S. Bernasconi, S. Merli

Clinica Pediatrica

Università di Parma

EVOLUZIONE DELLE CONOSCENZE

1° fase : comprensione del metabolismo della vitamina D ...

Vitamin D metabolism, functions and needs: from science to health claims

Eur J Nutr

2012

S. Battault · S. J. Whiting · S. L. Peltier · S. Sadrin · G. Gerber · J. M. Maixent

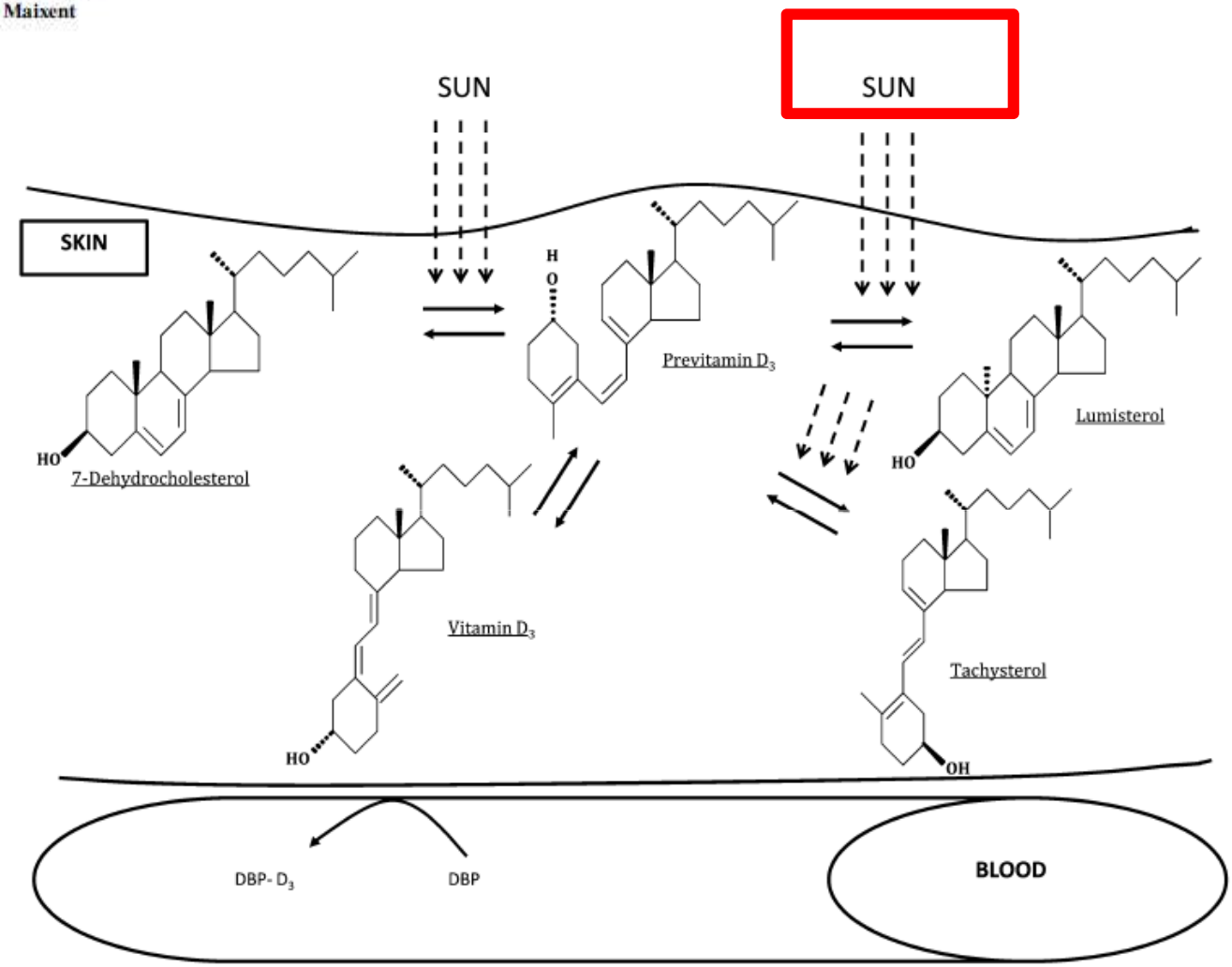


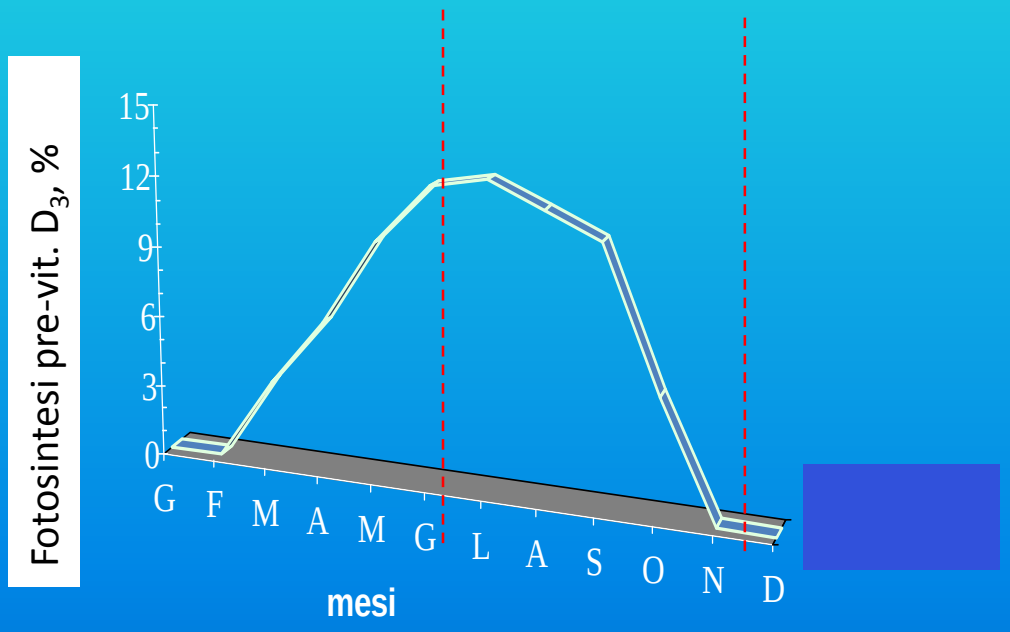
Fig. 1 Schematic of vitamin D3 synthesis in skin, adapted from [4]

ESPOSIZIONE AL SOLE E STATO VITAMINICO D

FATTORI CHE INFLUENZANO L'EFFICACIA DELLA RADIAZIONE SOLARE

- pigmentazione cutanea
- massa corporea
- latitudine
- stagione
- inquinamento atmosferico
- percentuale di cute esposta
- tipo di vestiario (motivi culturali e religiosi)
- utilizzo di filtri solari

PERCENTUALE DI FOTOSINTESI DELLA PRE-VITAMINA D_3 DAL 7-DEIDROCOLESTEROLO DURANTE I MESI DELL'ANNO, *IN VITRO*

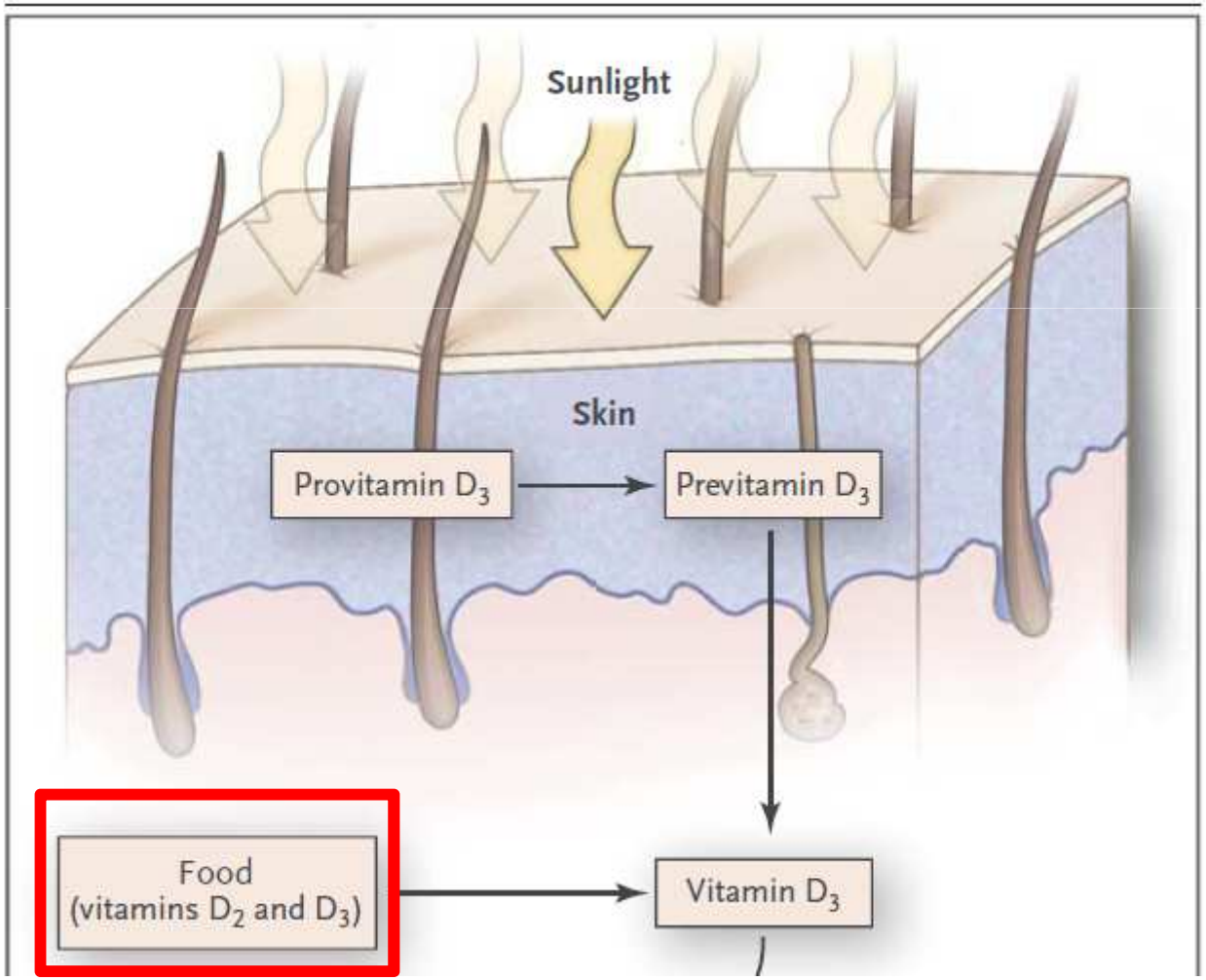


(Saggese G et al. Riv Ital Pediatr 18: 30, 1992)

Vitamin D Insufficiency

Clifford J. Rosen, M.D.

N Engl J Med 2011;364:248-54.



Vitamin D is initially generated in the skin from the nonenzymatic conversion of provitamin D3 to previtamin D3.

Dietary intake of vitamin D is usually relatively limited, since few foods, with the exception of certain kinds of fish, contain sizable amounts; supplements are commonly used.

Vitamin D Insufficiency

Clifford J. Rosen, M.D.

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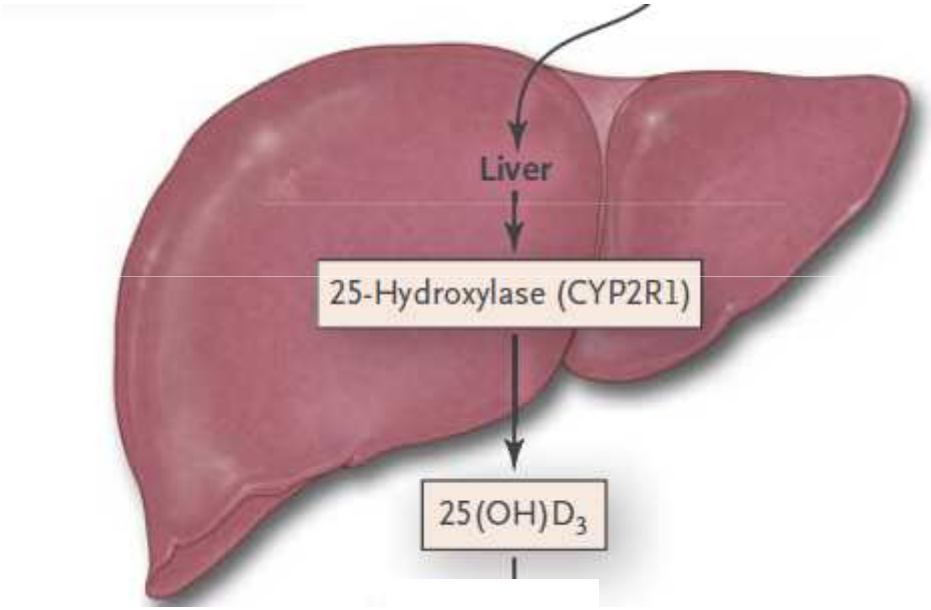
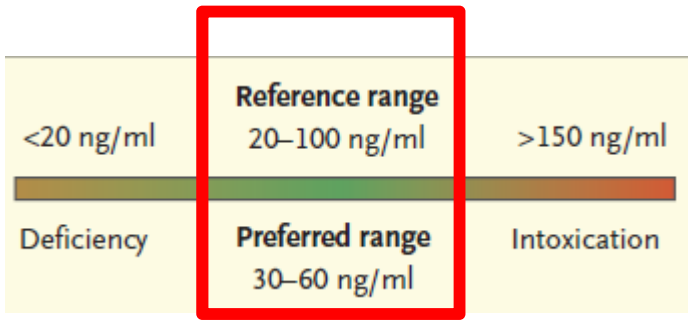


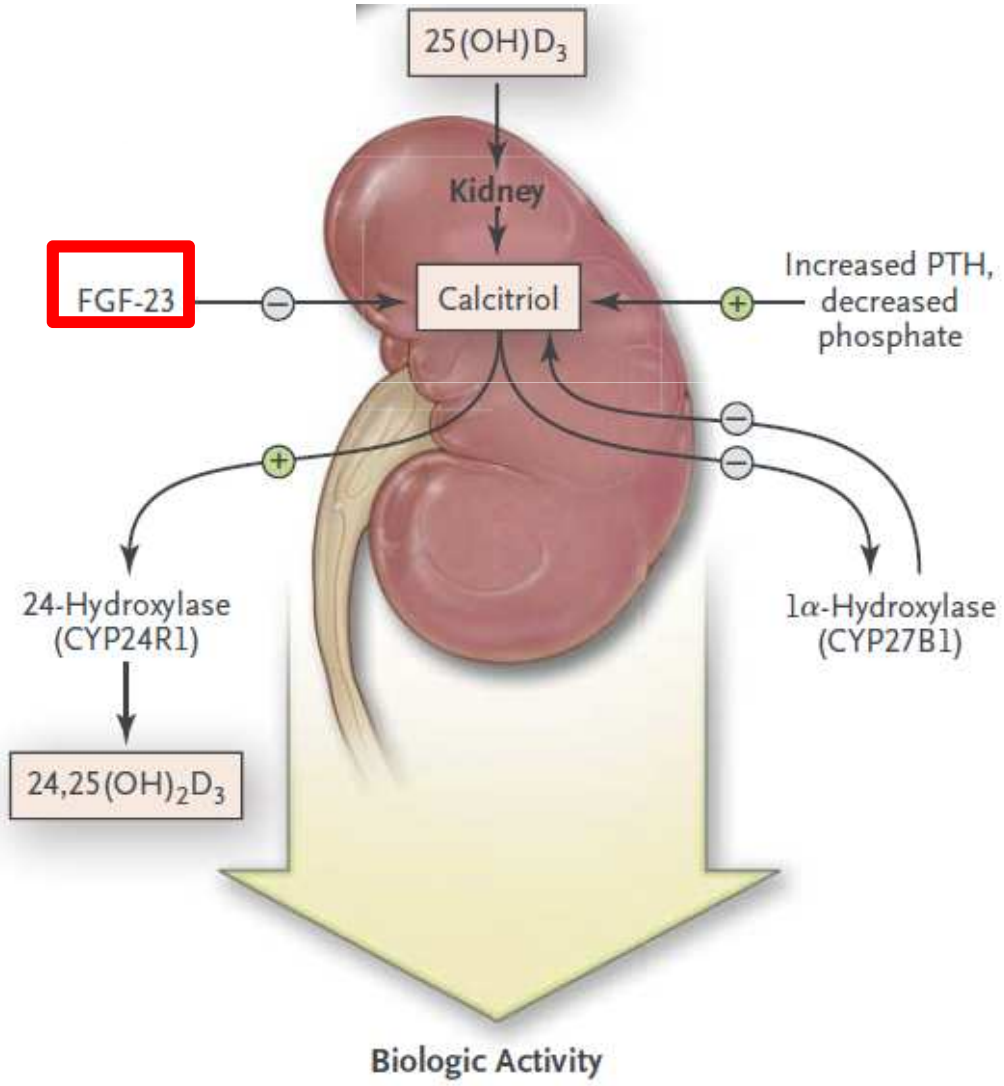


Vitamin D is either stored in adipose tissue or converted in the liver by the enzyme 25-hydroxylase to 25-hydroxyvitamin D3 (25[OH]D3), the form that circulates in the highest concentration and reflects solar and dietary exposure.

Vitamin D Insufficiency

Clifford J. Rosen, M.D.

N Engl J Med 2011;364:248-54.



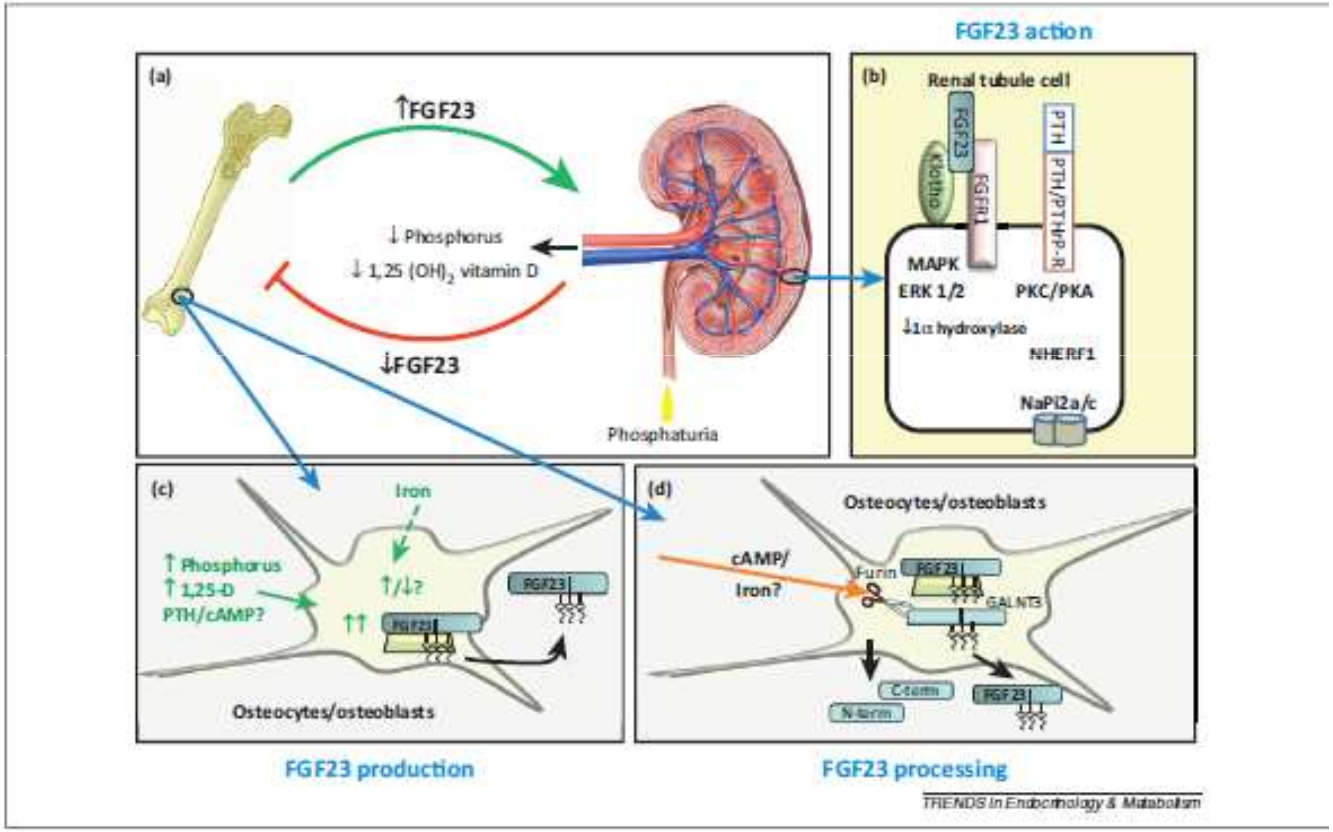
It is converted to the active metabolite, 1,25-hydroxyvitamin D or calcitriol, in the kidney, although other tissues have 1α-hydroxylase enzymatic activity. The synthesis of calcitriol is enhanced (+) by increasing levels of parathyroid hormone (PTH), which rise in response to lower levels of serum calcium. Reduced levels of serum phosphate can also increase (+) the production of calcitriol. **Its synthesis is suppressed (–) by the production of fibroblast growth factor 23 (FGF-23), which is secreted by osteocytes in the bone matrix**. Calcitriol inhibits the activity of 1α-hydroxylase and stimulates the activity of 24-hydroxylase , an enzyme that promotes production of 24,25(OH)2D3, a vitamin D product that is not biologically active.

Fibroblast growth factor 23: state of the field and future directions

Trends in Endocrinology and Metabolism

In press

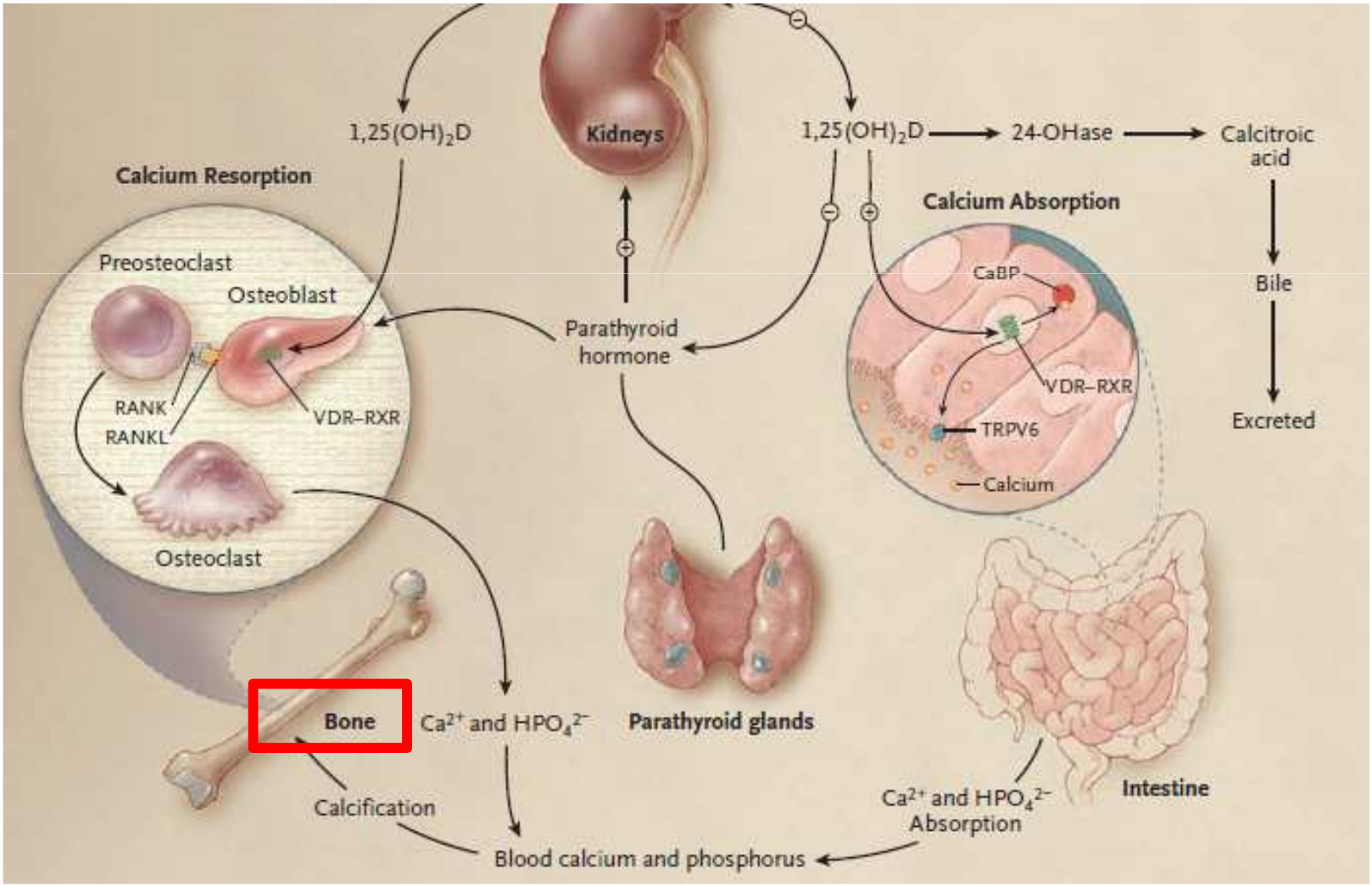
Nisan Bhattacharyya, William H. Chong, Rachel I. Gafni and Michael T. Collins



Vitamin D Deficiency

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

N Engl J Med 2007;357:266-81.

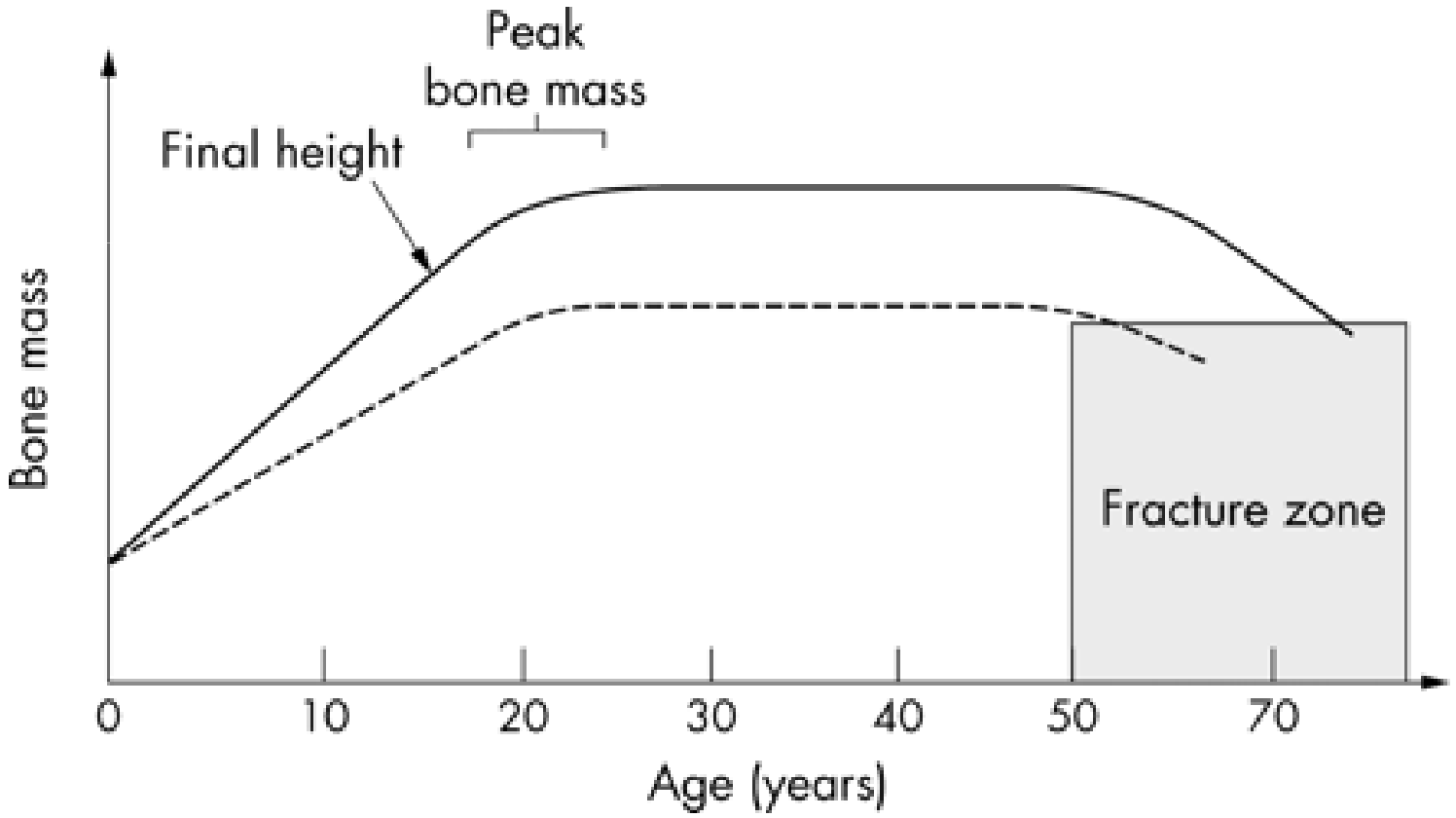


REVIEW

Bone mass acquisition in healthy children

J H Davies, B A J Evans, J W Gregory

Arch Dis Child 2005;**90**:373–378.



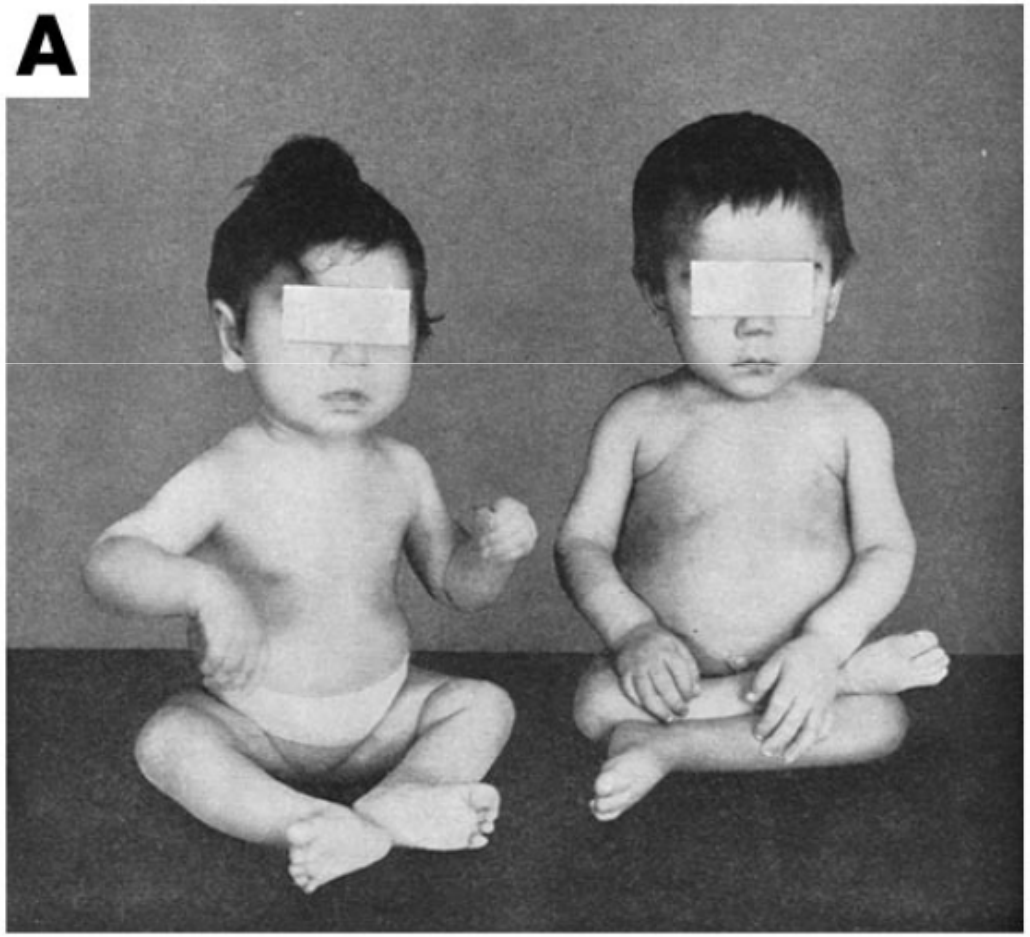
EVOLUZIONE DELLE CONOSCENZE

1° fase : comprensione del metabolismo della vitamina D e

della patogenesi del rachitismo.

The Journal of Clinical Investigation

Volume 116 Number 8 August 2006



Le "performance" da vitamina D: non solo rachitismo!

Sergio Bernasconi

Not all rickets is vitamin D deficiency

Meghan Treitz

Current Opinion in Pediatrics 2010, 22:829–832

Table 1 Classification and biochemical findings in rickets

Type of rickets	Cause	Calcium	Phosphate	Alkaline phosphatase	Parathyroid hormone	25(OH)D	1,25$(OH)_2$D	Urine calcium	TmP/GFR
Vitamin D-deficient	Insufficient 1,25$(OH)_2$D (due to diet, inadequate sun exposure, or malabsorption) which leads to inadequate calcium absorption	N or ↓	↓	↑	↑	↓	N or ↑	↓ or N	
Calcium-deficient	Insufficient dietary calcium	↓	↓		↑	N	↑	↓	
Vitamin D-dependent type 1	Insufficient 1,25$(OH)_2$D due to mutation in the 25-hydroxyvitamin D-1α-hydroxylase gene which leads to inadequate calcium absorption	↓	↓ or N	↑↑	↑	N	↓↓	↓	
Vitamin D-dependent type 2	Mutation in vitamin D receptor gene resulting in end-organ resistance to 1,25$(OH)_2$D	↓	↓ or N	↑↑	↑	N	↑↑	↓	
X-linked hypophosphatemic	Mutation in the PHEX gene resulting in increased renal loss of phosphate	N	↓↓	↑	N	N	N or ↓	↓	↓
Autosomal dominant hypophosphatemic		N	↓		N	N	N	N	↓
Hereditary hypophosphatemic with hypercalcuria		N	↓↓	↑	N or ↓	N	↑	↑	↓
Fanconi syndrome	Renal tubular damage resulting in increased renal loss of phosphate	N	↓		N or ↑	N	N or ↓	N or ↑	

↓, decreased; ↑, increased; N, normal; TmP/GFR, maximum tubular phosphate transport per glomerular filtration rate, calculated from TRP using a nomogram. Adapted from [1–3].

Le "performance" da vitamina D: non solo rachitismo!

Sergio Bernasconi

EVOLUZIONE DELLE CONOSCENZE

1° fase : comprensione del metabolismo della vitamina D e della patogenesi del rachitismo.

Terapia

EVOLUZIONE DELLE CONOSCENZE

1° fase : comprensione del metabolismo della vitamina D e della patogenesi del rachitismo.

Terapia

Profilassi

Le "performance" da vitamina D: non solo rachitismo!
Sergio Bernasconi

Prevention. Cod-liver oil has been given as preventative medicine for decades

(*left, British* children in 1938 are presumably getting their spoonful).

APPORTI RACCOMANDATI DI VITAMINA D DURANTE L'ETÀ EVOLUTIVA

Età	LARN*-'96 UI/die
Lattanti	
0 - 6 mesi	400 - 1000
6 - 12 mesi	400 - 1000
Bambini	
1 - 3 anni	400
4 - 10 anni	0 – 400
Adolescenti	
11 - 18 anni	0 - 600

° tutti gli allattati al seno o che assumono < 500 ml/die di una formula supplementata con 400 UI/l.

EVOLUZIONE DELLE CONOSCENZE

2° fase : "scomparsa" del rachitismo nei Paesi economicamente sviluppati

RACHITISMO CARENZIALE NEI PAESI IN VIA DI SVILUPPO

Principali fattori etiologici

Ridotta sintesi di vitamina D
(scarsa esp.solare,pigment.melaninica,eccessiva copertura)

Deficienza materna di vitamina D

Prolungato allattamento al seno senza profilassi con vit.D

Ridotto apporto dietetico di calcio

Ridotto assorbimento intestinale di calcio
(eccessivo consumo di alimenti ad elevato contenuto di fitati)

Alterato metabolismo vit. D → aumentato catabolismo 25-OH-D

Fattori genetici

EVOLUZIONE DELLE CONOSCENZE

3° fase : ricomparsa del rachitismo nei Paesi economicamente sviluppati.

Science in medicine

Resurrection of vitamin D deficiency and rickets

Michael F. Holick

Department of Medicine, Section of Endocrinology, Nutrition, and Diabetes, and Vitamin D, Skin and Bone Research Laboratory, Boston University Medical Center, Boston, Massachusetts, USA.

The Journal of Clinical Investigation 116, 8,2062, 2006

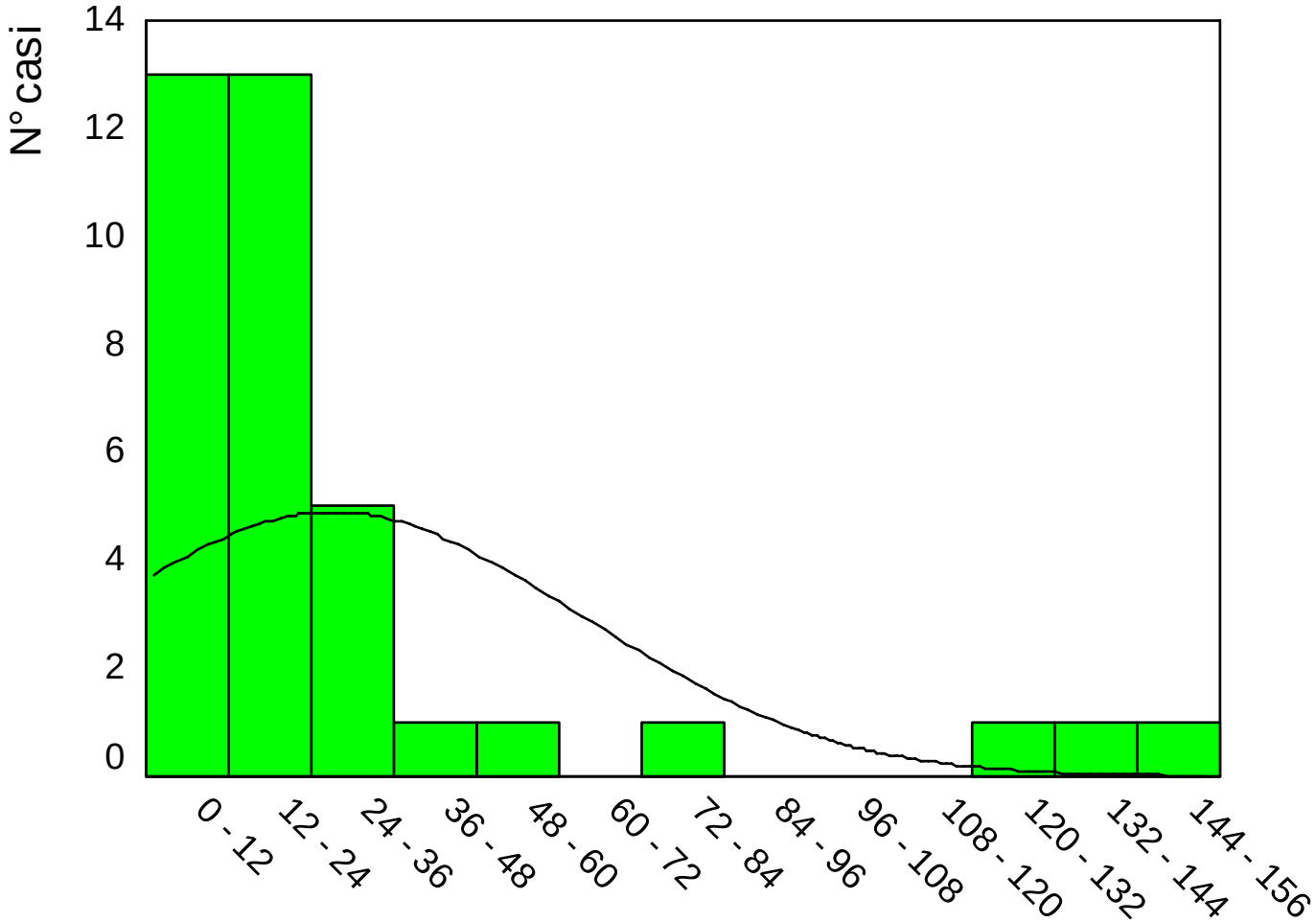
The re-emerging burden of rickets: a decade of experience from Sydney

P D Robinson, W Högler, M E Craig, C F Verge, J L Walker, A C Piper, H J Woodhead, C T Cowell, G R Ambler

Arch. Dis. Child. 2006;91;564-568

Clinica Pediatrica Università di Parma 1999-2004

Distribuzione per classi di età



R A C H I T I S M O

CAUSE DI UNA RICOMPARSA DEL RACHITISMO

- immigrazione di soggetti a rischio per motivi di pigmentazione cute e culturali
- minore esposizione al sole (motivi sociali, ignoranze igieniche, prevenzione melanoma, etc)
- aumento dell'allattamento al seno e di deficit di vit D nelle madri
- aumento bambini a rischio per problemi medici (diete, terapie, sopravvivenza prematuri ed altri cronici, etc)
- caduta di attenzione per il problema da parte dei pediatri e dei sanitari

EVOLUZIONE DELLE CONOSCENZE

4° fase :

- Studi epidemiologici

A global representation of vitamin D status in healthy populations

Arch Osteoporos 2012

D. A. Wahl · C. Cooper · P. R. Ebeling · M. Eggersdorfer · J. Hilger · K. Hoffmann · R. Josse · J. A. Kanis · A. Mithal · D. D. Pierroz · J. Stenmark · E. Stöcklin · B. Dawson-Hughes

20ng/ml

GREEN	>75 nmol/L
YELLOW	50-74 nmol/L
ORANGE	25-49 nmol/L
RED	<25 nmol/L

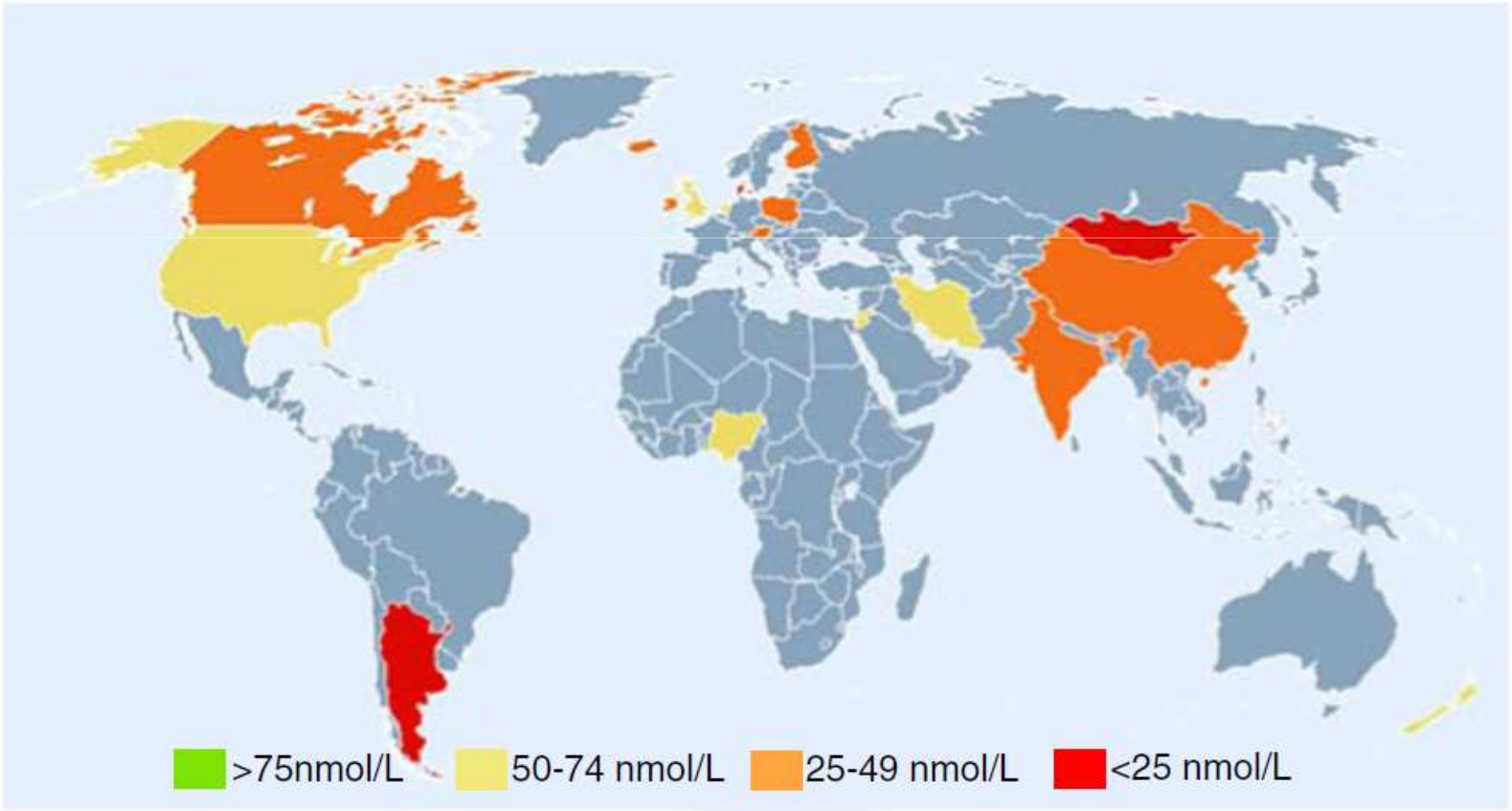
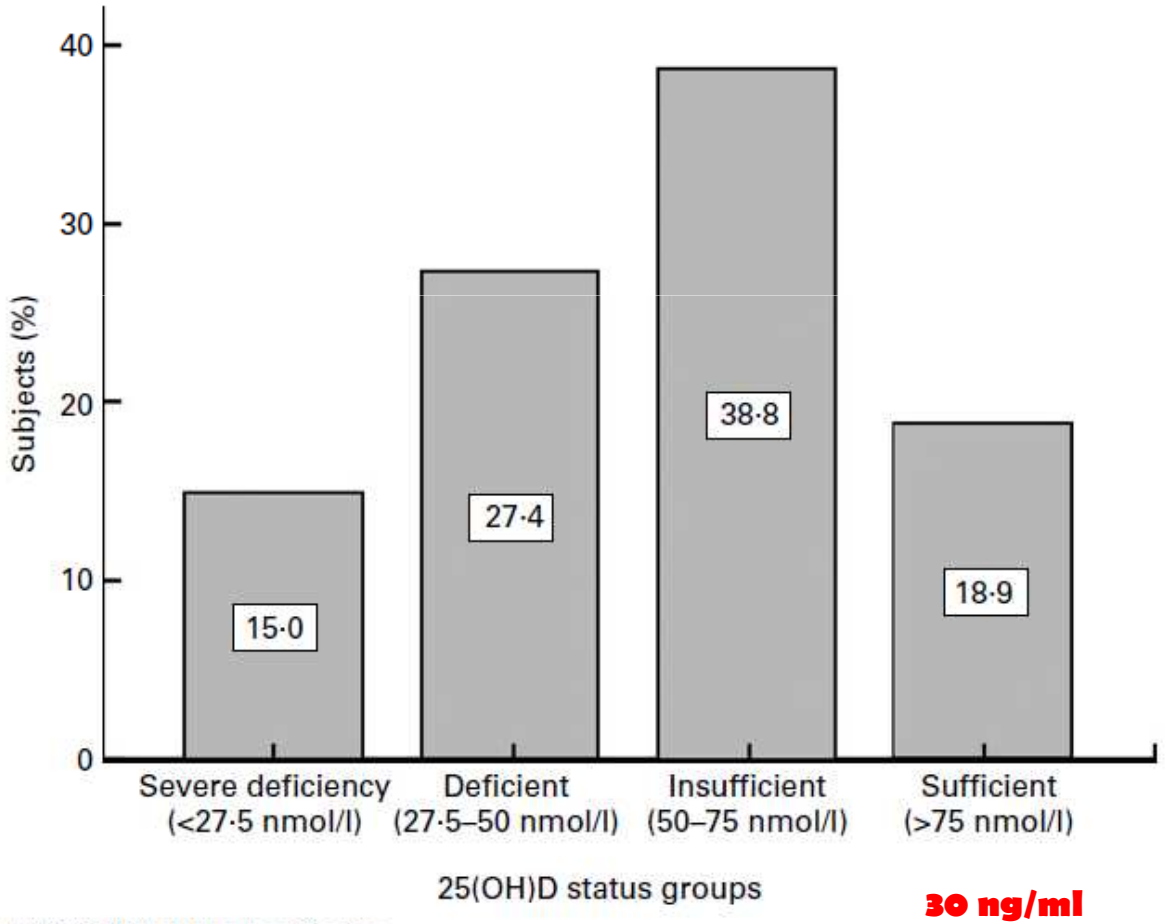


Fig. 1 Vitamin D status in children and adolescents (1–18 years) around the world when available; winter values were used to calculate the mean 25(OH)D levels

Vitamin D status among adolescents in Europe: the Healthy Lifestyle in Europe by Nutrition in Adolescence study

British Journal of Nutrition (2012), **107**, 755–764



30 ng/ml

Fig. 1. 25-Hydroxycholecalciferol (25(OH)D) status classification.

Is vitamin D status known among children living in Northern Italy?

Giuseppina Marrone · Ilaria Rosso · Raffaella Moretti · Francesca Valent · Carla Romanello

Eur J Nutr (2012) 51:143–149

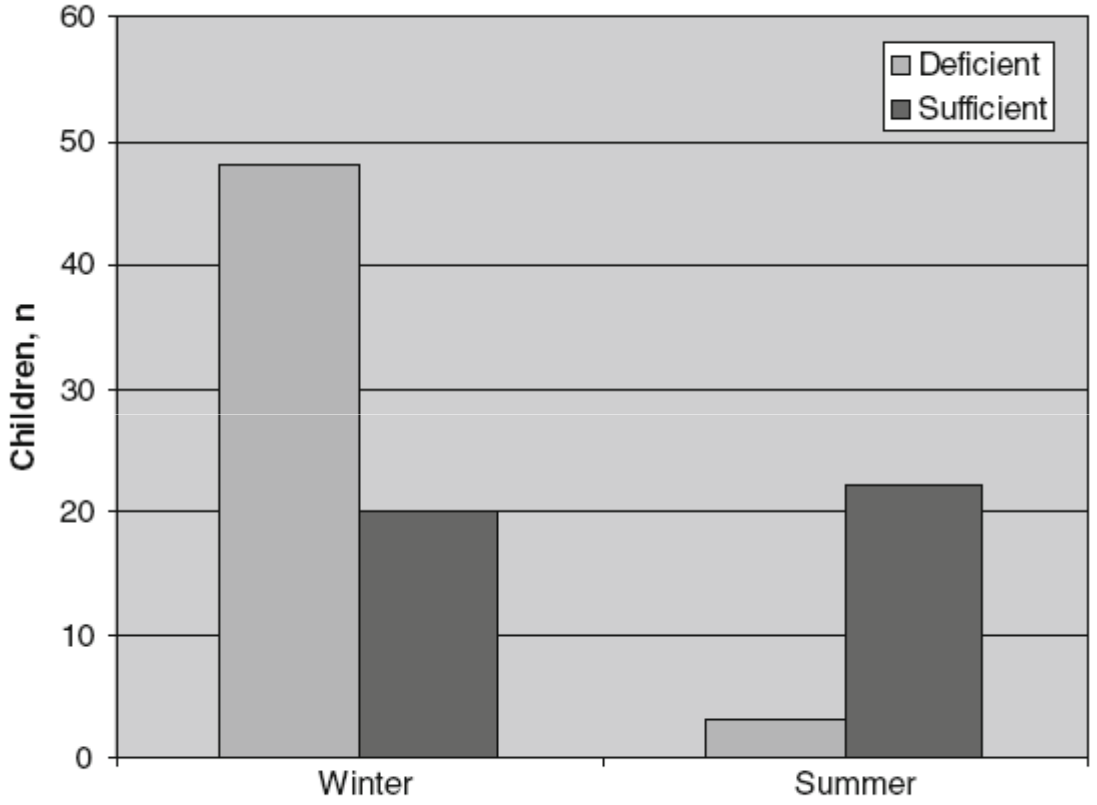


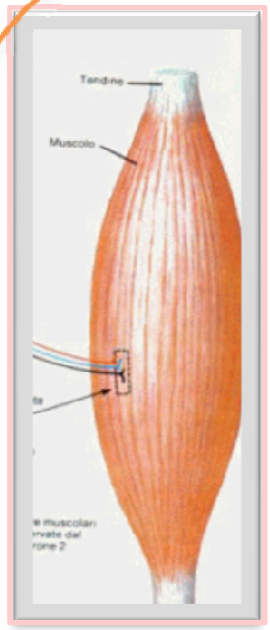
Fig. 1 25OHD concentration in winter (November–May) and in summer (June–October). Chi-square, $p < 0.0001$

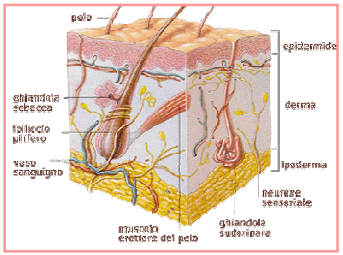
EVOLUZIONE DELLE CONOSCENZE

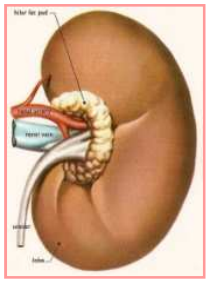
4° fase :

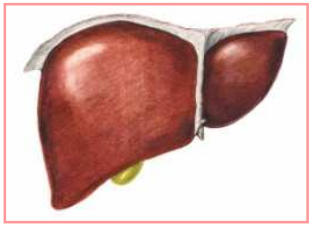
- Studi epidemiologici

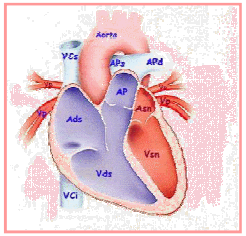
- Evidenze di azioni extra metabolismo calcio della vit. D.

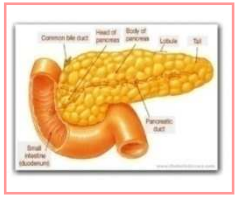


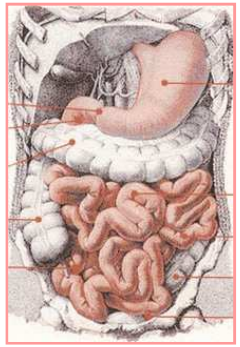




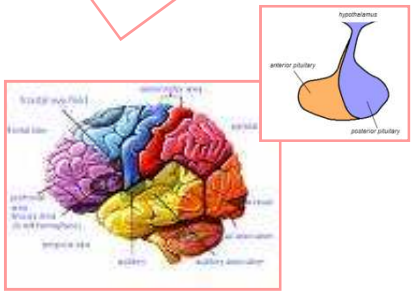


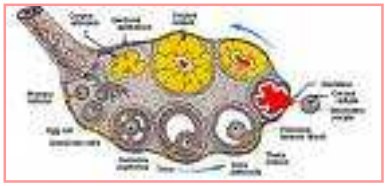


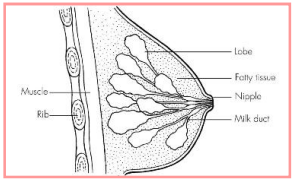


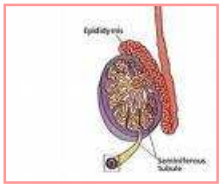


Recettore VITAMINA D









Holick MF. N Engl J Med, 2007; 357:266-81

Bouillon R et al. Endocr Rev, 2008; 29:726-76

EVOLUZIONE DELLE CONOSCENZE

5° fase :

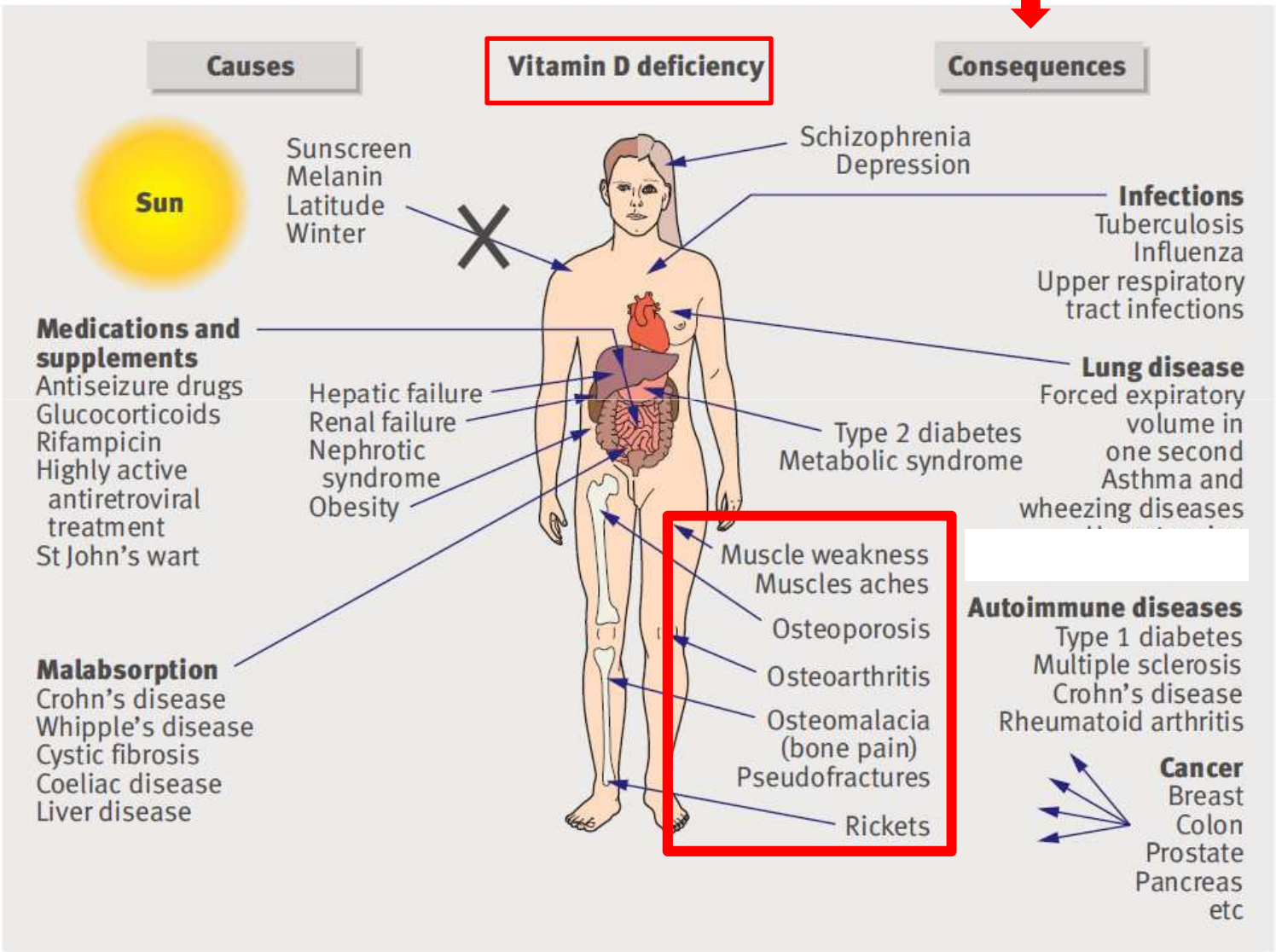
- Ruolo della carenza di vit. D in vari stati patologici

Deficiency of sunlight and vitamin D

Fortification of foods and advice on sensible sun exposure are urgently needed

Michael F Holick

BMJ 2008;336:1318-9



Causes and consequences of vitamin D deficiency

Vitamin D, Calcium, and Dairy Intakes and Stress Fractures Among Female Adolescents

Kendrin R. Sonneville, ScD, RD; Catherine M. Gordon, MD, MSc; Mininder S. Kocher, MD, MPH; Laura M. Pierce, BA; Arun Ramappa, MD; Alison E. Field, ScD

Arch Pediatr Adolesc Med. 2012;166(7):595-600.

Table 2. Age-Adjusted and Fully Adjusted Associations of Dairy, Vitamin D, and Calcium Intakes With Stress Fracture Among All Girls in the Growing Up Today Study

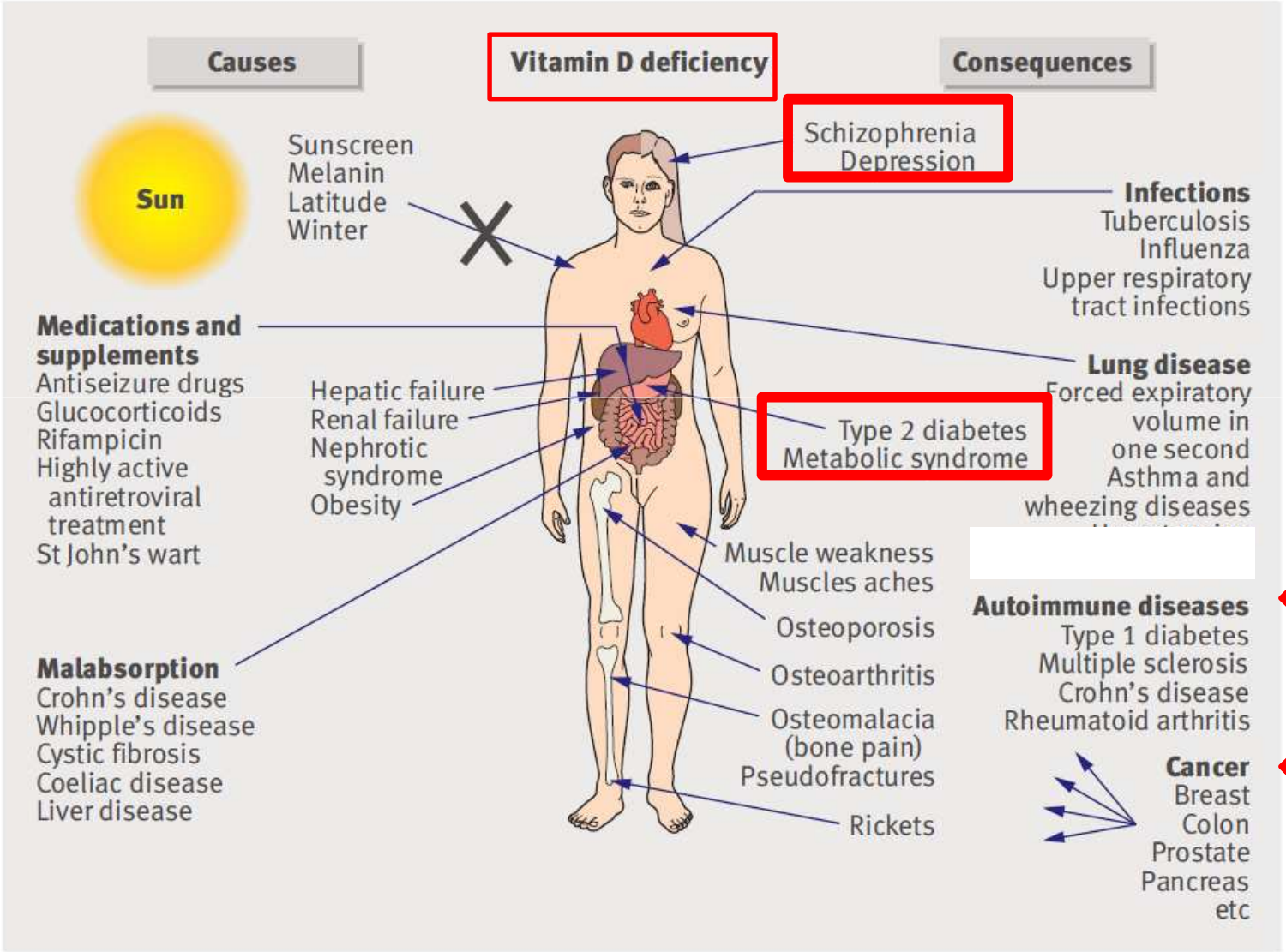
	HR (95% CI)	
Intake	**Age-Adjusted**	**Fully Adjusted[a]**
Dairy		
Servings/d		
0	1 [Reference]	1 [Reference]
1	1.28 (0.87-1.89)	1.21 (0.81-1.81)
2	0.98 (0.64-1.52)	0.91 (0.58-1.43)
≥3	1.13 (0.72-1.75)	1.02 (0.65-1.61)
P_{trend}	.83	.82
Vitamin D		
Quintile[b]		
1	1 [Reference]	1 [Reference]
2	0.93 (0.59-1.49)	0.95 (0.59-1.55)
3	0.86 (0.53-1.38)	0.72 (0.42-1.24)
4	0.92 (0.58-1.47)	0.78 (0.44-1.39)
5	0.72 (0.44-1.19)	0.49 (0.24-1.01)
P_{trend}	.25	.07
Calcium		
Quintile[c]		
1	1 [Reference]	1 [Reference]
2	0.93 (0.56-1.54)	0.94 (0.55-1.61)
3	1.12 (0.69-1.83)	1.28 (0.74-2.22)
4	0.87 (0.52-1.44)	0.99 (0.54-1.81)
5	1.22 (0.76-1.94)	1.57 (0.77-3.17)
P_{trend}	.52	.29

Deficiency of sunlight and vitamin D

Fortification of foods and advice on sensible sun exposure are urgently needed

Michael F Holick

BMJ 2008;336:1318-9



Causes and consequences of vitamin D deficiency

Vitamin D metabolism, functions and needs: from science to health claims

S. Battault · S. J. Whiting · S. L. Peltier · S. Sadrin · G. Gerber · J. M. Maixent

Eur J Nutr

2012

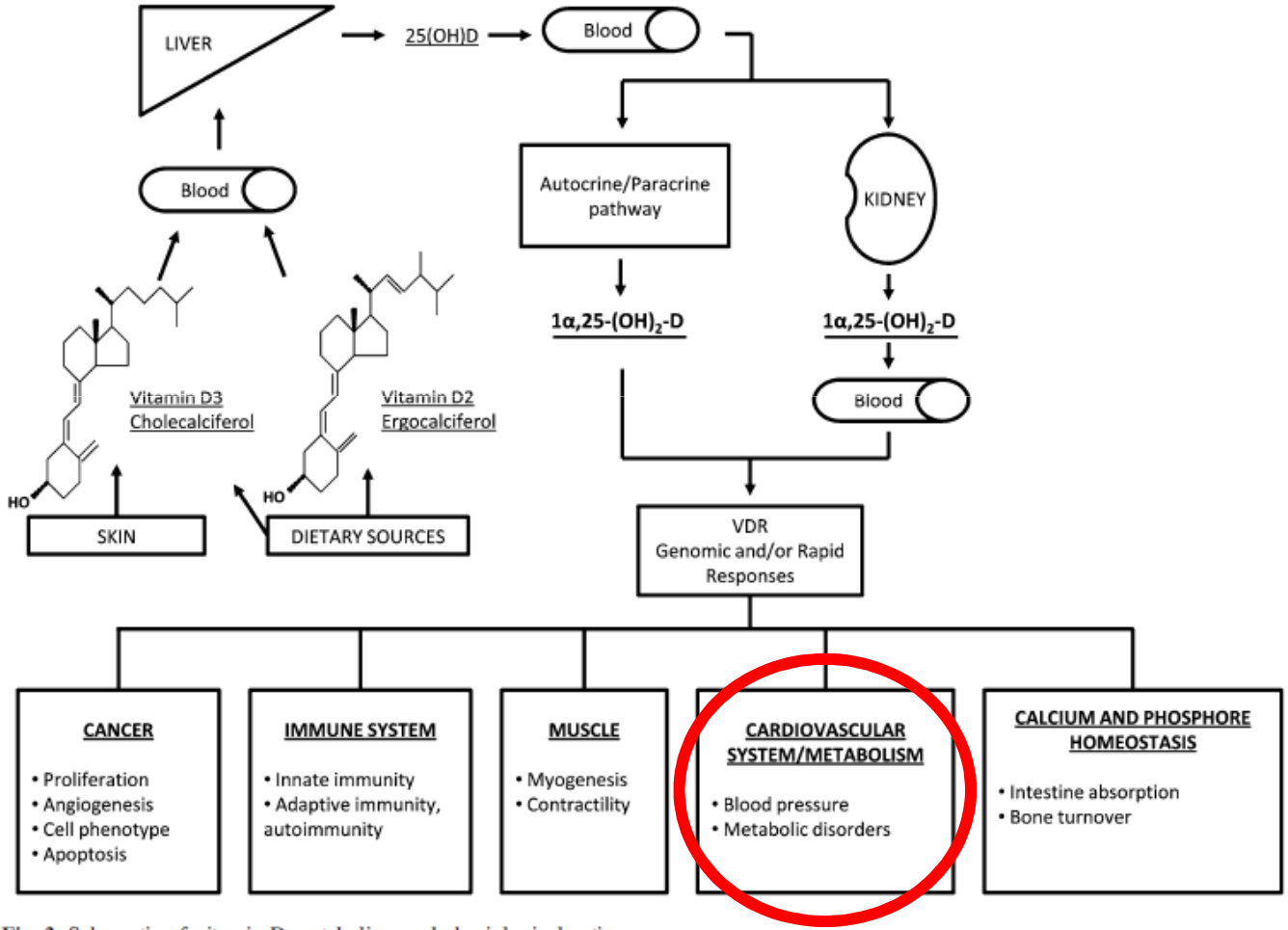
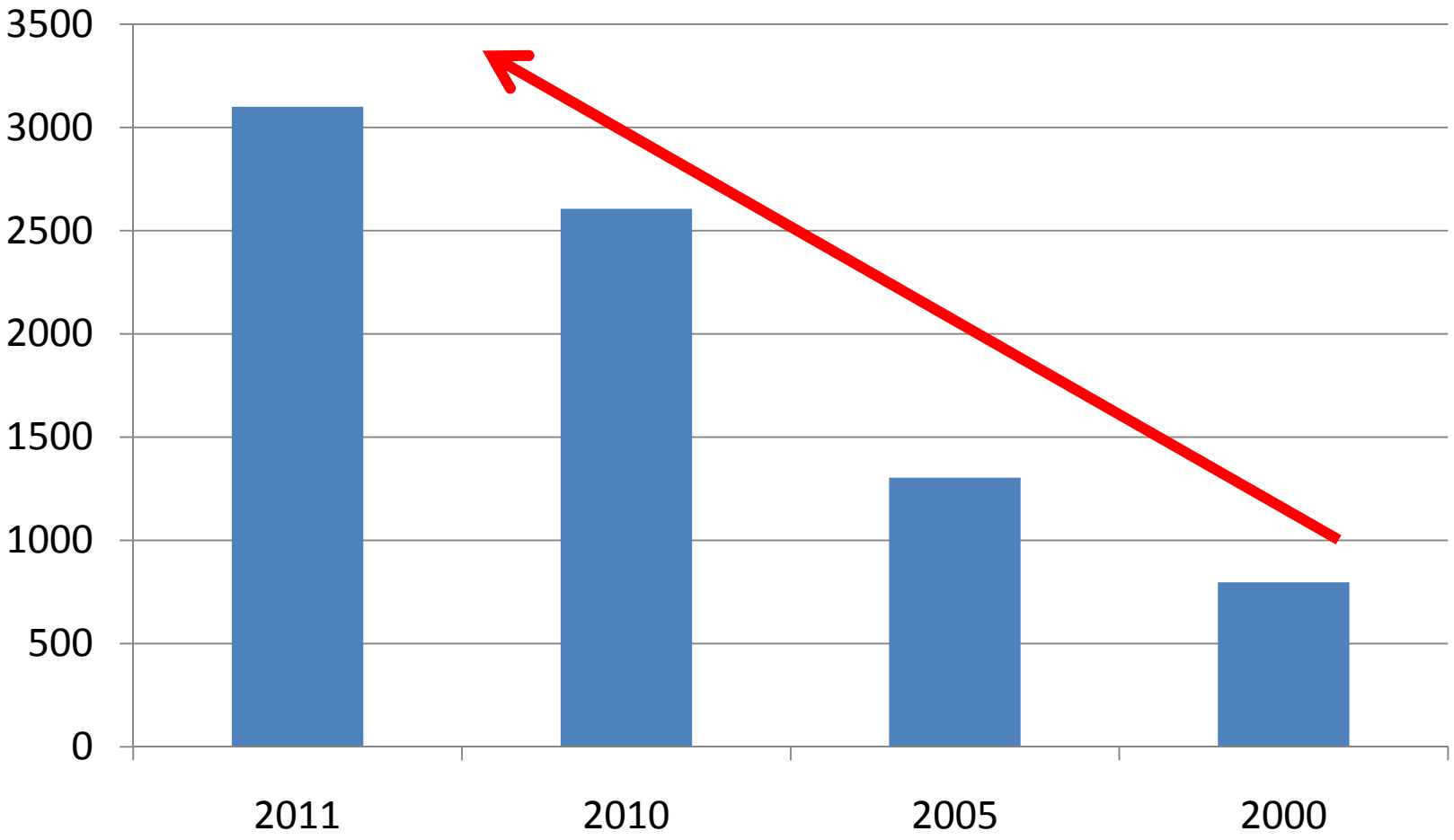


Fig. 2 Schematic of vitamin D metabolism and physiological actions

Le "performance" da vitamina D: non solo rachitismo!
Sergio Bernasconi

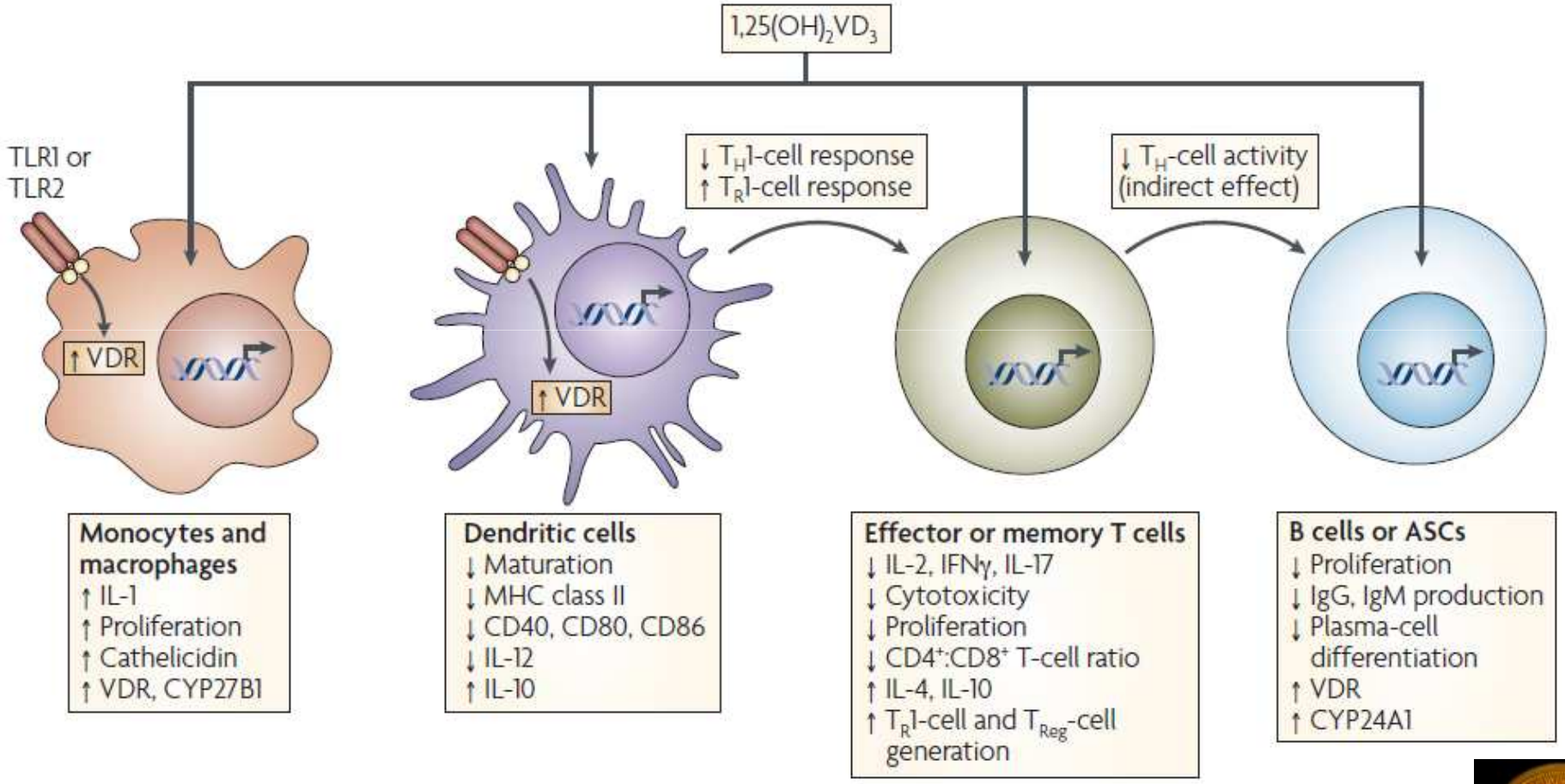
n. pubblicazioni con vit D nel titolo o nell'abstract



Vitamin effects on the immune system: vitamins A and D take centre stage

J. Rodrigo Mora*, Makoto Iwata‡ and Ulrich H. von Andrian§

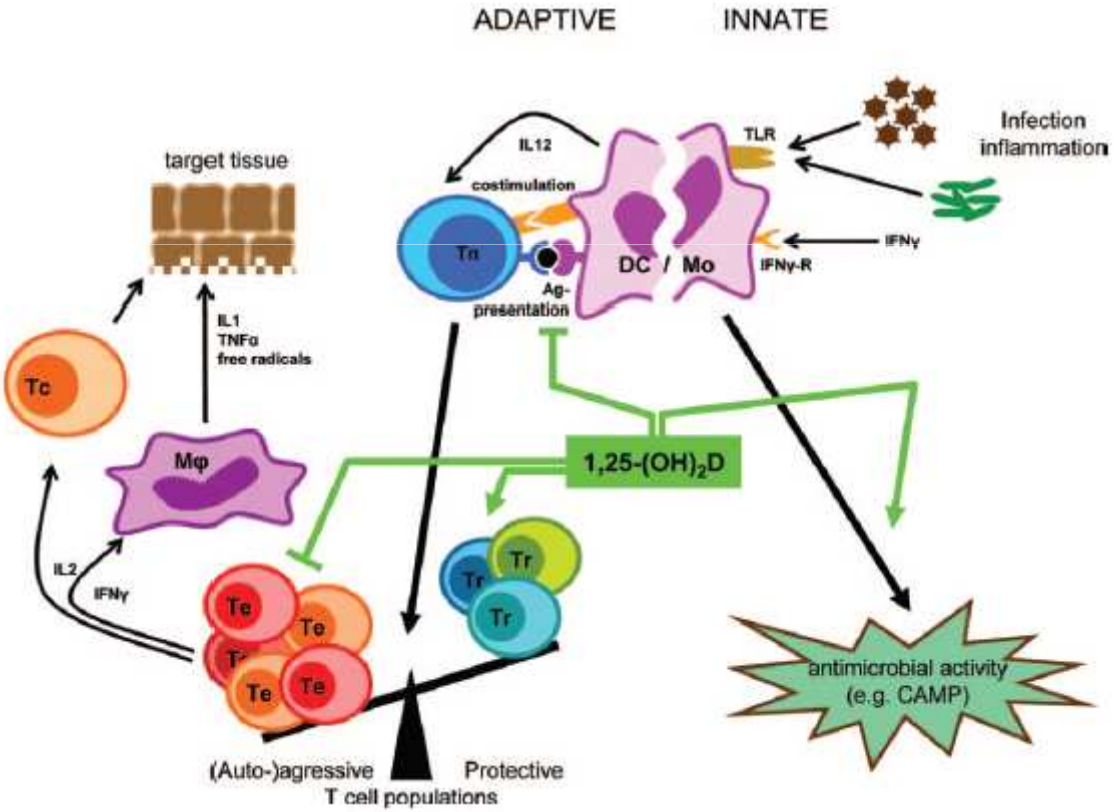
NATURE REVIEWS | IMMUNOLOGY
VOLUME 8 | SEPTEMBER 2008



Vitamin D and Human Health: Lessons from Vitamin D Receptor Null Mice

Roger Bouillon, Geert Carmeliet, Lieve Verlinden, Evelyne van Etten, Annemieke Verstuyf, Hilary F. Luderer, Liesbet Lieben, Chantal Mathieu, and Marie Demay

Endocrine Reviews 29(6):726–776



1,25-Dihydroxyvitamin D improved the free fatty-acid-induced insulin resistance in cultured C2C12 cells

Qiu Gen Zhou
Fan Fan Hou*
Zhi Jian Guo
Min Liang
Guo Bao Wang
Xun Zhang

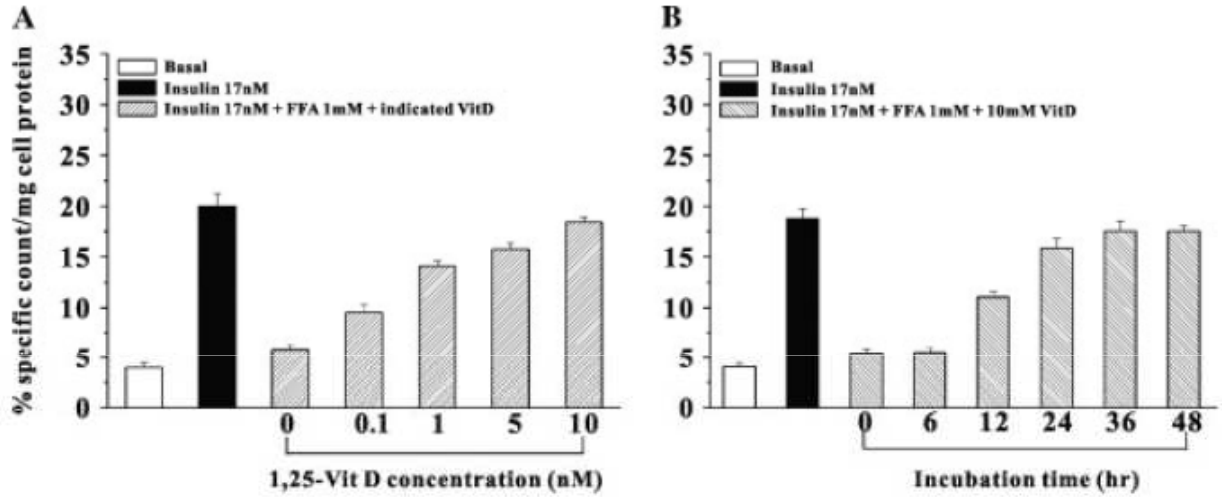


Figure 1. Effect of 1,25-dihydroxyvitamin D on 2-deoxyglucose uptake in myotubes treated with FFA. (A) Dose-dependent effect of 1,25-dihydroxyvitamin D on 2-deoxyglucose uptake. Myotubes were treated with 1 mM FFA alone or co-treated with indicated concentration of 1,25-dihydroxyvitamin D for 48 h. The cells were then stimulated with insulin (17 nM) for 15 min. Glucose uptake was quantified with radiolabelled 2-deoxyglucose. The values were expressed as mean ± SD of three independent experiments. ANOVA, $p < 0.001$. (B) Time course of 1,25-dihydroxyvitamin D on 2-deoxyglucose uptake. Myotubes were treated with 1 mM FFA alone or co-treated with 1,25-dihydroxyvitamin D (10 nM) for the indicated time. The cells were then stimulated with insulin (17 nM) for 15 min. Glucose uptake was quantified with radiolabelled 2-deoxyglucose. The values were expressed as mean ± SD of three independent experiments. ANOVA, $p < 0.01$

Vitamin D Serum Levels and Markers of Asthma Control in Italian Children

Iolanda Chinellato, MD, Michele Piazza, MD, Marco Sandri, MD, Diego Peroni, MD,
Giorgio Piacentini, MD, and Attilio L. Boner, MD

J Pediatr 2011;158:437-41

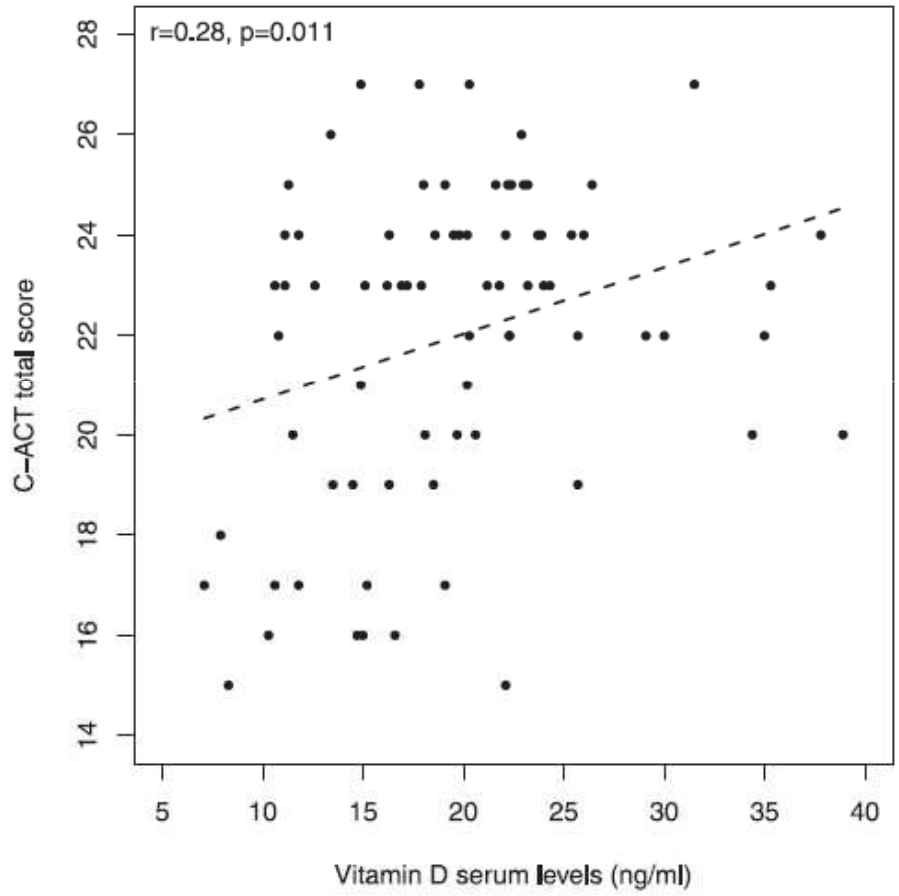
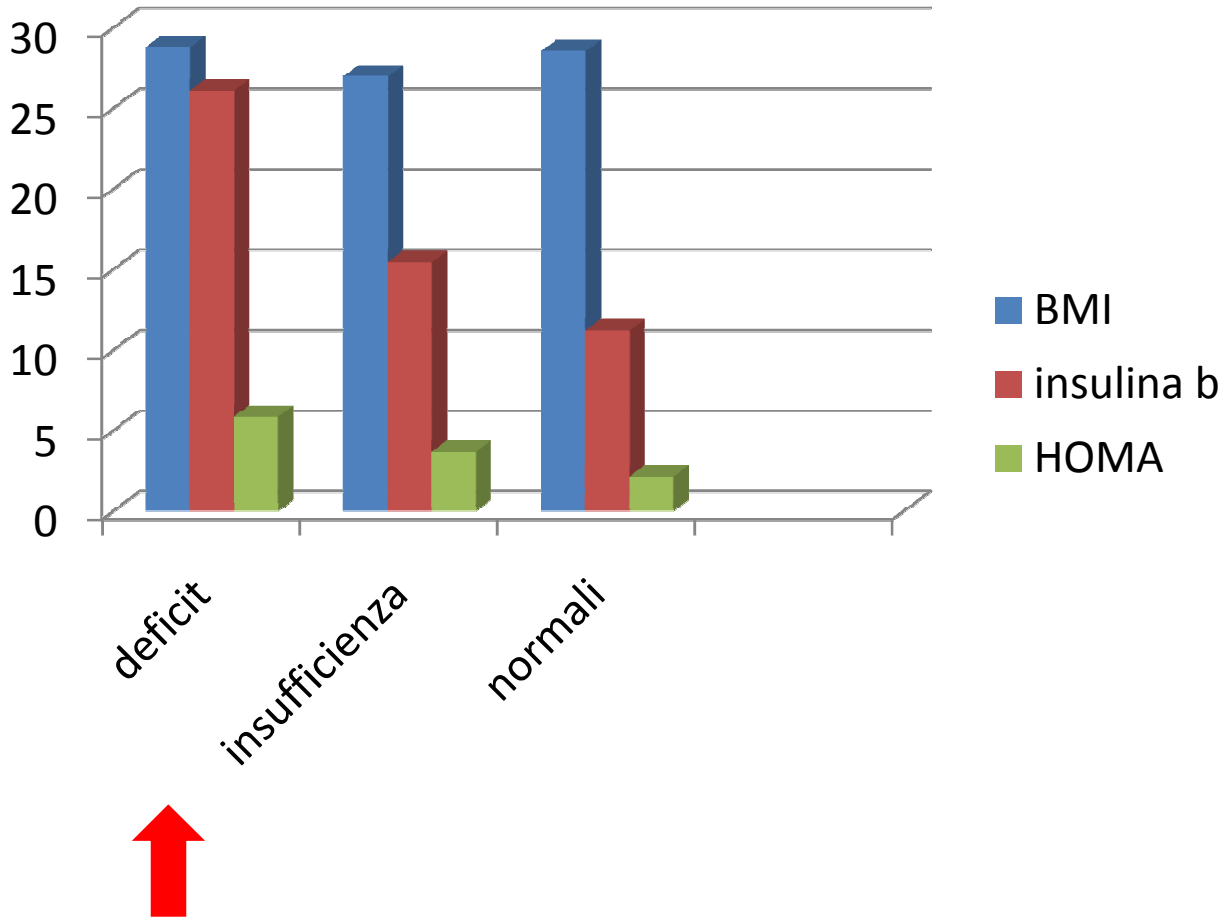
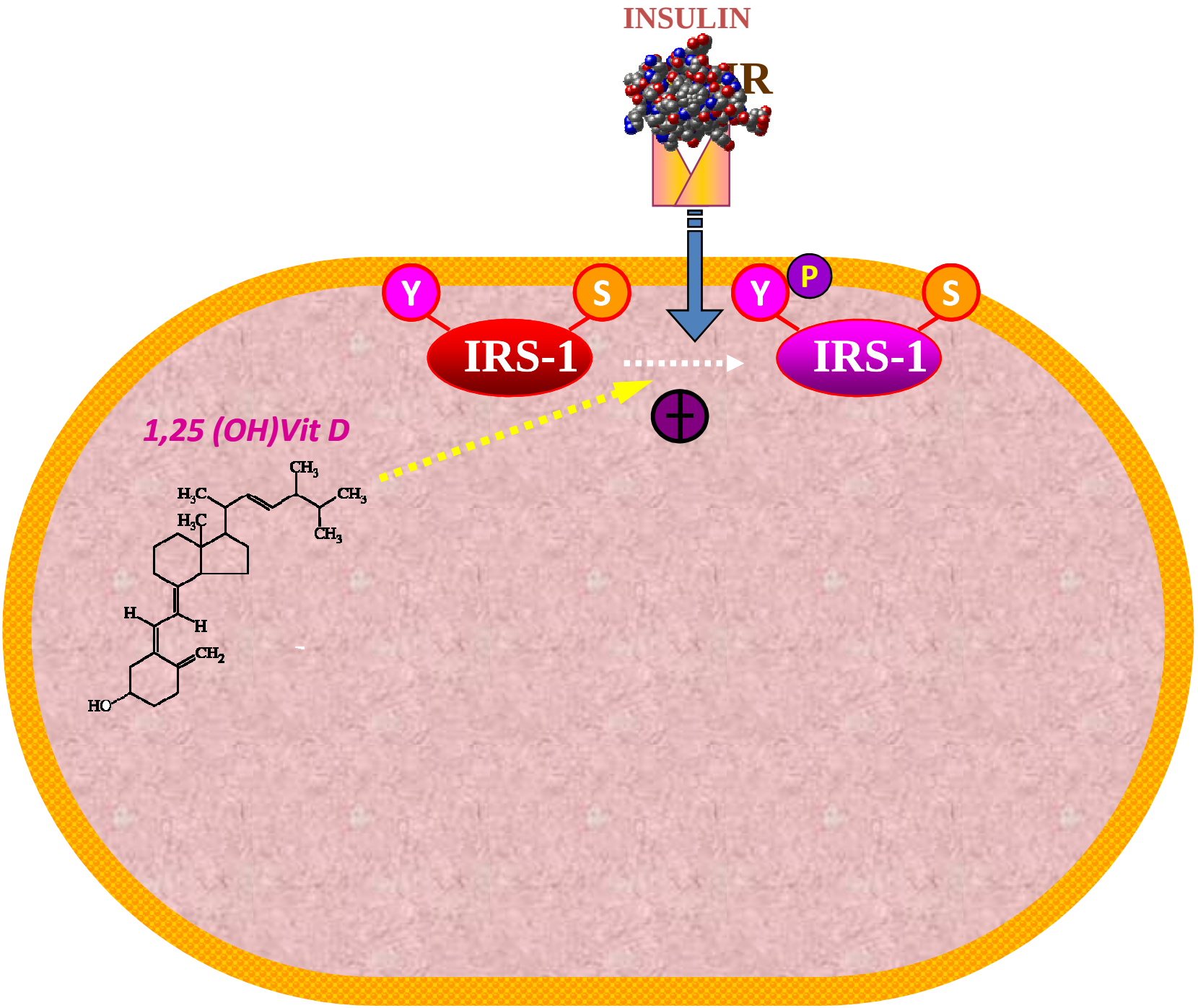


Figure 1. Scatter plot shows the relationship existing between vitamin D serum levels and C-ACT scores. Partial correlation analysis is reported.

The relation of vitamin D deficiency with puberty and insulin resistance in obese children and adolescents

J Pediatr Endocr Met 2012;25(1-2):83—87 © 2012




INSULIN
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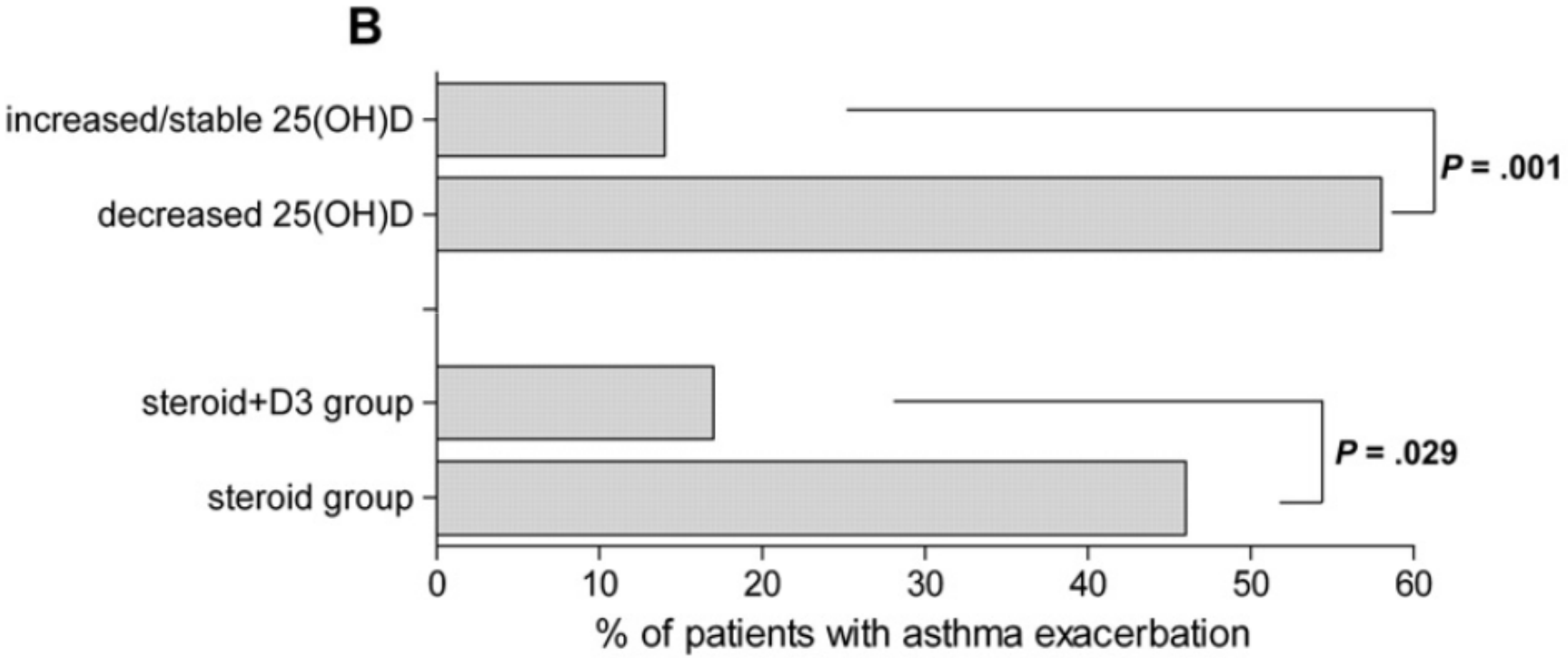
IRS-1
1,25 (OH)Vit D
CH3
H3C
CH3
H3C
CH3
H
H
CH2
HO

Vitamin D supplementation in children may prevent asthma exacerbation triggered by acute respiratory infection

Paweł Majak, MD, PhD
Małgorzata Olszowiec-Chlebna, MD
Katarzyna Smejda, MD
Iwona Stelmach, MD, PhD

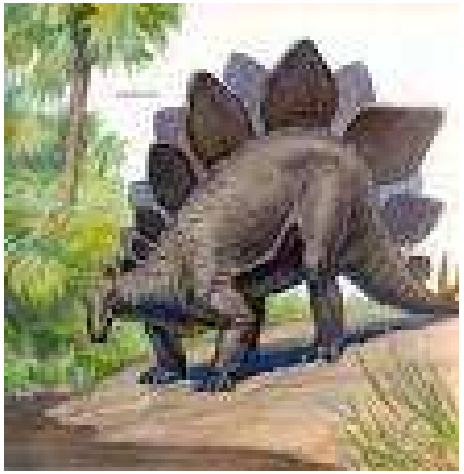
J ALLERGY CLIN IMMUNOL
MAY 2011



Asclepio

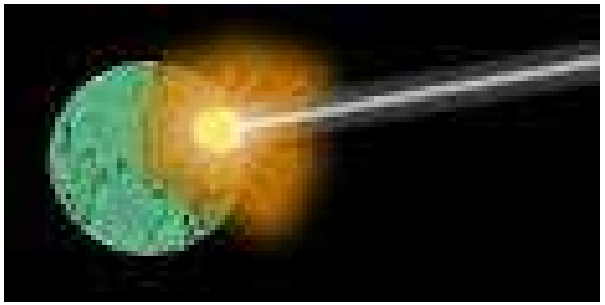
Panacea

Dea che lenisce e risana da tutti i mali, figlia di Asclepio e della ninfa Epione.



La carenza di vitamina D causa la scomparsa dei dinosauri ?

Il primo dinosauro conosciuto apparve approssimativamente 230 milioni di anni fa forse è l'Eoraptor lunensis
L'estinzione di massa del Cretaceo terziario, 65 milioni di anni fa, alla fine del Cretaceo, causò la scomparsa di tutti i dinosauri, con l'eccezione del ramo dei teropodi che, evolvendosi, avevano già portato alla comparsa dei primi uccelli.



Editorial

Vitamin D in asthma: Panacea or true promise?

Adit A. Ginde, MD, MPH,[a] and E. Rand Sutherland, MD, MPH[b,c] *Aurora and Denver, Colo*

J ALLERGY CLIN IMMUNOL
JULY 2010

To the skeptic, the results of many of these studies **seem too good to be true**, for they suggest that providing supplemental vitamin D to patients with asthma and low serum concentrations of vitamin D might

(1) prevent the development of asthma,

(2) reduce impairment and risk in patients who have the disease, and

(3) enhance clinical response to glucocorticoids, the most widely applied and effective treatment for persistent asthma.

Vitamin D Supplementation: What's Known, What to Do, and What's Needed

Stuart T. Haines, Pharm.D., FCCP, and Sharon K. Park, Pharm.D.

(Pharmacotherapy 2012;32(4):354–382)

Table 10. Vitamin D Supplementation: Potential Indications, Dosages, and Level of Evidence

Indication	Recommended Dosage (Duration)	Level of Evidence
General health		
Age 18–65 yrs, no chronic illnesses	Sensible sun exposure (indefinitely)	D
Age ≥ 65 yrs, for bone health	800–2000 IU/day (indefinitely)	A
Age ≥ 65 yrs, for fall prevention	800–5000 IU/day (indefinitely)	A
Age < 18 yrs, no chronic illnesses	400 IU/day (until age 18)	B
Vitamin D deficiency (< 20 ng/ml)	50,000 IU/wk (12 wks) or 50,000 IU 3 times/wk (6 wks)	B
Cardiovascular disease		
Hypertension	800–2000 IU/day (indefinitely)	C
Heart failure	800–2000 IU/day (indefinitely)	D
Atherosclerotic vascular disease	800–2000 IU/day (indefinitely)	D
Statin-induced myopathy	5000 IU/day (12 wks) or 50,000 IU/wk (12 wks)	C
Endocrine disorders		
Diabetes mellitus	800–2000 IU/day (indefinitely)	C
Neurologic disease		
Multiple sclerosis	10,000 IU/day (1 yr)	B
Depression	5000 IU/day (indefinitely)	C
Dementia	800–2000 IU/day (indefinitely)	D
Migraine headache	1200–2000 IU/day (indefinitely)	D
Respiratory disease		
Asthma	800–2000 IU/day (indefinitely)	C
COPD	800–2000 IU/day (indefinitely)	C
Infectious diseases		
Tuberculosis	10,000 IU/day (6 wks) or 100,000 IU every 2 wks (42 days)	B
Upper respiratory tract infections	800–2000 IU/day (indefinitely)	B
Cancer		
Cancer prevention	800–2000 IU/day (indefinitely)	B
Colorectal cancer	800–2000 IU/day (indefinitely)	D
Breast cancer	800–2000 IU/day (indefinitely)	D

Levels of evidence are as follows: A = supported by multiple randomized controlled trials; B = supported by a single randomized controlled trial, multiple uncontrolled studies, or multiple cohort studies; C = supported by a single cohort study or uncontrolled trial; D = epidemiologic association but no data to support supplementation.

EVOLUZIONE DELLE CONOSCENZE

6° fase :

Domande :

- **Di quale intake necessitiamo ?**

INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

Advising the Nation. Improving Health.

Committee to Review Dietary Reference Intakes for Vitamin D and Calcium
Food and Nutrition Board

A. Catharine Ross, Christine L. Taylor, Ann L. Yaktine, and
Heather B. Del Valle, *Editors*

Evaluation, Treatment, and Prevention of Vitamin D Deficiency: an Endocrine Society Clinical Practice Guideline

Michael F. Holick, Neil C. Binkley, Heike A. Bischoff-Ferrari,
Catherine M. Gordon, David A. Hanley, Robert P. Heaney, M. Hassan Murad,
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IOM Committee Members Respond to Endocrine Society Vitamin D Guideline

Clifford J. Rosen, Steven A. Abrams, John F. Aloia, Patsy M. Brannon,
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(*J Clin Endocrinol Metab* 97: 1146–1152, 2012)

Clifford J. Rosen, Steven A. Abrams, John F. Aloia, Patsy M. Brannon, Steven K. Clinton, Ramon A. Durazo-Arvizu, J. Christopher Gallagher, Richard L. Gallo, Glenville Jones, Christopher S. Kovacs, JoAnn E. Manson, Susan T. Mayne, A. Catharine Ross, Sue A. Shapses, and Christine L. Taylor

However, there are three major points of disagreement.

First, we disagree that serum 25-hydroxyvitamin D (25OHD) levels of 30 ng/ml or higher compared with 20 ng/ml provide increased health benefits.

Second, we disagree that all persons are deficient if serum 25OHD levels are below 20 ng/ml.

Third, the guideline incorrectly characterizes several large subgroups as at risk that, as discussed below, do not fit this category.

Vitamin D Supplementation in Infants, Children, and Adolescents

CATHERINE F. CASEY, MD; DAVID C. SLAWSON, MD; and LINDSEY R. NEAL, MD
University of Virginia Medical Center, Charlottesville, Virginia

American Family Physician

March 15, 2010 • Volume 81, Number 6

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	*Evidence rating*	*References*	*Comments*
Infants ingesting less than 1 L (33.8 fl oz) of formula per day, as well as all breastfed or partially breastfed infants, should receive 400 IU of supplemental vitamin D daily.	C	13, 19, 20	Based on disease-oriented evidence and expert opinion
Children and adolescents consuming less than 1 L of vitamin D–fortified milk per day should receive 400 IU of supplemental vitamin D daily.	C	21, 22	Based on disease-oriented evidence and case series
Limiting sunlight exposure may predispose children to vitamin D deficiency.	C	23, 25-27	Based on disease-oriented evidence and expert opinion
The best available biomarker of vitamin D status is serum 25-hydroxyvitamin D levels.	C	28, 29	Based on consensus and disease-oriented evidence
Children at increased risk of vitamin D deficiency may require higher dosages of supplemental vitamin D.	C	32-34	Based on disease-oriented evidence and expert opinion

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to http://www.aafp.org/afpsort.xml.

Le "performance" da vitamina D: non solo rachitismo!
Sergio Bernasconi

Vitamin D supplementation: guidelines and evidence for subclinical deficiency

Pornpoj Pramyothin[a,b] *and Michael F. Holick*[a]

Curr Opin Gastroenterol 2012, 28:139–150

- Difference in the recommendations from the US IOM report and the US Endocrine Society guideline reflects different goals and views on current evidence; future recommendations will be guided by results from vitamin D treatment studies assessing changes in patient outcomes at various 25(OH)D levels.

Uncertain Verdict as Vitamin D Goes On Trial

SCIENCE VOL 337 21 SEPTEMBER 2012

–KAI KUPFERSCHMIDT

Vitamin D on Trial

NAME	PLACE	PARTICIPANTS	DOSE	MAIN OUTCOMES	CURRENT STATE	RESULTS EXPECTED
VITAL	U.S.	20,000, men: 50+ women: 55+	2000 IU D_3 daily	Cancer, Cardiovascular disease	Recruitment to finish end of 2012	2017
FIND	Finland	18,000 men: 60+, women: 65+	1600 IU D_3 daily or 3200 IU D_3 daily	Cancer, Cardiovascular disease, Diabetes	Recruitment started in spring, supplementation to start in autumn	2020
ViDA	New Zealand	5100, 50+	100,000 IU D_3 a month (200,000 IU in June)	Cardiovascular disease, Respiratory disease, Fractures	Recruitment to finish this year	2017
DOHealth	8 European cities	2150, 70+	2000 IU D_3 daily	Infections, Fractures, Blood pressure, Cognitive function, Lower extremity function	Recruiting	2017
VIDAL	U.K.	20,000, 65–84	60,000 IU monthly	Longevity and others	Planned 2-year feasibility study on 1600 patients is recruiting	2020 (if main study gets go-ahead)

Le "performance" da vitamina D: non solo rachitismo!
Sergio Bernasconi

QUALI RACCOMANDAZIONI PER LA PEDIATRIA

NELLA POPOLAZIONE GENERALE ?

Dietary Guidelines for Calcium and Vitamin D: A New Era
Steven A. Abrams
Pediatrics 2011;127;566; originally published online February 21, 2011;
DOI: 10.1542/peds.2010-3576

TABLE 1 Selected Calcium and Vitamin D DRI Values for Children and Adolescents

Age	Calcium, mg/d	Vitamin D, IU/d
	Recommended Intake[a]	Recommended Intake[a]
0–6 mo	200	400
6–12 mo	260	400
1–3 y	700	600
4–8 y	1000	600
9–18 y	1300	600

[a] Recommended intake values are the RDA values for children aged 1 year and older and AI values for infants younger than 1 year.

Intakes vitamina D UI/die

	IOM	AAP	End. Soc.		LARN
	2011	2008	2011		2012
Età				Età	
0-6 mesi	400	400	400-1000	0,5-1 anno	400
6-12 mesi	400	400	400-1000	1-3 anni	400
1-3 anni	600	400	600-1000	4-6 anni	600
4-8 anni	600	400	600-1000	7-10 anni	600
9-18 anni	600	400	600-1000	11-14 anni	600
				15-17 anni	600

Vitamin D: Still a topical matter in children and adolescents. A position paper by the Committee on Nutrition of the French Society of Paediatrics☆

Available online at
SciVerse ScienceDirect
www.sciencedirect.com

M. Vidailhet[a,*], E. Mallet[b], A. Bocquet[c], J.-L. Bresson[d], A. Briend[e], J.-P. Chouraqui[f], D. Darmaun[g], C. Dupont[h], M.-L. Frelut[h], J. Ghisolfi[i], J.-P. Girardet[h], O. Goulet[d], R. Hankard[j], D. Rieu[k], U. Simeoni[l], D. Turck[m,*], Comité de nutrition de la Société française de pédiatrie

7.2.1. In individuals with no underlying risk

Recommendations are as follows *(table III)*:

- in breastfed infants: 1000 to 1200 IU/day throughout breastfeeding;
- in children under 18 months of age consuming milk fortified in vitamin D_3: add an additional 600 to 800 IU/day;
- in children under 18 months of age consuming cow's milk that is not fortified with vitamin D_3: 1000 to 1200 IU/day;
- in children 18 months to 5 years old: 2 80,000- or 100,000-IU doses in winter, 1 in November, the other in February;
- in adolescents from 10 to 18 years old: 2 80,000- or 100,000-IU doses in winter, 1 in November, the other in February, which can be replaced by a single 200,000-IU dose when the risk of forgetting the 2nd dose seems high.

Vitamin D: Still a topical matter in children and adolescents. A position paper by the Committee on Nutrition of the French Society of Paediatrics☆

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M. Vidailhet[a,*], E. Mallet[b], A. Bocquet[c], J.-L. Bresson[d], A. Briend[e], J.-P. Chouraqui[f], D. Darmaun[g], C. Dupont[h], M.-L. Frelut[h], J. Ghisolfi[i], J.-P. Girardet[h], O. Goulet[d], R. Hankard[j], D. Rieu[k], U. Simeoni[l], D. Turck[m,*], Comité de nutrition de la Société française de pédiatrie

Given the current uncertainty as to the causal relationship between vitamin D deficiency and diseases independent of phosphocalcic metabolism, these were not taken into consideration in these guidelines.

Table II
Examples of recommended vitamin D allowances (μg/day) at different ages in 13 European and North American countries.

Year	Country	3 months	9 months	5 years	10 years	15 years	Adults
2004	Germany + Austria + Switzerland	10	10	5	5	5	5
2009	Belgium	10	10	10	10	10–15	10–15
2007	Spain	10	10	10	5	5	5
2001	France	20–25	20–25	5	5	5	5
1996	Italy	10	17.5	5	5	7.5	5
2004	Denmark + Finland + Sweden	10	10	7.5	7.5	7.5	7.5
1991	United Kingdom	8.5	7	0 (§)	0 (§)	0 (§)	0 (§)
2010	United States + Canada	10	10	15	15	15	15

(§): 10 μg/day in cases of insufficient UVB exposure.

EVOLUZIONE DELLE CONOSCENZE

6° fase :

Domande :

- Di quale intake necessitiamo ?

- Quali sono i livelli ematici ottimali di vitamina ?

IOM Committee Members Respond to Endocrine Society Vitamin D Guideline

J Clin Endocrinol Metab 97: 1146–1152, 2012)

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What are the Skeletal Health Indicators for Vitamin D?

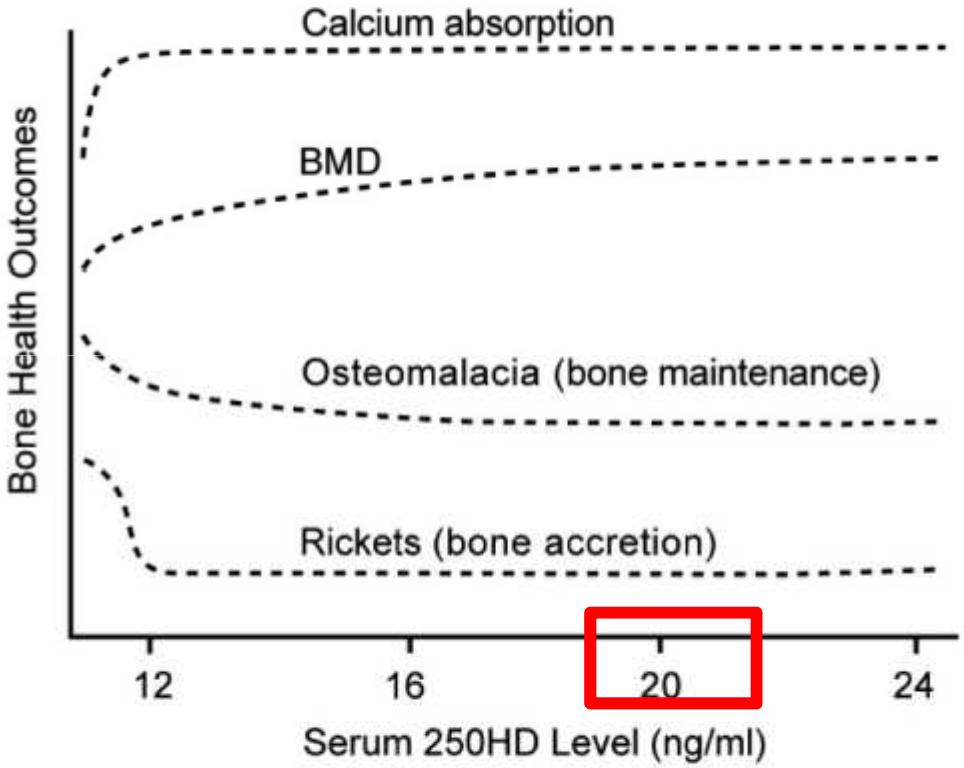

FIG. 1. IOM committee integration of optimal bone health outcomes (y-axis) and achieved serum 250HD levels (x-axis) revealing congruence of benefit between 16 and 20 ng/ml. BMD, Bone mineral density. [Reproduced from IOM (Institute of Medicine): Dietary reference intakes for calcium and vitamin D, p 293. Washington DC: The National Academies Press 2011 (2), with permission.]

EVOLUZIONE DELLE CONOSCENZE

6° fase :

Domande :

- Di quale intake necessitiamo ?

- Quali sono i livelli ematici ottimali di vitamina ?

- In quali condizioni aumentare l'intake ?

Vitamin D: Still a topical matter in children and adolescents. A position paper by the Committee on Nutrition of the French Society of Paediatrics☆

Available online at
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M. Vidailhet[a,*], E. Mallet[b], A. Bocquet[c], J.-L. Bresson[d], A. Briend[e], J.-P. Chouraqui[f], D. Darmaun[g], C. Dupont[h], M.-L. Frelut[h], J. Ghisolfi[i], J.-P. Girardet[h], O. Goulet[d], R. Hankard[j], D. Rieu[k], U. Simeoni[l], D. Turck[m,*], Comité de nutrition de la Société française de pédiatrie

7.2.2. In individuals with underlying risks

Certain cases warrant continuing supplementation all year long in children aged 1 to 5 years and in adolescents and maintaining it from 5 to 10 years. In certain pathological situations, the doses can be increased. If necessary, measurement of 25(OH)D levels will guide the prescription of vitamin D.

These underlying risks are the following:

- dark skin pigmentation;
- absence of summer sun exposure, a dermatological condition preventing such exposure, wearing skin-concealing clothing in summer;
- malabsorption, cholestasis, kidney failure, nephrotic syndrome;
- certain medical treatments (rifampicin; antiepileptic treatment: phenobarbital, phenytoin);
- obesity;
- children on certain extreme diets (veganism).

Vitamin D Deficiency in Obese Children and Its Relationship to Glucose Homeostasis

Micah L. Olson, Naim M. Maalouf, Jon D. Oden, Perrin C. White, and Michele R. Hutchison

(*J Clin Endocrinol Metab* 97: 279–285, 2012)

TABLE 4. Relationship between serum 25(OH)D and markers of glucose homeostasis and blood pressure by Spearman correlation in obese subjects

		Unadjusted		Adjusted[a]	
Variable	**n**	***r***	***P***	***R***	***P***
HOMA-IR	327	−0.27	<0.0001	−0.19	0.001
2-h Glucose	298	−0.14	0.02	−0.12	0.04
HgbA1c	384	−0.11	0.04	−0.07	0.18
SBP	406	−0.10	0.04	−0.07	0.14
DBP	406	0.01	0.77	−0.01	0.86

[a] Statistical analysis was conducted using partial correlation, adjusted for age and BMI Z score.

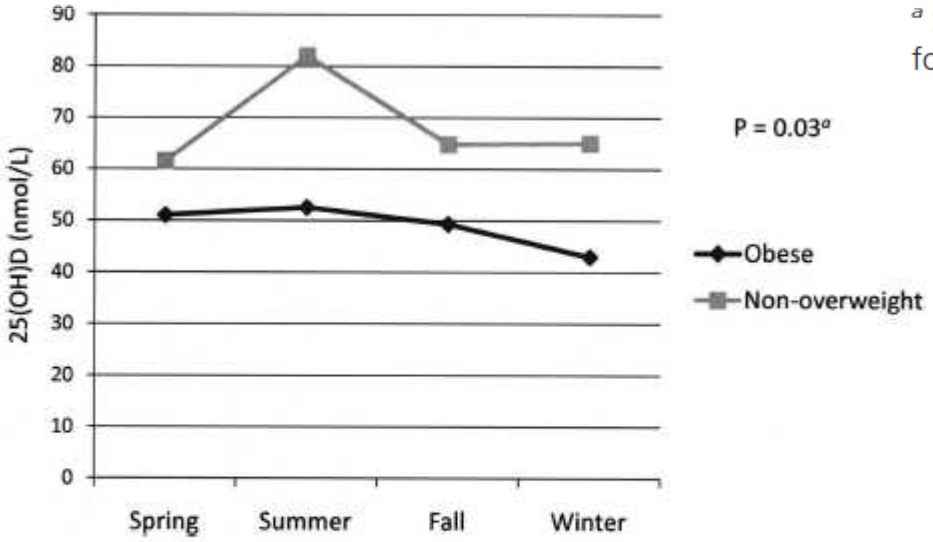


FIG. 1. Serum 25(OH)D concentration in obese *vs.* non-overweight subjects by season. Error bars denote SEM; error bars are smaller than the symbols for the obese group. $P = 0.03$ for interaction of group and season by ANOVA of 25(OH)D values.

Evaluation, Treatment, and Prevention of Vitamin D Deficiency: an Endocrine Society Clinical Practice Guideline

(*J Clin Endocrinol Metab* 96: 1911–1930, 2011)

Michael F. Holick, Neil C. Binkley, Heike A. Bischoff-Ferrari, Catherine M. Gordon, David A. Hanley, Robert P. Heaney, M. Hassan Murad, and Connie M. Weaver

Recommendation

2.5 We suggest that obese children and adults and children and adults on anticonvulsant medications, glucocorticoids, antifungals such as ketoconazole, and medications for AIDS be given at least two to three times more vitamin D for their age group to satisfy their body's vitamin D requirement (2|⊕⊕⊕⊕).

EVOLUZIONE DELLE CONOSCENZE

DUE DOMANDE FINALI DI INTERESSE PRATICO

1) QUALE FORMA DI VIT. D PER LA PROFILASSI ?

Vitamin D3 will be preferred over vitamin D2, which seems less active. (Vidailhet 2012)

Vitamin D2 is as effective as vitamin D3 in treating and preventing recurrence of vitamin D deficiency. (Pramyothin 2012)

EVOLUZIONE DELLE CONOSCENZE

DUE DOMANDE FINALI DI INTERESSE PRATICO

1) QUALE FORMA DI VIT D PER LA PROFILASSI ?

2) QUALI I LIMITI DI SICUREZZA ?

Vitamin D metabolism, functions and needs: from science to health claims

S. Battault · S. J. Whiting · S. L. Peltier · S. Sadrin · G. Gerber · J. M. Maixent

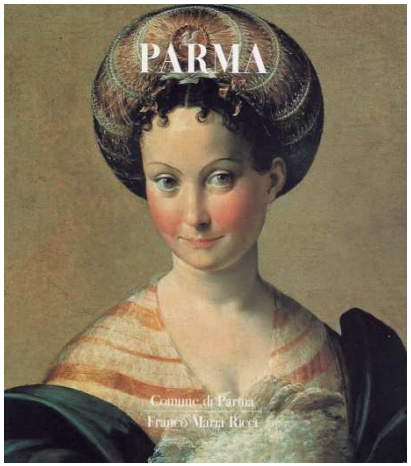
Eur J Nutr

Table 3 Upper levels for vitamin D

	Age group	Tolerable upper intake level (UL)	Comment
European Food and Safety Authority (EFSA)	0–10 year	25 μg/day (1,000 IU)	Depending on the amount of sunlight the risk of adverse effects at an intake at the upper level could increase. It should also be noted that higher doses of vitamin D might be needed, particular in the elderly, to achieve optimal serum levels of 25(OH)D for optimal mineralisation of the skeleton. The UL for adults does also apply to pregnant and lactating women
	11 year+	50 μg/day (2,000 IU)	
IOM	0–6 month	1,000 IU	
	6–12 month	1,500 IU	
	1–3 year	2,500 IU	
	4–8 year	3,000 IU	
	9 year+	4,000 IU	The UL also apply to pregnant and lactating women

Reference source: EFSA [70], IOM [69]

GRAZIE DELL'ATTENZIONE



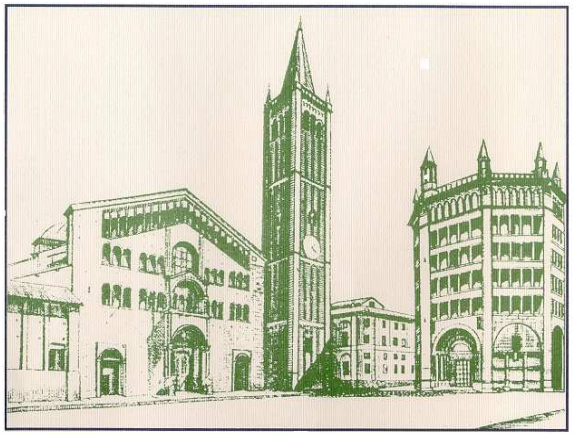


Table I

Equivalences, abbreviations, and synonyms.

Equivalences	Abbreviations and synonyms
Vitamin D	
1 μg = 2.5 nmol	25 hydroxyvitamin D = 25(OH)D = calcidiol
1 μg = 40 IU	1–25 dihydroxyvitamin D = 1.25$(OH)_2$ D = calcitriol
Plasma 25(OH)D	
1 ng/mL = 2.5 nmol/L	Vitamin D = Calciferol Vitamin D_3 = Cholecalciferol Vitamin D_2 = Ergocalciferol

Modulation of the immune system by UV radiation: more than just the effects of vitamin D?

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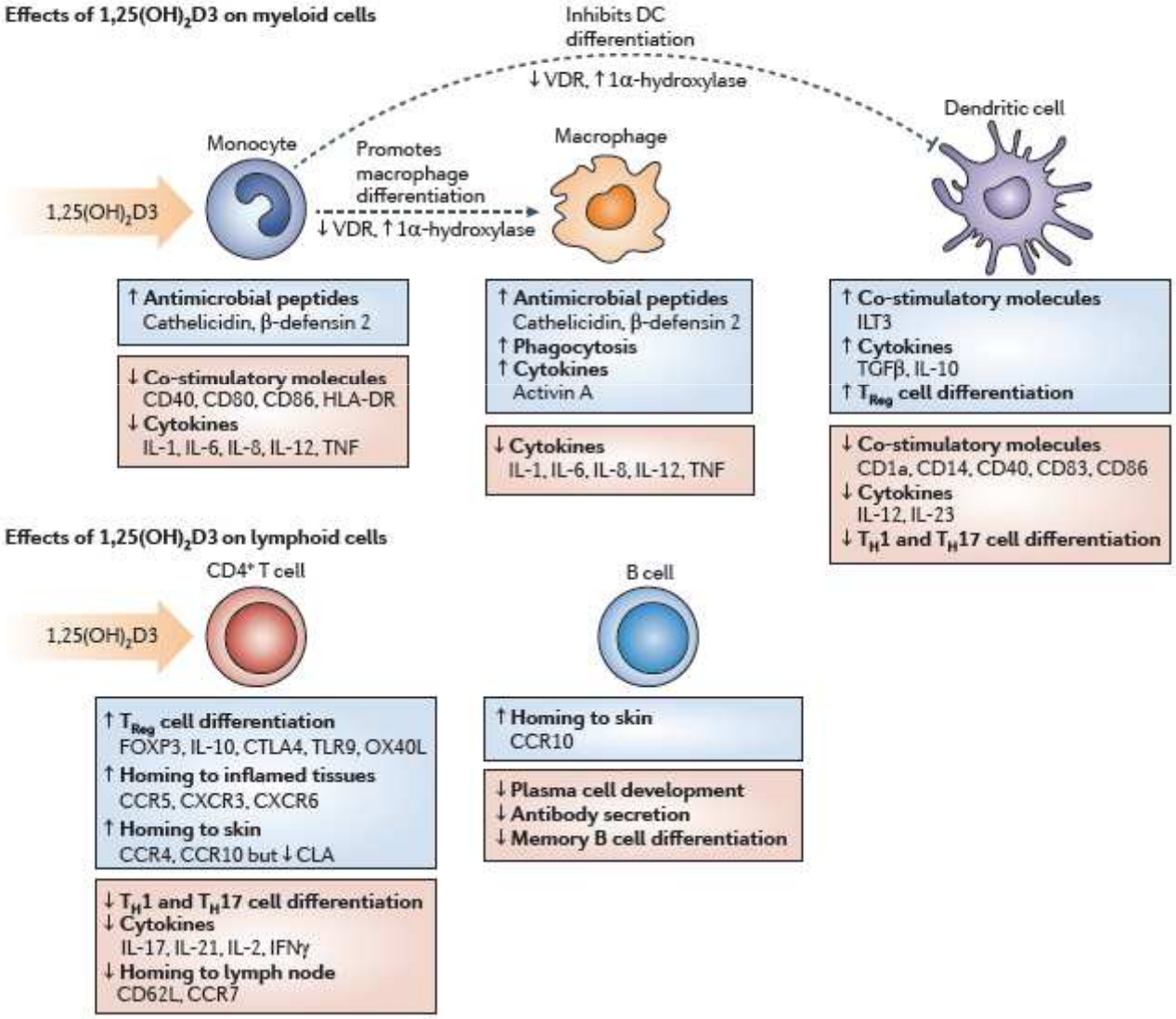
Prue H. Hart, Shelley Gorman* and John J. Finlay-Jones‡*