Vitamin  deficiency

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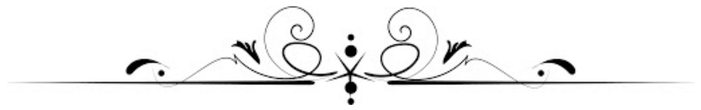
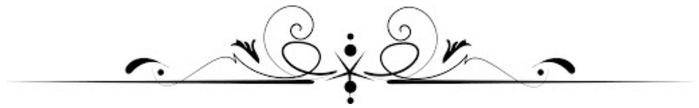
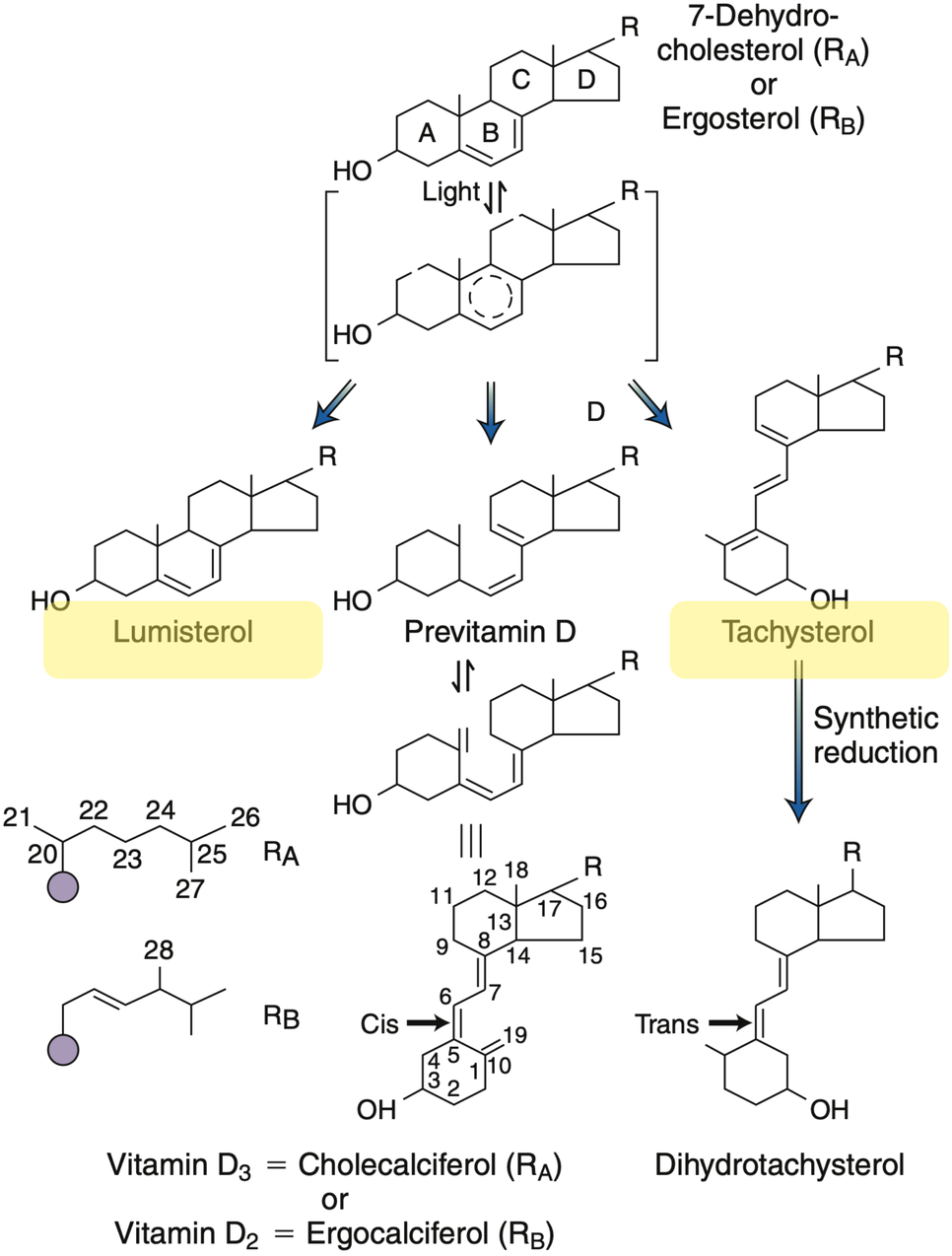
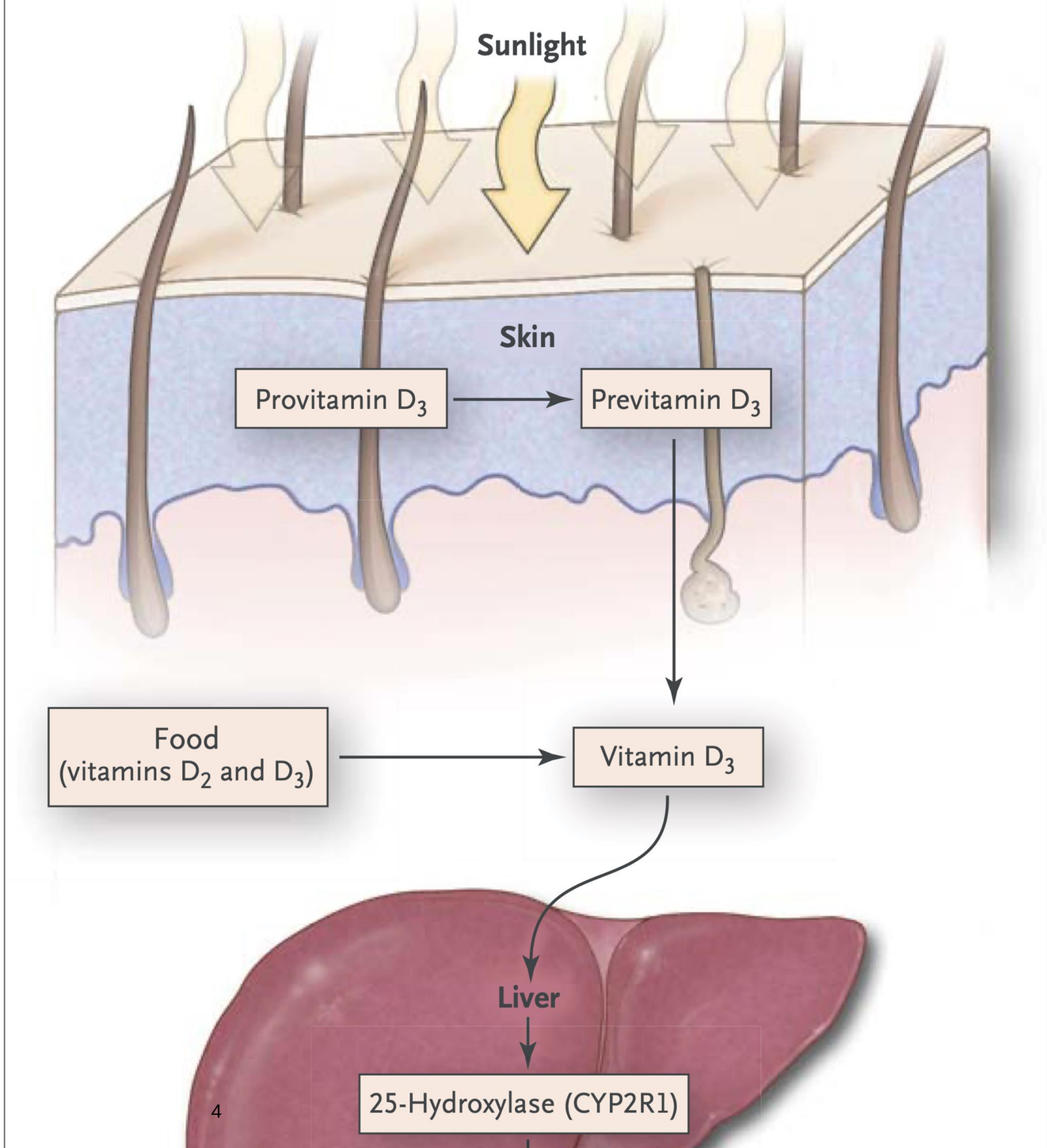
Vitamin D is a fat-soluble vitamin involved in the regulation of calcium homeostasis and bone health.

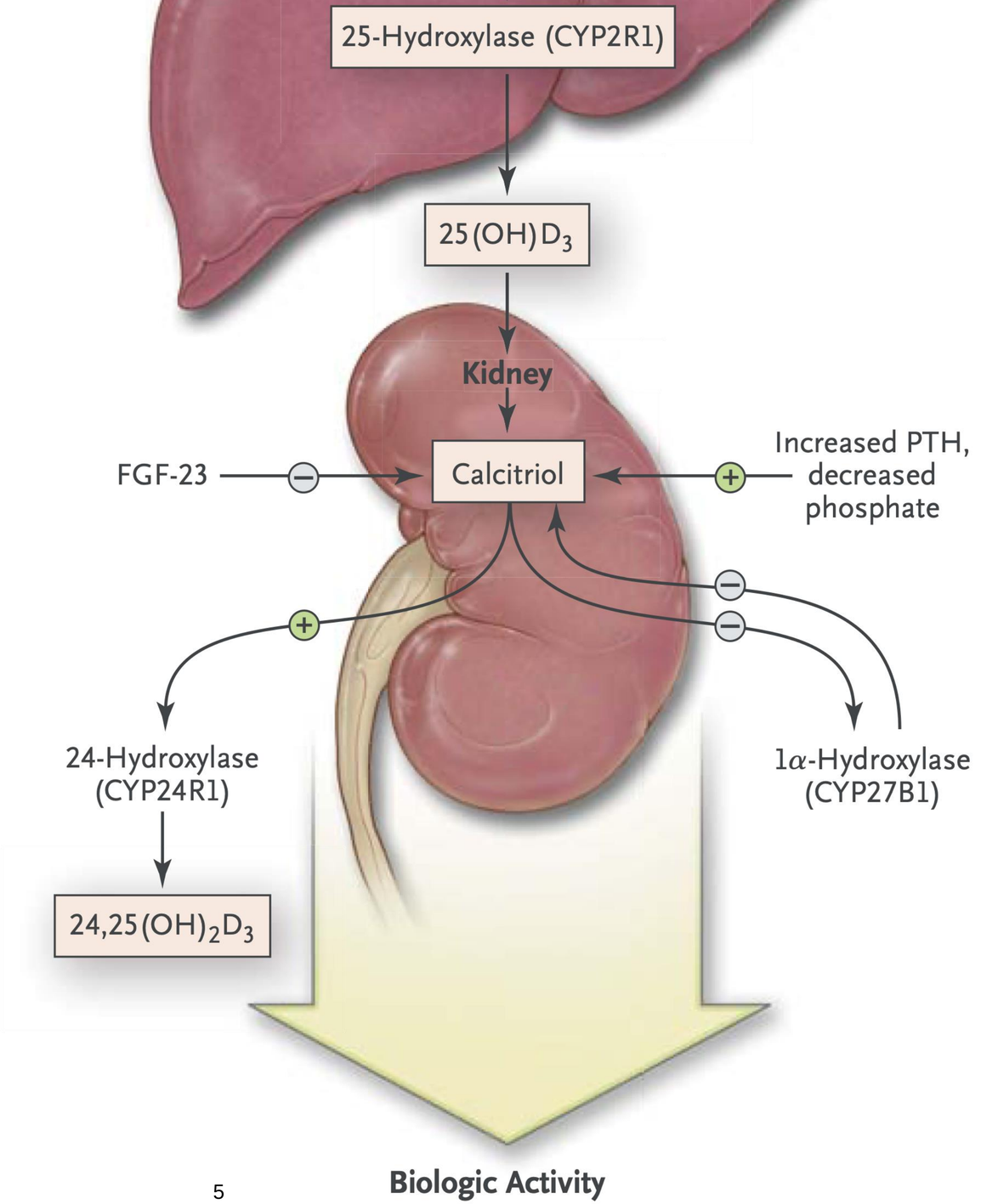


Vitamin D metabolism

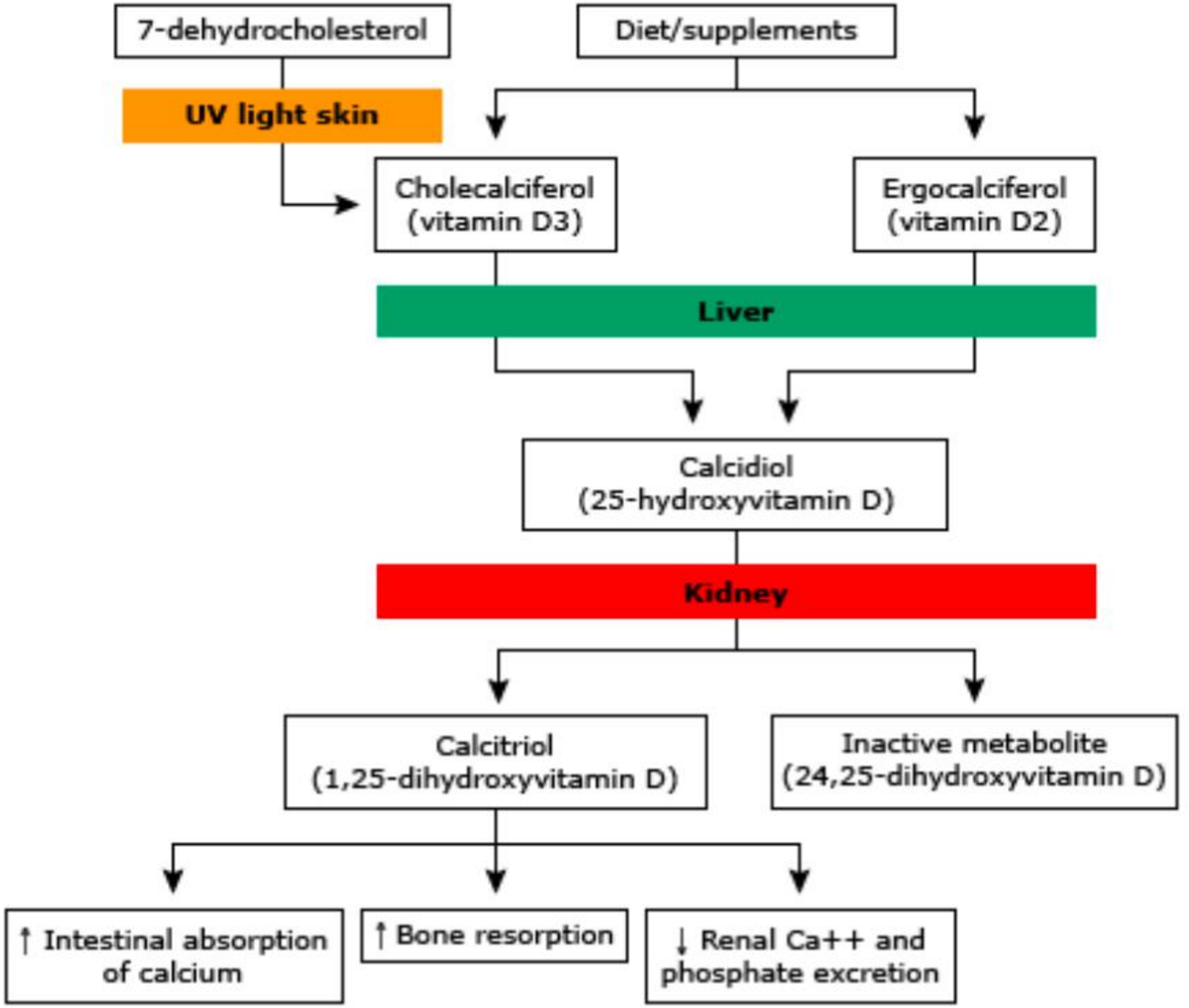



7-Dehydro-
cholesterol (R_A)
or
Ergosterol (R_B)
Light
D
Lumisterol
Previtamin D
Tachysterol
Synthetic
reduction
Cis
Trans
R_A
R_B
Vitamin D_3 = Cholecalciferol (R_A)
or
Vitamin D_2 = Ergocalciferol (R_B)
Dihydrotachysterol


Sunlight
Skin
Provitamin D_3
Previtamin D_3
Food
(vitamins D_2 and D_3)
Vitamin D_3
Liver
25-Hydroxylase (CYP2R1)


25-Hydroxylase (CYP2R1)
25(OH)D3
Kidney
FGF-23
Calcitriol
Increased PTH, decreased phosphate
24-Hydroxylase (CYP24R1)
1α-Hydroxylase (CYP27B1)
24,25(OH)2D3
Biologic Activity

Pathways of vitamin D synthesis



Casual exposure to sunlight provides amounts of vitamin D that are adequate to prevent rickets in many people but is influenced by geographic location, season, use of sun block lotion, and skin pigmentation

Sources of vitamin D

Sunlight

Cheese

Milk

Eggs

Salmon

Yogurt

Healthbring.com

Dietary Reference Intakes (DRIs)

- EAR - Estimated Average Requirements (The median intake needs of the population)
- RDA - Recommended Dietary Allowance (The requirements of at least 97.5% of the population)
- AI - Adequate Intake
- UL - Upper Level intake

The Journal of Clinical Endocrinology and Metabolism

J Clin Endocrinol Metab. 96(1): 53-58

The 2011 Report on Dietary Reference Intakes for Calcium and Vitamin D from the Institute of Medicine: What Clinicians Need to Know

A. Catharine Ross, JoAnn E. Manson, 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, Susan T. Mayne, Clifford J. Rosen, Sue A. Shapses

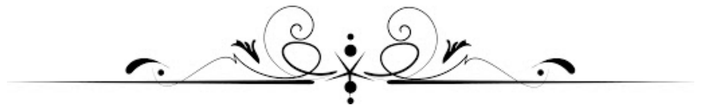
Department of Nutritional Sciences (A.C.R.), Pennsylvania State University, University Park, Pennsylvania 16802; Department of Medicine (J.E.M.), Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts 02215; Department of Pediatrics (S.A.A.), Baylor College of Medicine, Houston, Texas 77030; Department of Medicine (J.F.A.), State University of New York at Stony Brook, Stony Brook, New York 11794; Winthrop University Hospital (J.F.A.), Mineola, New York 11501; Division of Nutritional Sciences (P.M.B), Cornell University,

Life-stage group (age and gender)	Vitamin D		
	RDA (IU/d) (intake that covers needs of ≥97.5% of population)	Serum 25OHD level (ng/ml) (corresponding to the RDA)[b]	UL (IU/d)[a]
1–3 yr (M+F)	600	20	2500
4–8 yr (M+F)	600	20	3000
9–13 yr (M+F)	600	20	4000
14–18 yr (M+F)	600	20	4000
19–30 yr (M+F)	600	20	4000
31–50 yr (M+F)	600	20	4000
51–70 yr (M)	600	20	4000
51–70 yr (F)	600	20	4000
71+ yr (M+F)	800	20	4000
Pregnant or lactating (F)			
14–18 yr	600	20	4000
19–50 yr	600	20	4000
Infants			
0–6 months (M+F)	400[c]	20	1000
6–12 months (M+F)	400[c]	20	1500

Food*	Micrograms (mcg) per serving	IUs* per serving	Percent DV**
Cod liver oil, 1 tablespoon	34.0	1360	170
Trout (rainbow), farmed, cooked, 3 ounces	16.2	645	81
Salmon (sockeye), cooked, 3 ounces	14.2	570	71
Mushrooms, white, raw, sliced, exposed to UV light, 1/2 cup	9.2	366	46
Milk, 2% milkfat, vitamin D fortified, 1 cup	2.9	120	15
Sardines (Atlantic), canned in oil, drained, 2 sardines	1.2	46	6
Soy, almond, and oat milks, vitamin D fortified, various brands, 1 cup	2.5−3.6	100−144	13−18
Ready-to-eat cereal, fortified with 10% of the DV for vitamin D, 1 serving	2.0	80	10
Egg, 1 large, scrambled (vitamin D is in the yolk)	1.1	44	6
Liver, beef, braised, 3 ounces	1.0	42	5
Tuna fish (light), canned in water, drained, 3 ounces	1.0	40	5
Cheese, cheddar, 1 ounce	0.3	12	2
Mushrooms, portabella, raw, diced, 1/2 cup	0.1	4	1
Chicken breast, roasted, 3 ounces	0.1	4	1
Beef, ground, 90% lean, broiled, 3 ounces	0	1.7	0
Broccoli, raw, chopped, 1/2 cup	0	0	0
Carrots, raw, chopped, 1/2 cup	0	0	0
Almonds, dry roasted, 1 ounce	0	0	0

Clinical importance of vit D

Vitamin D and its metabolites have a significant clinical role because of their interrelationship with calcium homeostasis and bone metabolism.



- Without the presence of activated vitamin D, normal bone metabolism is altered so that only **10 percent of calcium** and **60 percent of phosphorus** are absorbed.
- As a result, the skeleton becomes the body's primary source of calcium.
- lead to osteomalacia, and precipitate and exacerbate osteopenia and osteoporosis.

Vitamin D deficiency

↓ Intestinal absorption of calcium and phosphate

Hypophosphatemia and then hypocalcemia

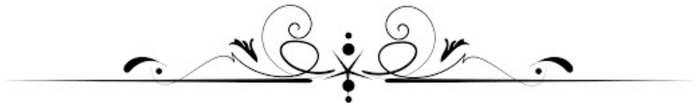
Secondary hyperparathyroidism

Phosphaturia and demineralization of bone

Osteomalacia in adult

Osteomalacia and rickets in children

Vitamin D deficiency cause serious health concern like rickets, osteomalcia, osteoporotic fracture and falls in elderly.



Extra-skeletal effects: vit D deficiency is shown to be associated with infections, asthmas, autoimmune diseases and cancer.

Extra-skeletal effects

Cardiovascular Diseases and Vitamin D

- A strong association between Vitamin D deficiency and **cardiovascular mortality**
- 40% higher risk of **death due to CVD and stroke** in black population with calcitriol level in the lowest quartile in data from NHANES.
- Higher risk of **metabolic syndrome, hypertension** and adverse cardiovascular events.
- High risk for developing CVD in subjects with lower levels of 25(OH)D.
- a study from South India reported that very high levels of 25(OH)D were associated with increased risk of IHD

Extra-skeletal effects

Cardiovascular Diseases and Vitamin D

- RCTs on vitamin D supplementation have not consistently demonstrated a positive effect on reducing BP

- Two studies that prospectively examined vitamin D supplementation on cardiovascular mortality did not show better survival compared with controls.

- A recent meta-analysis of 51 RCTs showed that vitamin D was associated with non-significant effect on death (RR 0.96), MI (RR 1.02), and stroke (RR 1.05) with no change in BP, resulting in the conclusion that data available to date are unable to show a significant decrease in mortality and cardiovascular risk associated with vitamin D.

Extra-skeletal effects

Diabetes and Vitamin D

- Animal studies suggest that the immunomodulatory and anti-inflammatory actions of vitamin D may reduce the autoimmune insulinitis of type I DM.
- By modulation of immune and inflammatory process, Vitamin D may decrease insulin resistance and increase insulin secretion in type II DM.
- Vitamin D deficiency may also impair insulin secretion through its associated increase in parathormone levels.
- It may reduce insulin resistance by its immunomodulatory and anti-inflammatory effects.

Extra-skeletal effects

Diabetes and Vitamin D

- There is some evidence to suggest that Vitamin D may play a role in the prevention and treatment of type I and II DM through its action on systemic inflammation, insulin secretion and resistance.

- The potential role of vitamin D and calcium supplementation in alleviating the increasing menace of diabetes needs to be further studied.

Extra-skeletal effects

Cancer and Vitamin D

- Women with mutations of VDR gene have higher risk of breast cancer.

- Women who had low blood level of 25(OH)D (<12 ng/ mL) at the start of study had significantly higher risk of development of colorectal cancer compared with those who had 25(OH)D level >24 ng/ mL.

Extra-skeletal effects

Cancer and Vitamin D

- A double-blind placebo-controlled trial to determine if 1,25(OH)2D could be used in pre-leukemia showed promising results initially but was proved to be unsuccessful in the end because of development of hypercalcemia and blast crisis.

- In prostatic cancer, even though administration of 2000 IU Vitamin D per day resulted in fall in PSA levels, severe hypercalcemia necessitated the halting of the trial

- More studies will be needed to confirm and approve Vitamin D as a co-prescription with anti-cancer drugs.

Extra-skeletal effects

Autoimmune Diseases and Vitamin D

- 1,25(OH)2D inhibits T cells proliferation and prevents formation of gamma interferon and interleukin-2 (IL-2) by the helper T cells (TH1).

- It also enhances suppressor T cell (TH2) activity, thereby enhancing production of IL-4, IL-5 and IL-10.

- Use of Vitamin D receptor ligands have increased the action of natural killer cells and enhanced the activation of phagocytes. 1,25(OH)2D has been shown to be useful in animal models of **multiple sclerosis** and **Crohn's disease**

Extra-skeletal effects

Autoimmune Diseases and Vitamin D

- Women who had the highest intake of Vitamin D had reduced risk of developing multiple sclerosis by 42%.

- Similar observations have been made in rheumatoid arthritis, and children born to mothers who were Vitamin D deficient had increased risk of wheezing disorders during early childhood.

Extra-skeletal effects

Innate Immunity and Vitamin D

- Since the prevalence of Vitamin D concentration of <30 ng/mL was observed in 86% of patients with active tuberculosis, it had been used earlier to treat patients with tuberculosis.

- However, Vitamin D supplementation cannot be recommended as treatment for tuberculosis unless more prospective studies come up with evidence-based criteria.

- In the case of HIV also, some in vitro studies have shown favorable effect on induction of autophagy.

- Direct correlation was observed between lower levels of 1,25(OH)2D with lower CD4+ T cell count, higher tumor necrosis factor level and speed of HIV disease progression.

Extra-skeletal effects

Psoriasis and Vitamin D

- Active Vitamin D is a potent inhibitor of keratinocytes and could be used safely for non-malignant hyper-proliferative skin disorders like psoriasis.

- Topically applied 1,25(OH)2D or some if its analogs could be used as a first-line therapy in psoriasis.

“The IOM Committee concluded that the evidence that vitamin D or calcium reduced risk of nonskeletal chronic disease outcomes was inconsistent, inconclusive, and did not meet criteria for establishing cause-and-effect relationships. ”

VITAMIN D DEFICIENCY

The major cause of vitamin D deficiency is lack of sun exposure.

Risk Factors for Vitamin D Deficiency

- Age > 65 years
- Breastfed exclusively without vitamin D supplementation
- Dark skin
- Insufficient sunlight exposure
- Medication use that alters vitamin D metabolism (e.g., anticonvulsants, glucocorticoids)
- Obesity (BMI>30)
- Sedentary lifestyle

Causes of vitamin D deficiency or resistance

Deficient intake or absorption
Dietary
Malabsorption
Gastric bypass (bariatric surgery, gastrectomy)
Small bowel disease
Pancreatic insufficiency
Decreased skin synthesis
Inadequate sunlight exposure
Full sunscreen use
Darkly pigmented skin
Defective 25-hydroxylation
Cirrhosis
Increased catabolism of vitamin D to inactive metabolites
Anticonvulsants
Loss of vitamin D binding protein
Nephrotic syndrome
Defective 1-alpha 25-hydroxylation
Hypoparathyroidism
Renal failure
1-alpha hydroxylase deficiency (vitamin D-dependent rickets, type 1)
Defective target organ response to calcitriol
Hereditary vitamin D-resistant rickets (vitamin D-dependent rickets, type 2)

How to diagnose vitamin D deficiency

The blood level of **25(OH)D** is the best method to determine vitamin D status.

Although 1,25 (OH) 2 D is the biologically active form, it provides no information about vitamin D status because it is often normal or even elevated in children and adults who are vitamin D deficient.

Assay issues

- Total 25(OH) D - clinically important one
- Levels vary with the assay method used.
- Assay variability is still a major issue.
- Since 2010, Vitamin D Standardization Program to standardize the gold standard reference assays or reference measurement by National Institute for Standards and Technology (NIST)

Diagnostic Criteria

- Deficient : <30 **nmol/l** (12 ng/ ml)
- Insufficiency : 30-50 **nmol/L** (12-20 ng/ml)
- Sufficiency : >50 **nmol/L** (>20 ng/ml)

Age and Ageing 2014; 43: 592–595 doi: 10.1093/ageing/afu093

Vitamin D status in Asia

INDIA

- In healthy pregnant women in Delhi the mean serum 25(OH)D was **23.2 nmol/l**
- Hypovitaminosis D (25(OH)D < 50 nmol/l) was observed in **96·3 %** of the subjects.
- In healthy school children aged 6-18 years the mean serum 25(OH)D level was 31.9nmol/l with 29.9% having a level <22.4nmol/l.

Vitamin D status in Asia

BANGLADESH

Vitamin D insufficiency (< 40 nmol/l) was common (**80%**) regardless of age, lifestyle and clothing in study from Dhaka

- 25(OH)D < 37.7nmol/l was seen in **50%** of those in low income groups (median 36.7nmol/l) compared to **38%** of high income groups (median (43.5nmol/L).

Vitamin D status in Asia

VIETNAM

- In a cross sectional study from Vietnam the mean 25(OH)D level was **91.8nmol/l** in men and **75.1 nmol/**l in women.

Vitamin D status in Asia

THAILAND

- Across Thailand 2641 adults aged 15-98 years were selected from the Thai 4th National Health Examination Survey (2008-9) cohort
- Subjects residing in Bangkok, had lower mean 25(OH)D levels than other parts of the country (Bangkok 64.8nmol/l, central 79.5nmol/l, northern 81.7nmol/l, north-eastern 82.2nmol/l and southern regions 78.3nmol/l)

Vitamin D status in Asia

MALAYSIA

- 71% of the Malay women had levels in the insufficient range (25-50nmol/l) compared to 11% of the Chinese women.
- Malay women commonly wear traditional dress with only face and hands exposed.

Vitamin D status in Asia

CHINA

- Vitamin D insufficiency is highly prevalent in China and Mongolia where rickets is still seen commonly.
- In a study of 301 healthy adolescent girls from Beijing, 57.8% had vitamin D insufficiency (serum 25(OH)D < 50nmol/l) , whilst 31.2% had levels <25nmol/l.
- A semi-arid mountainous area in central China, showed a mean 25(OH)D of 31.7nmol and 25% of the population had a serum level <19.5nmol/l

Vitamin D status in Asia

MYANMAR

Prevalence of vitamin D deficiency and its determinants in pre-defined Myanmar healthcare user populations.

Aung MW, Pyone ZC, Hlaing TT, Mitchell E, Aye M (2018)

- Cross sectional observational survey of vitamin D deficiency among Myanmar health care users at Yangon General hospital.
- Vitamin D deficiency found in **31.7%** in those who already had fragility fracture, **51.7%** in those who had fracture risk, in compared to higher rate of deficiency **81.7%** in control group of health care workers
- (60 persons in each group)

Myanmar Health Sciences Research Journal, Vol. 27, No. 1, 2015

Serum 25(OH)D_3, Calcium, Phosphorus Levels and Bone Mineral Density in Adult Women

Ei Ei Hlaing[1*], *Khin Moe Moe Nwe*[1], *May Pyone Kyaw*[1] & *Theingi Myint*[2]

[1]Department of Biochemistry
University of Medicine (Mandalay)
[2]University of Medicine 1(Yangon)

120 women

31-60 years of age

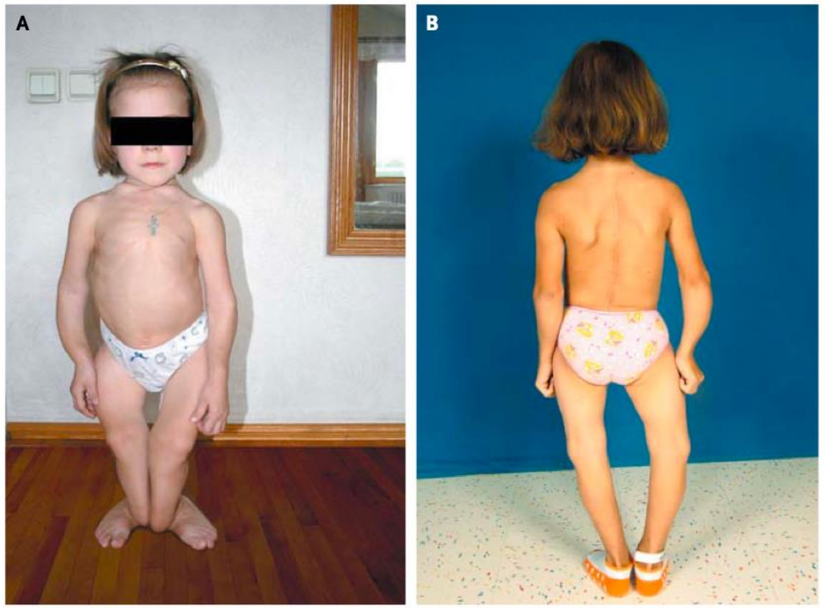
Divided:
Pre-menopausal and Post-menopausal
Age: 31-40, 41-50 and 51-60 years

Parameters	Age (years) (n=40)			ANOVA (p)
	31-40	41-50	51-60	
Serum calcium (mmol/L)	2.23 ±0.19	2.23 ±0.18	2.12 ±0.26	0.062
Serum phosphorus (mg/dl)	3.81 ±0.47	4.00 ±0.49	4.27 ±0.65	<0.001*
Serum 25(OH)D3 (nmol/L)	108.52 ±40.77	113.48 ±46.57	54.57 ±12.66	<0.0001*
BMD (T score)	-1.67 ±0.69	-1.93 ±0.64	-2.74 ±0.76	<0.0001*

*=Significant differences among groups

Rickets (children) and osteomalacia (children and adults) due to severe vitamin D deficiency are now uncommon

Severe Vitamin D Deficiency — Rickets



Subclinical vitamin D deficiency, as measured by low serum 25(OH)D, is very common.

Manifestations of Vitamin D Deficiency

- Bone discomfort or pain (often throbbing) in low back, pelvis, lower extremities
- Increased risk of falls and impaired physical function
- Muscle aches
- Proximal muscle weakness
- Symmetric low back pain in women

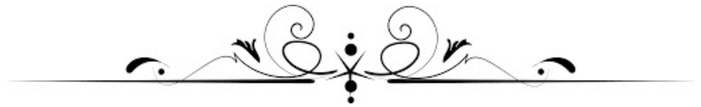
Patients who have musculoskeletal pain

Nonspecific musculoskeletal pain is a common symptom of vitamin D deficiency, and the prevalence of unrecognized vitamin D deficiency among patients with these symptoms is extremely high.

Patients who present with nonspecific musculoskeletal pain should be screened for vitamin D deficiency.

Screening for vitamin D deficiency

There is no evidence demonstrating benefits of screening for vitamin D deficiency at a population level.



Screening will be done only to clinically suspected vitamin D deficiency

1. Patients with bone diseases that may be improved with vitamin D treatment eg: **rickets**, **osteomalcia**, **fragility fractures**

2. Persons who need correcting vitamin D deficiency prior to **specific treatment** eg: pagets disease, potent antiresorptive therapy for osteoporosis

3. Patients with **musculoskeletal symptoms**, chronic muscle aches and widespread bone pain that could be attributed by vitamin D deficiency

4. **Low calcium/phosphate or high alkaline phosphtase**

5. **Low bone mineral densitometry or radiological osteopenia**

6. **CKD stage 4 or 5**

7. **Malabsorption syndrome** (measure at least annually)

Vitamin D replacement regimen

Serum 25(OH)D Level	Recommendations
<30 nmol/L	60,000 IU of vitamin D2 or D3 orally once per week for 5 to 6 weeks, and then 800 to 1000 IU of vitamin D3 daily thereafter
30 to 50 nmol/L	Initial supplementation with 800 to 1000 IU daily may be sufficient.
50 to 75 nmol/L	600 to 800 IU vitamin D3 daily
Patients with malabsorption	High doses of vitamin D of 10,000 to 50,000 IU daily may be necessary. Patients who remain deficient or insufficient on such doses will need to be treated with hydroxylated vitamin D metabolites

Varieties of Vitamin D

- Ergocalciferol (Vit D2)
- Cholecalciferol (Vit D3)
- Dihydrotachysterol
- Alphacalcidol (1α-hydroxy cholecalciferol)
- Calcitriol (1,25 Dihydroxycholecalciferol)

OPTIMAL INTAKE TO PREVENT DEFICIENCY

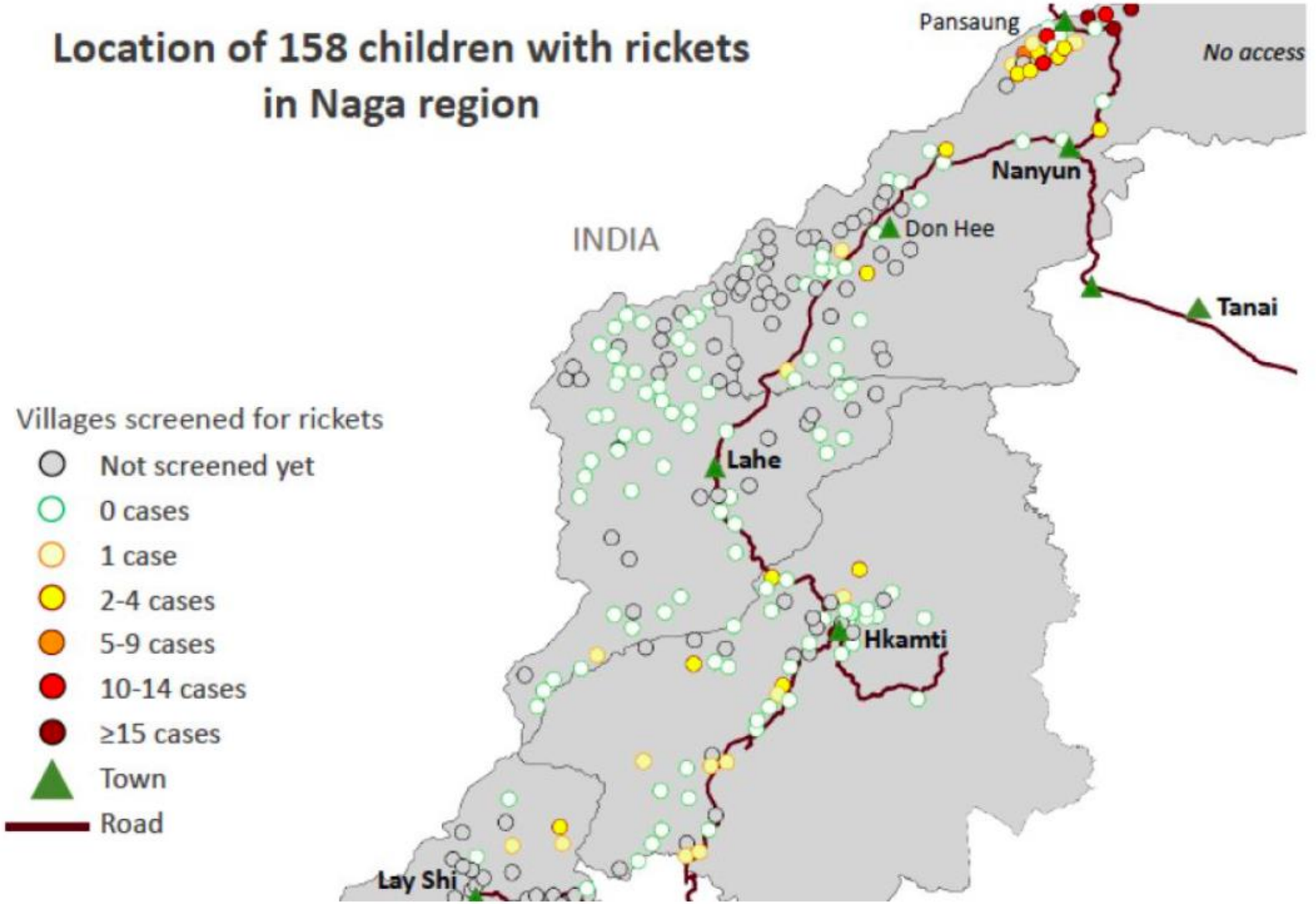
Adults who do not have regular, effective sun exposure year round should consume at least **600 to 800 IU** (15 to 20 micrograms) of vitamin D3 (cholecalciferol) daily.

Older persons confined indoors and other high-risk groups may have low serum 25-hydroxyvitamin D (25[OH]D) concentrations at this intake level and may require **higher intakes**.

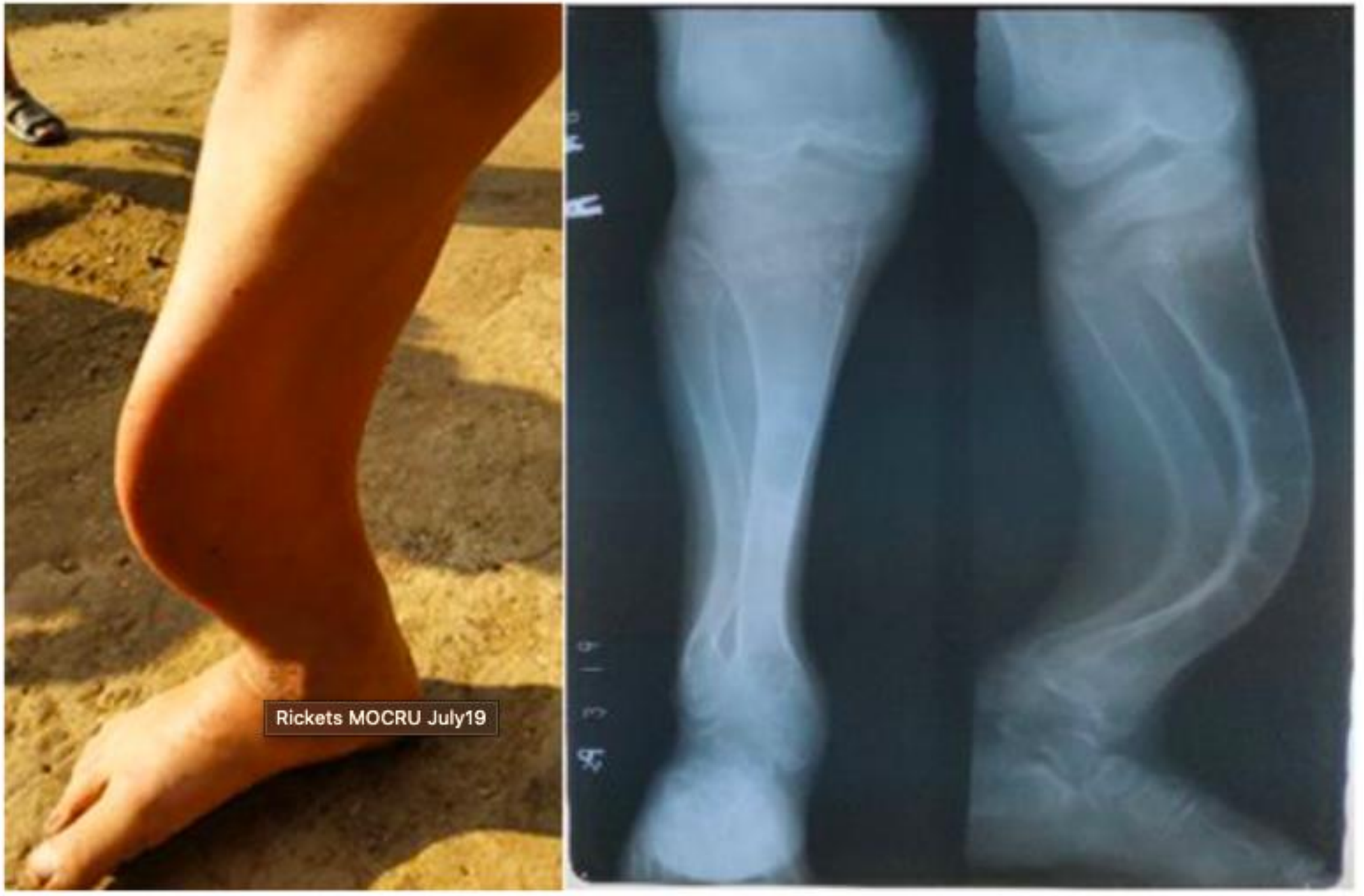
Myanmar being situated between latitude 14-24 North of the Equator, sufficient ultraviolet B (UVB) radiation is available throughout the year on its exposure to the skin to synthesize vitamin D.

Therefore, maximum Exposure of the arms and legs to UVB radiation (wavelength 290-370nm)

between 10 am to **3 pm** for **10-15 minutes** per time for **3 times per week** can be advised to maintain recommended daily requirement.



Medical Action Myanmar and MOCRU health teams identified a number of children with rickets in remote areas of Myanmar.


Rickets MOCRU July19

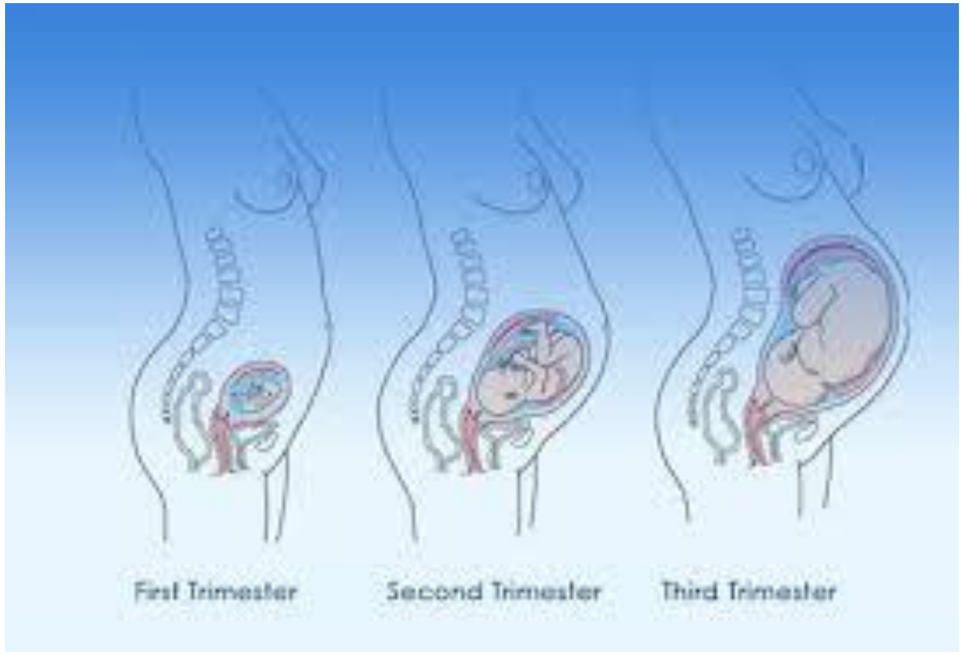
For high risk group (Asymptomatic patients)

- No investigation is required
- Offer lifestyle advice
- Suggest DRI (daily requirement intake) supplements : **600 - 800 IU/day**

High risk groups

- All pregnant and breastfeeding women, especially teenagers and young women
- All babies, particularly those who have had prolonged breast feeding without supplementation
- Elderly with history of falls and non-traumatic fracture
- People taking anticonvulsant, anti-TB, ART, long-term glucocorticoid
- Chronic Liver and kidney disease
- Those with risk factors such as diabetes mellitus, alcoholics, vegetarians
- Those not exposed to adequate sunlight (indoor workers, those who cover their skin for cultural reasons, who are housebound or confined indoors for long periods)

Treatment recommendation for special populations



- The optimal serum 25(OH)D level in pregnancy should be at least 50 nmol/L.
- For routine supplementation, daily allowance of 600 IU vitamin D for all reproductive-age women, including during pregnancy and lactation .
- vitamin D- insufficient pregnant women 600 to 800 IU of vitamin D3 daily.

Supplement Facts

Serving Size: 2 Softgels
Servings per Container:30

	Amount Per Serving	%DV
Vitamin A (as Beta Carotene)	5000 IU	100%
Vitamin C (as Ascorbic Acid)	60 mg	100%
Vitamin D3 (as Cholecalciferol)	800 IU	200%
Vitamin E (as D-Alpha-Tocopheryl Acetate)	40 IU	100%
Vitamin B1 (as Thiamine HCl)	5mg	333%
Vitamin B2 (as Riboflavin-5'-Phosphate)	5mg	294%
Vitamin B3 (as Niacinamide)	20mg	100%
Vitamin B5 (as D-Calcium Pantothenate)	8.8mg	88%
Vitamin B6 (as Pyridoxal-5'-Phosphate)	5mg	250%
Vitamin B9 (as L-Methylfolate)	800mcg	200%
Vitamin B12 (as Methylcobalamin)	20mcg	333%
Calcium (as Carbonate)	46mg	5%
Iron (as Ferrous fumarate)	5mg	28%
Magnesium (as Oxide)	50mg	13%
Zinc (as Sulfate Monohydrate)	7.5mg	50%
Selenium (as Sodium Selenite)	110mcg	157%
Molybdenum (as Sodium Molybdate)	51mcg	68%
DHA (Docosahexaenoic Acid)	200mg	**
Choline (as Bitartrate)	50mg	**
EPA (Eicosapentaenoic Acid)	40mg	**
Boron (as Sodium Tetraborate Decahydrate)	1mg	**

**Daily Value (DV) Not Established

- For pregnant women with vitamin D deficiency, 1000 to 2000 IU of vitamin D daily
- Urinary calcium excretion increases in pregnancy, and it should be monitored when treating vitamin D deficiency, especially in women with a history of renal stones.

Monitoring

- Healthy adults initiating vitamin D supplementation (600 to 800 IU daily) **do not require** an initial or follow-up serum 25(OH)D measurement after starting supplementation.

- Patients being treated specifically for serum 25(OH)D 50 nmol/L(<20 ng/mL) require a repeat 25(OH)D measurement approximately **three to four months** after initiating therapy.

- The dose of vitamin D may require further adjustment and additional measurements of 25(OH)D.

Vitamin D toxicity

- Liver - p450 enzyme system metabolize 25(OH)D to inactive metabolites but is insufficient to prevent vitamin D intoxication following the ingestion of large amounts of vitamin D.

- Liver - usual storage system for vit D.

- When large amounts of vitamin D are ingested, much of the excess vitamin D is stored in adipose tissue.

- As these sites become saturated, the vitamin D remains in serum and is converted to toxic levels of 25(OH)D.

25(OH)D > 375 nmol/l(150 ng/ml) = intoxication

- Symptoms of **acute intoxication** are due to hypercalcemia and include confusion, polyuria, polydipsia, anorexia, vomiting, and muscle weakness.

- Chronic intoxication may cause **nephrocalcinosis**, **bone demineralization**, and **pain**.

- The intake at which the dose of vitamin D becomes toxic is not clear.

- The Institute of Medicine (IOM) has defined the "tolerable upper intake level" (UL) for vitamin D as 100 micrograms (4000 IU) daily for healthy adults and children 9 to 18 years.

- The maintenance tolerable upper limits of vitamin D, which is **not to be exceeded** without medical supervision, should be
- 1000 IU/d for infants up to 6 months,
- 1500 IU/d for infants from 6 months to 1 yr,
- 2500 IU/d for children aged 1–3 yr,
- 3000 IU/d for children aged 4–8 yr, and
- 4000 IU/d for everyone over 8 yr.

- Vitamin D intoxication has been documented in adults taking more than **60,000** IU per day.

- Case reports have described hypervitaminosis D due to errors in manufacturing, formulation or prescription, including milk that was inadvertently excessively fortified with vitamin D

- Prolonged exposure of the skin to sunlight does not produce toxic amounts of vitamin D3 (cholecalciferol), due to photoconversion of previtamin D3 and vitamin D3 to inactive metabolite

- Multiple studies reveal that prolonged exposure of the skin to sunlight results in a maximum serum 25-hydroxyvitamin D (25[OH]D) level of 200 nmol/L(<80 ng/mL).

THE TAKE-HOME MESSAGE

The major cause of vitamin D deficiency is lack of sun exposure.

Risk Factors for Vitamin D Deficiency

- Age > 65 years
- Breastfed exclusively without vitamin D supplementation
- Dark skin
- Insufficient sunlight exposure
- Medication use that alters vitamin D metabolism (e.g., anticonvulsants, glucocorticoids)
- Obesity (BMI>30)
- Sedentary lifestyle

THE TAKE-HOME MESSAGE

- Deficient : <30 **nmol/l** (12 ng/ ml)
- Insufficiency : 30-50 **nmol/L** (12-20 ng/ml)
- Sufficiency : >50 **nmol/L** (>20 ng/ml)

THE TAKE-HOME MESSAGE

Serum 25(OH)D Level	Recommendations
<30 nmol/L	60,000 IU of vitamin D2 or D3 orally once per week for 5 to 6 weeks, and then 800 to 1000 IU of vitamin D3 daily thereafter
30 to 50 nmol/L	Initial supplementation with 800 to 1000 IU daily may be sufficient.
50 to 75 nmol/L	600 to 800 IU vitamin D3 daily
Patients with malabsorption	High doses of vitamin D of 10,000 to 50,000 IU daily may be necessary. Patients who remain deficient or insufficient on such doses will need to be treated with hydroxylated vitamin D metabolites

THE TAKE-HOME MESSAGE

Vitamin D toxicity

- Symptoms of **acute intoxication** are due to hypercalcemia and include confusion, polyuria, polydipsia, anorexia, vomiting, and muscle weakness.
- Chronic intoxication may cause **nephrocalcinosis**, **bone demineralization**, and **pain**.

25(OH)D >150 ng/ml (375 nmol/l) = intoxication


THANK YOU