Hypovitaminosis D

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Scenario 1

- Mrs. A, a 55 -year- old lady presented to OPD with the complaints of generalized body aches & pains.
- She was obese & known case of diabetes for 5 years.
- Examination was unremarkable except her BMI was 32.

- Her baseline investigations were normal.

- She was ***not improved*** after symptomatic measures, like pain killers, calcium supplements & antidepressants.

Her vitamin D level was done, which revealed-

Vitamin D level	Normal range	Interpretation
9.2 ng/mL	> 30 ng/mL	severe deficiency

Scenario 2

- 30 year old lady complaining of aches and pain in limbs . Difficulty in raising from squat position in wash room. She used to wear veil for 15 years. Her body weight is 49 kgs. Mildly anaemic. No other positive findings detected. Her husband staying abroad. She has one child of 2 yrs old.

- She has been treated with anti depressant, anxiolytic, Elemental calcium for many months with out benefit.
- Blood sugar and Thyroid function are normal
- All Routine tests are also normal
- Serum Vitamin D level was done

  Vit- D is : 17.1ng/ml

Scenario 3

- Mr. X , 45 year healthy gentleman is a Corporate Executive presented with fatigue, aches and pains all over the body for 6 months. Non diabetic , non hypertensive
- He did Executive health check up where mild hypercholesterolemia detected only , all routine tests are normal.

- Vitamin - D assay was done : 21.2 ng/ml

Correction of low vitamin D with supplements improved their symptoms *dramatically*.

- Despite abundant sunshine in Bangladesh, allowing vitamin D synthesis all the year round, ***why our people are developing hypovitaminosis D*** striked our mind.

DH Lab Reference Range

- INTERPRETIVE guidelines for Vitamin D (25-hydroxy):
-

> 80 ng/mL: Potential toxicity
30-80 ng/mL: Optimum level
20-29 ng/mL: Insufficiency
< 20 ng/mL: Deficiency

Vitamin D Basics

- Units: ng/mL vs. nmol/L
  - 2.5 nmol/L = 1 ng/mL
  - If data are in nmol/L, divide by 2.5 for ng/mL

- Rule of thumb
  - For every 100 IU vitamin D3 ingested, blood level of 25-OH-D increases by 1 ng/mL

    - 1 μg of D3 or D2 = 40 IU

Regional

- Northern China where 42% of infants were found to suffer from this disease during the winter/spring period.
- North China (Beijing) hypovitaminosis:

I. 89% of Chinese adolescent girls

II. 48% of old men had severe deficiency

Among postmenopausal women serum 25(OH)D level lower amongst the Malays (44±11nmol/L) than the Chinese (69±16nmol/L)

- In SEA ,80% of the apparently healthy population is deficient in vitamin D (<20 ng/mL) and up to 40% of the population is severely deficient (<9 ng/mL).

Holick MF. Vitamin D Deficiency. N Engl J Med 2007; 357: 266--281.
2. Arya V, Bhambri R, Godbole MM, Mithal A.Vitamin D tatus and its relationship with bone mineral density in healthy Asian Indians. Osteoporsis Int 2004; 15(1): 56-- 61.

Nazmul ahasan,Aparna das, editorial, Journal of Enam Medical College Vol 3 No 2 July 2013

Regional

- Prevalence of hypovitaminosis D (25(OH)D <75nmol/L) in postmenopausal women

I. 47% in Thailand,
II. 49% in Malaysia,
III. 90% in Japan
IV. 92% in South Korea

- The mean serum 25(OH)D concentration was 48nmol/L in premenopausal women from Indonesia (6°S) and Malaysia (2°N)

South East Asia, Middle East and North Africa

Middle East and North Africa					
Tunisia	62	Ariana (36.8°N)	Population mainly women 20–60 years	47.6%	<37.5
Iran	49	Zanjan (36.4°N)	Mothers and neonates	2/3 of mothers and neonates in winter; 46% mothers in summer; 35% neonates in summer	<25
	50	Tehran (35.4°N)	Children 7–18 years	50% girls; 11% boys	<20
	51	Tehran (35.4°N)	Men and women 20–64 years	9.5%	<12.5
Morocco	61	Rabat (34.0°N)	Women 24–77 years	91%	75
Lebanon	53	Beirut (33.5°N)	Children 10–16 years	55–74% in spring; 25–54% in winter	<50
	55	Beirut and Bekaa	Men and women 30–50 years	30.7–61.8%	<12.5
Jordan	57	Amman (31.5°N)	Men and women 18–45 years	62.3% in summer; 50% in winter	12.5–30.0
	58	Northern Jordan (31°N)	Premenopausal women and children 4 to 5 years	49% women; 61% children	<25
South Asia					
India	43	New Delhi (28°N)	Children 10–18 years	27–42.3%	<22.5
	42	Lucknow (26.8°N)	Pregnant women	42%	<25
Pakistan	40	Karachi (24.5°N)	Mothers and infants	55% infants; 45% mothers	<25
Bangladesh	38	Dhaka (23.4°N) Nandail (15.2°N)	Adult women 16–40 years	12–17% 38–50%	<25.0 <37.5

Pakistan

Pakistan:

- The median level of serum vitamin D was 18.8 (IQ range 12.65–24.62) ng/dL. A total of 253 (84.3%) respondents had low levels (30ng/dL) of 25OH vitamin D.
- In Karachi, 55% of infants and 45% of mothers had very low serum 25(OH)D levels (<25 nmol/L or 10 ng/mL).

Adil Sheikh1, Zeb Saeed1, Syed Ali Danial Jafri2, Iffat Yazdani2, Syed Ather Hussain2*Vitamin D Levels in Asymptomatic Adults-A Population Survey in Karachi, Pakistan. PLoS ONE | www.plosone.org 1 March 2012 | Volume 7 | Issue 3 | e33452

India

In North India (27ºN): Hypovitaminosis D in

- 96% of neonates , 91% of healthy school girls , 78% of healthy hospital staff and 84% of pregnant women .

In South India (13ºN): hypovitaminosis D

- Inverse relationship between measured serum 25(OH)D levels and PTH levels
- Vitamin D levels were significantly higher in rural compared to urban subjects

Lucknow,India found that 84%t of pregnant women had 25(OH)D values below 22 ng/mL

Sachan A, Gupta R, Das V, et al. (2005) High prevalence of vitamin D deficiency among pregnant women and their newborns in northern India. Am J Clin Nutr 81:1060-1064.

8. Puri S, Marwaha RK, Agarwal N, et al. (2008) Vitamin D status of apparently healthy schoolgirls from two different socioeconomic strata in Delhi: relation to nutrition and lifestyle. Br J Nutr 99:876-882.

Srilankna

- In Sri Lanka (7ºN), mean 25(OH)D among healthy females was 35.3nmol/L
- 40.5% of them had 25(OH)D values below 25nmol/L .
- High prevalences

I. Skin pigmentation
II. traditional clothing.
III. Air pollution
IV. limited outdoor activity
V. urban population

Rodrigo MD (2007) Peak bone mass measured by phalangeal BMD and its association with nutritional status, socioeconomics status and physical activity: a community based cross sectional study in Galle district, Sri Lanka. In. Extract from PHD thesis (unpublished).

Bangladesh

- In Bangladesh (24ºN) hypovitaminosis D:
- In women regardless of age, lifestyle and clothing
- 25(OH)D levels below 37.5nmol/L was

  38% from high income group and

  50% in women from low income groups .

Islam MZ, Akhtaruzzaman M, Lamberg-Allardt C (2006) Hypovitaminosis D is common in both veiled and nonveiled Bangladeshi women. Asia Pac J Clin Nutr 15:81-87.

. Islam MZ, Lamberg-Allardt C, Karkkainen M, et al. (2002) Vitamin D deficiency: a concern in premenopausal Bangladeshi women of two socio-economic groups in rural and urban region. Eur J Clin Nutr 56:51-56.

Bangladesh

- Vitamin D deficiency (serum 25-OHD level <25 nmol/l) was detected in 39% of young women (university students), 30% in veiled women and 38% in diabetic women, respectively.

- Vitamin D insufficiency defined as serum 25-OHD concentration <40 nmol/l was detected in 78% of group A, 83% in group B and 76% in group C, respectively.

Md Zahirul Islam PhD1, Mohammed Akhtaruzzaman PhD2 and Christel Lamberg-Allardt PhD, **Hypovitaminosis D is common in both veiled and nonveiled Bangladeshi women.** *Asia Pac J Clin Nutr 2006;15 (1): 81-87*

Knowledge in bangladesh (rural and Urban)

- Though the rural students are less familiar with vitamin D ($p<0.001$) and osteoporosis ($p=0.0056$) than urban students, they exercise a healthy diet in terms of milk consumption ($p<0.0001$) and engage themselves more in outdoor activities
- Spend more time in sunlight ($p<0.0001$) than the urban students.
- Thus the rural students may require less supplemental support of calcium and/or vitamin D than the urban students ($p<0.0001$).

Dewan Taslima Akhter1†, Riaz Uddin2†*, Dilshad Yasmin2 and Rajia Sultana Nijhu2
Calcium and Vitamin D Related Knowledge in 16-18 Years Old Adolescents: Does Living in Urban or Rural Areas Matter J Nutr Food Sci Volume 3 • Issue 6 • 1000240

Men (Husband) versus Pregnant Women in Bangladesh

- 50% of the men but only 23% of women spent ≥2 hours outdoors per day during daytime hours (n = 82, p=0.0007).
- 24% of men and 0% of women reported outdoor professions (p<0.0001).
- Men's mean 25(OH)D (55.2 ±17.5 nmol/L) was significantly higher than women's (21.6 ±10.7nmol/L)
- (mean difference = 30.7 nmol/L; p<0.0001).
- A significantly lower proportion of men (6.0%) were vitamin D deficient (25(OH)D<30nmol/L) vs women (21.7%; p<0.0001)

Joy Shi2, Eszter Papp2, Abdullah Al Mahmud3, Alison Gernand4 and aniel Roth1,2 Lindsay Ruiter1,2, **JHPN,Vol 10:11-16Vitamin D Status of Husbands of Pregnant Women in Dhaka, Bangladesh**

D3 ≠ D2 ≠ 1α,25-di(OH)-D3

- D3 is made in the skin* (or ingested in supplements) – not biologically active
  - Cholecalciferol
- D2 is from plants** (not humans) – only 1/3 as active as D3
  - Ergocalciferol
- 1α,25-di(OH)-D3 is converted in the kidney and other tissues - biologically active
  - "Vitamin D"
  - Calcitriol
- 25-OH-D is the storage form, NOT biol. active

***From 7-dehydrocholesterol**

****From ergosterol**

- Recently, we are observing this sort of presentation very frequently in our clinical practice, which are incorrectly diagnosed as fibromyalgia or chronic fatigue or depression.

Background

- Vitamin-D is a fat soluble steroid pro-hormone which has been appreciated for its role in **calcium homeostasis and bone health** since its identification in 1921.

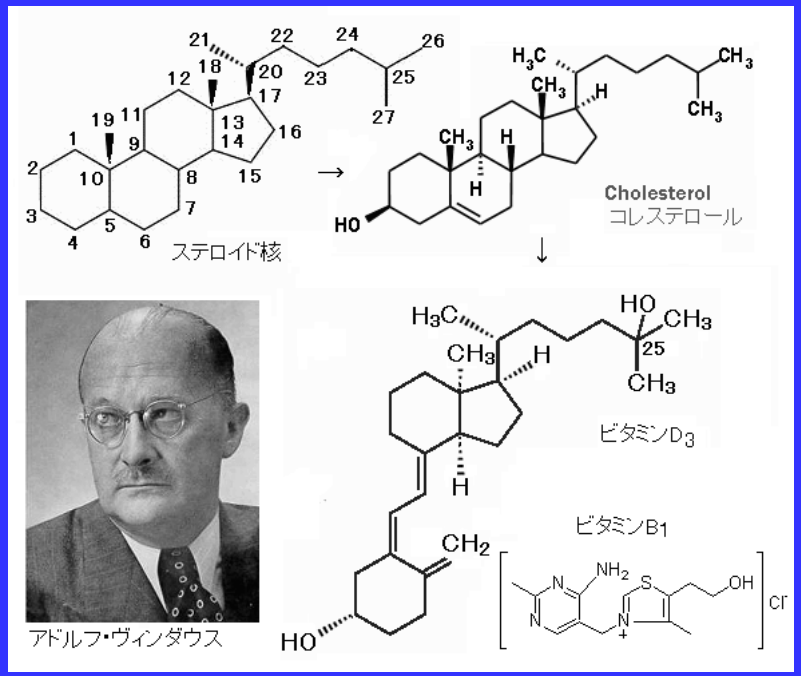
History

- In 1921, Elmer McCollum identified an antirachitic substance found in certain fats that could prevent rickets.

- Because the newly discovered substance was the **fourth** vitamin identified, it was called vitamin D.

History..contd..

- The 1928 Nobel Prize in Chemistry was awarded to Adolf Windaus, who discovered the steroid 7-dehydrocholesterol, the precursor of vitamin D.



Why we are so much concern?

- Vitamin D has received considerable interest from the medical community due to recent evidence for -

✓ the non-skeletal effects of vitamin D combined with the finding of

✓ widespread global deficiency.

Prevalence

- Vitamin D deficiency is more common than previously thought.

- It has been estimated that almost **1 billion people in the world** suffer from vitamin D deficiency or insufficiency. (1)

[Ref- *Masood SH, Iqbal MP, Prevalence of vitamin D in South Asia. Pak J Med Sci, 2008; 24(6)]*

Prevalence..contd..

- In SEA, **80%** of the apparently healthy population is **deficient** in vitamin D (<20 ng/ml).

Forms of Vitamin D

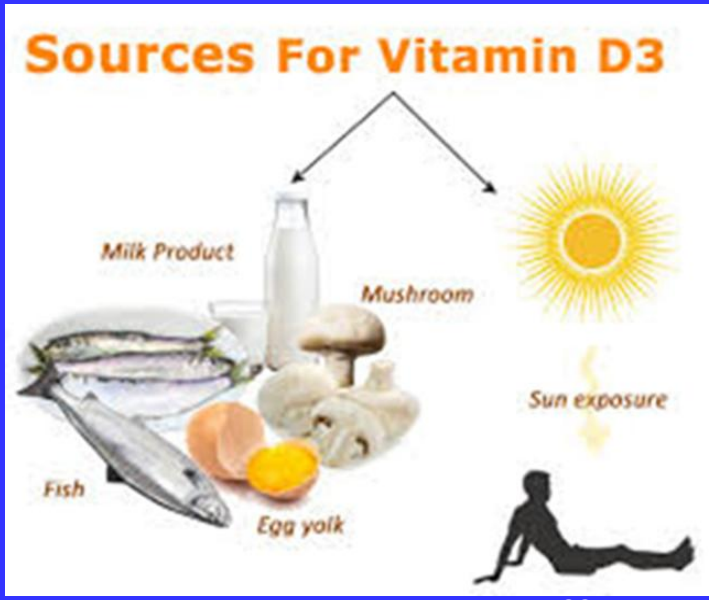
Vitamin D consists of 2 bioequivalent forms.

Form	Other Name	Source
Vitamin D2 (D2)	Ergocalciferol	• dietary vegetable sources • oral supplements
Vitamin D3 (D3) 	Cholecalciferol	• skin exposure to UVB radiation in sunlight • food sources such as oily fish and variably fortified foods • oral supplements

Sources

- In normal individuals, vitamin D comes from 2 sources:

%	Source
About **70-90%**	is made in the skin by the action of ultraviolet light from the sun
10-30%	from diet.



Sources..contd..

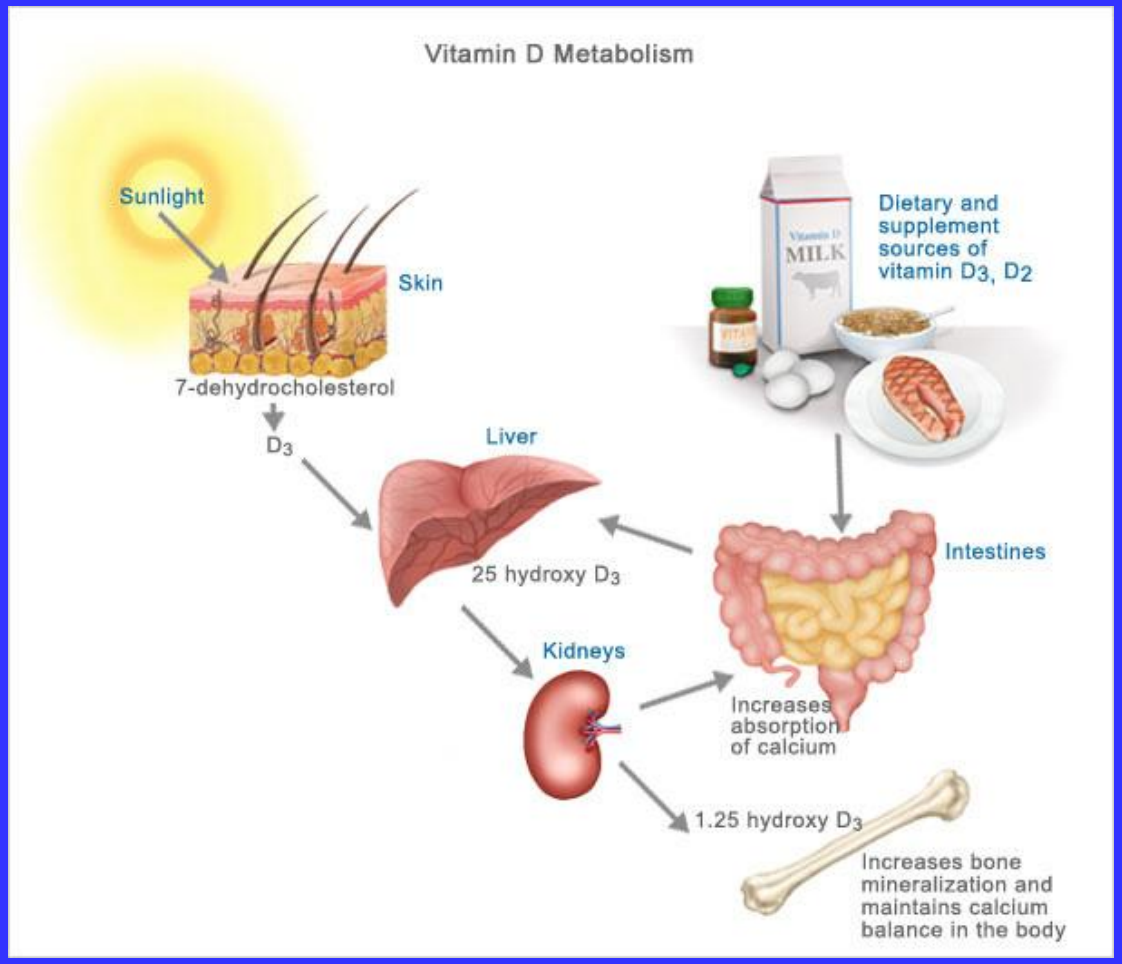
- Aside from rich sources such as oily fish, the vitamin D content of most foods is between 50 and 200 IU per serving.

- This value varies greatly by region of the world because fortification markedly improves the availability of vitamin D through diet.

Relation of sunlight & Vitamin D

- During exposure to solar UVB radiation, 7-dehydrocholesterol in the skin is converted to pre- vitamin D3, which is immediately converted to vitamin D3 in a heat-dependent process.

Relation of sunlight & Vitamin D

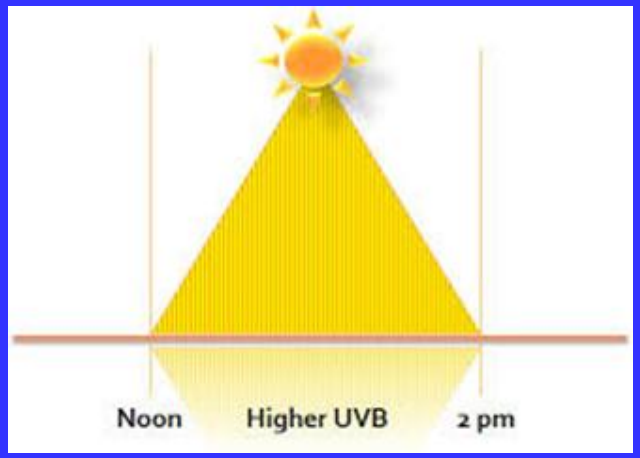


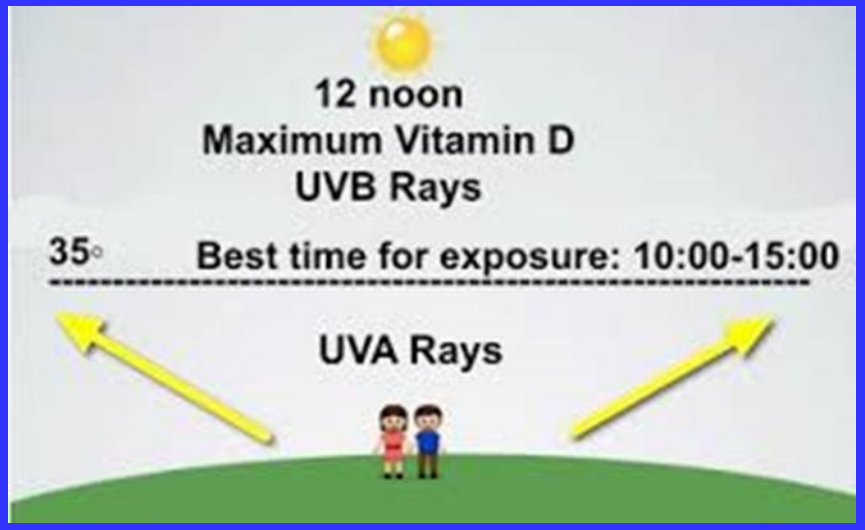
Factors influencing photosynthesis and bioavailability of vitamin D

Factors influencing photosynthesis and bioavailability of vitamin D

a. Environmental factors-

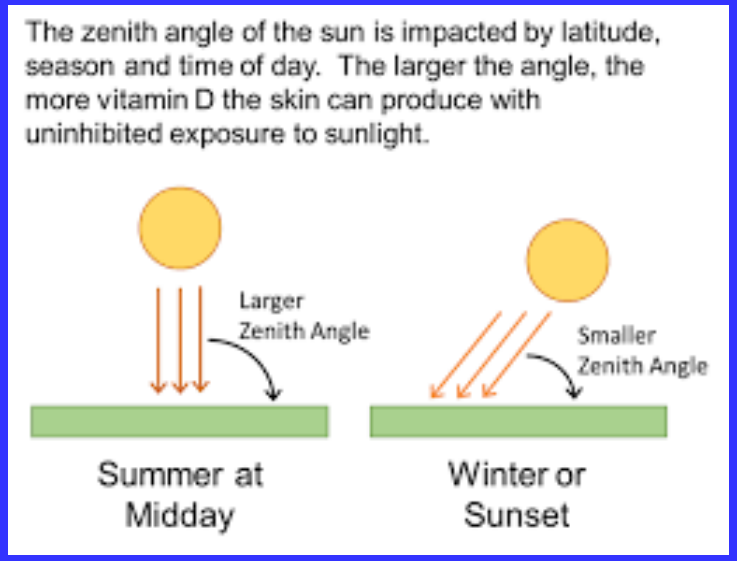
1. Duration and time of sun exposure-skin produces more vitamin D if exposed it during the middle of the day.

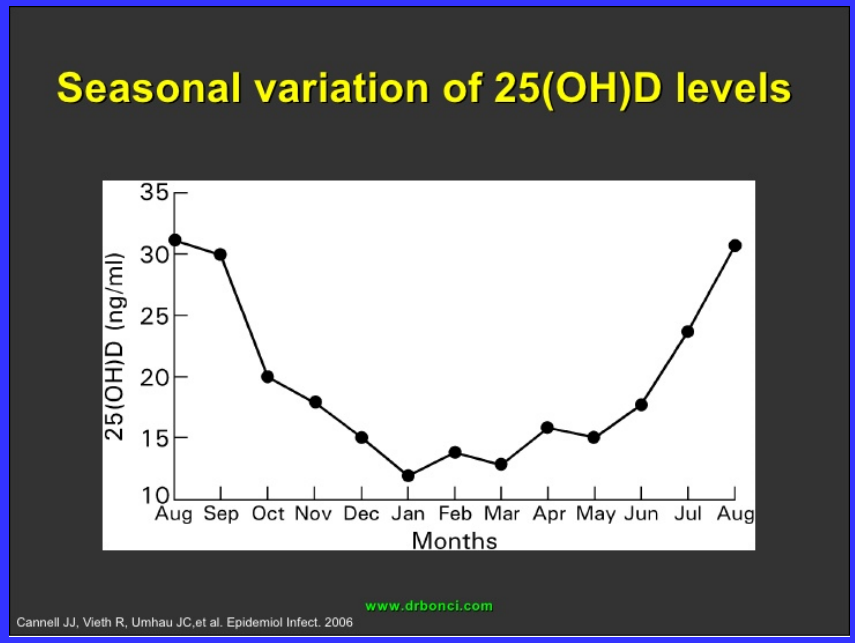




Factors influencing photosynthesis and bioavailability of vitamin D..contd..

2. Season

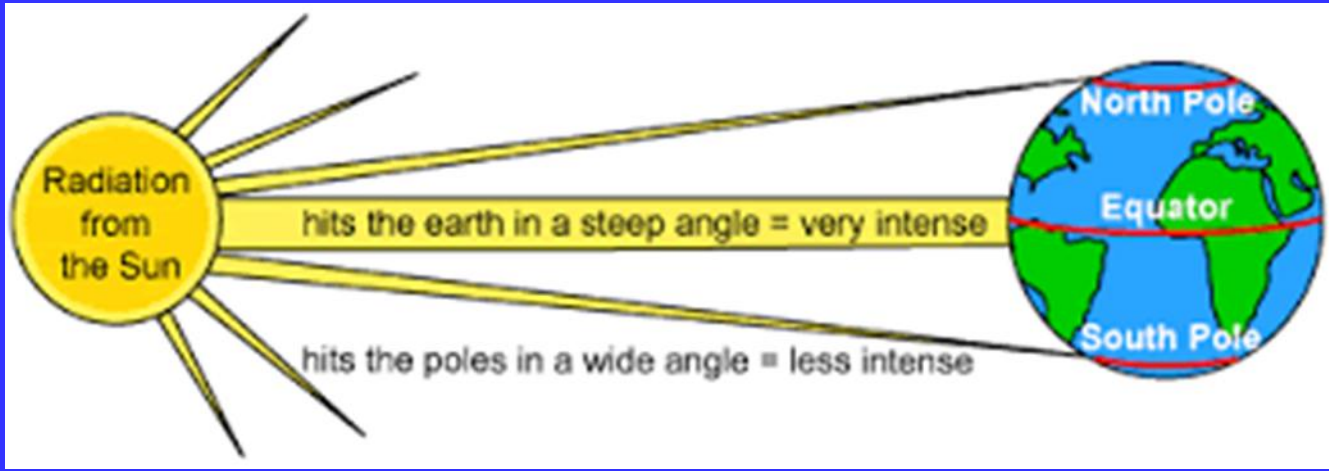




Factors influencing photosynthesis and bioavailability of vitamin D..contd..

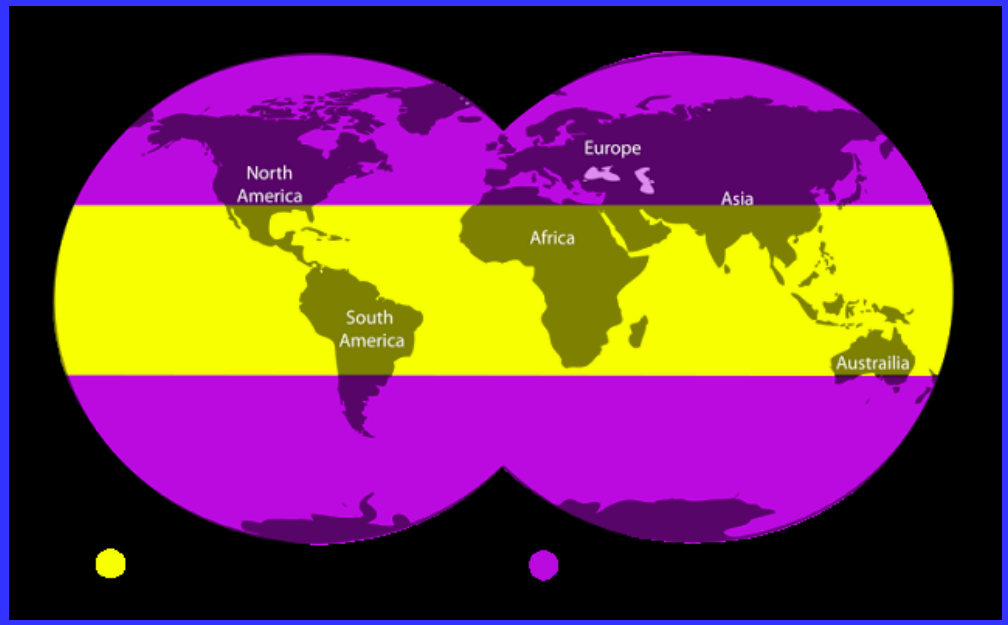
3. Latitude

- Moving away from the equator, the intensity of UV light decreases, so that at a latitude above 50° (including northern Europe), vitamin D is not synthesized in winter



Factors influencing photosynthesis and bioavailability of vitamin D..contd..

- the closer to the equator one lives, the easier it is to produce vitamin D from sunlight all year round.



Factors influencing photosynthesis and bioavailability of vitamin D..contd..

- 4. Atmospheric pollution-

Causes insufficient cutaneous absorption of UVB

Factors influencing photosynthesis and bioavailability of vitamin D..contd..

b. Patient related factors-

1. clothing style (using veils)

Factors influencing photosynthesis and bioavailability of vitamin D..contd..

2.use of sun blocks

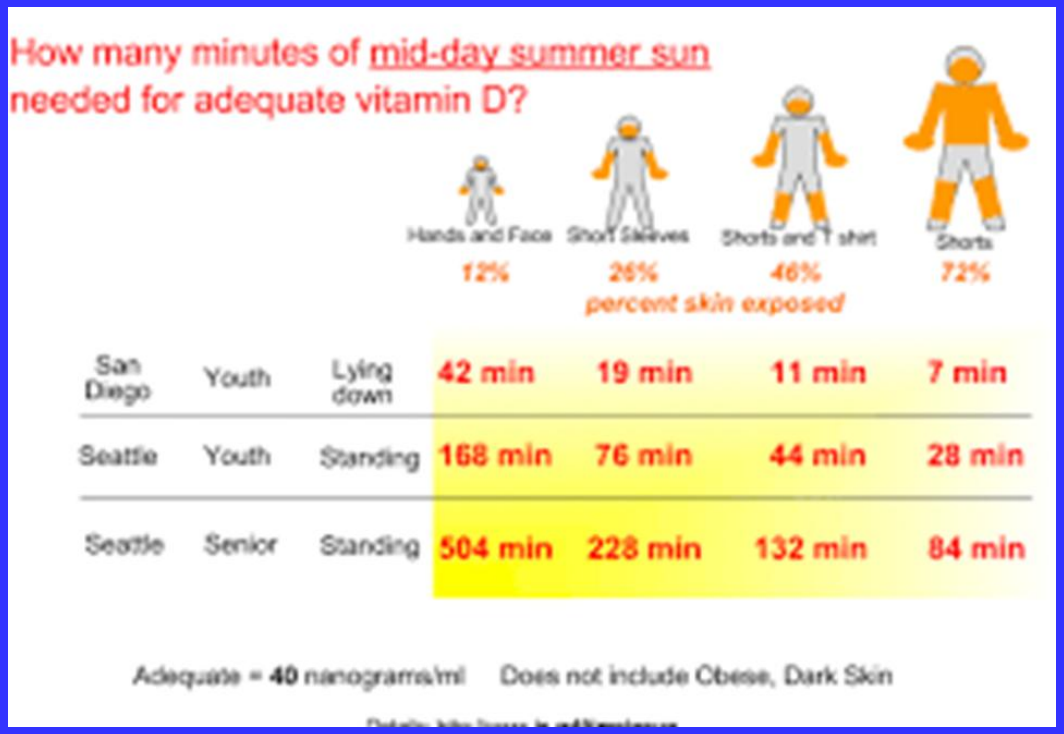
Factors influencing photosynthesis and bioavailability of vitamin D..contd..

3. The color of skin –

- Whiter skin make vitamin D more quickly than darker skin.
- Darker skins with more melanin allow less UVB to enter the skin.

Factors influencing photosynthesis and bioavailability of vitamin D..contd..

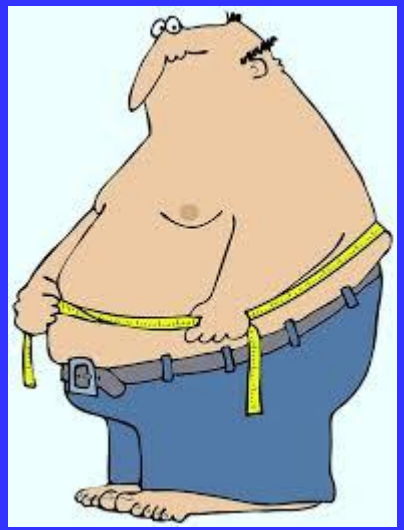
- 4. The amount of skin exposed – the more skin one exposes, the more vitamin D body will produce.



Factors influencing photosynthesis and bioavailability of vitamin D..contd..

5. obesity-

- vitamin D is accumulate in adipose tissue with decreased bioavailability and lower serum levels in persons with higher BMI



Factors influencing photosynthesis and bioavailability of vitamin D..contd..

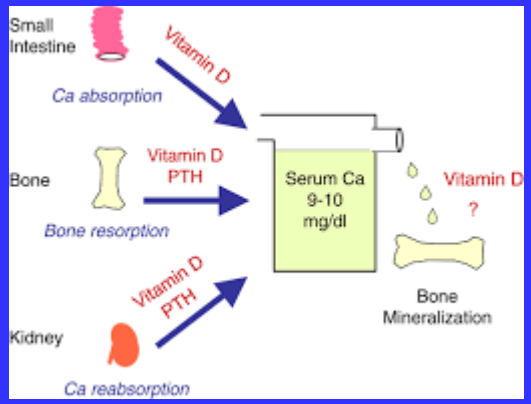
6. Aging –

- ✓ Even if regularly exposed to sunlight, elderly people produce 75% less cutaneous D3 than young adults .
- ✓ Production of $1,25(OH)_2D$ is reduced by 50% as a result of an age-related decline in renal function

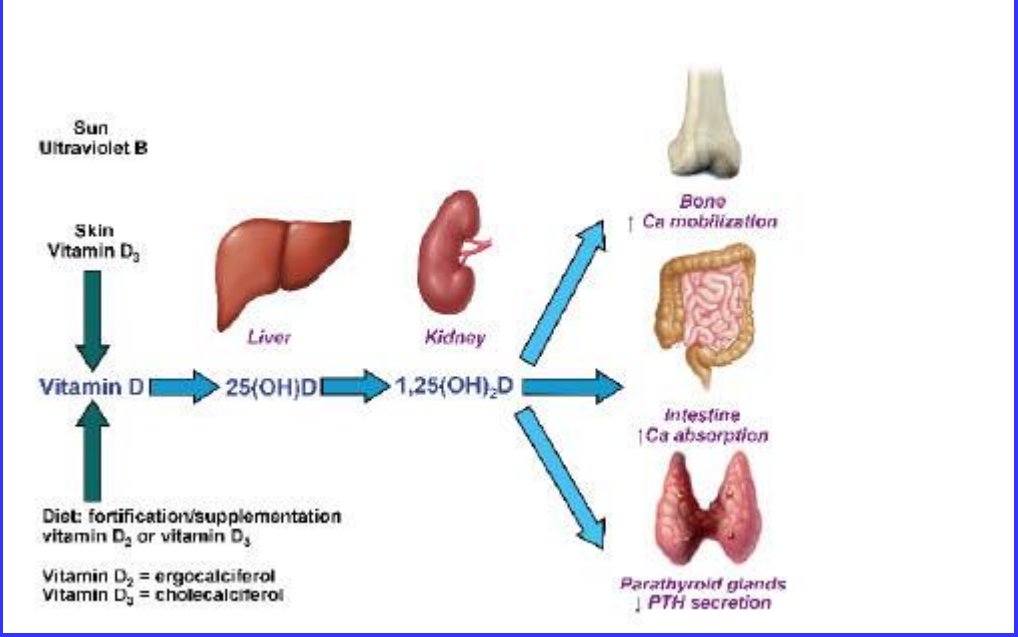
7. presence of several chronic diseases

(like CKD)

Actions of Vitamin D…



Actions of Vitamin D



Non-classical Actions of Vitamin D

- Suppress cell growth/proliferation
- Regulate apoptosis

- Modulate immune responses
  - Susceptibility to infections
  - Susceptibility to autoimmune disorders , like Multiple sclerosis , T_1DM
  - Effects in transplantation immunity

Non-classical Actions of Vitamin D..contd..

- Modulate keratinocyte differentiation and function
  - Key role in psoriasis therapy
- Suppress renin-angiotensin system
- Stimulate insulin secretion
- Control neuromuscular function and the brain
- Anti-oxidative/neuroprotective

Number of First Nonvertebral Fractures among All Subjects, According to Skeletal Site

TABLE 5. NUMBER OF FIRST NONVERTEBRAL FRACTURES AMONG ALL SUBJECTS, ACCORDING TO SKELETAL SITE.

SITE OF FRACTURE	PLACEBO GROUP (N = 202)	CALCIUM–VITAMIN D GROUP (N = 187)
Face	1	1
Shoulder, humerus, or clavide	4	3
Radius or ulna	5	1
Hand	1	1
Ribs	2	2
Pelvis	2	0
Hip	1	0
Tibia or fibula	1	1
Ankle or foot	7	2
Multiple sites	2	0
Total	26	11

Dawson-Hughes B et al. N Engl J Med 1997;337:670-676

The NEW ENGLAND JOURNAL of MEDICINE

Vitamin D and Fracture Risk

- A meta-analysis of 7 RCT's evaluating fracture risk in pts given 400 IU of vit D3 per day revealed little benefit.

- In studies using 700-800 IU of of vitamin D3 per day, the RR of hip fracture and nonvertebral fracture were reduced by 26% and 23% respectively compared to calcium and placebo.

Bischoff-Ferrari, Am J Clin Nutr 2006

Vitamin D and Falls

- Skeletal muscle has a vitamin D receptor for maximal function.
- A meta-analysis of 5 RCT with 1237 subject ---- increased vitamin D reduced the risk of falls by 22%.

--- 400 IU of vitamin D per day was not as effective 800 IU vitamin D per day

- In an RCT done in a NH:

---- residents receiving 800 IU of vitamin D2 per day plus calcium had a 72%reduction in the risk of falls compared with placebo.

(Bischoff-Ferrari, Am J Clin Nutr 2006)
(Broe, J Am Geriatr Soc, 2007)

Evidence for Role of Vitamin D in CVD

- Framingham Offspring Study
  - 1739 subjects (mean 59 yr, 55% F, all C)
  - No prior CVD
  - Mean 25-OH-D 19.7 ng/mL
    - 28% with 25-OH-D <15 ng/mL
    - 9% with 25-OH-D <10 ng/mL
  - 5.4 yr follow-up
  - 120 developed first CV event

Wang TJ, et al. *Circulation* 2008;117:503-511.

Evidence for Role of Vitamin D in CVD: Framingham Offspring

	Hazard ratios ng/mL	Adj. for age, sex	Adj for *covar.	Adj. for *covar., CRP
Hypertension	25-OH-D ≥15	1.00	1.00	1.00
	10 to <15	2.07 (1.19-3.61)	1.93 (1.09-3.42)	2.07 (1.16-3.69)
	<10	3.19 (1.70-5.99)	2.51 (1.30-4.82)	2.43 (1.23-4.80)
No HTN	25-OH-D ≥15	1.00	1.00	1.00
	10 to <15	1.45 (0.74-2.82)	1.06 (0.53-2.13)	1.05 (0.52-2.13)
	<10	1.66 (0.64-4.28)	1.00 (0.35-2.85)	1.08 (0.37-3.16)

Wang TJ, et al. *Circulation* 2008;117:503-511.

*Covar. SBP, anti-HTN, DM, cig, total-HDL, BMI, creat

Evidence for Role of Vitamin D in CVD

- Health Professionals Follow-up Study
  - Prospective trial nested case control
  - 18,225 M age 40-75 (mean 63.8 yr) 94% C
  - No known CVD, baseline 25-OH-D 24.5 vs. 23 ng/mL
  - 10 yr follow-up
  - 454 with nonfatal MI or fatal CHD

Compared with 25-OH-D ≥30 ng/mL	≤15 ng/mL	15-22.5 ng/mL	22.6-29.9 ng/mL
RR of MI after adjustment*	2.09 (1.24-3.54)	1.43 (0.96-2.13)	1.60 (1.10-2.32)

*FHx MI, BMI, EtOH, activity, DM, HTN, ethnicity, region, marine ω-3 intake, LDL, HDL, TG

Giovannucci E, Liu Y, Hollis BW, Rimm EB. *Arch Intern Med*. 2008; 168(11):1174-80.

Vitamin D and Hypertension

- 148 F age 75 yr with 25-OH-D level <50 nmol/L received calcium 600 mg plus 400 IU D_3 BID vs. calcium 600 mg alone BID over 8 weeks

	Initial		Final	
	Ca only	Vit. D + Ca	Ca only	Vit. D + Ca
25-OH-D (nmol/L)	24.6	25.7	44.4 (17.8 ng/mL)	64.8 (25.9 ng/mL)
PTH (pmol/L)	6.1	6.1	5.3	4.6
SBP (mmHg)	140.6	144.1	134.9	131.0
DBP (mmHg)	82.6	84.7	75.7	77.5
HR (mmHg)	74.1	75.4	73.9	71.3

Pfeifer M, et al. *J Clin Endocrinol Metab* 2001;86:1633-37.

Vitamin D and Hypertension

- In a study of hypertensive patients who were exposed to ultraviolet B radiation three times per week for 3 months

- 25 OH vitamin D levels increased by approximately 180% and both SBP and DBP were reduced by 6 mm Hg

. (Krause, Lancet 1998)

Vitamin D and Diabetes

- In 10,366 children in Finland- 2000 IU of vitamin D3 per day (1st yr) & follow up -the risk was reduced by 80%.
- In subset analysis, among children with vitamin D deficiency, the risk was increased by 200%
- Combined 1200 mg of calcium+ 800 IU of vitamin D lowered the risk by 33 % compared to <600 mg calcium+ < 400 IU of vitamin D.

(Hyponen, Lancet 2001)

(Pittas, Diabetes Care 2006)

Vitamin D and MS

Multiple Sclerosis: Vitamin D levels of 40 ng/ml or higher may confer some protection against MS.

Patients receiving Magnesium, Calcium and 5000 IU vitamin D significantly reduced MS exacerbations (14 vs 32).

Vitamin D and Dementia

- Vitamin D may be primarily associated with cognitive domains other than memory , such as executive cognitive functions, depression, bipolar disorders, and schizophrenia.
- Low 25(OH)D may be a risk factor for cognitive impairment (41-60%).
- Receptors for Vitamin D are present in brain cells. Increased Vitamin D may improve cognitive function in patients with Alzheimer's

Vitamin D and Cancer

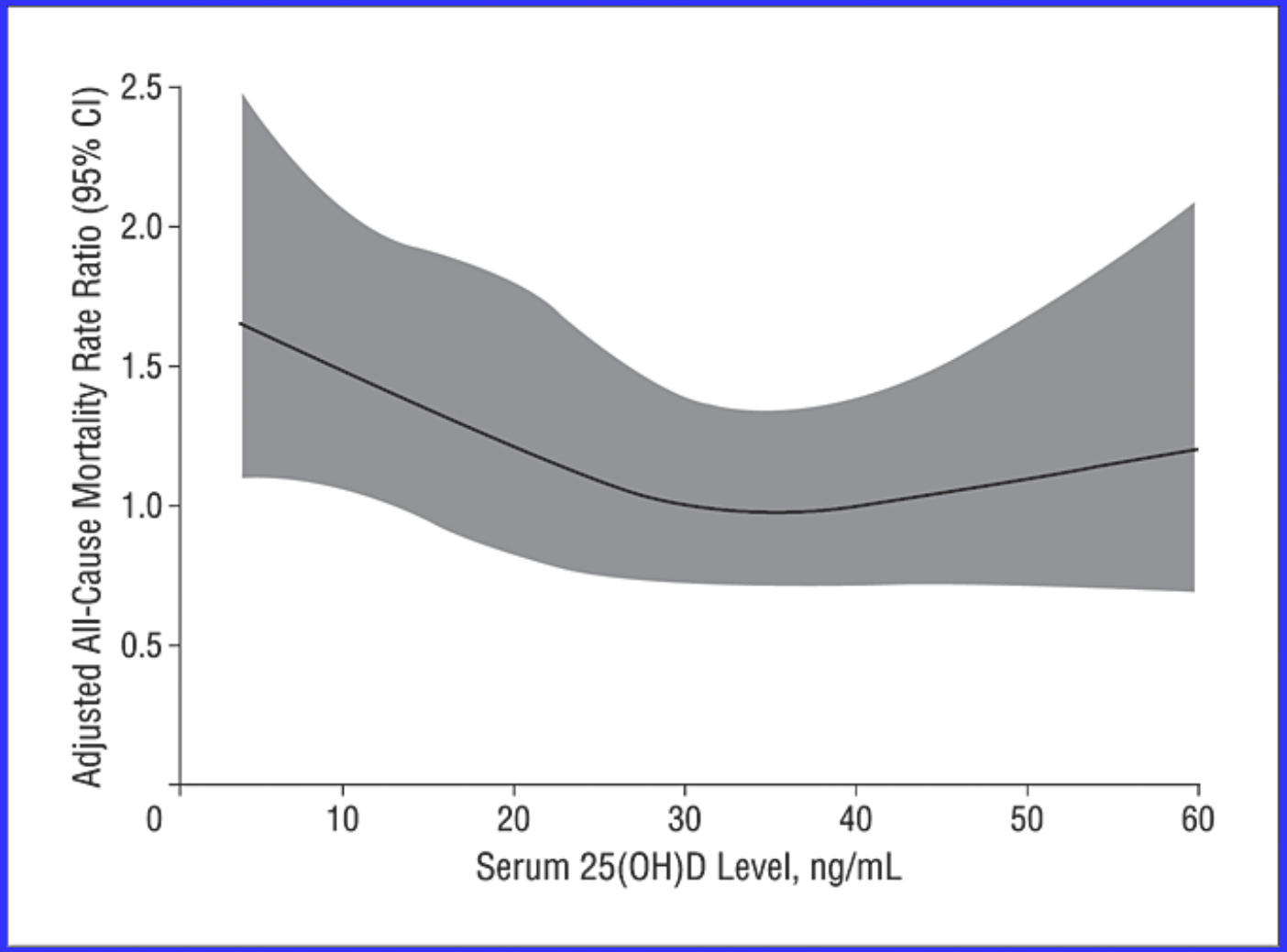
- 25 OH vitamin D below 20 ng/ml :
- 30-50% increased risk of incident and mortality of colon, prostate and breast cancer.
- D 1-alpha hydroxylase and produce 1,25 OH vitamin D locally to control genes
- Prevent cancer by limiting cellular proliferation and differentiation by inhibiting angiogenesis and inducing apoptosis

Vitamin D Deficiency and All Cause Mortality

- 13,331 adults 20 years or older from NHANES III testing association of low 25 OH vitamin D and all cause, cancer and cardiovascular mortality
- Median follow up was 8.7 years
- 1806 deaths, including 777 from CVD
- In multivariate models (25 OH vitamin D <17.8 ng/ml) was associated with a 26% increased rate of all cause mortality, (95% CI, 1.08-1.46.)

(Melamed, Arch Intern Med, 2008)

Restricted cubic spline showing the fully adjusted associations between serum 25-hydroxyvitamin D (25[OH]D) levels and all-cause mortality in 13 331 participants of the Third National Health and Nutrition Examination Survey



Melamed, M. L. et al. Arch Intern Med 2008;168:1629-1637.

ARCHIVES OF INTERNAL MEDICINE

Association Between 25- OH Vitamin D and URTI

- 18,883 subjects 12 and older from NHANES III
- The median serum 25 OH vit D was 29 ng/mL
- Recent URTI was reported by

I. 24% with 25 OH vit D < 10 ng/mL,

II. 20% with levels of 10 to < 30 ng/mL and

III. 17% with levels of ≥30 ng/mL ($p<0.001$).

- The association were higher in those with asthma (OR 5.67) and COPD (OR 2.26)
- Conclusion: Serum 25 OH vit D levels are inversely associated with recent URTI.

Ginde et al, Arch Intern Med 2009

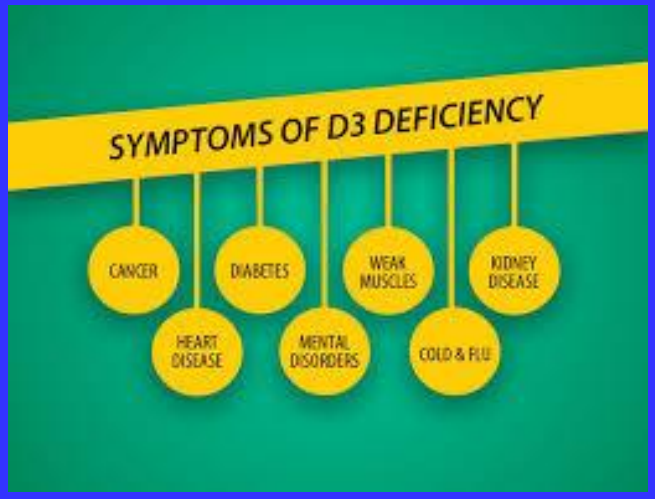
Vitamin D Deficiency and Other Conditions

- Linked to increased incidence of :
- Schizophrenia
- Depression
- Reactive Airway Disease

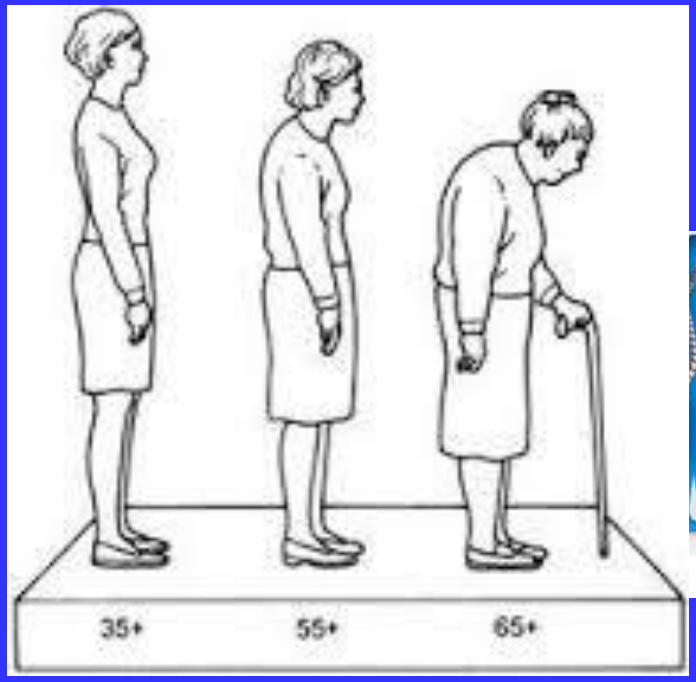
Who Should Be Screened for Vitamin D Deficiency

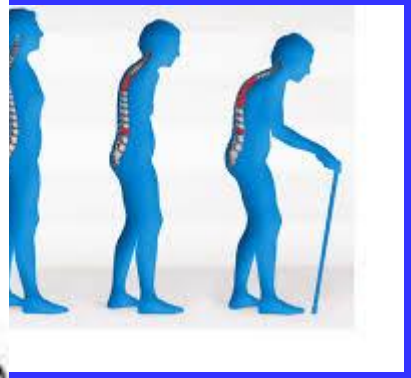
- Elderly
- Home bound or institutionalized patients
- Patients with known or suspected malabsorption
- Patients with osteoporosis or osteopenia
- CKD patients
- Chronic liver disease patients
- Patients with nonspecific musculoskeletal pain
- Patients on medications that induce P-450 enzyme activity
- Obese

Features of Vitamin D deficiency…..

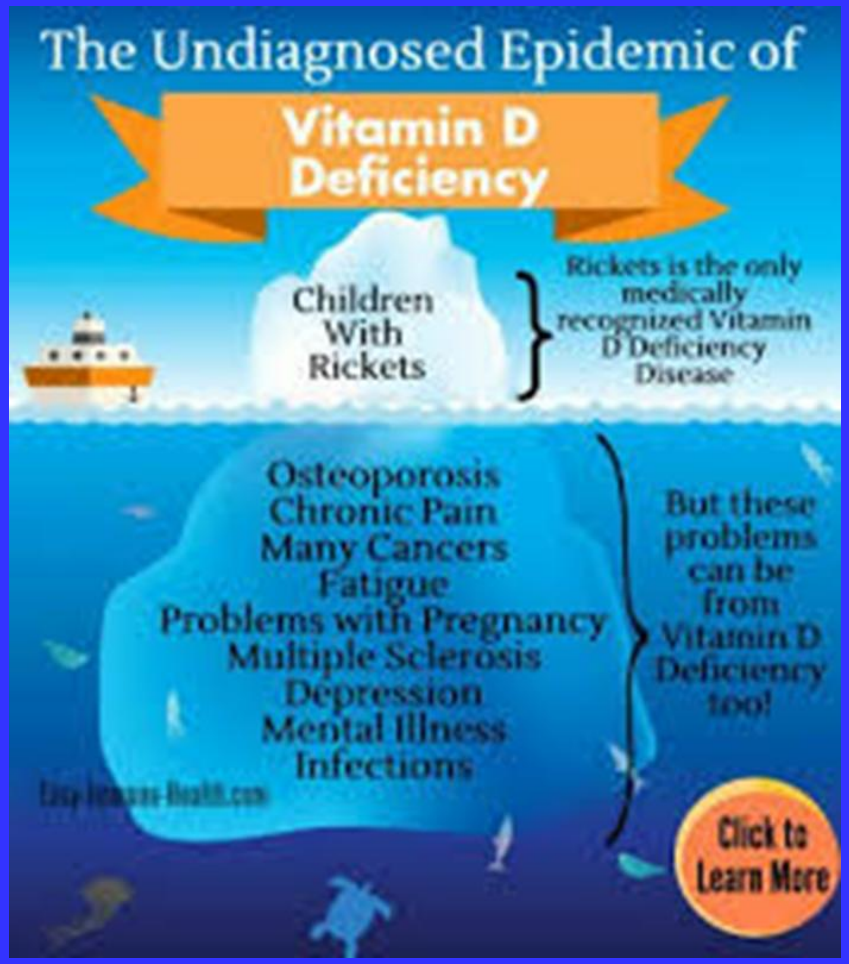


Features of Vitamin D deficiency..contd..


35+
55+
65+



Features of Vitamin D deficiency..contd..



Features of Vitamin D deficiency..contd..

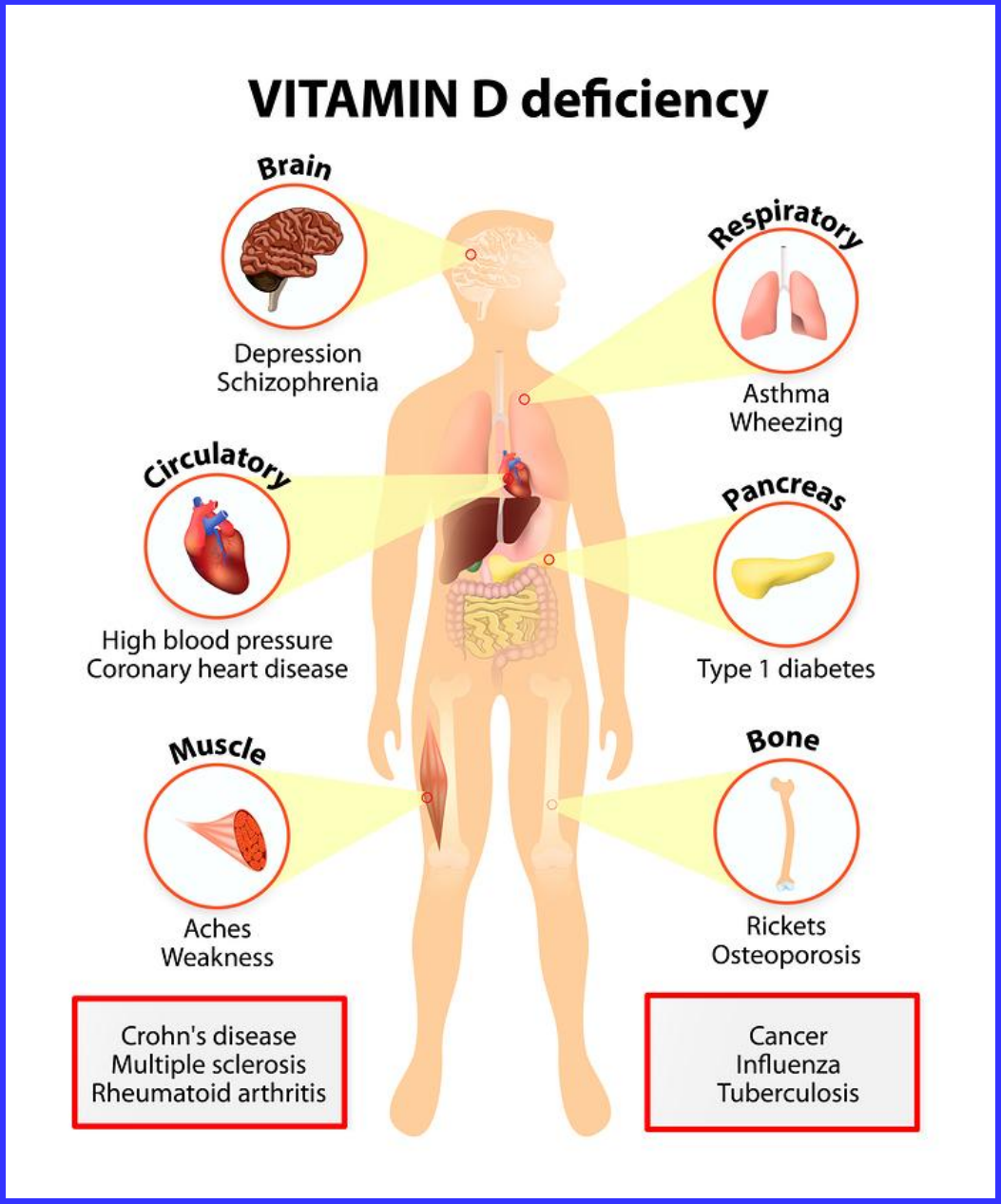
Clinical manifestations of Vitamin D deficiency

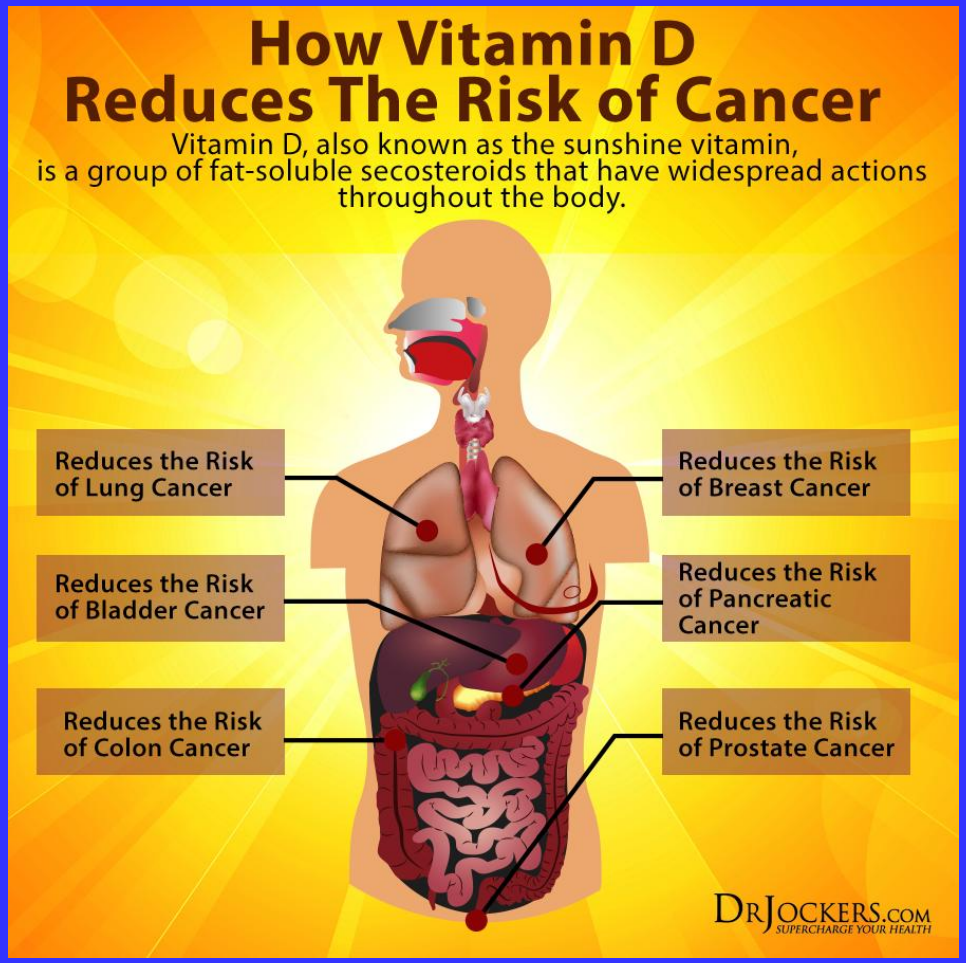
Musculoskeletal disorders:

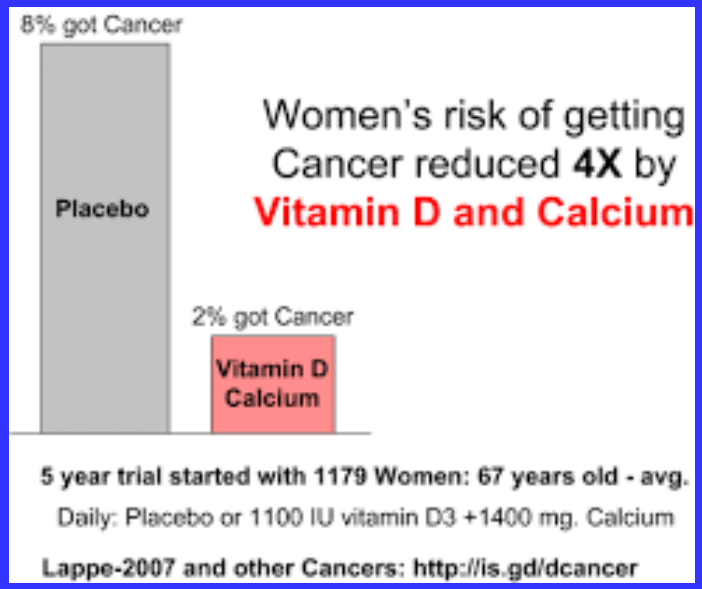
- non specific muscle pain,
- poor muscle strength
- Proximal muscle weakness
- low BMD (osteoporosis)
- ↑ risk of fall & fracture

Non-musculoskeletal disorders:

- ↑ risk of RTI,
- diabetes mellitus
- possibly cardiovascular diseases, hypertension
- Schizophrenia & depression
- Cancer (eg- colon, breast, ovarian & prostate)


VITAMIN D deficiency
Brain
Depression
Schizophrenia
Respiratory
Asthma
Wheezing
Circulatory
High blood pressure
Coronary heart disease
Pancreas
Type 1 diabetes
Muscle
Aches
Weakness
Bone
Rickets
Osteoporosis
Crohn's disease
Multiple sclerosis
Rheumatoid arthritis
Cancer
Influenza
Tuberculosis


How Vitamin D
Reduces The Risk of Cancer
Vitamin D, also known as the sunshine vitamin,
is a group of fat-soluble secosteroids that have widespread actions
throughout the body.
Reduces the Risk of Lung Cancer
Reduces the Risk of Breast Cancer
Reduces the Risk of Bladder Cancer
Reduces the Risk of Pancreatic Cancer
Reduces the Risk of Colon Cancer
Reduces the Risk of Prostate Cancer
DrJockers.com
SUPERCHARGE YOUR HEALTH


8% got Cancer
Placebo
Women's risk of getting Cancer reduced 4X by Vitamin D and Calcium
2% got Cancer
Vitamin D Calcium
5 year trial started with 1179 Women: 67 years old - avg.
Daily: Placebo or 1100 IU vitamin D3 +1400 mg. Calcium
Lappe-2007 and other Cancers: http://is.gd/dcancer

How to evaluate vitamin D status?

How to evaluate vitamin D status?

- The **serum 25(OH)D** is the most reliable marker of vitamin D status.
- reflecting the sum of cutaneous synthesis and oral intake.

What is an optimal 25(OH)D level?

25(OH) D level (ng/ml)	Interpretation
>=30-80	**Normal**
21- 29	Insufficient
10-20	**Deficient**
< 10	Severely deficient

Who should be tested for Vitamin D deficiency???

- Although vitamin D deficiency is prevalent, measurement of serum 25(OH)D levels is expensive,
- and universal screening is **not** supported.
- However, vitamin D testing may benefit those at risk for severe deficiency

Clinical Risk Factors for Vitamin D Deficiency

I. Decreased intake

- Inadequate oral intake
- Malnutrition (poor oral intake)

Clinical Risk Factors for Vitamin D Deficiency

- Limited sun exposure –

1. Home bound/ institutionalized
2. Dark skin
3. Living in High latitude
4. Winter season
5. Sunscreen users
6. Wearing skin covering clothes

Clinical Risk Factors for Vitamin D Deficiency

II. Gastrointestinal

Malabsorption

III. Hepatic

- Some antiepileptic medications (increased 24-hydroxylase activity)
- Severe liver disease or failure (decreased 25-hydroxylase activity)

Clinical Risk Factors for Vitamin D Deficiency

IV. Renal

- Aging (decreased 1-α hydroxylase activity)
- Renal insufficiency, GFR <60% (decreased 1-α hydroxylase activity)
- Nephrotic syndrome (decreased levels of vitamin D–binding protein)

Clinical Risk Factors for Vitamin D Deficiency

V. Elderly patients (> 50 years)

VI. Obesity (BMI> 30 kg/m2)-body fat sequesters the vitamin

Clinical Risk Factors for Vitamin D Deficiency

It has been suggested that clinicians should ***routinely test for hypovitaminosis D*** *in patients with* ***musculoskeletal symptoms****, such as bone pain, myalgias, and generalized weakness, because these symptoms are often associated with hypovitaminosis D .*

Management

Management

- Many patients and physicians think that adequate vitamin D intake can be obtained via diet alone.

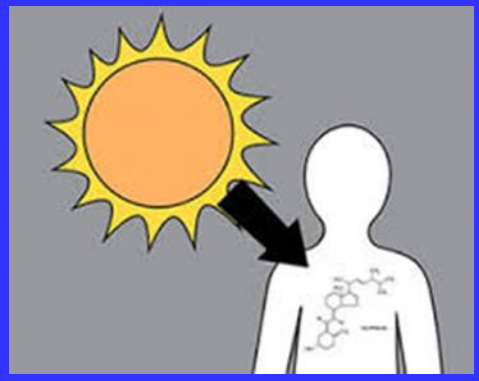
- *This assumption is erroneous.*

Management..contd..

As there are only small amounts of vitamin D in food there are only 2 sure ways to get enough vitamin D:

1. Taking vitamin D supplements.

2. Exposing bare skin to sunlight to get ultraviolet B (UVB).



Vitamin D supplements

Vitamin D supplements

Available forms of vitamin D supplements are

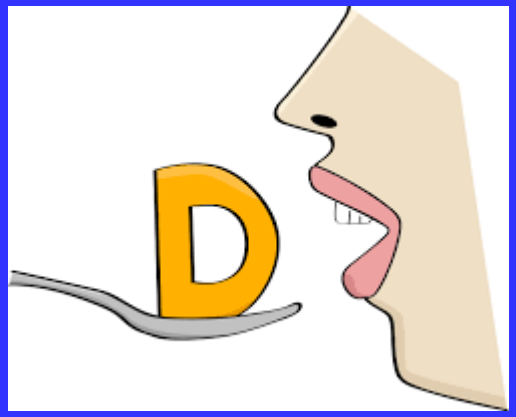
1. Ergocalciferol (vitamin D2)
2. Cholecalciferol (vitamin D3).

Vitamin D3 is preferred , as

- ✓ It is the naturally occurring form of the vitamin
- ✓ Vitamin D3 >3 times as effective as D2
- ✓ Longer duration of action

Vitamin D supplements

- **Dosing** — The recommended dose of vitamin D depends upon the **nature and severity** of the vitamin D deficiency.



Vitamin D supplements

- The lower the 25(OH)D serum concentration is before treatment, the higher is the dosage that is needed in order to quickly reach an acceptable serum level.

Vitamin D supplements

- Treatment involves an ***initial high-dosage treatment phase***, which can be given on a daily or weekly basis until the required serum levels are reached,

- followed by the ***maintenance*** of the acquired levels.

Vitamin D supplements

- Therapy prescriptions vary, and there ***is no consensus yet*** on how best to arrive at an optimum serum level.

Vitamin D supplements :Dosage

- According to ***Endocrine Society Practice Guideline:***

Age	Initial Therapy	Duration	Maintenance
Upto 1 year	2000 IU/ day or	6 weeks	400-1000 IU/day
	50,000 IU/ week		
1- 18 years	2000 IU/ day or	6 weeks	600-1000 IU/day
	50,000 IU/ week		
> 18 years	6000 IU/ day or	8 weeks	1500- 2000 IU/day
	50,000 IU/ week		

Vitamin D supplements

- ✓ In obese patients ,
- ✓ patients with malabsorption syndromes &
- ✓ patients on medications affecting vitamin D metabolism

2- 3 times higher doses are required.

Vitamin D supplements

- If the 25(OH)D concentration remains **persistently low** despite several attempts at correction with oral vitamin D,
- a trial of **ultraviolet B light therapy** (ie, by tanning lamps) may be considered to improve vitamin D status.

Vitamin D supplements

- For every 100 IU vitamin D3 ingested, blood level of 25-OH-D increases by 1 ng/mL

- 1 IU vitamin D is the biological equivalent of 0.025 µg cholecalciferol/ergocalciferol.


D-Rise® 20000
Cholecalciferol 20000 IU
BEXIMCO PHARMACEUTICALS LTD.
D-Rise® 40000
Cholecalciferol 40000 IU
10 capsules
Each capsule contains:
Cholecalciferol USP 40000 IU.
BEXIMCO PHARMACEUTICALS LTD.


Vitamine D3 B.O.N.®
200 000 UI/ml
Cholecalciferolum

Management..contd..

- **Need for other vitamins or minerals? —**

✓ During treatment for vitamin D deficiency, it is important to consume **calcium**.

✓ Calcium can be found in food sources or dietary supplements

Group	Dose
Men & premenopausal women	1000 mg/ day
postmenopausal women	1200 mg/ day

Management..contd..

Monitoring —

- A blood test is recommended to monitor blood levels of 25(OH)D **3 months** after beginning treatment.

- The dose of vitamin D may need to be adjusted based on these results.

Management..contd..

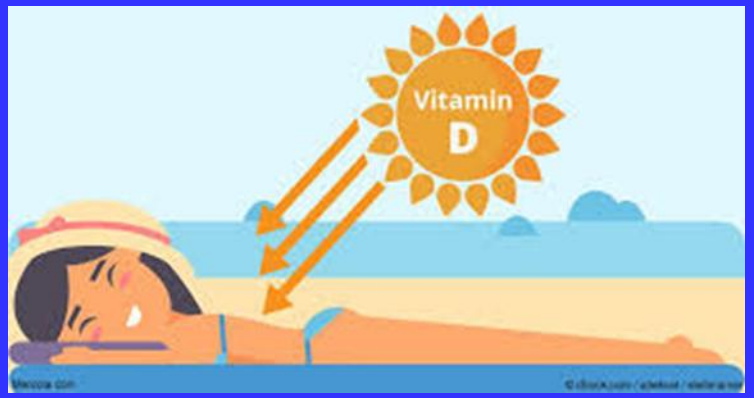
Side effects —

- Side effects of vitamin D are uncommon unless the 25(OH)D level becomes
- ✓ very elevated (>100 ng/mL) and
- ✓ the person is taking high dose calcium supplements.

Management..contd..

2.Exposing bare skin to sunlight (ultraviolet B)

- Full-body sun exposure producing slight pinkness in light-skinned persons results in vitamin D production equivalent to ingesting 10,000-25,000 IU



Management..contd..

- *5-10 minutes of direct exposure to the arms and legs = 3000 IU of vitamin D3*

- In a study of in Boston, 36% had 25 OH vit D level < 20 ng/ml at the end of winter. The prevalence decreased to 4% by the end of summer.

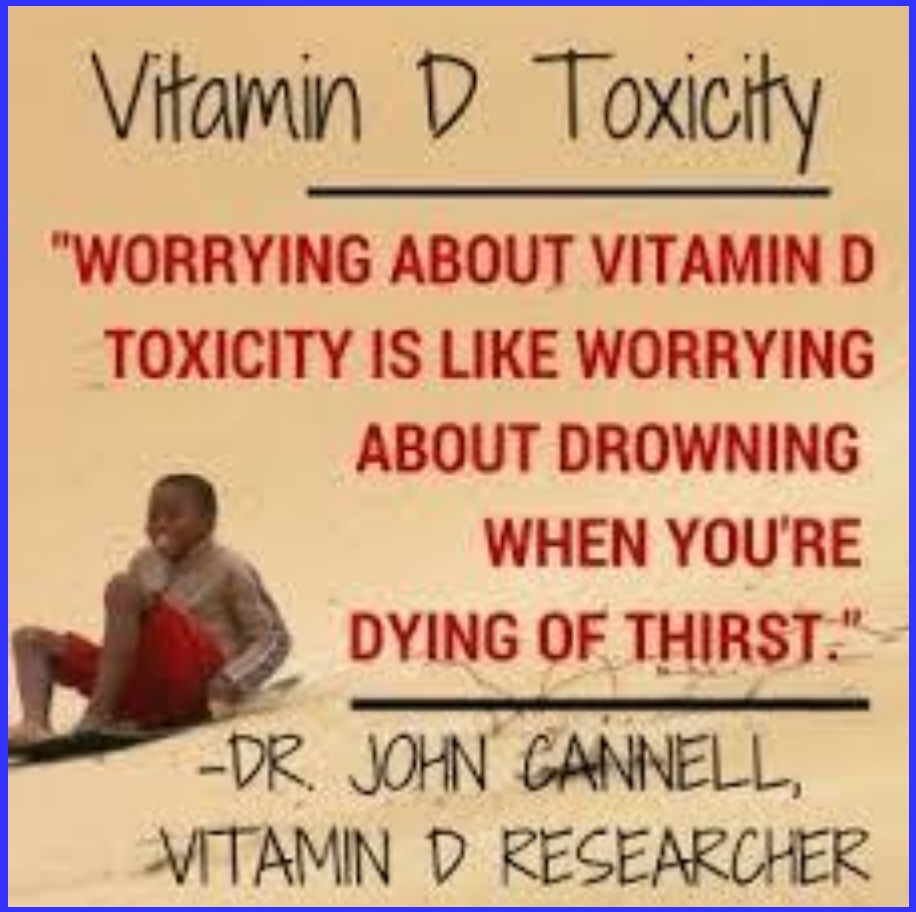
Exposing skin to UVB and the risk of skin cancer

- Research to date shows that moderate but frequent sun exposure is **healthy** but

- over exposure and intense exposure can **increase** risk of skin cancer.

Vitamin D toxicity

- Although excess vitamin D supplementation can lead to hypercalcemia, vitamin D toxicity is extremely rare
- generally occurs only after ingestion of large doses of vitamin D (>10,000 IU/d) for prolonged periods in patients with normal gut absorption or in patients who may be concurrently ingesting generous if not excessive amounts of calcium.


Vitamin D Toxicity
"WORRYING ABOUT VITAMIN D TOXICITY IS LIKE WORRYING ABOUT DROWNING WHEN YOU'RE DYING OF THIRST."
-DR. JOHN GANNELL, VITAMIN D RESEARCHER

Vitamin D toxicity

- Excessive intakes of vitamin D can lead to hypercalcemia.
- The symptoms of this are

✓ weakness,
✓ confusion,
✓ constipation,
✓ loss of appetite, and
✓ development of painful calcium deposits.

Prevention

- Unprotected sun exposure is the major source of vitamin D for both children and adults.

- ***10- 15 minutes exposure of hands, arms and face without sunscreen 2-3 times / week may be sufficient*** especially between the hours of 10 am and 3 pm (depending on skin sensitivity)

Prevention..contd..

- Sensible sun exposure, produces vitamin D in the skin that may last twice as long in the blood compared with ingested vitamin D

Prevention..contd..

Prevention..contd..

- Recommended dietary intake of vitamin D for patients at risk of vitamin D deficiency is as follows :

Age group	Vitamin D supplement
In infants and children up to 1 year old	at least 400 IU/day, to maximize bone health
In children and adolescents 1-18 years of age	at least 600 IU/day to maximize bone health
In adults 19-70 years of age	at least **600 IU/day** to maximize bone health and muscle function
> 70 year of age	800 IU/day

Prevention..contd..

- The Canadian Paediatric Society recommends that pregnant or breastfeeding women consider taking 2000 IU/day, that all babies who are exclusively breastfed receive a supplement of 400 IU/day.

- **Study of Serum Vitamin D level in different socio-demographic population- A Pilot study**

Highlights of our study….

Objectives

- ✓ To determine the prevalence of hypovitaminosis D &
- ✓ its association with different socio-demographic population
- in adult patients of PMCH.

Methodology…

Methodology

- A cross sectional observational study was conducted
- among the adult patients aged 18 years and above
- presented with generalized body aches and pains
- attended both outpatient and inpatient department of Popular Medical College Hospital
- during the period of March'16- August'16 (6 months).

Inclusion criteria

- Total 212 adult patients, both male and female were recruited in the study who gave consent after explanation.

Exclusion criteria

- Following subjects were excluded from the study-
- Age <18 years
- Patients who were not willing to participate in the study
- Patients who were taking vitamin D, Calcium with vitamin D or Multivitamins as supplement

Exclusion criteria

- Individuals who suffer from chronic diseases that affect the absorption of Vitamin D such as chronic liver disease & kidney disease

- Subjects who are taking drugs that could influence vitamin D like steroid and anti-epileptics

Results …

Table 1: Vitamin D status among the study population (Range: 3.3- 29.0)

Vitamin D level (ng/ml)	Vitamin D status	Frequency (n)	Percent (%)
>=30	Normal	00	00
21- 29.9	Insufficient	09	4.2
10- 20.9	Deficient	147	68.9
< 10	Severely deficient	56	26.9

Vitamin D level

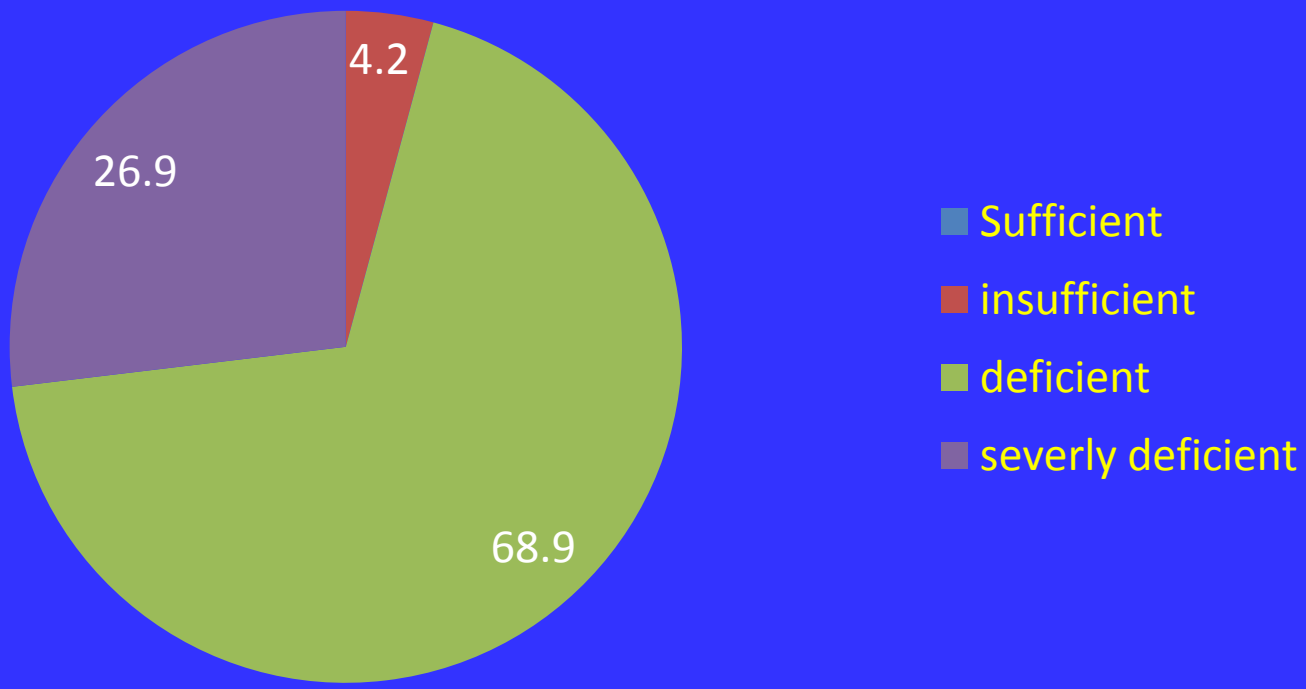
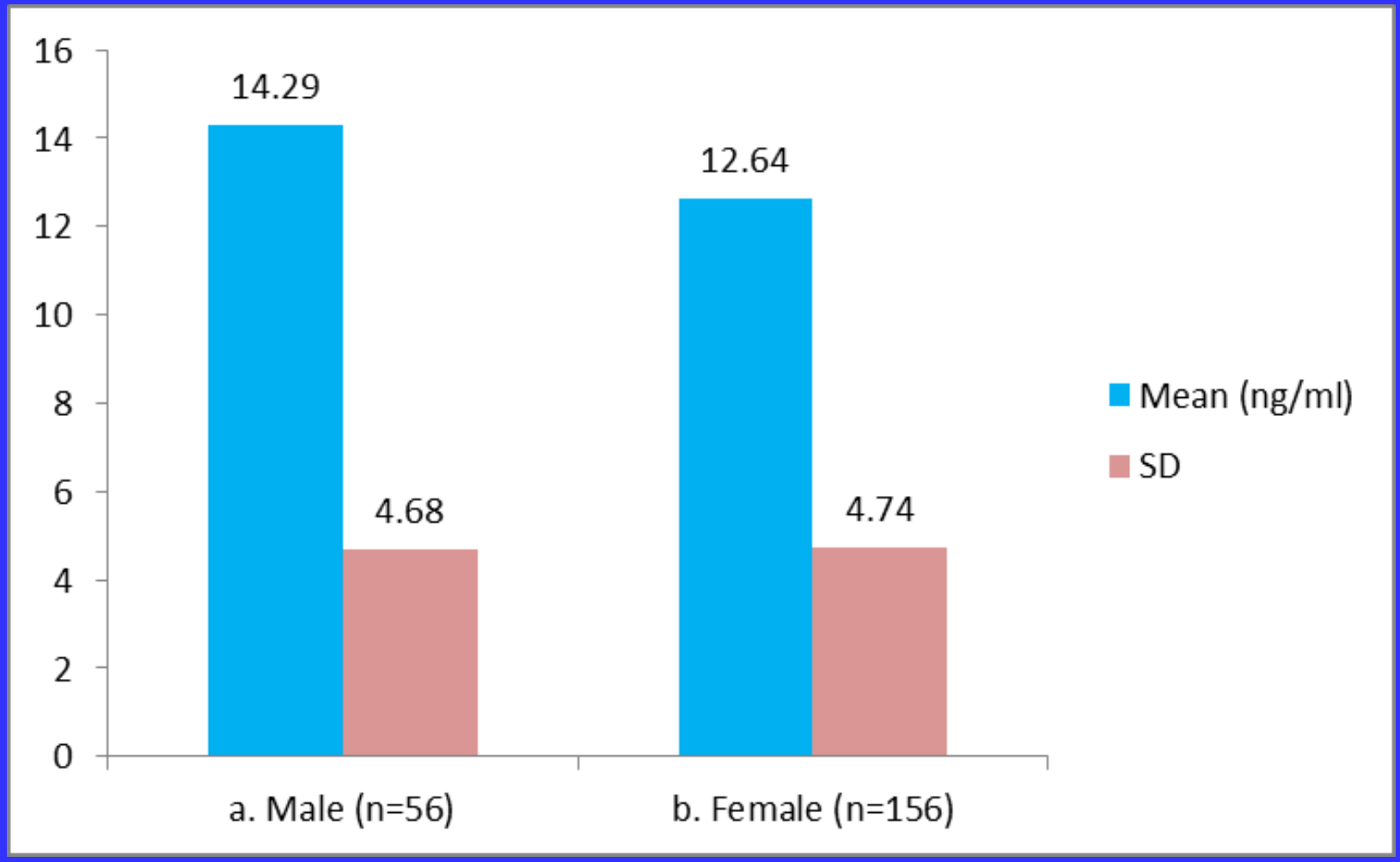


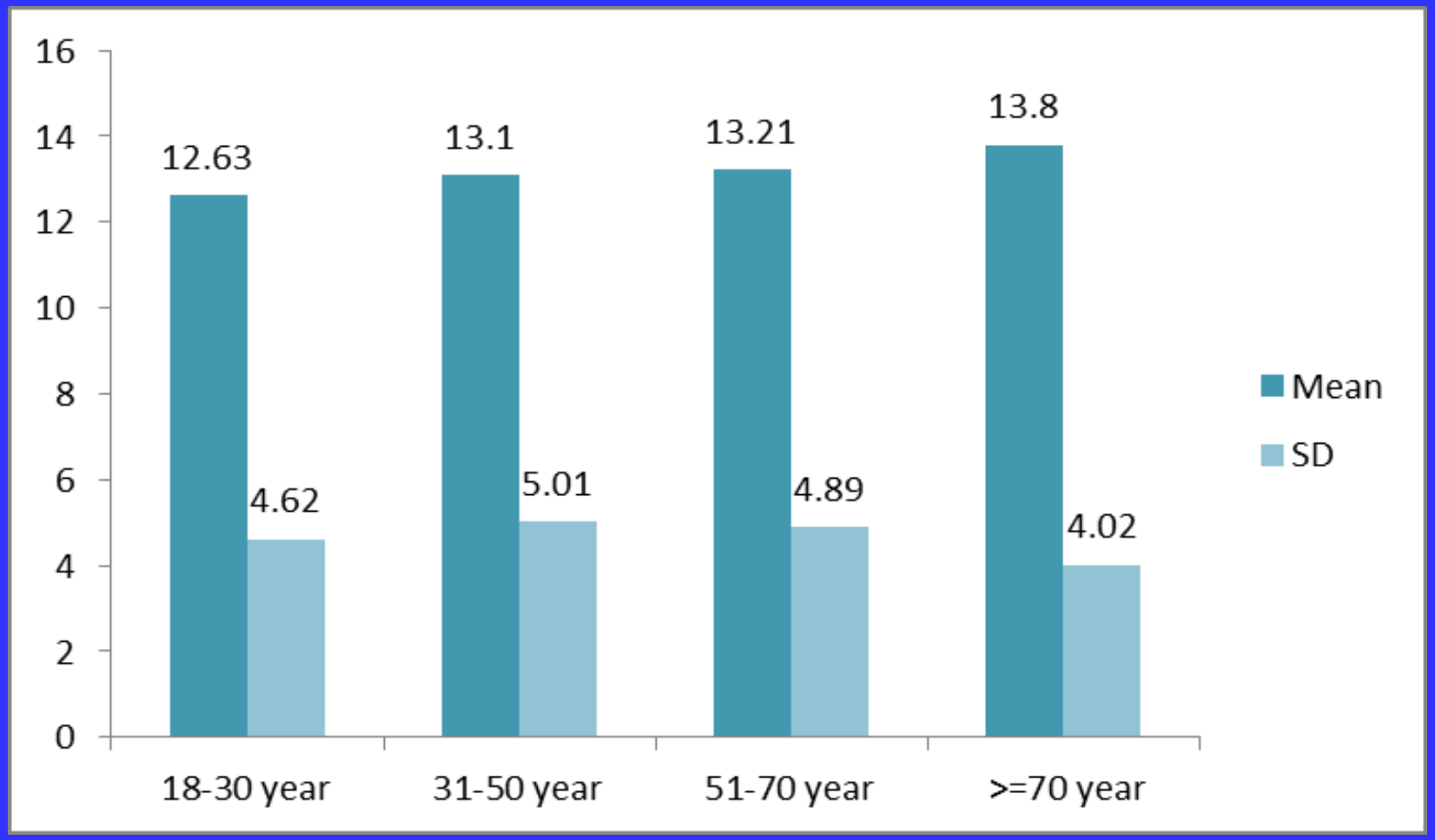
Table 2-Comparison of vitamin D levels with socio-demographic factors

Socio-demographic factors	Frequency (n)	Mean (ng/ml)	SD
Sex	a. Male (n=56) b. Female (n=156)	14.29 12.64	4.68 4.74
Age	a.18-30 year(n=38) b.31-50 year(n=80) c.51-70 year(n=76) d. >=70 year(n=12)	12.63 13.10 13.21 13.80	4.62 5.01 4.89 4.02

Gender distribution of Vitamin D level

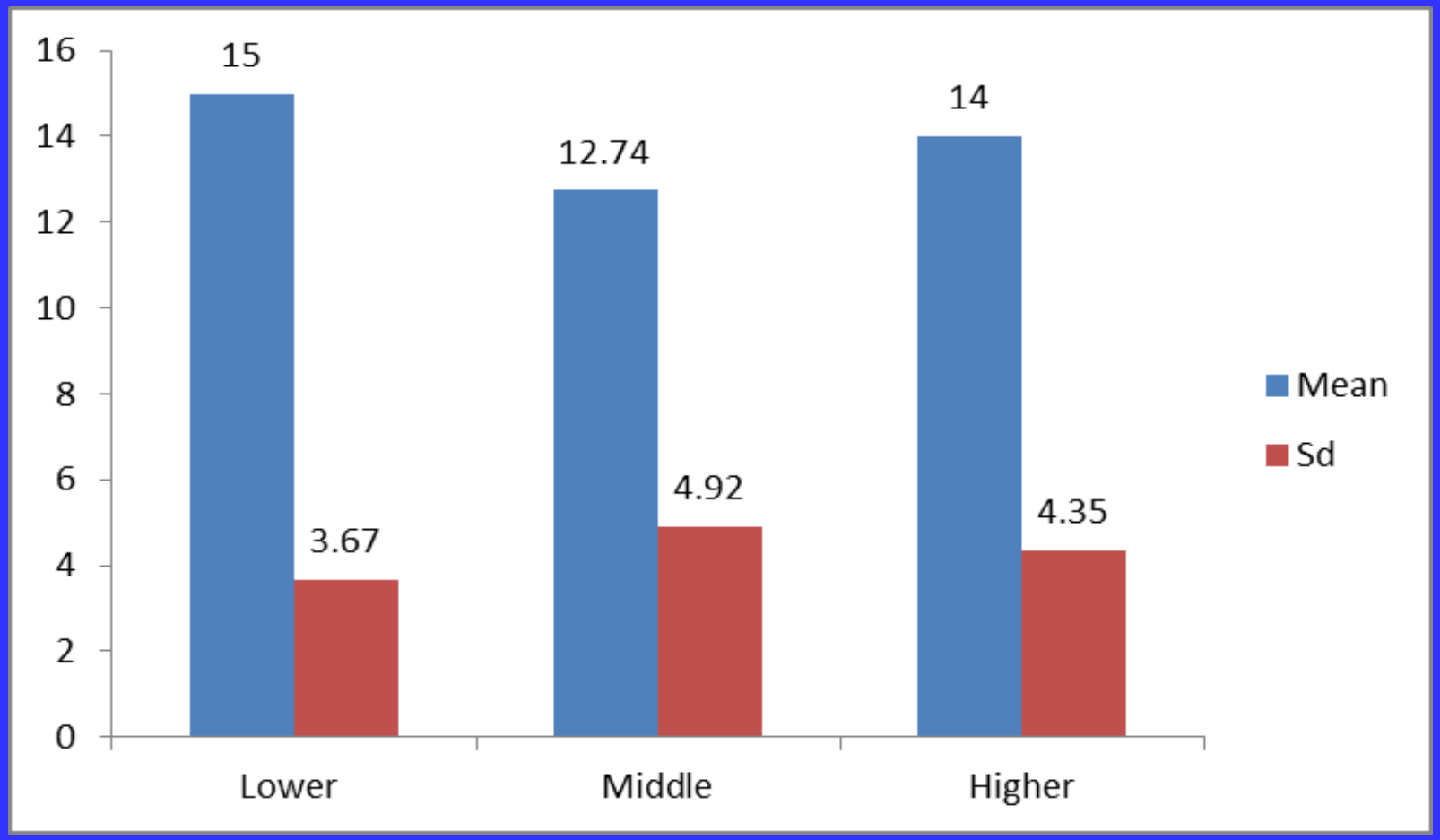


Vitamin D level in different Age group

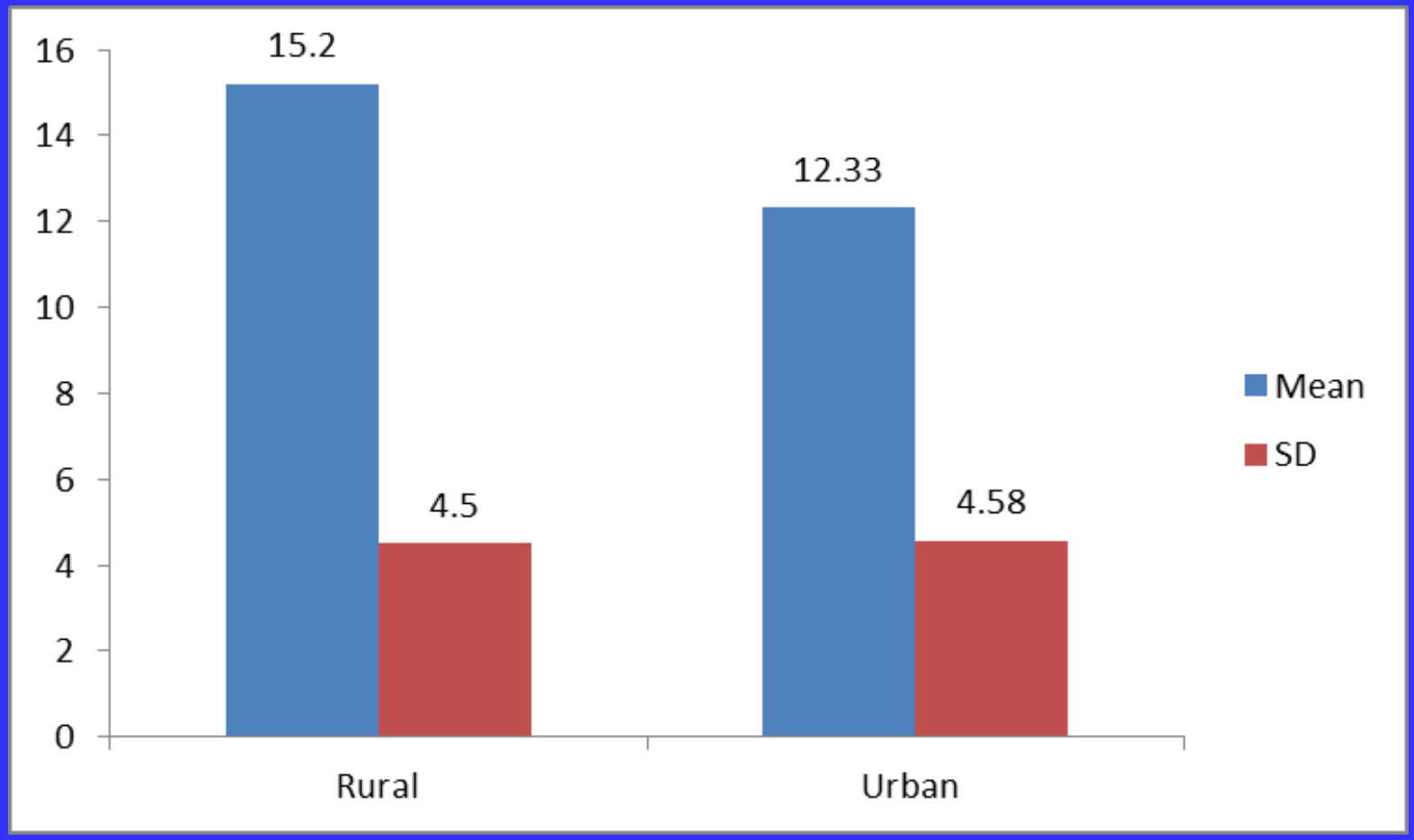


Socio-demographic factors	Frequency (n)	Mean (ng/ml)	SD
Socio-economic status	a. Lower (n=18) b. Middle(n=180) c. Higher(n=14)	15.0 12.74 14.0	3.67 4.92 4.35
Location	a. Rural (n=54) b. Urban (n=158)	15.20 12.33	4.50 4.58
BMI	a. Normal (n=98) b. Underweight (n=14) c. Overweight (n=70) d. Obese (n=30)	13.55 12.82 13.19 11.10	5.12 4.21 4.41 4.71

Vitamin D level in different Socio-economic status

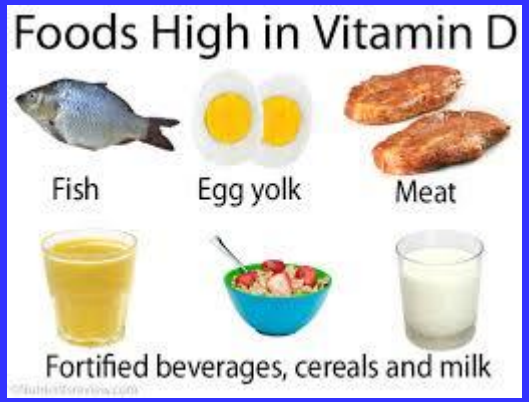


Vitamin D level in different locale

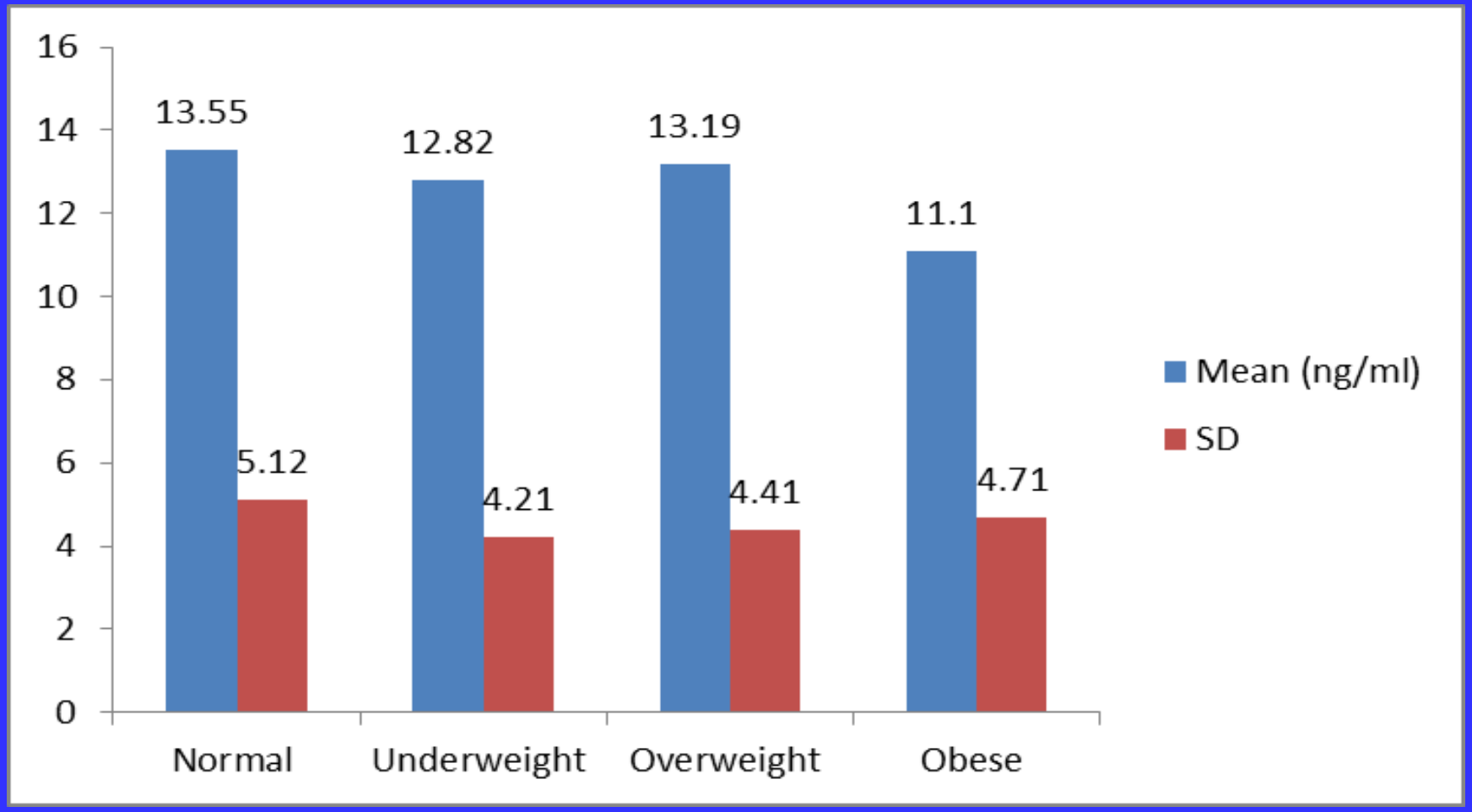


- All our study subjects were consuming vitamin D enriched food like eggs, fish, milk (except cheese) in different proportion & amount.

- So, food was **not** an important determinant of hypovitaminosis D in our study.



Vitamin D level in different BMI

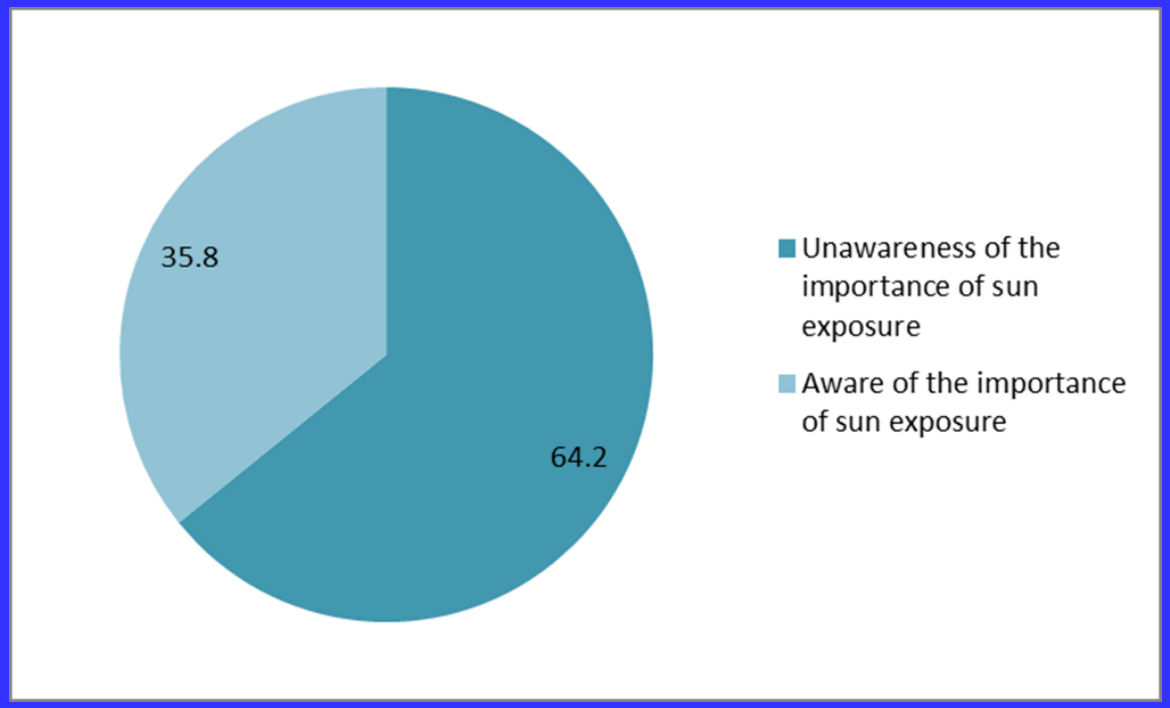


- The mean difference between normal and obese population was statistically significant (p value 0.007).

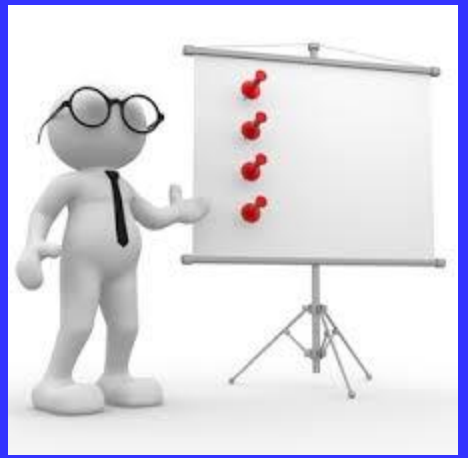
- This indicates obesity is an independent risk factor for hypovitaminosis D.

Awareness of the importance of sun exposure

- One of the most striking finding from our study is the unawareness of the importance of sun exposure among 2/3 of our study population (64.2%).



Conclusion ...



- Despite abundant sunlight in Bangladesh, the prevalence of vitamin D deficiency among adult patients presenting with generalized aches and pains is found to be 100% across all age groups & both sexes.

- **Some of the important factors associated with hypovitaminosis D in Bangladesh are-**

✓ Female gender

✓ urbanization

✓ obesity

✓ dark skin complexion

✓ wearing skin covering veils

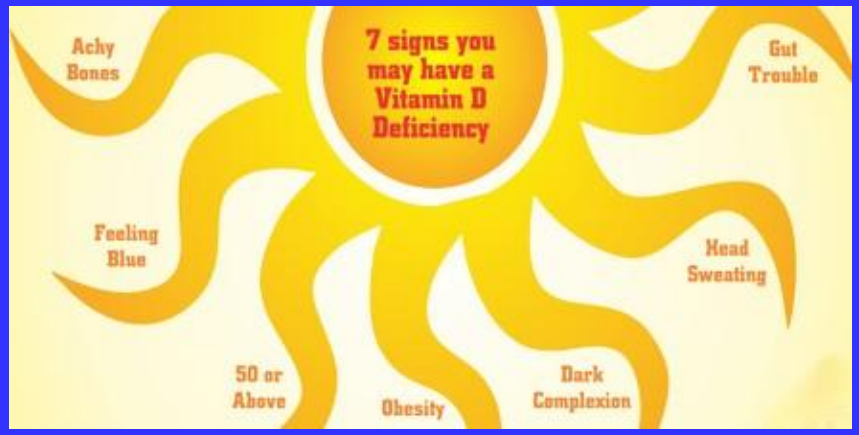
✓ lifestyle factors (staying inside home/ office/ car- lack of sunlight exposure)

Take Home Messages…

Take Home Messages

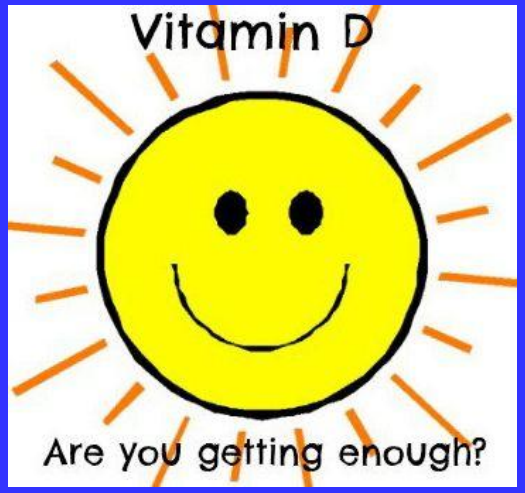
- Vitamin D deficiency is common worldwide
- 25 OH vitamin D is a predictor of bone health in terms of fracture risk and risk of falls
- 25 OH vitamin D is also an independent predictor of risk of

✓ Cardiovascular disease,
✓ hypertension,
✓ cancer,
✓ diabetes,
✓ all cause mortality, and
✓ URTI



Take Home Messages..contd..

- Sensible sun exposure is a great way to maintain vitamin D sufficiency



Take Home Messages..contd..

- Physicians should **screen for** vitamin D deficiency who **are at risk** based on diet, sun exposure, obesity indices, age, sex & lifestyle factors, ***as features of hypovitaminosis D are mostly reversible with proper replacement.***

Take Home Messages..contd..

- Public health efforts in Bangladesh should try to

✓ Increase awareness about the importance of sun exposure and

✓ encourage the consumption of natural food sources rich in vitamin D.