mariana Gosnell**

New studies highlight the importance of the forgotten vitamin.

Years ago, doctors believed that vitamin D, sometimes called "sunshine vitamin" because sunlight triggers the body to produce it, was important primarily in preventing rickets (a softening of bones) in children. Once milk became fortified with vitamin D, rickets pretty much disappeared, and the problem of vitamin deficiency seemed to have been solved. But according to Michael F. Holick, director of the Vitamin D, Skin, and Bone Research Laboratory at Boston University Medical Center, who has spent 30 years studying the vitamin, "rickets can be considered the tip of the vitamin D-deficiency iceberg."

Today a lack of the vitamin has been linked to a host of other diseases, including cancers of the colon, prostate, and breast; tuberculosis; schizophrenia; multiple sclerosis; hip fractures; and chronic pain. How can one vitamin play a role in so many diverse diseases? The answer seems to lie in the fact that most tissues in the human body (and not just those in the intestine



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## The 10 Biggest Medical Breakthroughs

TOP STORIES

### #8 | Early Test for Lung Cancer

A new blood test could aid earlier detection of the leading cause of U.S. cancer deaths by screening for a protein rarely seen in healthy people.

### #9 | New Source of Stem Cells

Amniotic fluid collected from afterbirth and amniocentesis tests contains stem cells that may be almost as malleable as the ones obtained from embryos.

### #10 | More Benefits of Vitamin D

A slew of new studies suggests that diets high in vitamin D may improve life expectancy and help ward off diabetes, gum disease, multiple sclerosis and maybe even cancer.

\* SPECIAL WEIGHT-LOSS ISSUE

# fitness

Mind, Body + Spirit

BONUS SECTION

## Drop 10 lbs This Month!

- \* No-Fail Diet Foods
- \* Stick-With-It Strategies
- \* Fat-Melting Moves

Great Skin All Winter  
9 Best Beauty Buys

## Get Your Dream Body

## 20 Healthy Meals for Less

Recipes p.115

FLAT  
ABS  
FAST  
WITHOUT  
CRUNCHES!

FEBRUARY 2009  
FITNESSMAGAZINE.COM

# Super Vitamin to the Rescue!

Faster than prescription meds! More powerful than an ordinary supplement! Able to stop tall health problems in their tracks! Vitamin D is the new health hero, so why aren't you taking it? BY RICHARD LALIBERTE

**B**illie Jo Coomer, 31, couldn't figure out what the heck was wrong with her. For more than six years she had suffered from headaches and pain in her stomach, back, arms and legs. "I hurt constantly and couldn't sleep at night," says Billie Jo, an administrator in St. Clair Shores, Michigan. She saw more than a dozen doctors, but all they did was prescribe painkillers and antidepressants.





MAY  
**Teen**VOGUE

**GIRL HOT  
vs.  
GUY HOT**  
what's the deal?

**miley cyrus**

"I believe in love at first sight—it just hasn't happened to me"

**20 GREEN  
BEAUTY BUYS  
UNDER \$20**

**earth angels**

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teens are saving  
the planet

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# Sunny D

**Could sunlight, supplements, and milk be the simple solutions to an increasingly common teen-health concern?**

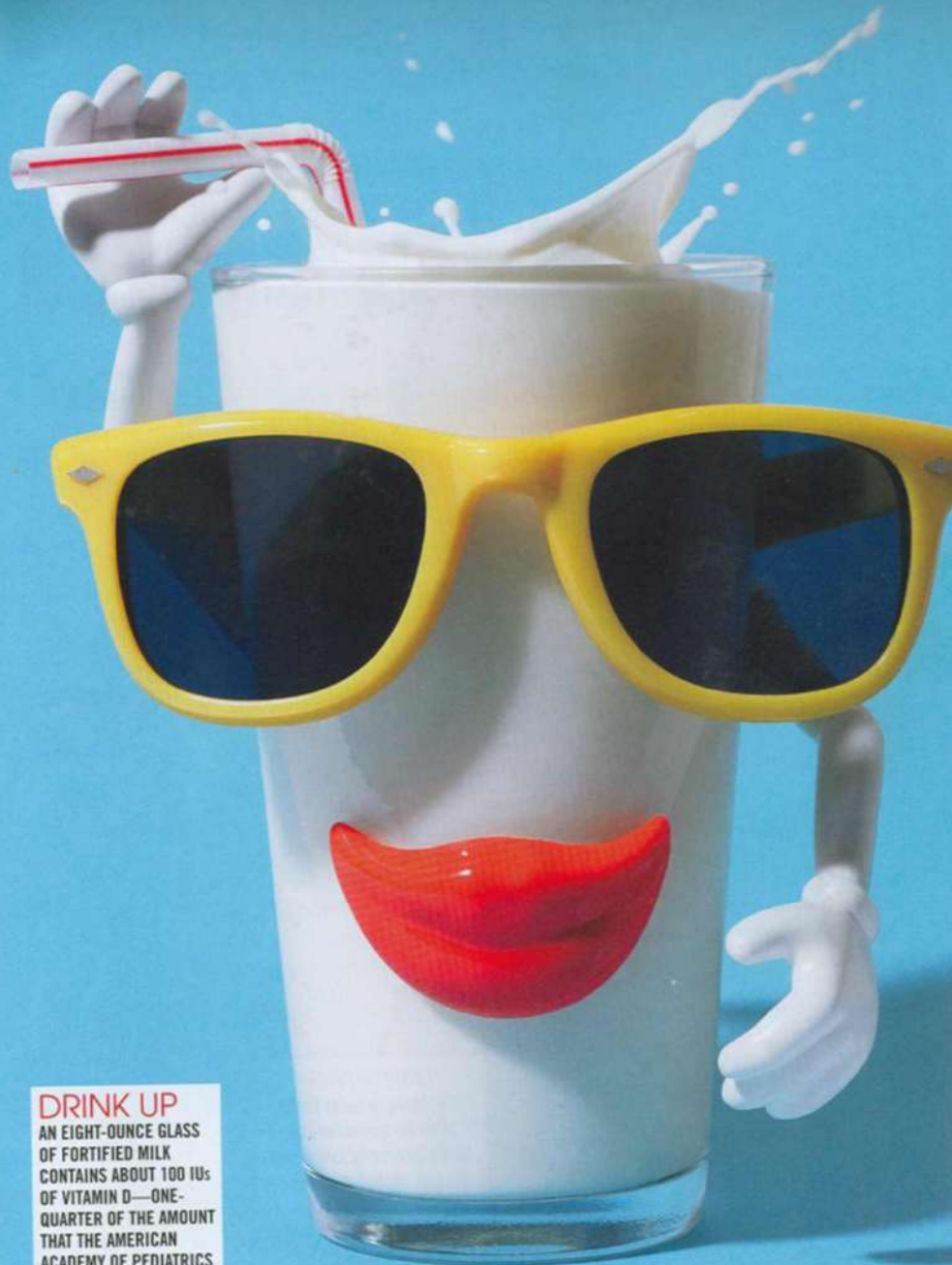
**T**outed by experts as the latest super-supplement, vitamin D may help ward off aches and pains, banish fatigue, increase muscle power, and slow weight gain, all while strengthening bones. It's an impressive list of pros—so why, then, did a recent study find that more than 40 percent of teens suffer from vitamin D deficiency?

The answer is simple: The body can't make vitamin D on its own. Few foods naturally contain the nutrient (fish like salmon and mackerel and foods like liver and egg yolks do). For that reason, public health officials mandated decades ago that milk be fortified with vitamin D. But reliance on milk may have caused part of the problem, says Darshak Sanghavi, M.D., of the University of Massachusetts. "Today teens have more beverage options than before, like soda, energy drinks, and coffee. Those have replaced milk as the central drink in their diet," she explains, "so they don't get the same amount of D that they used to. Plus, many people of color—including African-Americans, Asians, and Latinos—suffer from lactose intolerance and avoid milk altogether."

Certain diets may play a role in vitamin D deficiency as well. "Teen girls are more likely to experiment with diets like veganism, which cut out products such as eggs, fish, and fortified dairy, the common dietary sources of vitamin D," says Lisa Callahan, M.D., of the Women's Sports Medicine Center at New York's Hospital for Special Surgery. But food is just one way the body gets vitamin D.

The most abundant source of vitamin D by far is the sun (the body uses sunlight to convert a form of cholesterol in the skin into vitamin D). "Receiving enough sun exposure to make vitamin D isn't always easy," says Michael F. Holick, Ph.D., M.D., professor of medicine at the Boston University Medical School. "It depends on the season, time of day, latitude of where you live, and your skin pigment. Darker skin absorbs sunlight less easily than lighter skin does. Therefore, teens of color likely require more sunlight exposure to create enough D." Cities in the north receive less direct sun than those in the south, particularly in the winter, which is why vitamin D deficiency is more likely among teens who live in cities at higher latitudes. And sunscreen, too, is a factor. "UVB rays are necessary for the body to activate the vitamin D creation process in the skin. Sunscreen blocks that out," Holick notes. Which isn't to say you should sunbathe in order to get vitamin D. "Always use SPF and reapply during prolonged exposure," Callahan suggests.

So how can girls guard against skin cancer *and* still get enough vitamin D? First, check labels to see if any of your favorite foods are already fortified with the nutrient. Many products—like orange juice, cereal, and yogurt—have vitamin D added to them. If your levels from food are insufficient, then "take a multivitamin that includes D," Callahan advises. "I tell my patients to get between 800 and 1,000 IUs [international units] per day which, between supplements and food, is easily achieved. There's so much that modern medicine can't fix, but solving vitamin D deficiency is simple." —RICHIA GULATI



**DRINK UP**  
AN EIGHT-OUNCE GLASS OF FORTIFIED MILK CONTAINS ABOUT 100 IUs OF VITAMIN D—ONE-QUARTER OF THE AMOUNT THAT THE AMERICAN ACADEMY OF PEDIATRICS RECOMMENDS FOR TEENS. PHOTOGRAPHED BY BELA BORSODI.

**VITAMIN D**

**SUNSHINE**

**VITAMIN**

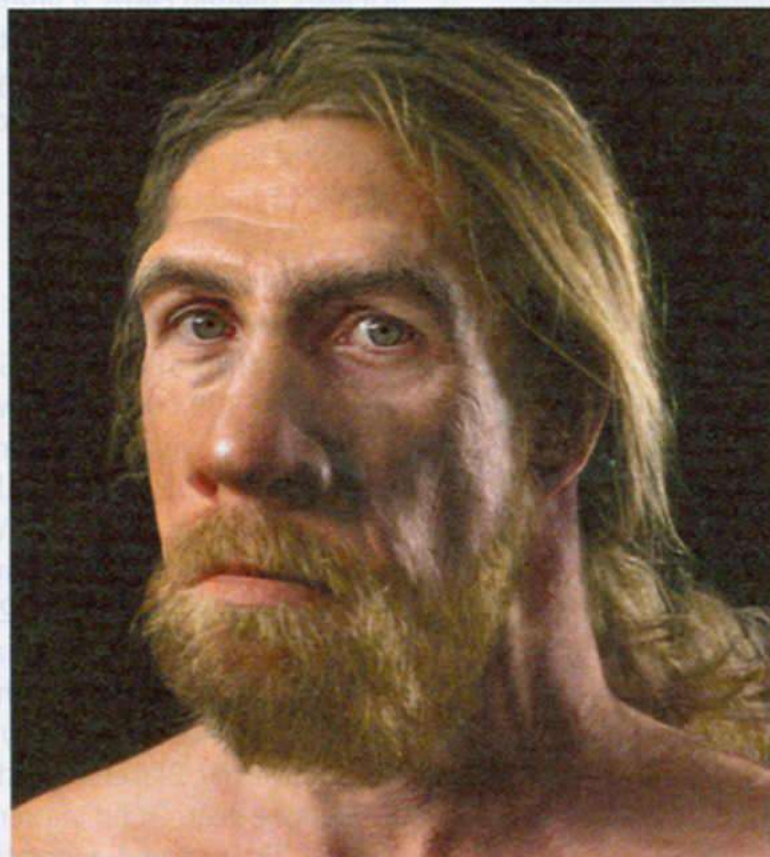


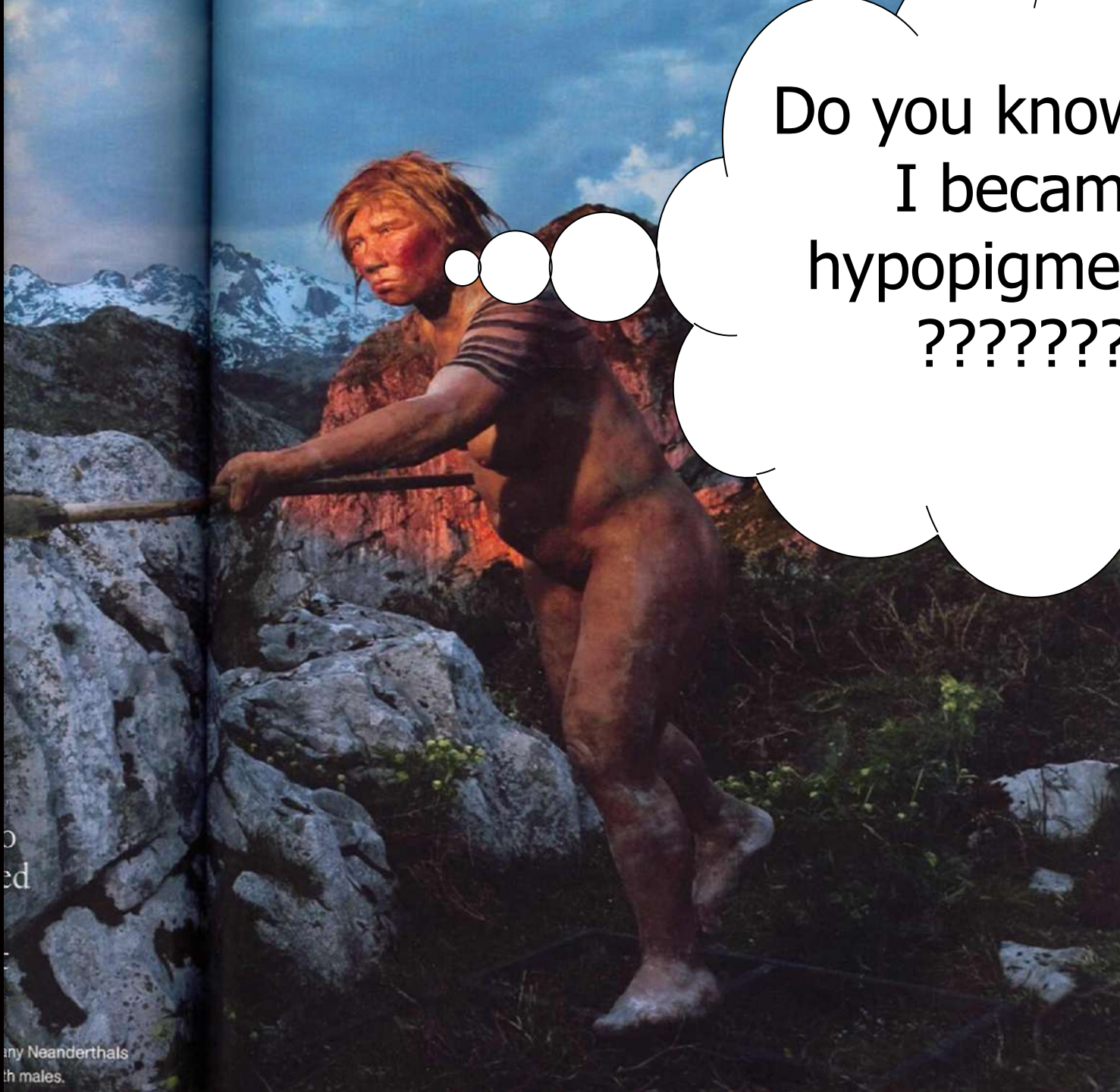
GENETICS

# Ancient DNA Reveals Neandertals

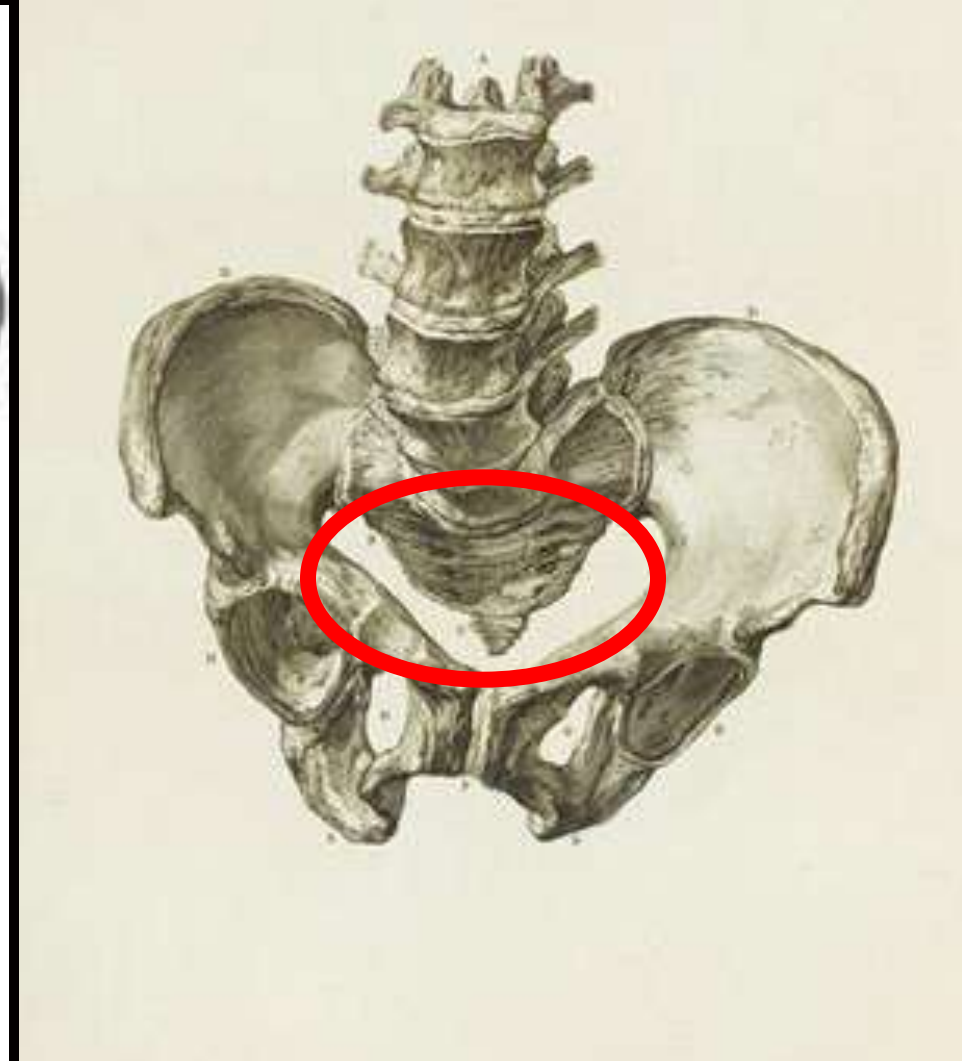
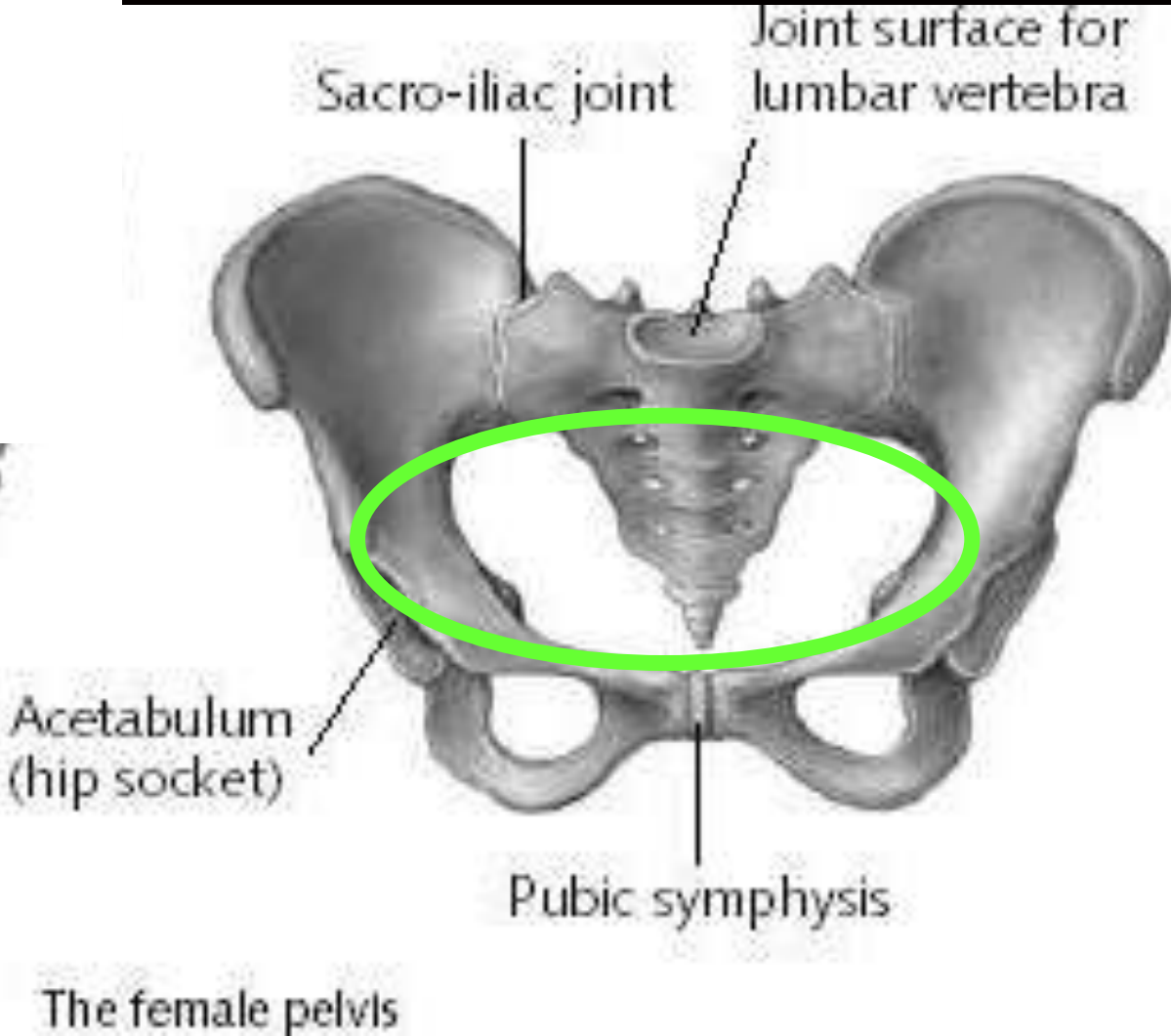
GENETICS

# Ancient DNA Reveals Neandertals With Red Hair, Fair Complexions





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



**Normal Female Pelvis**

**Rachitic Pelvis**



FINALLY  
WE CAN MAKE  
VITAMIN D  
!!!!!!!!!!

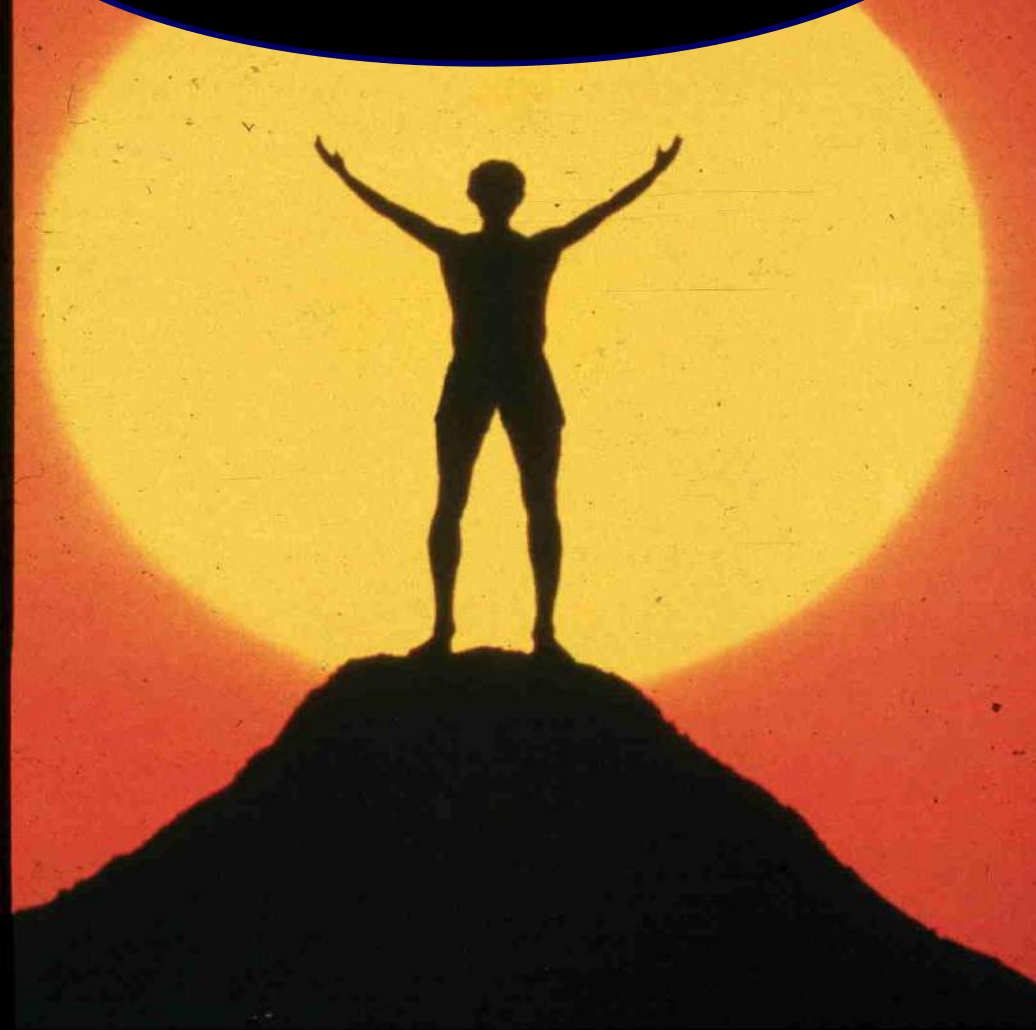


A photograph of a man in traditional African attire, including a red wrap and beaded jewelry, standing outdoors. A speech bubble is overlaid on the image, containing the text: "MY SKIN PIGMENT IS PERFECTLY DESIGNED !!!!!".

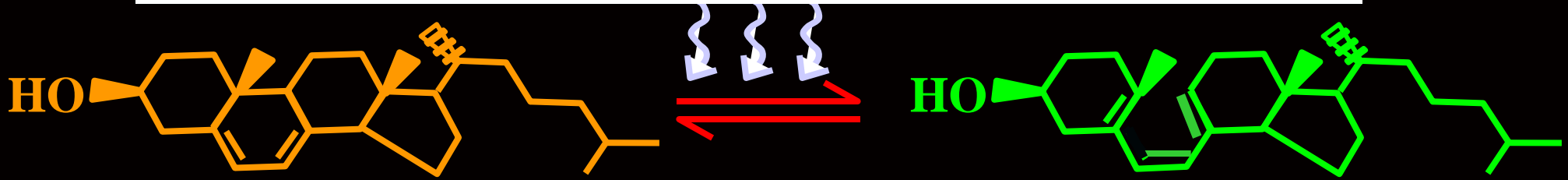
**MY  
SKIN PIGMENT  
IS PERFECTLY  
DESIGNED  
!!!!!!**

**COMPARE & CONTRAST**

**HOW DO YOU MAKE  
VITAMIN D ????**

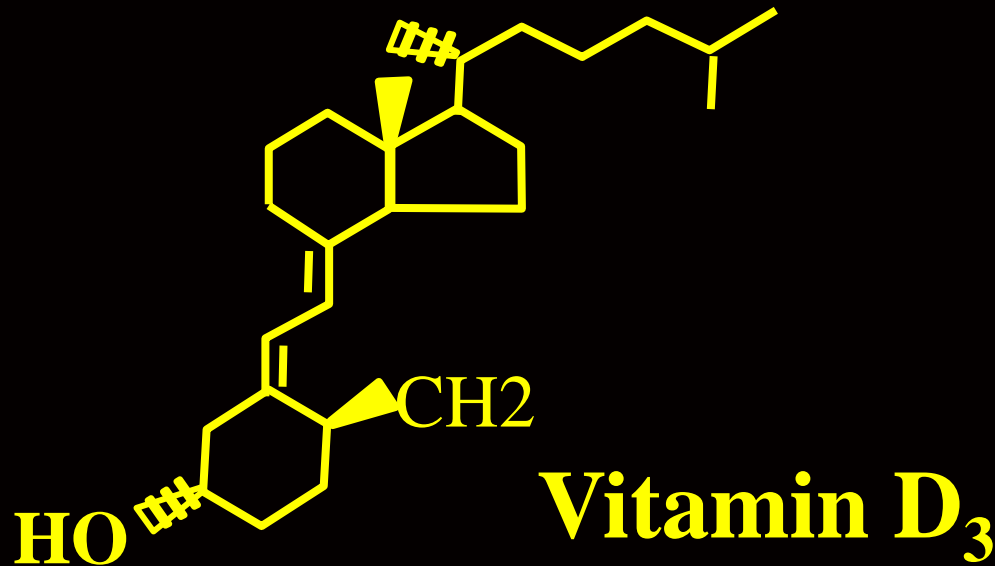


# Solar UV Radiation



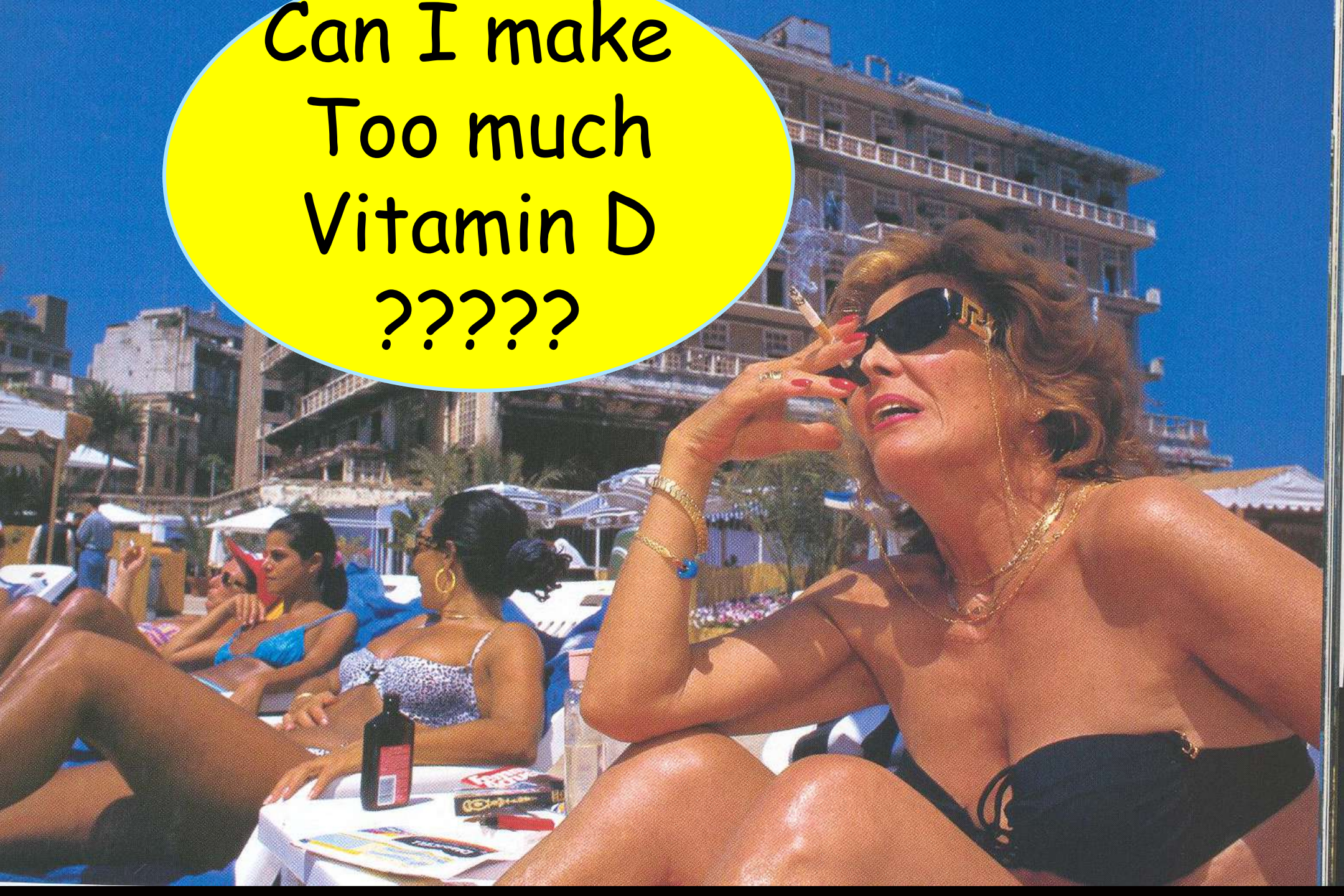
**7-DHC**

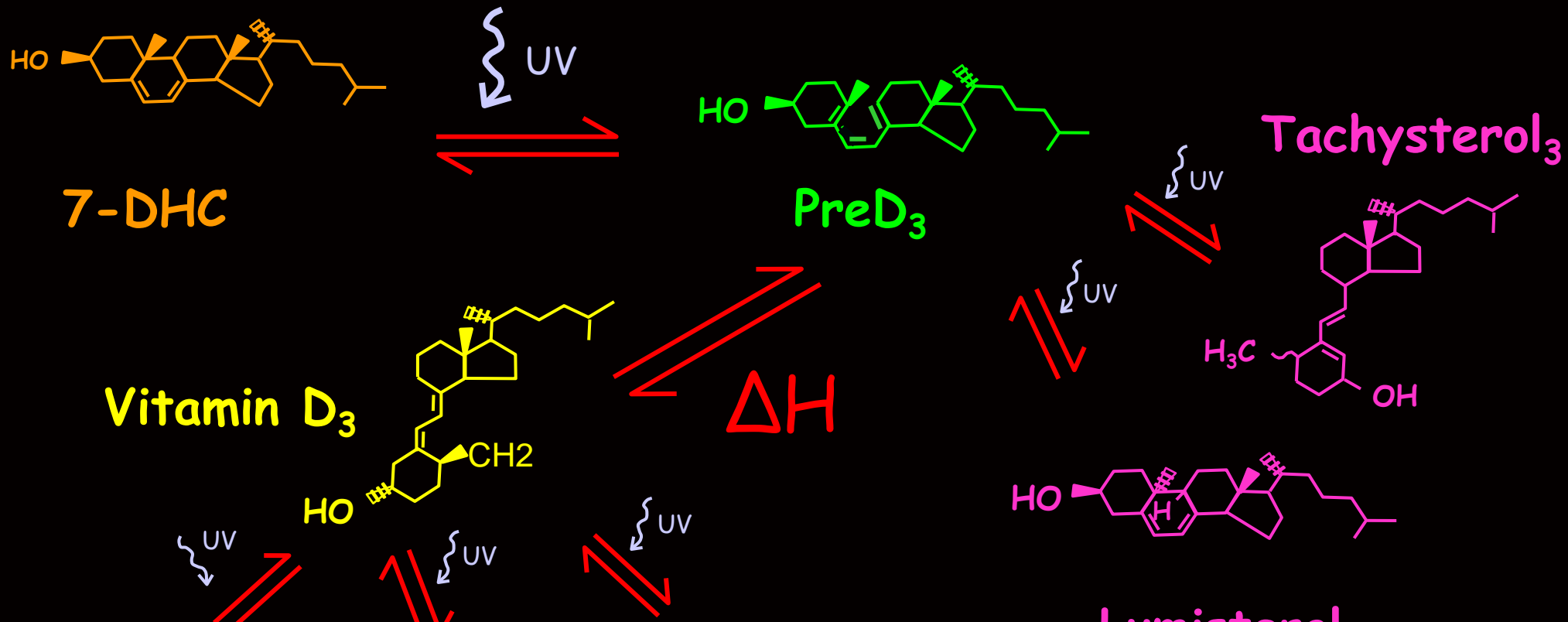
**PreD<sub>3</sub>**



**Vitamin D<sub>3</sub>**

Can I make  
Too much  
Vitamin D  
?????





**YOU CANNOT BECOME  
VITAMIN D TOXIC FROM  
SUN EXPOSURE**



**Did you know**  
**The Vitamin D**  
**Made in skin**  
**Lasts 2X longer**  
**Than vitamin D**  
**From the diet ???**

1600s



DARK ALLEY in Glasgow, photographed in about 1870, is typical

GLASGOW

essary for the synthesis of the hormone that prevent

S-T-E-C-K-R







**Sniadecki**

**1822**

**Association Study  
Rickets & Sunlight**

**“STRONG AND OBVIOUS IS THE INFLUENCE**  
**OF SUN ON THE CURE OF RICKETS AND THE**  
**FREQUENT OCCURANCE OF THE DISEASE**  
**IN DENSELY POPULATED TOWNS WERE**  
**THE STREETS ARE NARROW AND POORLY LIT**

***SNIADECKI 1822***

**HESS & UNGER**

**1921**

***SUN CURED RICKETS***



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

# SUNLIGHT *for* BABIES



U. S. DEPARTMENT OF LABOR

CHILDREN'S BUREAU

FOLDER NO. 5

1931

## GIVE THE BABY A COAT OF TAN

The baby should get tanned all over, but the tanning should take place gradually. Care should be taken not to burn him. Some babies tan more quickly than others; some burn more easily.

Dark-skinned babies need more sun to tan them and to protect them from rickets than fair-skinned babies.

In warm weather sun baths should be given



Give the baby a coat of summer tan.

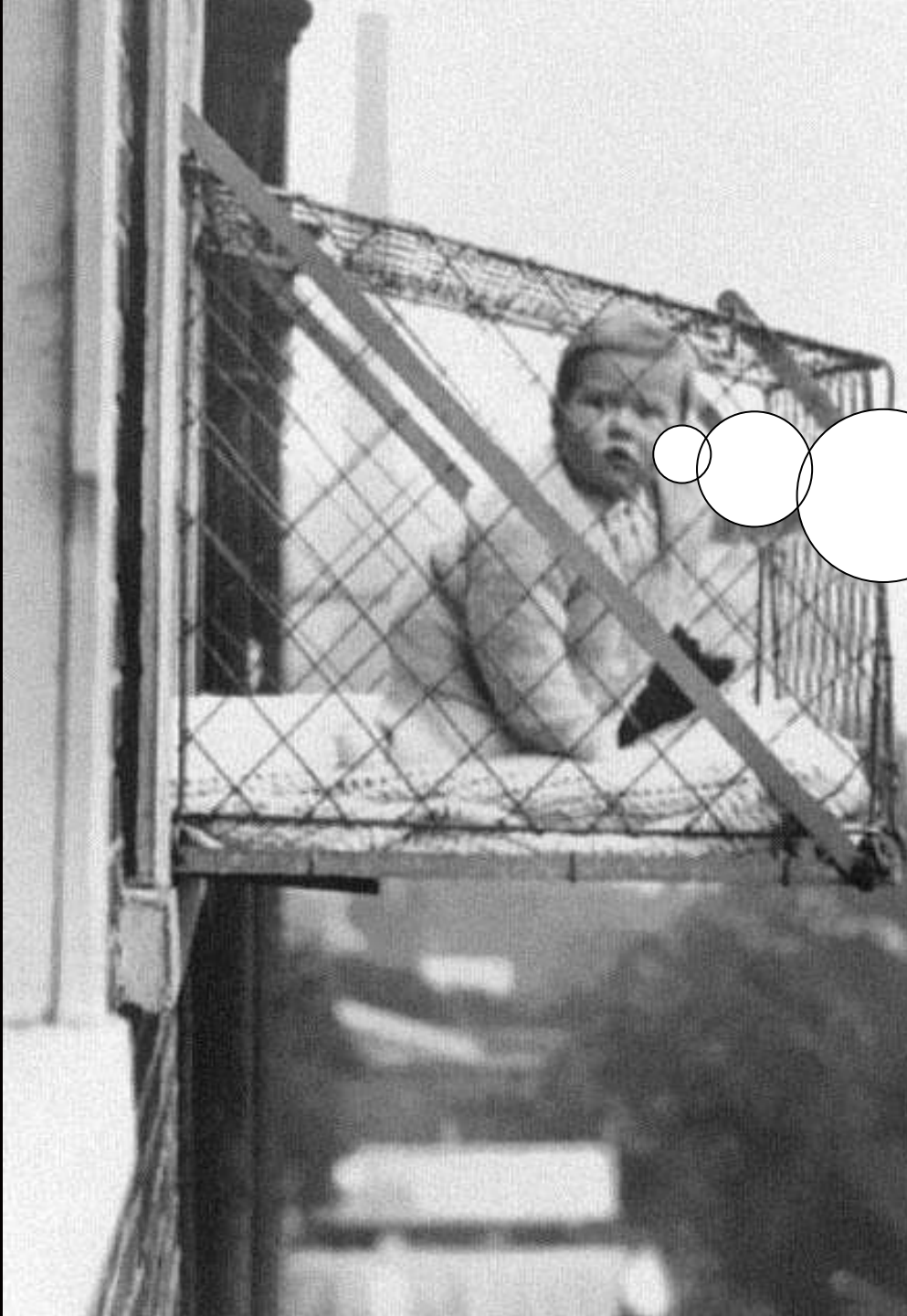
## SUNLIGHT, HEALTH, AND GROWTH

The sun that tans the child's skin helps him to grow normally. It gives his body the power



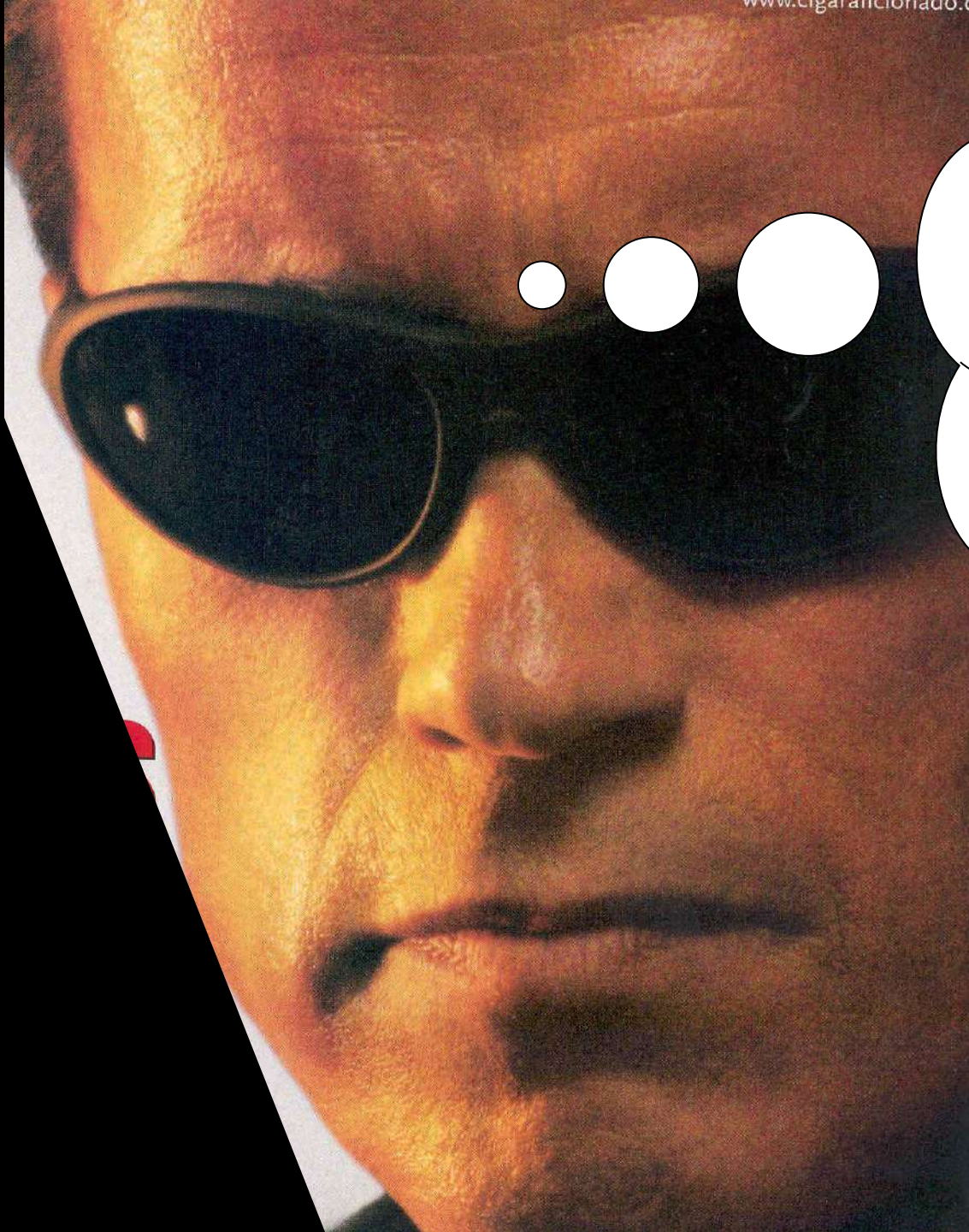
The first warm day is made sunny.

**US Department of Labor  
1931**



**Mommy**  
**Will I make**  
**Enough vitamin D**  
**????**

**What about skin**  
**Cancer**  
**????**



**Dermatology  
Societies  
FOR 50 YEARS  
ARE YOU  
SURE  
??????**



WHAT WILL  
HAPPEN IF MY  
CHILDREN GO  
OUT WITHOUT  
SUNSCREEN ?





**Child Abuse**

A close-up photograph of a black and white cow's face, looking out from a wooden stall. The cow's nose is prominent in the foreground, showing a black patch. The background shows other cows in a barn setting.

**Is it true we  
put vitamin D  
in milk ?????**

**we don't**

**put VITAMIN D  
in  
MILK**



THE STORY OF  
IRRADIATED VITAMIN 'D' MILK

THE *Magic* OF  
VITAMIN D

•  
STEENBOCK  
PROCESS OF  
IRRADIATION  
with  
ULTRA-VIOLET  
LIGHT  
•

WISCONSIN ALUMNI RESEARCH FOUNDATION

MADISON, WISCONSIN

PROTECTION



Grade A  
Pasteurized Homogenized



**vitamin**  
**D**  
**milk**

# VITAMIN D DEFICIENT RICKETS



NO  
CALCIFICATION

RICKETS



CALCIFICATION

VITAMIN D TREATED  
AFTER 2 MONTHS



SWOLLEN  
WRIST

POOR  
CALCIFICATION



3 YEARS OLD

NORMAL  
CALCIFICATION



STEENBOCK 1920s

VITAMIN D

is

ESSENTIAL

FOR

BONE HEALTH

# Case #1

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





**KIMANI**

**KIKI**

Franklin ZOO



**MY  
BONES  
HURT!!!!**



**MY DAUGHTER  
NEEDS HELP  
IMMEDIATELY**

**!!!**





**Please CALL  
Dr. HOLICK  
!!!!!!!!!!!!!!**



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



**D-ficient**




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

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



**1<sup>st</sup> Birthday**





**MOMMY**  
**Will my**  
**GROWTH**  
**Be STUNTED**  
**????**

**YES**  
**!!!!!!!**

**1889**

**BOSTON**

**80% INFANTS**

***RICKETS***

**BUT IS RICKETS**


**A PROBLEM**

**2019 ???? ?**

**Yes!!!**



**BOSTON MEDICAL CENTER**

A close-up photograph of a woman with a large hoop earring, wearing a red t-shirt with a graphic, breastfeeding her baby. The baby is wearing a red and white checkered shirt. A white speech bubble with a black outline is positioned over the top left of the image, containing text.

MY DOCTOR SAID  
BREAST MILK PROVIDES  
ALL THE NUTRITION  
MY INFANT NEEDS.

**Breastmilk - the Best Fast Food!**

The Breastfeeding Center  
88 East Newton St. Vose 3  
[breastfeeding@bmc.org](mailto:breastfeeding@bmc.org)

Boston Medical Center  
Boston, MA 02118

CYBILL SHEPHERD MOUTHS OFF

# Ms.

Special Report

## BREAST VS. BOTTLE

A NEW  
THE

THERE IS  
LITTLE VITAMIN D  
BREAST MILK

~ 25 IU/L

ISA  
On Ero  
Love, Grien,  
and Life



DISPLAY UNTIL APRIL 27, 1998

VOLUME VIII Number 5 \$5.95 U.S. \$6.95 CANADA

Harper's  
**BATH**

**FALL**  
SHOPPING  
PREVIEW

GET  
PERFECT  
SKIN

GREAT  
FASHION  
FOR EVERY  
AGE

Nothing to wear?

**487** Best  
new ideas  
inside

**CAN I BE AT  
RISK ???????**

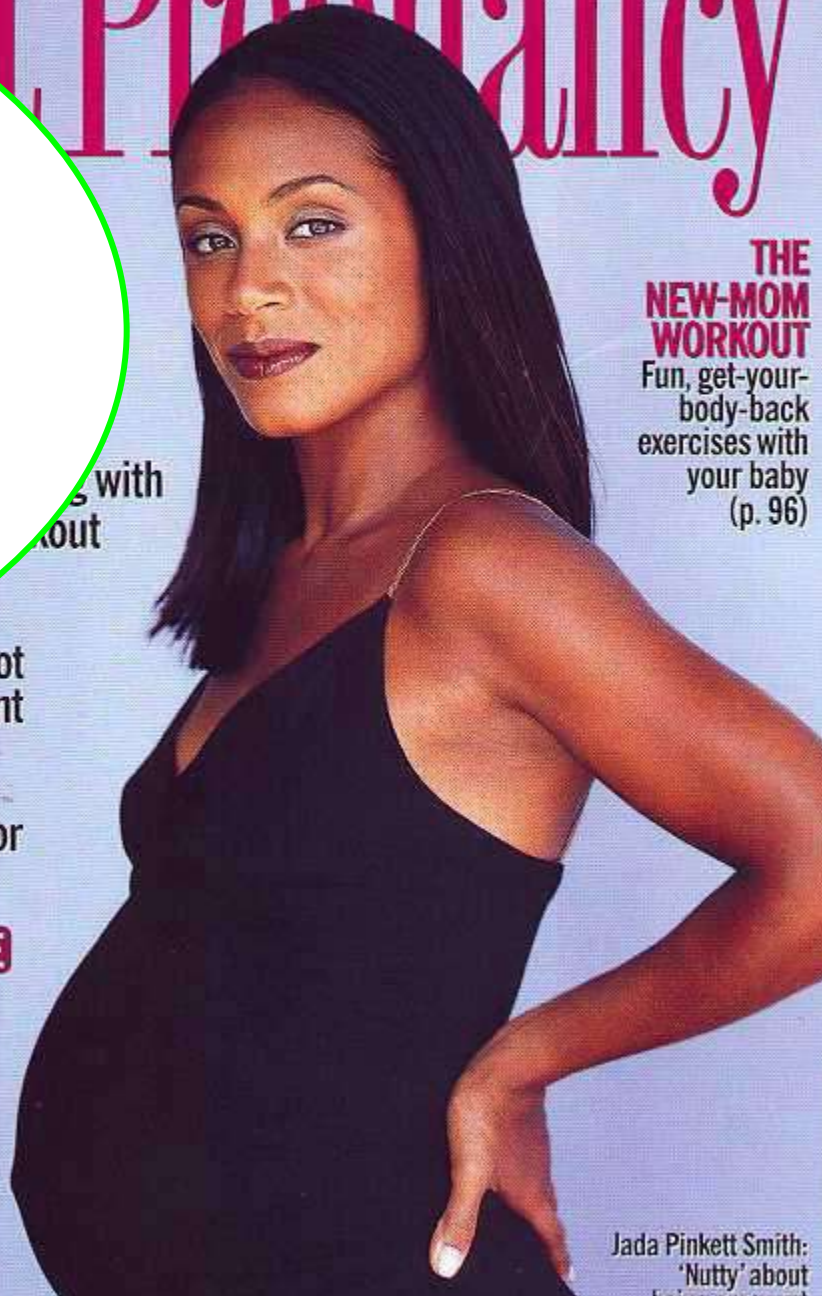




**IS VITAMIN D DEFICIENCY  
A COMMON PROBLEM  
FOR PREGNANT WOMEN  
???????**

For the Whole Nine Months . . . and Beyond  
**Fit Pregnancy**

**THE  
NEW-MOM  
WORKOUT**  
Fun, get-your-  
body-back  
exercises with  
your baby  
(p. 96)



**Super foods**  
Complete nutrition for  
you and your baby

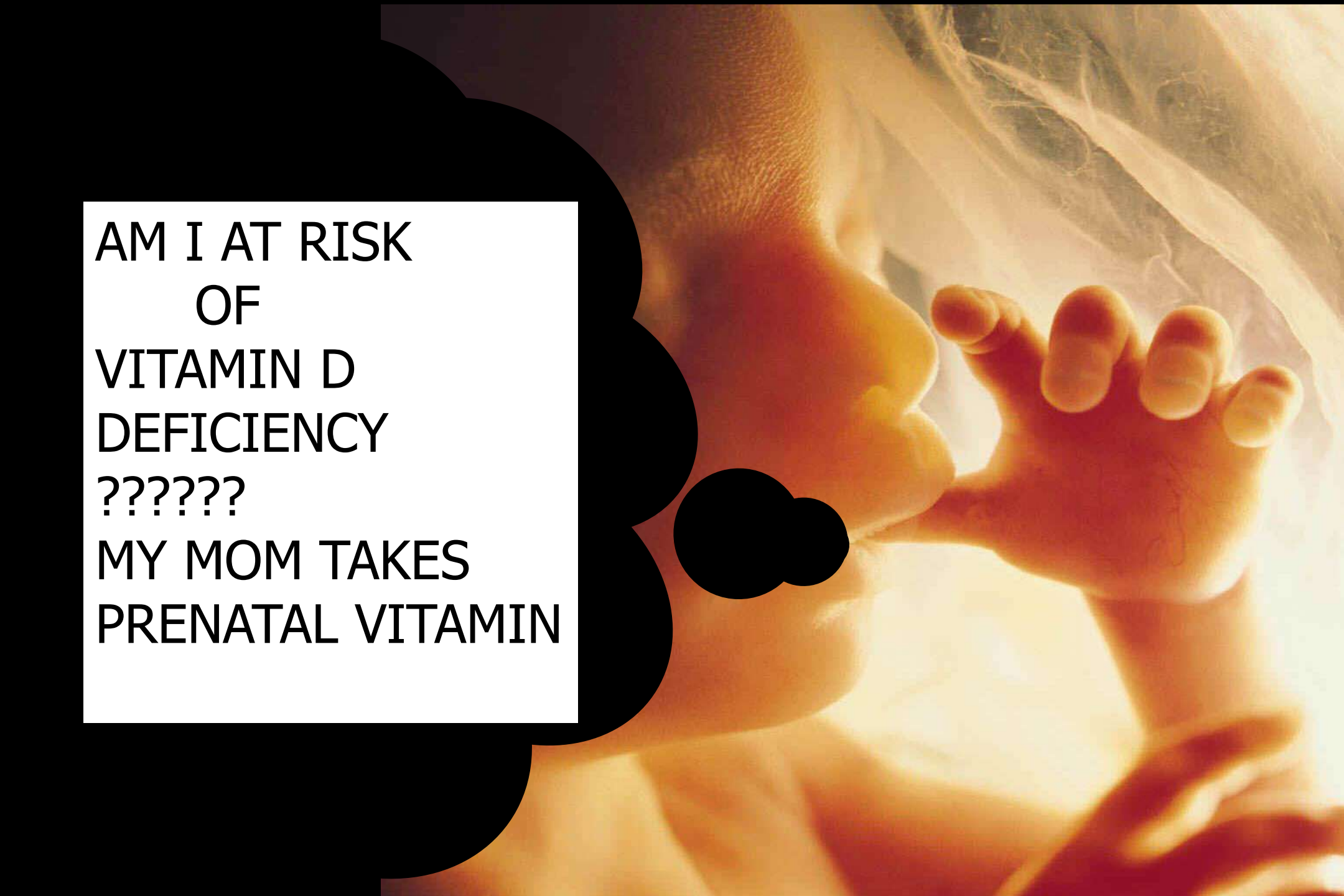
**SEXY HOLIDAY STYLE**

**Baby-care basics**  
We take the fear  
out of those first  
days home

\$4.95 US/\$5.95 Can Dec/Jan 2001  
Display until January 23, 2001



Jada Pinkett Smith:  
'Nutty' about  
being pregnant



AM I AT RISK  
OF  
VITAMIN D  
DEFICIENCY  
??????  
MY MOM TAKES  
PRENATAL VITAMIN

# 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)

N(%)

Race

Black	25 (62.5%)
Caucasian	10 (25%)

**Daily Intake Vitamin D  
~600 IU**

Drinks milk	37 (92.5%)
Eats fish	44(89.7%)
MVI(400 IU Vit D)	28(70%)
Ca supplement	4(10%)
Vit D supplement	0 (0%)

**70% MTV**

	Mean Val
Age (years)	28.8 ± 6.5
Milk Consumption (8 oz. glasses/day)	2.3±2.4
Fish Consumption (servings a month)	6.2±5

**DRANK  
2.3 GLASSES  
MILK/D**

**76% Mothers**

**81% Newborns**

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

**Vitamin D Deficient**



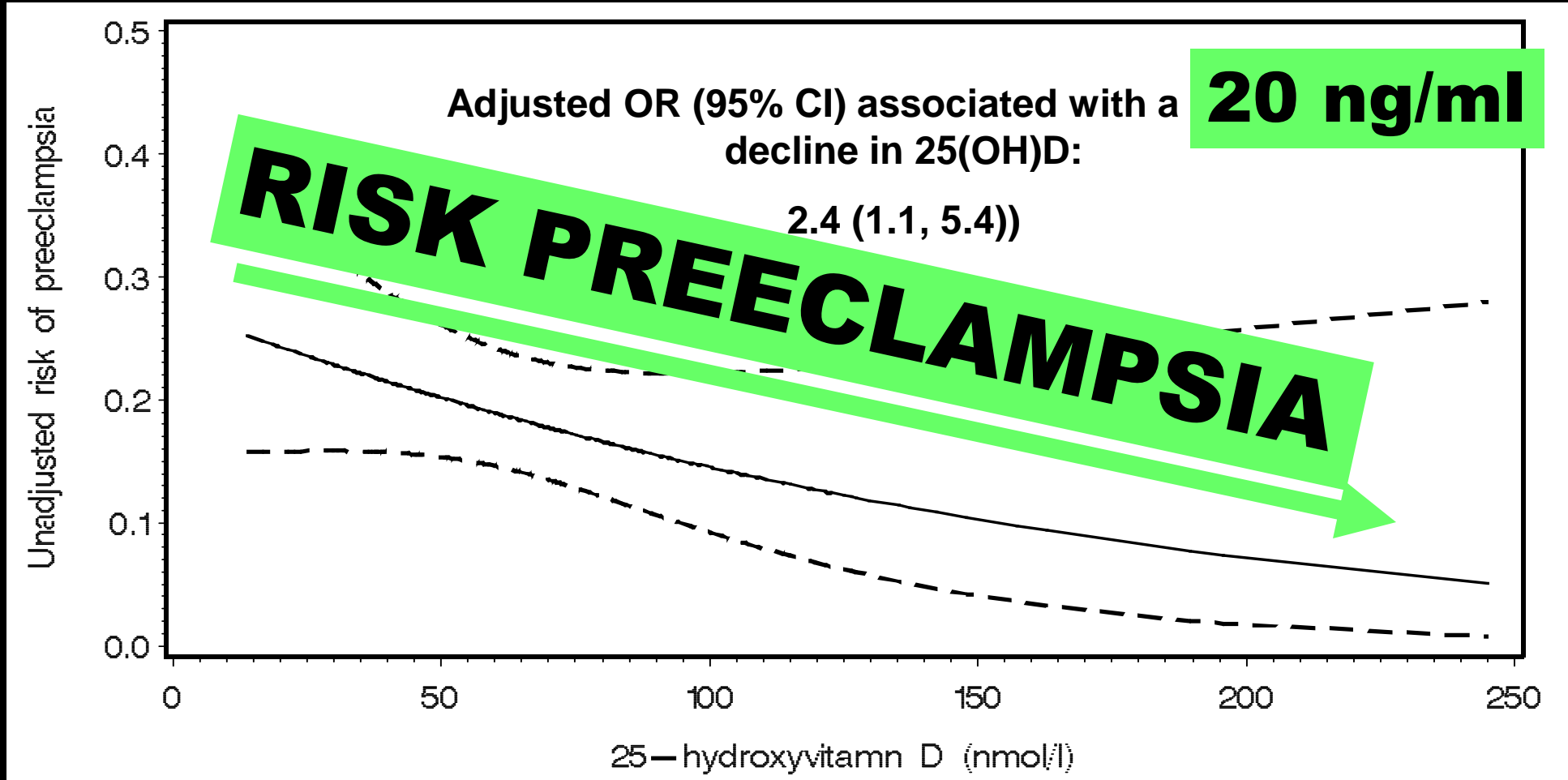
**PREECLAMPSIA**

## Preeclampsia

Preeclampsia is an increased blood pressure and protein in the urine (as a result of kidney problems) related condition starts after the 20th week of pregnancy.



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





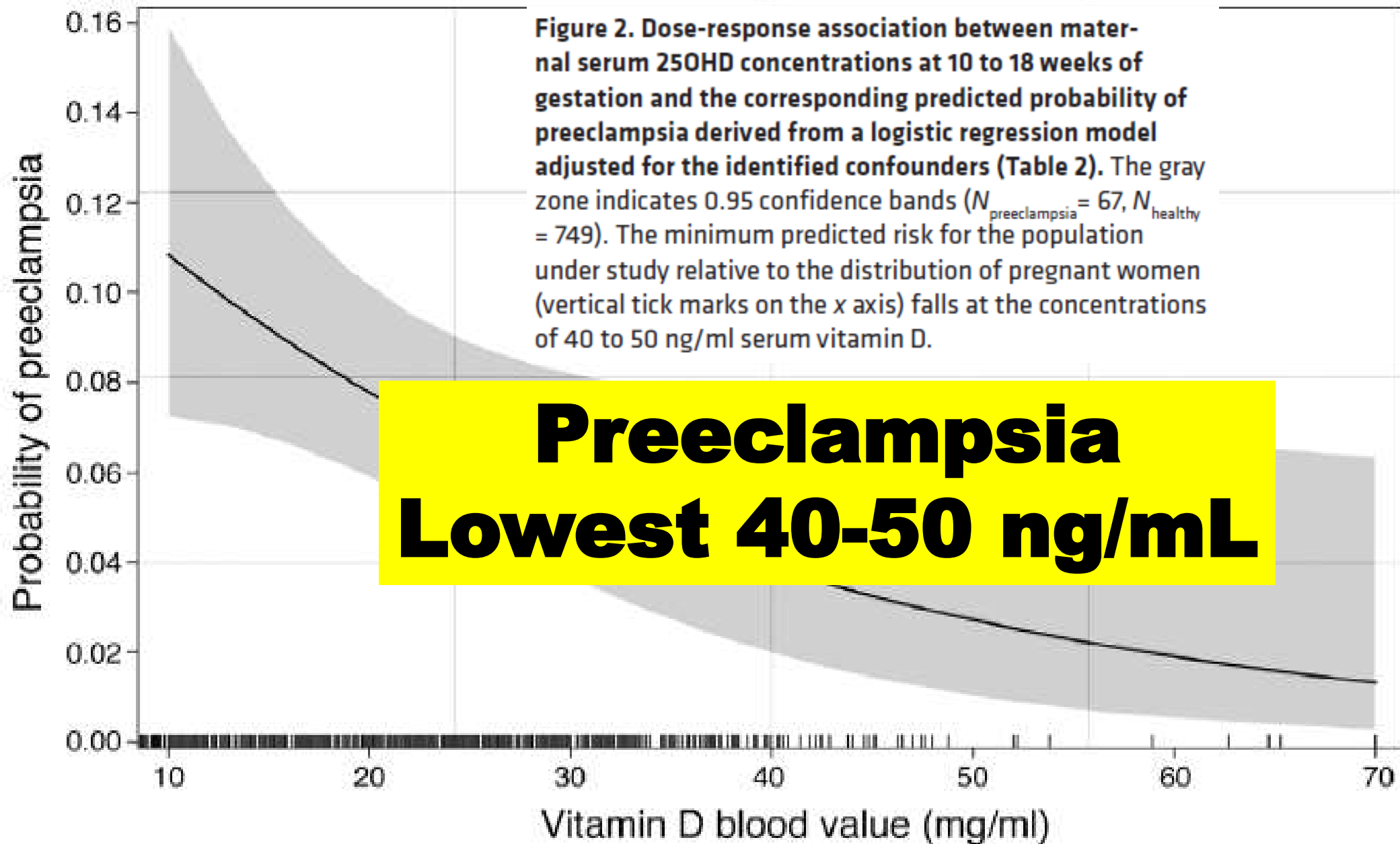


Figure 2. Dose-response association between maternal serum 25OHD concentrations at 10 to 18 weeks of gestation and the corresponding predicted probability of preeclampsia derived from a logistic regression model adjusted for the identified confounders (Table 2). The gray zone indicates 0.95 confidence bands ( $N_{\text{preeclampsia}} = 67$ ,  $N_{\text{healthy}} = 749$ ). The minimum predicted risk for the population under study relative to the distribution of pregnant women (vertical tick marks on the x axis) falls at the concentrations of 40 to 50 ng/ml serum vitamin D.

**Preeclampsia  
Lowest 40-50 ng/mL**

# Early pregnancy vitamin D status and risk of preeclampsia

Hooman Mirzakhani,<sup>1</sup> Augusto A. Litonjua,<sup>1,2</sup> Thomas F. McElrath,<sup>3</sup> George O'Connor,<sup>4</sup> Aviva Lee-Parritz,<sup>5</sup> Ronald Iverson,<sup>5</sup> George Macones,<sup>6</sup> Robert C. Strunk,<sup>7</sup> Leonard B. Bacharier,<sup>7</sup> Robert Zeiger,<sup>8</sup> Bruce W. Hollis,<sup>9</sup> Diane E. Handy,<sup>10</sup> Amitabh Sharma,<sup>1</sup> Nancy Laranjo,<sup>1</sup> Vincent Carey,<sup>1</sup> Weilliang Qiu,<sup>1</sup> Marc Santolini,<sup>1,11</sup> Shikang Liu,<sup>12</sup> Divya Chhabra,<sup>13</sup> Daniel A. Enquobahrie,<sup>14</sup> Michelle A. Williams,<sup>15</sup> Joseph Loscalzo,<sup>16</sup> and Scott T. Weiss<sup>1,17</sup>

BACKGROUND. Low vitamin D status in pregnancy was proposed as a risk factor of preeclampsia.

METHODS. 400 vs 4400 IU/D 10-18 wks (10-18 weeks), of

preeclampsia incidence at trial entry and in the third trimester (27-28 weeks) were studied. We also conducted a nested case-control study of 157 women to investigate the expression profiles at 10 to 18 weeks in 47 participants who developed preeclampsia.

RESULTS. Of 881 women randomized, outcomes were 67 (8.2%) developing preeclampsia. There was no significant difference between treatment groups in the incidence of preeclampsia (8.08% vs. 8.33%, respectively).

However, a significant reduction in preeclampsia incidence was observed in women with insufficient vitamin D levels (<0.05 in the multivariate model) and network analysis of differentially expressed genes implicated inflammatory pathways.

CONCLUSIONS. Vitamin D supplementation initiated in weeks 10-18 of pregnancy did not reduce preeclampsia incidence in the intention-to-treat paradigm. However, vitamin D levels of 30 ng/ml or higher at trial entry and in late pregnancy were associated with a lower risk of preeclampsia. Differentially expressed vitamin D-associated transcriptomes implicated the emergence of an early pregnancy, distinctive immune response in women who went on to develop preeclampsia.

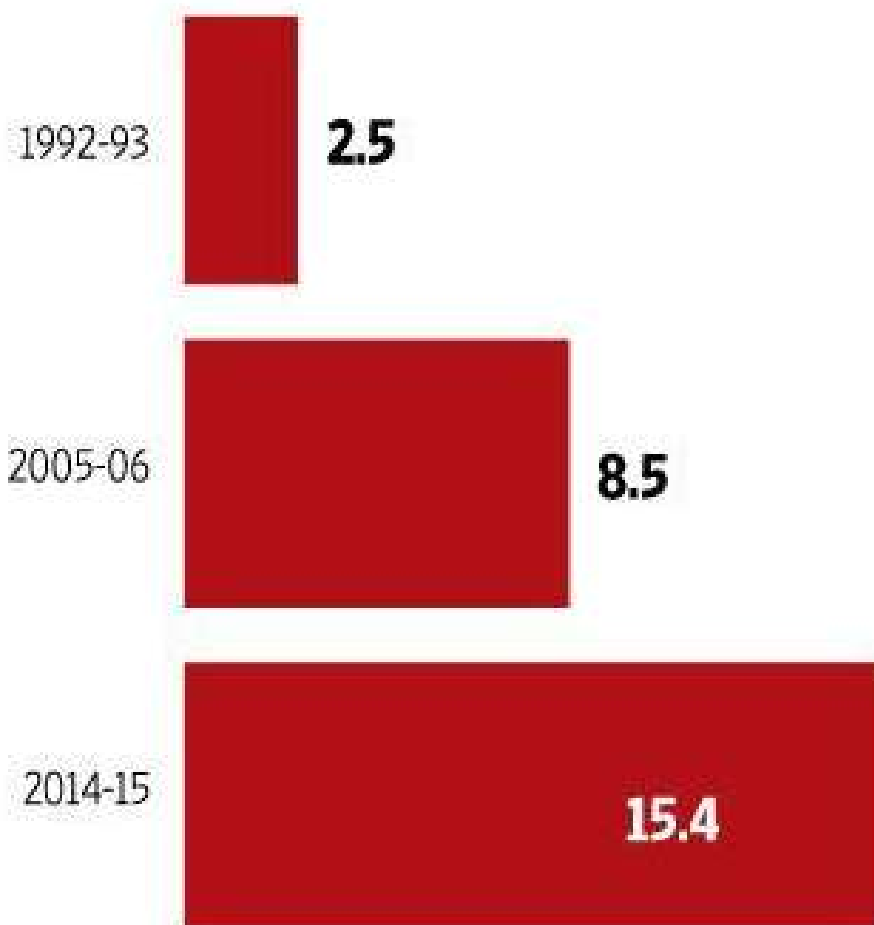
TRIAL REGISTRATION. ClinicalTrials.gov NCT00920621.

# The alarming increase in caesarean births in India

The past decade has seen India cross that WHO threshold for caesareans at an overall level

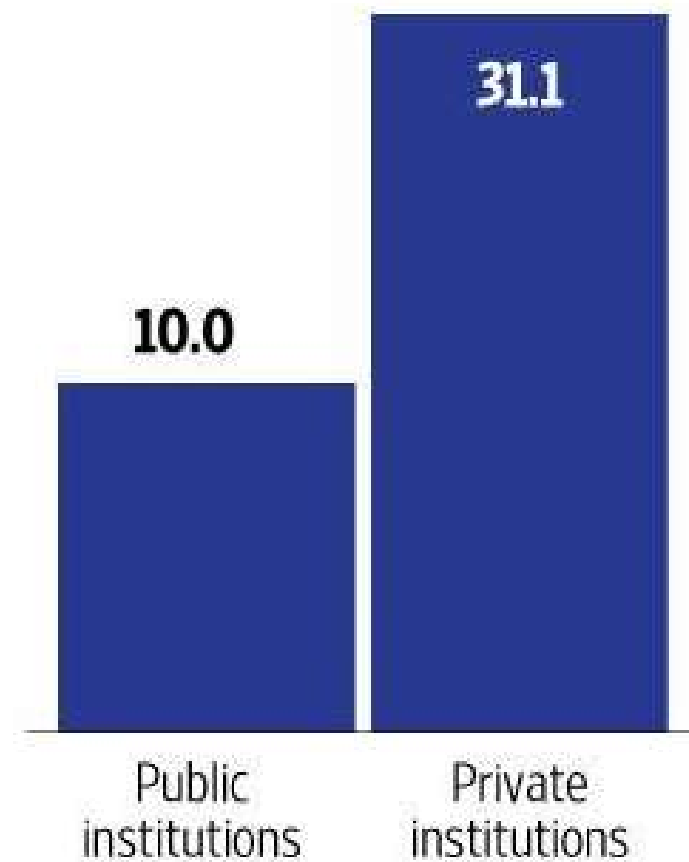
## Caesarean deliveries in India (%)

By year



## Caesarean deliveries (%)

By type of hospital



Figures for 2014-15

# **Association Between Severe Vitamin D Deficiency and Primary Caesarean**

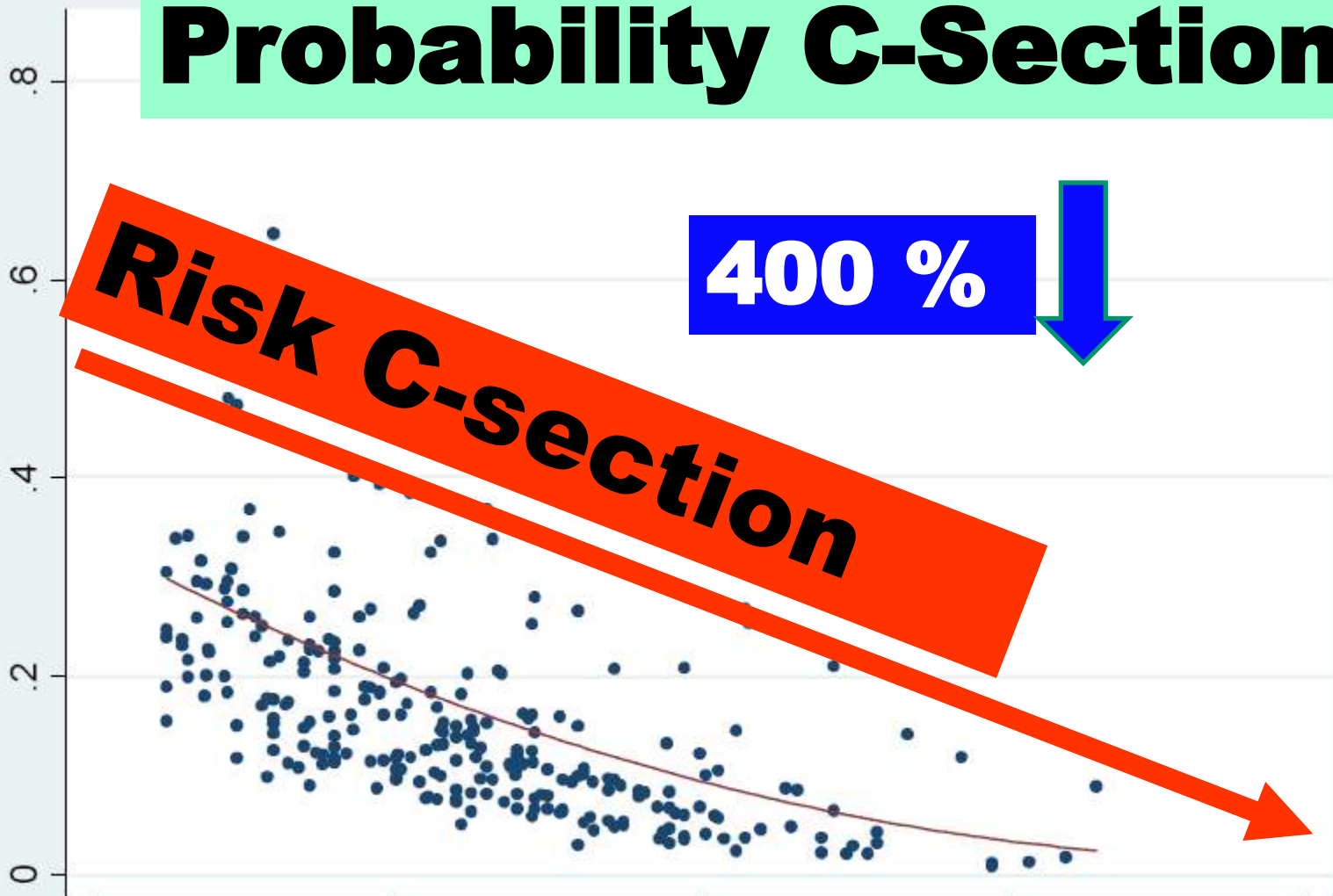
---

## **Section**

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

# Probability C-Section

Predicted Probability of Cesarean Section



**0 20 40 60 80**

**Mother's 25(OH)D ng/ml**

# **Maternal Vitamin D Insufficiency Early in Pregnancy Is Associated with Increased Risk of Preterm Birth in Ethnic Minority Women in Canada<sup>1,2</sup>**

Negar Tabatabaei,<sup>3,9</sup> Nathalie Auger,<sup>5</sup> Catherine M Herba,<sup>3,6</sup> Shuqin Wei,<sup>3,4</sup> Catherine Allard,<sup>7</sup> Guy D Fink,<sup>7,8</sup> and William D Fraser<sup>3,7,9\*</sup>



**Could I have  
been delivered  
At **Term**  
If Mom had  
taken  
**Vitamin D**  
**?????****



Maternal 25(OH)D concentrations  $\geq 40$  ng/mL  
associated with 60% lower preterm birth risk  
among general obstetrical patients at an  
urban medical center

Sharon L. McDonnell<sup>1</sup>, Keith A. Baggerly<sup>2</sup>, Carole A. Baggerly<sup>1</sup>, Jennifer L. Aliano<sup>1</sup>,  
Christine B. French<sup>1\*</sup>, Leo L. Baggerly<sup>1</sup>, Myla D. Ebeling<sup>3</sup>, Charles S. Rittenberg<sup>3</sup>,  
Christopher G. Goodier<sup>3</sup>, Julio F. Mateus Niño<sup>3</sup>, Rebecca J. Wineland<sup>3</sup>, Roger  
B. Newman<sup>3</sup>, Bruce W. Hollis<sup>3</sup>, Carol L. Wagner<sup>3</sup>

Zoom of Fitted LOESS Curve (MUSC, N=1064)

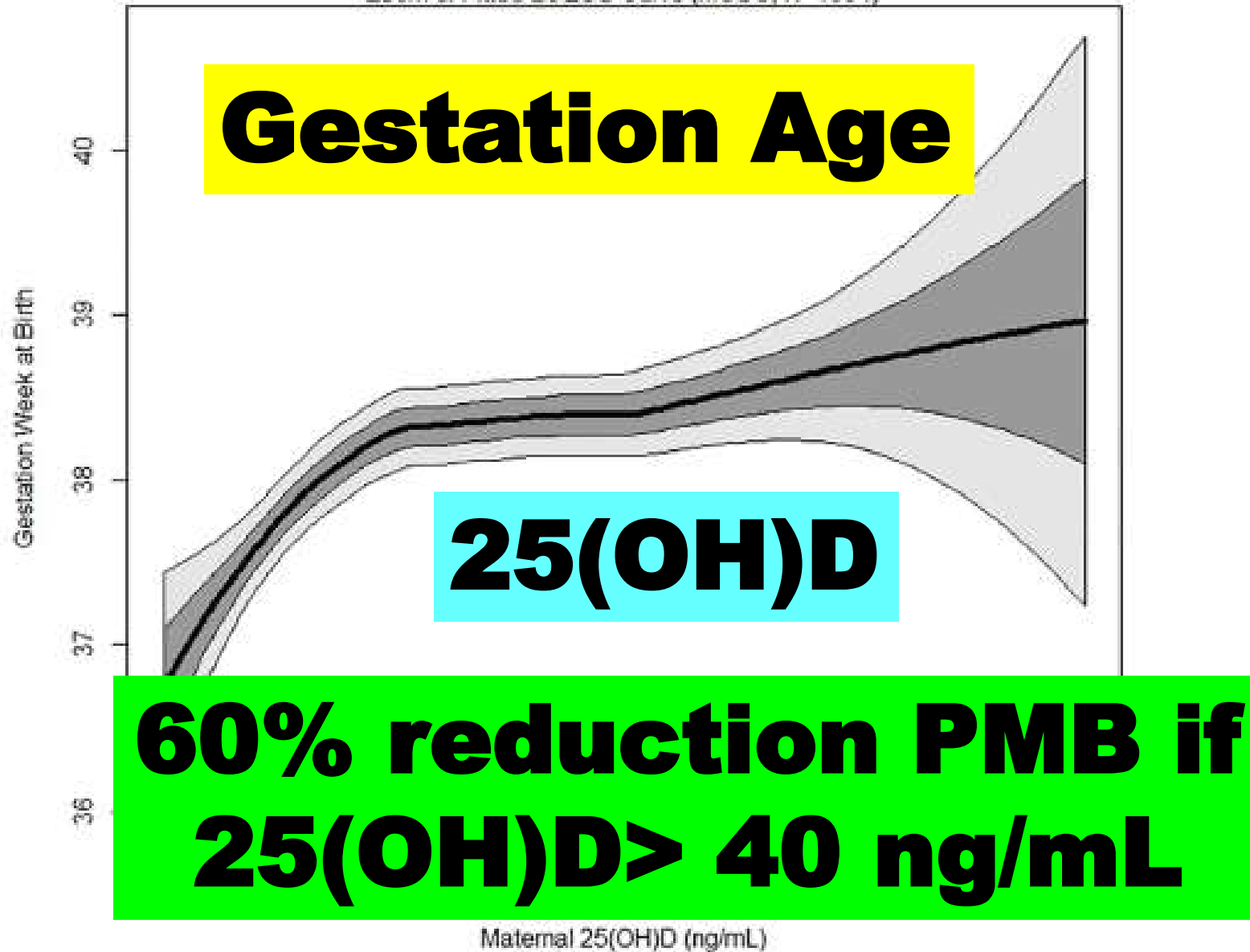


Fig 2. Zoom of the fitted LOESS curve of maternal 25(OH)D concentration and gestational age (weeks) at birth with 1 and 2 SD windows superimposed. Black line represents fitted LOESS curve, dark gray area represents 1 standard deviation, and light gray area represents 2 standard deviations.

**Mom  
Thanks for Taking  
Vitamin D**



JOIN OUR NEW BOOK CLUB!

January 2008

# marie claire

## SEXY WINTER SKIN

57 SMART BEAUTY BUYS

**LOVE REHAB**  
"I SAID NO TO SEX... AND GOT SEXIER"

**TANNING, BLEACHING, BOTOXING**  
ARE YOU OBSESSED?

# 101

IDEAS FOR EASY WEEKEND STYLE

"HOW I LEARNED TO LOVE THE MOTHER I HATED"

I NEED **2000 IU** VITAMIN D/DAY TO PROVIDE ENOUGH VITAMIN D FOR ME & MY INFANT

THE BUSY GIRL GUIDE TO A **BETTER BODY**

Christina Aguilera **REVEALED**

AMAZING PICTURES INSIDE

"WHEN I FOUND OUT, I STARTED SHAKING"



**Ms.**

CYBILL SHEPHERD MOUTHS OFF

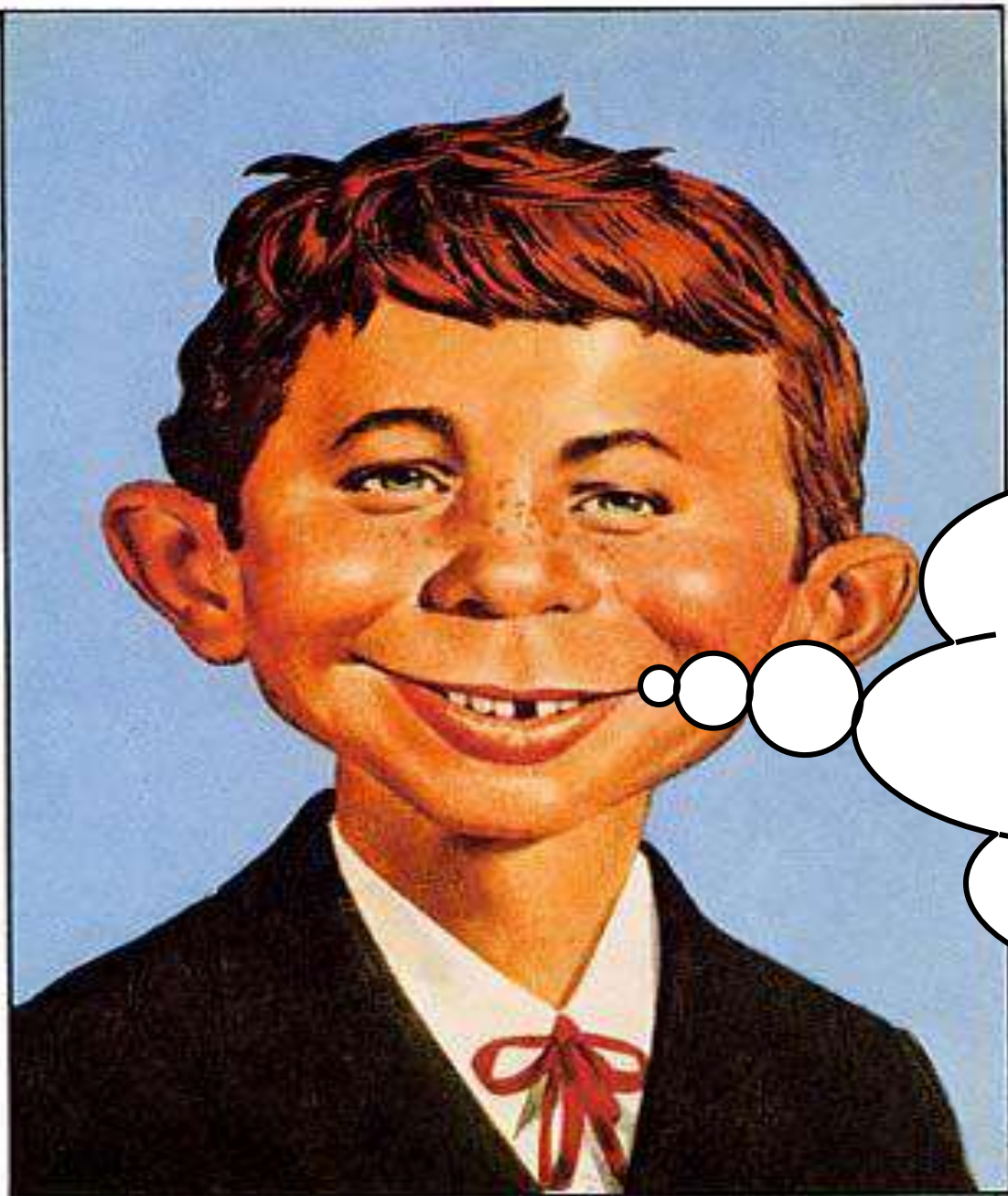
**How much does  
my Mother need  
to provide me with  
my Vitamin D in  
Breast milk ????**

**6000 IU/D**


**Hollis and Wagner AJCN 2004**

DISPLAY UNTIL APRIL 27, 1998

VOLUME VII NUMBER 5 \$5.95 U.S. \$6.95 CANADA

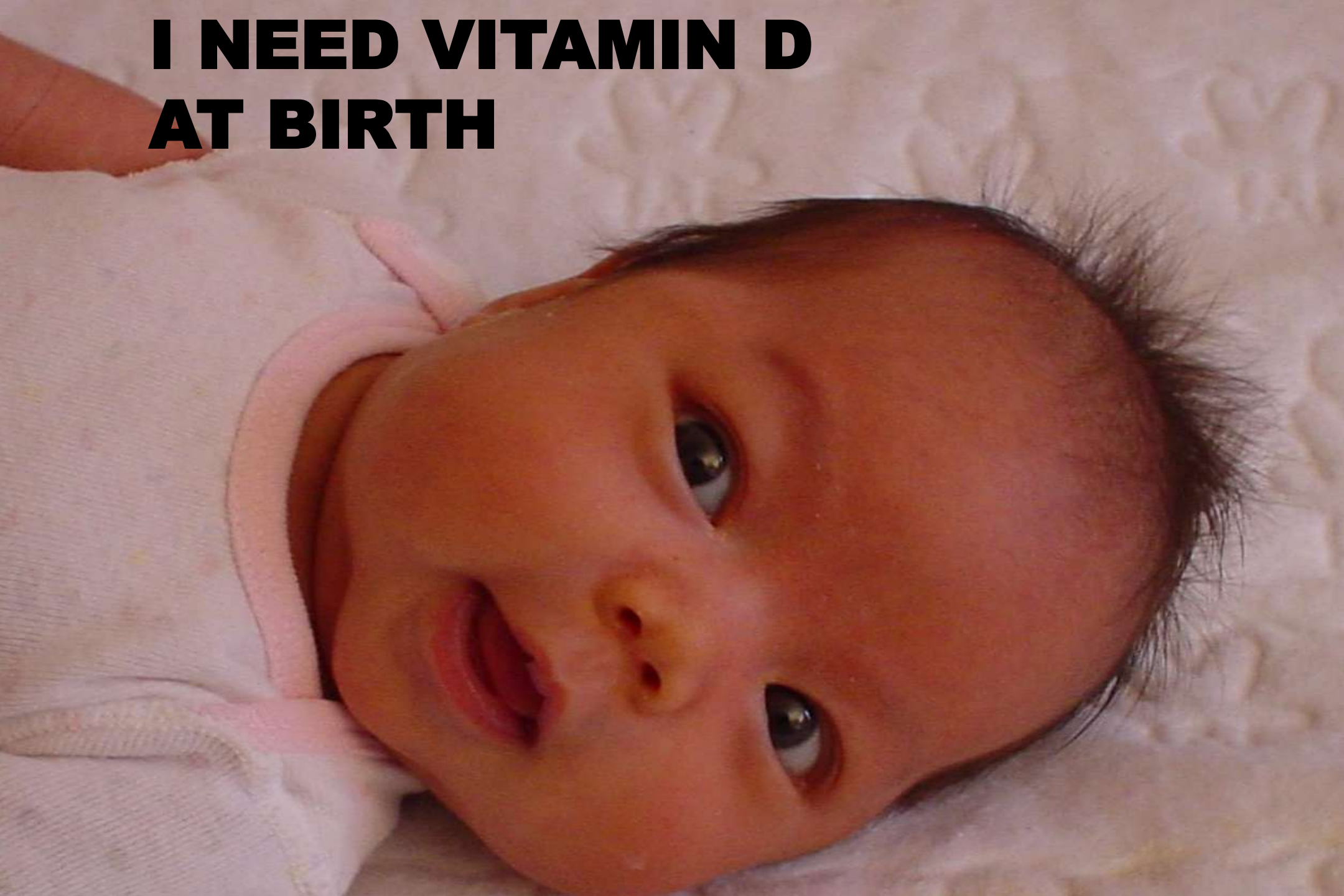


BUT INFANTS ARE  
MORE  
SUSCEPTIBLE  
TO VITAMIN D  
INTOXICATION  
!!!!!!!!!!!!



**How Much Do  
I Need To  
Prevent  
Vitamin D  
Deficiency  
??????**

**I NEED VITAMIN D  
AT BIRTH**





SEARCH

The Web  CNN.com

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Weather

Business at CNNMONEY

## Breast-fed infants need extra vitamin D

Monday, April 7, 2003 Posted: 10:07 AM EDT (1407 GMT)

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

News

News

News

SEARCH


international units of vitamin D, available as over-the-counter liquid drops or tablets. Supplements containing only vitamin D generally are too concentrated to be safe for routine use, it says.

The new recommendation also applies to:

# Case #2

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





# JURASSIC SYNDROME

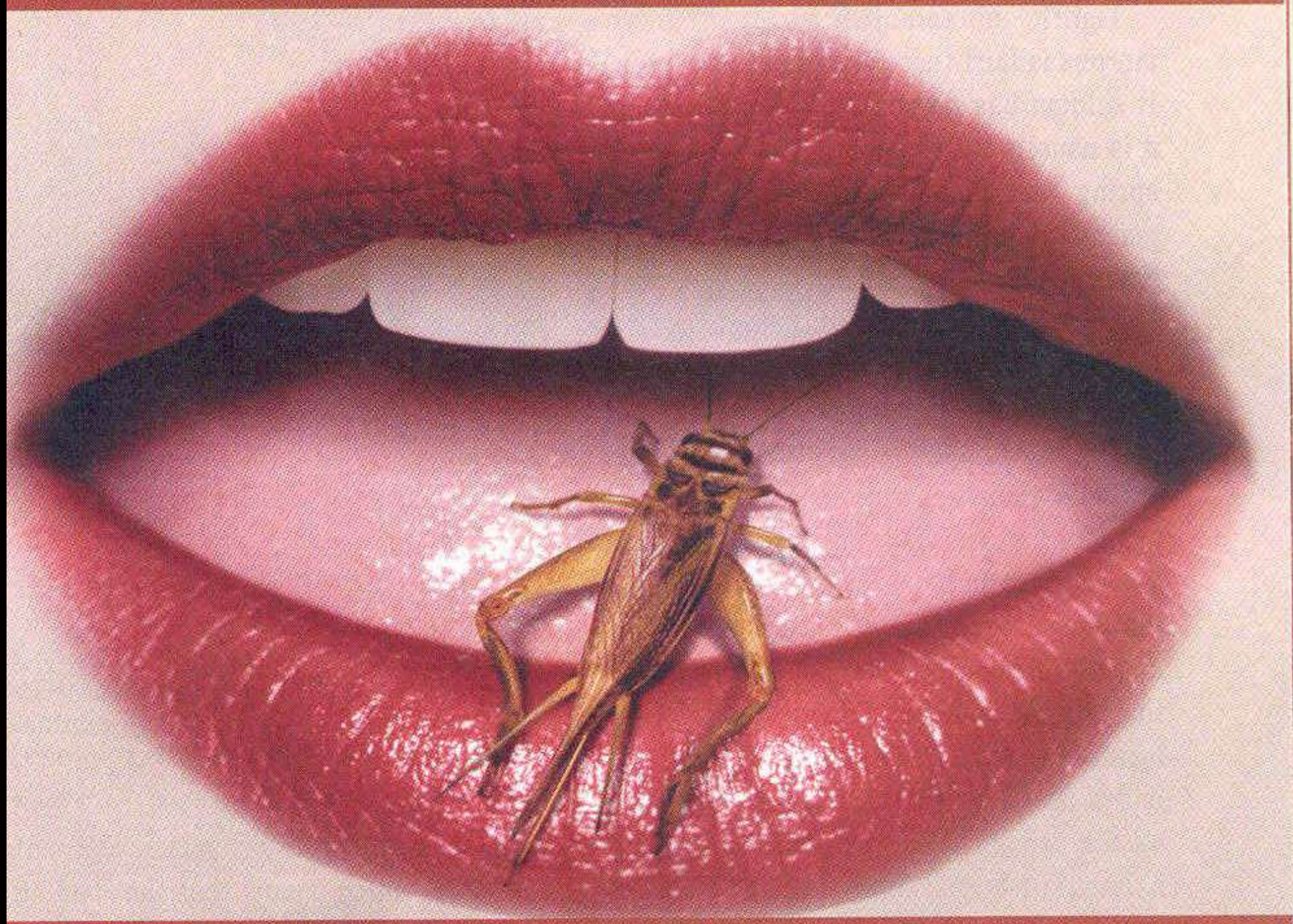
JURASSIC PARK™

750,000 young at risk

# Diet

- Lettuce
- Crickets

**Dx ?**



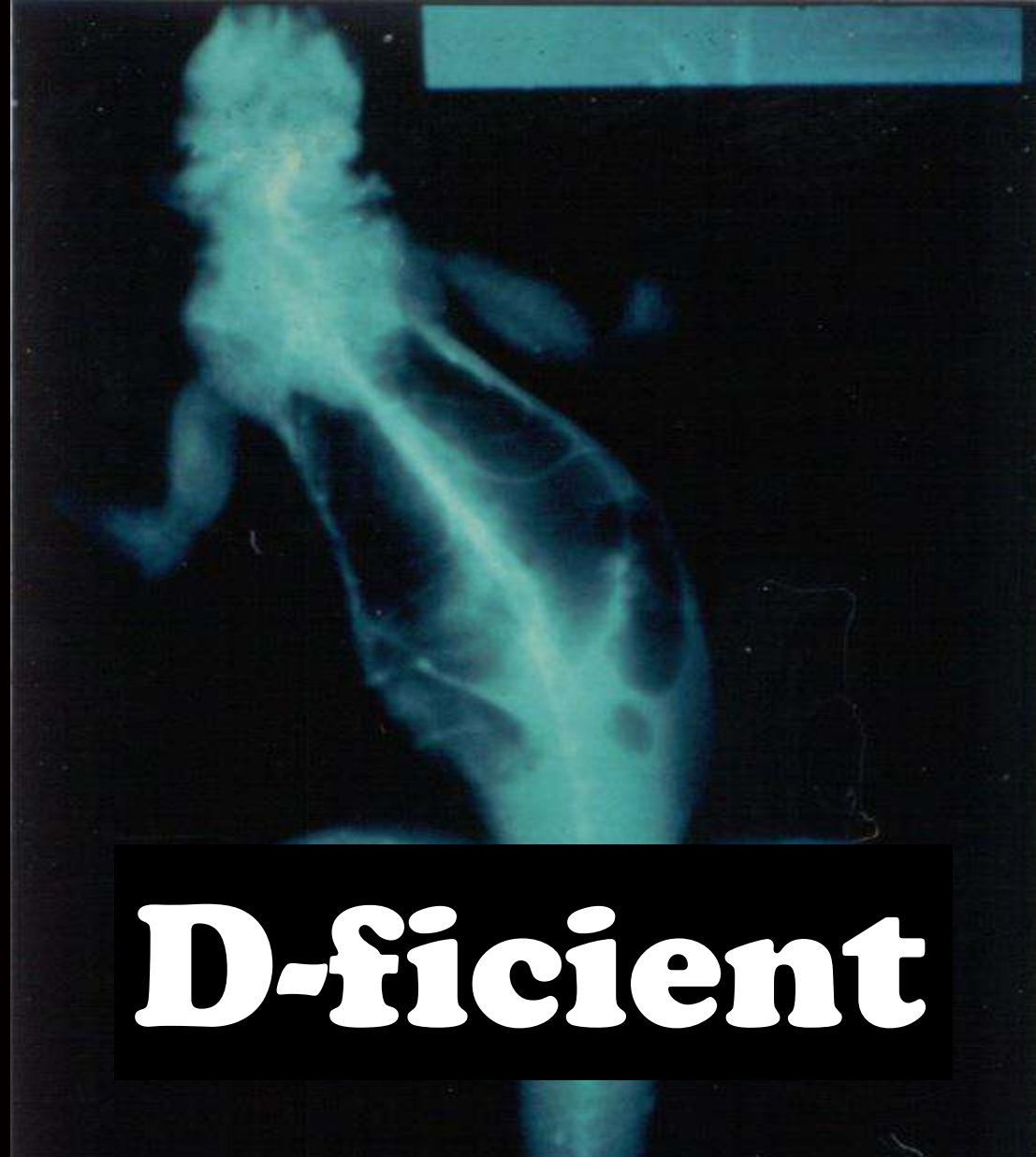
Dinner is Served.



**750,000 IMPORTED/YEAR**







**D-ficient**

Osteoporosis & Osteomalacia

August 1997

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ISSUE!

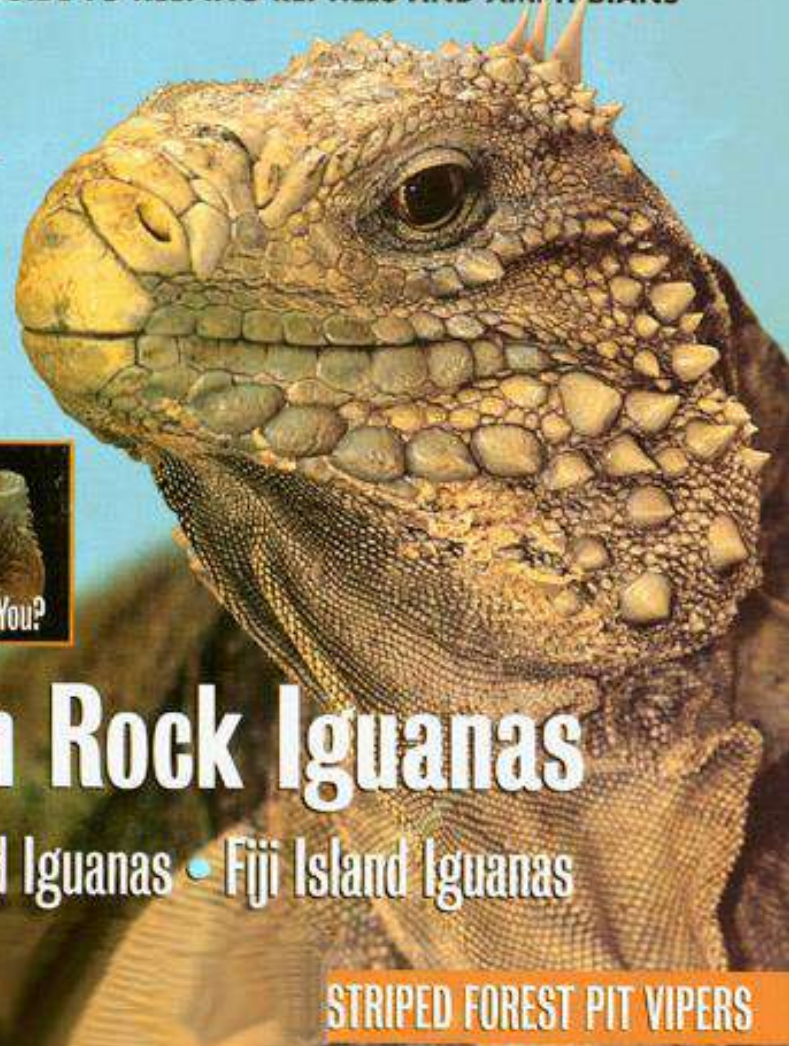


Is a Green Iguana  
the Pet for You?

## Cuban Rock Iguanas

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.



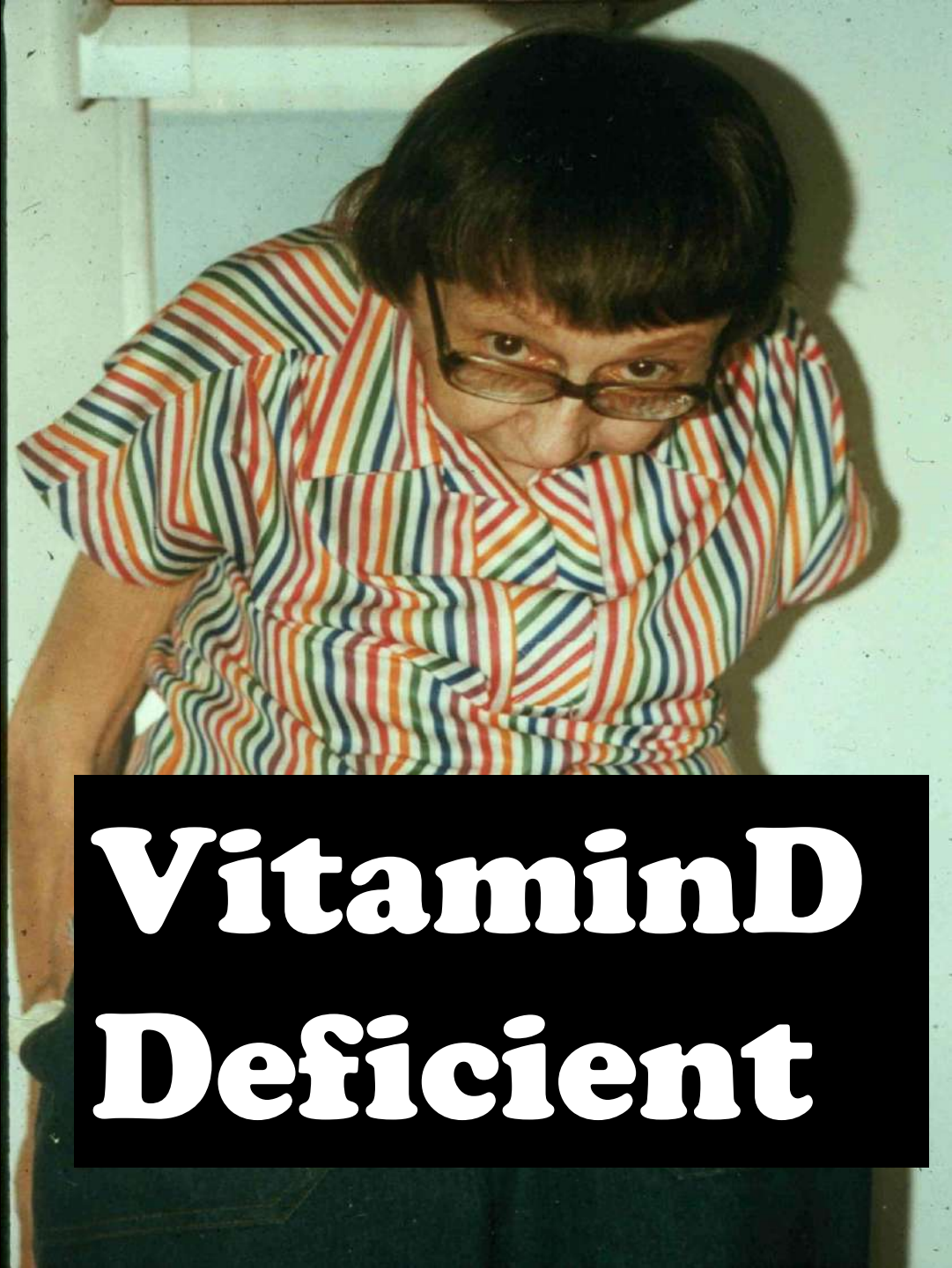
article by  
margaret  
a. wissman,  
dvm, dabvp

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

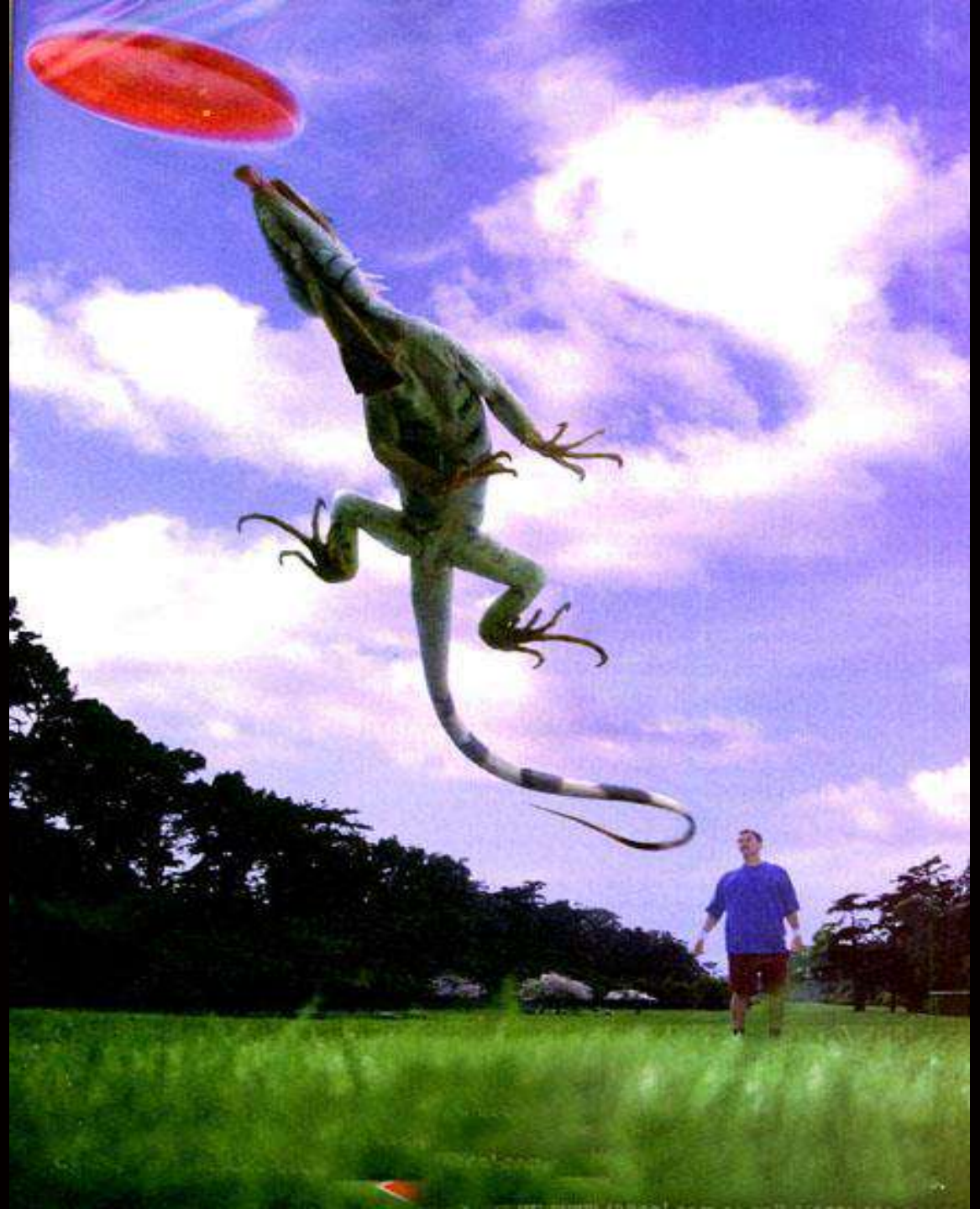




**VITAMIN D**

**SUNLIGHT**

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



# REPTA SUN™

LONG LIFE FULL SPECTRUM LIGHTING

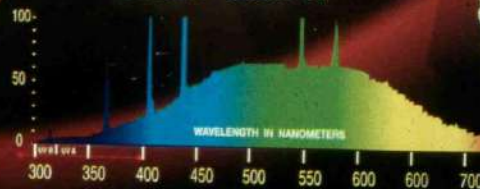
## FULL SPECTRUM

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 animal's 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.

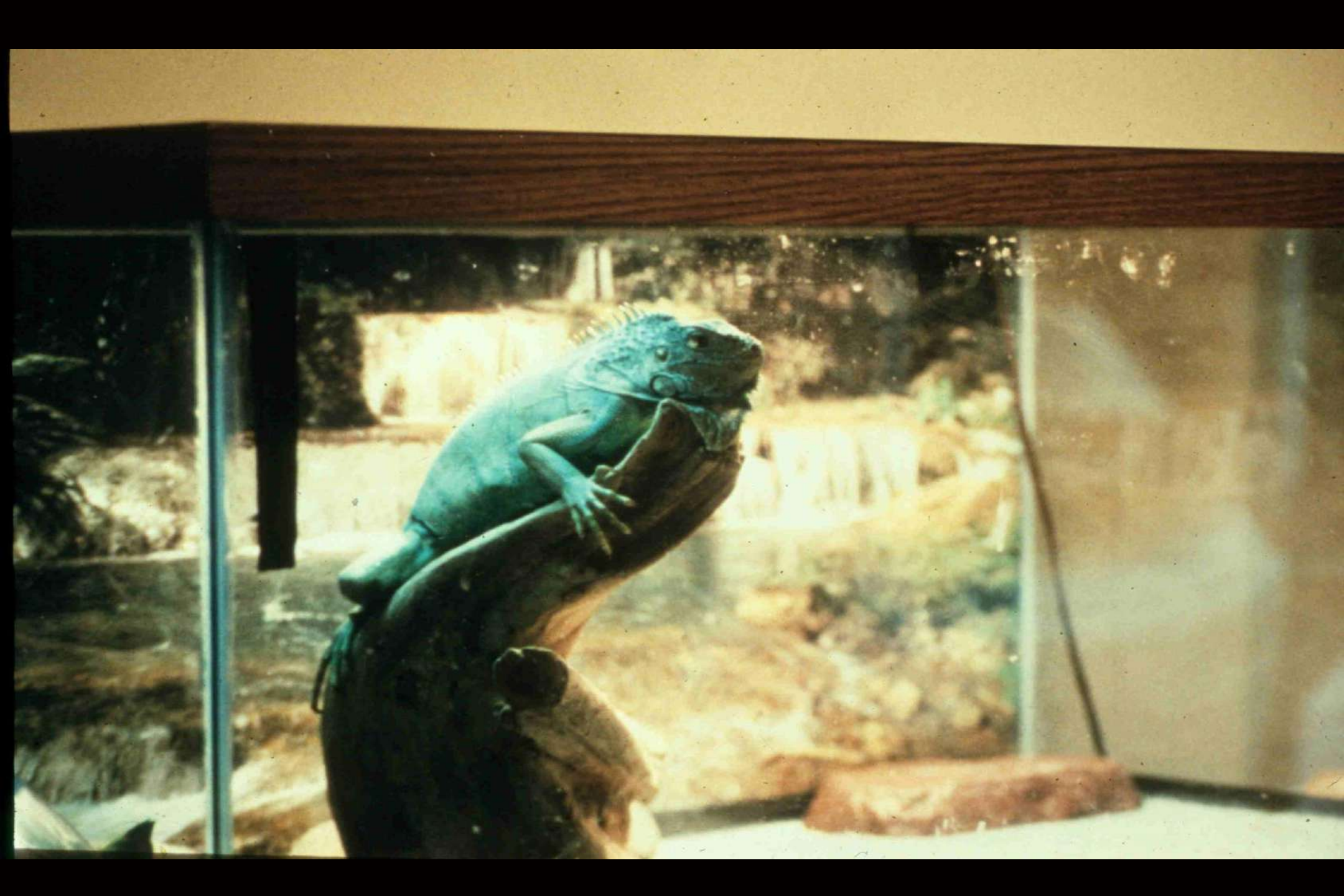
## SPECTRAL GRAPH CRI-91 5600 K

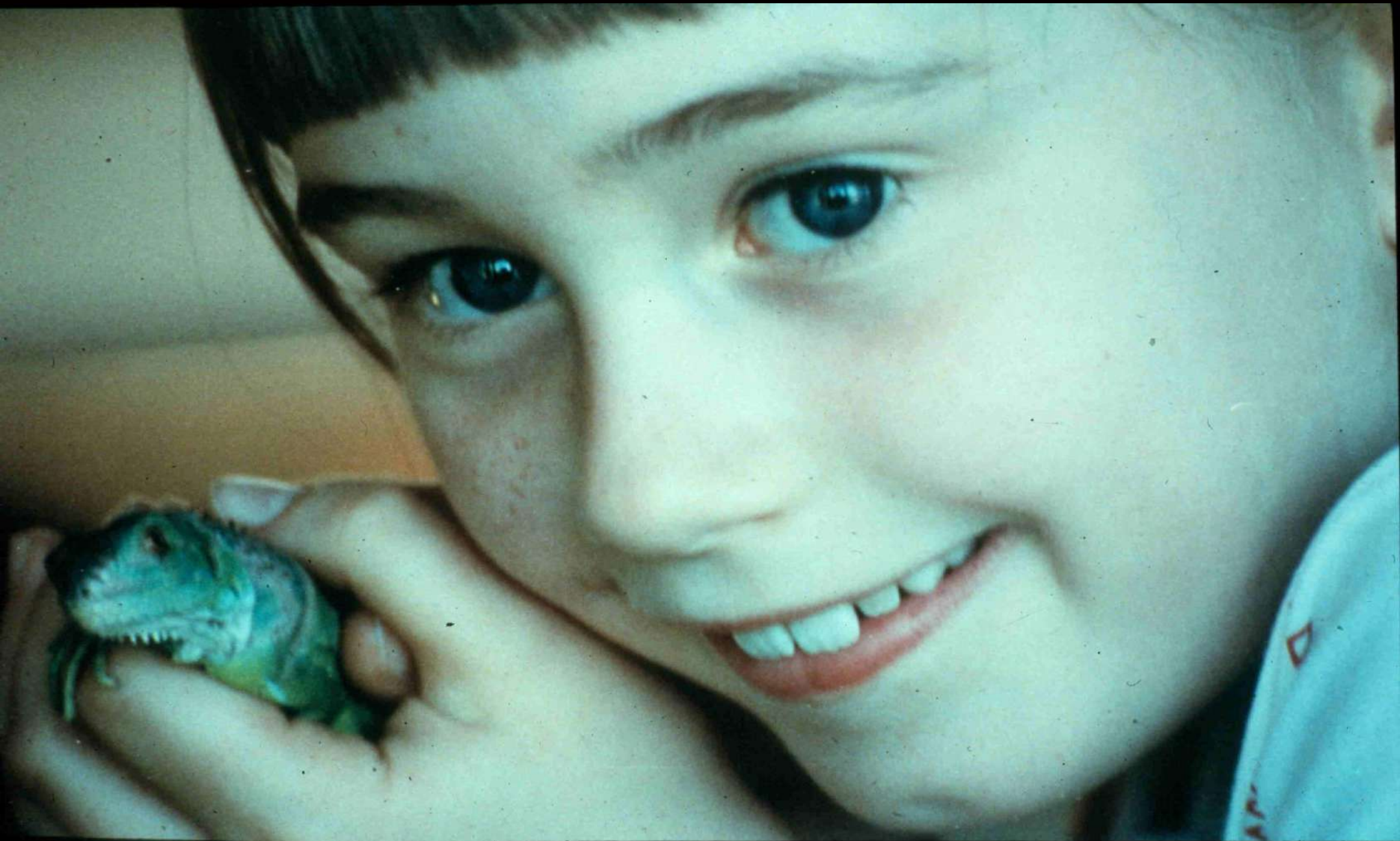


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**\$40**





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







# Case #3

- **6 month old twins**
- **Muscle Weakness**
- **Boney Deformities**
- **Failure to Thrive**



6

Pronghorn  
Skull  
12/16/84



7

Pronghorn  
Skeleton  
12/16/84



**Vitamin D-deficient  
Severe  
proximal muscle weakness**



**Vitamin D + TLC**

# Case #4

- **5 Year Old Female**
- **Poor Dentition**
- **Dental Caries**
- **Delayed tooth eruption**

A close-up photograph of a person's mouth, showing the upper and lower teeth. The teeth appear to be in poor health, with visible decay and discoloration. The background is dark, and the lighting is focused on the teeth. The image has a slightly grainy texture.

**D-ficient**

**Dental Problems**

## Dental Caries is on the Rise

The Centers for Disease Control and Prevention report that dental caries is the most common childhood disease in America today, five times more common than asthma.

Even more alarming is the fact that the decay rate is on the rise. Today, 8% of our nation's infants and toddlers have "Early Childhood Caries", formerly called Baby Bottle Tooth Decay. Approximately 18% of three year old children have more than one cavity. That number increases to 40% in five year olds with over 95% of eighteen-year-olds having had at least one cavity. Of concern is the association between early





# Prenatal Vitamin D and Dental Caries in Infants

**Inverse relationship with  
maternal 25(OH)D  
vs  
amount of decay  
In infants**

RES  
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had  
child  
child  
Pois  
inve  
enar

levels ( $P = .02$ ) were significantly associated with ECC.

**CONCLUSIONS:** This study found that maternal prenatal 25OHD levels may have an influence on the primary dentition and the development of ECC.

The  
mel  
36%  
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an  
that  
OHD

# Periodontitis Tooth Loss



**D-ficient**

# Association between serum concentrations of 25-hydroxyvitamin D<sub>3</sub> and periodontal disease in the US population<sup>1-3</sup>

Thomas Dietrich, Kaumudi J Joshipura, Bess Dawson-Hughes, and Heike A Bischoff-Ferrari

## ABSTRACT

**Background:** Periodontal disease (PD) is a common chronic inflammatory disease and an important risk factor for tooth loss. Vitamin D might affect periodontal disease risk via an effect on bone mineral density (BMD) or via immunomodulatory effects.

**Objective:** The objective was to evaluate whether serum 25-hydroxyvitamin D<sub>3</sub> [25(OH)D<sub>3</sub>] concentrations are associated with PD in the third National Health and Nutrition Examination Survey.

**Design:** We analyzed data on periodontal attachment loss (AL) and serum 25(OH)D<sub>3</sub> concentrations from 11 202 subjects aged ≥20 y. Mean AL was modeled in a multiple linear regression with quintile of serum 25(OH)D<sub>3</sub> concentration as an independent variable. The model was stratified by age and sex and was adjusted for age within age groups, race or ethnicity, smoking, diabetes, poverty income ratio, body mass index, estrogen use, and gingival bleeding.

**Results:** 25(OH)D<sub>3</sub> concentrations were significantly and inversely associated with AL in men and women aged ≥50 y. Compared with men in the highest 25(OH)D<sub>3</sub> quintile, those in the lowest quintile had a mean AL that was 0.39 mm (95% CI: 0.17, 0.60 mm) higher; in women, the difference in AL between the lowest and highest quintiles was 0.26 mm (0.09, 0.43 mm). In men and women younger than 50 y, there was no significant association between 25(OH)D<sub>3</sub> and AL. The BMD of the total femoral region was not associated with AL and did not mediate the association between 25(OH)D<sub>3</sub> and AL.

**Conclusions:** Low serum 25(OH)D<sub>3</sub> concentrations may be associated with PD independently of BMD. Given the high prevalence of PD and vitamin D deficiency, these findings may have important public health implications. *Am J Clin Nutr* 2004;80:108-13.

# Case #5

- **Fertile couple from Indonesia**
- **Relocated to Washington DC for diplomatic reasons**
- **Had nonviable offspring**

# Komodo Dragons



**NATIONAL ZOO  
KOMODO DRAGONS**

**UVB**

**WHY???**

**Vitamin D-ficient**

**NON-VIABLE HATCHLINGS**





A scientist in a white lab coat and red gloves is working in a laboratory. He is holding a dark, curved object, possibly a piece of equipment or a sample, and looking at it intently. The background shows various lab equipment, including a Bunsen burner and a beaker.

**UVB**

**NEEDED VITAMIN D**



**Did you know???**

**Vitamin D Deficiency  
Associated**

**Infertility**

**Low Birth Wt**

**Poor Birth Outcomes**



# Dubai centre warns of vitamin D deficiency link to infertility

90 per cent of UAE residents are vitamin D deficient, says the International Osteoporosis Federation



Image Credit: Organiser

Josephine Piralta with her baby. When 25-year-old Josephine Peralta and her 28-year-old husband started planning a family, they never imagined that it would take them six years of continuous struggle to achieve their dream.



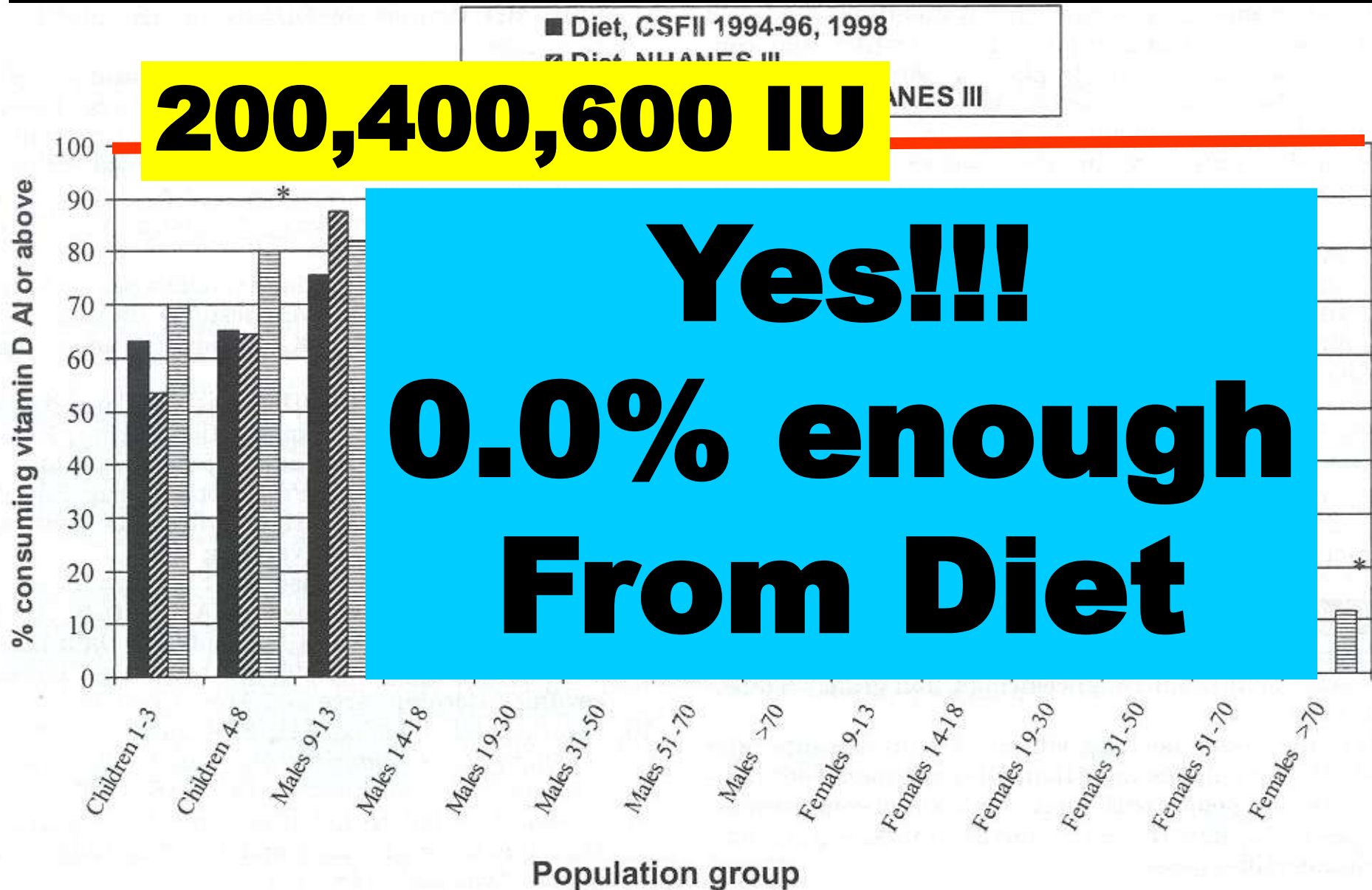
Is it

True Vitamin D

is Rare in

Foods???

# % US POPULATION USUAL VITAMIN D INTAKE FROM DIET ALONE OR DIET + SUPPLEMENTS



**Did you Know  
Mushrooms  
Make Vitamin D  
??????**



# GROWING?



## VITAMIN

Helps GROWTH.  
TEETH.  
BONES

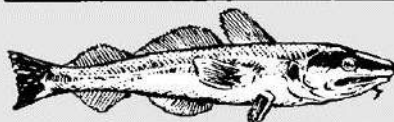
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SCOTT'S EMULSION is a natural food supplement containing the vitamins A and D in a form that is easily absorbed by the body. It is a rich source of Vitamin A and D, and is also a source of Vitamin E. It is a natural food supplement and is suitable for all ages.



3217



**I EAT  
FISH  
Do  
All fish  
Have a lot  
of vitamin D  
???**



WHAT TYPE  
DO WE NEED  
TO EAT??????

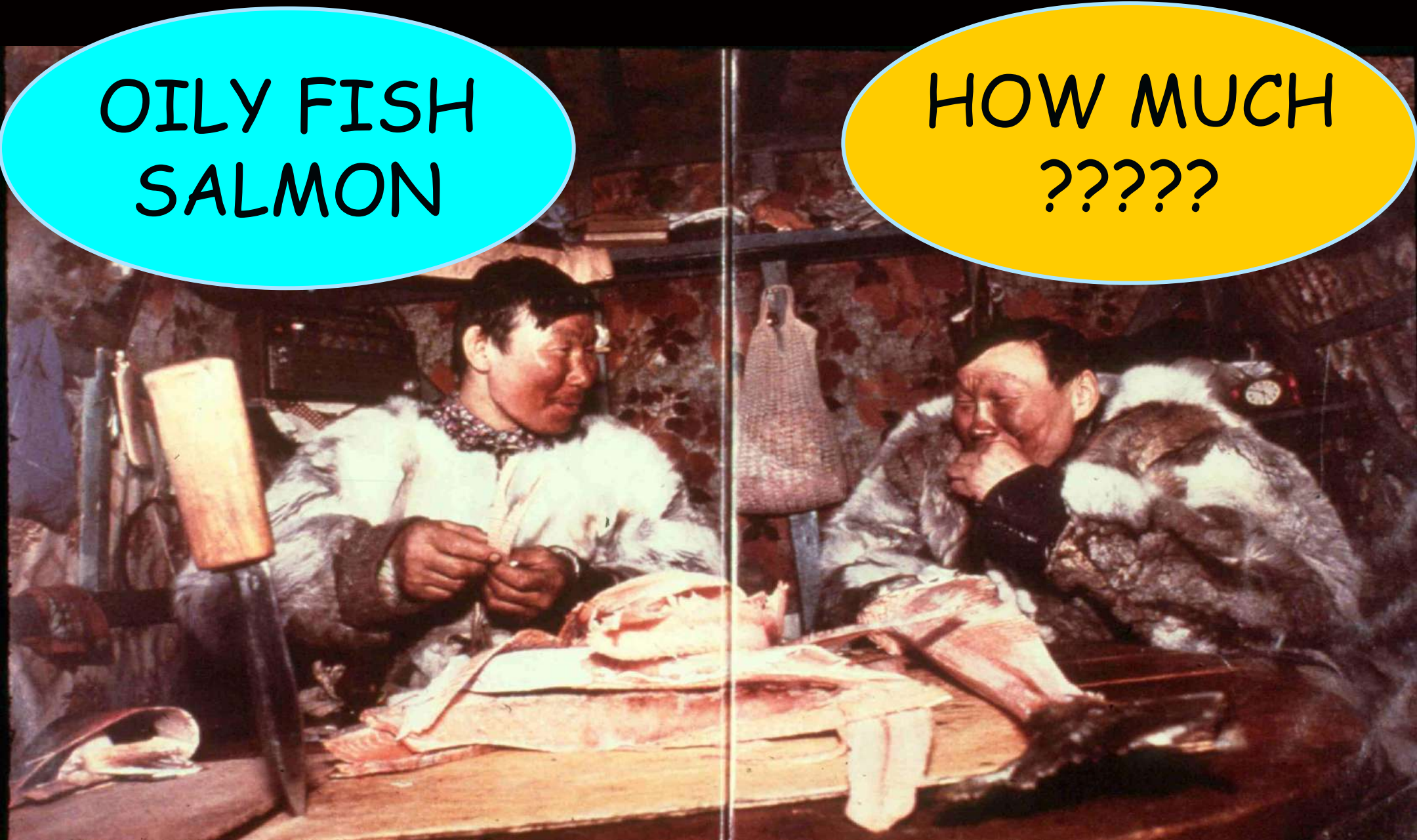
NO  
Sailfish  
Have  
NONE !!!



Nor Do  
Rooster Fish !!!

OILY FISH  
SALMON

HOW MUCH  
?????



A man wearing a maroon long-sleeved shirt, yellow rubber gloves, and a colorful headband is smiling and holding up a large, fresh salmon fillet. He is standing behind a stainless steel counter in what appears to be a commercial kitchen or food processing area. The background shows various kitchen equipment and a checkered floor.

**500-1000 IU/3.5 oz**

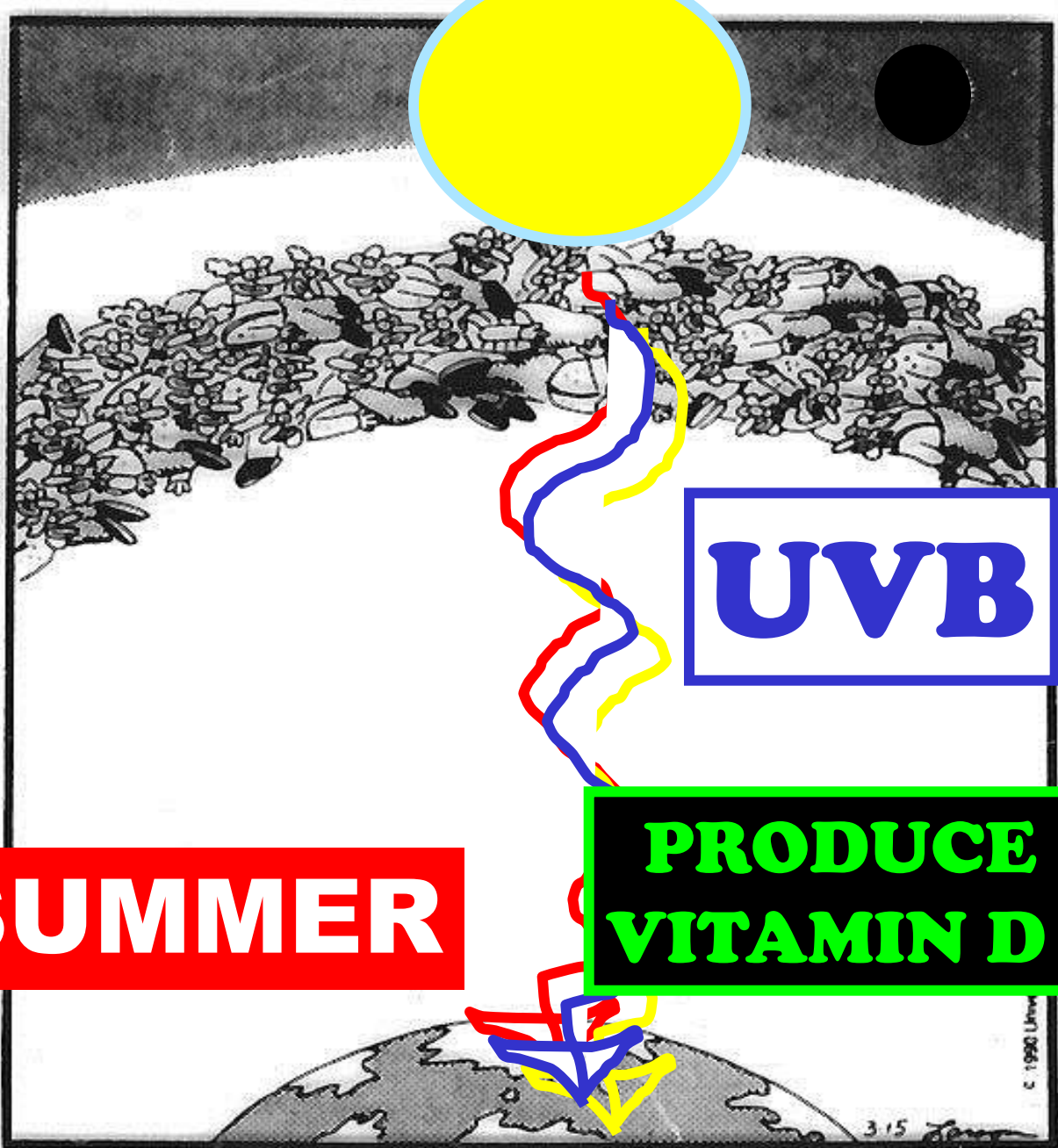
**5-7 Times/Week**







**Sunlight makes us  
feel good !**

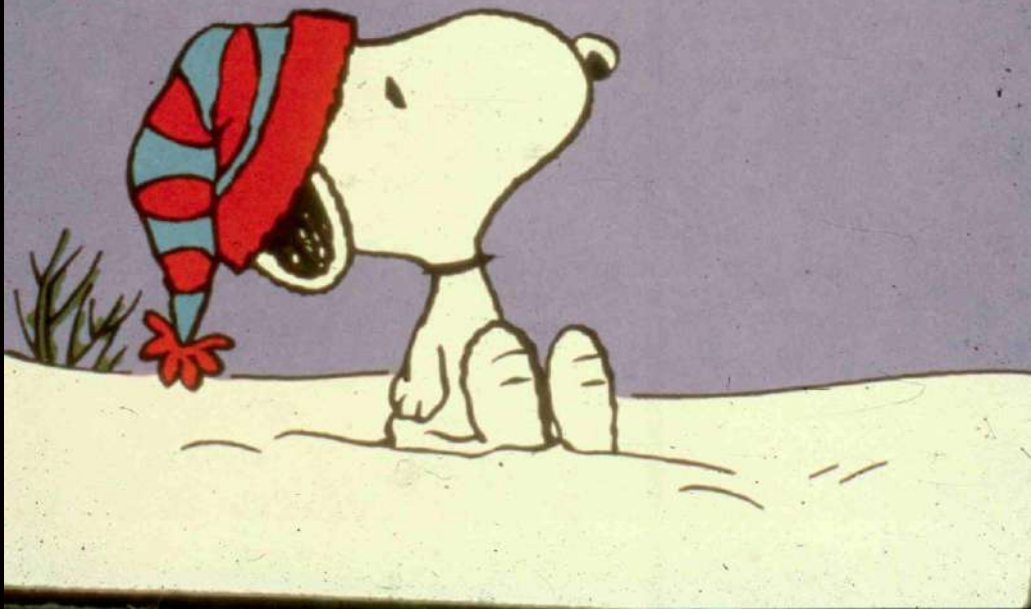


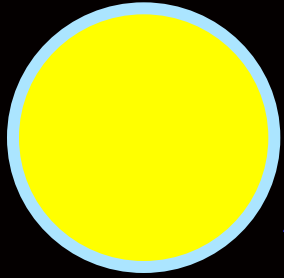
**SUMMER**

**PRODUCE  
VITAMIN D**

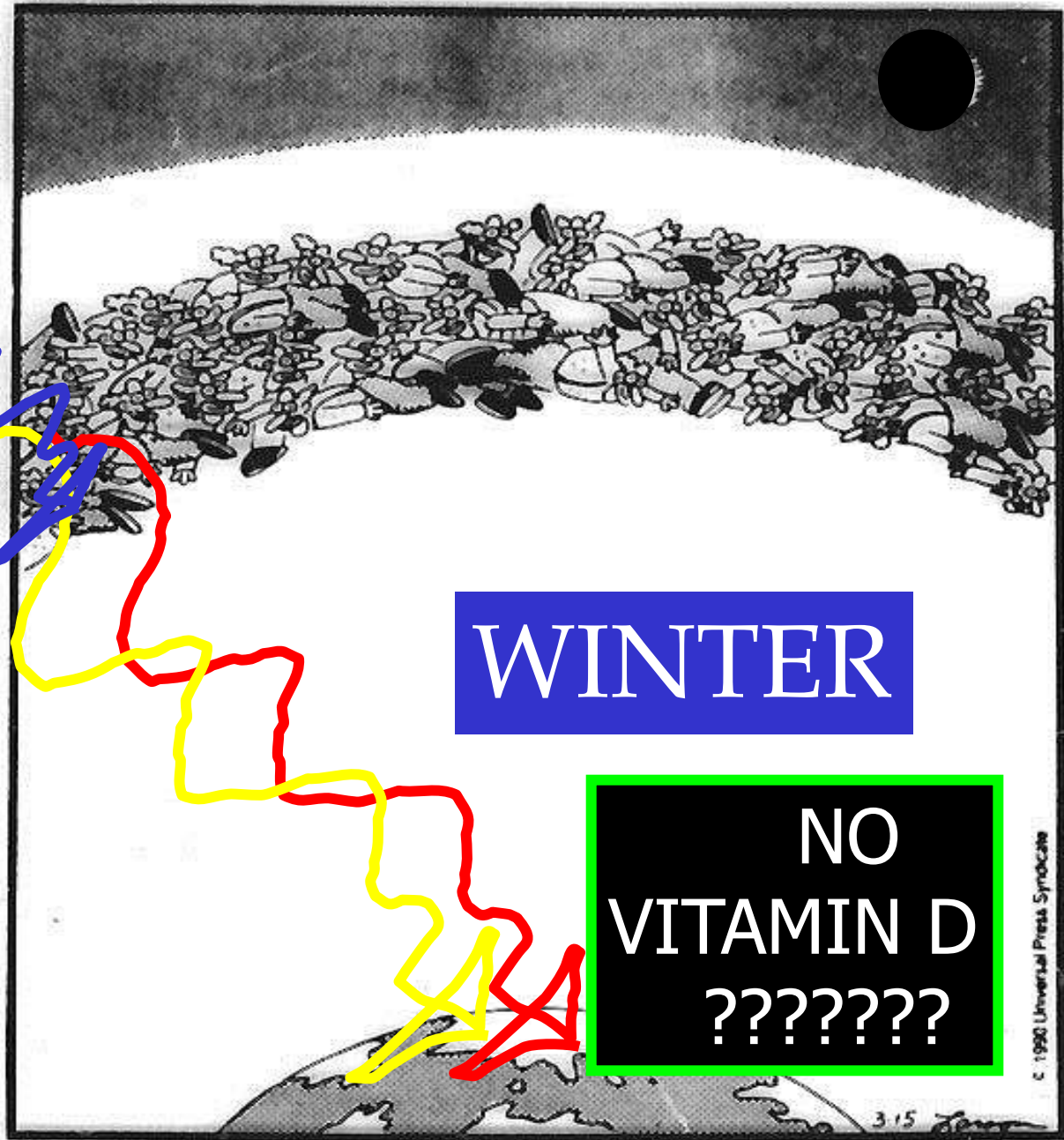
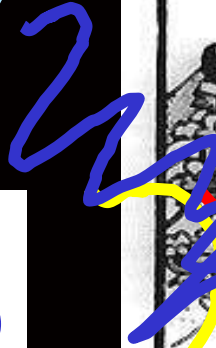
The bozone layer: shielding the rest of the solar system from the Earth's harmful effects.

IS VITAMIN D<sub>3</sub> MADE  
IN SKIN  
DURING THE WINTER?





UVB



WINTER

NO  
VITAMIN D  
???????

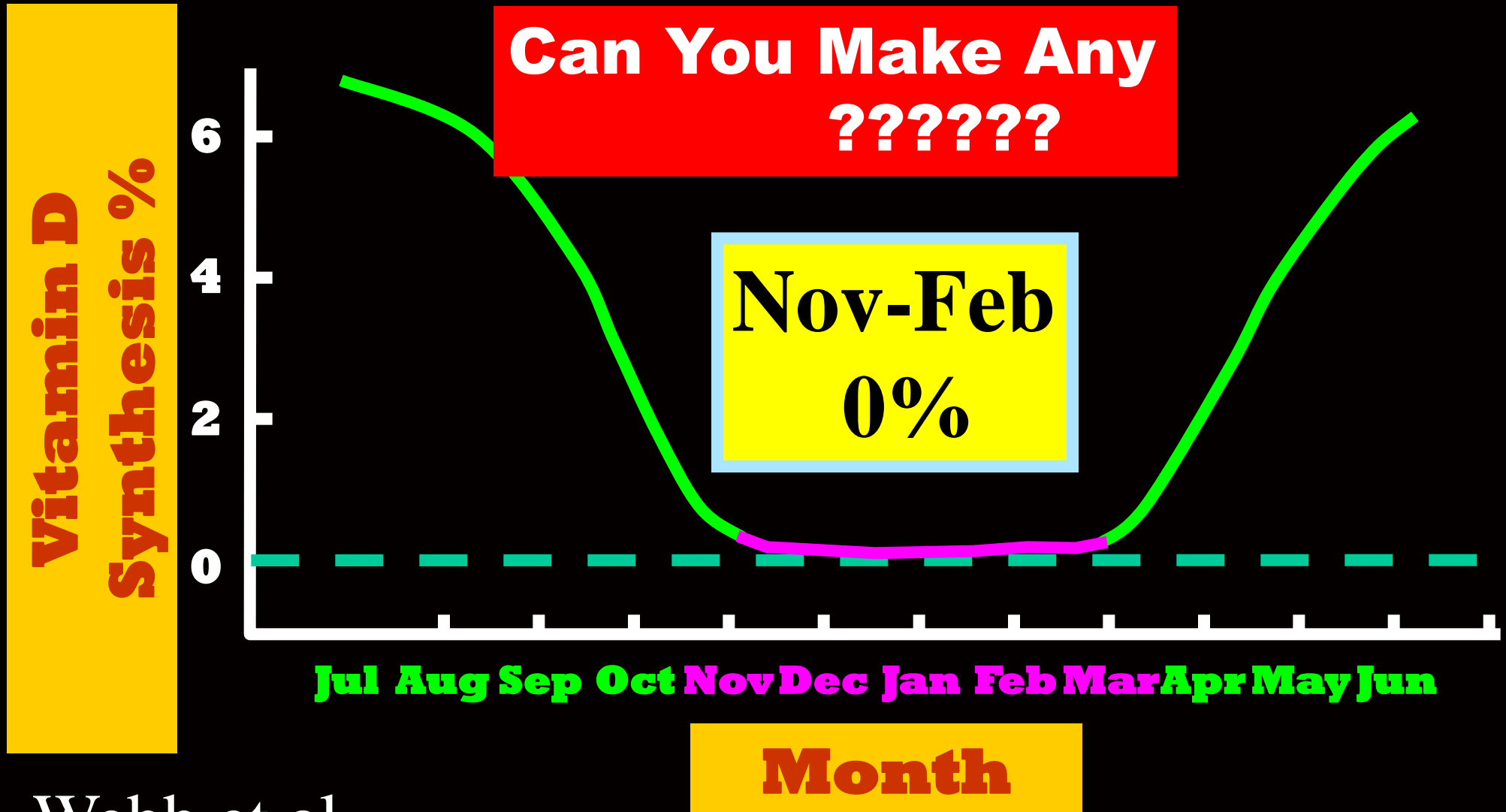
c. 1990 Universal Press Syndicate

315

The bozone layer: shielding the rest of the solar system from the Earth's harmful effects.



# Seasonal Effect on Cutaneous Vitamin D Synthesis in Boston

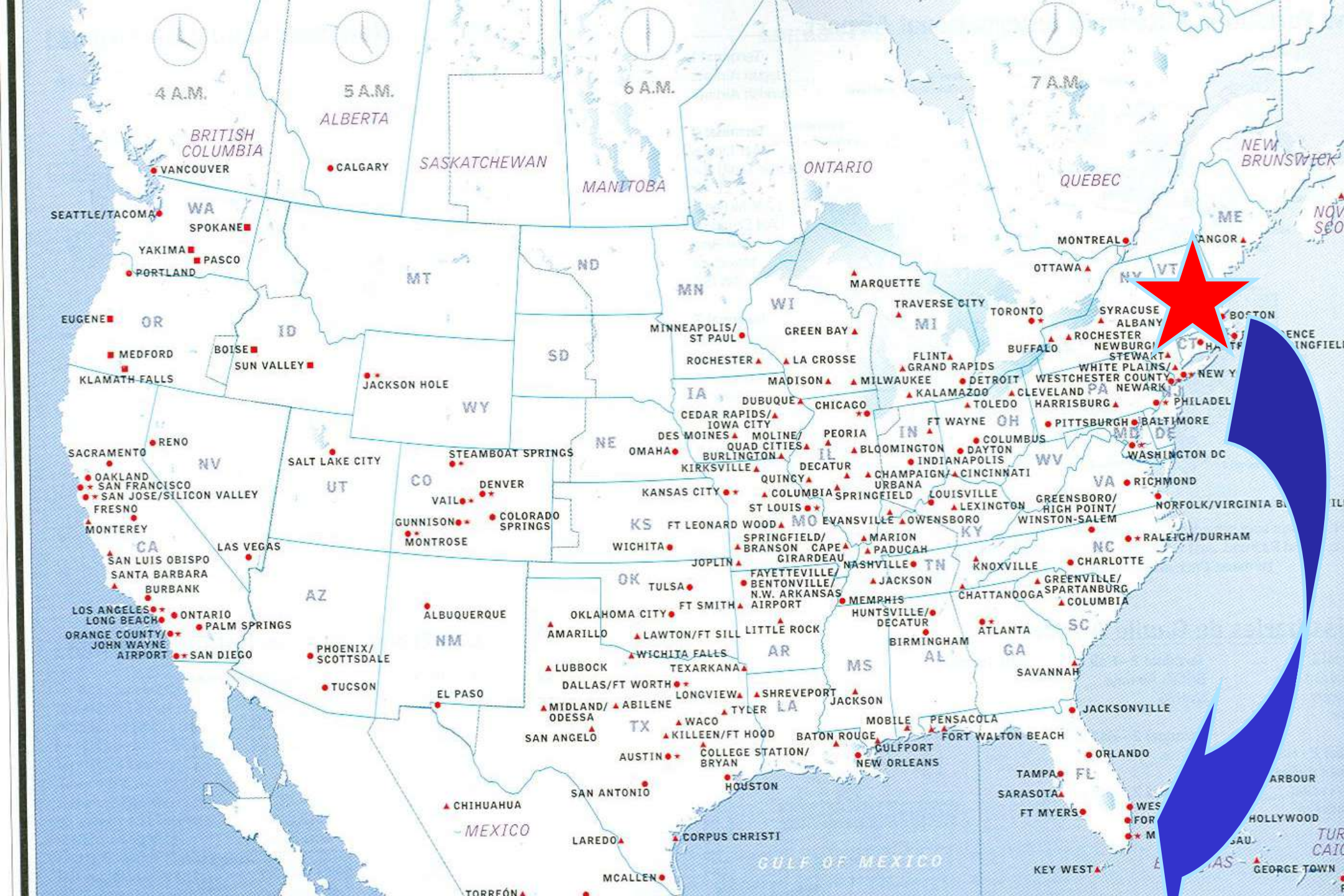


Webb et al

**Not In The  
Winter**



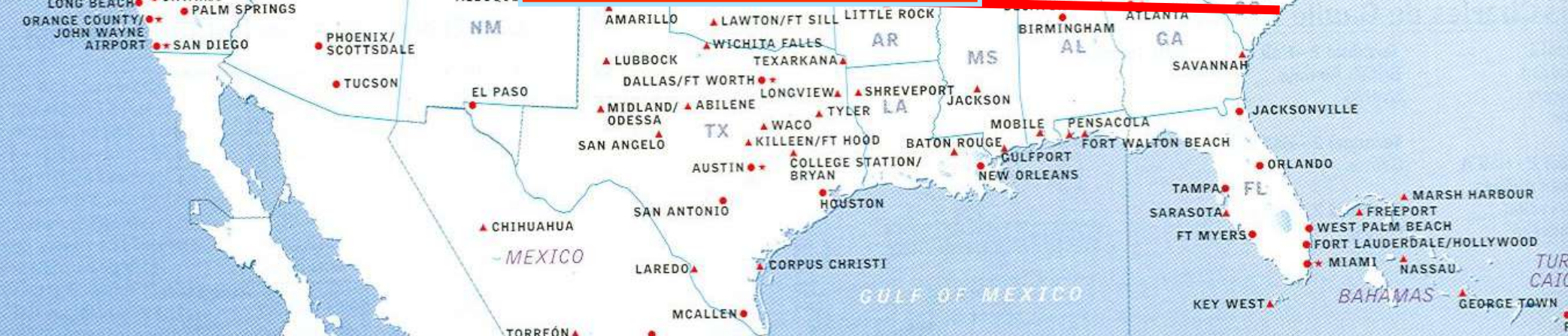
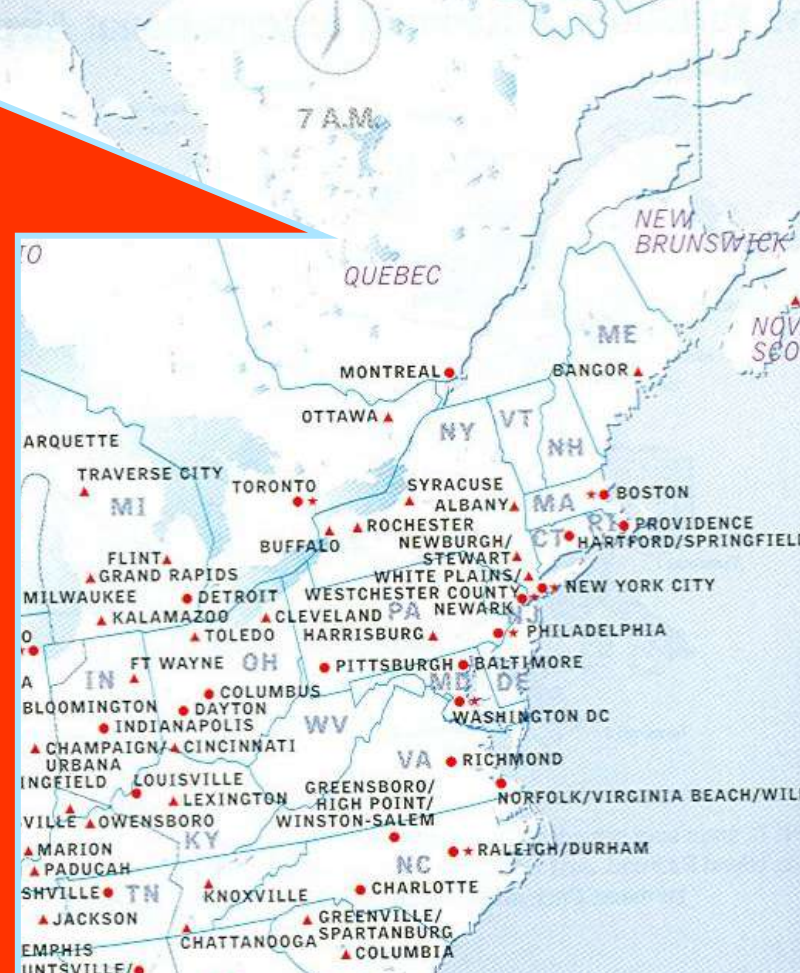


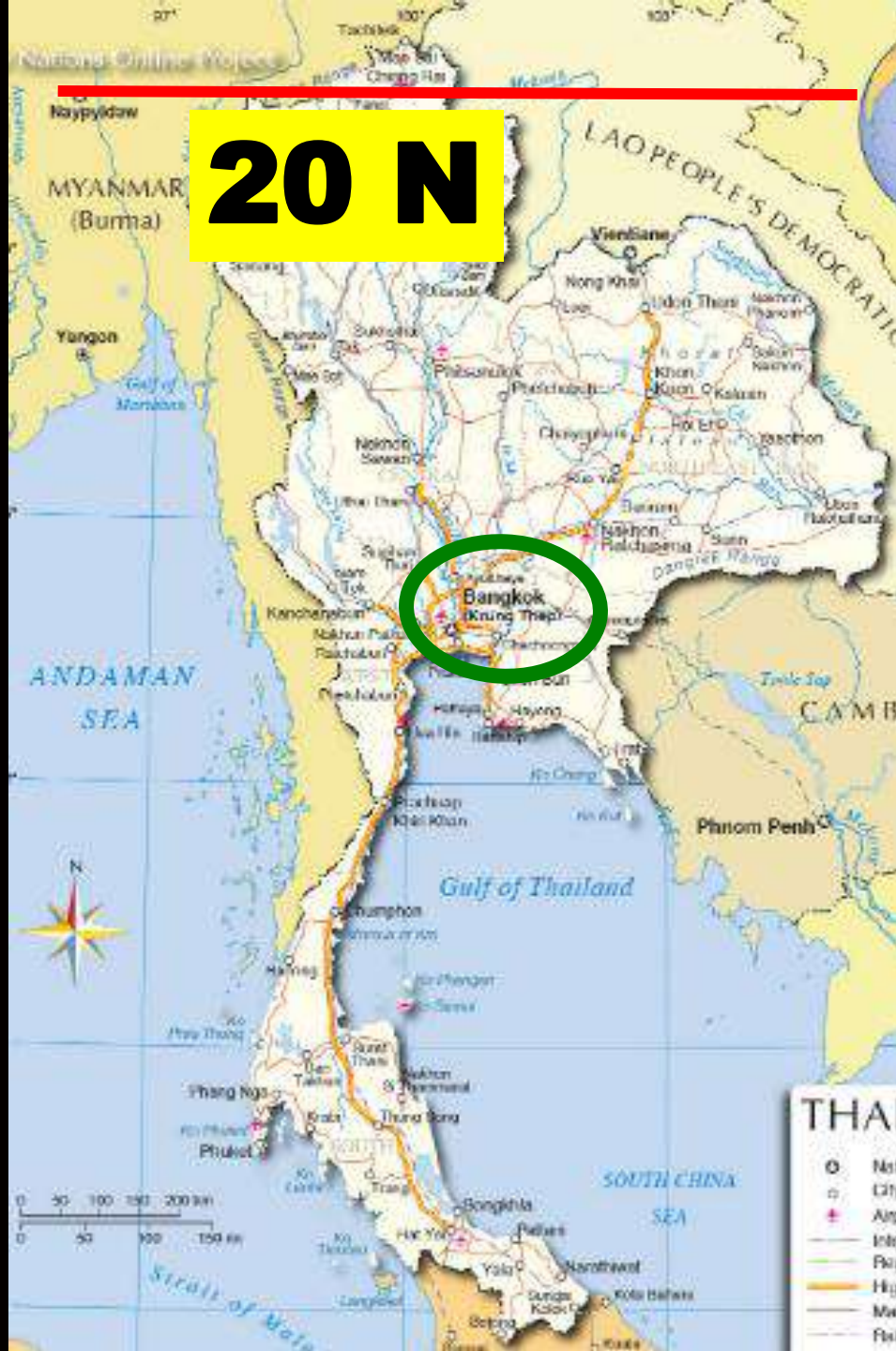


A photograph of a beach scene. In the foreground, a woman with sunglasses and a white polo shirt stands on the sand. Behind her is a colorful beach chair. In the background, two people are playing in the shallow water near the shore. The ocean waves are breaking on the beach. A large yellow circle with a white border is overlaid on the left side of the image, containing text.

**All Year  
In  
Miami Florida  
Latitude  
25.8 N**

**Cannot  
Make  
Vitamin D  
In  
Winter  
Above  
32 N**







**Ozone**

**NO<sub>2</sub>**

**SO<sub>2</sub>**



**Can I make vitamin D  
While jogging in early  
Morning sun ????**

**Great for Romance  
Not for Vitamin D**

**10am-3pm**







# **NO KIDDING?**

---

## **THE PRICE OF A TAN Skin Cancer in the U.S.**

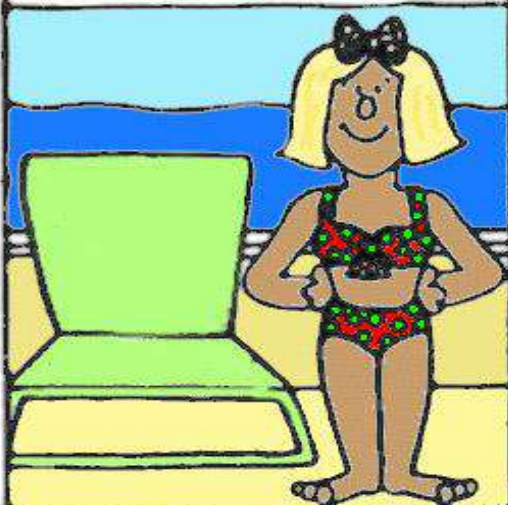
1. Primary cause - sun in 90% of cases
2. New cases — 1,370 each day
3. 63 life-threatening cases each day
4. 1 in 7 will contract in a lifetime
5. Risk of life-threatening skin cancer in lifetime — 1 in 150 persons

Source: The Skin Cancer Foundation

CATHY

By Cathy Guisewite

Q: BEACHWEAR EVOLUTION Q:  
1951: THE TWO-PIECE



1971: THE ONE-PIECE



1991: THE 36-PIECE

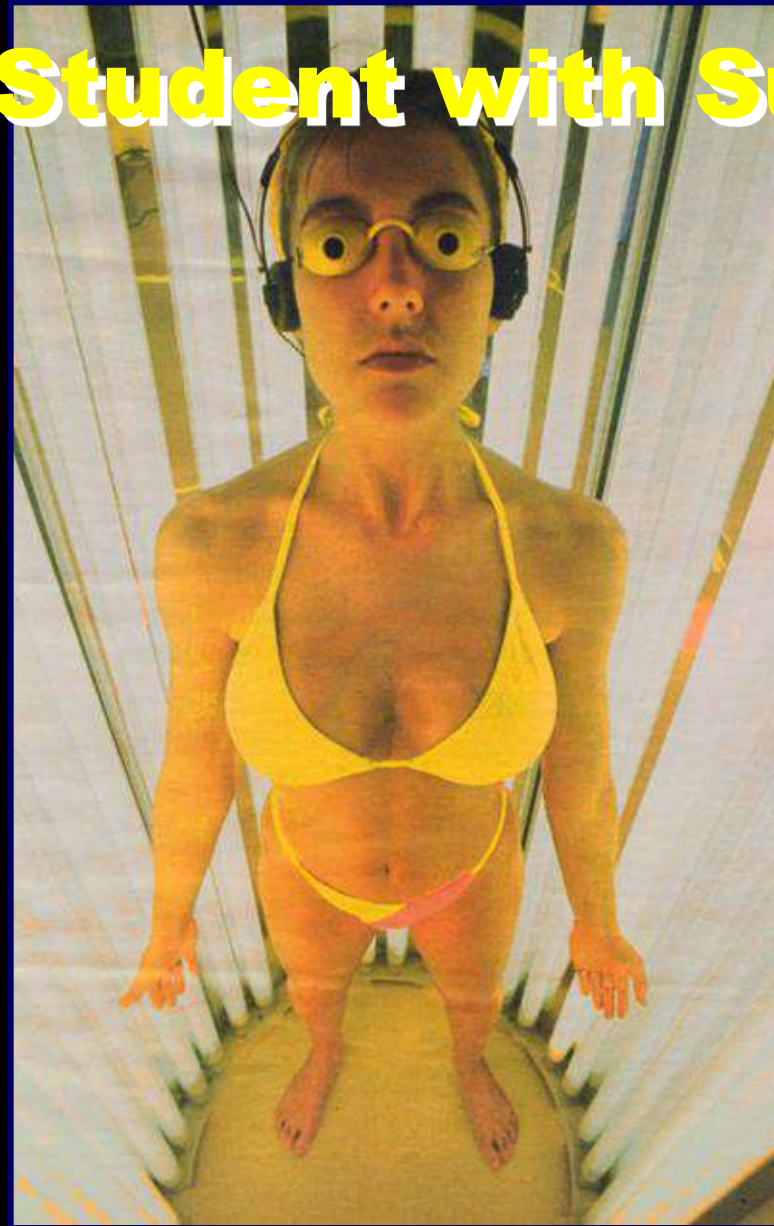






**Is it True  
Suncscreens Reduce  
Vitamin D Synthesis  
????????????**

# Medical Student with Sunscreen



**Serum Concentration  
of Vitamin D (ng/ml)**

**Without Sunscreen**

**SPF30 ↓ ~95%**

**With Sunscreen**



Holick, 1987

**Days**

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





**HOW MUCH**

**SUN**

**EXPOSURE**

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

**NEVER**

***BURRN***



NEVER BURN





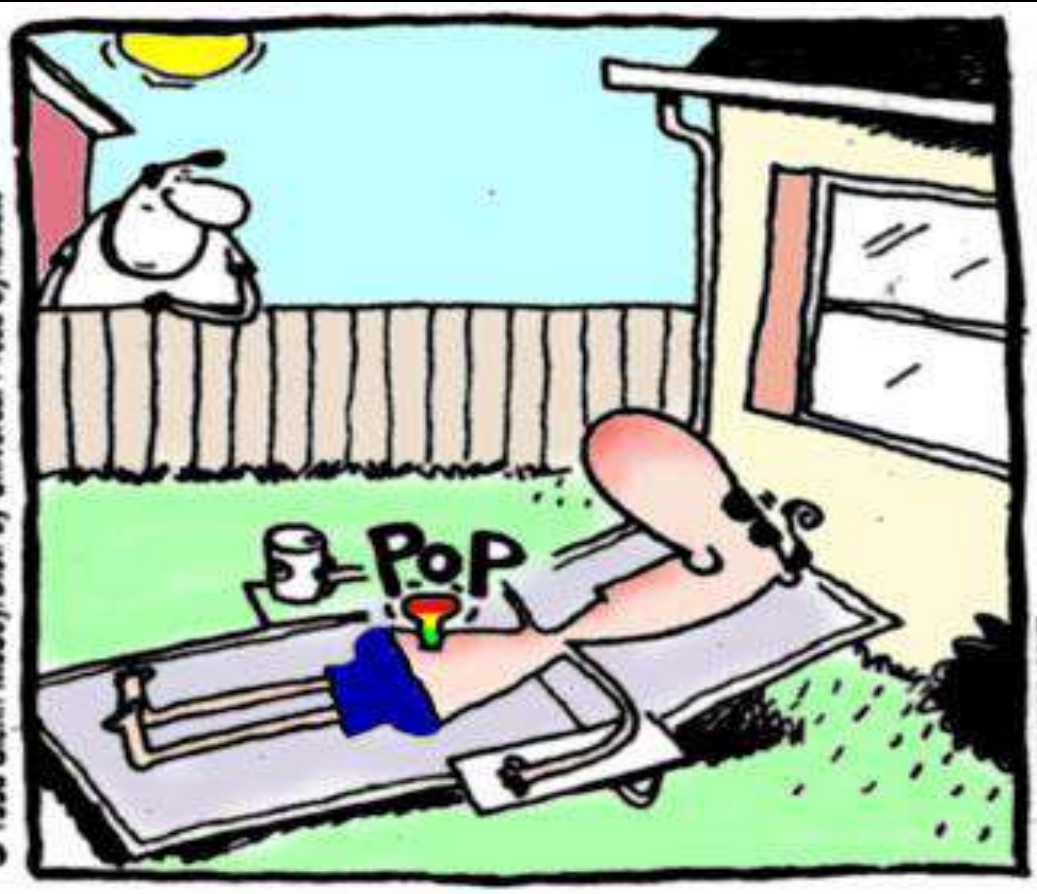
HOW DO YOU  
KNOW WHEN  
YOU MADE ENOUGH  
VITAMIN D?

© 1998 Glenn McCoy/Dist. by Universal Press Syndicate

7/20



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www.uexpress.com

# Total Body

1X

ORAL  
VITAMIN D





**1 minimal  
erythematol  
dose**





Exposure to  
1 Minimum Erythema  
Dose

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

(RDA 600-800 IU)


# Therefore -

To get the RDA of 1500-2000 IU  
of vitamin D<sub>3</sub>

Need to expose **15-20%**  
of Body Surface



**Is it True  
I washing off  
The Vitamin D I just  
Made from the Sun  
?????**

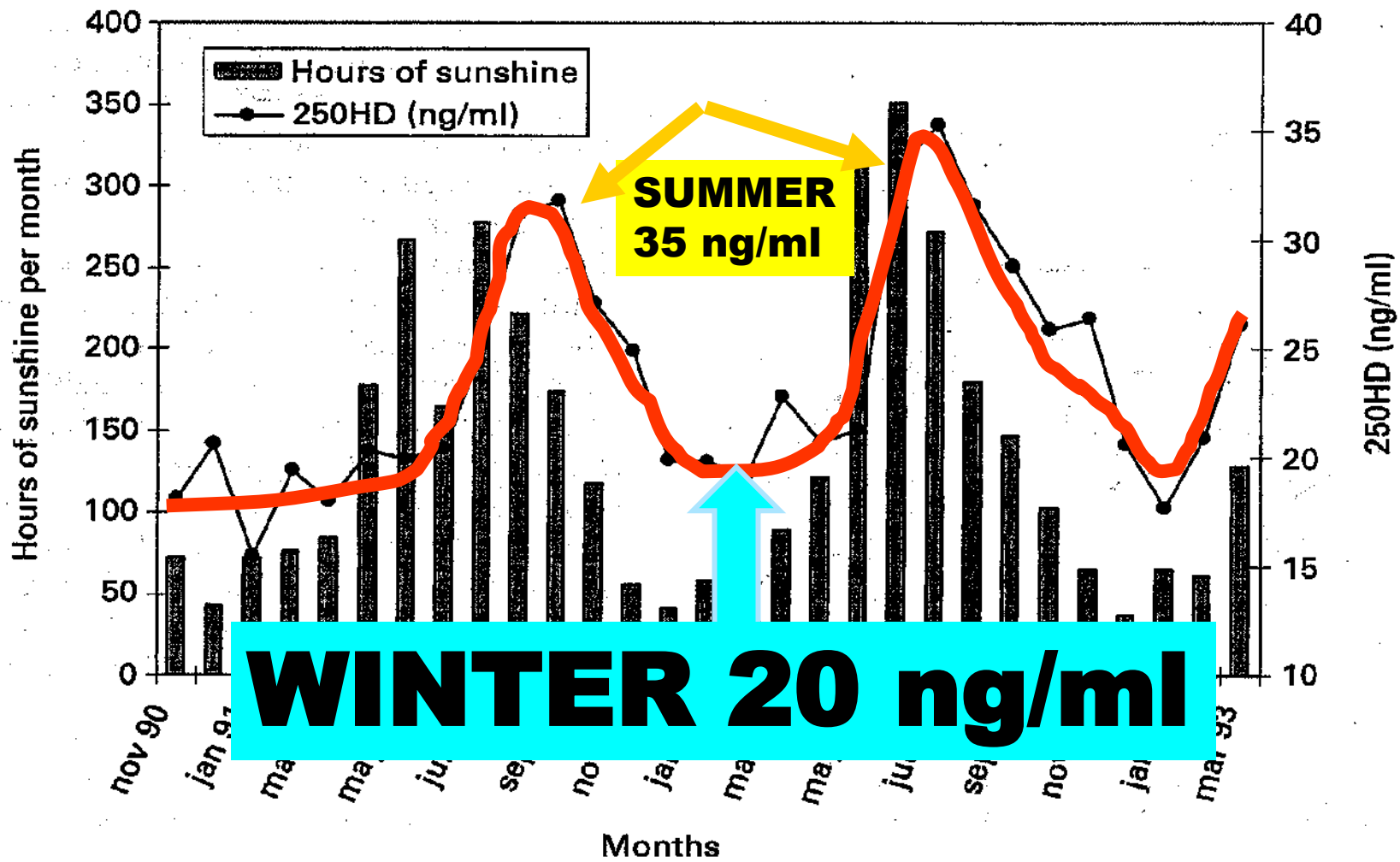
A young girl with long blonde hair is looking into an aquarium tank. She has a wide-eyed, surprised expression with her mouth open. The tank is filled with blue water and several colorful fish, including a clownfish and a striped fish. The background is a blue wall with a white door handle.

**Not True  
Vitamin D  
Is made in the  
Living cells in  
The skin !!!!**

Does Sunlight Really  
Provide us with Vitamin D

???????





# Mr Burns

**IS IT TRUE AGING  
AFFECTS VITAMIN D  
SYNTHESIS ????**







**YES**  
**75% REDUCTION**  
**Holick et al Lancet 1989**

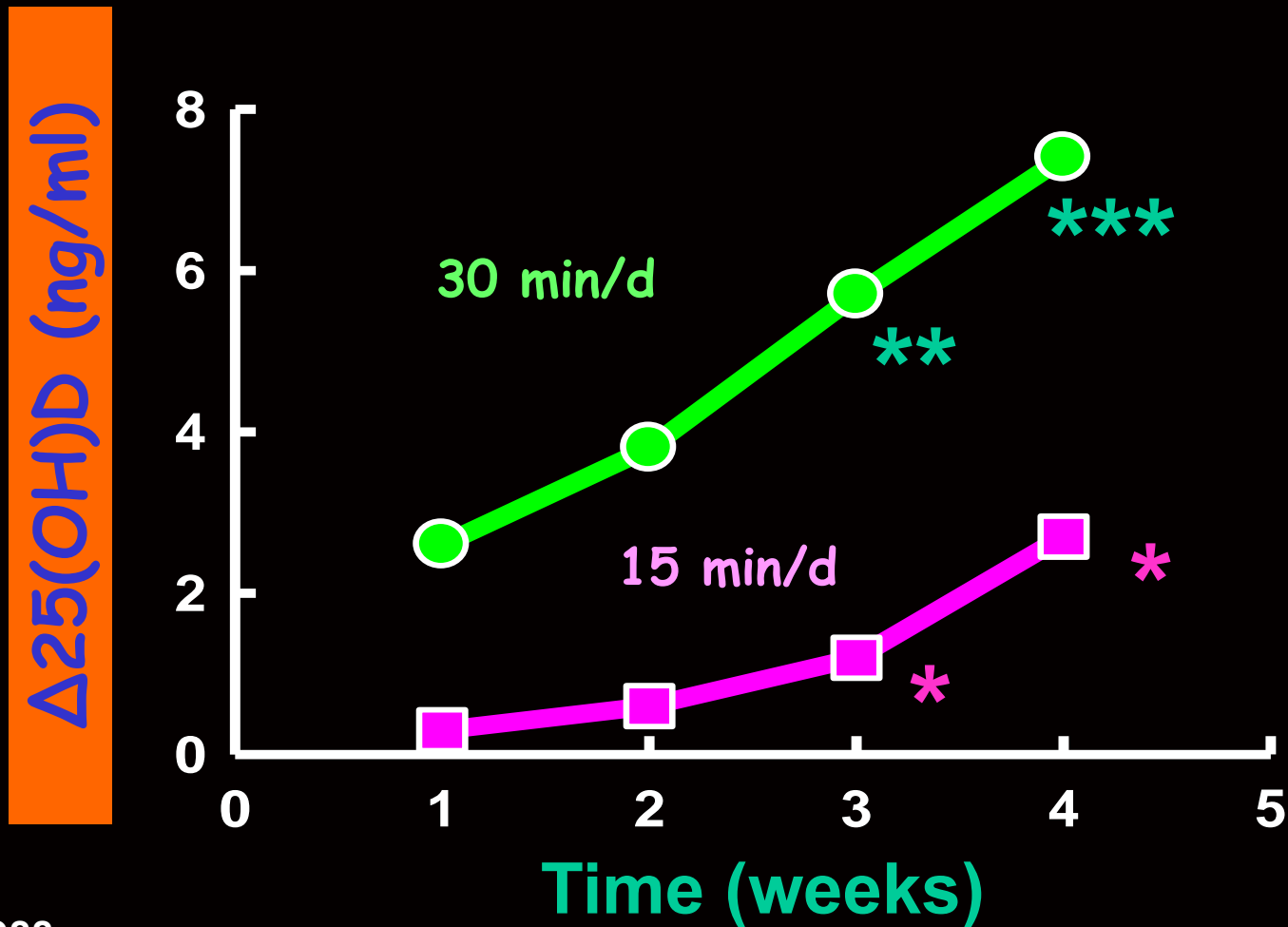


IS IT TRUE  
CAN I STILL MAKE A  
SUFFICIENT AMOUNT  
??????????

**YES  
THE SKIN HAS  
A LARGE CAPACITY  
TO MAKE VITAMIN D**



# Changes in Serum 25(OH)D with Sunlight Exposure



STAR  
WAR

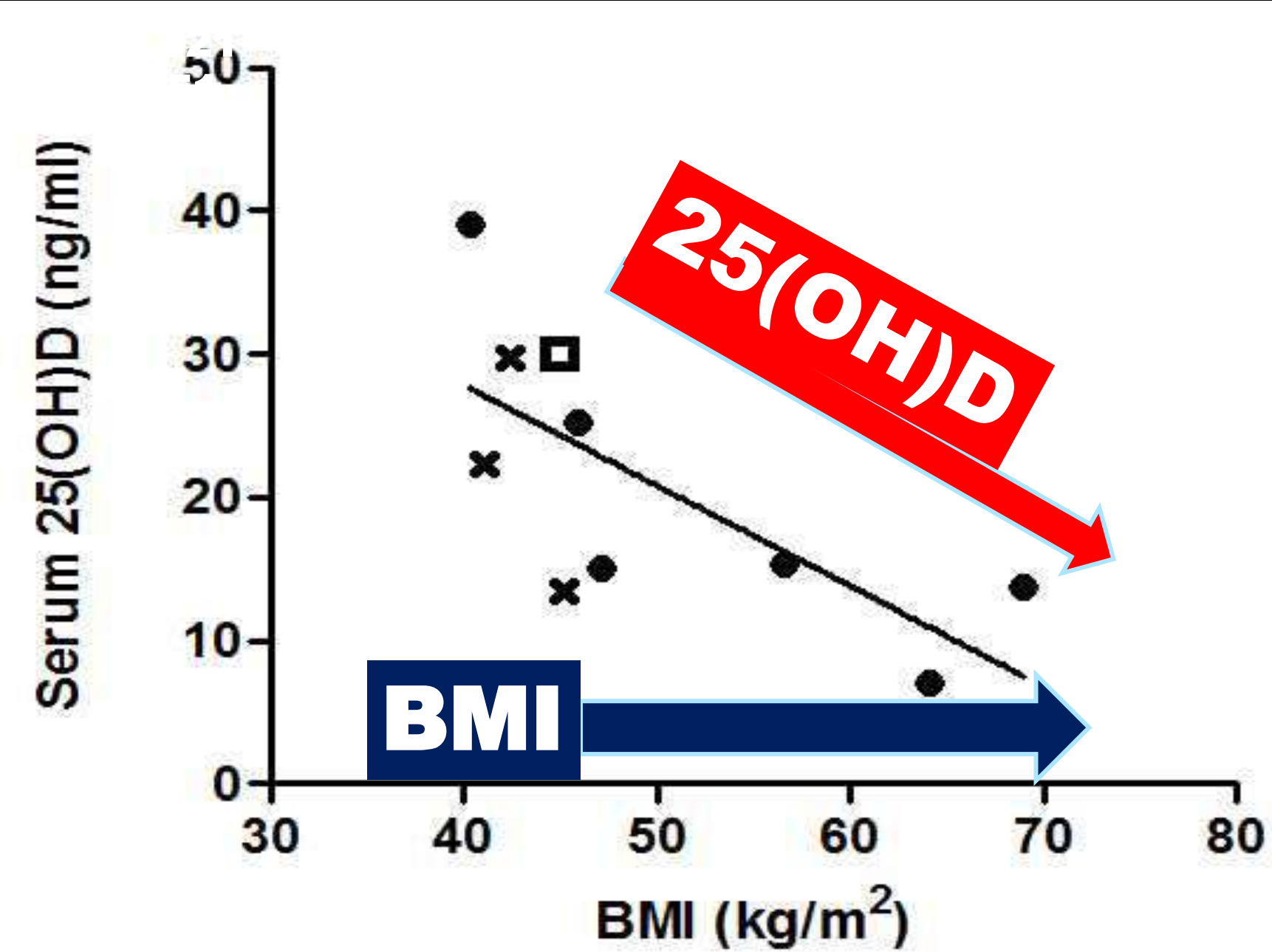


A cartoon illustration of a diner scene. On the left, a man with a long nose and glasses is talking on a blue mobile phone. In the center, a woman with a large pink shirt and a yellow top is sitting at a table. The background shows a window with a view of a city, a blue vending machine, and a counter with glasses. The scene is brightly lit with a yellow sun in the top right corner.

**Wow !!!**

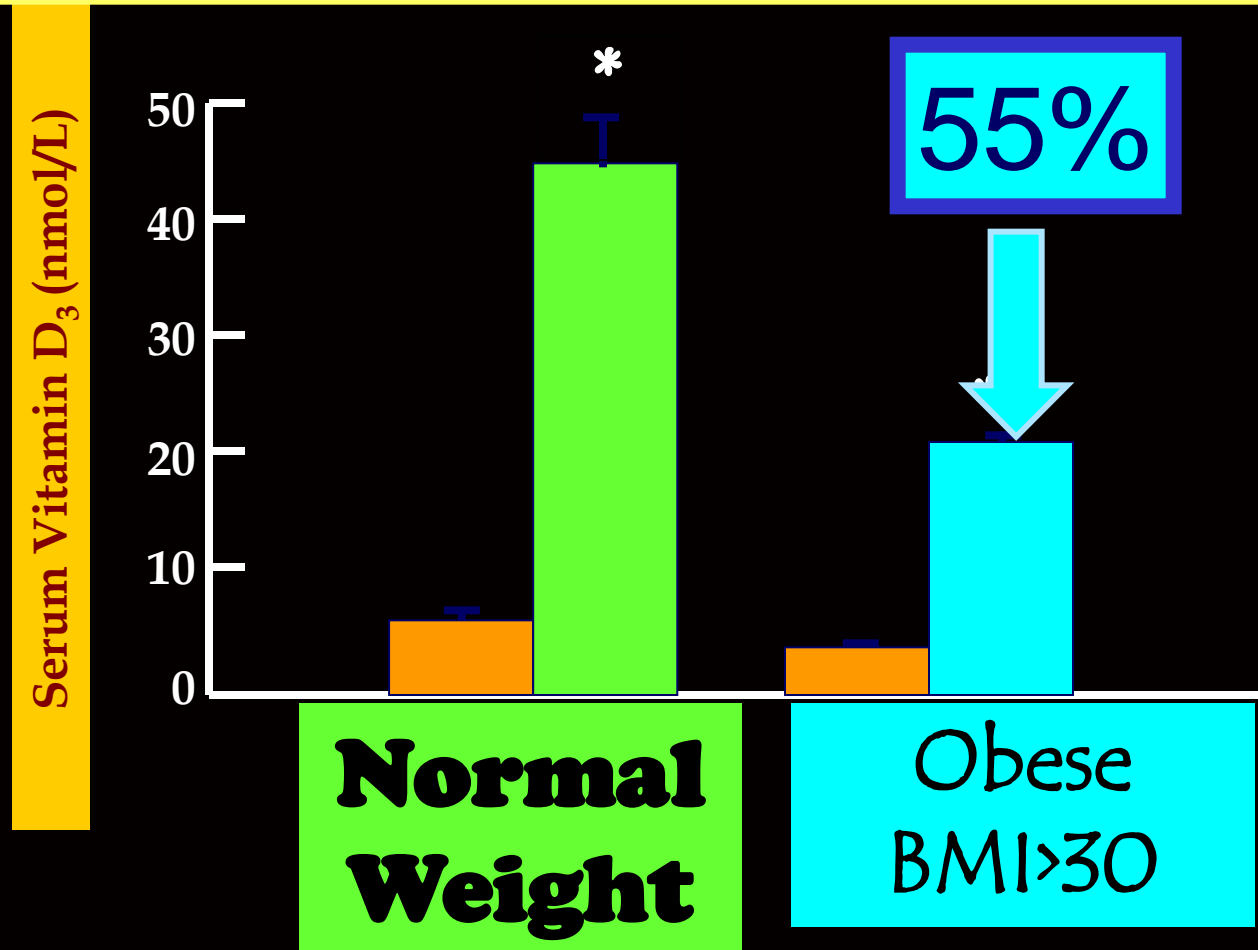
**Did You Know  
Obesity Causes  
Vitamin D Deficiency?**

# BMI vs. serum 25(OH)D (N= 10)





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





Is Vitamin D  
Stored In Fat  
???????



**Rx Obese pts  
need**

**2-3 X vitamin D**

**50,000 IU vitamin D/wk**

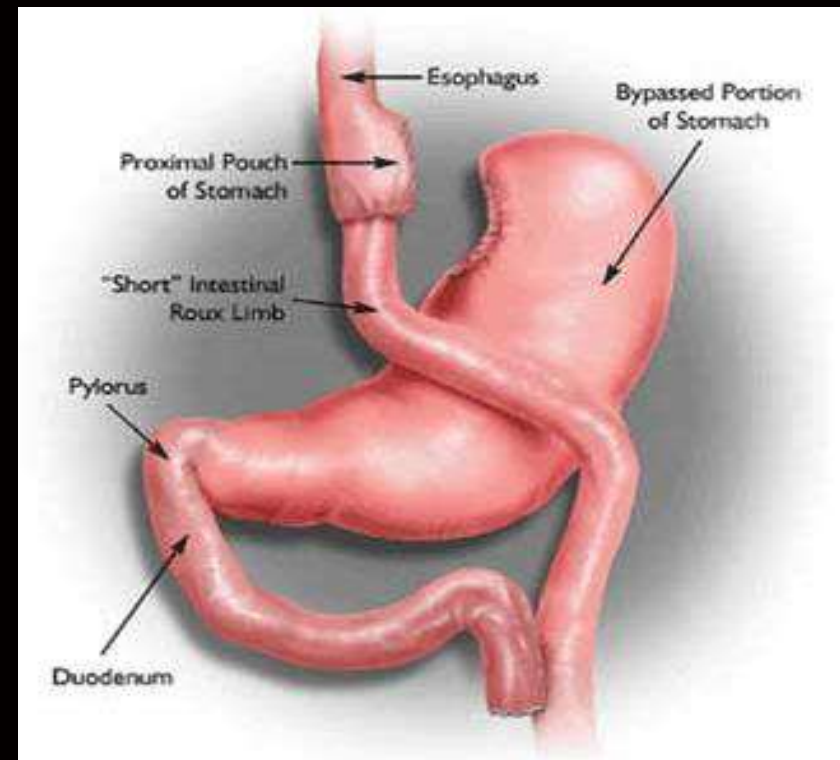
**4-52011g/g**

**Vitamin D**

**Both  
D2&D3**

# What Happens to Serum 25(OH)D with Massive Weight Loss after RYGB ?

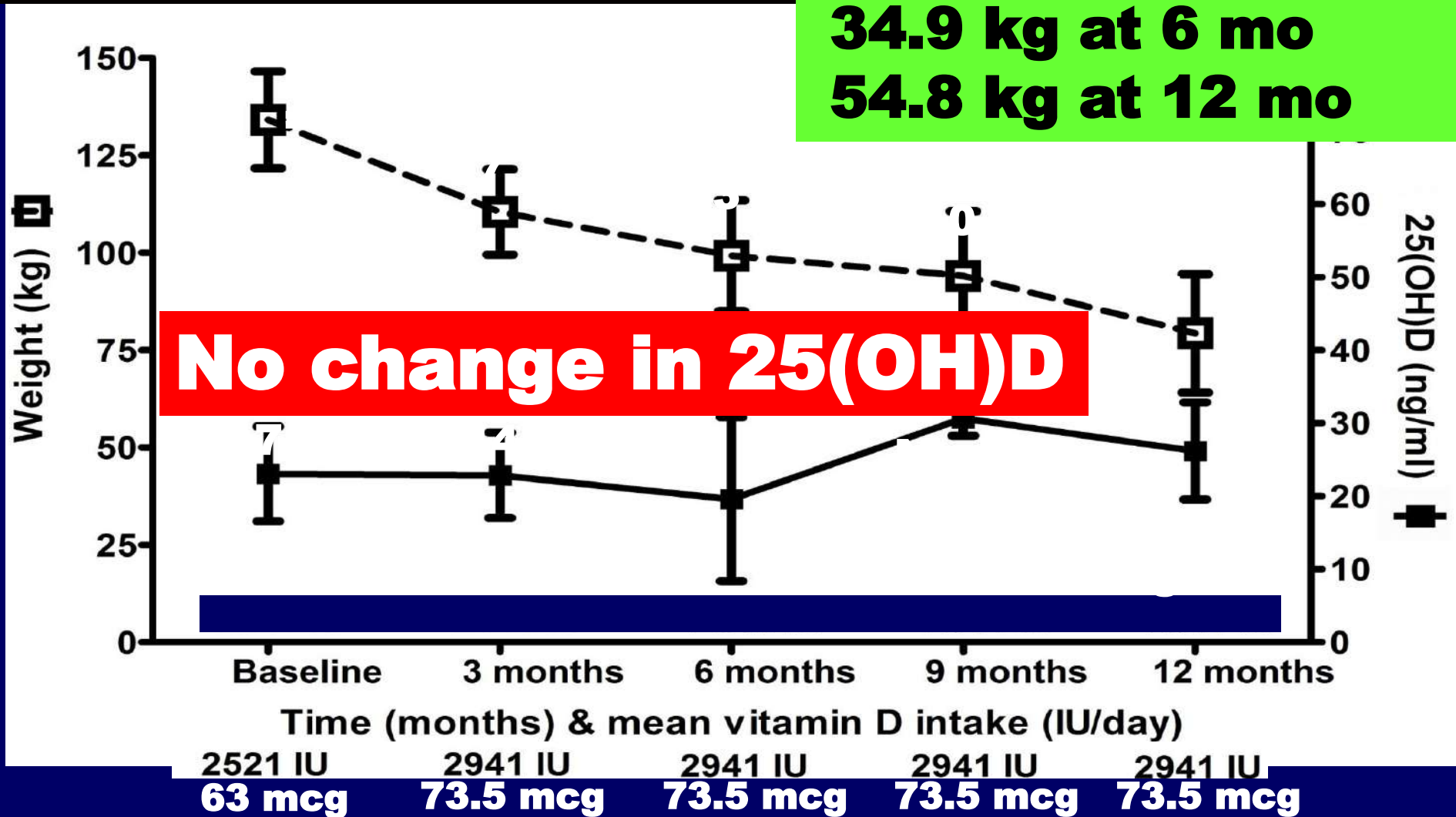
- Available reports of 25(OH)D levels after RYGB are discrepant
  - Decreased (1,2)
  - Unchanged (3,4)
  - Increased (5,6)



- (1) Aasheim ET et al. *Am J Clin Nutr* 2009;90:15-22.
- (2) Johnson JM et al. *Ann Surg* 2006;243:701-4
- (3) Coates PS et al. *J Clin Endocrinol Metab* 2004;89:1061-5.
- (4) Fleischer J et al. *J Clin Endocrinol Metab* 2008;93:3735
- (5) Stein EM et al. *Clin Endocrinol (Oxf)* 2009;71:176-83.
- (6) Bruno C et al. *J Clin Endocrinol Metab*;95:159-66.

# Mean weight, 25(OH)D and Vitamin D Intake

**Weight loss :**  
**34.9 kg at 6 mo**  
**54.8 kg at 12 mo**





**Skin  
Pigment affects  
Vitamin D  
Synthesis  
Need 4 to 10X  
more exposure  
Than my friend**

**Therefore do I**

**Need 2X more**

**Vitamin D???**

**No I need the  
Same amount  
As a White adult**





**How do  
You Define  
Vitamin D  
Deficiency  
????**

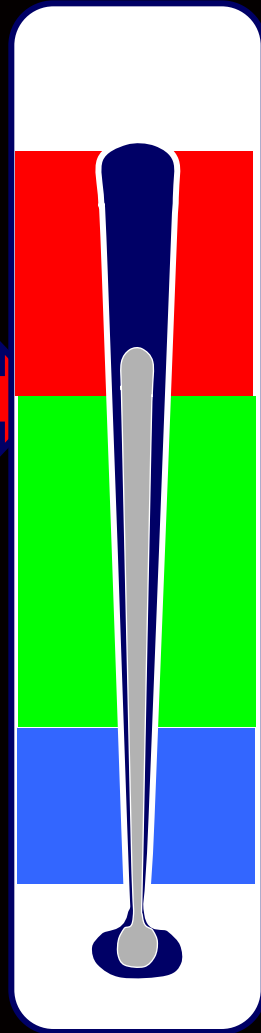


**Serum 25(OH)D is  
the barometer for  
vitamin D status**

# 25(OH)D

**H**

**100 ng/ml**

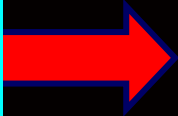


**Excess**

**N**

**Normal**

**20 ng/ml**



**Deficient**

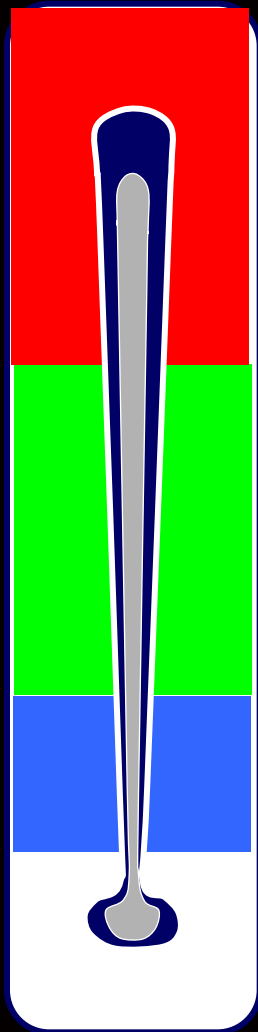
**L**

# 25(OH)D in Lifeguards



110 ng/mL

100 ng/mL



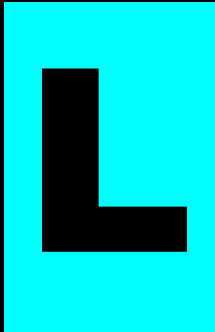
110  
ng/mL



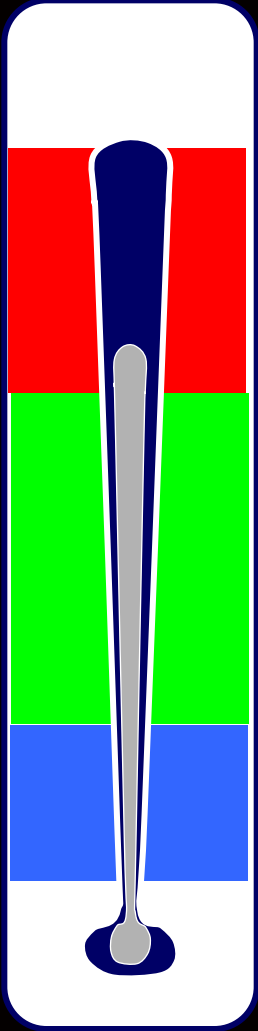
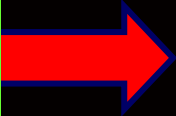
# Vitamin D Intoxication

25(OH)D > 150 ng/ml

# 25(OH)D



**20 ng/mL**



**Normal**

**Deficient**  
**??????????**

**EXCLUSIVE**

**Holick**  
**What evidence**  
**Is there**  
**For**  
**25(OH)D > 30/ng/ml**  
**For better**  
**Health**



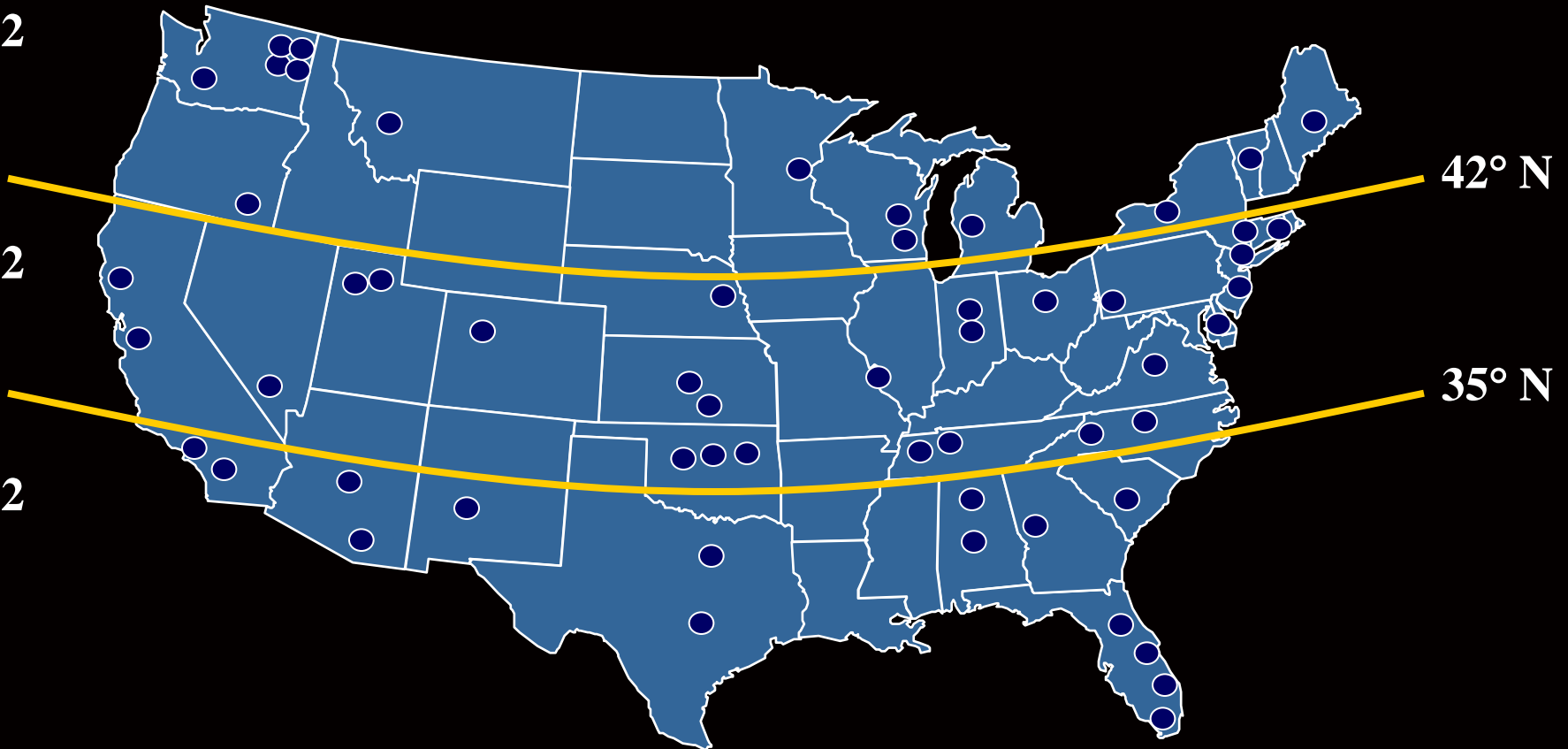
# Vitamin D Inadequacy (<30 ng/ml) Prevalence by Latitude

Sites also in Alaska and Hawaii  
P=NS for test of trend

N=259/532  
(48.7%)

N=342/642  
(53.3%)

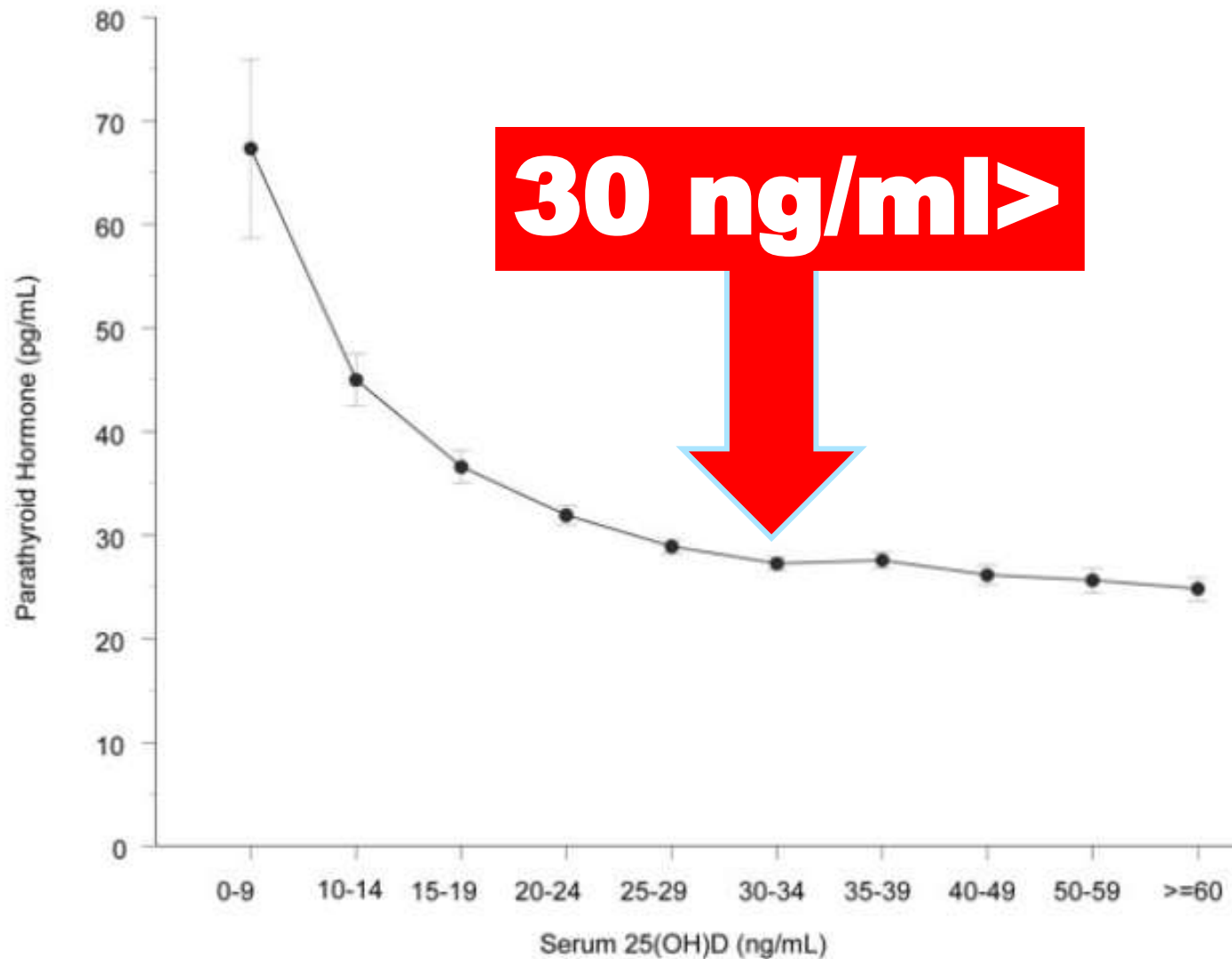
N=198/362  
(54.7%)



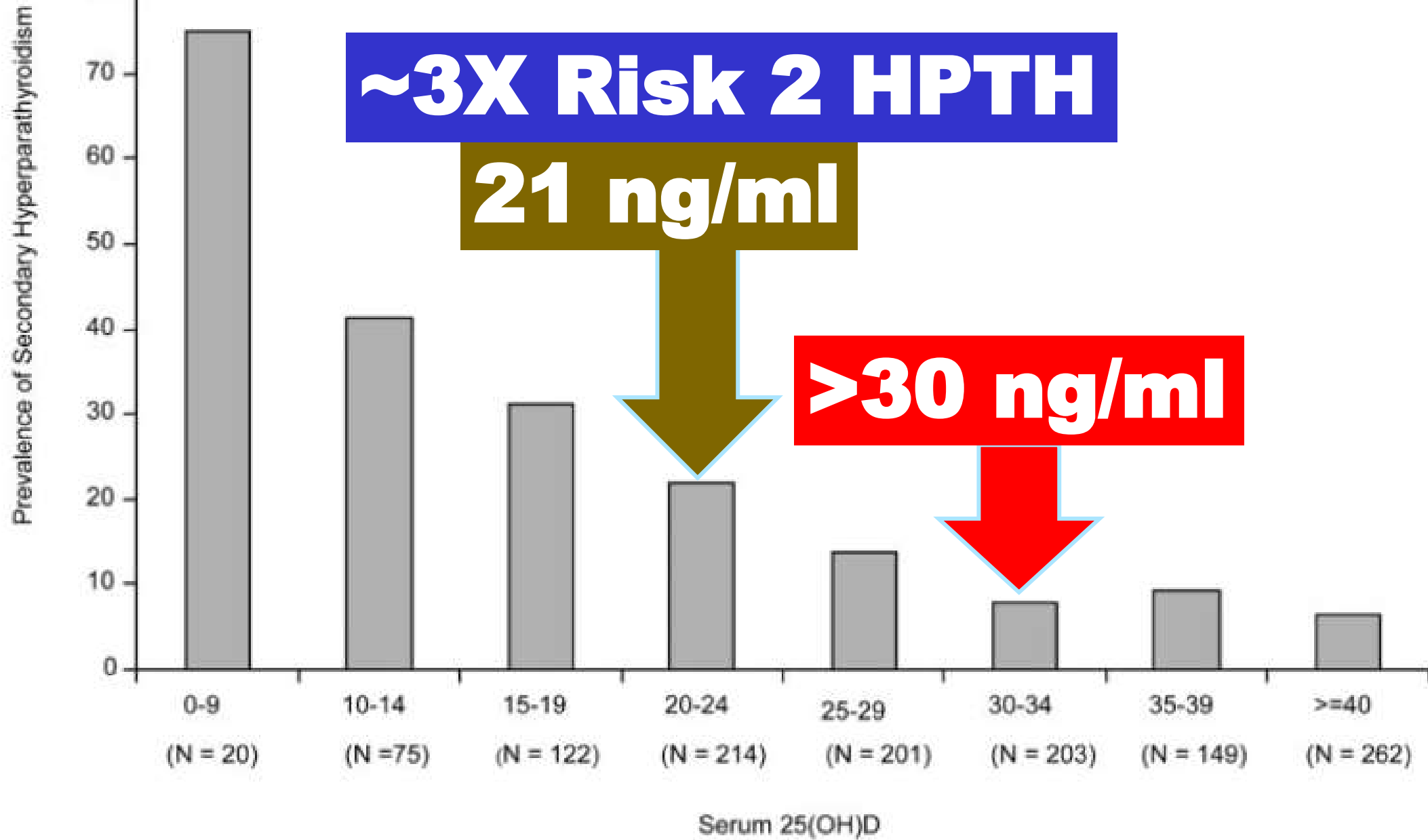


# Prevalence of Vitamin D Inadequacy among Postmenopausal North American Women Receiving Osteoporosis Therapy

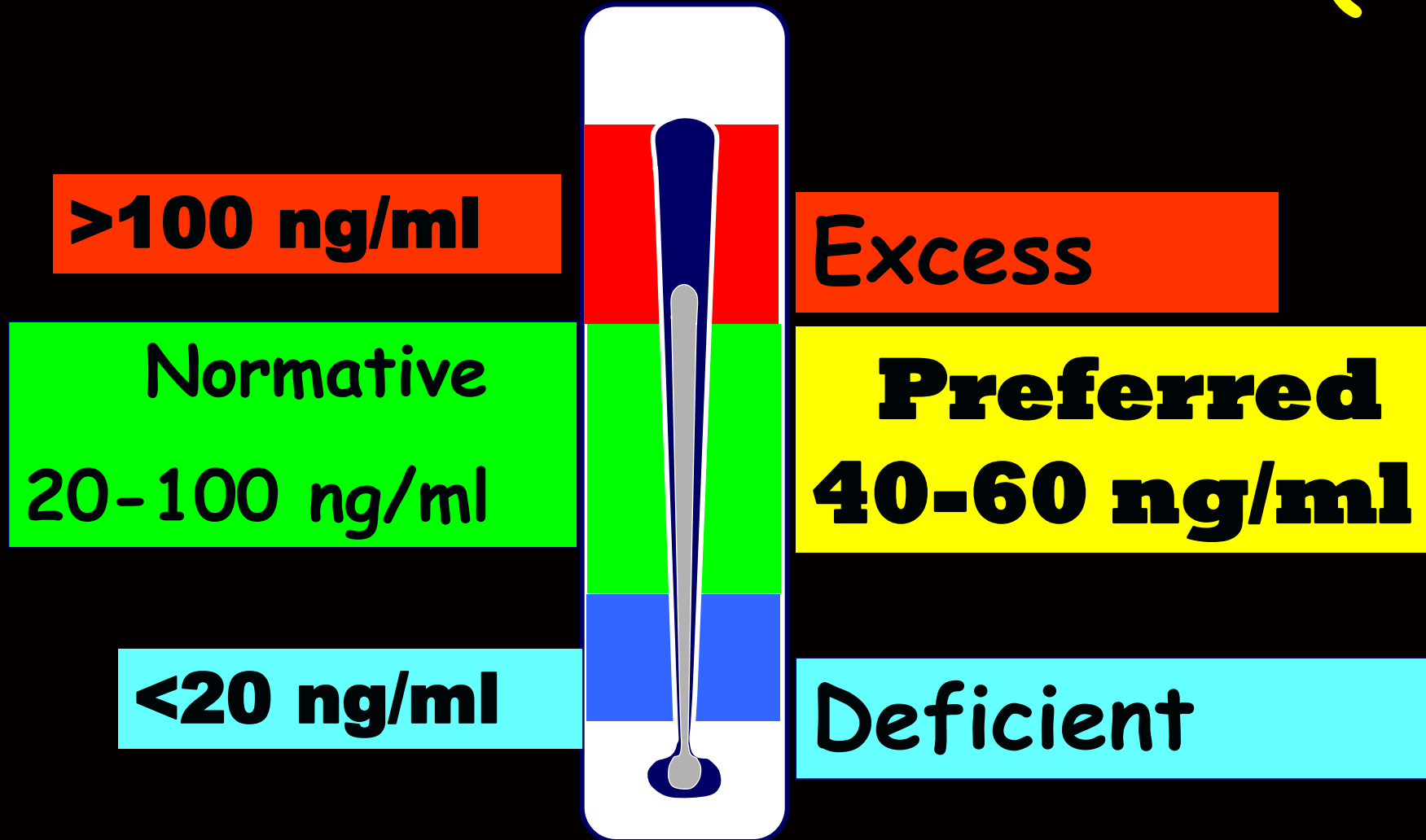
Michael F. Holick, Ethel S. Siris, Neil Binkley, Mary K. Beard, Aliya Khan, Jennifer T. Katzer, Richard A. Petruschke, Erluo Chen, and Anne E. de Papp

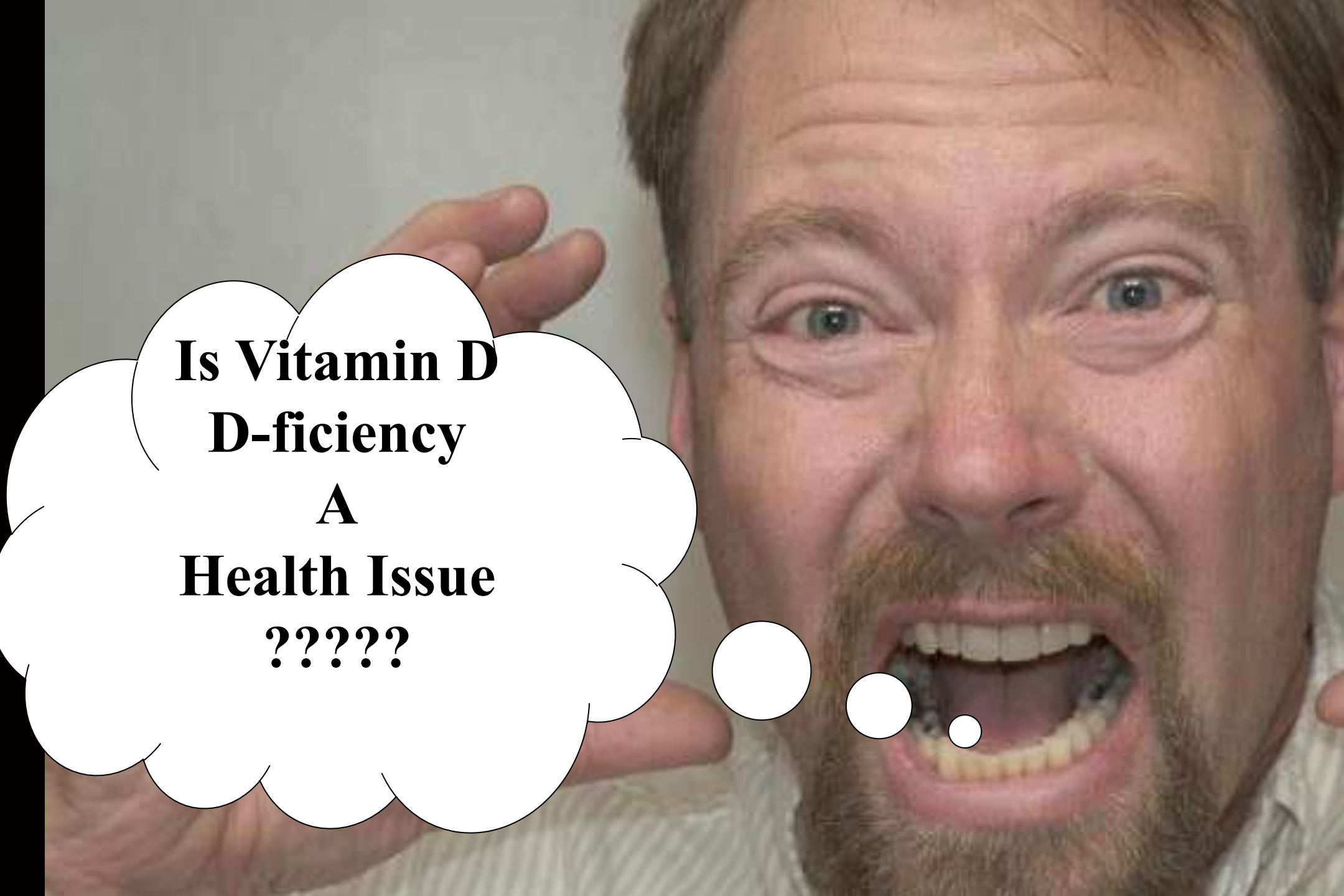


# Prevalence of 2<sup>nd</sup> Hyperparathyroidism



# Endocrine Society's Recommendation 25(OH)D



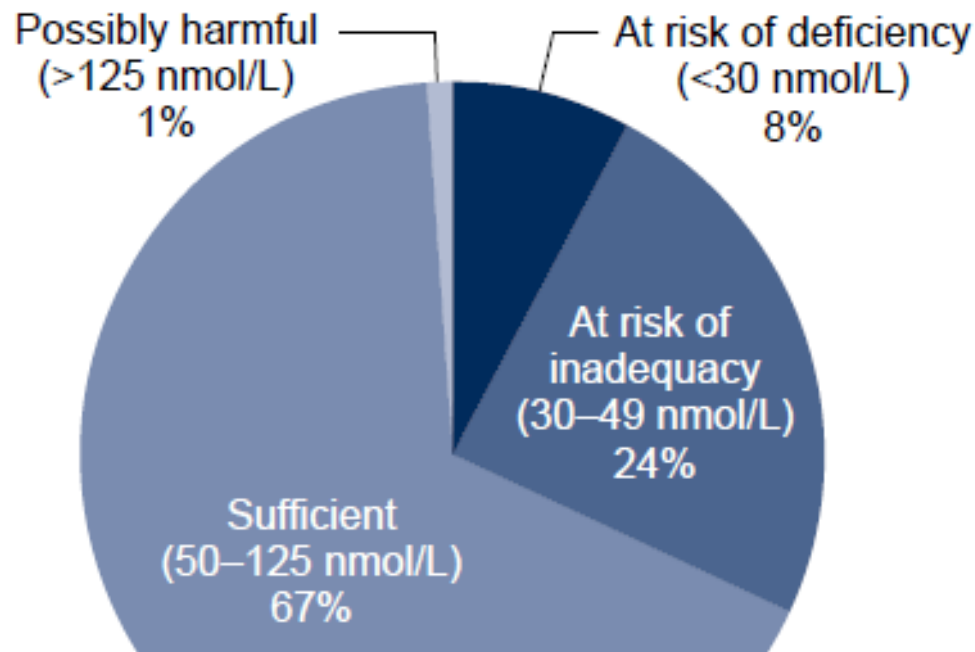
A close-up photograph of a man with a surprised or excited expression, his mouth wide open showing his teeth. He has a mustache and goatee. A large white thought bubble with a black outline is positioned on the left side of the image, containing text. Three smaller white circles with black outlines lead from the bottom of the thought bubble towards the man's mouth, suggesting the thought is coming from him.

**Is Vitamin D  
D-ficiency  
A  
Health Issue  
?????**

# Vitamin D Status: United States, 2001–2006

Anne C. Looker, Ph.D.; Clifford L. Johnson, M.P.H.; David A. Lacher, M.D.; Christine M. Pfeiffer, Ph.D.  
Rosemary L. Schleicher, Ph.D.; and Christopher T. Sempos, Ph.D.

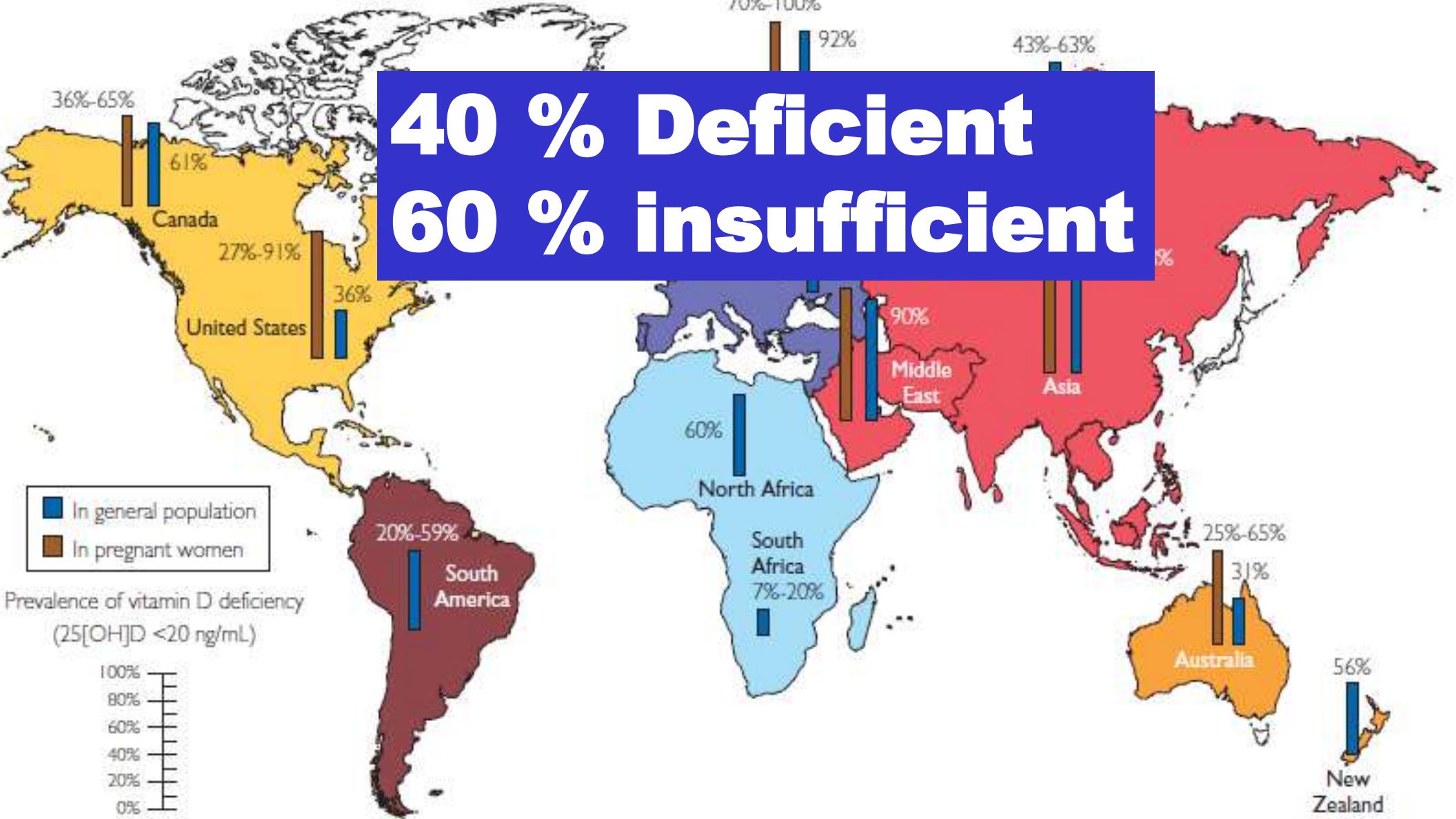
Figure 1. Serum 25OHD status of persons aged 1 year and over: United States, 2001–2006



**32%**  
**25(OH)D < 20 ng/ml**

NOTES: 25OHD is 25-hydroxyvitamin D.  
SOURCE: CDC/NCHS, National Health and Nutrition Examination Survey (NHANES) 2003–2006.

from NHANES



**FIGURE 5.** Reported incidence of vitamin D deficiency defined as a 25-hydroxyvitamin D (25[OH]D) level below 20 ng/mL around the globe in pregnant women and the general population. To convert 25(OH)D values to nmol/L, multiply by 2.496. Copyright Holick 2013, reproduced with permission.

## Vitamin D deficiency in Thailand<sup>☆</sup>

[Oranan Siwamogsatham](#), MD

Samitivej Srinakarin Hospital, Bangkok Hospital Group, Bangkok, Thailand

[Boonsong Ongphiphadhanakul](#), MD

Department of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

[Vin Tangpricha](#), MD, PhD<sup>\*</sup>

Division of Endocrinology, Metabolism and Lipids, Department of Medicine, Emory University School of

Life style and environmental factors are the major factors that determine vitamin D status in Thai people. Thai women are at risk for vitamin D insufficiency likely due to sunscreen usage and sun avoidant behavior due to the desire to maintain a fair complexion. Living in urban areas such as in Bangkok, increases the risk of vitamin D insufficiency due to increased pollution, which decreases the amount of UVB available for cutaneous vitamin D synthesis. Also at increased risk for vitamin D insufficiency are young Thai people living in urban areas in Thailand who have less leisure time and spend less time in the sunlight. Furthermore, in Thailand dairy products are not fortified with vitamin D and very few vitamin D-rich foods are part of the Thai diet. Thus, dietary intake of vitamin D in Thai people is generally low.

## ORIGINAL ARTICLE

# Vitamin D status in Thai dermatologists and working-age Thai population

Natta RAJATANAVIN,<sup>1</sup>  Silada KANOKRANGSEE,<sup>1</sup> Wichai AEKPLAKORN<sup>2</sup>

<sup>1</sup>Division of Dermatology, Department of Medicine, Faculty of Medicine, <sup>2</sup>Department of Community Medicine, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

levels in both groups were measured using liquid chromatography coupled with mass spectrometry. The majority of dermatologists were of Fitzpatrick skin type III ( $n = 61, 61.3\%$ ) or IV ( $n = 32, 33.3\%$ ). The mean serum 25(OH)D and 25(OH)D<sub>3</sub> levels were 18.9 and 18.2 ng/mL, respectively, whereas the corresponding levels in the general population were 26.5 and 25.8 ng/mL. None of the dermatologist had serum 25(OH)D sufficiency ( $>30$  ng/mL), 38 (38.78%) had vitamin D insufficiency (20–30 ng/mL) and 60 (61.22%) had vitamin D deficiency ( $<20$  ng/mL). The frequency of vitamin D deficiency in dermatologists was significantly higher than in the general population (61.2% vs 19.2%,

$P < 0.001$ ). Ninety percent of dermatologists used sunscreen daily and spent time mostly indoors. Dermatologists used physical sun-protection more than half of the time when outdoors, for example, a book or paper as a sunshade (70.3%), an umbrella (48.4%), a long-sleeved shirt (20.4%) or a hat (9.7%). In conclusion, dermatologists showed a remarkably high prevalence of vitamin D deficiency which may be due to inadequate exposure to sunlight, regular use of sunscreen and practicing various sun-protection activities.



# **Vitamin D Deficiency**

- **Osteomalacia**
- **2° HPTH**
- **↑ Osteoporosis**



**Does Vitamin D  
Reduce Risk  
Of  
Fractures  
??????**

# Deconstructing Vitamin D Deficiency

**Lorenz C. Hofbauer<sup>1,2,\*</sup> and Christine Hamann<sup>3</sup>**

<sup>1</sup>*Division of Endocrinology, Diabetes and Bone Diseases, Dresden Technical University Medical Center, D-01307 Dresden, Germany.*

<sup>2</sup>*Center for Regenerative Therapies Dresden, D-01307 Dresden, Germany.*

<sup>3</sup>*Department of Orthopedics, Dresden Technical University Medical Center, D-01307 Dresden, Germany.*

<sup>4</sup>*Corresponding author. E-mail: [lorenz.hofbauer@uniklinikum-dresden.de](mailto:lorenz.hofbauer@uniklinikum-dresden.de)*

*Science Translational Medicine* 10 Jul 2013:

Vol. 5, Issue 193, pp. 193fs27

DOI: [10.1126/scitranslmed.3006566](https://doi.org/10.1126/scitranslmed.3006566)

# SECONDARY HYPERPARATHYROIDISM

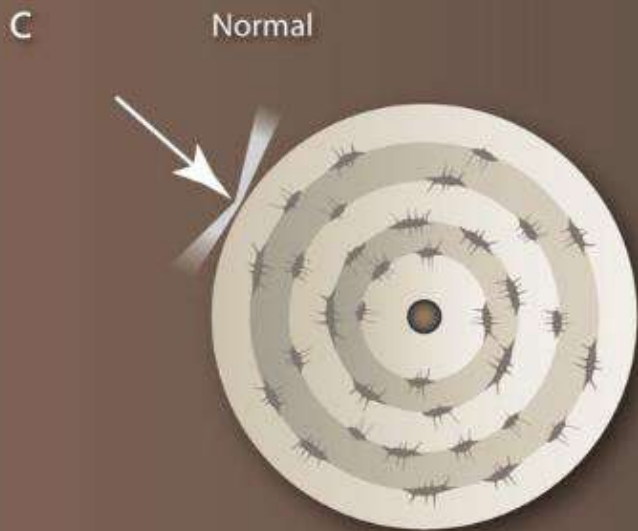
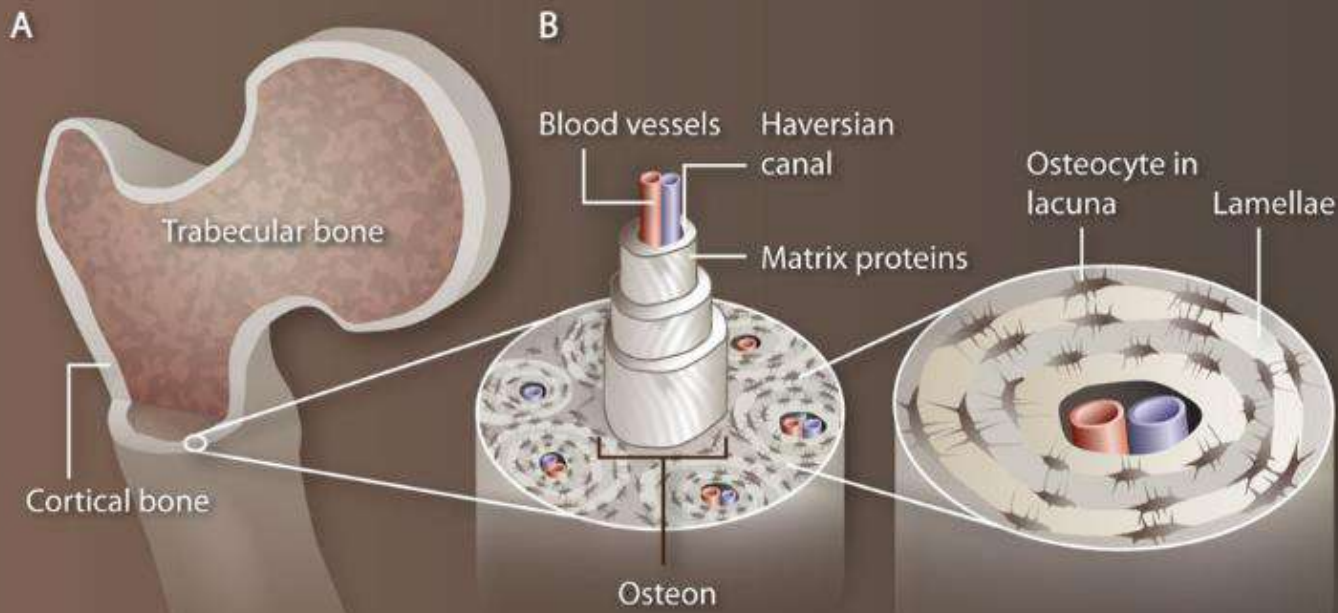
A histological slide of bone tissue stained with hematoxylin and eosin (H&E). The image shows several layers of bone tissue. In the center, there is a prominent osteoclast, a large multinucleated cell with a clear cytoplasm and a distinct nucleus. The surrounding bone matrix appears somewhat porous and less dense, consistent with the effects of secondary hyperparathyroidism.

**Osteoclast**



**Loss of Matrix & Mineral**

**Osteopenia/Osteoporosis**



**Fig. 1 Cortical bone quality in vitamin D deficiency.**

(A) Cortical bone is a major determinant of bone strength and resistance to fractures. This type of bone is separate from trabecular bone, which is the spongy interior bone. (B) At the microstructural level, cortical bone is built of cylinders called osteons. Osteons are composed of bone proteins and matrix concentrically arranged in lamellae around a central Haversian canal, which provides the vascular supply. Osteocytes are located in lacunae between these lamellae. (C) Poor crack control in vitamin D-deficient bone. Vitamin D-deficient bone displayed wider Haversian canals, larger osteocytic lacunae, and increased cortical porosity as compared with those of normal bone (4). Mineralized bone has a higher mineralization and crystallinity degree and older collagen properties; as a result of this poor bone quality, cracks were not deflected or bridged but rather spread transversally.

# Vitamin D Deficiency Induces Early Signs of Aging in Human Bone, Increasing the Risk of Fracture

**Björn Busse<sup>1,2,\*</sup>, Hrishikesh A. Bale<sup>2</sup>, Elizabeth A. Zimmermann<sup>1,2,3</sup>, Brian Panganiban<sup>2</sup>, Holly D. Barth<sup>2,3</sup>, Alessandra Carriero<sup>2</sup>, Eik Vettorazzi<sup>4</sup>, Josef Zustin<sup>5</sup>, Michael Hahn<sup>1</sup>, Joel W. Ager III<sup>2</sup>, Klaus Püschel<sup>6</sup>, Michael Amling<sup>1</sup> and Robert O. Ritchie<sup>2,3</sup>**

+ Author Affiliations

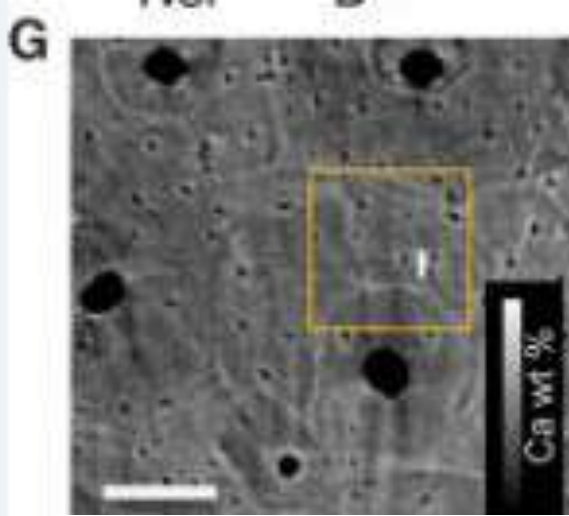
\*Corresponding author. E-mail: b.busse@uke.uni-hamburg.de

*Science Translational Medicine* 10 Jul 2013:

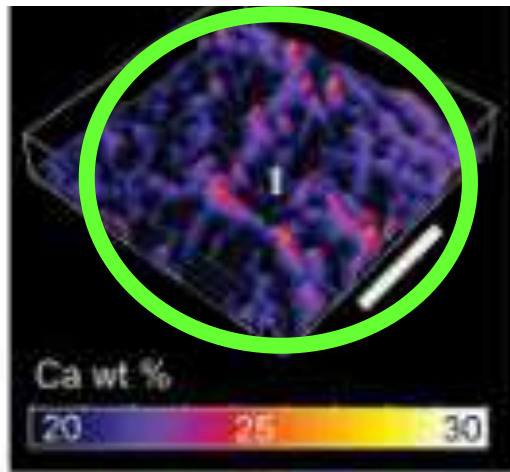
Vol. 5, Issue 193, pp. 193ra88

DOI: 10.1126/scitranslmed.3006285

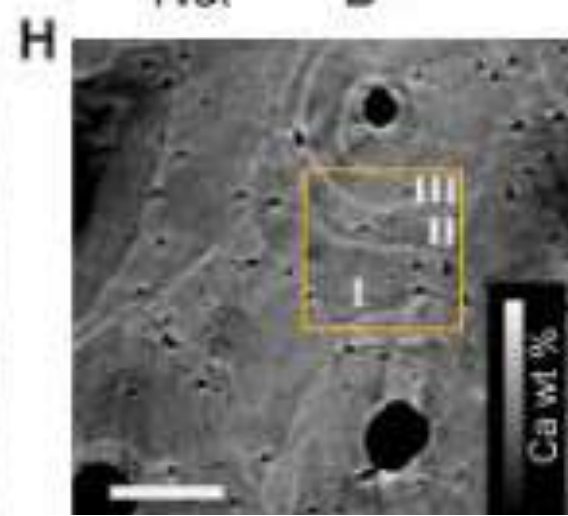
and its greatly decreased fracture resistance. Through a combination of characterization techniques spanning multiple size scales, our study expands the current clinical understanding of the pathophysiology of vitamin D deficiency and helps explain why well-balanced vitamin D levels are essential to maintain bone's structural integrity.



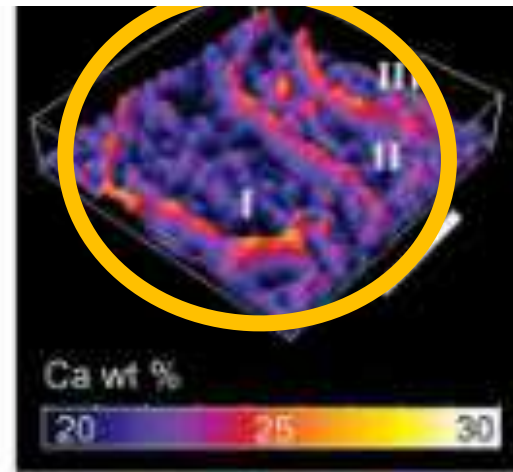
**Normal**



Normal



**Deficient**



Vitamin D-

Microtomography slices (scale bars, 100  $\mu\text{m}$ ) (G and H) and corresponding bone surface plots (scale bars, 50  $\mu\text{m}$ ) (I and J) from regions within the yellow boxes depict mineral content and extent of mineralization in both the cement lines (Roman numerals) and bone in normal and vitamin D-deficient samples.

**Subclinical**

**Vitamin D Deficiency**

**PRECIPITATES**

**&**

**EXACERBATES**

**OSTEOPOROSIS**



**OSTEOPOROSIS**

**IS OFTEN A**

**SILENT DISEASE**

OSTEOMALACIA/RICKETS

IS **NOT** A

SILENT DISEASE

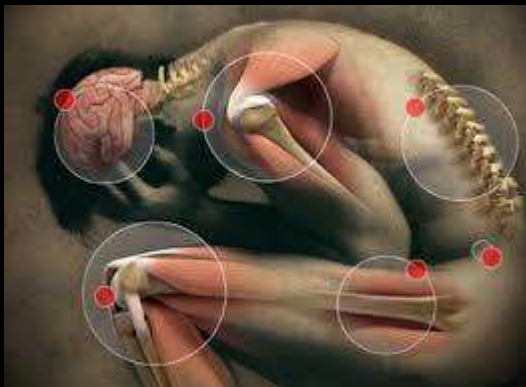


**Curiously**

**Your aches and pains  
In your bones and muscles  
Always occur during  
The winter**

**I wonder why**

**??????**



# Symptoms

- Generalized bone pain
- Isolated bone pain
- Muscle aches



40-60% OSTEOMALACIA

***FIBROMYALGIA***



**MAYO CLINIC**

**December 2003**

*Volume 78*

*Number 12*

# *Mayo Clinic Proceedings*

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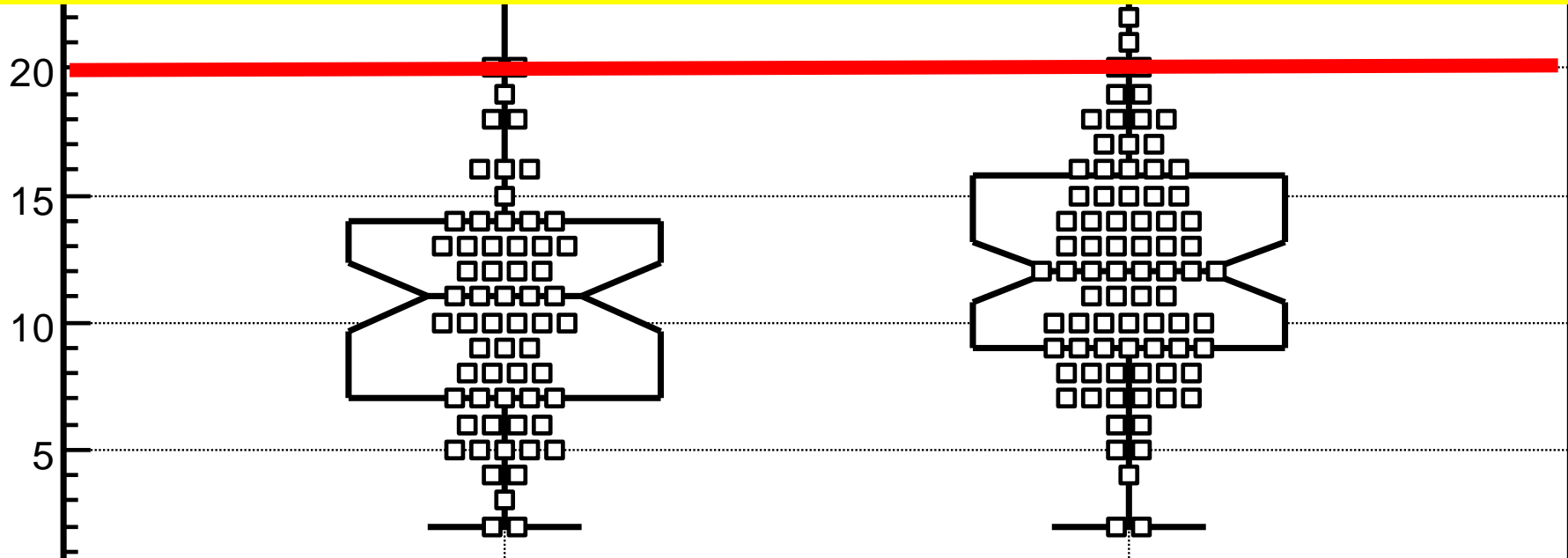
**Original Article**

## **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**

**78 Y/O M**

**MUSCLE WEAKNESS**

**ATROPHY, DENERVATION**

We present  
weakness

less  
tor

neuron disease. 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

Amyotroph Lateral Scler Other Motor Neuron Disord. 2000 Sep;1(4):283-6. Related  
Articles Links

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

Whitaker CH, Malchoff CD, Felice KJ.

**KRAFT  
SPORT**  
*Revue*

EINE GUTTE FÜHRER BIS ZUM SOMMER

*Mr. Germany 1967*

WORLD  
HAUPTSPORT UND KÖRPERTRAINING

33

2 DM



*Arnold  
Schwarzenegger*

# Rickets



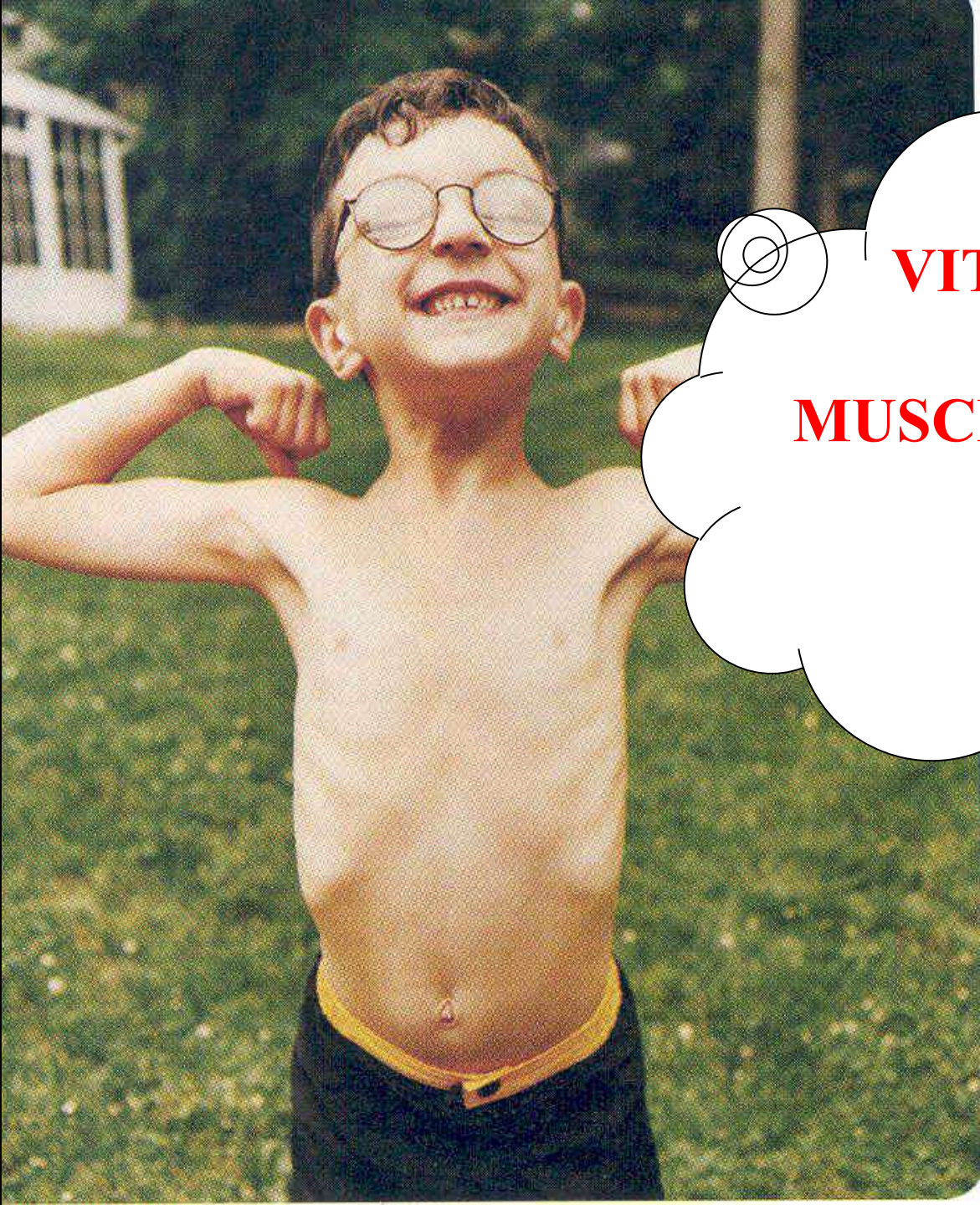


**Is it True that  
Vitamin D can  
Improve Muscle  
Strength**

**!!!**



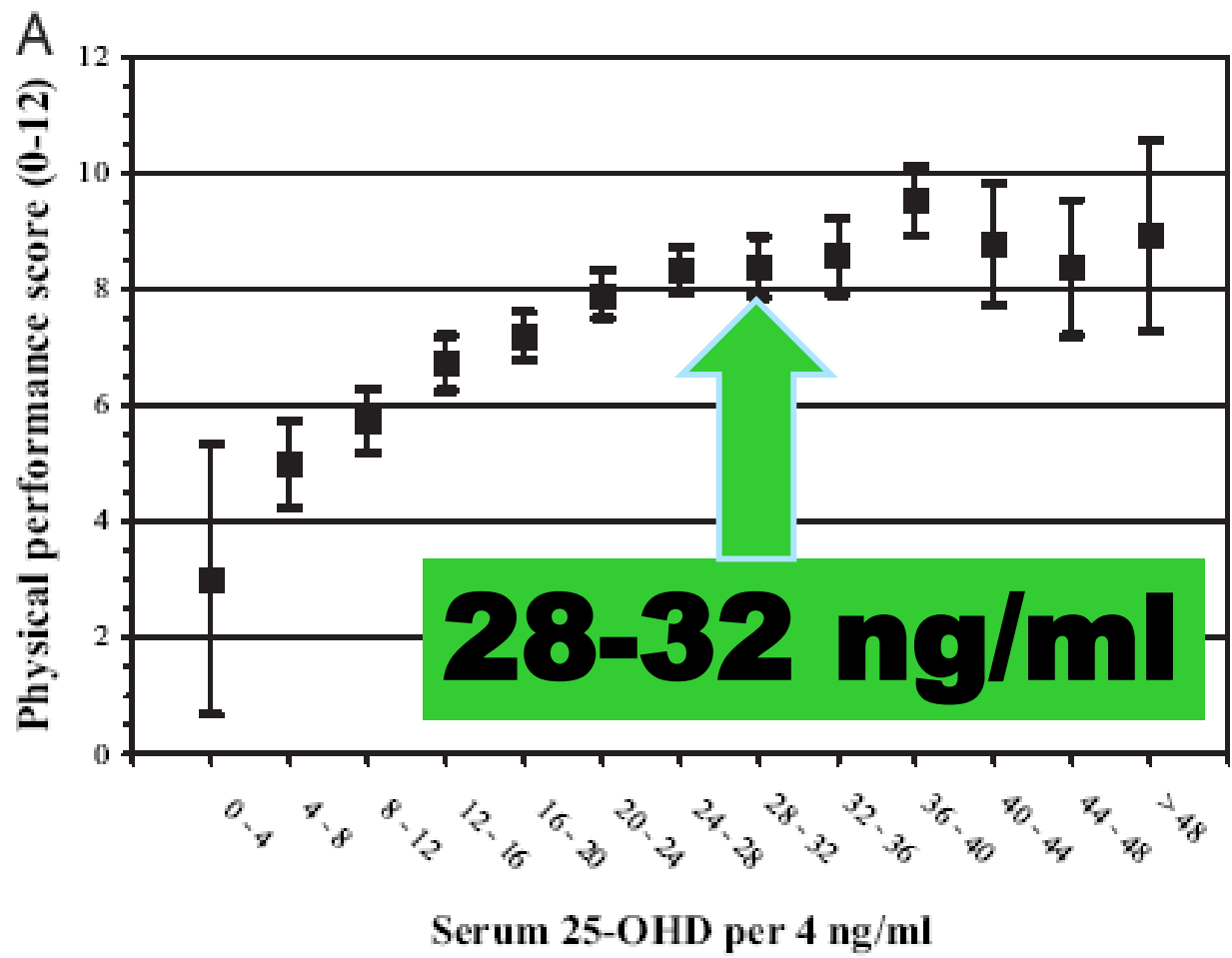
**SUN & MUSCLE STRENGTH**



**VITAMIN D IS  
GOOD FOR  
MUSCLE STRENGTH**

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

Ilse S. Wicherts, Natasja M. van Schoor, A. Joan P. Boeke, Marjolein Visser, Dorly J. H. Deeg, Jan Smit, Dirk L. Knol, and Paul Lips



JCEM 2007

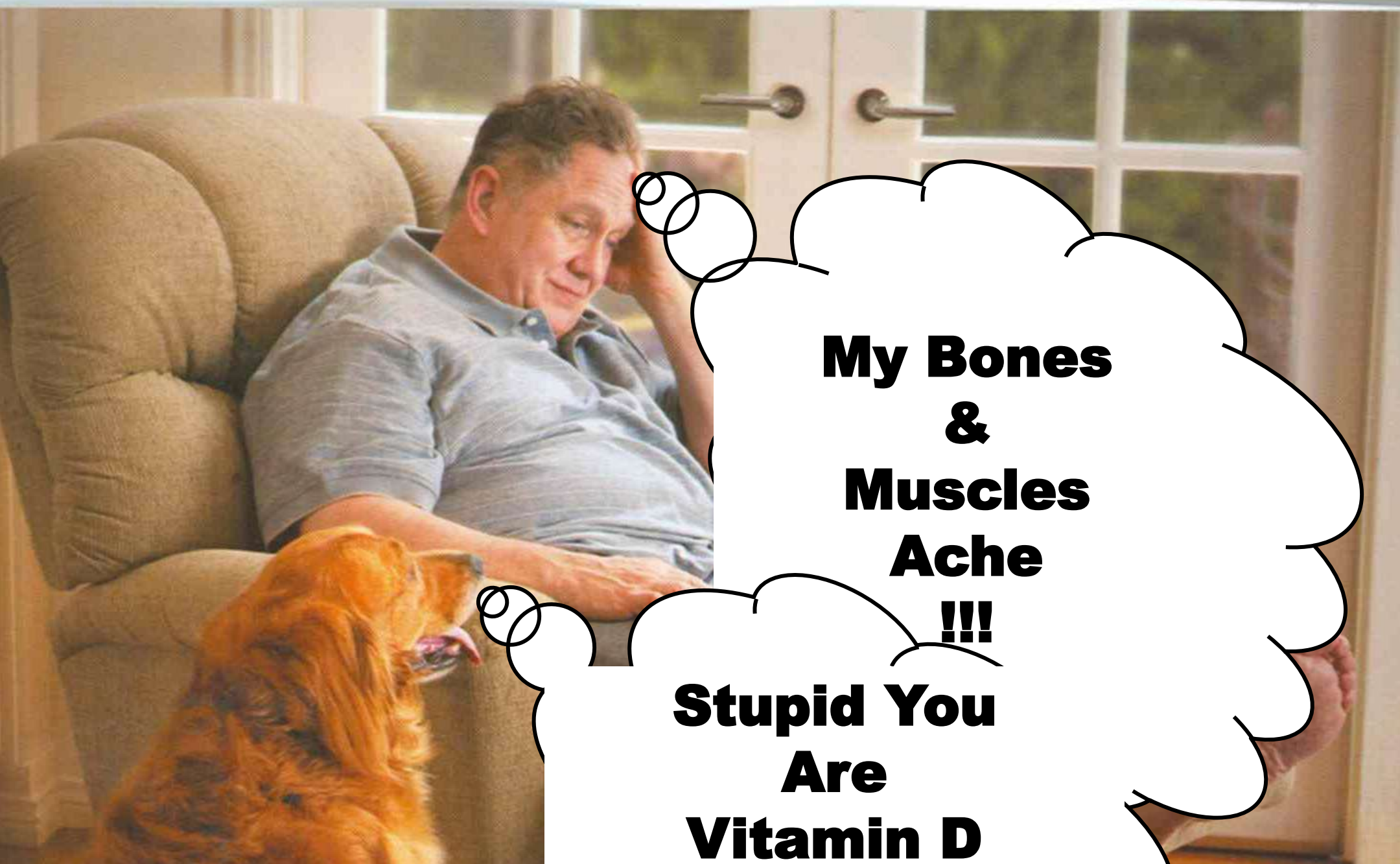
A Higher Dose of Vitamin D Reduces the Risk of Falls in Nursing Home Residents: A Randomized, Multiple-Dose Study

**72% Less Falls**  
**800 IU/d 5 months**

group taking an 800 IU vitamin D supplement had fewer falls (6.1%) compared with the 500 IU/d group (6.8%)

**No Benefit**  
**200,400 or 600 IU/d**





**My Bones  
&  
Muscles  
Ache  
!!!**

**Stupid You  
Are  
Vitamin D**

25(OH)D > 30 ng/ml

↑Muscle strength,  
↑balance,  
↑lower extremity function

↑ BMD

↓Fall risk

↓ **Fxs**

**HOW DO YOU TREAT**

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

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



TREAT VITAMIN D DEFICIENCY

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

~6500 IU/d

ONCE/WEEK

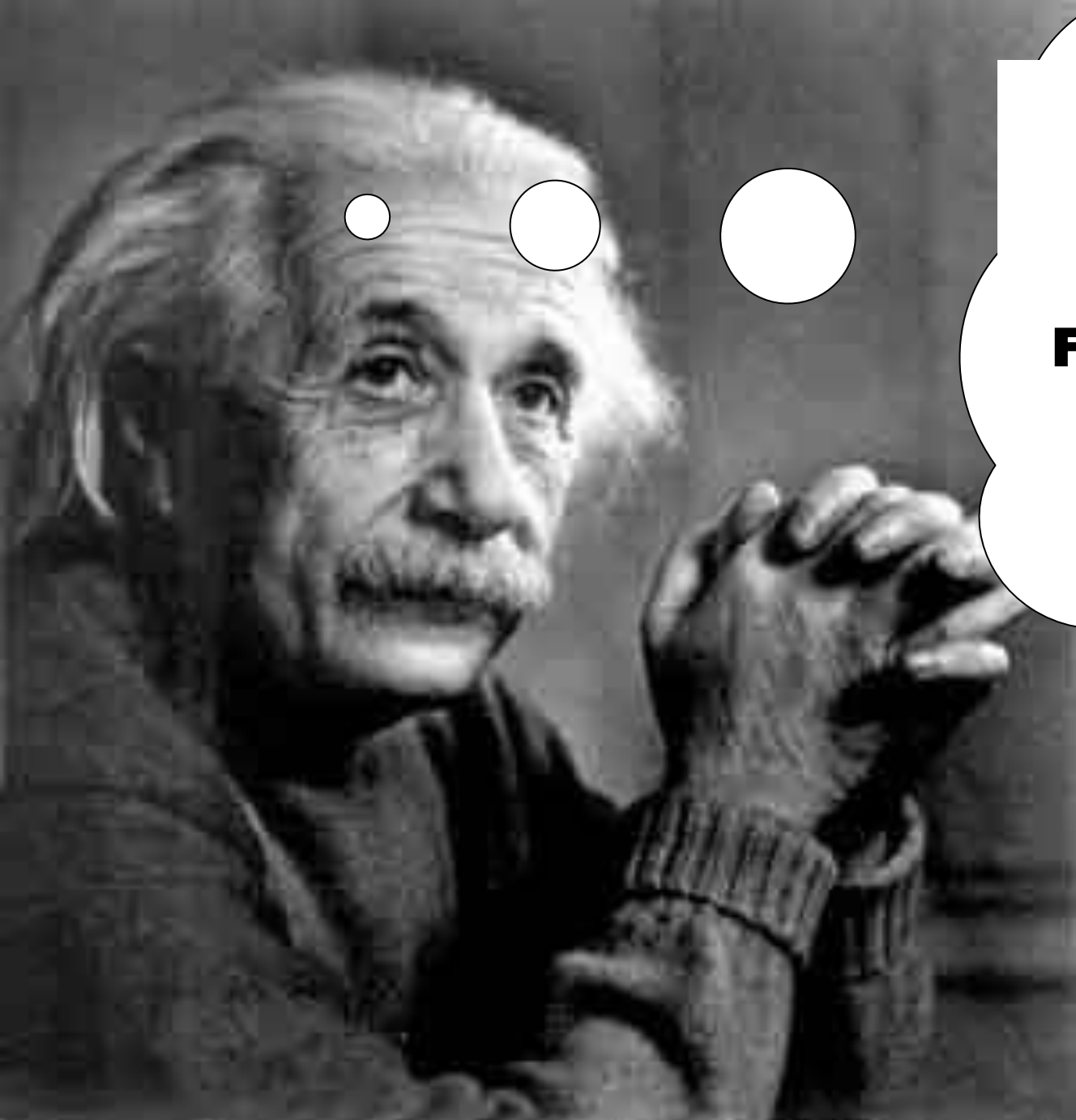
8 WEEKS

MAINTAIN VITAMIN D SUFFICIENCY

50 000 IU VITAMIN D

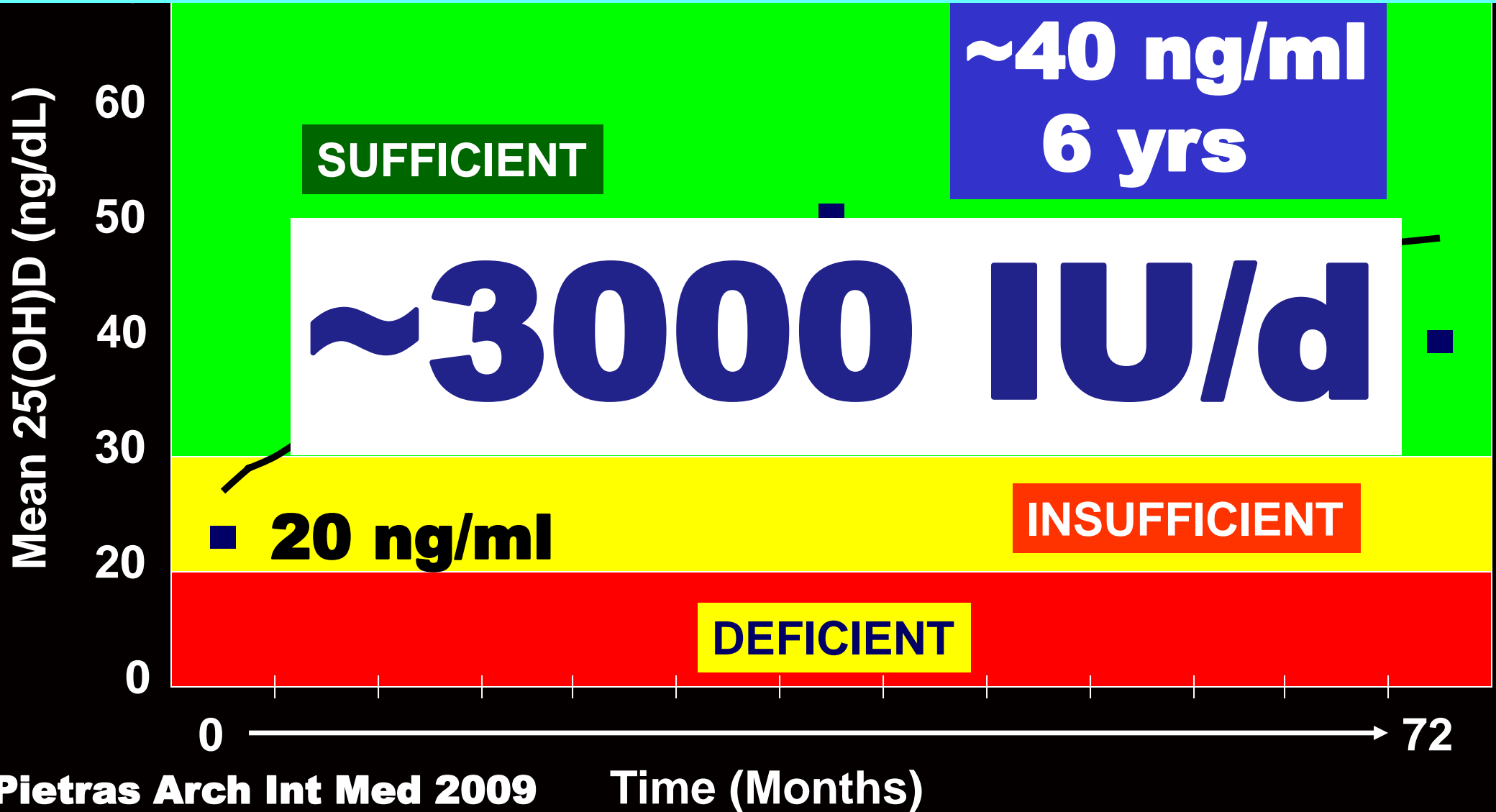
**~3000 IU/d**

ONCE/ 2 WEEKS



**WILL Rx  
VITAMIN D2 FOR  
6 Years  
Be Effective & Safe  
For Maintaining 25(OH)D  
Levels  
???????**

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







**Can I give  
50,000 IU  
twice a month  
Without screening  
For 25(OH)D  
????????????**

The Endocrine Society's  
CLINICAL | GUIDELINES

# **Endocrine Society's Practice Guidelines**

Evaluation, Treatment, and Prevention  
of Vitamin D Deficiency:

An Endocrine Society Clinical Practice Guideline

### 3.4. Evidence

A dose of 50,000 IU of vitamin D<sub>3</sub> once a week for 8 wk is often effective in correcting vitamin D deficiency (3, 16). Doses of 50,000 IU of vitamin D<sub>3</sub> once every other week were

**50,000IU twice a month  
25(OH)D were  
35-50 ng/mL**

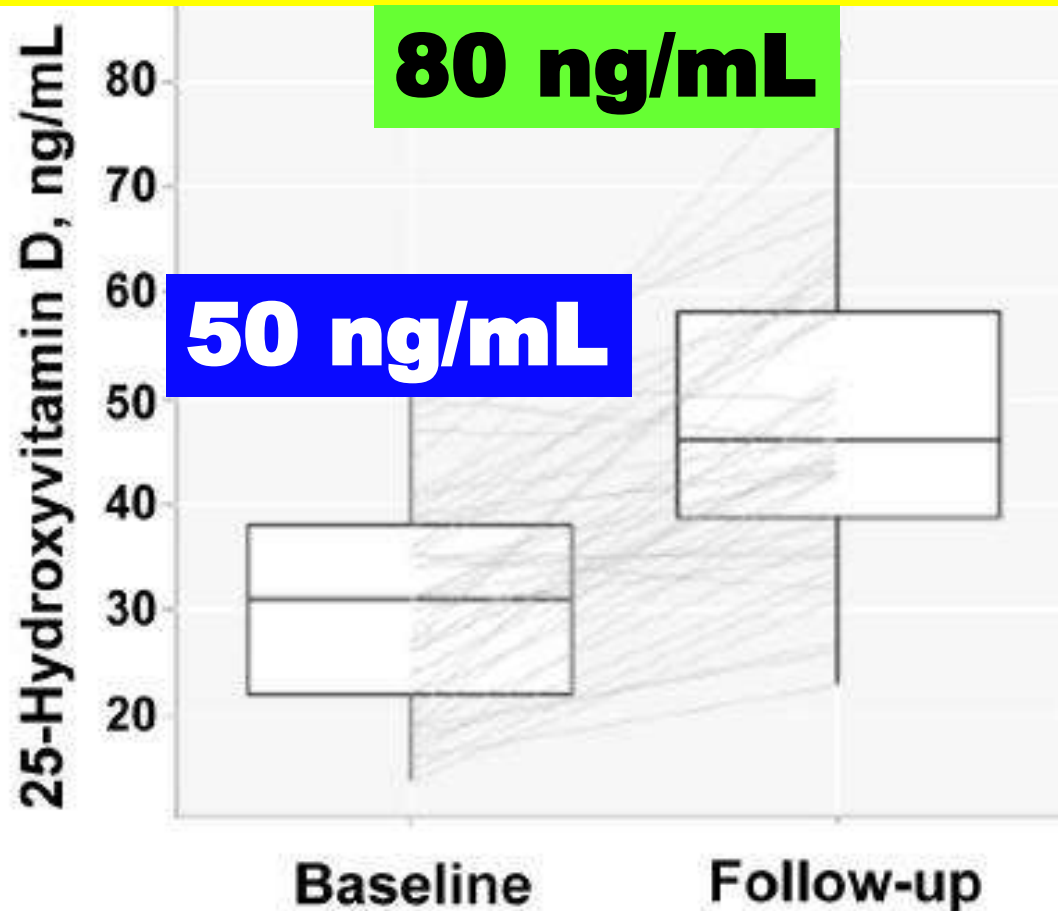
50,000 IU of vitamin D<sub>3</sub> once every other week was effective in maintaining blood levels of 25(OH)D between 35 and 50 ng/ml without any untoward toxicity (102). Obese adults need at least two to three times more vitamin D to treat and prevent vitamin D deficiency (38, 42).

**TREATMENT WITH 50 000 IU VITAMIN D<sub>2</sub> EVERY OTHER WEEK  
AND EFFECT ON SERUM 25-HYDROXYVITAMIN D<sub>2</sub>,  
25-HYDROXYVITAMIN D<sub>3</sub>, AND TOTAL 25-HYDROXYVITAMIN D  
IN A CLINICAL SETTING**

*Emily T. W. Demetriou, MD<sup>1</sup>; Thomas G. Travison, PhD<sup>2,3</sup>;  
Michael F. Holick, PhD, MD<sup>2,3</sup>*

***Conclusions:* 50 000 IU vitamin D<sub>2</sub> repletion and maintenance therapy substantially increases total 25(OH)D and 25(OH)D<sub>2</sub> despite a decrease in serum 25(OH)D<sub>3</sub>. This treatment program is an appropriate and effective strategy to treat and prevent vitamin D deficiency. (Endocr Pract. 2012;18:pp)**

**50,000 IU twice a month  
For up to 6 Years  
No baseline measurement of  
25(OH)D**





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

**Heaney et al 2005**

**C3PO**

**R2D2**

**IS D3  
MORE  
EFFECTIVE  
THAN D2  
????**



**IS VITAMIND2  
REALLY BETTER  
THAN VITAMIN D3  
???????**

MYTHBUSTERS

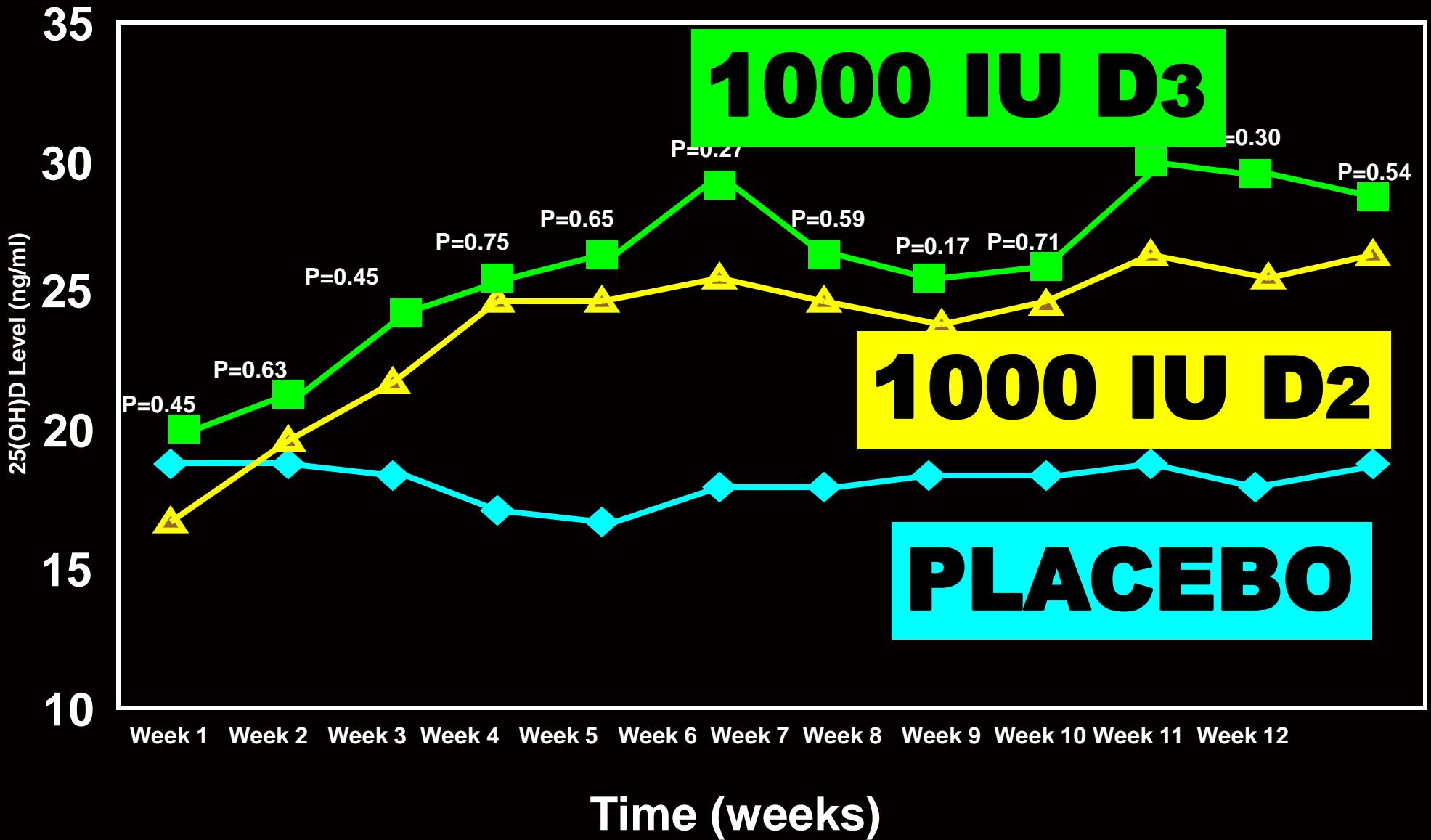


**1000 IU Vitamin D<sub>3</sub>/d**

**or**

**1000 IU Vitamin D<sub>2</sub>/d**

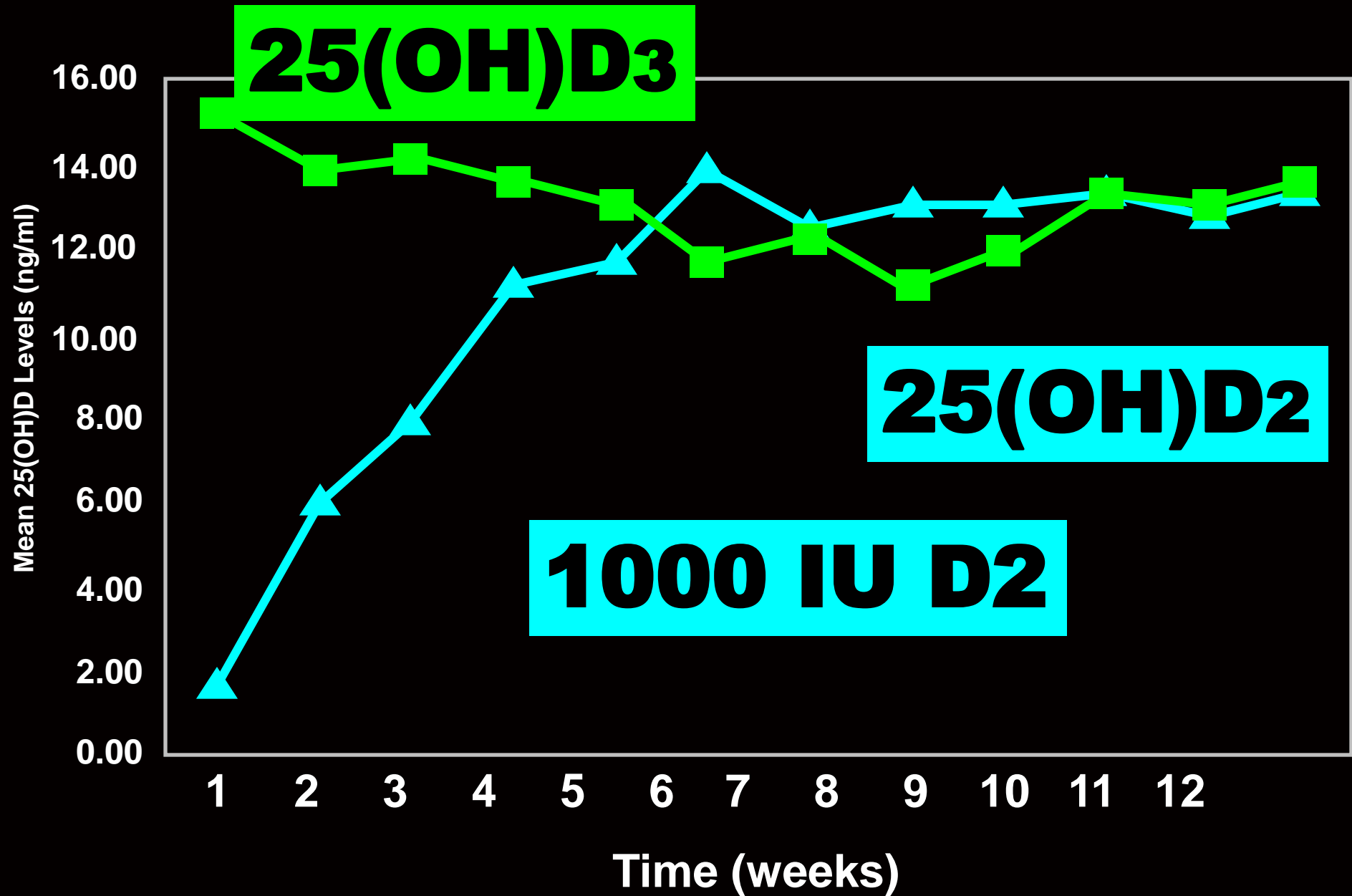
# Mean Serum Total 25(OH)D Levels

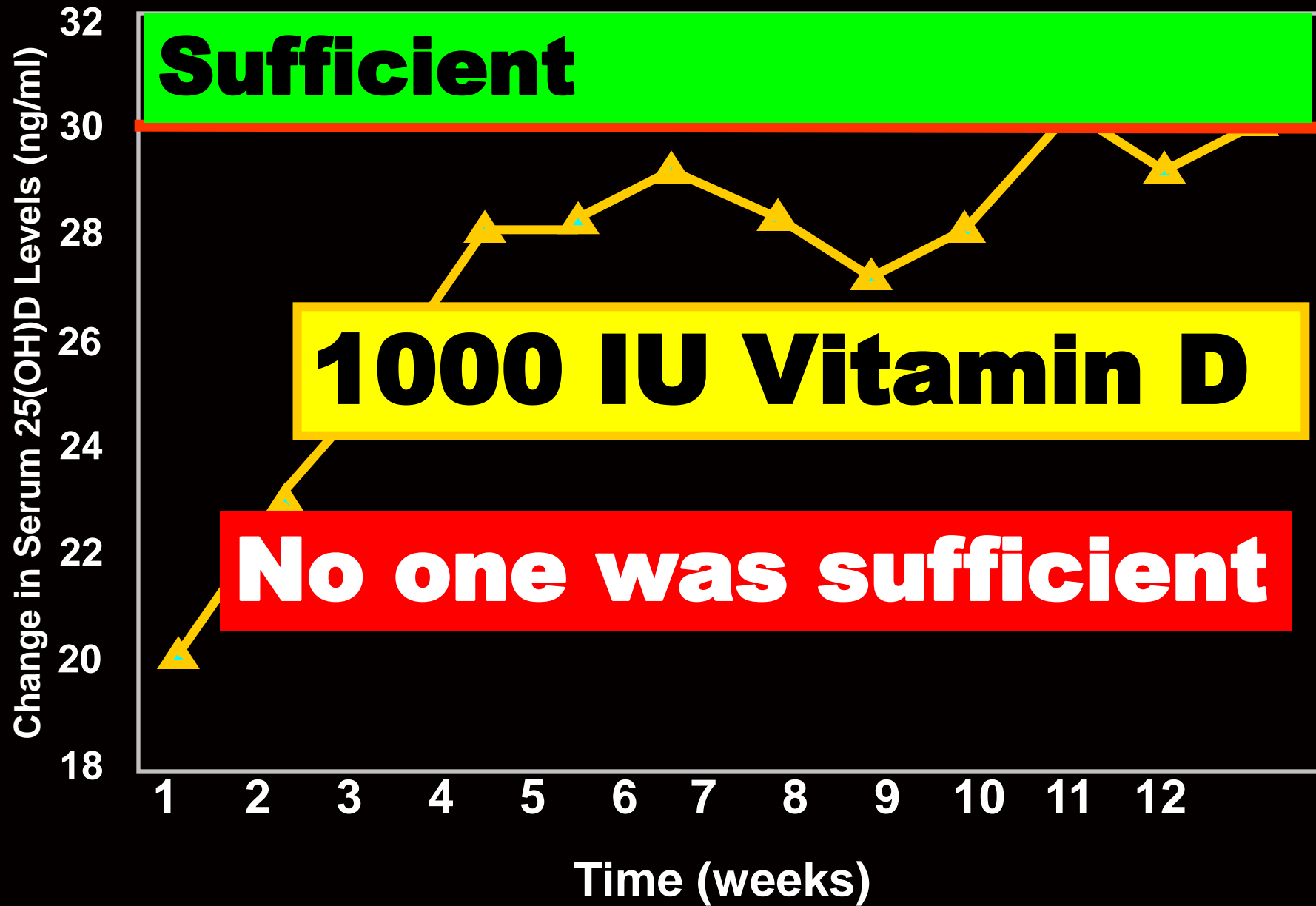





**BUT VITAMIN D<sub>2</sub>  
INCREASES THE  
DESTRUCTION  
OF VITAMIN D<sub>3</sub>  
!!!!!!!**

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







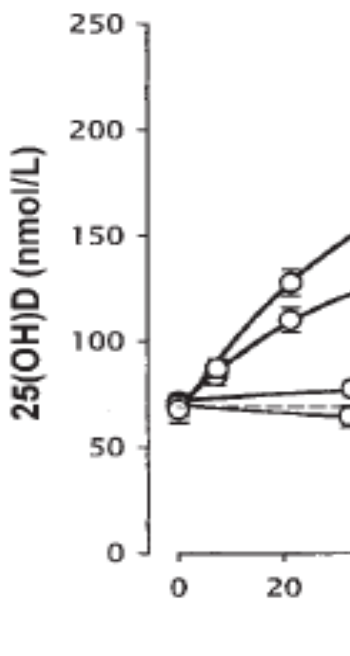


WILL YOU BECOME  
VITAMIN D  
INTOXICATED  
????

**,ELEVATED  
Ca,Pi,25(OH)D  
CALCIFY  
BLOOD  
VESSELS  
&KIDNEYS**

# Human serum 25-hydroxycholecalciferol response to extended oral dosing with cholecalciferol<sup>1-3</sup>

Robert P Heaney, K Michael Davies, Tai C Chen, Michael F Holick, and M Janet Barger-Lux



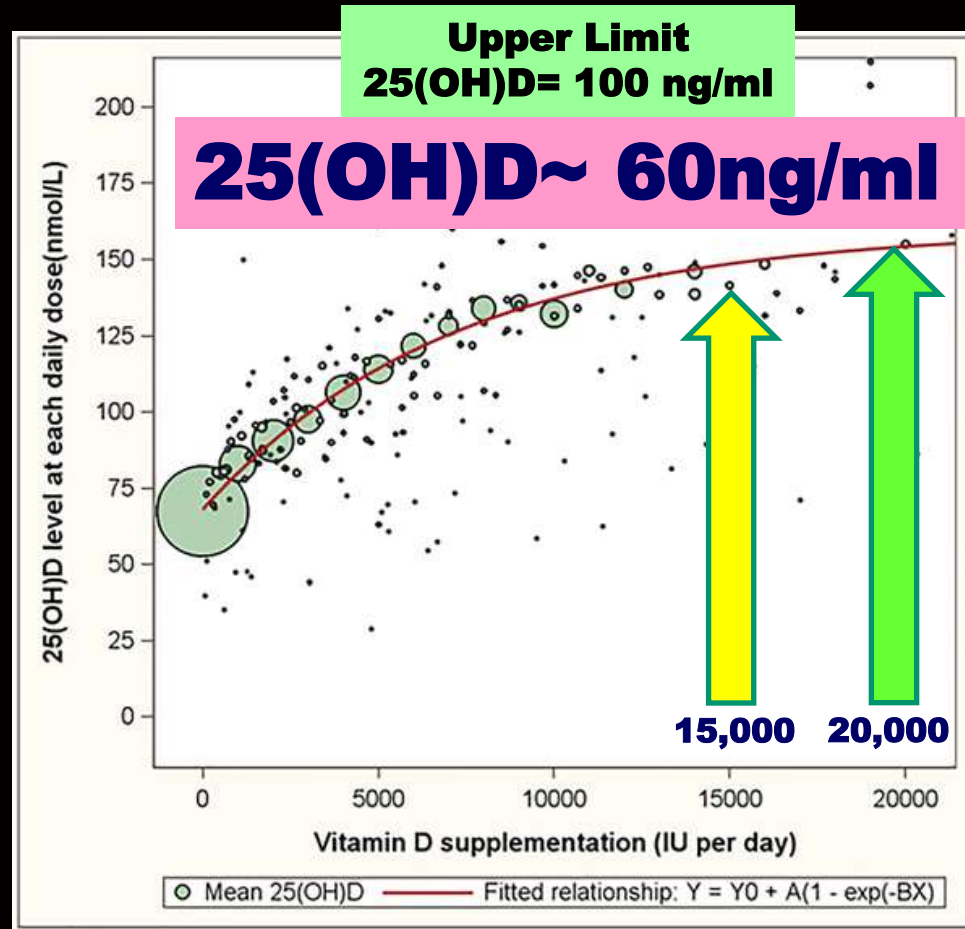
**10,000 IU/d  
Is Safe**

2.0  $\mu$ mol/L  
Before treatment      After treatment

FIGURE 4. Plot of total serum calcium concentrations before and after treatment in the 31 participants who had received  $\approx 130$  d of treatment with 137.5 and 275  $\mu$ g cholecalciferol (analyzed dose)/d. The horizontal dashed lines represent the reference normal range.



The dose response relationship between oral vitamin D supplementation and serum 25(OH)D levels based on 22,214 observations of healthy volunteers.



Ekwaru JP, Zwicker JD, Holick MF, Giovannucci E, et al. (2014) The Importance of Body Weight for the Dose Response Relationship of Oral Vitamin D Supplementation and Serum 25-Hydroxyvitamin D in Healthy Volunteers. PLoS ONE 9(11): e111265. doi:10.1371/journal.pone.0111265  
<http://www.plosone.org/article/info:doi/10.1371/journal.pone.0111265>



**What about  
Infants and  
Children  
??????**

# Treatment of Hypovitaminosis D in Infants and Toddlers

Catherine M. Gordon, Avery LeBoff Williams, Henry A. Feldman, Jessica May, Linda Sinclair, Alex Vasquez, and Joanne E. Cox

Division of Adolescent Medicine (C.M.G., A.L.W., J.M., L.S.), Division of Endocrinology (C.M.G., H.A.F.), Clinical Research Program (H.A.F.), and Division of General Pediatrics (J.E.C.), Children's Hospital Boston, Boston, Massachusetts 02115; and Biotics Research Corp. (A.V.), Rosenberg, Texas 77471

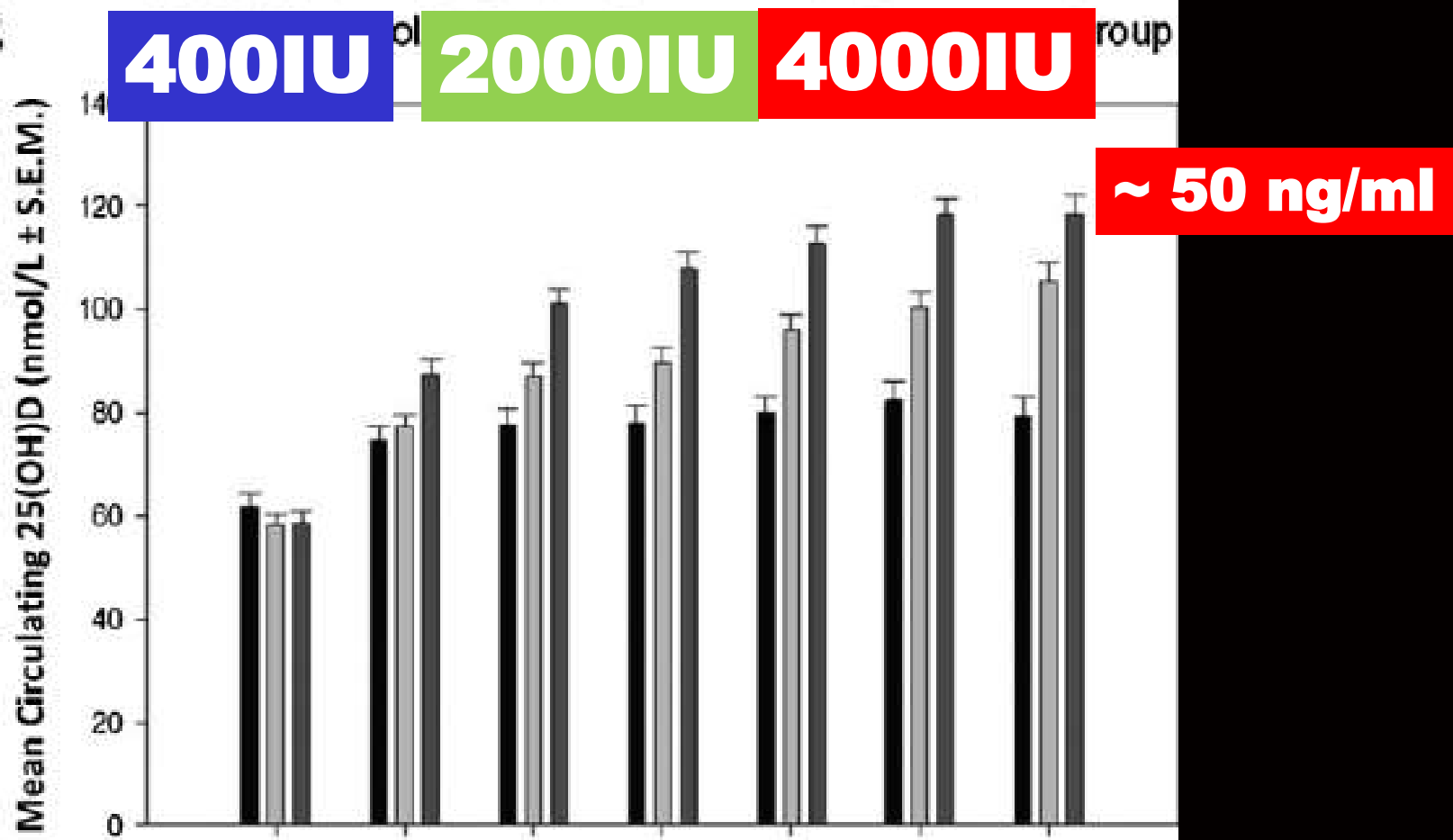
**Conclusions: Short-term vitamin D2 2,000 IU daily, vitamin D2 50,000 IU weekly, or vitamin D3 2,000 IU daily yield equivalent outcomes in the treatment of hypovitaminosis D among young children.** Therefore, pediatric providers can individualize the treatment regimen for a given patient to ensure compliance, given that no difference in efficacy or safety was noted among these three common treatment regimens. (*J Clin Endocrinol Metab* 93: 2716–2721, 2008)

**Infants & Toddlers**

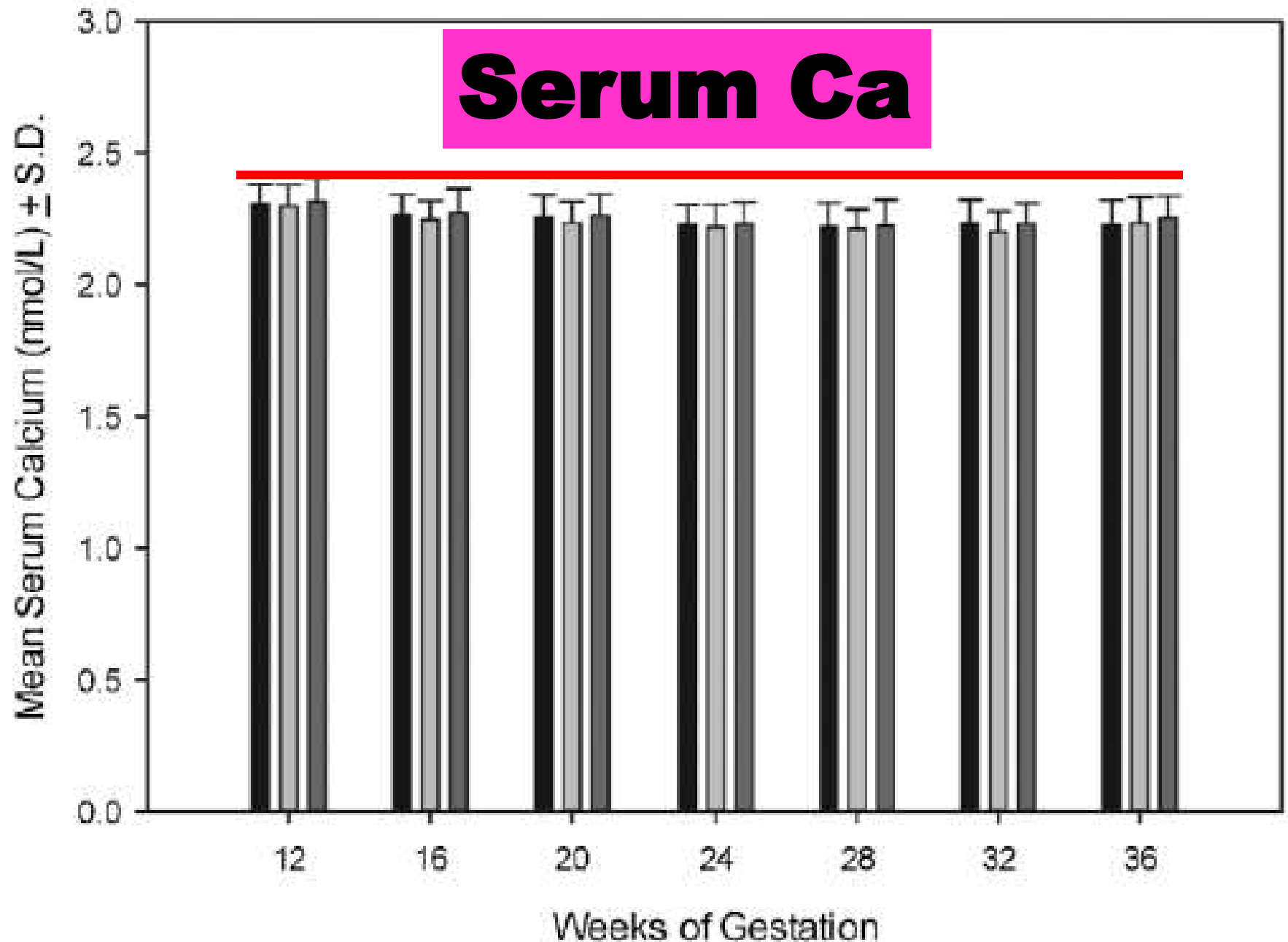
**2000 IU/d; 50,000 IU/wk**

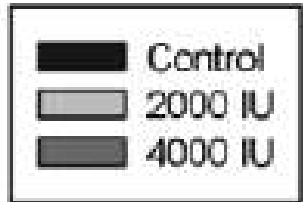
**Safe**

# Vitamin D Supplementation During Pregnancy: Double-Blind, Randomized Clinical Trial of Safety and Effectiveness

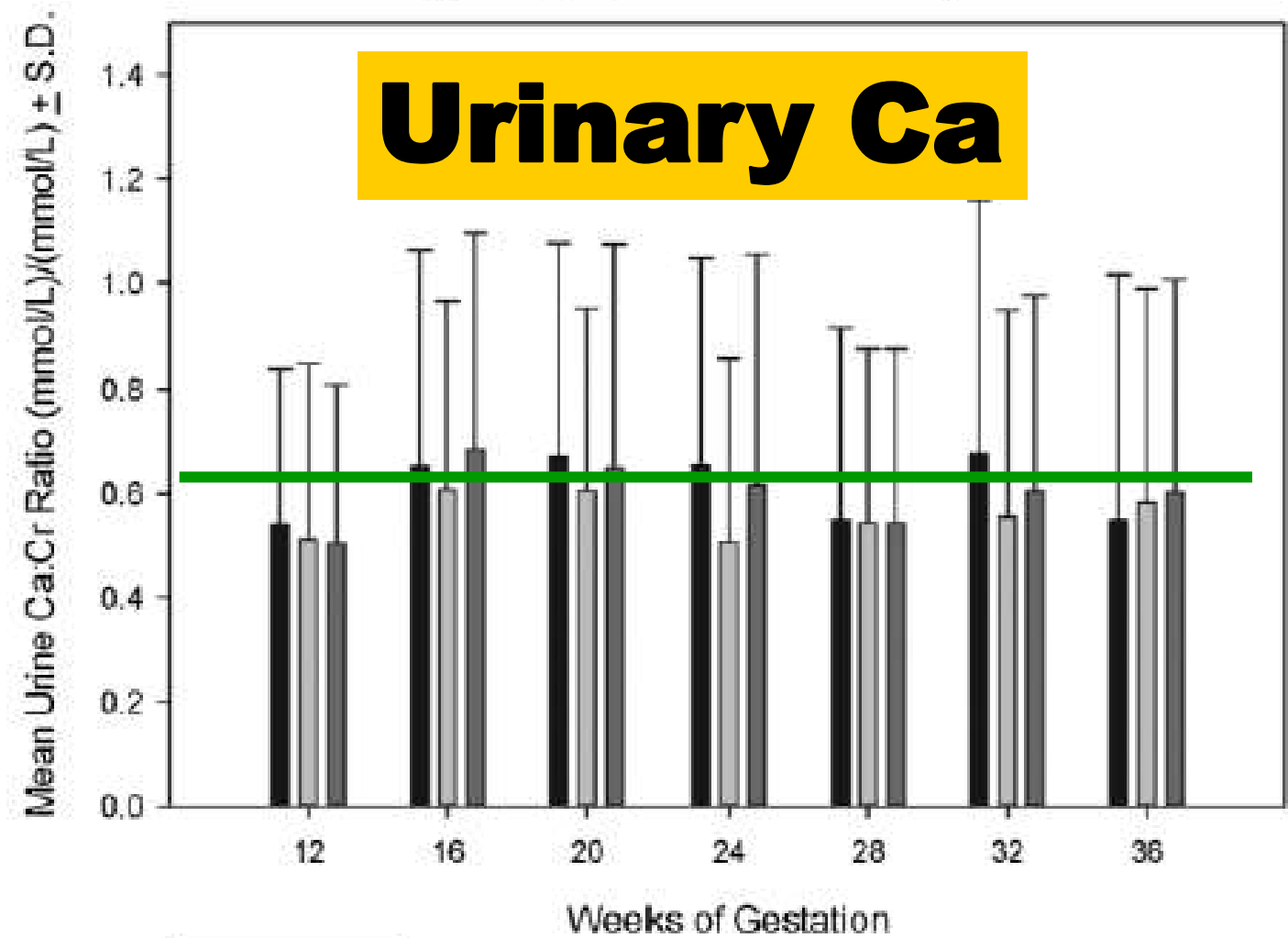


# A Serum Calcium (nmol/L) During Pregnancy by Treatment Group





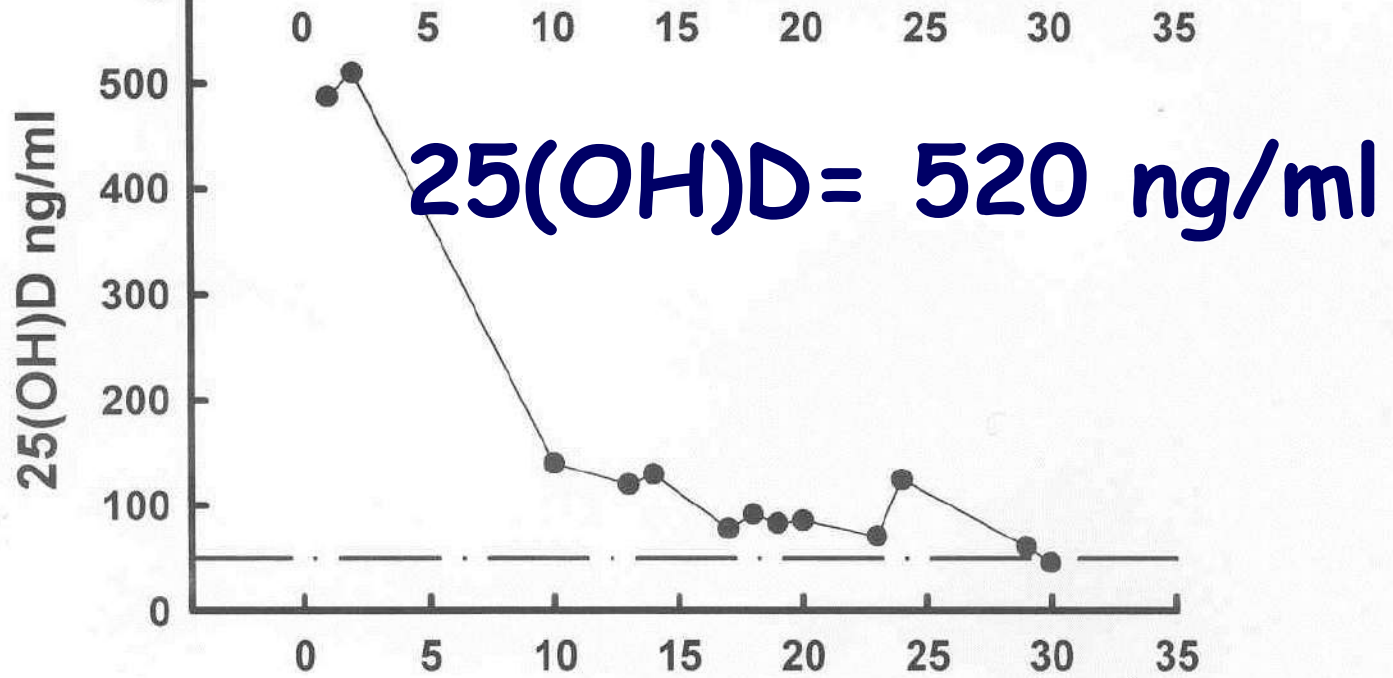
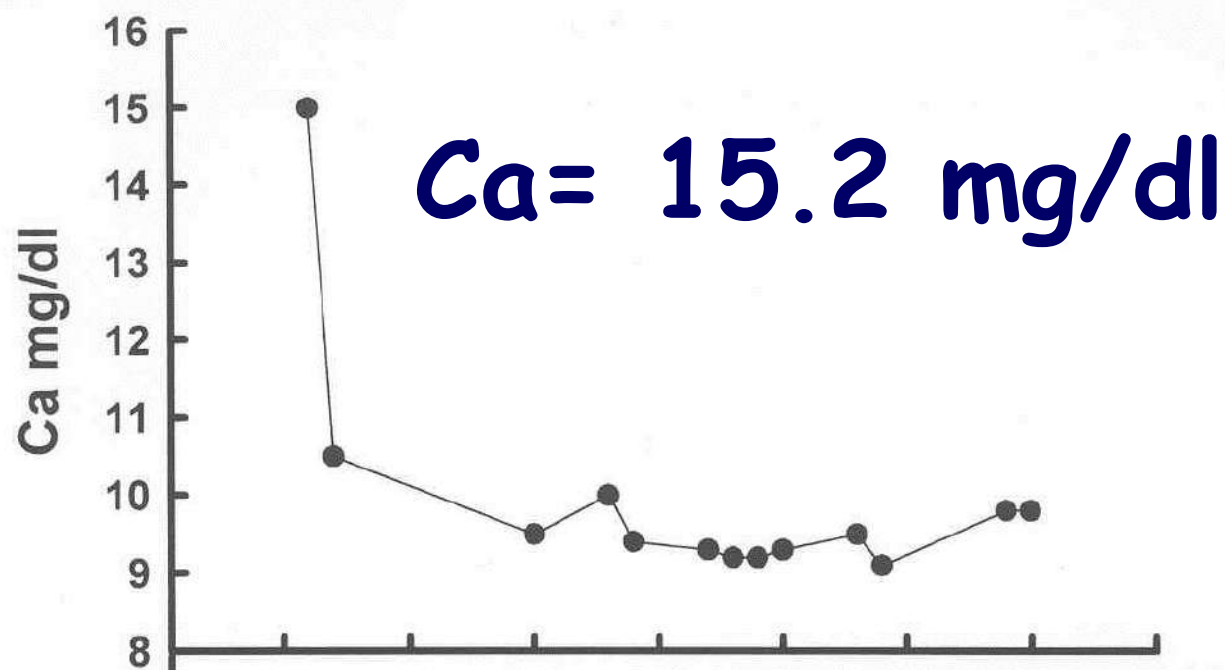
**B** Urine Calcium Creatinine Ratio (mmol/L)/(mmol/L) During Pregnancy by Treatment Group



**1 MILLION IU  
VITAMIN D/DAY**

Vitamin  
**CHOLECALCIFEROL  
POWDER**  
30 GRAMS

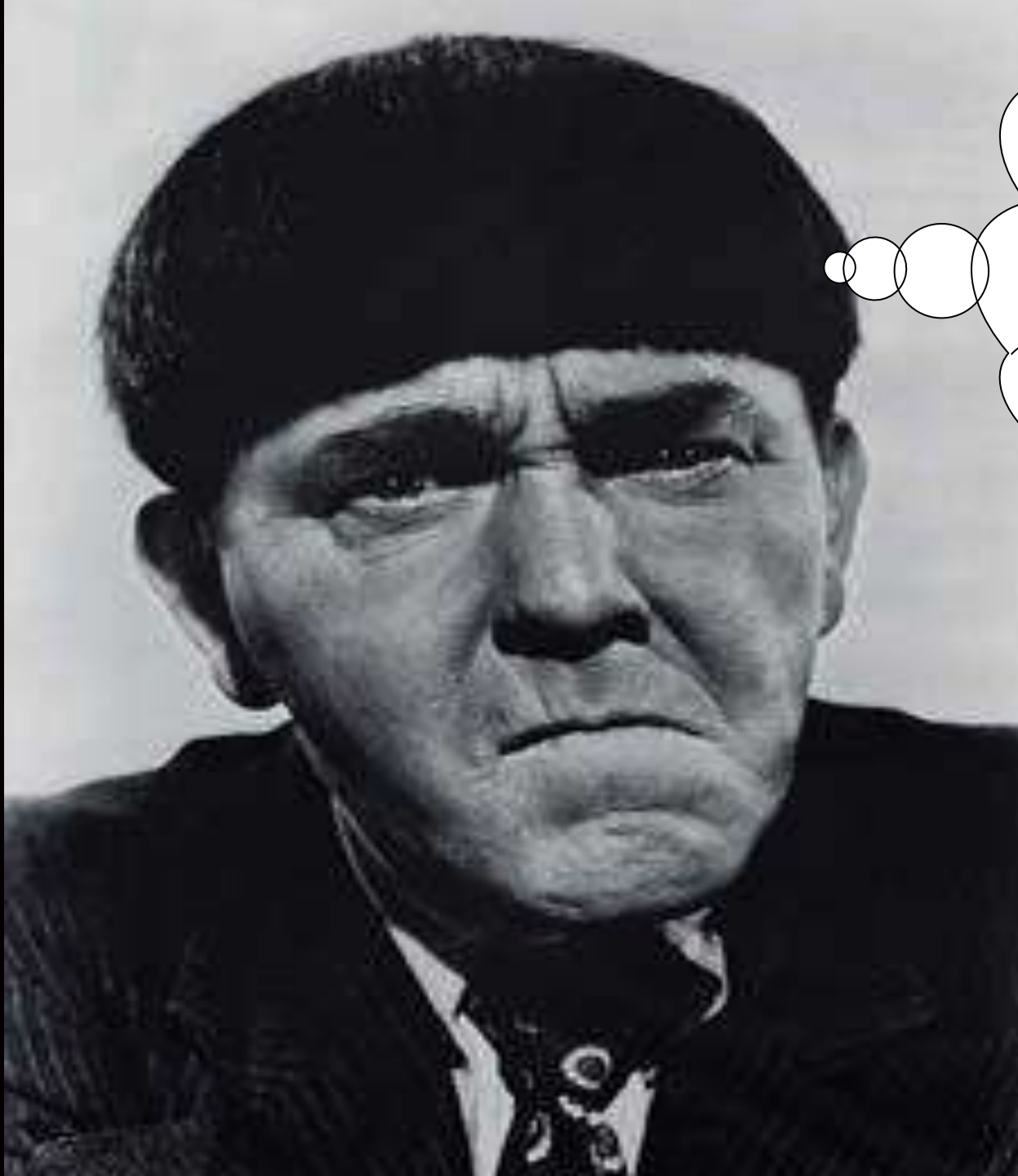
**1000 IU/TSP**



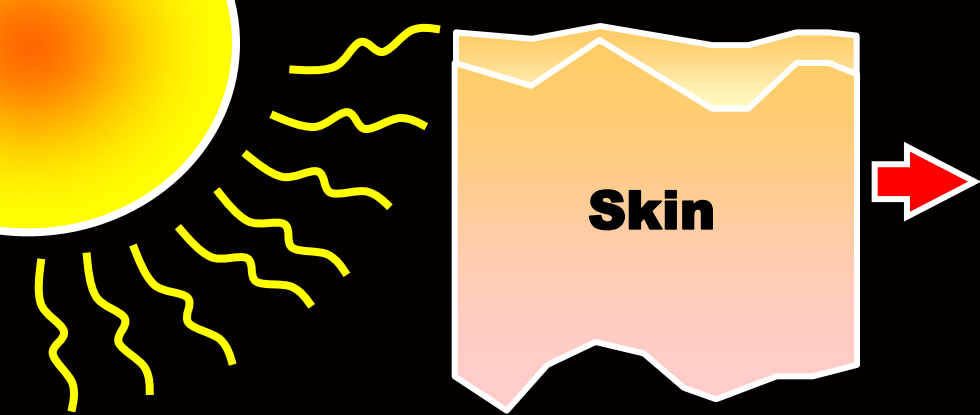


**IT IS  
DIFFICULT  
TO BECOME  
VITAMIN D  
INTOXICATED**

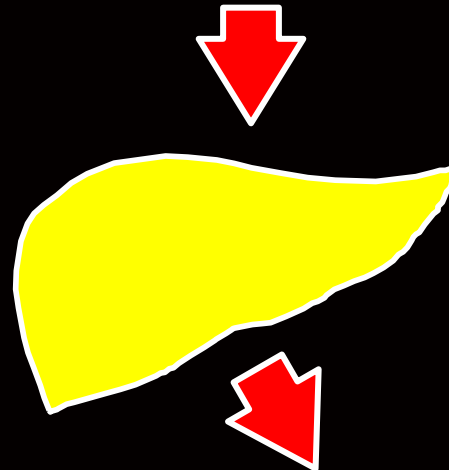




WHY SHOULD  
I CARE ???????



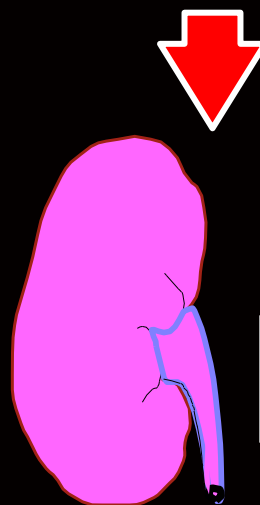
**VITAMIN D**



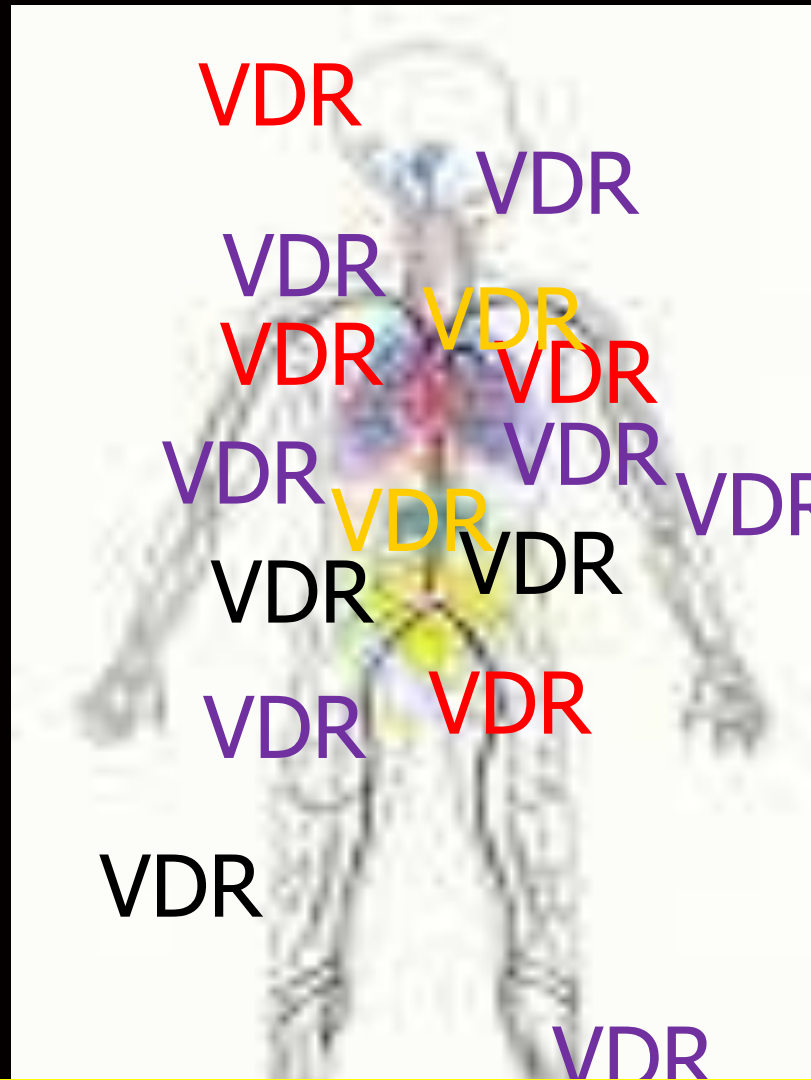
**Liver**  
**25-OHase**

**25(OH)D<sub>3</sub>**

**Kidney**  
**1 $\alpha$ -OHase**



**1,25(OH)<sub>2</sub>D<sub>3</sub>**

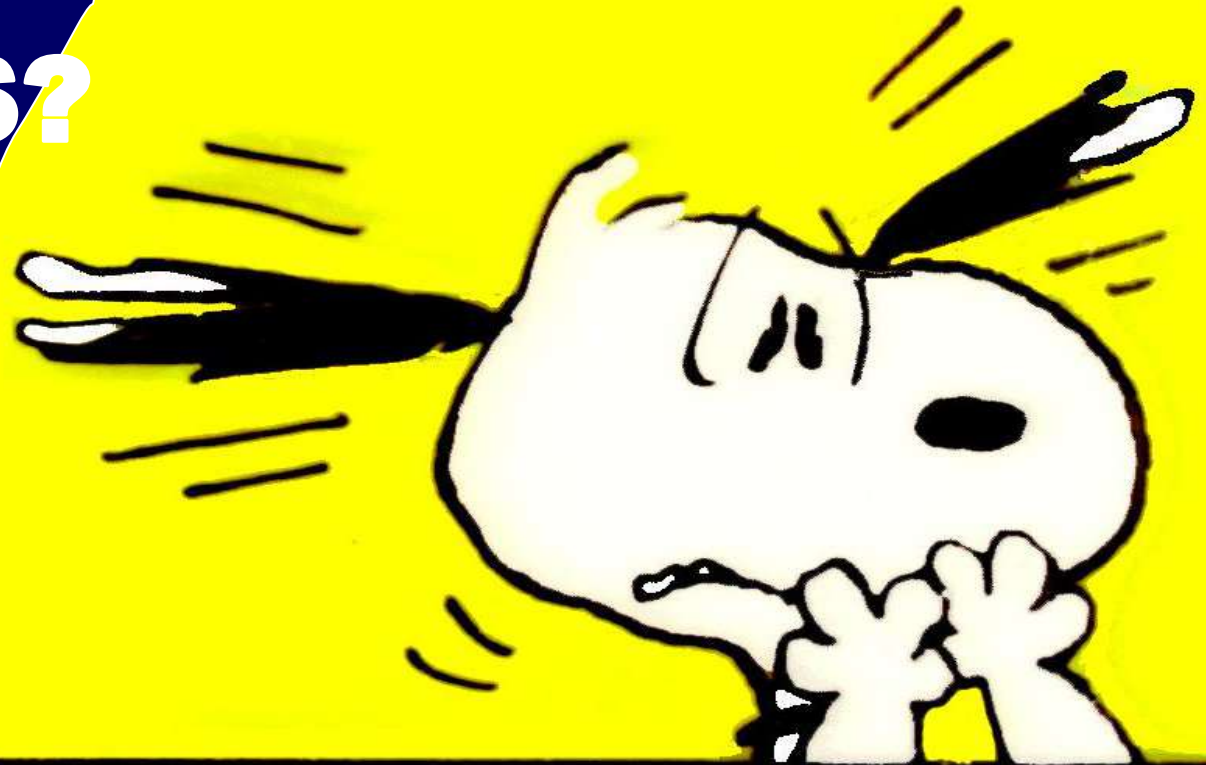


**ESSENTIALLY EVERY TISSUE AND CELL HAS A VDR**

**WHAT ARE  
THE  
FUNCTIONS?**

**???????**

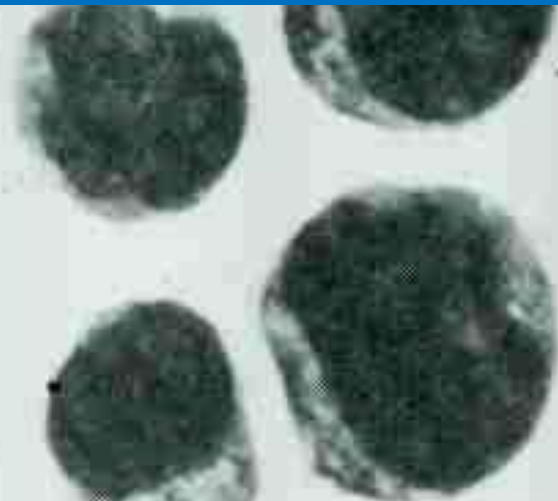
**WHY???????**



# HL-60 LEUKEMIC CELLS

**CONTROL**

**+VDR**



**B**



**C**



**RX - 1,25(OH)<sub>2</sub>D<sub>3</sub>**

**Suda et al 1979**

VITAMIN D

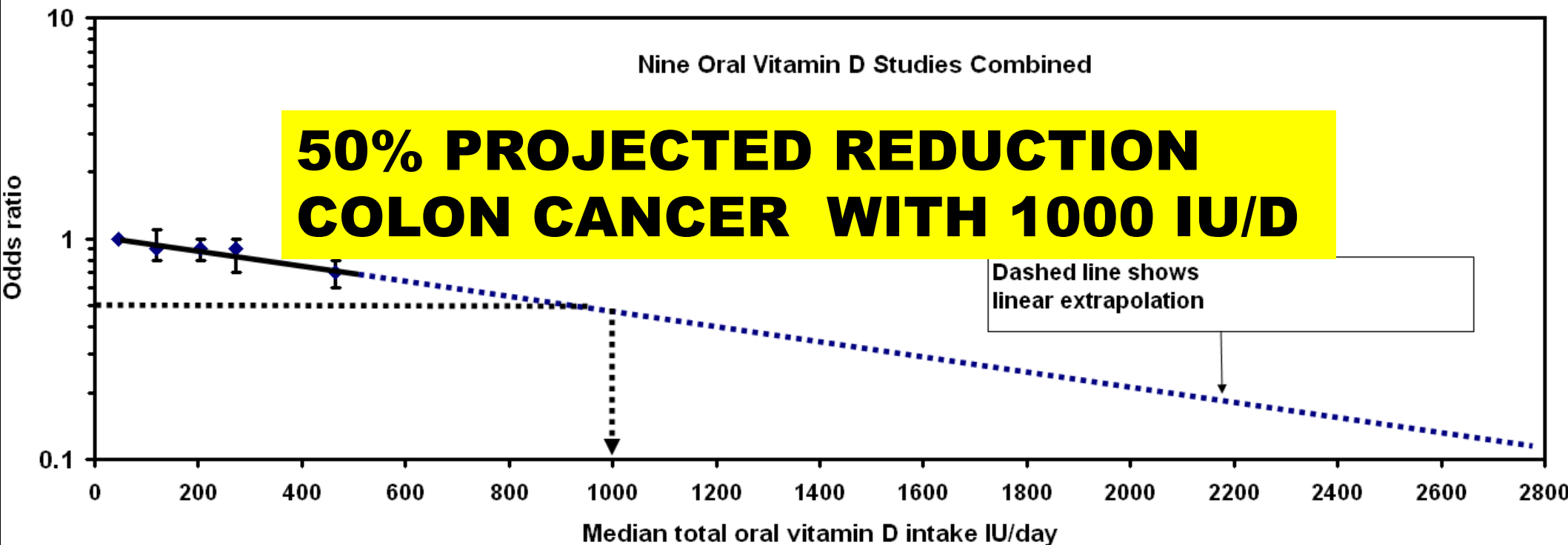
&

CANCER

**WHAT IS THE  
EVIDENCE THAT  
VITAMIN D AND  
SUNLIGHT  
DEFICIENCY  
INCREASES  
RISK OF DEADLY  
CANCERS  
?????????**





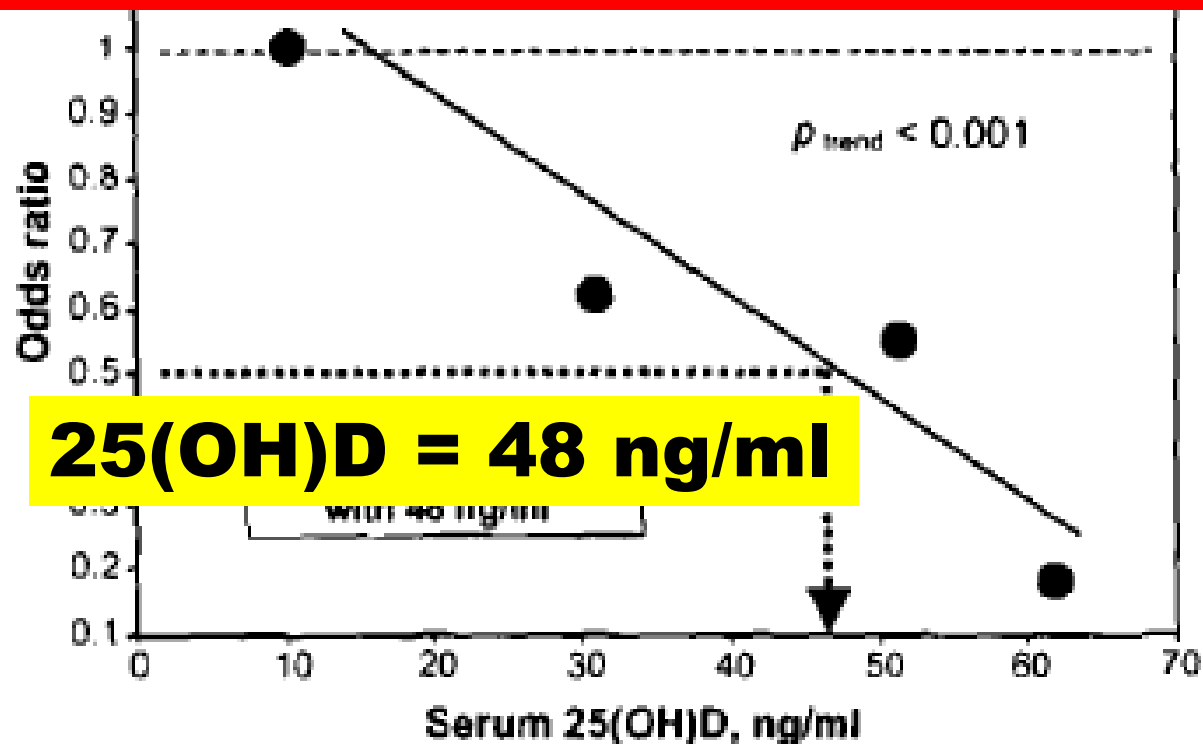


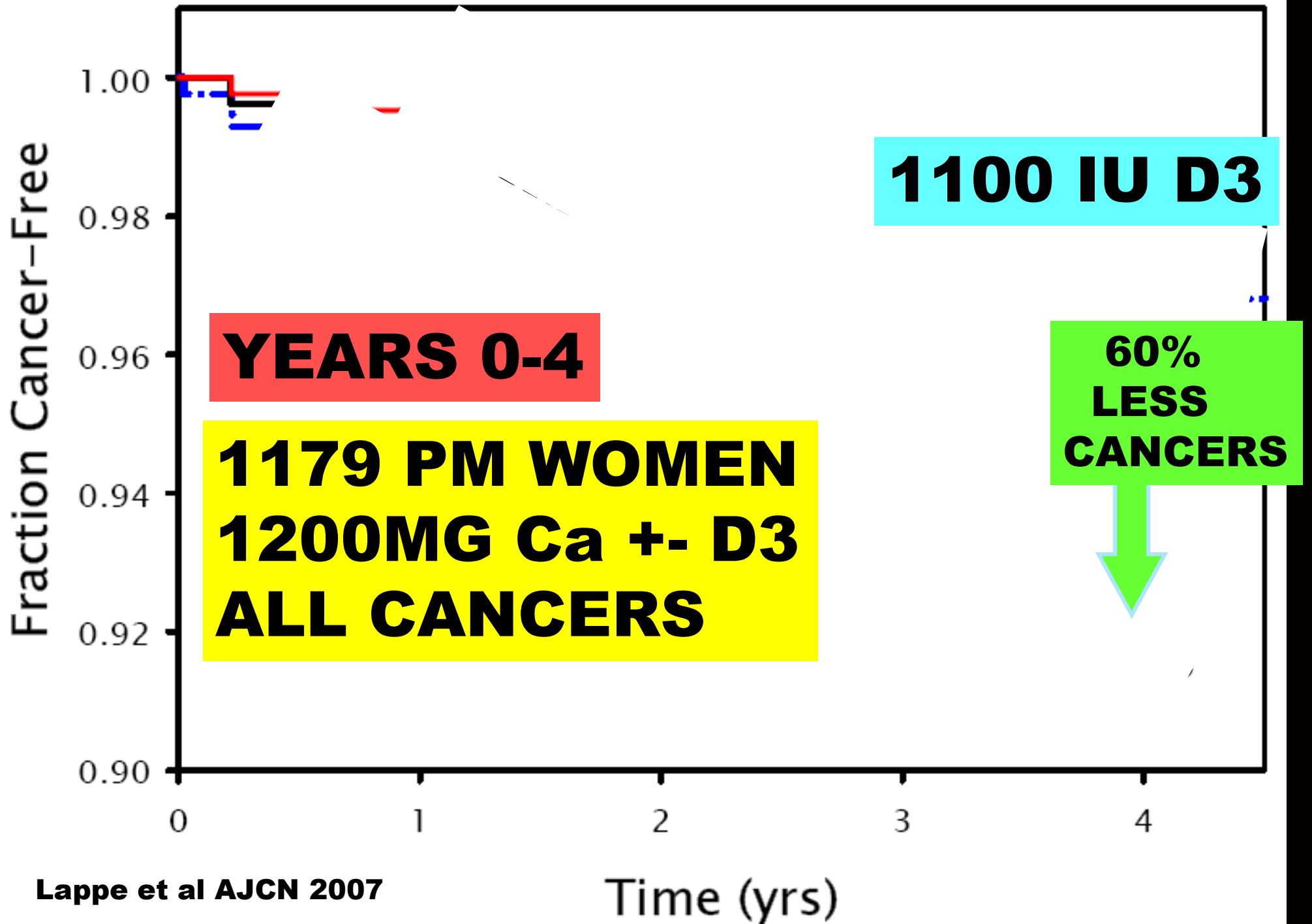
**Garland et al 2005**

# 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>

**50% LOWER RISK**





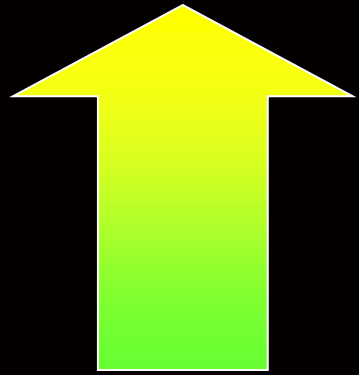
**WHAT IS THE  
POSSIBLE CONNECTION  
BETWEEN  
VITAMIN D & CANCER  
????????**

**ACTIVATED VITAMIN D**

**INHIBITS**

**CANCER CELL GROWTH**

**BUT**

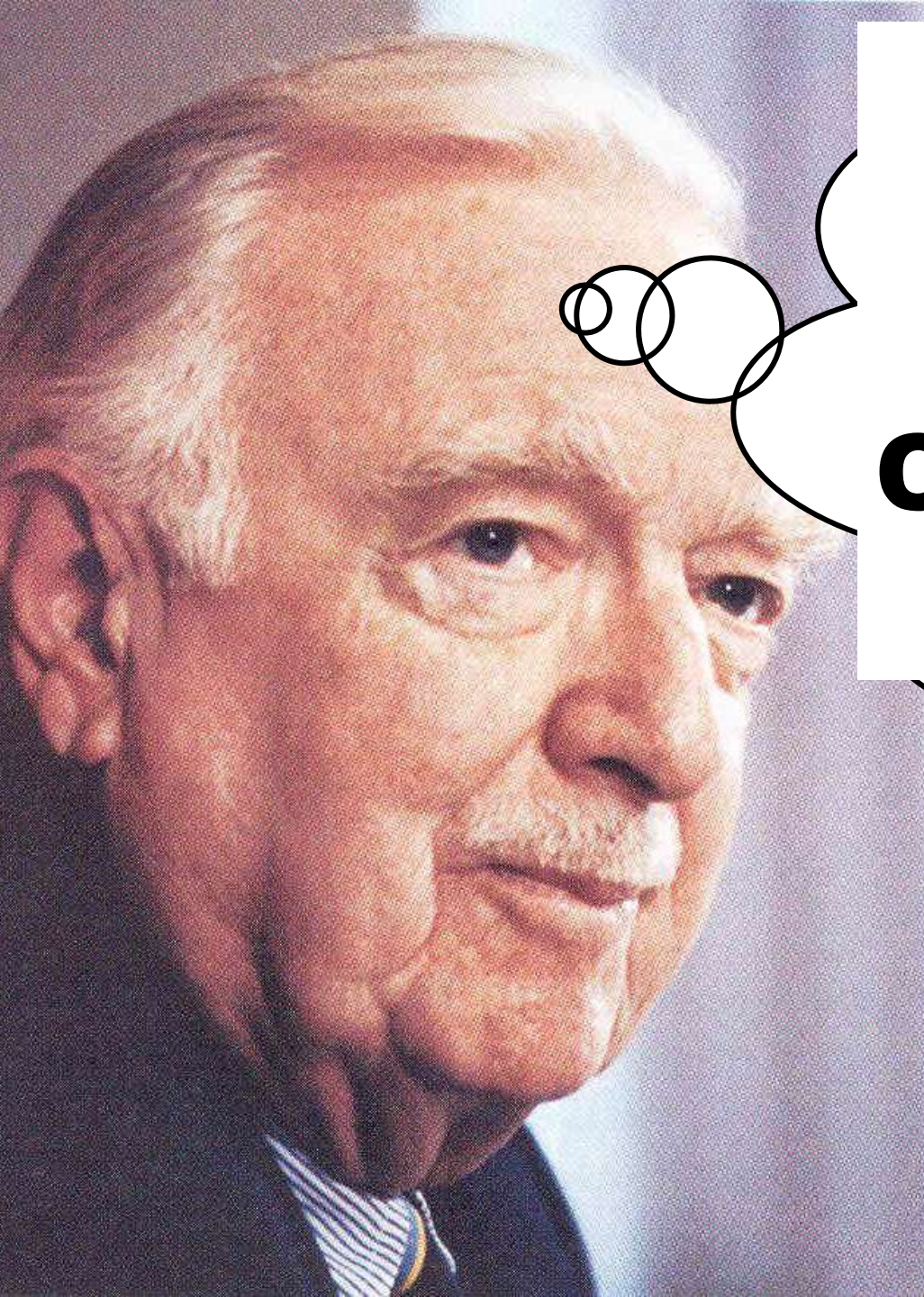


**VITAMIN D**

**INTAKE OR SUNLIGHT**

**DOES NOT INCREASE**

**1,25(OH)<sub>2</sub>D<sub>3</sub>**



**This is a  
REAL  
CONUNDRUM  
!!!!!!!**

**IS IT POSSIBLE  
PROSTATE CELLS MAKE**

***1,25(OH)<sub>2</sub>D<sub>3</sub>***

**TO REGULATE  
CELL  
GROWTH**

**????????**



# Autocrine Regulation of Cell Growth

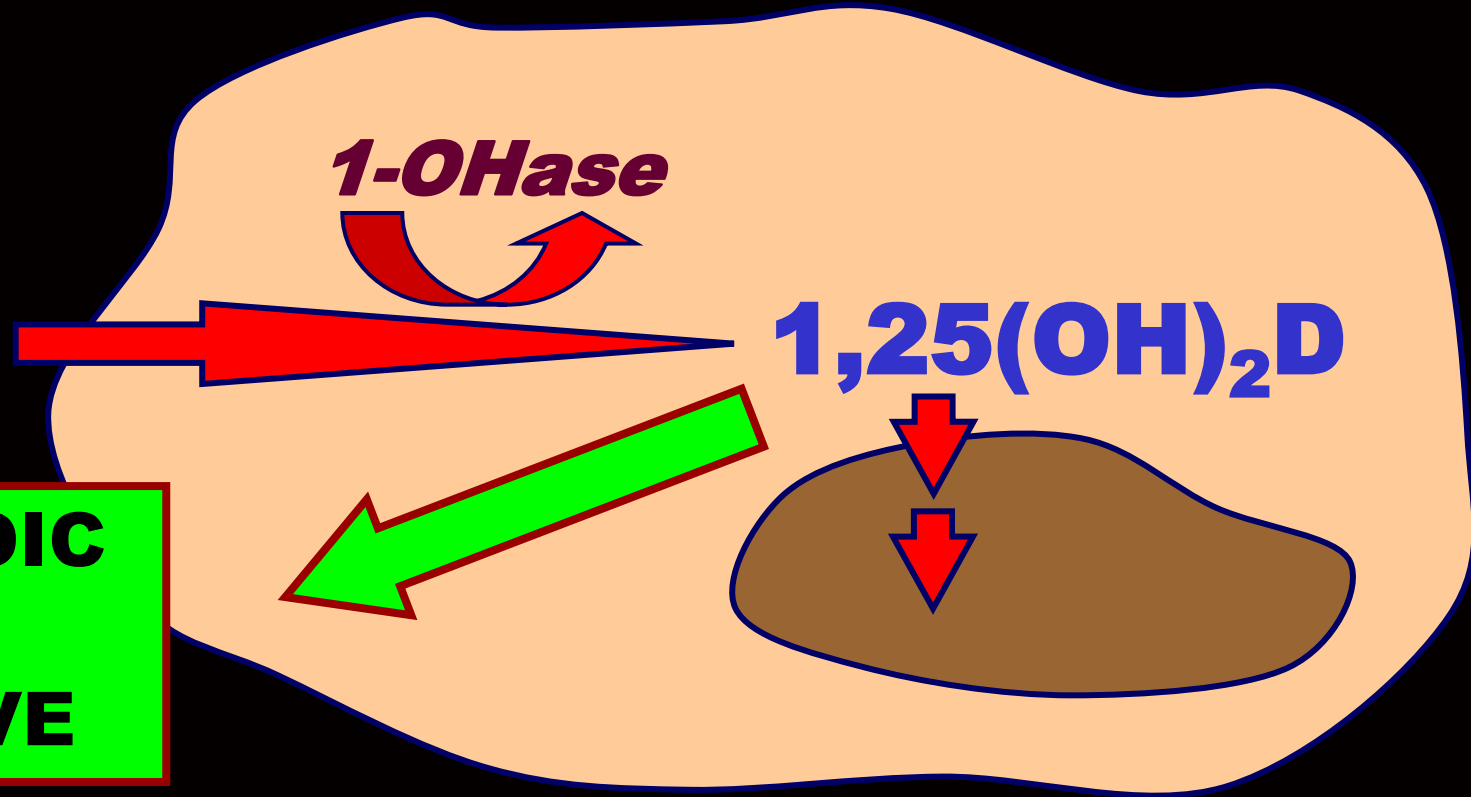
**25(OH)D**

**CALCITROIC  
ACID  
INACTIVE**

*1-OHase*

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

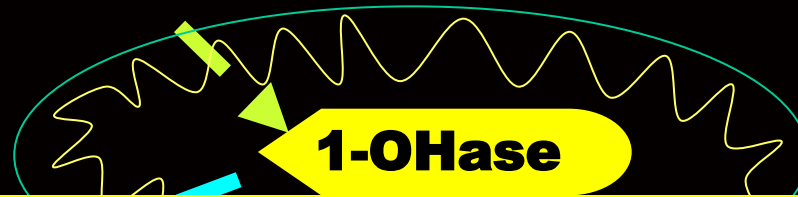
**Control of cell growth**



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

**Colon Cell**

**Mitochondria**



**1-OHase**

**~ 2000 Genes  
Affected  
By 1,25(OH)<sub>2</sub>D**

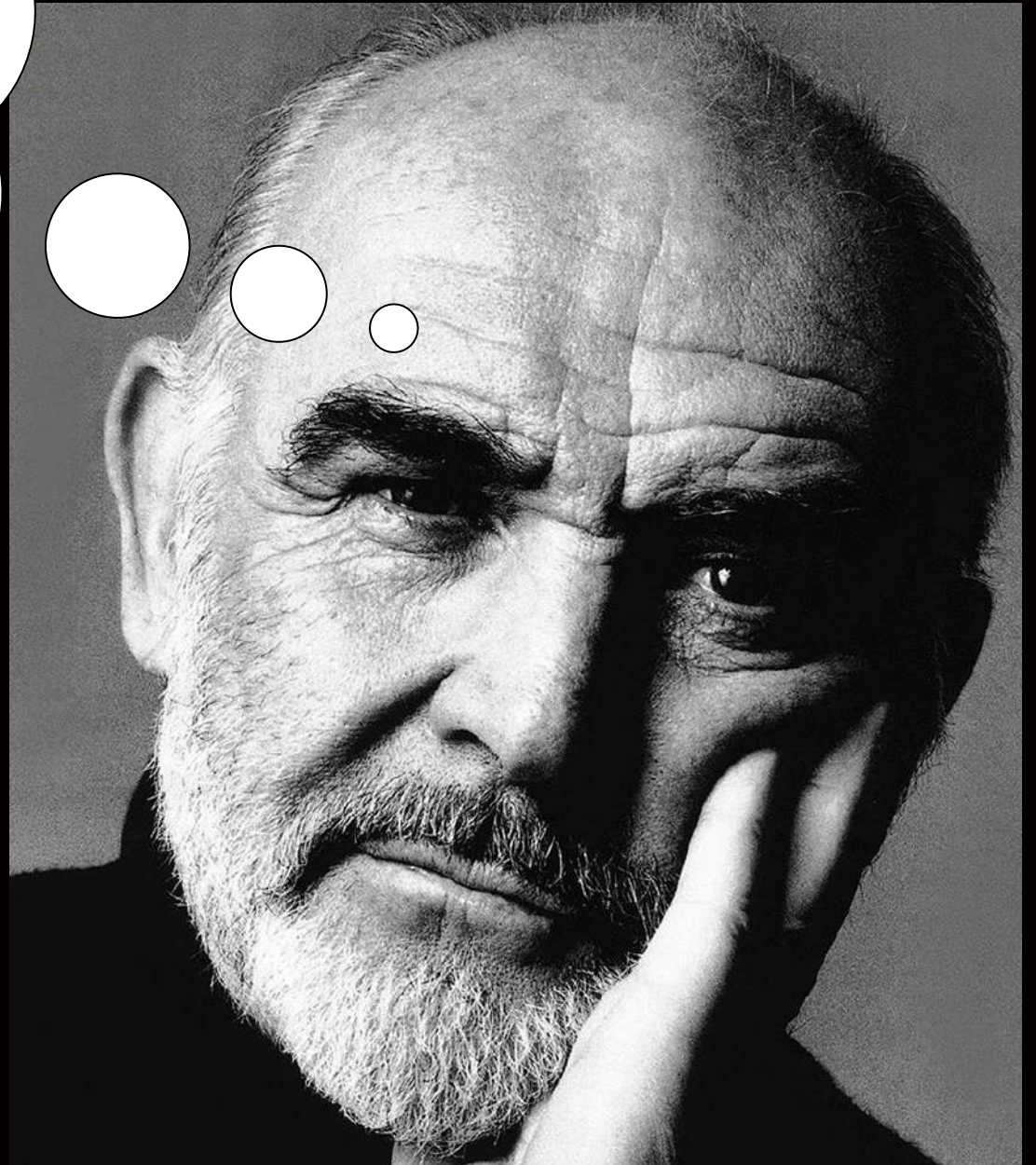
**Bcl-2  
Bcl-X  
Mcl-1  
BAG1  
XIAP  
cIAP1  
cIAP2**

**Differentiation  
MATURATION**

**CDK2, p21, p27, p53  
Ki67, E-Cadherin**

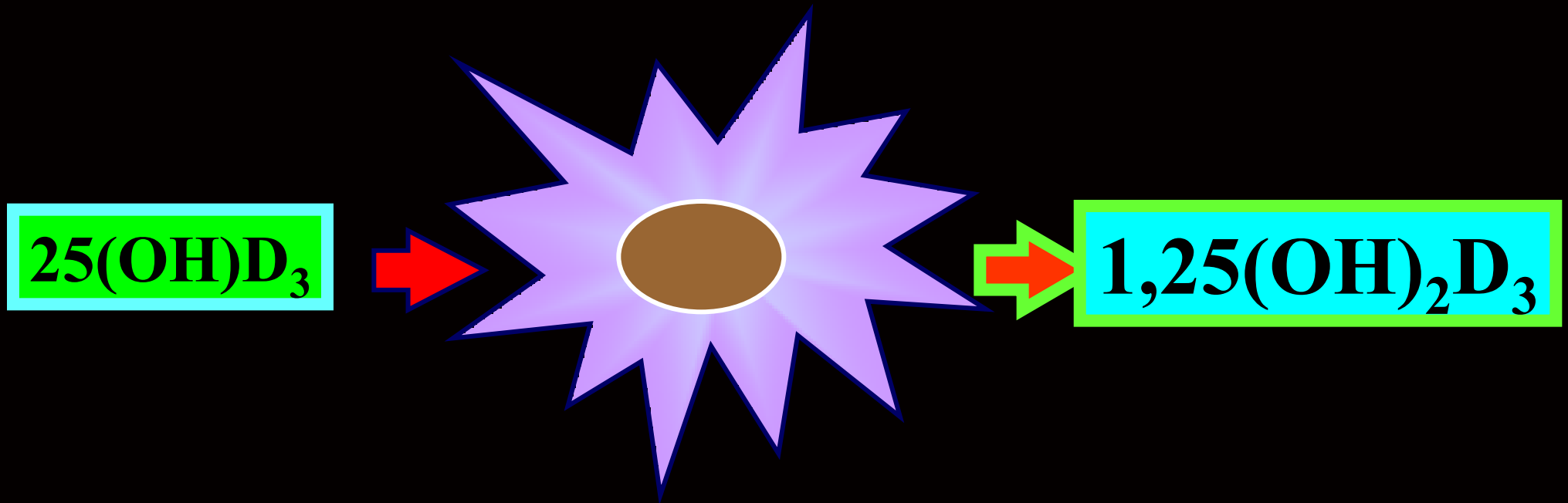
**le  
Arrest**

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



# ACTIVATED MACROPHAGES

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





**1849**

**Codliver oil - Rx Tuberculosis**

**Brompton Hospital  
Records, 38 1849**

# Vitamin D Protects Against Tuberculosis

02.23.06, 12:00 AM ET

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

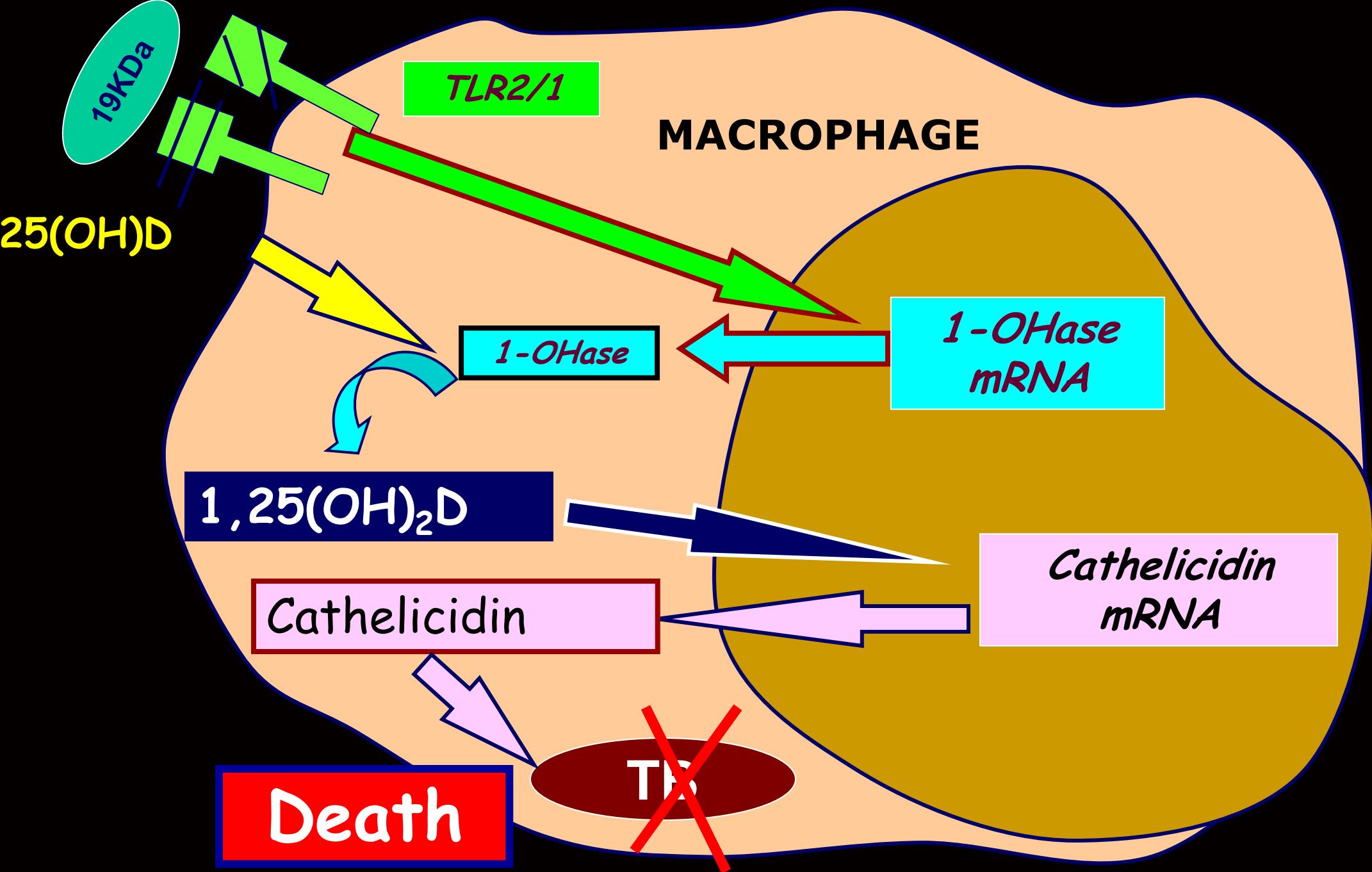
## REPORTS

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>





„Der Zauberberg“ (Thomas Mann 1924)

# Treat and Prevent TB





**Why is flu  
Season always  
In the WINTER  
?????????**



**1981 Edgar  
Hope-Simpson  
Suggested a  
“SEASONAL  
STIMULUS”**

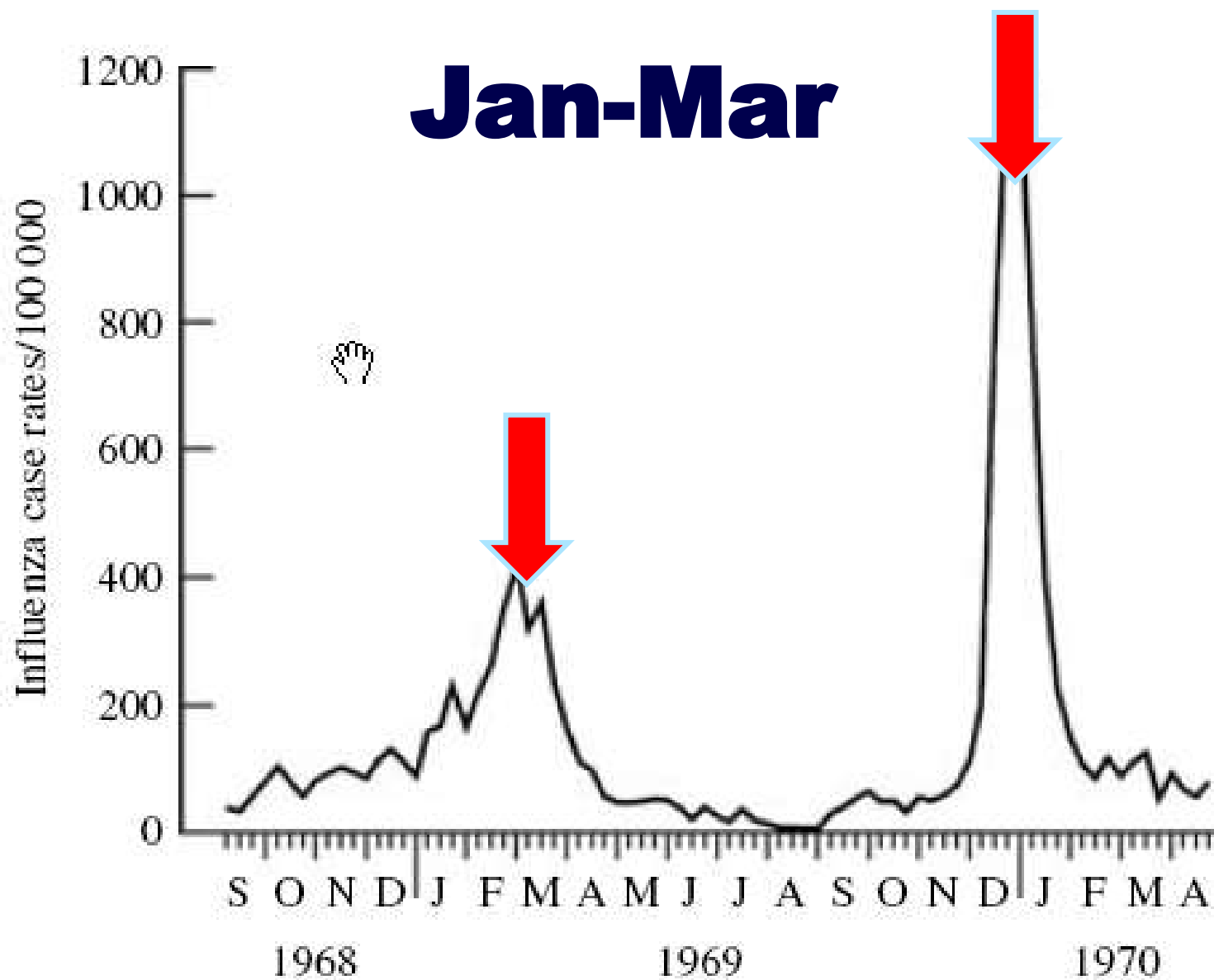


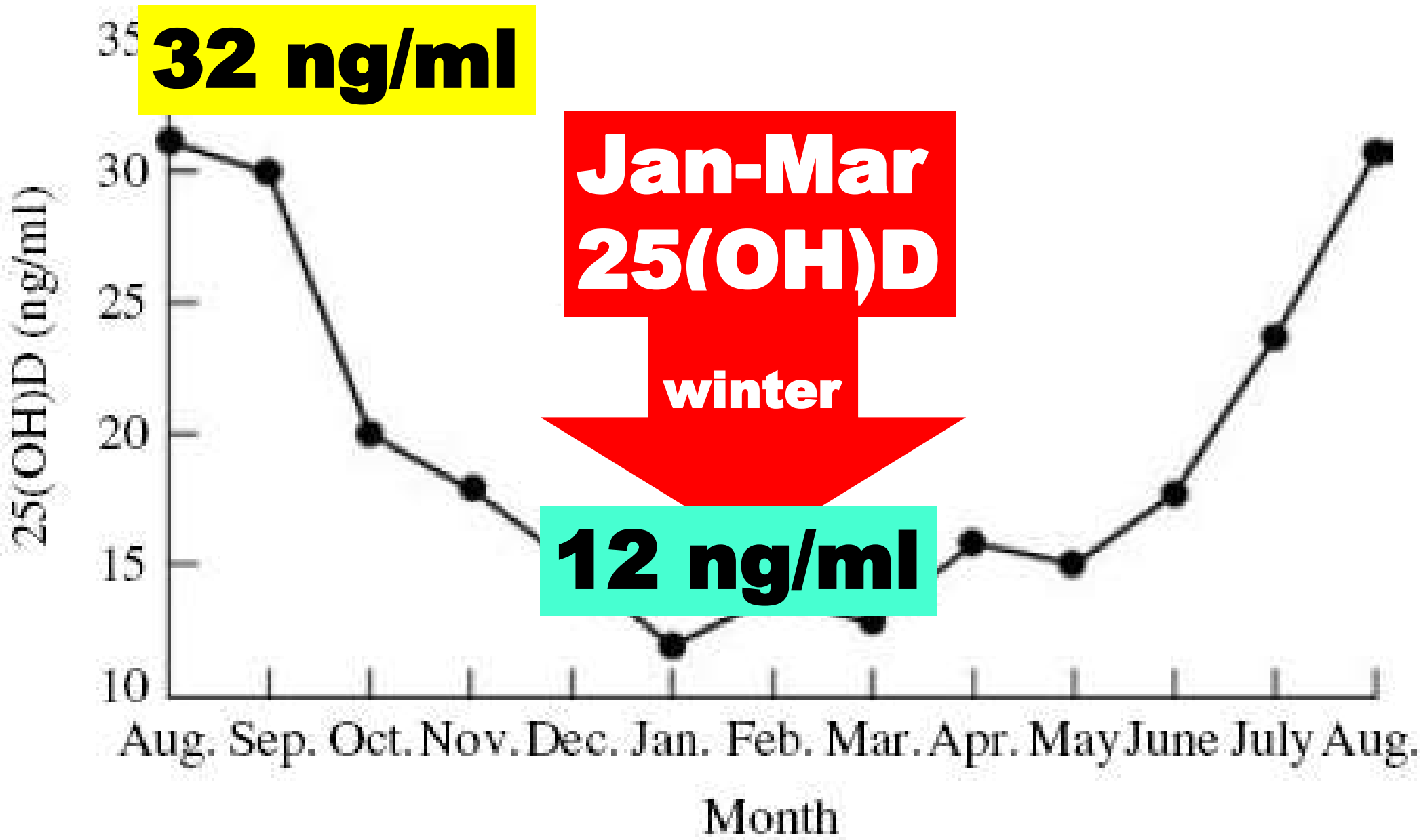
Fig. 2. Weekly consultation rates for illnesses diagnosed clinically as influenza or influenza-like, calculated from re-

**32 ng/ml**

**Jan-Mar  
25(OH)D**

**winter**

**12 ng/ml**



# Serum 25-Hydroxyvitamin D and the Incidence of Acute Viral Respiratory Tract Infections in Healthy Adults

James R. Sabetta<sup>1,2\*</sup>, Paolo DePetrillo<sup>3</sup>, Ralph J. Cipriani<sup>2</sup>, Joanne Smardin<sup>2</sup>, Lillian A. Burns<sup>2</sup>, Marie L. Landry<sup>4</sup>

*Methodology/Findings:* In this prospective cohort study serial monthly concentrations of 25-hydroxyvitamin D were measured over the fall and winter 2009–2010 in 198 healthy adults, blinded to the nature of the substance being 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-five (98.5%) of the enrolled participants completed the study. Light skin pigmentation, lean body mass, and supplementation with vitamin D were found to correlate with higher concentrations of 25-hydroxyvitamin D. Concentrations of 38 ng/ml or more were associated with a significant ( $p < 0.0001$ ) two-fold reduction in the risk of developing acute respiratory tract infections and with a marked reduction in the percentages of days ill.

**25(OH)D=38 ng/ml**

**2X**



Randomized trial of vitamin D supplementation to prevent seasonal influenza A in schoolchildren<sup>1-3</sup>

*Mitsuyoshi Urashima, Takaaki Segawa, Minoru Okazaki, Mana Kurihara, Yasuyuki Wada, and Hiroyuki Ida*

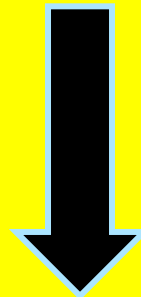
## Influenza A + School Children

**Placebo**

**18.6%**

**+1200 IU Vitamin D 10.8%**

**42%**





# **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. Mathieu*

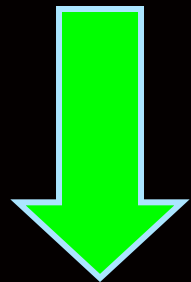
Laboratory for Experimental Medicine and Endocrinology (LEGENDO), Catholic University of Leuven, UZ Gasthuisberg, Onderwijs en Navorsing, Leuven, Belgium



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

**Vitamin D**

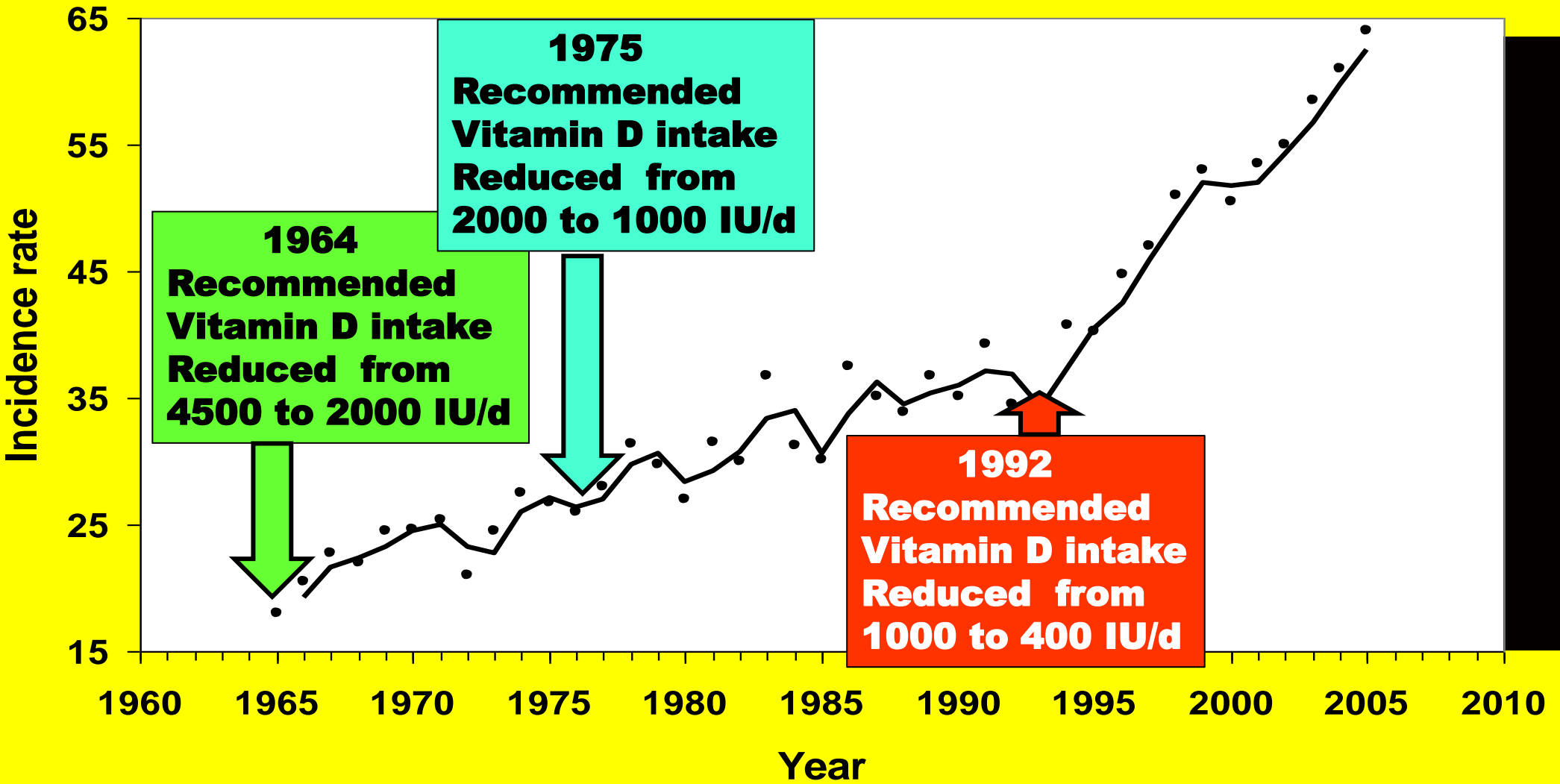
**Risk Type 1 Diabetes After 31 Years**



**88%**

**Hypponen et al. Lancet 2001**

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

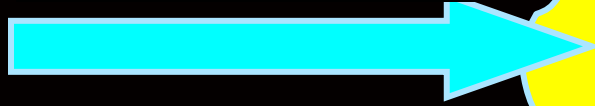


**WHAT IS THE  
EVIDENCE  
&  
MECHANISM  
????????**

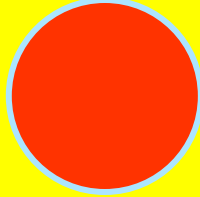


Beta-ISLET CELL

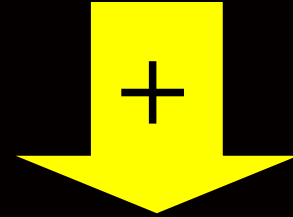
1,25(OH)D<sub>3</sub>



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

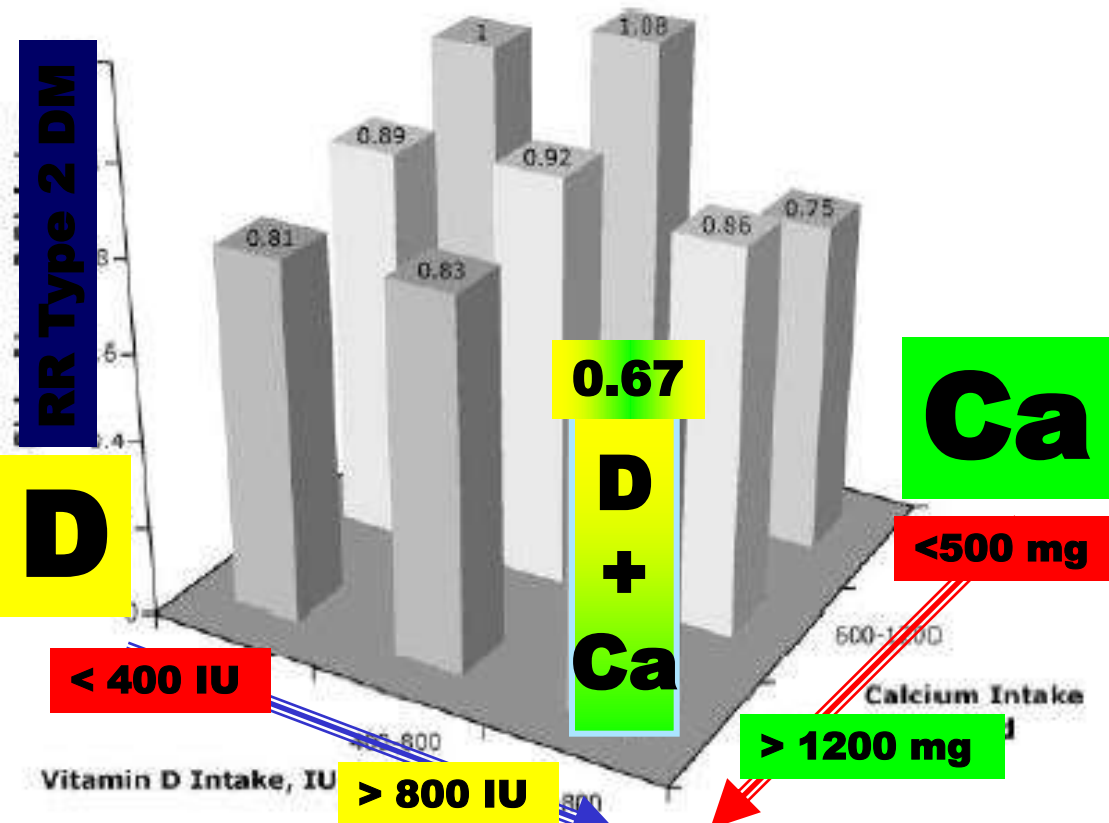


FIG. 1. Adjusted relative risk of incident type 2 DM in the Nurses Health Study by calcium and vitamin D intake (52).

**RR**

**33%**

**Ca > 1200 MG**

**+**

**VIT D > 800 IU**

# North-South Gradient in Mortality from MS

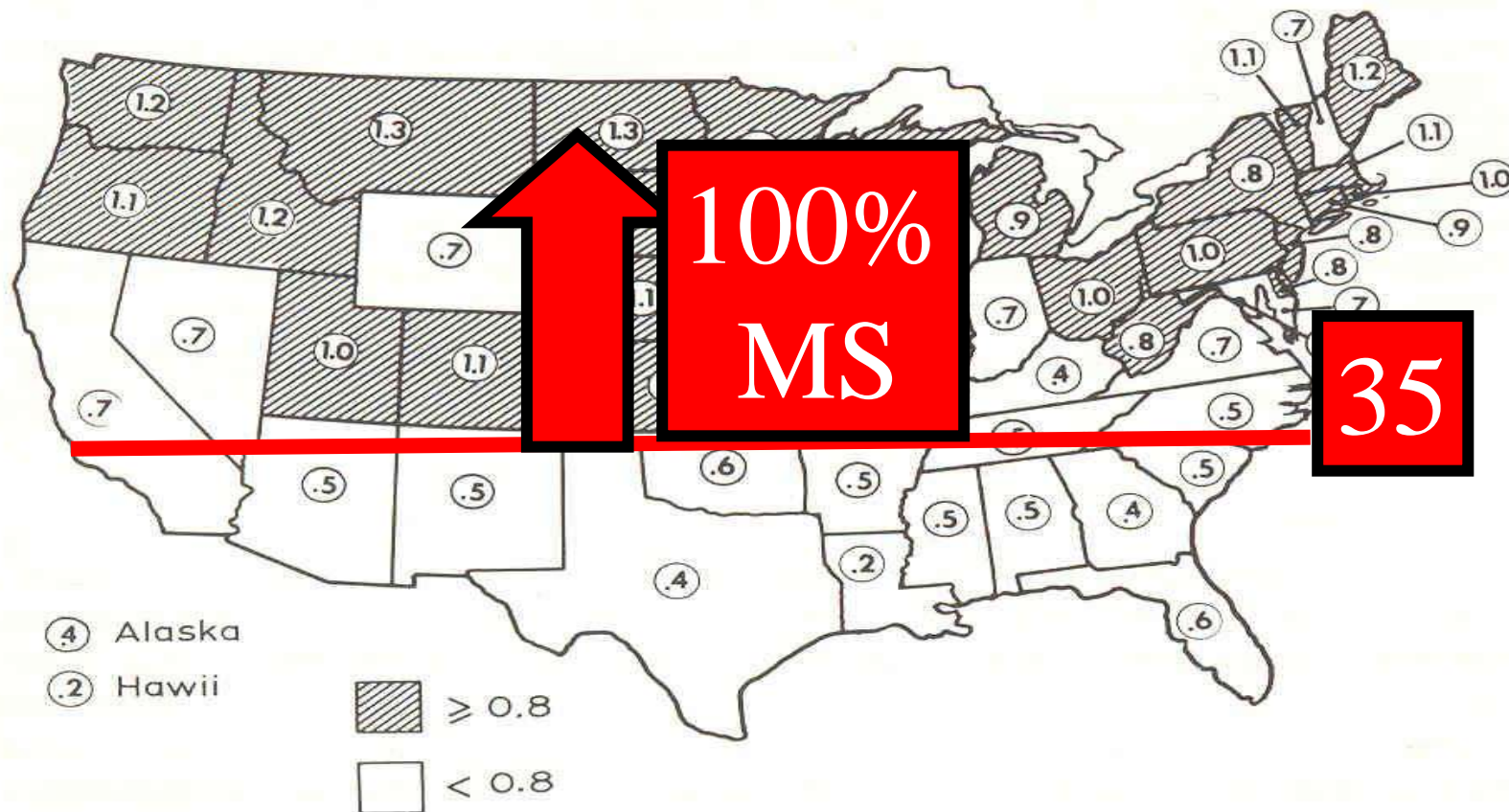


Fig. 3.4 Average annual age adjusted death rates for multiple sclerosis per 100 000 population by state of residence at death: United States, 1959–61. From Kurtzke *et al.* (1971).



# 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%**

Last Updated: Sunday, 22 June, 2003, 22:59 GMT 23:59 UK

[E-mail this to a friend](#)[Printable version](#)

## Vitamin could prevent arthritis

**Scientists hope adding vitamin D to the diet could help prevent one of the most common and painful forms of arthritis.**

Osteoarthritis affects more than a million people in the UK, many of them elderly.

There is currently no cure and all doctors can do is control pain and keep patients active and mobile.



Over one million in UK have osteoarthritis

# OSTEOARTHRITIS

### Study

But scientists at the Royal National Orthopaedic Hospital (RNOH), in Stanmore, Middlesex and University College, London, are to study 600 patients to see if they can help prevent osteoporosis of the knee.

They will study the patients over a three-year period to see whether a simple tablet or supplement can help prevent cartilage destruction and reduce pain.

They will measure the effects on the cartilage with X-rays

“ We hope that by preventing



Beneficial effects of UV radiation  
on diseases other than cancer

# Arteriosclerosis, Thrombosis, and Vascular Biology

JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart  
Association® 

*Learn and Live* SM

**Serum 25-Hydroxyvitamin D Levels and the Prevalence of Peripheral Arterial  
Disease. Results from NHANES 2001 to 2004**

Michal L. Melamed, Paul Muntner, Erin D. Michos, Jaime Uribarri, Collin Weber,  
Jyotirmay Sharma and Paolo Raggi

*Arterioscler. Thromb. Vasc. Biol.* published online Apr 16, 2008;

# Vitamin D deficiency in humans is associated with heart failure.

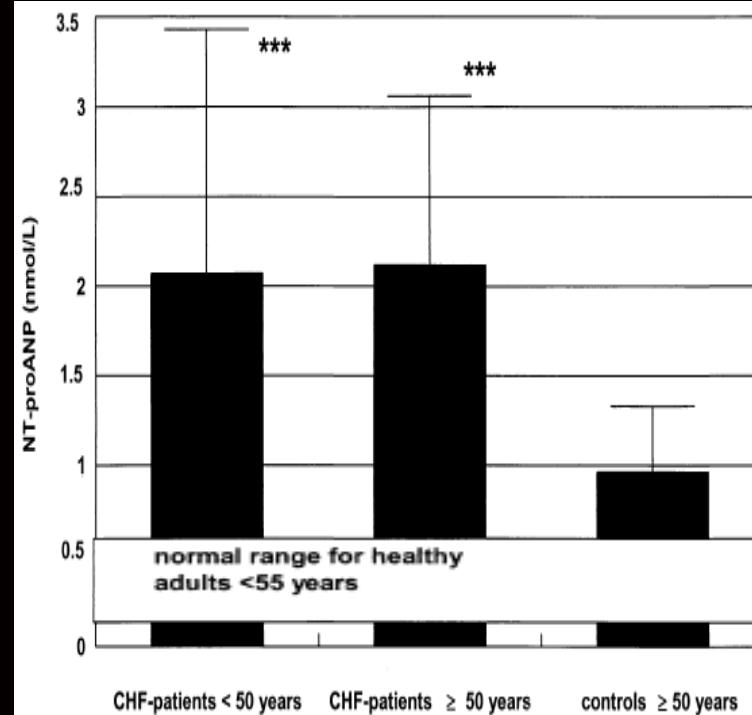
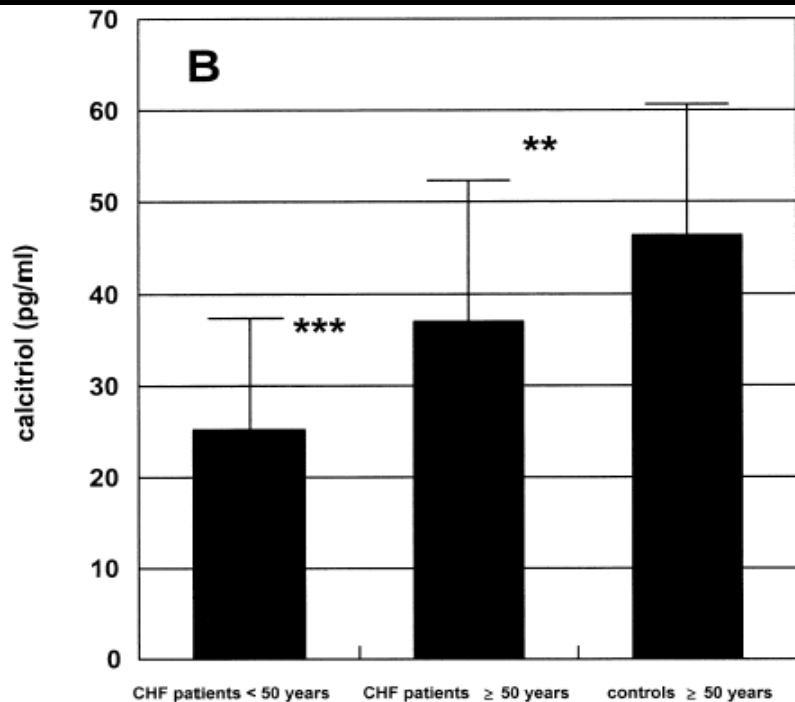
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Vol. 41, No. 1, 2003  
ISSN 0735-1097/03/\$30.00  
PII S0735-1097(02)02624-4

## Heart Failure

### Low Vitamin D Status: A Contributing Factor in the Pathogenesis of Congestive Heart Failure?

Armin Zittermann, PhD,\* Stefanie Schulze Schleithoff,\* Gero Tenderich, MD,†  
Heiner K. Berthold, MD, PhD,‡ Reiner Körfer, MD,† Peter Stehle, PhD\*  
*Bonn, Bad Oeynhausen, and Rotenburg a.d. Fulda, Germany*



**Holick**

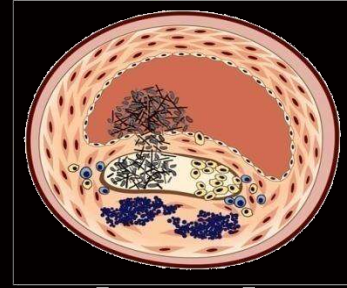
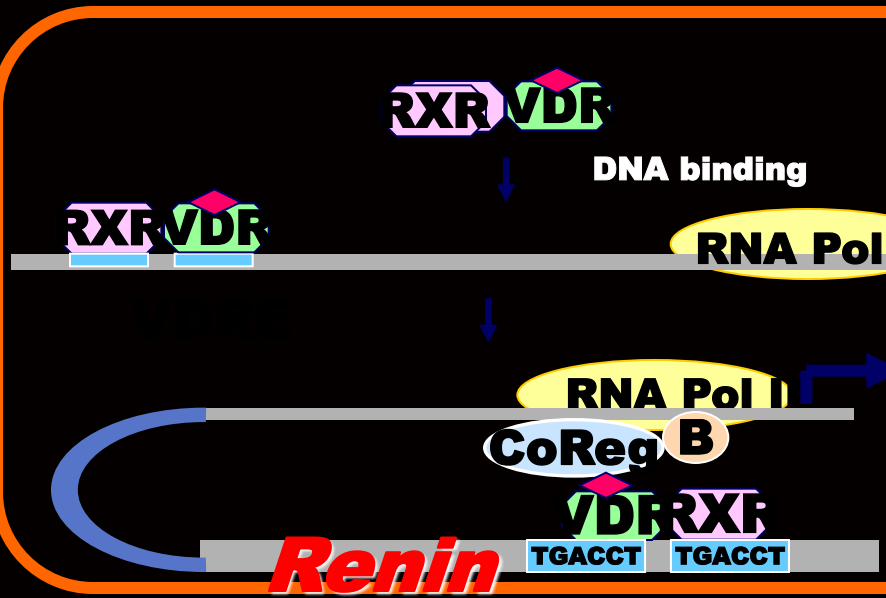
**What are the  
Mechanisms**

**??????????**



# Suppression of Renin Transcription by VDR Activation

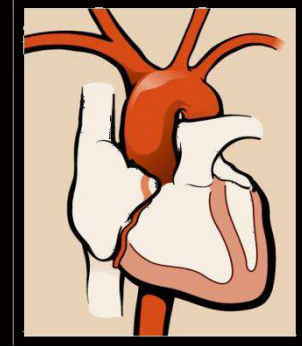
> 200 Genes in Heart & Vessels



Atherosclerosis, Inflammation, oxidative stress



Blood Pressure



LVH





# Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart  
Association



*Learn and Live...*

## Vitamin D Deficiency and Risk of Cardiovascular Disease

Thomas J. Wang, Michael J. Pencina, Sarah L. Booth, Paul F. Jacques, Erik Ingelsson,  
Katherine Lanier, Emelia J. Benjamin, Ralph B. D'Agostino, Myles Wolf and  
Ramachandran S. Vasan

*Circulation* published online Jan 7, 2008;

DOI: 10.1161/CIRCULATIONAHA.107.706127

*Circulation* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX  
75234

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ISSN: 1524-4539

**First MI >50% Increase  
Associated  
With Vitamin D Deficiency**

# Vitamin D Supplementation and Total Mortality

*A Meta-analysis of Randomized Controlled Trials*

*Philippe Autier, MD; Sara Gandini, PhD*



**All Cause Mortality**

**Decreased 25%**

**Optimal 25(OH)D > 30 ng/ml**



**Cliff Rosen**

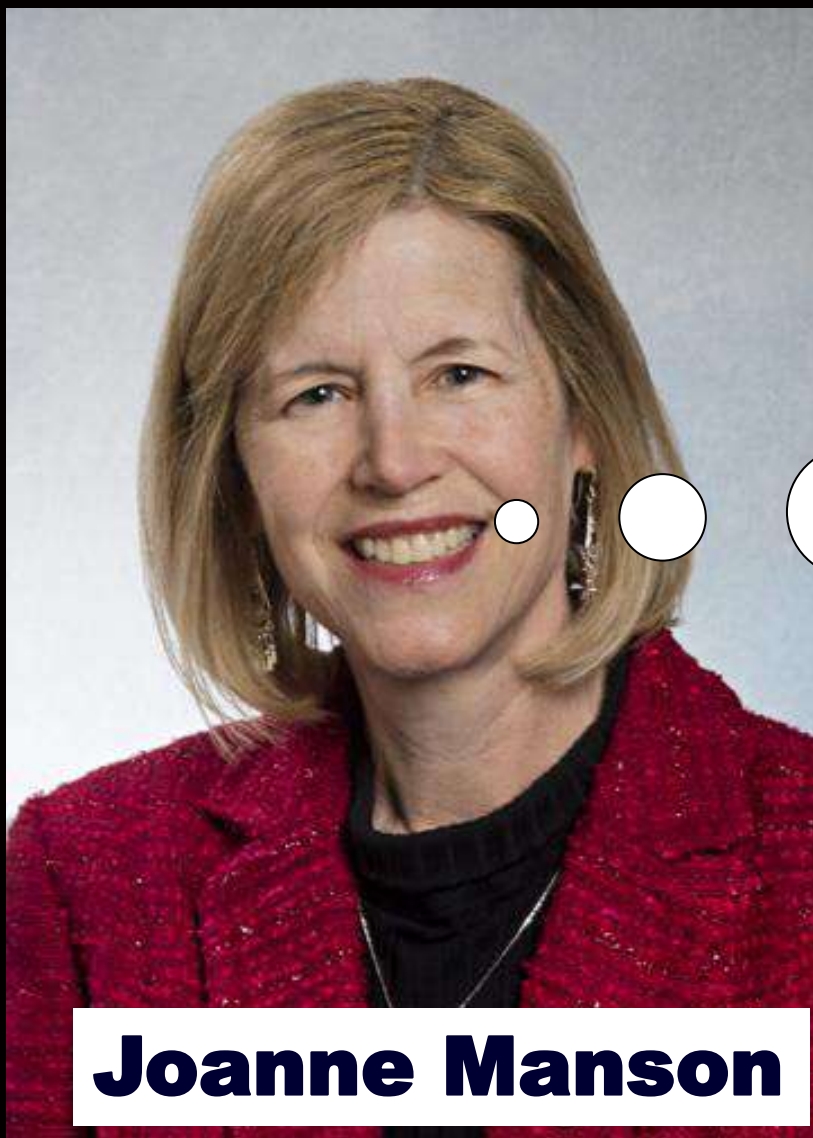
**Holick  
What Else  
Do you Have  
???????**

**Is there any evidence  
That vitamin D  
Can Have  
Non-Calcemic  
Health Benefits  
In light of the  
VITAL Study  
???????**

## Specific attributes of the VITAL trial design that are relevant to

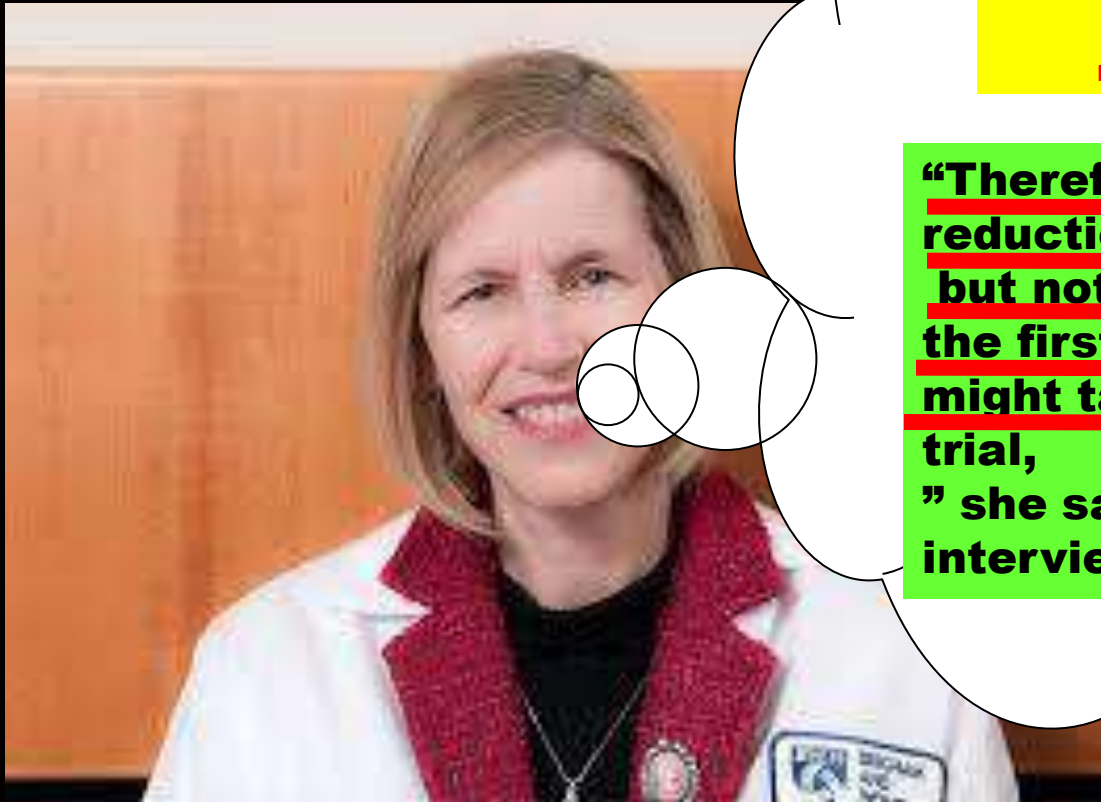
- 15,787 had blood samples available for analysis
- The mean ( $\pm$ SD) serum total 25-hydroxyvitamin D level at baseline was
  - **30.8 $\pm$ 10.0 ng/mL**
  - **Males 28.7 ng/mL**      **Females 30 ng/mL**
  - **12.7% had levels below 20 ng/mL (50 nmol/L)**
  - 32.2% had levels from 20 to less than 30 ng/mL (50 to <75 nmol/L).

- ***By inference, 55.1% had “optimal levels” of 25-hydroxyvitamin D***



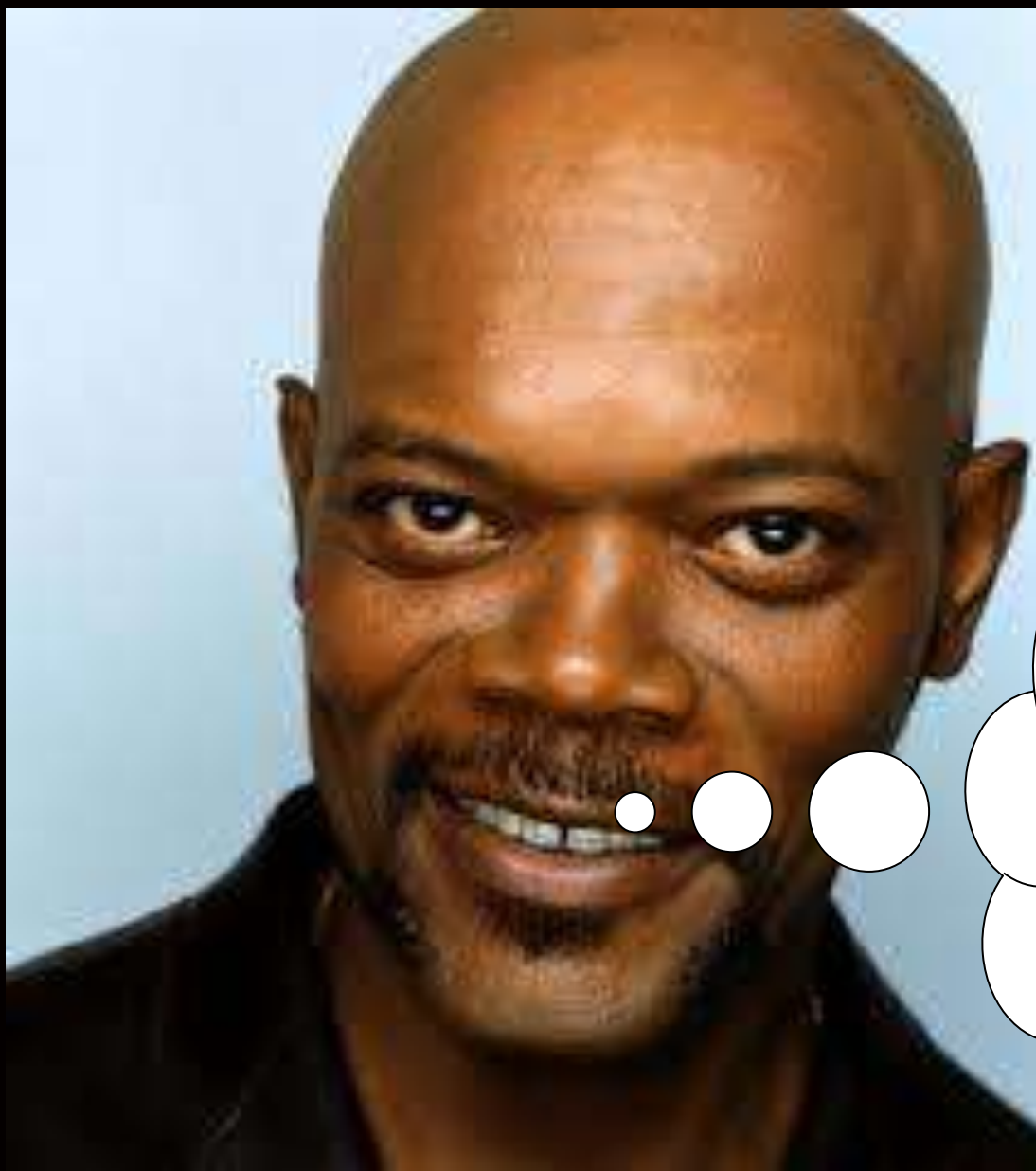
**Joanne Manson**

VITAL Study  
No benefit for  
Reducing  
Cancer or CVD  
Risk

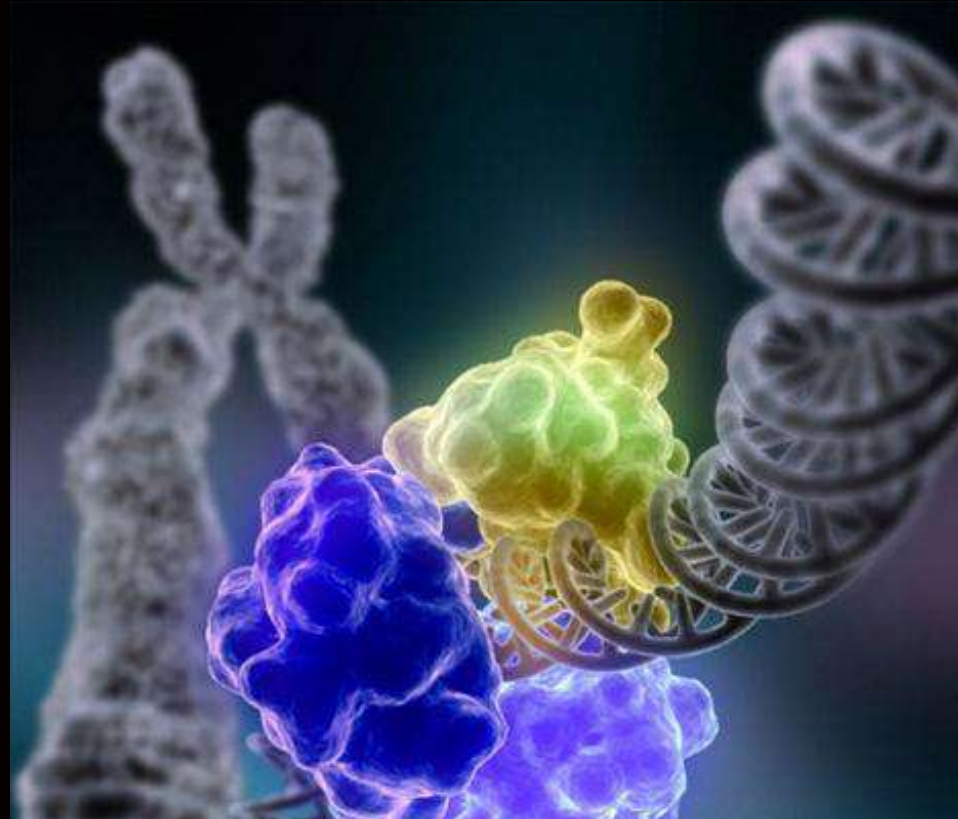


**There was a 25%  
Significant Decrease  
Cancer Mortality**

**“Therefore, you may see a  
reduction in cancer death  
but not see a reduction in  
the first diagnosis, which  
might take a much longer  
trial,  
” she said in a telephone  
interview.**



**Is there any evidence  
That vitamin D  
Can improve  
Immune Health  
??????**



# **Gene Expression With Vitamin D**



**Influence of vitamin D status  
and vitamin D<sub>3</sub> supplementation  
on genome wide expression of  
healthy adult white blood cells**

**8 Adults 12 weeks Received  
400 or 2000 IU/d X12 wks  
Buffy Coat time 0 and 12 wks**

**Chip Analysis 22,500 genes**

Expression of 82 genes decreased

Expression of 209 genes increased

**Low Expression**

**High Expression**

**Before Vitamin D  
291 Genes**

**After Vitamin D**

**Higher Expression**

**Lower Expression**

After Supplementation

Serum 25(OH)D levels

35.2 ± 8.2 ng/ml

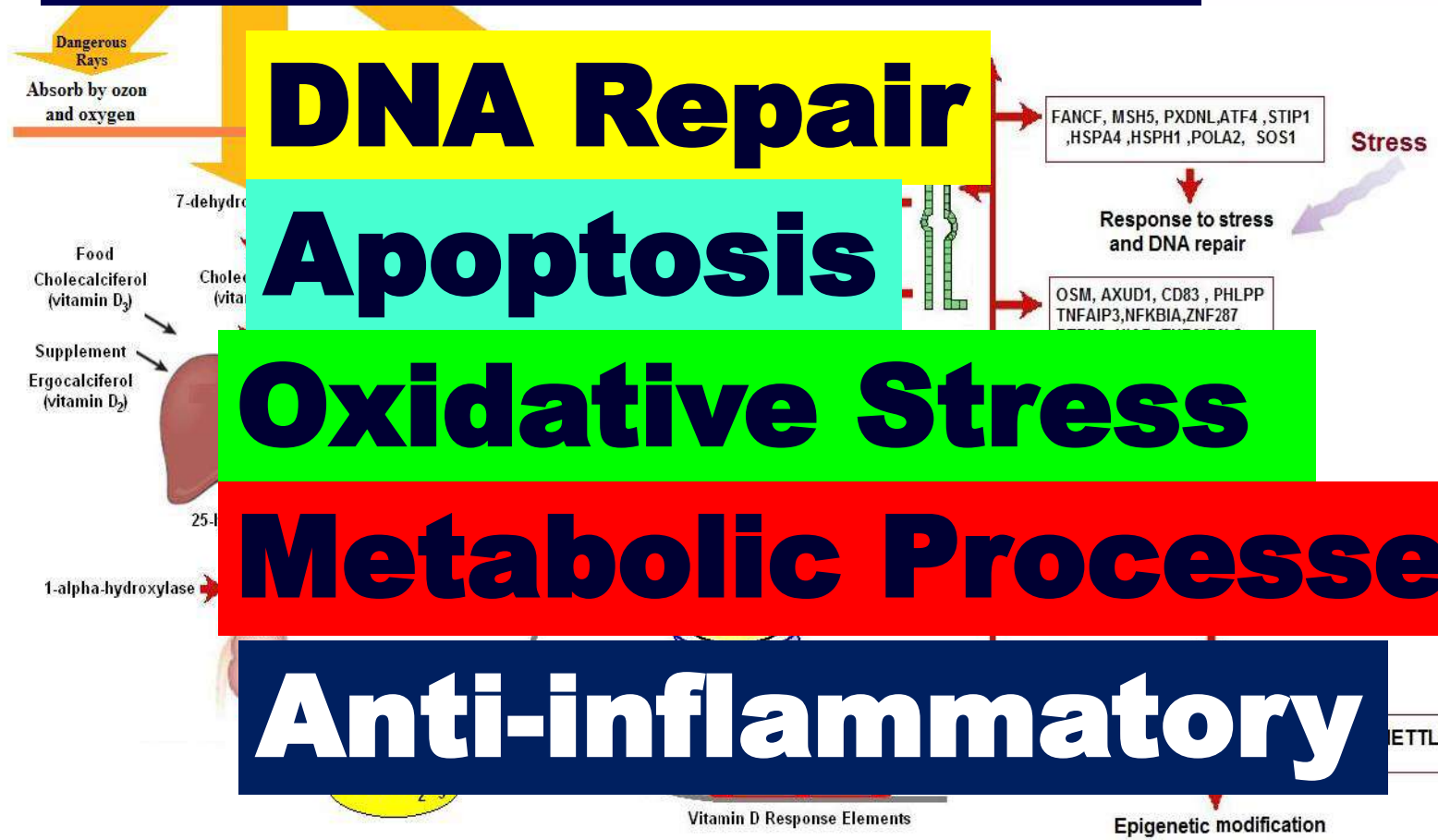
27.3 ± 6.4 ng/ml

25.1 ± 4.7 ng/ml

16.2 ± 4.2 ng/ml

# >80 Pathways Influenced by Vitamin D Supplementation

A2,ZNF225,ZNF607,,ZNF616,  
F,ZNF223, ZNF175,MED7,  
D17,ZNF235,NF780A,  
,NAPC3,TRIP11,JRKL,  
780B



**DNA Repair**

**Apoptosis**

**Oxidative Stress**

**Metabolic Processes**

**Anti-inflammatory**

Vitamin D Response Elements

Epigenetic modification

SETTL4



Can you Dissociate  
Vitamin D's Calcium  
Effect from  
Non-Calcium Effects?  
?????

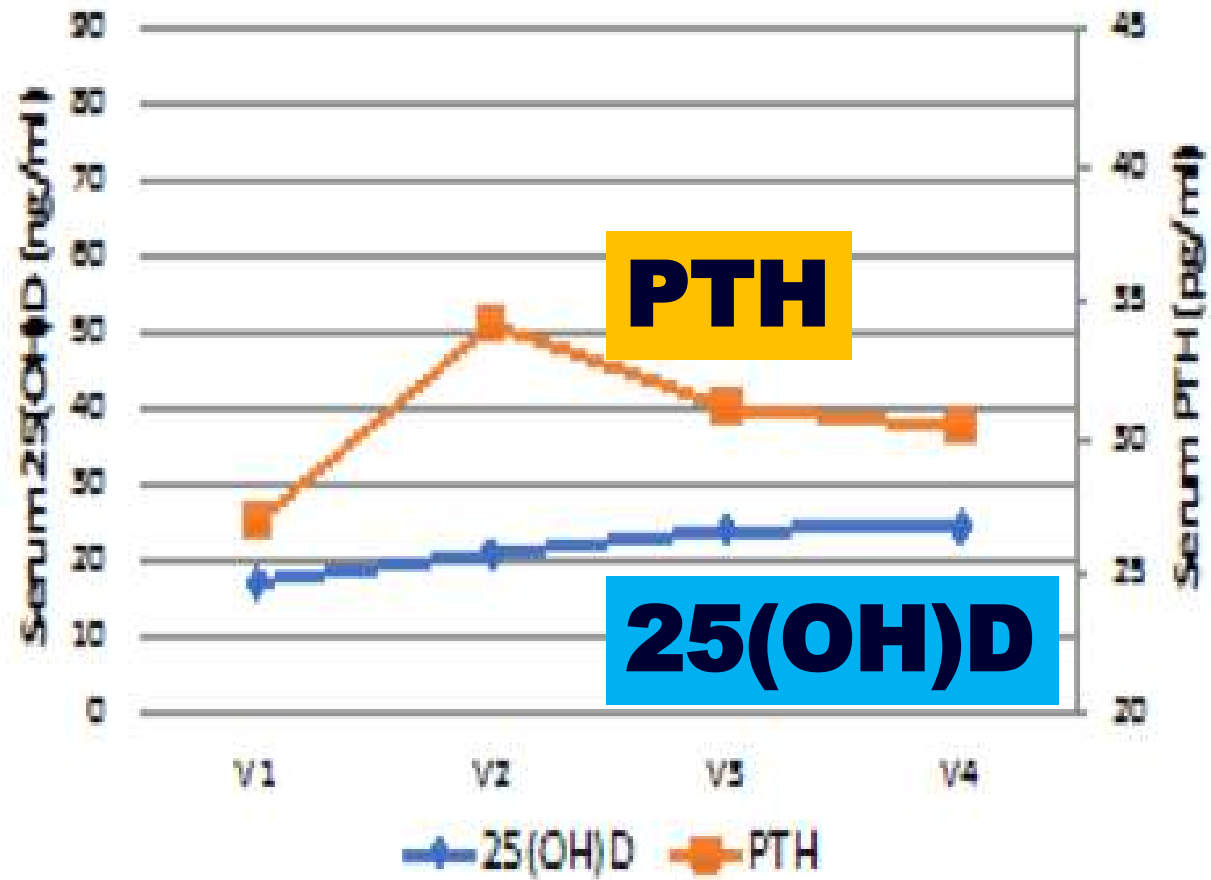
Just Say No

## **Dose dependent effect of Vitamin D on Calcium metabolism (PTH) and Immunity**

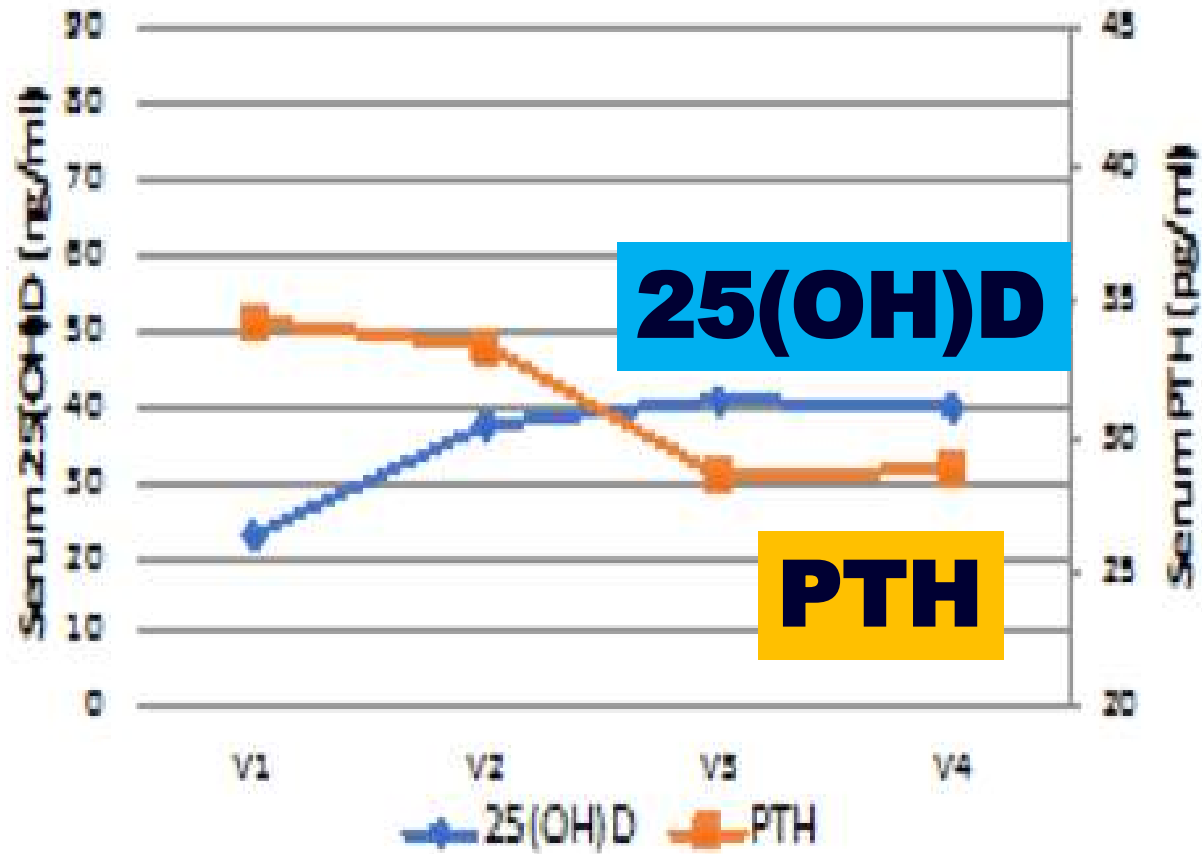
- A) 600 IU/day for 6 months**
- B) 4,000 IU/day for 6 months**
- C) 10,000 IU/day for 6 months**

<b>Vitamin D Dose</b>	<b>600 IU/D (N=9)</b>	<b>4000 IU/D (N=13)</b>	<b>10,000 IU/D (N=8)</b>
<b>Sex (Women)</b>	<b>6</b>	<b>8</b>	<b>5</b>
<b>Race (Non-White)</b>	<b>6</b>	<b>5</b>	<b>4</b>
<b>Age (years)</b>	<b>26.3±2</b>	<b>25.3±2</b>	<b>26.1±2</b>
<b>25(OH)D(ng/mL)before supplementation</b>	<b>17.1±5.9</b>	<b>22.5±5.7</b>	<b>17.8±3.3</b>
<b>25(OH)D(ng/mL)after supplementation</b>	<b>24.3±4.1</b>	<b>39.7±3.8</b>	<b>78.6±13.</b>

600 IUs/day

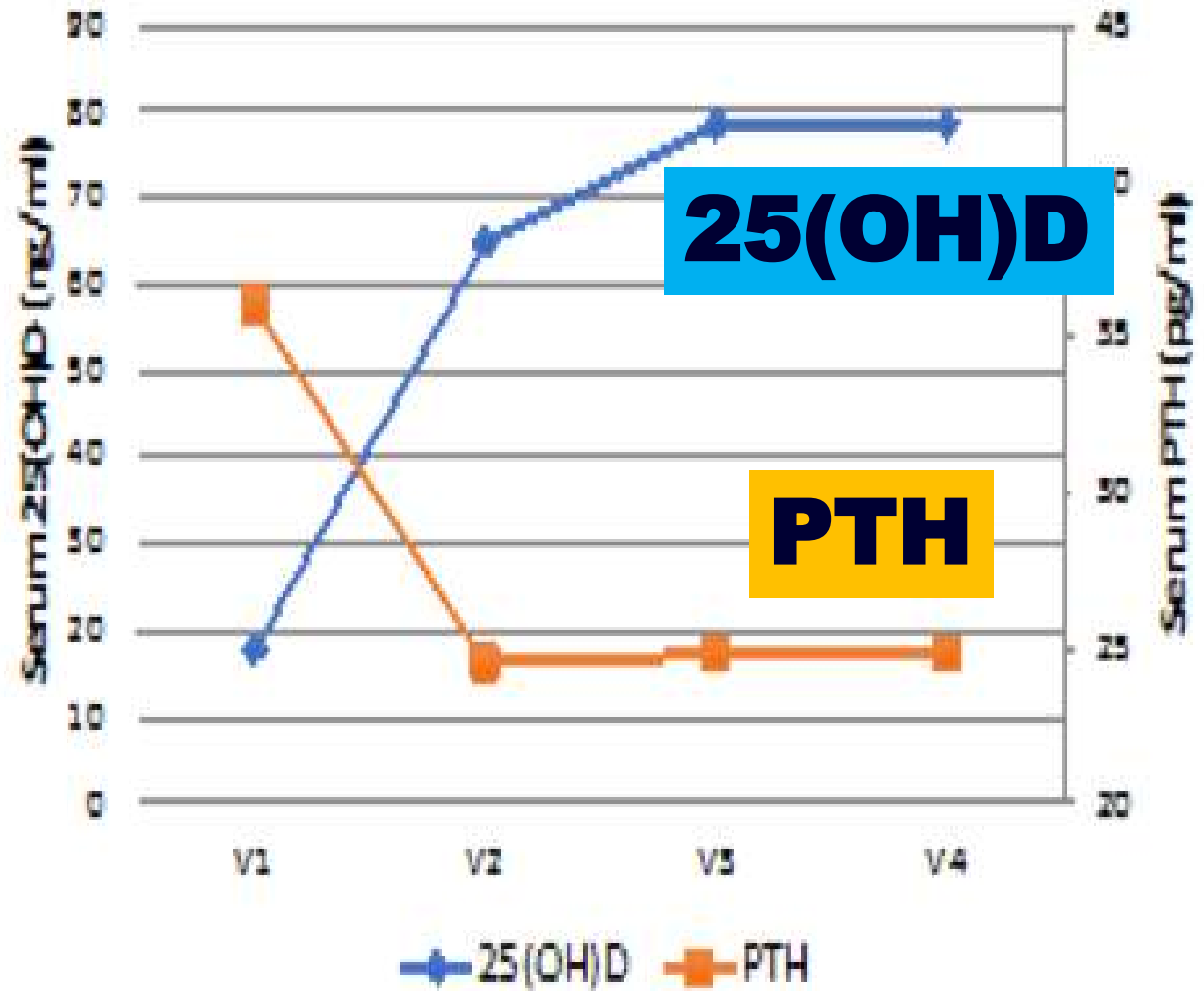


4,000 IUs/day





10,000 IUs/day



PTH	17	13	28	22	21	53	29	31	35
25(OH)D	26	45	15	34	20	13	34	18	43
	1	1	55-1	55-4	57-1	64-1	64-4	65-1	65-4

SNORA1	1.78
SNORA2	2.00
SNORA3	2.08
SNORA4	2.16
SNORA5	2.24
SNORA6	2.32
SNORA7	2.40
SNORA8	2.48
SNORA9	2.56
SNORA10	2.64
SNORA11	2.72
SNORA12	2.80
SNORA13	2.88
SNORA14	2.96
SNORA15	3.04
SNORA16	3.12
SNORA17	3.20
SNORA18	3.28
SNORA19	3.36
SNORA20	3.44
SNORA21	3.52
SNORA22	3.60
SNORA23	3.68
SNORA24	3.76
SNORA25	3.84
SNORA26	3.92
SNORA27	4.00
SNORA28	4.08
SNORA29	4.16
SNORA30	4.24
SNORA31	4.32
SNORA32	4.40
SNORA33	4.48
SNORA34	4.56
SNORA35	4.64
SNORA36	4.72
SNORA37	4.80
SNORA38	4.88
SNORA39	4.96
SNORA40	5.04
SNORA41	5.12
SNORA42	5.20
SNORA43	5.28
SNORA44	5.36
SNORA45	5.44
SNORA46	5.52
SNORA47	5.60
SNORA48	5.68
SNORA49	5.76
SNORA50	5.84
SNORA51	5.92
SNORA52	6.00
SNORA53	6.08
SNORA54	6.16
SNORA55	6.24
SNORA56	6.32
SNORA57	6.40
SNORA58	6.48
SNORA59	6.56
SNORA60	6.64
SNORA61	6.72
SNORA62	6.80
SNORA63	6.88
SNORA64	6.96
SNORA65	7.04
SNORA66	7.12
SNORA67	7.20
SNORA68	7.28
SNORA69	7.36
SNORA70	7.44
SNORA71	7.52
SNORA72	7.60
SNORA73	7.68
SNORA74	7.76
SNORA75	7.84
SNORA76	7.92
SNORA77	8.00
SNORA78	8.08
SNORA79	8.16
SNORA80	8.24
SNORA81	8.32
SNORA82	8.40
SNORA83	8.48
SNORA84	8.56
SNORA85	8.64
SNORA86	8.72
SNORA87	8.80
SNORA88	8.88
SNORA89	8.96
SNORA90	9.04
SNORA91	9.12
SNORA92	9.20
SNORA93	9.28
SNORA94	9.36
SNORA95	9.44
SNORA96	9.52
SNORA97	9.60
SNORA98	9.68
SNORA99	9.76
SNORA100	9.84

**128**  
**Total genes**  
**Regulated**  
**600 IU**

**46 genes**  
**Up**  
**regulated**

**80 genes**  
**Down**  
**regulated**

PTH	34	55	40	48	21	38	14	11	35	33	18	34	20	18
25(OH)D	9	18	10	25	13	26	18	30	23	29	27	20	15	27
Sam ple ID	17-1	17-4	30-1	30-4	49-1	49-4	50-1	50-4	67-1	67-4	68-4	69-1	61	64



**309  
Total genes  
Regulated  
4,000 IU**

**157 genes  
Up  
regulated**

**142 genes  
Down  
regulated**

**25-Hydroxyvitamin D**

PTH	5	27	9	12
25(OH)D	1	70	8	88
ID				

**20**

**56**

**21**

**87**

**23**

**96**

**14**

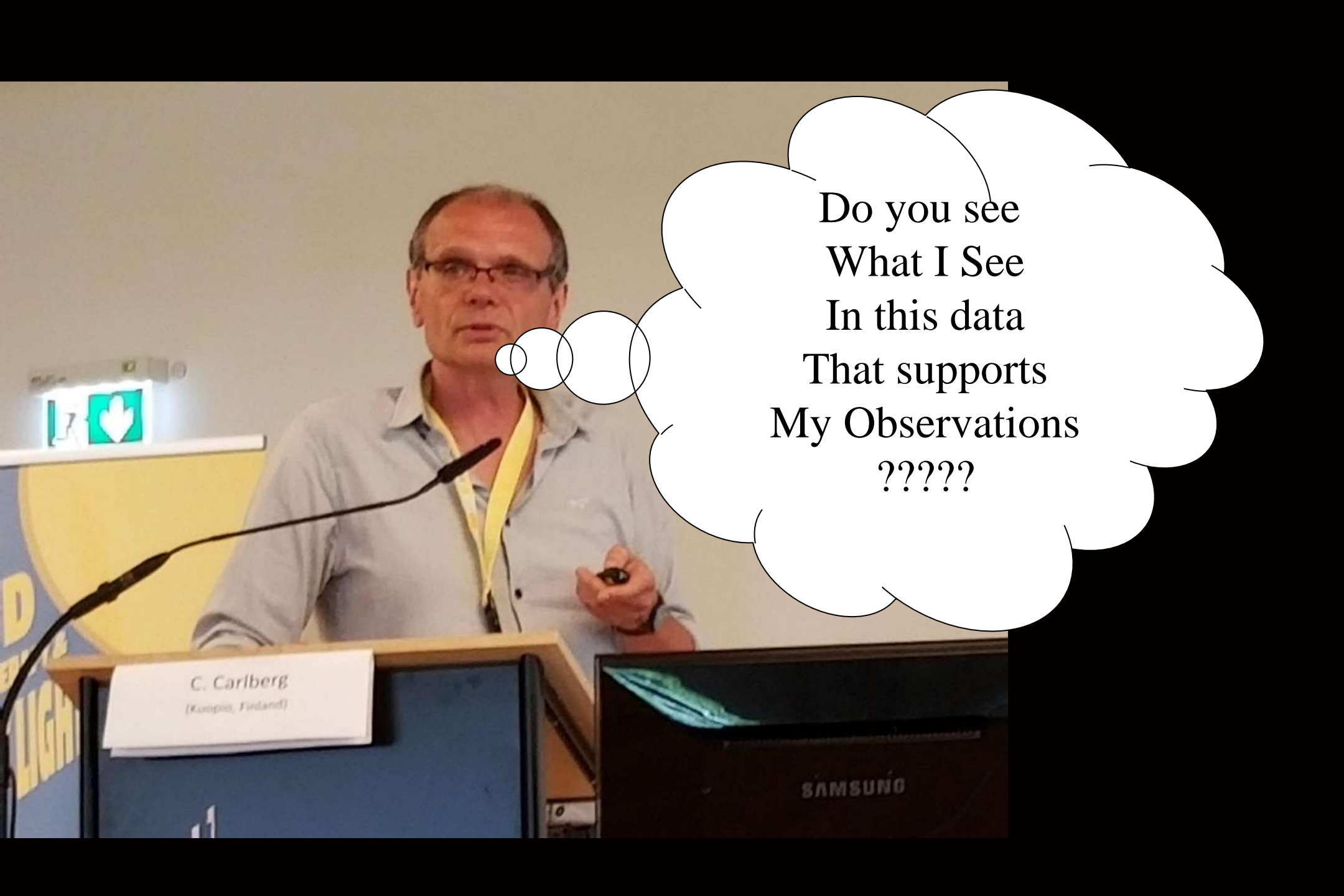
**84**



**2,273**  
**Total genes**  
**Regulated**  
**10,000 IU**

**815 genes**  
**Up**  
**regulated**

**1458 genes**  
**Down**  
**regulated**



Do you see  
What I See  
In this data  
That supports  
My Observations  
?????

C. Carlberg  
(Kuopio, Finland)

SAMSUNG

# 25-Hydroxyvitamin D

PTH	5	27	59	12
25(OH)D	1	70	18	88
ID				

20

56

21

87

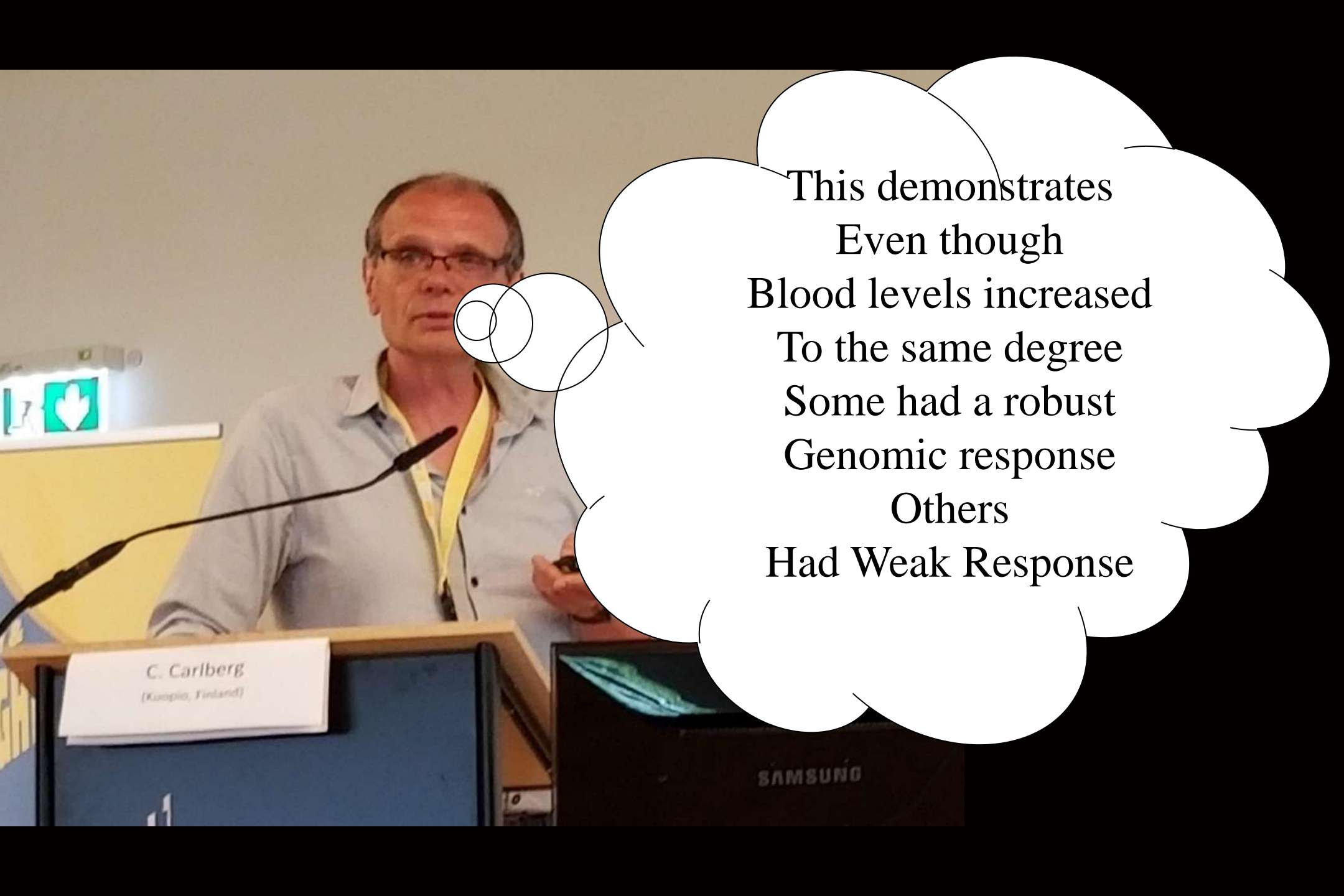
23

96

14

84



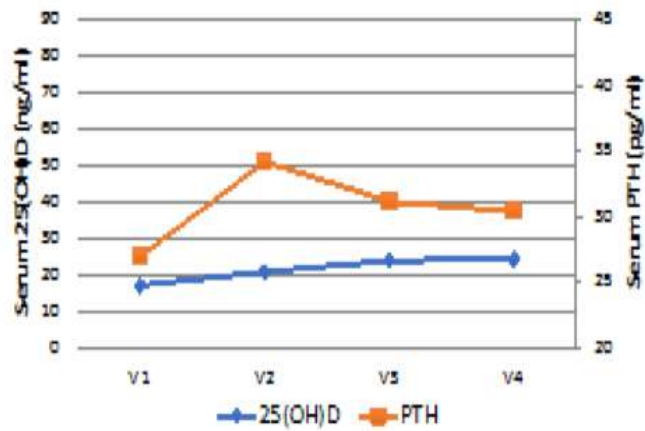


This demonstrates  
Even though  
Blood levels increased  
To the same degree  
Some had a robust  
Genomic response  
Others  
Had Weak Response

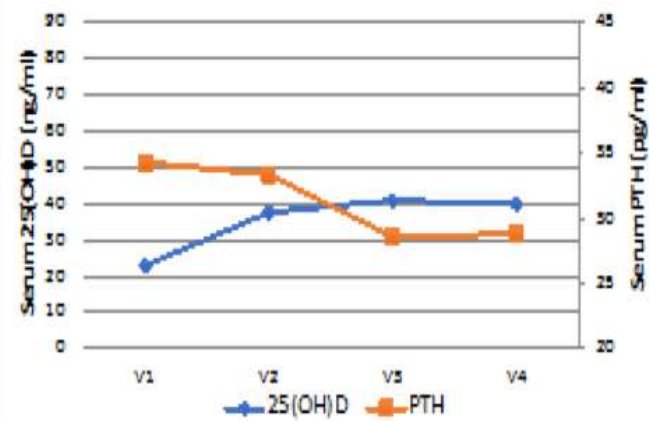
C. Carlberg  
(Kuopio, Finland)

SAMSUNG

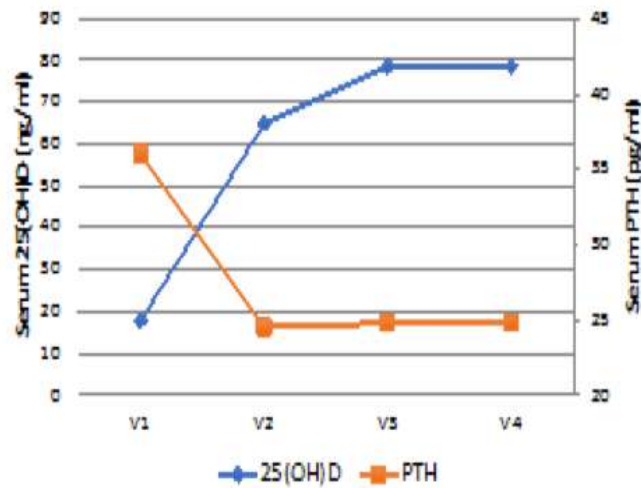
600 IU/day



4,000 IU/day

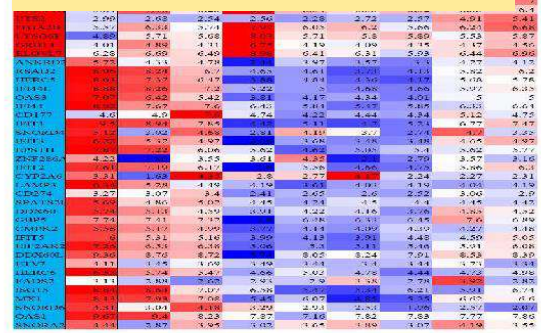


10,000 IU/day

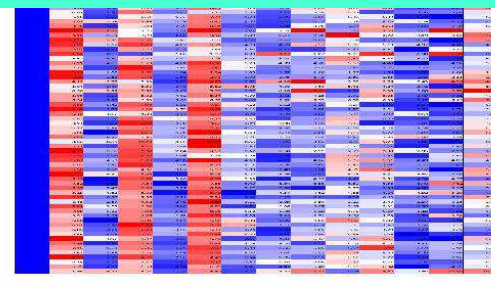




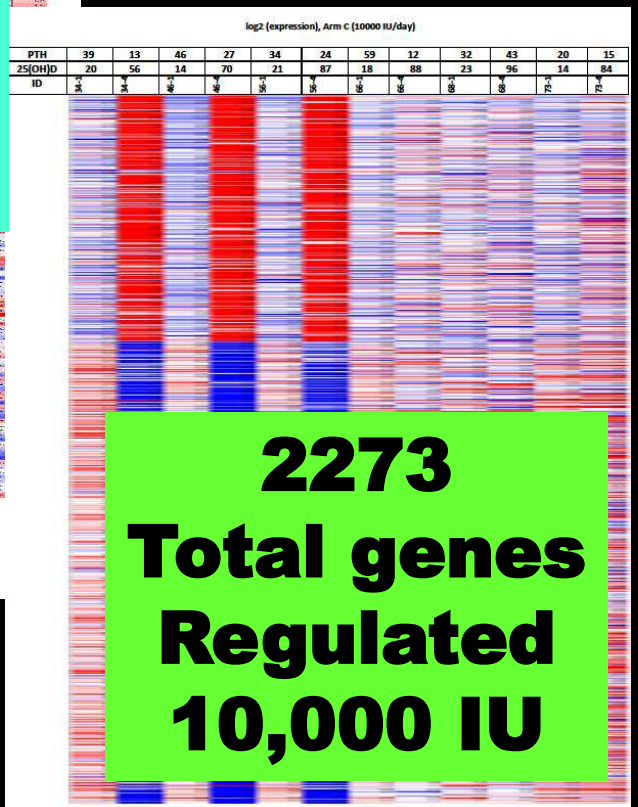
**126  
Total genes  
Regulated  
600 IU**



**309  
Total genes  
Regulated  
4,000 IU**



**2273  
Total genes  
Regulated  
10,000 IU**





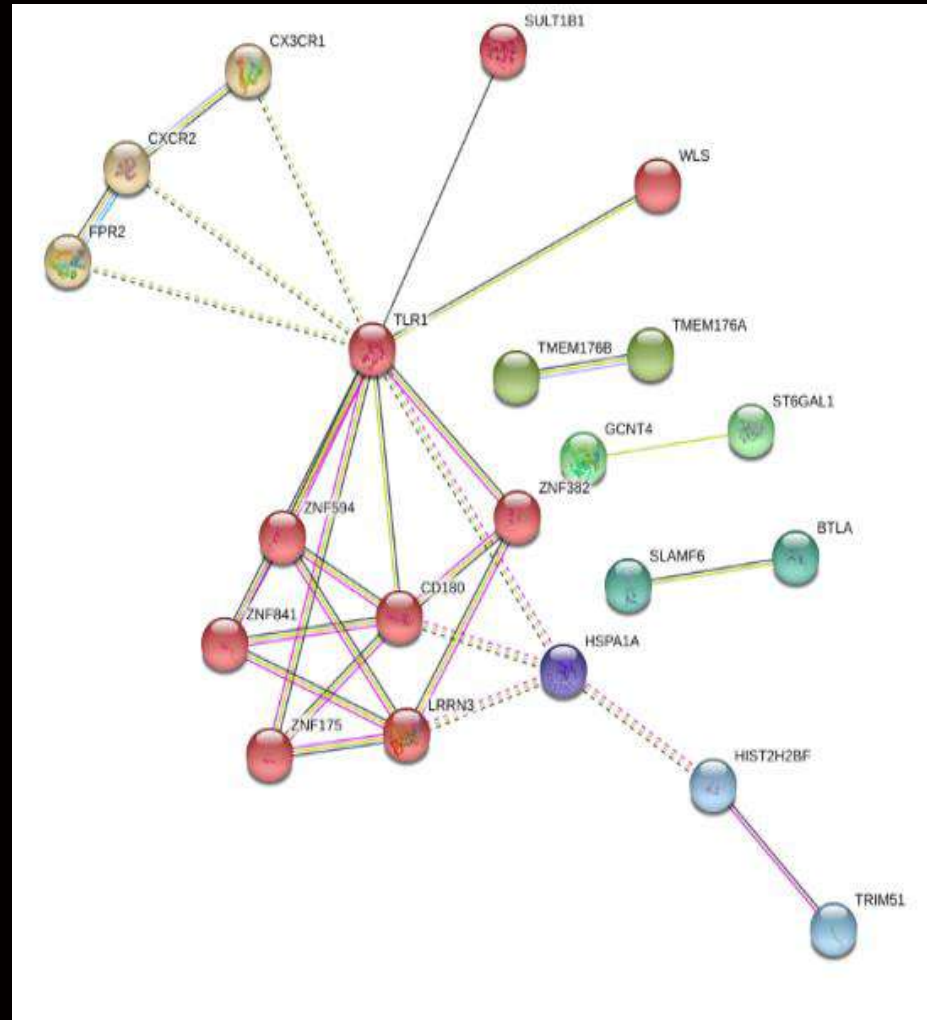
**The upregulated genes**

**This network includes 4 clusters that shows by 4 different colors.**

**The key genes in these clusters are HIST1H2B, JUN, NFKB, TNF, IL8, HSPA8, EIF4A and PRS. That**

**Control cellular proliferation,  
inflammatory activity and  
immune function**

**45 downregulated genes after 10000 IU/day for 24 weeks.**



**The downregulated genes are involved in the below molecular network . The key genes in this network are TLR1, CD180 and LRRN3.**

**The down regulated genes are involving in the pathways related to integral component of membrane (specially in immune system).**

**The nutrigenomics breakthrough**  
Reverse age-related DNA damage • Prevent inherited disease  
Lose weight and feel better

**FEED**

Eat to Turn Off

**YOUR**

Disease-Causing Genes

**GENES**

and Slow Down Aging

**RIGHT**

**With Vitamin D**

A close-up photograph of a woman with long, wavy brown hair and bright blue eyes. She has a surprised or excited expression, with her mouth wide open and her hands framing her face. The background is a warm, out-of-focus orange and yellow. A white circular callout box is overlaid on the right side of the image, containing text.

**What about  
Maintaining serum  
Vitamin D levels**

**Is there any**

**Benefit**

**???**



# Dietary Vitamin D and Its Metabolites Non-Genomically Stabilize the Endothelium

Christopher C. Gibson<sup>1,2,3</sup>✉, Chadwick T. Davis<sup>1,3,4</sup>✉, Weiquan Zhu<sup>1</sup>, Jay A. Bowman-Kirigin<sup>1</sup>, Ashley E. Walker<sup>5</sup>, Zhengfu Tai<sup>6</sup>, Kirk R. Thomas<sup>1,3</sup>, Anthony J. Donato<sup>5</sup>, Lisa A. Lesniewski<sup>5</sup>, Dean Y. Li<sup>1,3,4,6,7,8,9</sup>\*

min D pathway. Our data suggests the presence of an alternative signaling modality by which D<sub>3</sub> acts directly on endothelial cells to prevent vascular leak. The finding that D<sub>3</sub> and its metabolites modulate endothelial stability may help explain the clinical correlations between low serum vitamin D levels and the many human diseases with well-described vascular dysfunction phenotypes.

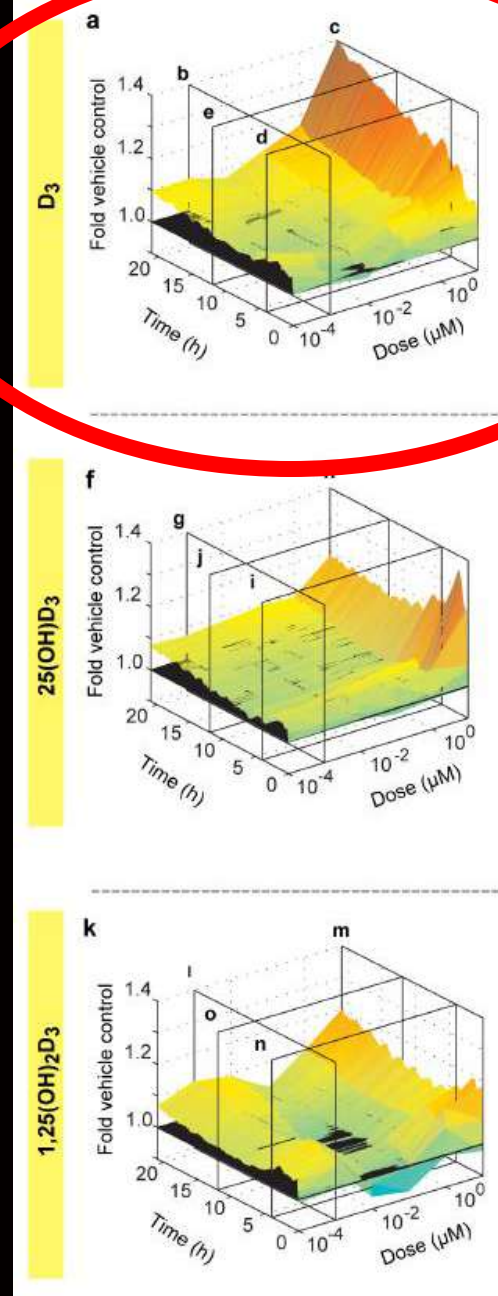


A hallmark of inflammation is the activation and destabilization of the endothelial cells lining the vasculature, leading to dysfunctional nutrient exchange, inflammatory cell migration, and dysregulated activation of the clotting cascade [17, 18]. Endothelial destabilization and activation occurs as a result of injury, altered hemodynamics, response to cytokines or other inflammatory cues, as well as genetic diseases [19, 20]. Therapies designed to stabilize

# Vitamin D<sub>3</sub>

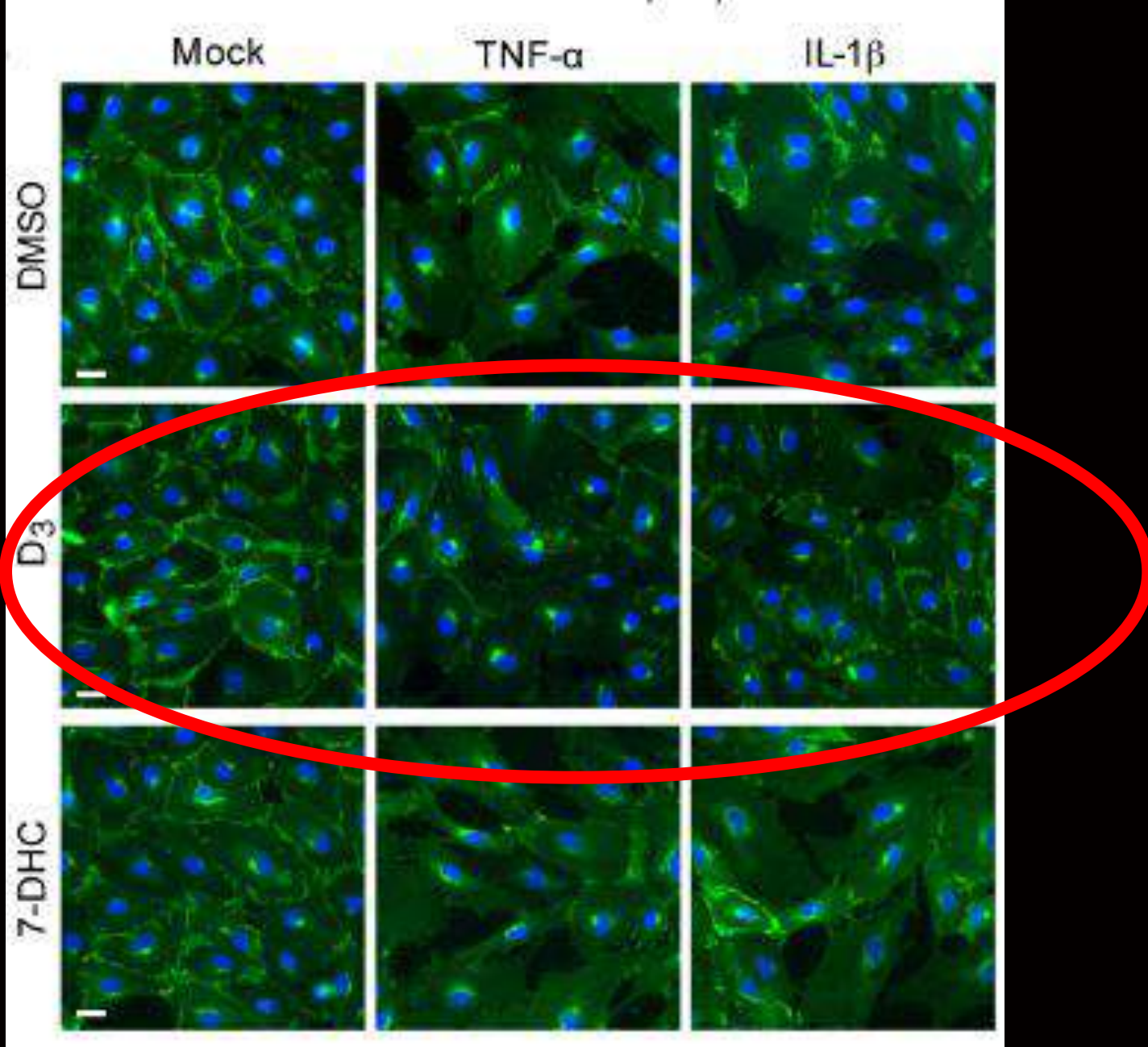
# 25(OH)D<sub>3</sub>

# 1,25(OH)<sub>2</sub>D<sub>3</sub>

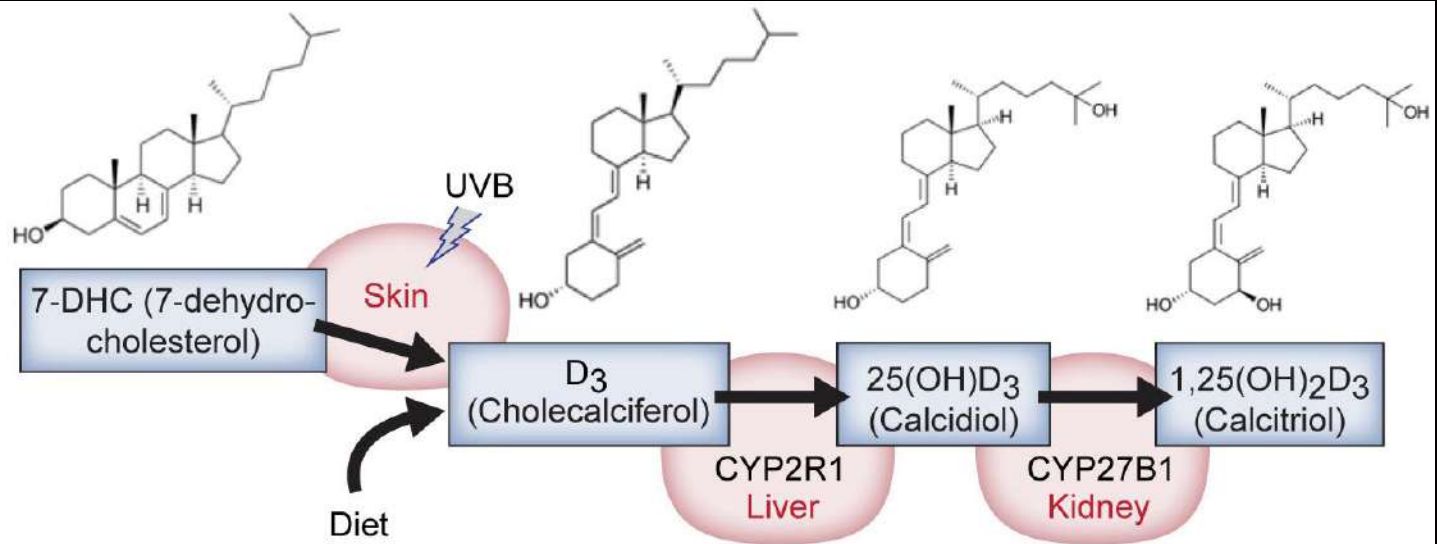


**Fig 1. Vitamin D stabilizes the endothelium.** Dose/time resistance (endothelial stability) surfaces generated with ECIS are shown from 100 pM to 10 µM and from zero to 21 hours for: (A) D<sub>3</sub>; (F) 25(OH)D<sub>3</sub>; (K) 1,25(OH)<sub>2</sub>D<sub>3</sub>. Detailed time-responses are shown at 1 nM and 10 µM respectively for: (B and C) D<sub>3</sub>; (G and H) 25(OH)D<sub>3</sub>; and (L and M) 1,25(OH)<sub>2</sub>D<sub>3</sub>. Detailed dose-response are shown at 4 hours and 12 hours respectively for (D and E) D<sub>3</sub>, (I and J) 25(OH)D<sub>3</sub>, and (N and O) 1,25(OH)<sub>2</sub>D<sub>3</sub>.

# Vitamin D3



**Fig 1. Vitamin D stabilizes the endothelium.** Dose/time resistance (endothelial stability) surfaces generated with ECIS are shown from 100 pM to 10 μM and from zero to 21 hours for: (A) D<sub>3</sub>; (F) 25(OH)D<sub>3</sub>; (K) 1,25(OH)<sub>2</sub>D<sub>3</sub>. Detailed time-responses are shown at 1 nM and 10 μM respectively for: (B and C) D<sub>3</sub>; (G and H) 25(OH)D<sub>3</sub>; and (L and M) 1,25(OH)<sub>2</sub>D<sub>3</sub>. Detailed dose-response are shown at 4 hours and 12 hours respectively for (D and E) D<sub>3</sub>, (I and J) 25(OH)D<sub>3</sub>, and (N and O) 1,25(OH)<sub>2</sub>D<sub>3</sub>.



Normal circulating levels*	NA	1-90 nM	30-80 nM	50-100 pm
Enhancement of endothelial stability (minimum active dose)	NA	<100 pM	100 nM	1 nM
Enhancement of endothelial stability	Inactive	Active	Active	Active

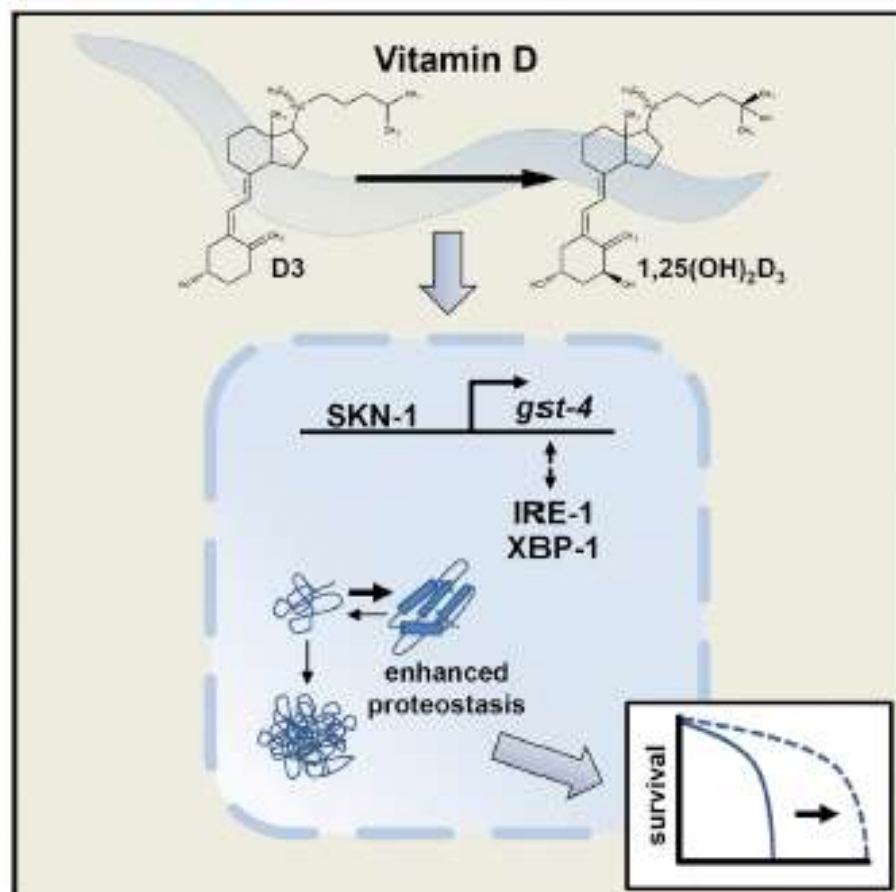


**Vitamin D  
Improves longevity  
In  
Nematodes  
!!!!!!!**

# Cell Reports

## Vitamin D Promotes Protein Homeostasis and Longevity via the Stress Response Pathway Genes *skn-1*, *ire-1*, and *xbp-1*

### Graphical Abstract



### Authors

Karla A. Mark, Kathleen J. Dumas, Dipa Bhaumik, ..., Arvind Ramanathan, Bradford W. Gibson, Gordon J. Lithgow

### Correspondence

kdumas@buckinstitute.org (K.J.D.),  
glithgow@buckinstitute.org (G.J.L.)

### In Brief

Maintenance of protein homeostasis is crucial to cellular health and contributes significantly to the lifespan of organisms. Mark et al. demonstrate that vitamin D supplementation promotes protein homeostasis and slows aging in the nematode, *C. elegans*. These findings identify a mechanism by which vitamin D influences aging.

## Highlights

- Vitamin D metabolism is conserved between nematodes and mammals
- Vitamin D prevents the age-dependent accumulation of SDS-insoluble proteins
- Vitamin D enhances lifespan and protein homeostasis via IRE-1, XBP-1, and SKN-1

## Vitamin D: A New Promising Therapy for Congenital Ichthyosis.

Sethuraman G<sup>1</sup>, Marwaha RK<sup>2</sup>, Challa A<sup>3</sup>, Yenamandra VK<sup>3</sup>, Ramakrishnan L<sup>4</sup>, Thulkar S<sup>5</sup>, Sharma VK<sup>3</sup>.

### ⊕ Author information

#### Abstract

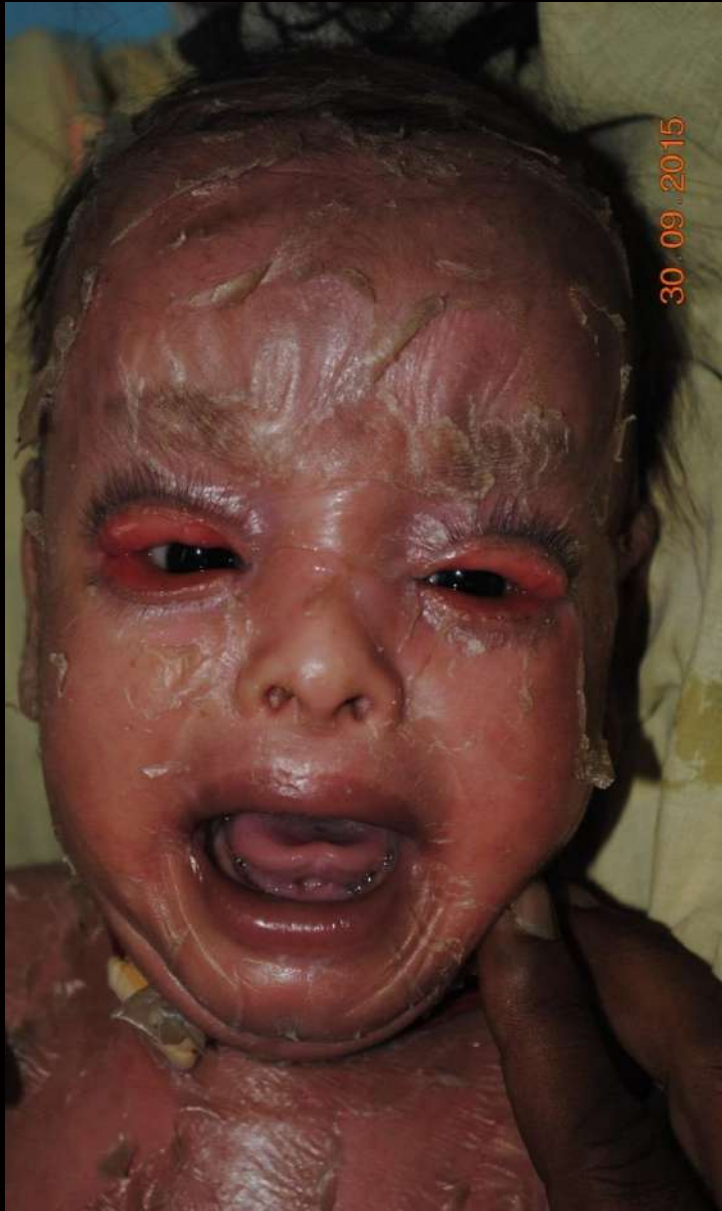
Severe vitamin D deficiency and rickets are highly prevalent among children with congenital ichthyosis. We report an incidental observation of a dramatic and excellent clinical response with regard to skin scaling and stiffness in children with congenital ichthyosis after short-term high-dose vitamin D supplementation that has not been previously described. Seven children with congenital ichthyosis (5 with autosomal recessive congenital ichthyosis; 2 with epidermolytic ichthyosis) and severe vitamin D deficiency (and/or rickets) were given 60,000 IU of oral cholecalciferol daily for 10 days under supervision. All children were subsequently put on recommended daily allowance of 400 to 600 IU of cholecalciferol. The

main outcome was that all children had severe vitamin D deficiency and radiologic evidence of rickets. Significant improvement in skin scaling and stiffness was observed. At 1 month, the skin had become smoother and less stiff. This response was also observed in all children. Supplementation with high-dose vitamin D followed by recommended daily allowance appears to be an effective form of therapy in the management of congenital ichthyosis with vitamin D deficiency.

**60,000 IU X 10 Days  
(600,000IU)**

Copyright © 2016 by the American Academy of Pediatrics.





**60,000 IU X10 days  
(600,000 IU)**

Lose weight and feel better

**FEEED**

Eat to Turn Off

**YOUR**

Disease-Causing Genes

**GENES**

and Slow Down Aging

**RIGHT**

**With Vitamin D**

VITAMIN D

***DEFICIENCY***

IS A DISEASE OF NEGLECT

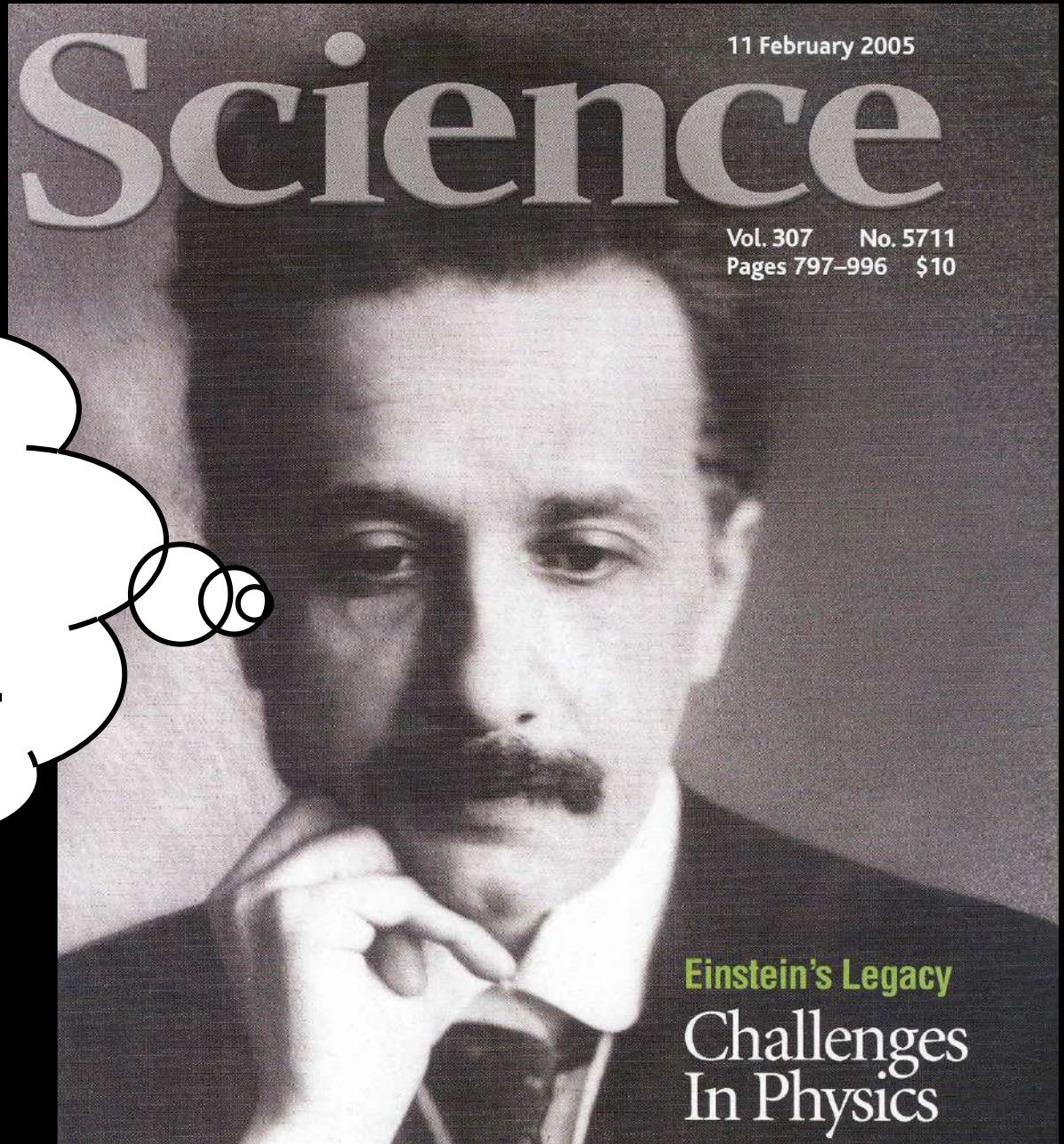
# Science

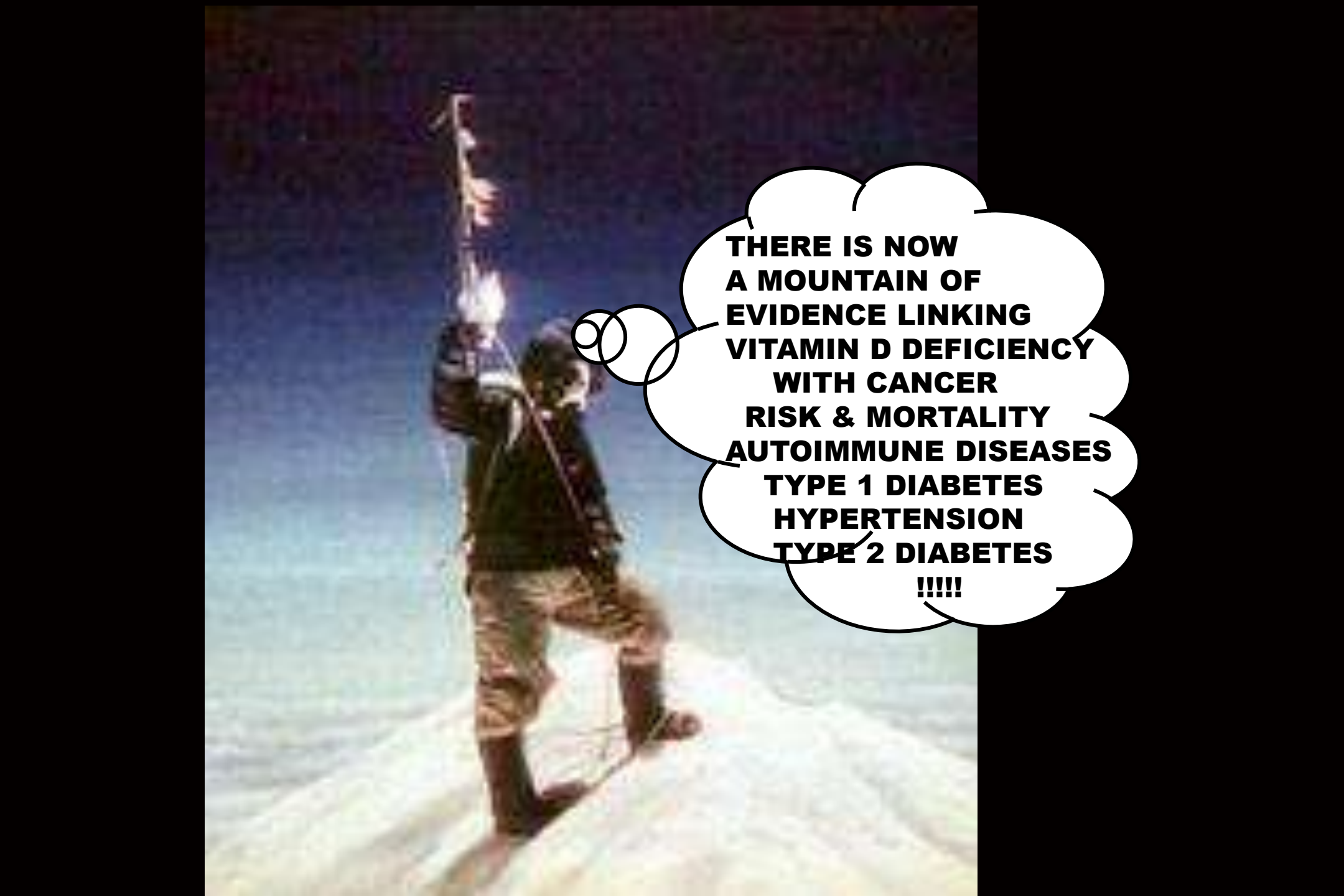
11 February 2005

Vol. 307 No. 5711  
Pages 797-996 \$10

**ADEQUATE  
VITAMIN D  
IS  
NECESSARY  
FROM BIRTH-  
DEATH**

**Einstein's Legacy**  
Challenges  
In Physics

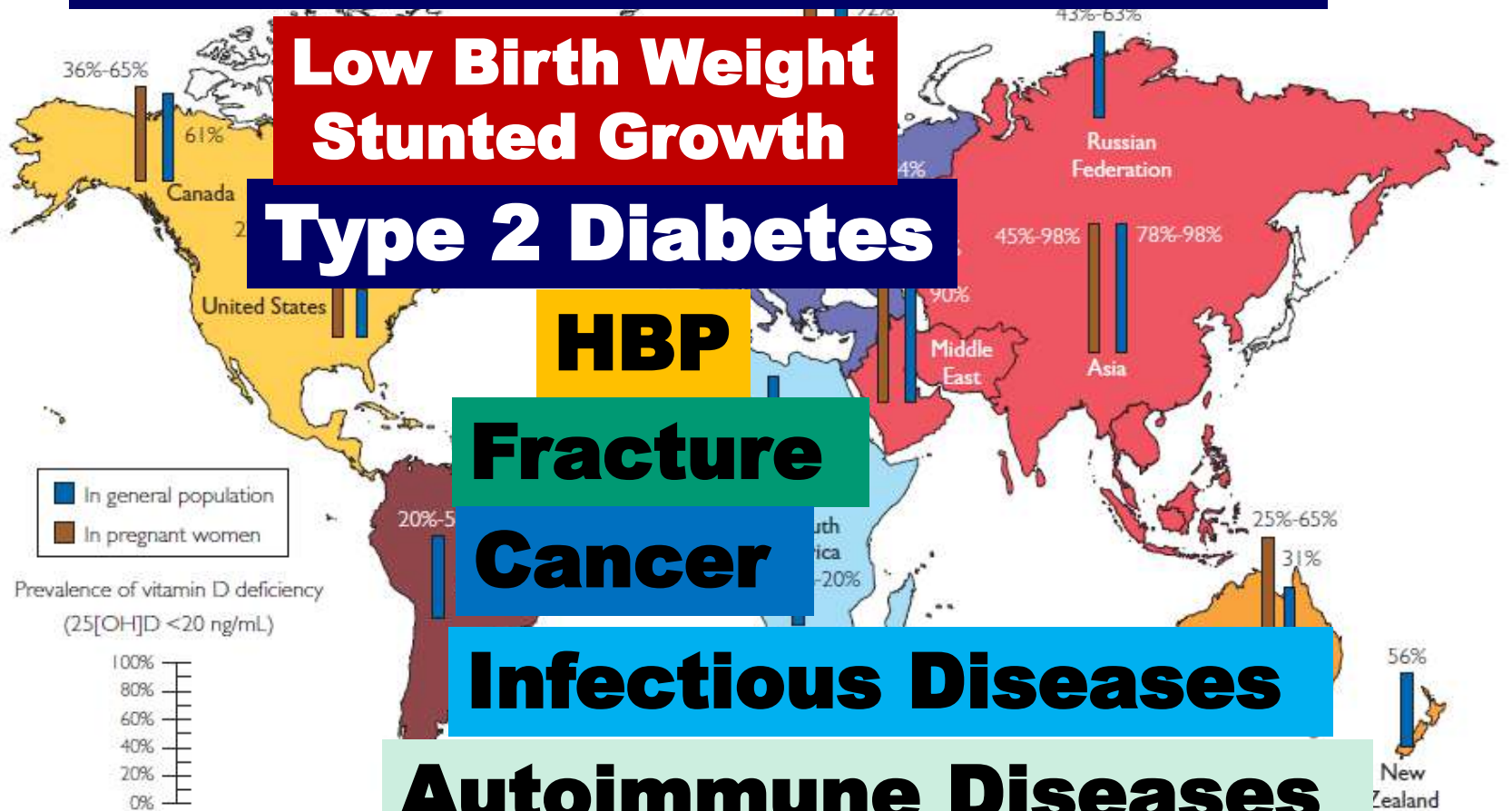


A person is climbing a rope on a mountain peak. The person is wearing a dark jacket and brown pants. The background is a clear blue sky and a white mountain peak. The person is holding the rope with both hands and is looking up. The rope is attached to a point above the person. The person is standing on a white, rocky surface. The overall scene is one of a high-altitude mountain climb.

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

**!!!!**

# Disease Burden & Vitamin D Deficiency



**Low Birth Weight  
Stunted Growth**

**Type 2 Diabetes**

**HBP**

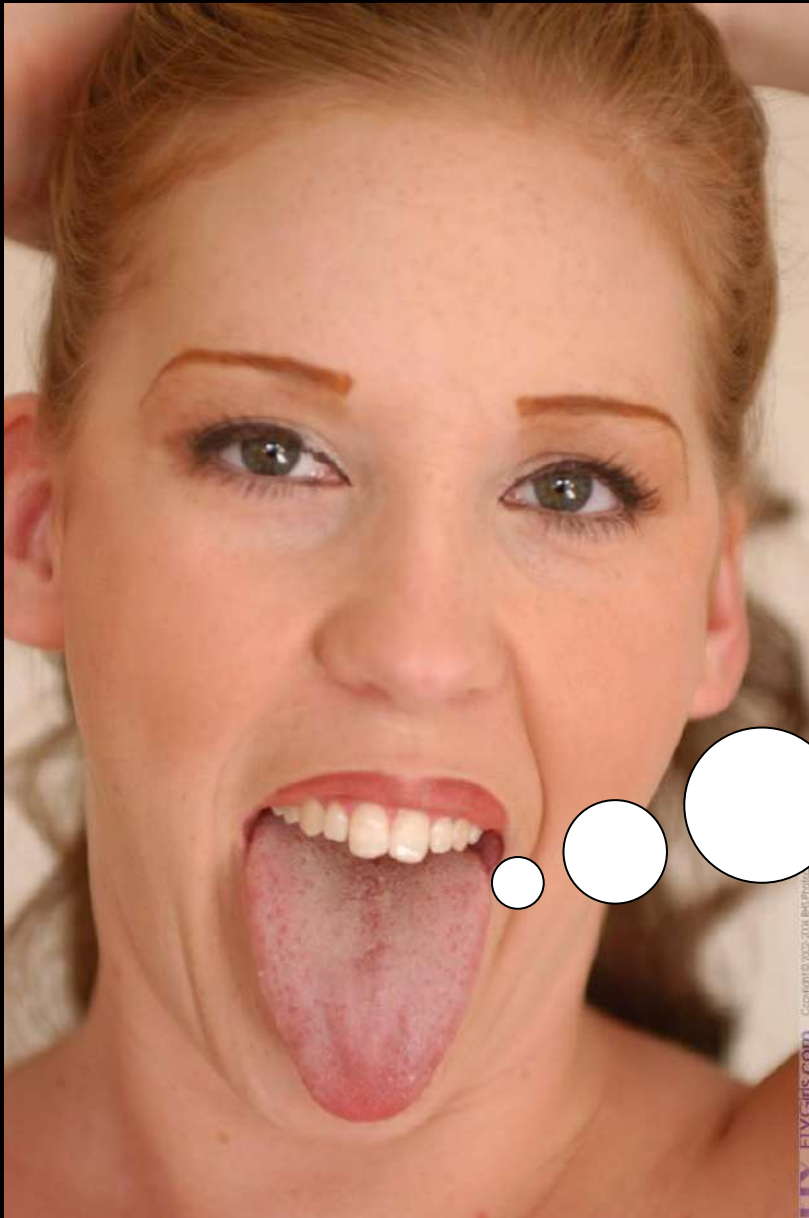
**Fracture**

**Cancer**

**Infectious Diseases**

**Autoimmune Diseases**

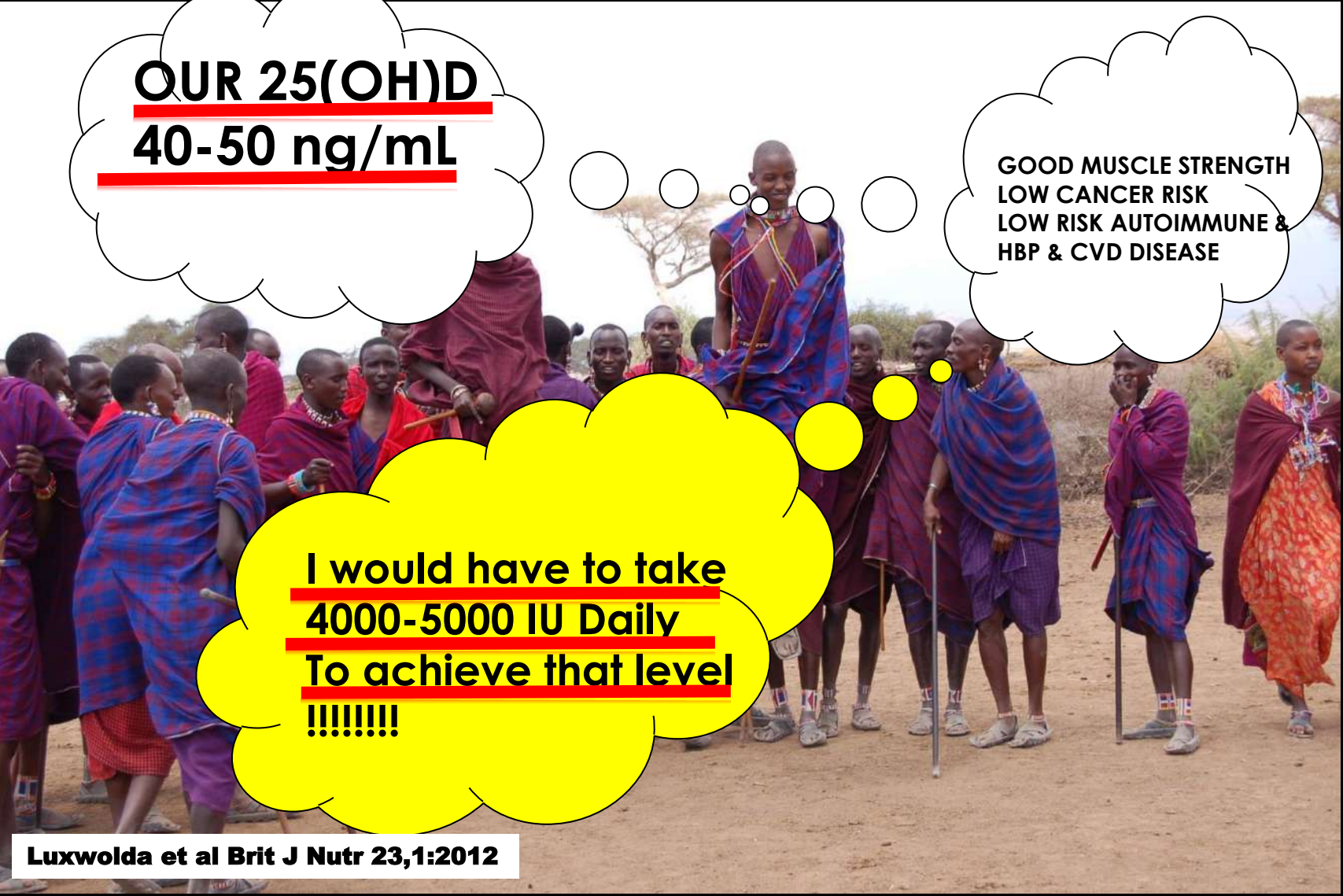
WHAT IS A  
**NORMAL**  
VERSUS  
**HEALTHY**  
25(OH)D LEVEL  
?????????



**How can we determine**  
**what the optimal**  
**25(OH)D Level should**  
**be**

**Since there are so**  
**Many health**  
**benefits/**  
**???????**





**OUR 25(OH)D**  
**40-50 ng/mL**

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

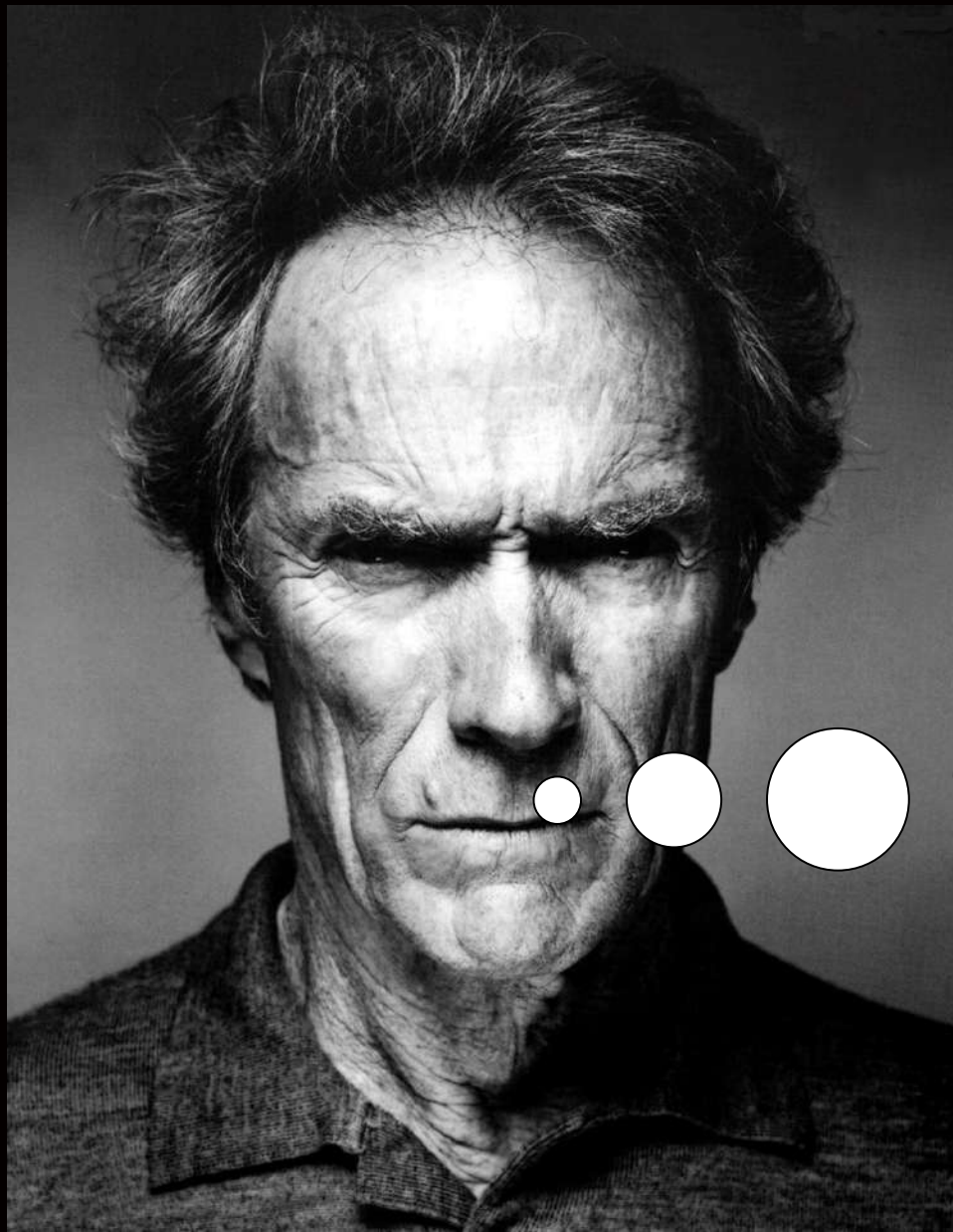
**I would have to take**  
**4000-5000 IU Daily**  
**To achieve that level**  
**!!!!!!!**

**Luxwolda et al Brit J Nutr 23,1:2012**

# GOAL

25(OH)D > 30 ng/ml

40-60 ng/mL preferred



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




**100 IU VITAMIN D3**

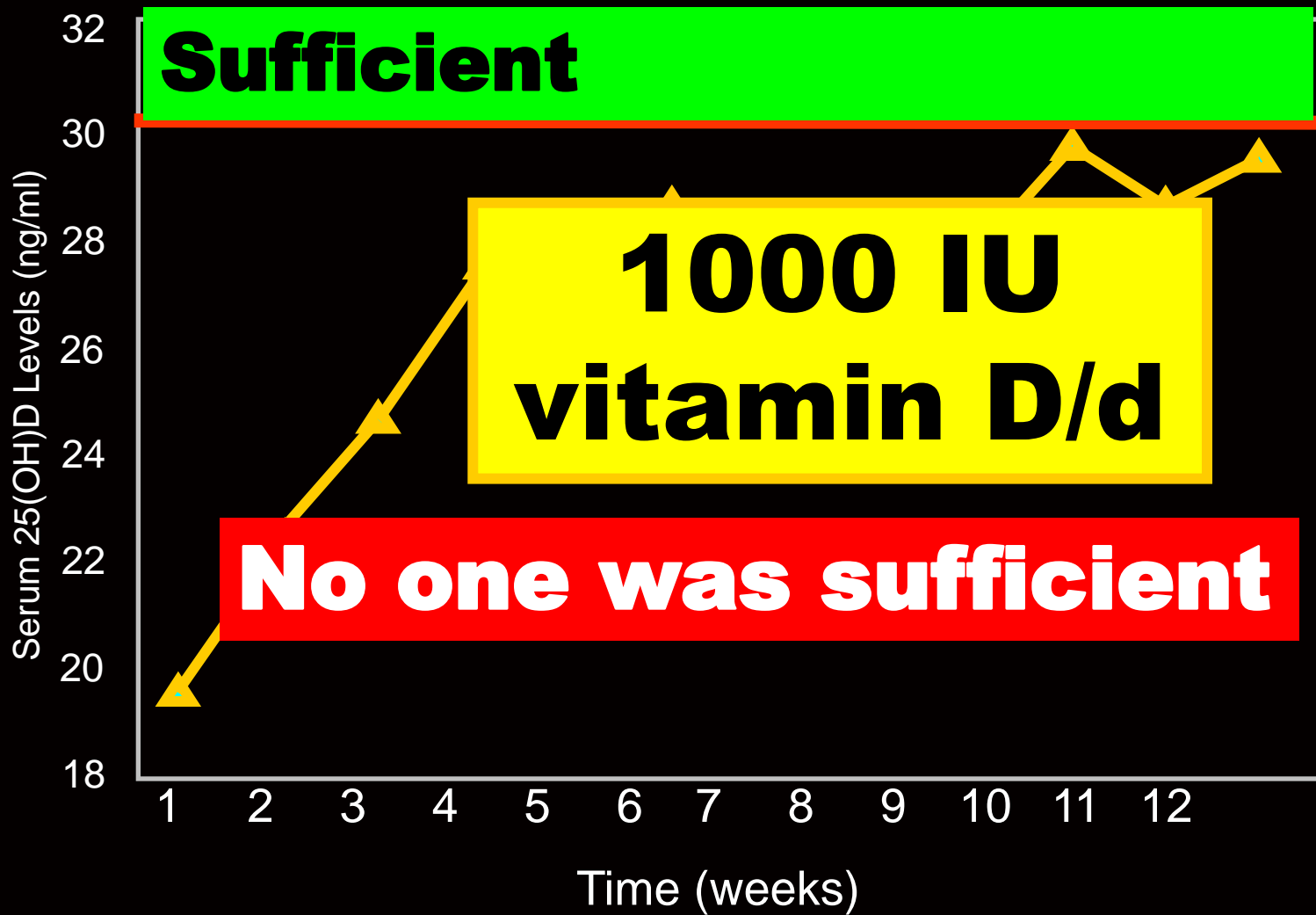
**RAISES 25(OH)D**

**BY ONLY**

**1 NG/ML**



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



**Adults 2000 IU**

**&**

**Children 1000 IU**

**Conquer**

**Vitamin D**

**Deficiency**



**What is the  
Best  
Source of  
Vitamin D  
?**

Capturing  
the sunshine vitamin  
(VITAMIN-D)

*in 88 new*

**Bond Bread**  
**Recipes**



# VITAL NEWS for Mothers!

## Bond Bread now brings sunshine vitamin-D

*Never before supplied in sufficient quantity  
by any table-food—now this scarcest  
of health-guarding elements can  
be had at every meal.*

*If your child ever  
cried in the night  
for you, one slice  
of Bond might do.*

*Write to General  
Baking Company,  
Route 960, 200  
Madison Avenue,  
New York City  
for 10¢ booklet.*



**T**O BUILD strong bones and sound teeth, to promote proper growth, to strengthen resistance to colds and illness, everybody—especially children—needs sunshine vitamin-D every day. But until now much of it could be obtained only from direct sunshine, from sun lamps, and from medicines.

Now scientists have found a way to provide this vital, health-building food element in bread. And Bond Bread has been chosen exclusively to offer you the benefits of this discovery. They guarantee that one to two slices of Bond Bread at each meal will give you all the extra sunshine vitamin-D you need.

Ask your grocer for sunshine vitamin-D Bond Bread—the same home-like flavor, the same firm texture that Home-Perk

Rising insures—the bread that more than a million housewives buy every day. And with this priceless improvement, it costs you no more than you have been paying.

**OFFICIALLY APPROVED BY  
HIGHEST AUTHORITIES**

Every claim made in this advertisement has been specifically checked and approved by recognized scientific authorities. Bond Bread, analyzed and tested as to its sunshine vitamin-D content, has been found the official bread of several national agencies at the following:

THE AMERICAN MEDICAL ASSOCIATION'S COMMITTEE ON FOODS  
Wisconsin Alumni Research Foundation  
Good Housekeeping Bureau of Food  
Physical Culture Institute  
Home-Making Center  
The Paediatric Research Foundation  
Child Health Magazine  
Parents Magazine

Guaranteed by  
The General Baking Company

# Bond Bread

**FOR HAPPIER HEALTH**

Get the sunshine Vitamin-D you need with Bond Bread... Bond Bread and Bond Baking... Write to the General Baking Company for the booklet on this vitamin-D you need...

FIFTEEN CENTS

October 12, 1936

# TIME

*The Weekly Newsmagazine*



*Kinzy Bros. from Illustrated Weekly of India*



Volume XXVIII

**THE VICEROY OF INDIA**

*"Trust me — I'll trust you!"*  
(See FOREIGN NEWS)

Number 15

Serve  
*Sunny* Energy



**Schlitz**

the beer with *Sunshine*

**VITAMIN-D**

**S**WISH . . . sings the racket. Flash . . . goes the ball. That's energy—vigor—life.

SCHLITZ gives you energy like that! It's the beer with SUNSHINE VITAMIN D\*.

First the quick, invigorating tang of fine malt and hops perfectly brewed under PRECISE ENZYME CONTROL.

Then the more lasting benefits of SUNSHINE VITAMIN D—priceless aid to vigor . . . life . . . and buoyant health.

Modern living; clothing; hours spent indoors or in the shade—rob us of sunshine benefits even in mid-summer. But SCHLITZ in brown bottles and cans gives you the Vitamin D you need for vigorous health.

It's cooling . . . refreshing . . . energizing. With all the tangy, old-time SCHLITZ flavor and bouquet—plus new health benefits—and at no increase in price.

Beer is good for you . . . but SCHLITZ, the beer with SUNSHINE VITAMIN D, is extra good for you. Drink it each day—for health with enjoyment. Jos. Schlitz Brewing Company, Milwaukee, Wis.

\*Each 12-ounce bottle or can of SCHLITZ contains 100 U. S. P. X. Units of Sunshine Vitamin D. SCHLITZ brewer's yeast contains the pro-vitamin D which is activated directly by the ultra-violet rays of the sun to form Vitamin D. (Protected by U. S. Letters Patent.)



Copyright 1936, J.S.B. Co.

The Beer That Made Milwaukee Famous

**KEEP SUNNY  
SUMMER ENERGY**



**DRINK SCHLITZ  
ALL WINTER**



**T**O help retain the peak of sunny summer energy—to help maintain rugged resistance all through Fall and Winter—drink SCHLITZ, with SUNSHINE VITAMIN D.

As the summer sun heads south; as days grow shorter and stormier—we get less and less of sunshine's benefits. Likewise, our ordinary foods are lacking in Sunshine Vitamin D, so essential to robust vitality.

SCHLITZ, with SUNSHINE VITAMIN D\*, gives you the sunny source of energy you need the

whole year around. Beer is good for you—but SCHLITZ, with SUNSHINE VITAMIN D, is extra good for you. It has all the old-time SCHLITZ FLAVOR AND BOUQUET brewed to mellow ripe perfection under PRECISE ENZYME CONTROL, with new health benefits . . . and at no increase in price.

Drink SCHLITZ regularly—every day—for enjoyment—for energy.  
Jos. Schlitz Brewing Company,  
Milwaukee, Wisconsin.

\*Each 12-ounce bottle or can of SCHLITZ contains 100 U.S.P. XI. Units of Sunshine Vitamin D. SCHLITZ brewer's yeast contains pro-vitamin D which is activated directly by the ultra-violet rays of the sun to form Vitamin D. (Protected by U. S. Letters Patent.)

**Schlitz**

**WITH SUNSHINE VITAMIN-D**



Copyright 1935, J.S.B. Co.

**The Beer That Made Milwaukee Famous**

1  
9  
3  
4





**"Look, Johnnie, over there is a little spot of sunshine,  
go over and play in and get your vitimin D."**

Published September 17, 1953





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



OCTOBER 2003

\$4.95 US

"PEOPLE SHOULD HAVE THE OPPORTUNITY TO BENEFIT FROM  
DR. HOLICK'S INSIGHTS WITHOUT FURTHER DELAY."  
—JANE E. BRODY, THE NEW YORK TIMES

THE MEDICAL BREAKTHROUGH THAT SHOWS HOW TO  
HARNESS THE POWER OF THE SUN FOR YOUR HEALTH

# THE UV

## ADVANTAGE

**MICHAEL HOLICK, PH.D., MD.**  
Professor of Medicine, Physiology, and Biophysics Boston University Medical Center

**AND MARK JENKINS**

# THE BOOK

Dr. Holick's new book shatters the myths about UV and tanning and establishes some new realities

# MAY 04



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

# The Influence of Painful Sunburns and Lifetime Sun Exposure on the Risk of Actinic Keratoses, Seborrheic Warts, Melanocytic Nevi, Atypical Nevi, and Skin Cancer

Cornelis Kennedy, Chris D. Bajdik,\* Rein Willemze, Frank R. de Gruijl, and Jan N. Bouwes Bavinck, for the members of the Leiden Skin Cancer Study

Departments of Dermatology, Leiden University Medical Center, Leiden, The Netherlands; \*British Columbia Cancer Agency, Vancouver, British Columbia, Canada

**Lifetime sun exposure was predominantly associated with an increased risk of squamous cell carcinoma (p-value for trend = 0.03) and actinic keratoses (p-value for trend < 0.0001) and to a lesser degree with the two types of basal cell carcinoma. By contrast, lifetime sun exposure**



I should Avoid ALL  
Sunlight to Prevent  
Melanoma

!!!!!!



Did you Know  
Most Melanomas

**Occur on the  
Least Sun Exposed Areas**

???????



**Occupational  
sun exposure  
Decreases risk  
melanoma**



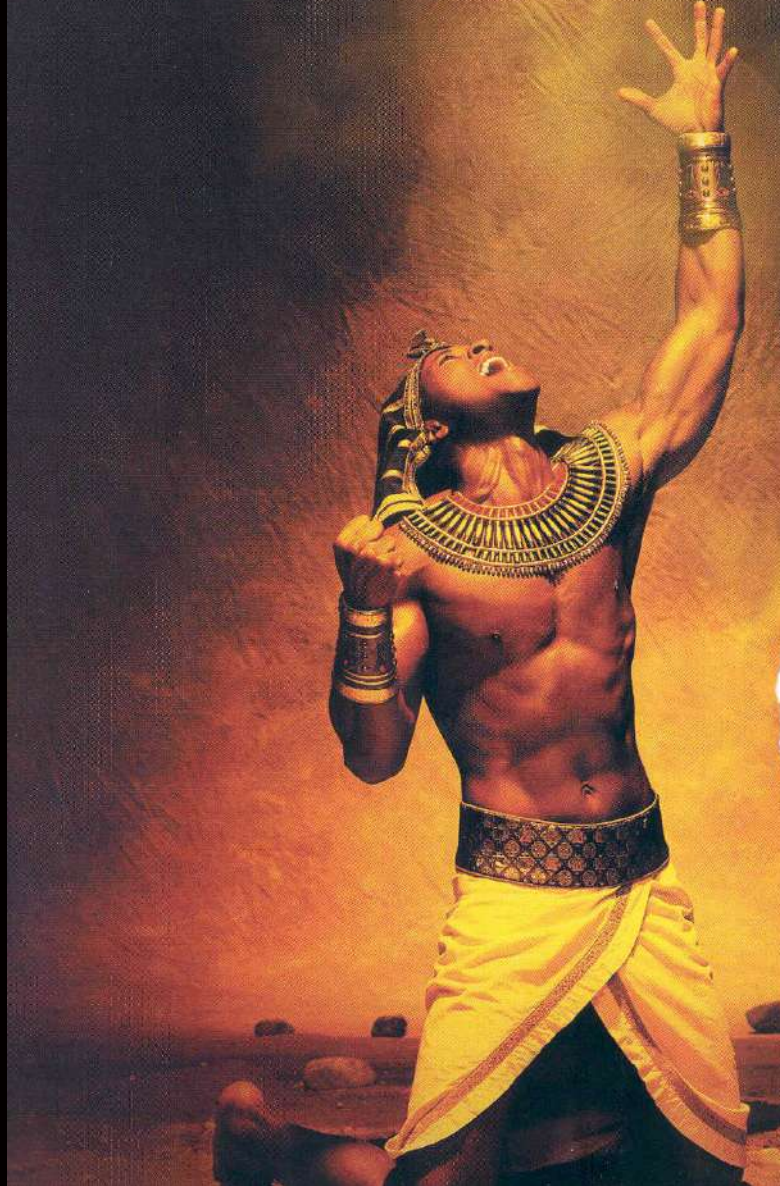
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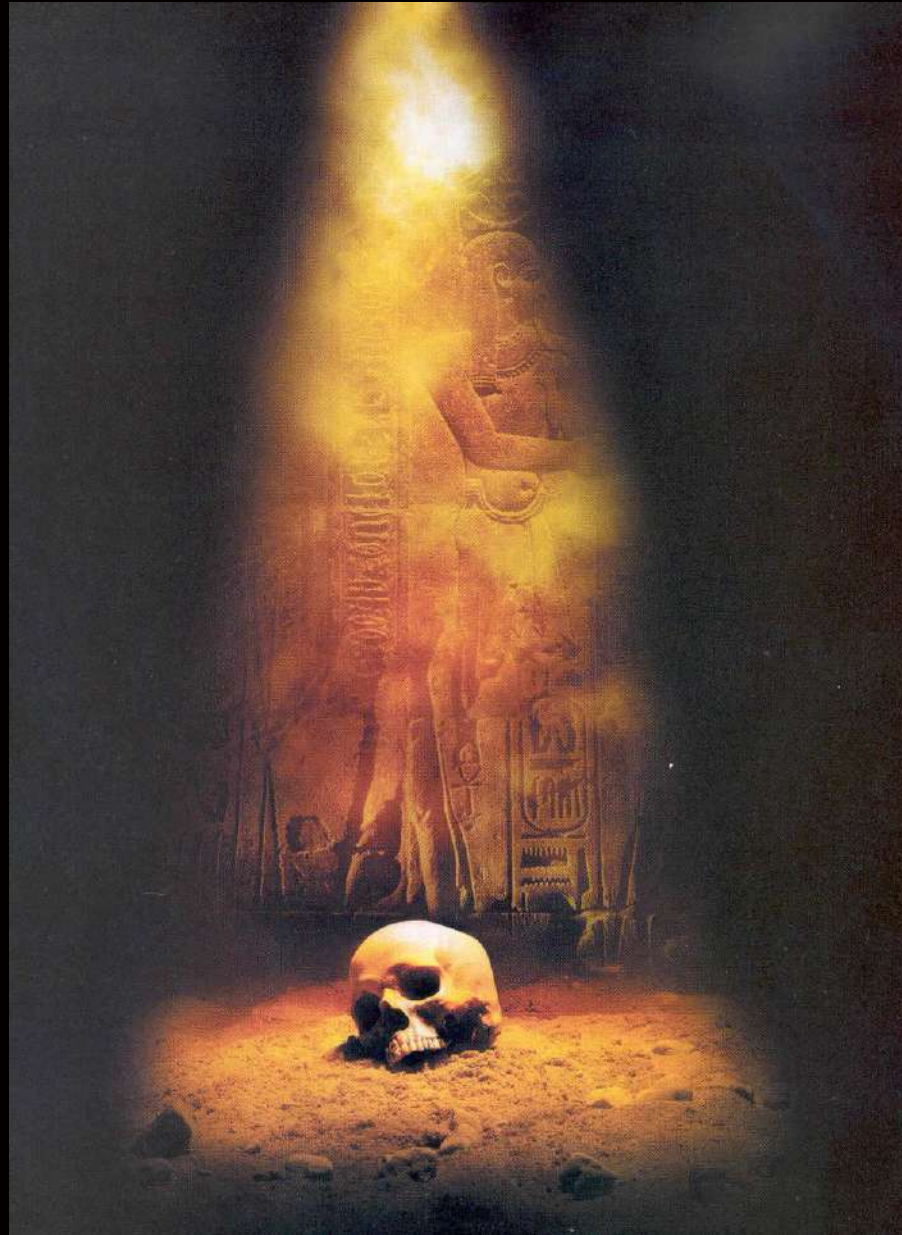
Departments of Dermatology, Leiden University Medical Center, Leiden, The Netherlands; \*British Columbia Cancer Agency, Vancouver, British Columbia, Canada

By contrast, lifetime sun exposure appeared to be associated with a lower risk of malignant melanoma, despite the fact that lifetime sun exposure did not diminish the number of melanocytic nevi or atypical nevi. Neither painful sunburns nor lifetime sun exposure were associated with an increased risk of seborrheic warts. *Key words: actinic keratoses/atypical nevi/melanocytic nevi/seborrheic warts/skin cancer/ultraviolet light. J Invest Dermatol 120:1087–1093, 2003*

# ANCESTORS APPRECIATION OF THE SUN FOR ITS LIFE GIVING BENEFITS



UNENLIGHTENED DERMATOLOGISTS  
VIEW OF THE SUN'S EFFECT ON HEALTH





ALWAYS WEAR  
A SUNSCREEN

DERMATOLOGIST ADVISING ABOUT SUN EXPOSURE





CHARLES M. SCHULZ  
1922 - 2000

Thank You For Giving The World Such Happiness.

Classic  
**PEANUTS**

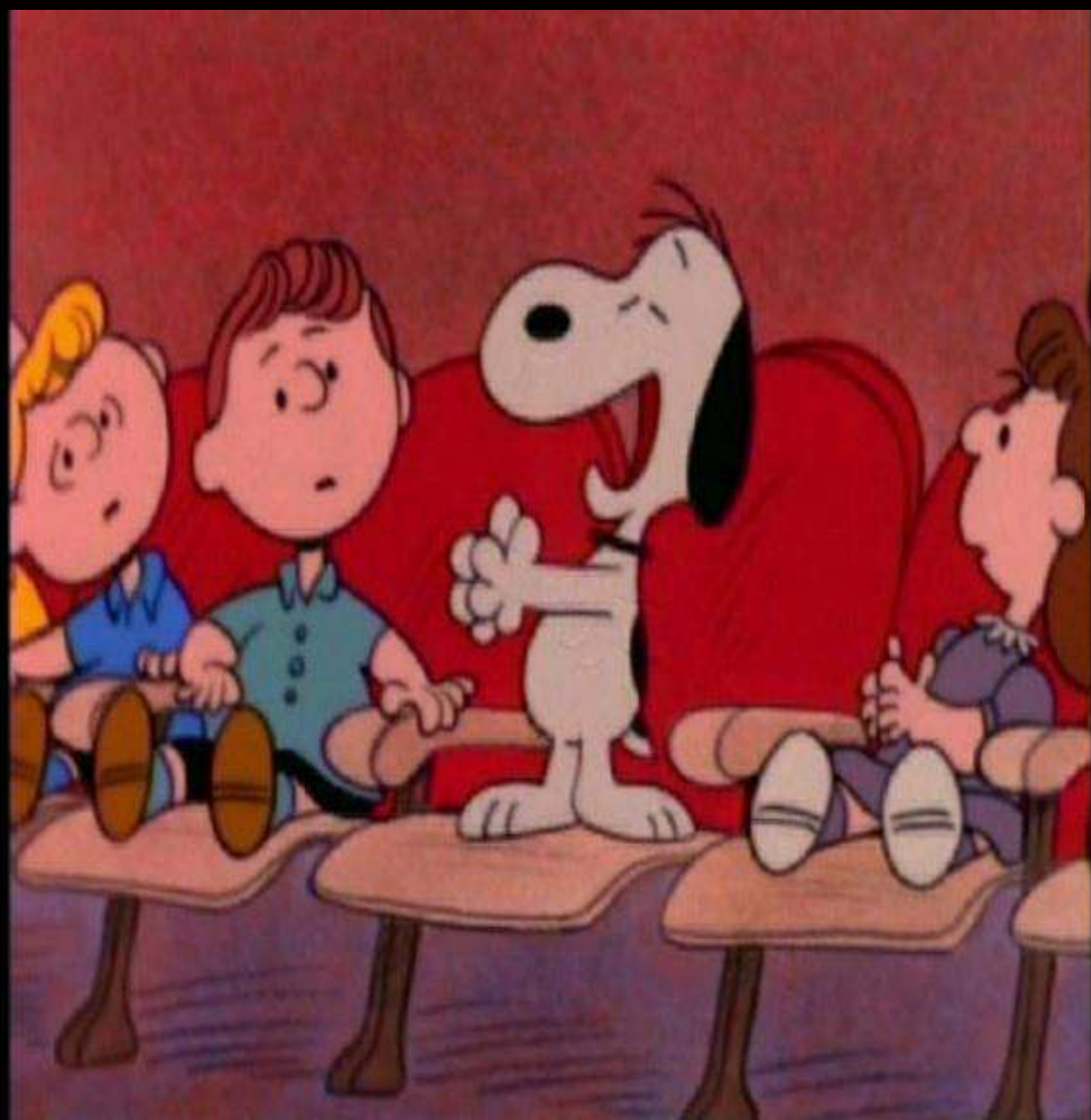
featuring  
"Good ol'  
Charlie Brown"

by SCHULZ

GOOD  
GRIEF!

ANOTHER  
NOTE!

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







**NEVER BE  
EXPOSED  
TO THE SUN  
!!!!!!!!!!!!!!!!!!!!**

# Stopping the burn

Blankets designed to stop the sun's rays

**By Benjamin Smith**  
STAFF WRITER

Anne Hinck admits she might have been a little obsessed with protecting her newborn from the sun, but she's turned that obsession into the start up business, Baby Capes.

The Sudbury mother of two has designed and developed an infant-size, sun-block blanket to help protect newborns from over exposure to the sun. The blankets are being sold on the company's Web site and at 15 retail locations in New England and New York.

"The rate that skin cancer is growing is unbelievable," Hinck said. "You need to protect them while their infants to help prevent cancer later."



**D-ficient**

Baby Capes founder Anne Hinck models one of her

# Slip, Slap, Slop



**~ 40% Australians D-Ficient**

# 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**

**Holick**

**What about skin  
cancer**

**And**

**Sun damage**

**????????**





**Can you have your  
Cake  
and  
Eat it T O O O O O O O O O O O  
????????**

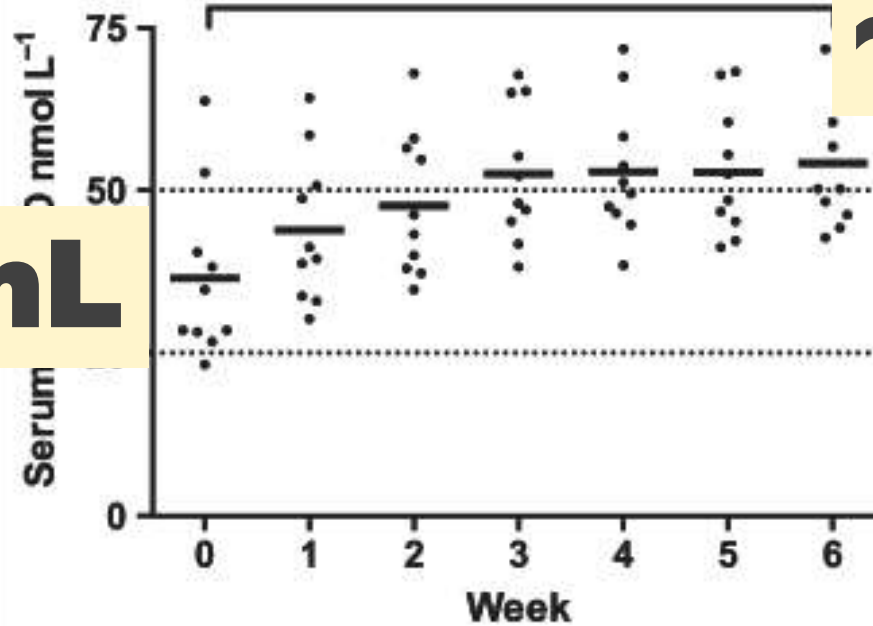
# Concurrent beneficial (vitamin D production) and hazardous (cutaneous DNA damage) impact of repeated low-level summer sunlight exposures\*

S.J. Felton,<sup>1</sup> M.S. Coombs,<sup>2</sup> R. Kift,<sup>3</sup> J.L. Berry,<sup>4</sup> A.R. Webb,<sup>3</sup> P.M.W. Lam,<sup>5</sup> F.R. de Graaff,<sup>6</sup> A. Vail<sup>7</sup> and L.E. Rhodes<sup>1</sup>

**Conclusions** Low-dose summer sunlight exposures confer vitamin D sufficiency in light-skinned people concurrently with low-level, nonaccumulating DNA damage. The same exposures produce minimal DNA damage but less vitamin D in brown-skinned people. This informs tailoring of sun-exposure policies.

(a)

**Skin type 2**

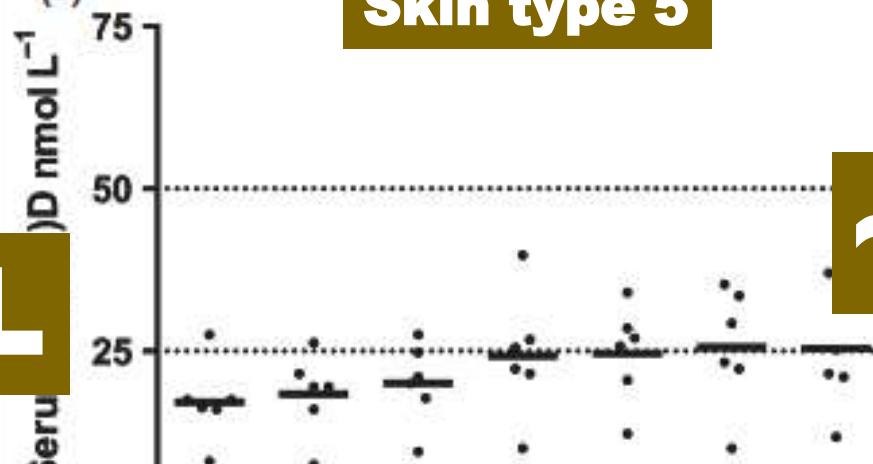


**~21 ng/mL**

**~15 ng/mL**

(b)

**Skin type 5**



**~10 ng/mL**

**~8 ng/mL**

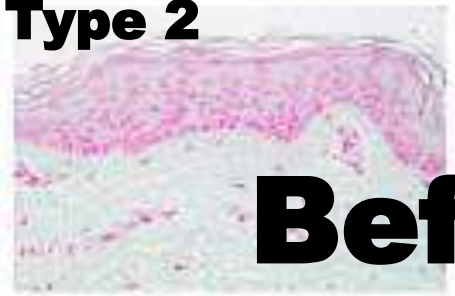
**6 wks UVR in UK Summer**



Type 2

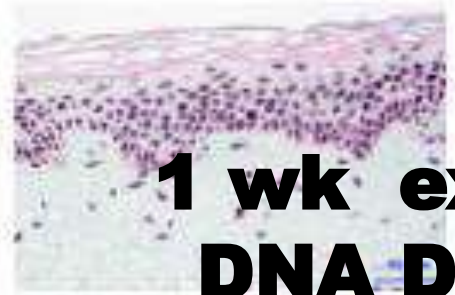
Type 5

(a)



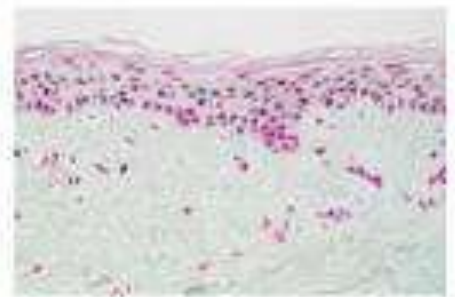
**Before**

(b)

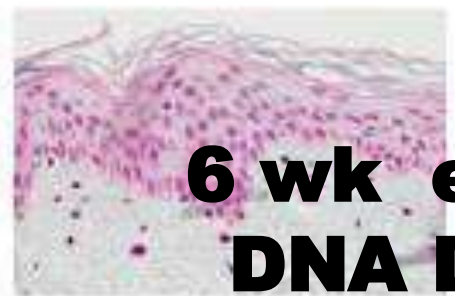


**1 wk exposure  
DNA Damage**

(c)



(d)



**6 wk exposure  
DNA Damage**

• Phototype II   • Phototype V



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



**YOU CANNOT  
GET IT FROM  
DIET**

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

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

*Michael F. Holick  
Ph.D., M.D.*



**What is the  
Best  
Source of  
Vitamin D  
?**



**WHEN CAN YOU MAKE  
VITAMIN D ????**

**How about an App???**

**<http://dminder.info>**

SPF 30



**+ 4000 IU Vitamin D3**

**+ MTV=1000 IU**

**+ 3 glasses milk = 300 IU**

**My Vitamin D Intake  
~6000 IU/Day**

**My 25(OH)D = 62 ng/ml**

Patent Pending  
AUSTL 174934  
Practitioner Only

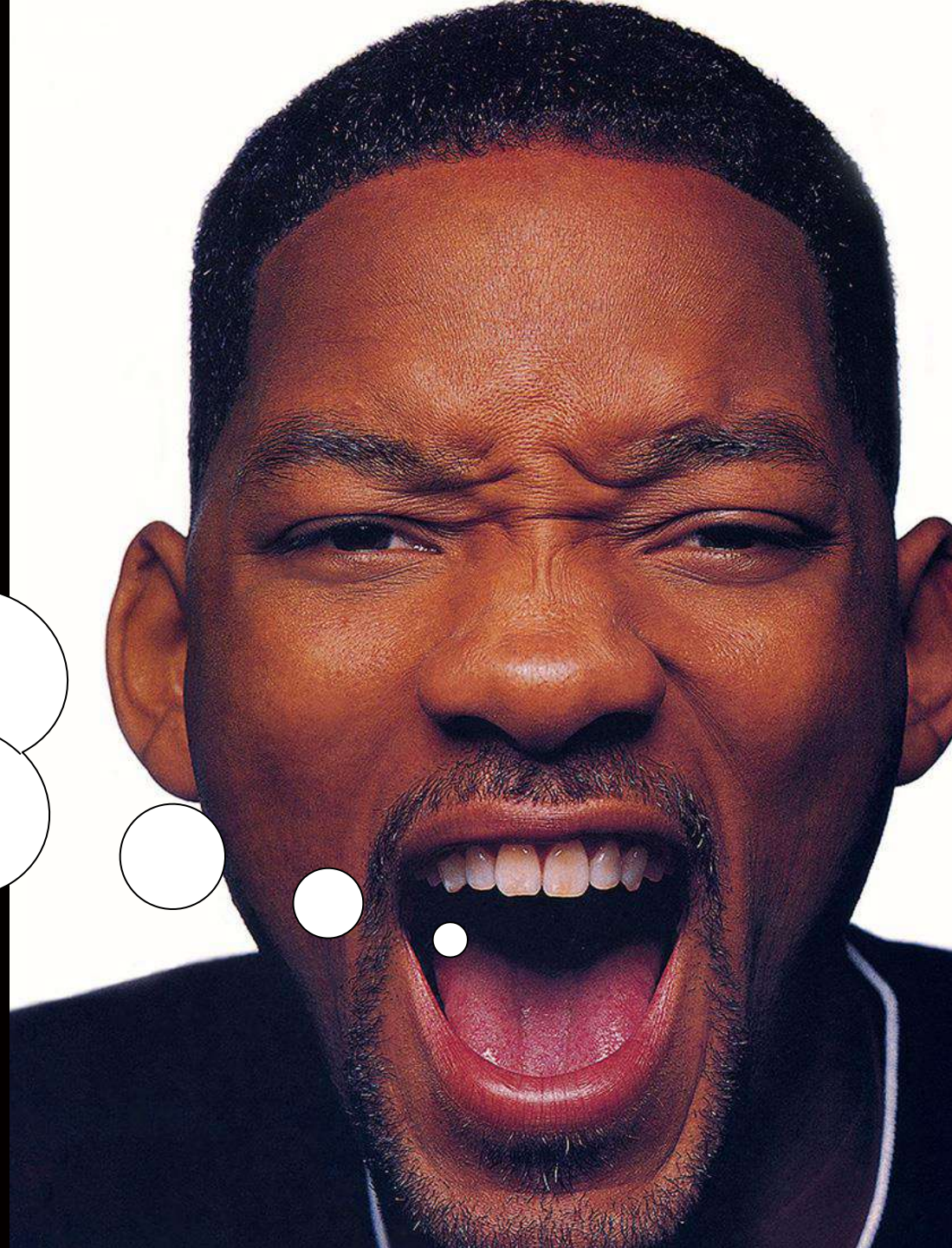
Wild Alaskan  
Sockeye Salmon Oil  
+ Vitamin D3

Dietary Supplement

Pure and Natural Source of  
Vitamin D3 and Omega-3 Fatty Acids



**Vitamin D  
Deficiency  
Is The  
Most COMMON  
Medical Condition**



***DrHolick.com***

**CAUSES**

***VITAMIN D DEFICIENCY*** **CONSEQUENCES**

**Holick NEJM July 07**

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



***DrHolick.com***

A man in a suit is shown from the chest up, looking slightly to the right. He has a serious expression. A large white thought bubble is positioned to his left, containing blue text. Another white thought bubble is positioned to his right, containing red text. The background is a blurred, light-colored wall.

**We Need  
Sensible  
Sun  
&  
Supplement  
Recommendations**

**This is  
NOT  
HYPOTHESIS**

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



**Do we need to  
Screen everyone  
For their**

**25(OH)D levels**

**????????????????**

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

**But Yes**  
**BMI>30**  
**Malabsorption**  
**Meds/AEs., Glc**  
**Sarcoidosis**

Ben quoi ?



**MICHAEL F. HOLICK, Ph.D., M.D.**

Foreword by ANDREW WEIL, M.D.

# THE VITAMIN D SOLUTION

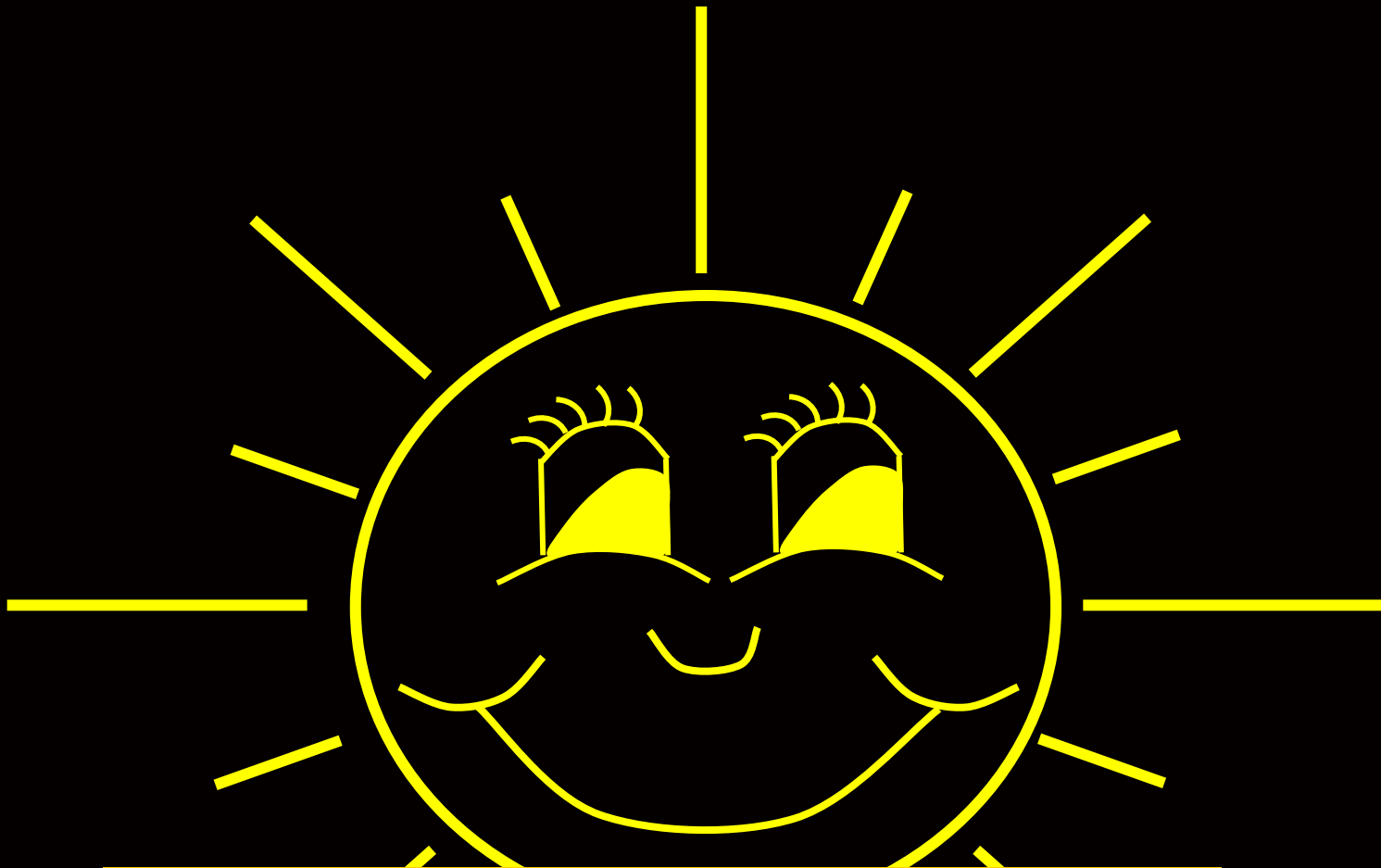
A 3-Step Strategy to Cure Our  
Most Common Health Problems

**DrHolick.com**



**Vitamin D  
Can help Improve  
Your Health**





**DrHolick.com**

**<http://dminder.info>**