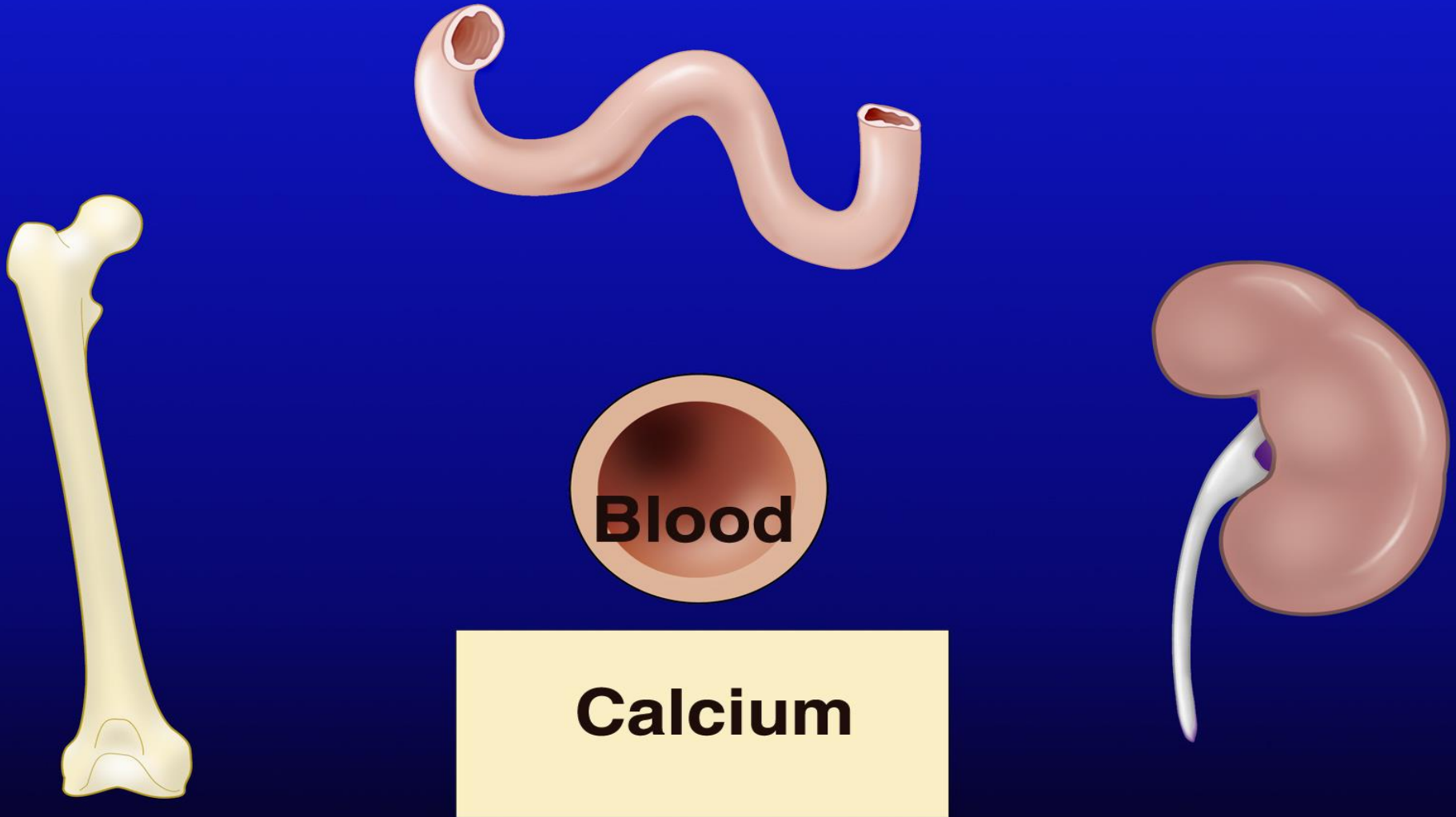


Nutrition as a Key to Economic Development: The Case for Armenia

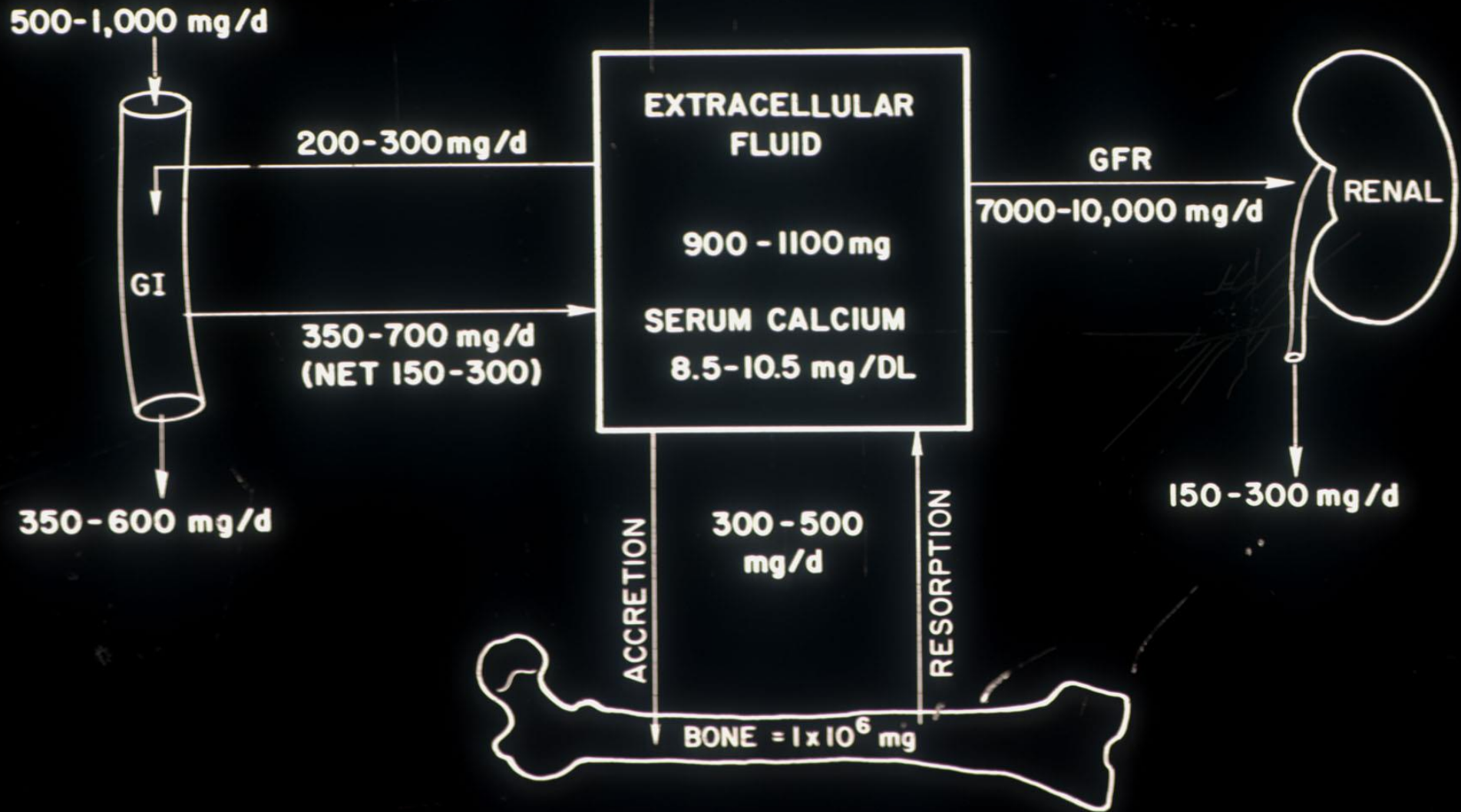
Calcium, Vitamin D and Bone Health

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College of Physicians and Surgeons
New York, NY USA
May 26-27, 2014

Regulation of Serum Calcium



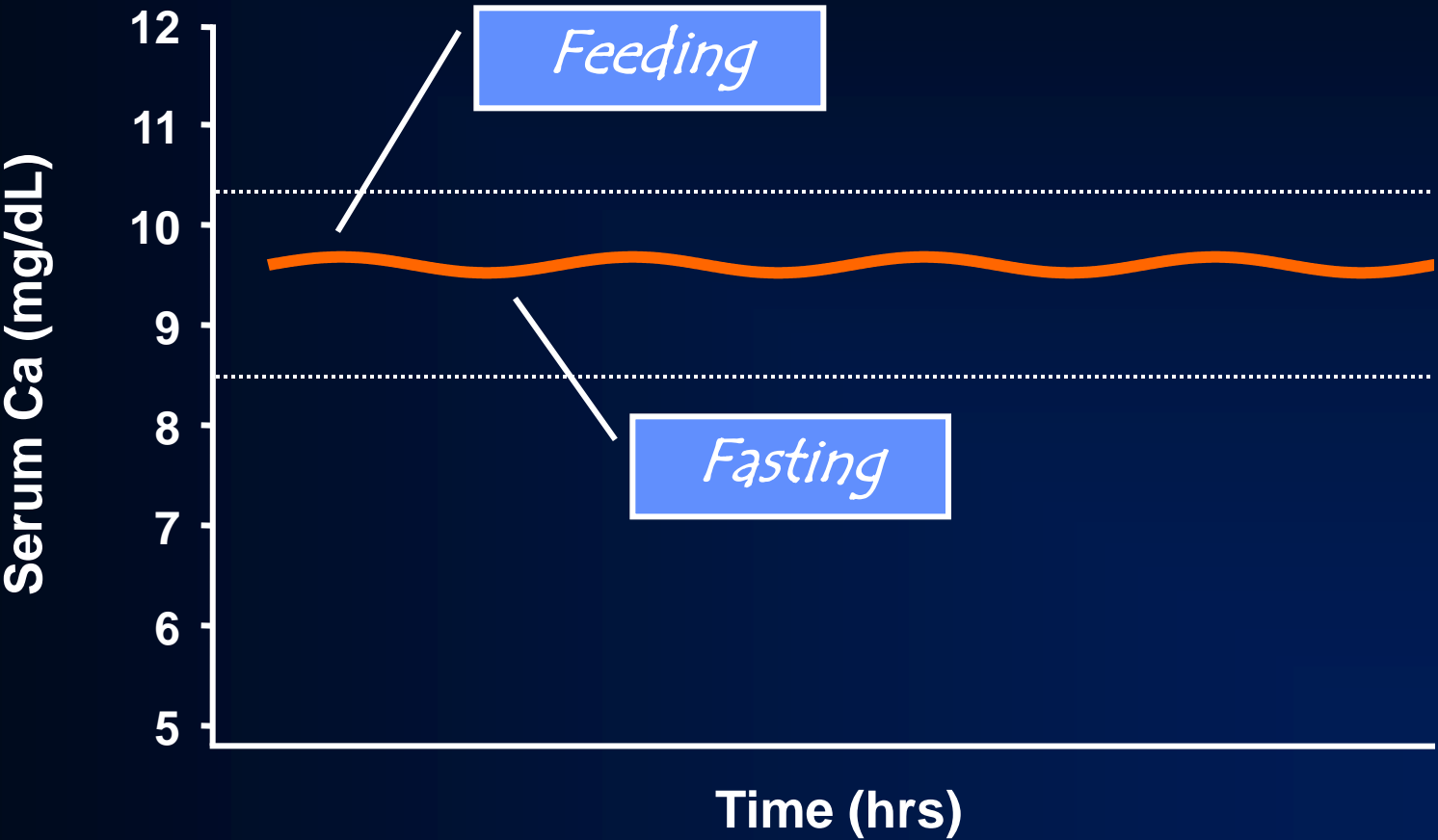
ADULT CALCIUM BALANCE



Key principle #1

Hormonal mechanisms keep the serum calcium within normal limits "at all times" under general homeostatic conditions- even if calcium balance is negative

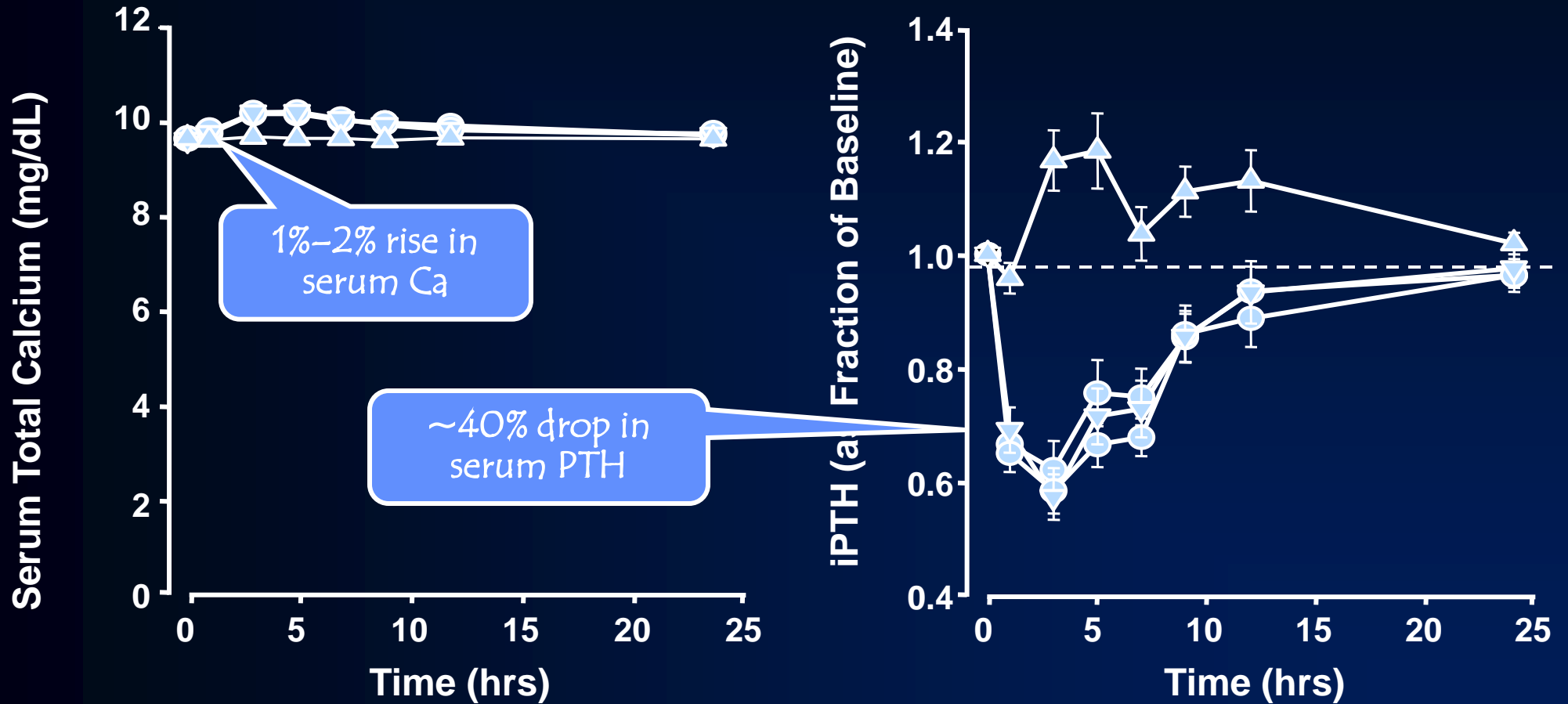
Normal Function



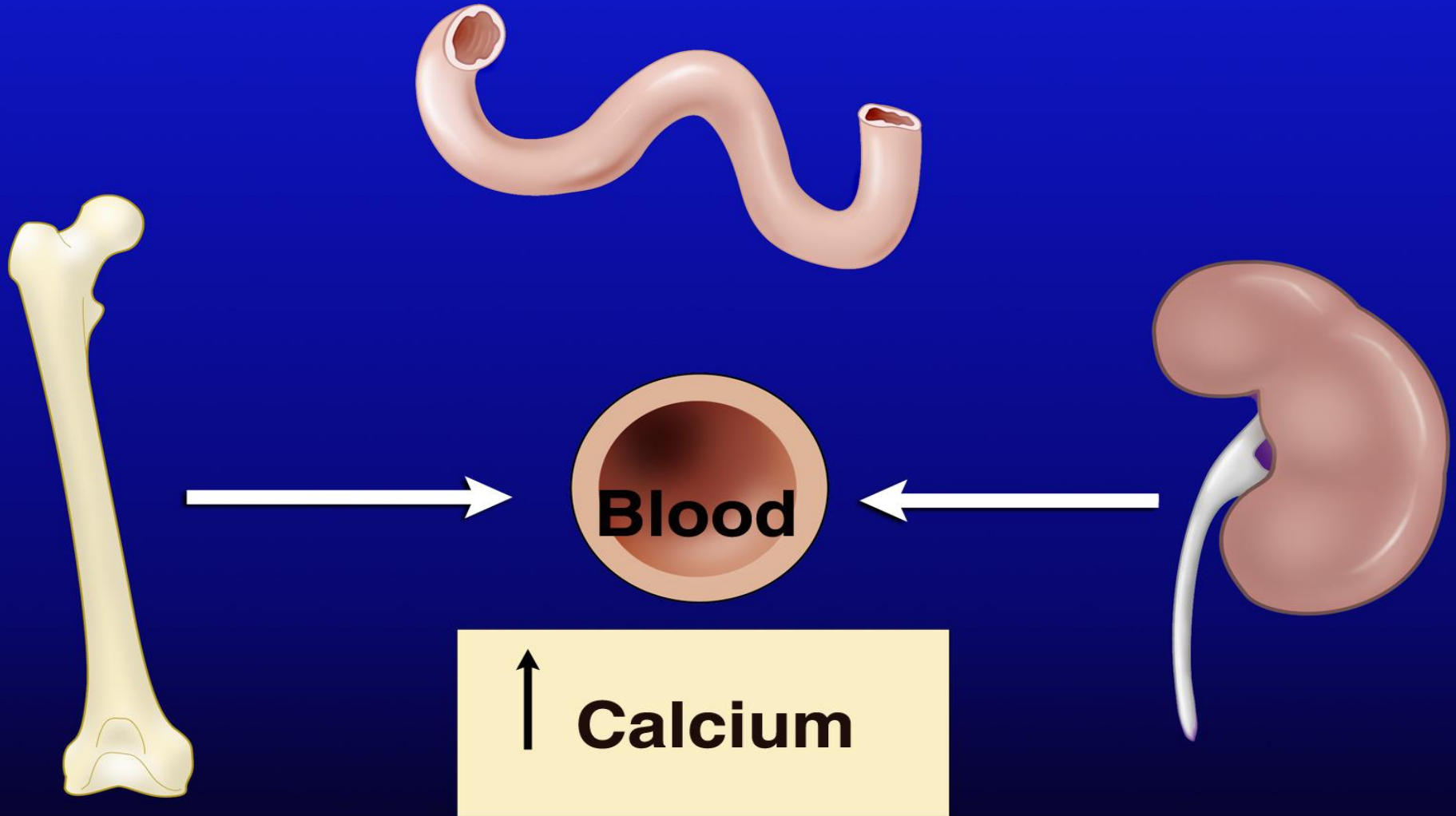
Hormonal regulation of the serum calcium level

- **Parathyroid hormone**
- Vitamin D

PTH Responsiveness

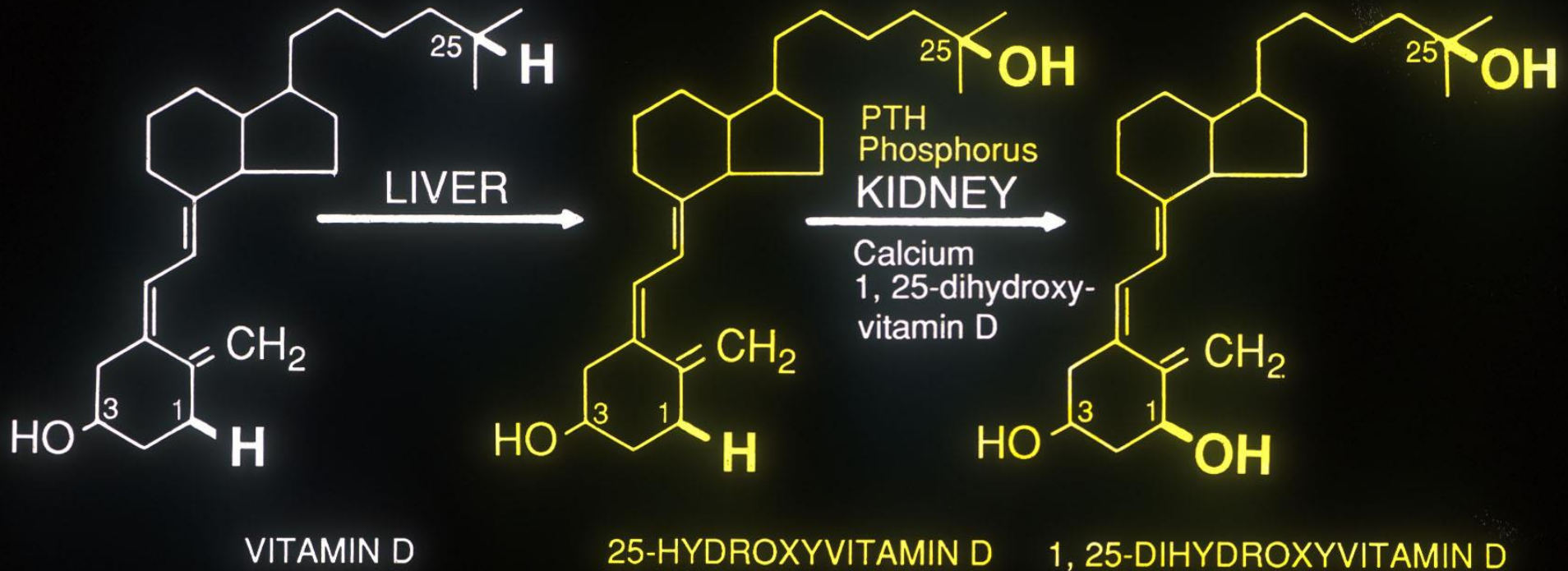


PTH: Effect on Serum Calcium



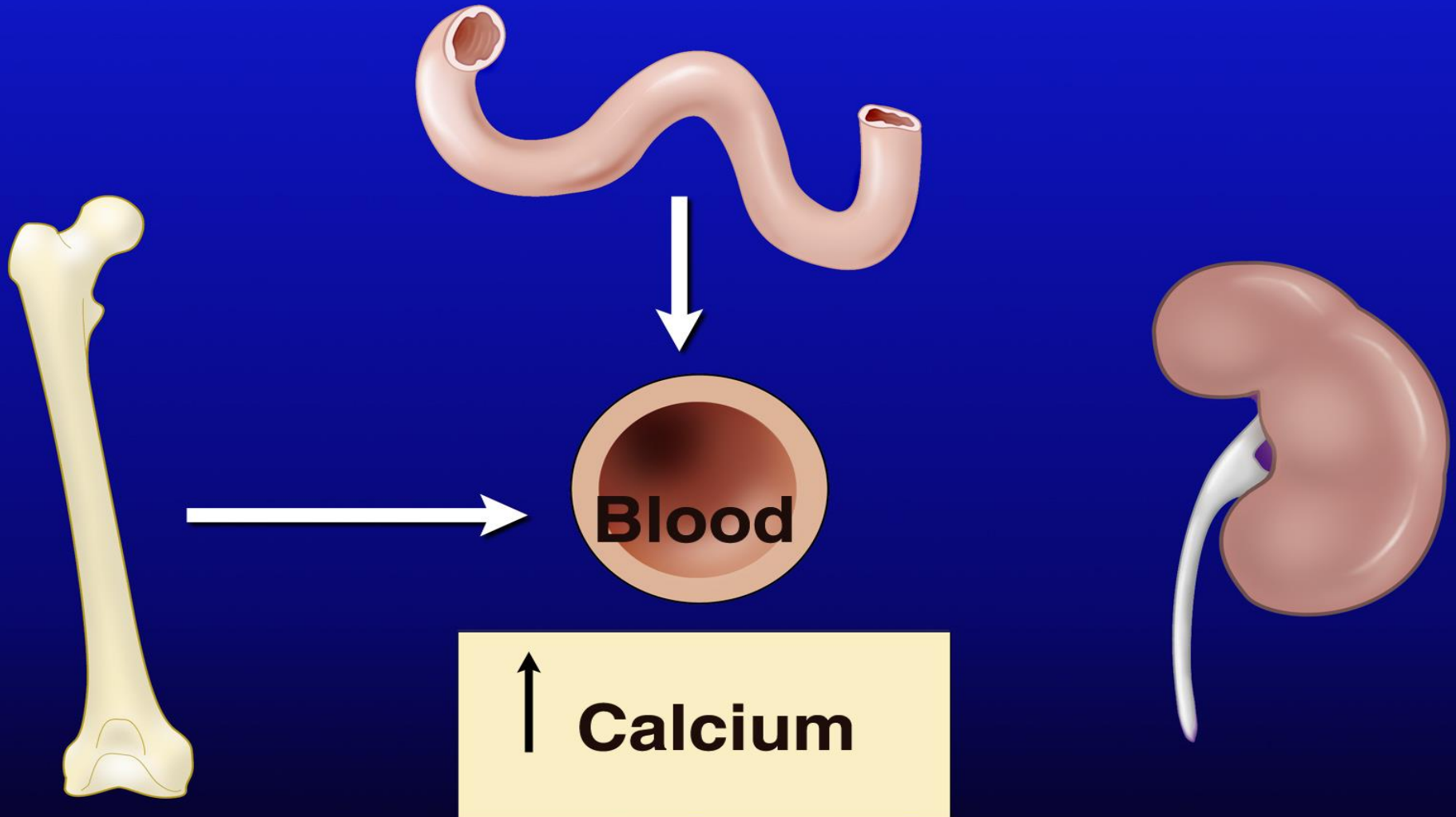
Hormonal regulation of the serum calcium level

- Parathyroid hormone
- Vitamin D



**Storage form: index of vitamin D
sufficiency or insufficiency**

1,25(OH)₂D: Effect on Serum Calcium

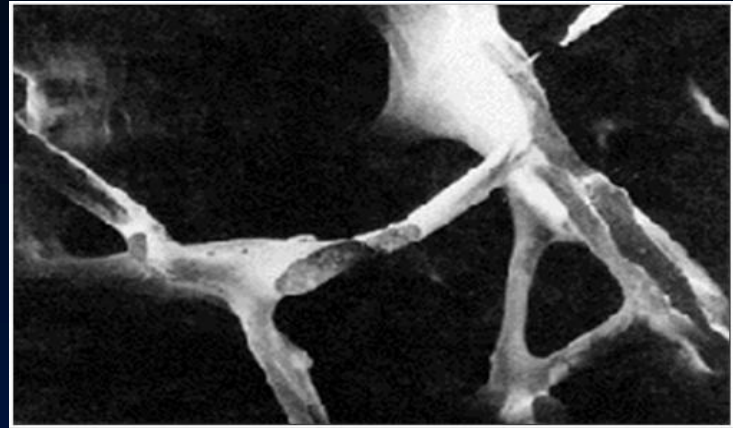


Principle #2

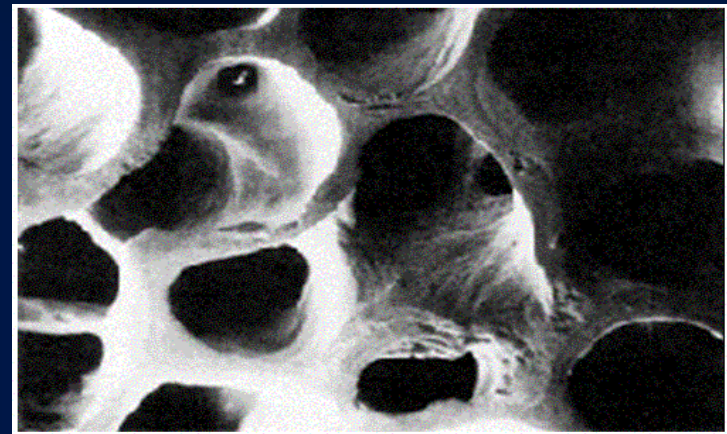
- Osteoporosis is a state of *skeletal* calcium deficiency; not of abnormalities in the serum calcium
- The serum calcium in osteoporosis is typically:
 - Normal
 - High
 - Low

Osteoporosis: Identifying the Problem

“ A skeletal disorder characterized by compromised bone strength predisposing to an increased risk of fracture.”



Osteoporotic bone

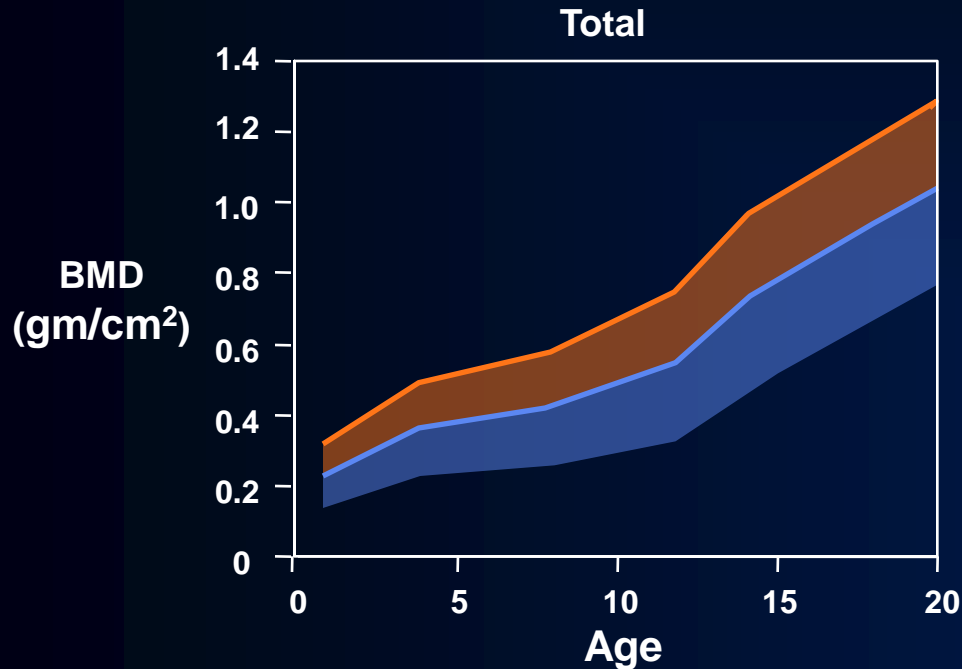


Healthy bone

Osteoporosis

- A skeletal calcium deficiency state (not a state of abnormal serum calcium concentration) associated with bone loss and microarchitectural deterioration
- Childhood nutrition is a key element in the disease that is seen in adulthood

Increase in Bone Mass with Age in Children



Peak attained in early 20s-30

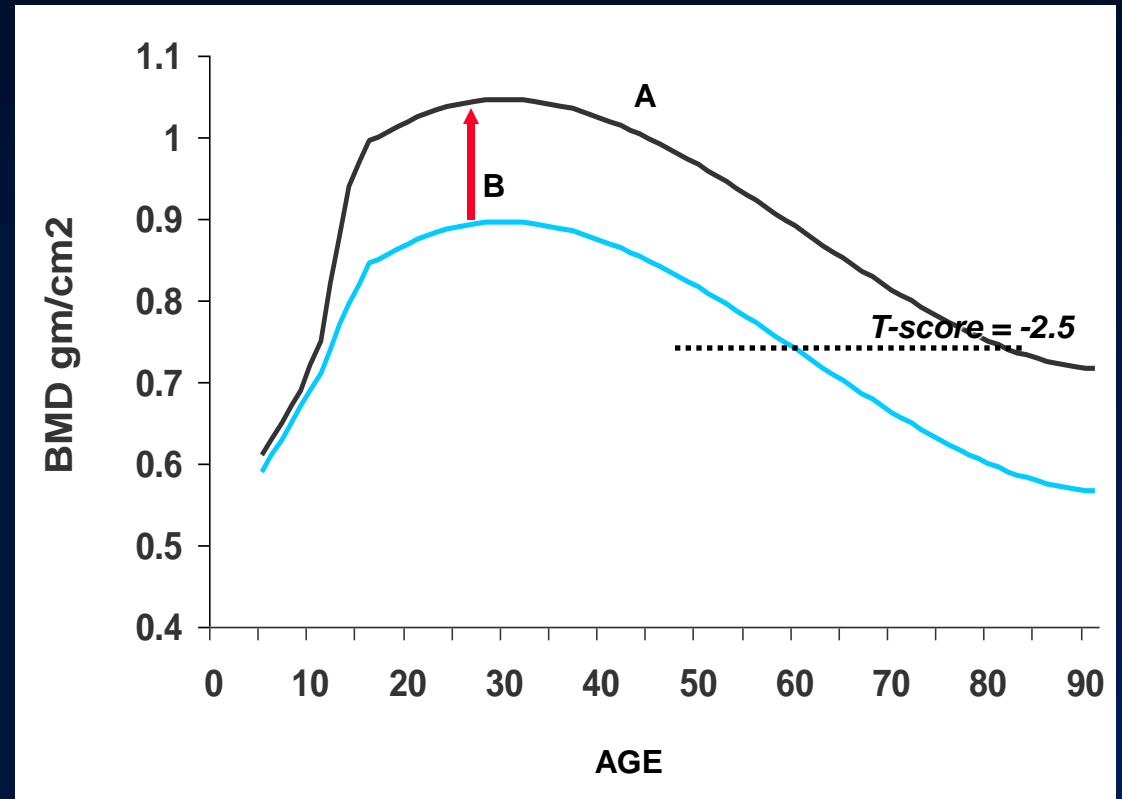
Maintained until 30s or 40s

Peak bone mass is a major determinant of bone density and strength throughout life

The beginning of the end result: Failure to Achieve Optimal Peak Bone Mass

A. Optimal Peak Bone Mass

B. Low normal peak bone mass



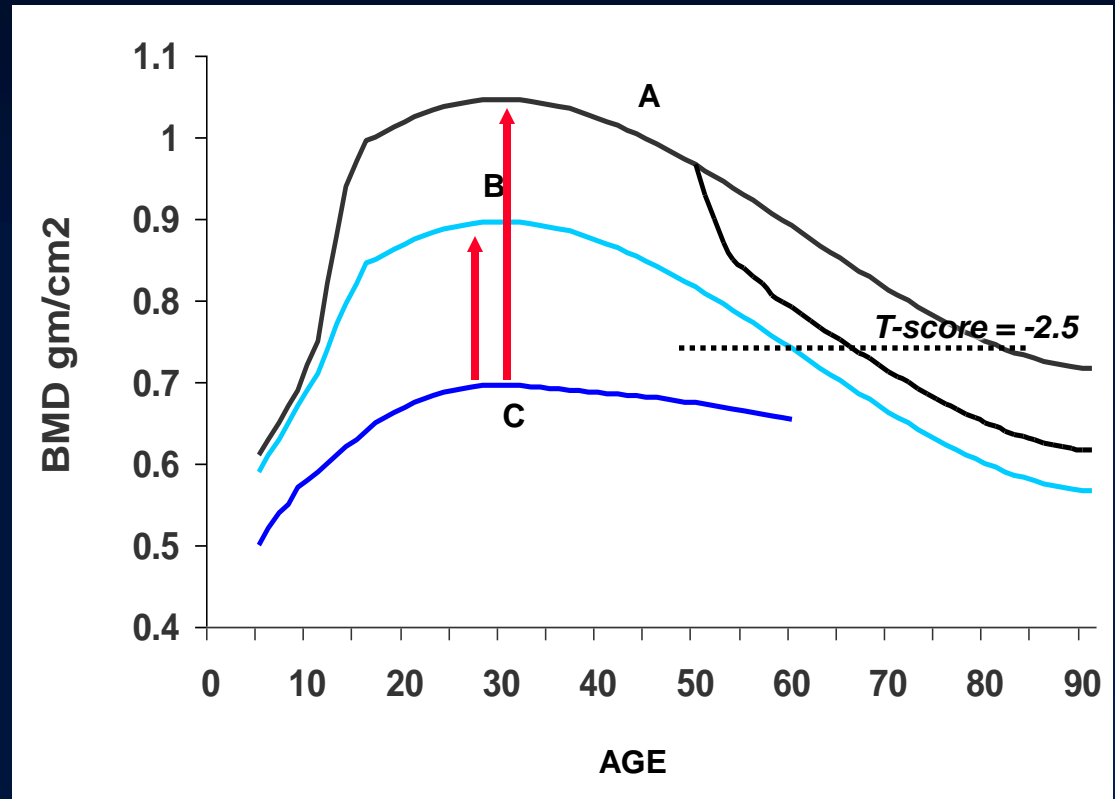
The beginning of the end result: Failure to reach even low normal peak bone mass

A. Optimal Peak Bone Mass

B. Low normal peak bone mass

C. Failure to acquire bone mass even in the low normal range:

- small size
- heredity
- late or missed puberty
- *Stunting?*



Determinants of Peak Bone Mass

- Factors that determine peak bone mass
 - Genetic (approximately 60-80%)
 - Disease susceptibility genes, “high BMD” gene
 - ***Nutrition - calcium, vitamin D and protein***
 - Body size and weight
 - Exercise
 - Smoking
 - Sex hormones during adolescence

Principle #3

Strongest predictor of bone mineral density in the later years is low bone mineral density at younger ages

Calcium intake in Childhood in Armenia

- By UN survey in 2005, the average intake of dairy was 2.5 servings per week (8% of caloric intake) and well under nutritional recommendations

Institute of Medicine Recommended Requirements for Calcium

RDA	mg/d*	Upper Limit (mg/d)
1–3 yr	700	2500
4–8 yr	1000	2500
9–18 yr	1300	3000
Pregnant or lactating (Female)		
14–18 yr	1300	3000
19–50 yr	1000	2500
Infants		
0–6 months	200	1000
6–12 months	260	1500

*Intake that covers needs of $\geq 97.5\%$ of population

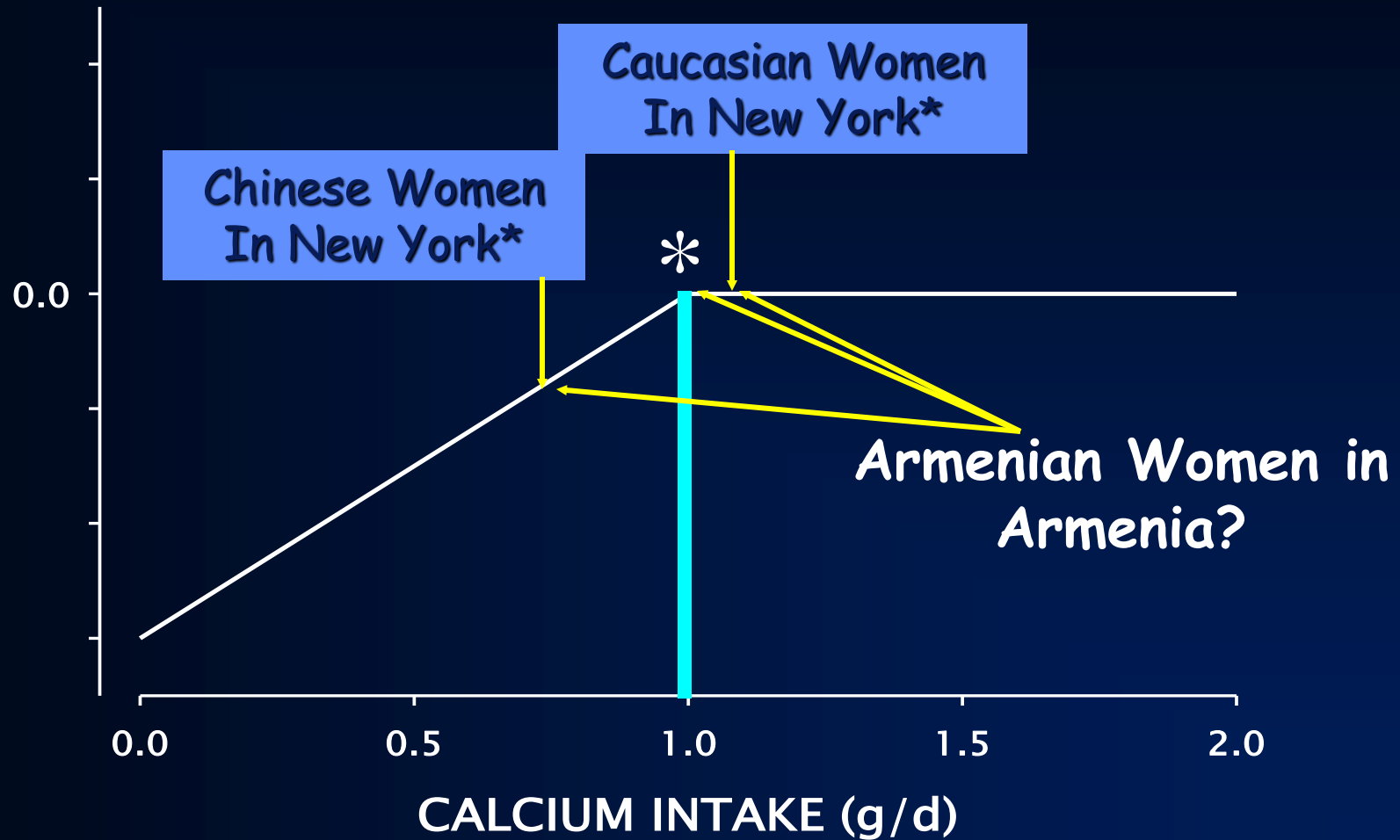
Calcium

- Preferably, calcium intake should come from natural sources (i.e., dairy)
- Calcium supplementation is used only to make up the difference between amount in foods (including calcium-supplemented foods) and what is needed.
- Only 500-600 mg advised at a time for better absorption
- Should be taken with food (protein meal) for better absorption efficiency

The best sources of Calcium

- **Dietary**
 - Dairy products
 - Green vegetables
 - Certain nuts like almonds
- **Calcium Supplements**
 - Calcium carbonate (40% calcium)
 - Requires a source of acid (gastric or food)
 - Absorption is enhanced by food
 - Calcium Citrate (20% calcium)
 - Does not require acid for absorption
 - Absorption is enhanced with food
 - Is thought to cause fewer GI issues

MAINTENANCE THRESHOLD: (Heaney, 2006)





DRINK YOUR LOW OR
NON-FAT MILK;
EAT YOUR LOW OR
NON-FAT YOGURT, CHEESE;
USE CALCIUM SUPPLEMENTS
ONLY TO SUPPLEMENT!

CALCIUM

A photograph of a log cabin with a wooden post in the foreground. A bright yellow rectangular sign with rounded corners is superimposed over the center of the image. The sign contains the text "VITAMIN D" in a bold, black, sans-serif font. The background shows the log cabin's exterior and a clear sky.

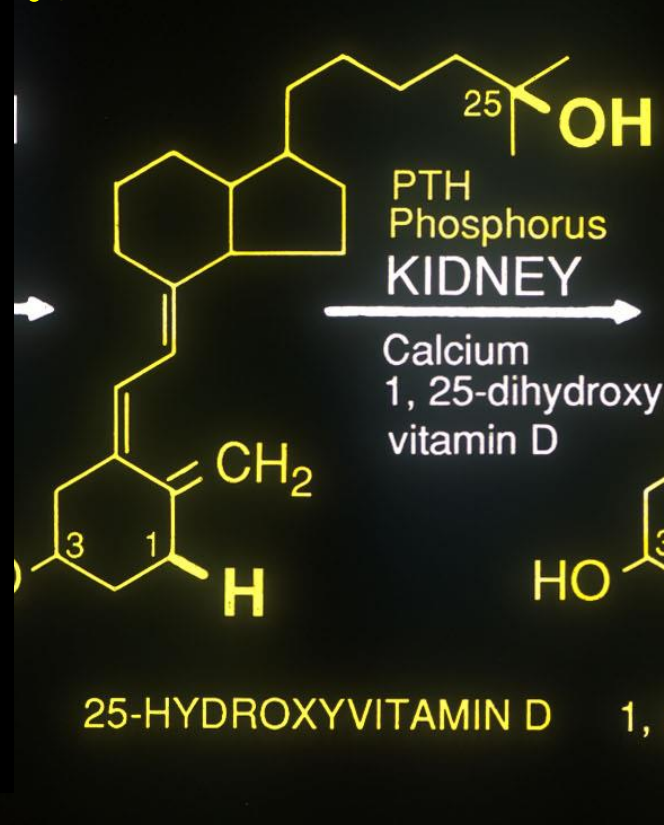
VITAMIN D

Without sufficient vitamin D

- Calcium absorption is reduced
- Even a calcium sufficient diet, therefore will not be adequate, in the presence of vitamin D deficiency

Vitamin D:

What is the metabolite to measure?



In Armenia

- It is very expensive to measure 25-hydroxyvitamin D: (\$25-US per sample)
- Essentially no data, therefore, on vitamin D adequacy here
- Abundant data, though, throughout the world

VITAMIN D DEFICIENCY IS COMMON

- How common is vitamin D deficiency?
- What are common sources of Vitamin D
 - The sun?
 - Dairy? What dairy?
 - Other sources
- How is Vitamin D deficiency defined?
- The stages of Vitamin D deficiency
 - Early, moderate, severe

Sources of Vitamin D: THE SUN

but why is it difficult to get sufficient Vitamin D from the sun?

THE SUN IS NO LONGER A
MAJOR SOURCE OF VITAMIN
D THROUGHOUT THE WORLD

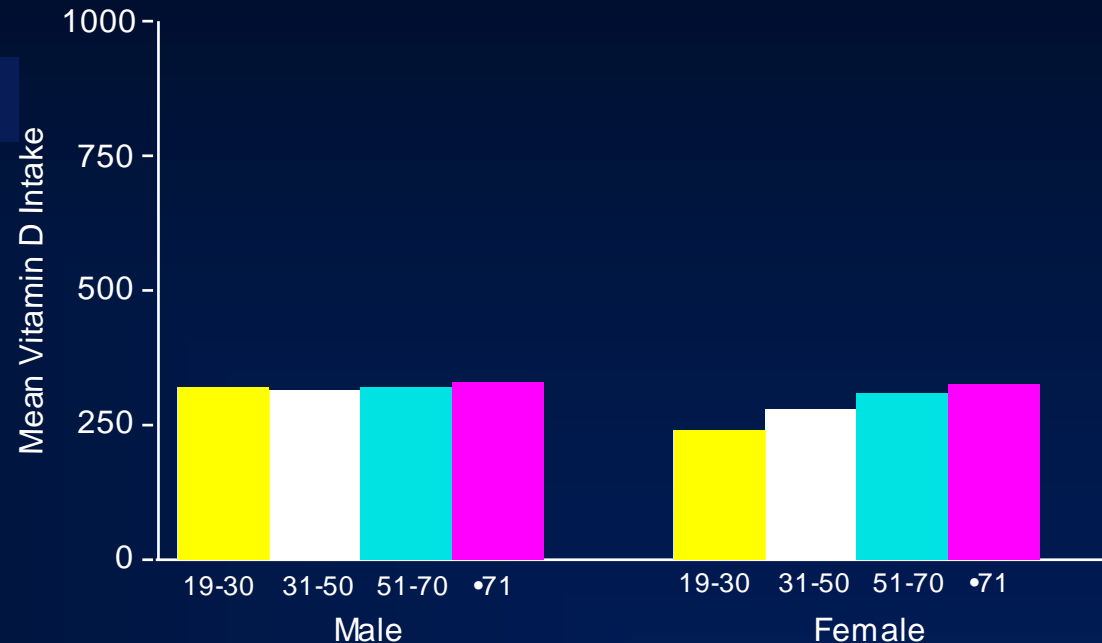
A sunset over a body of water. The sun is low on the horizon, creating a bright orange and red glow. The sky transitions from orange near the horizon to a pale blue at the top. The water is dark blue with some ripples. A small sailboat is visible on the left side of the horizon.

**If we do not get our
Vitamin D from Sunlight...**

**Is food an alternative
source of Vitamin D?**

Vitamin D is Rare in Food; as a Result, Intake is Low At All Ages

<u>Food</u>	<u>IU</u>
Cod Liver Oil, 1 Tsp	400
Salmon, 3.5 oz	360
Mackerel, 3.5 oz	345
Milk, 1 cup	100
Fortified cereal, 3/4 cup	50
Liver, 3.5 oz	30
Egg, one whole	25

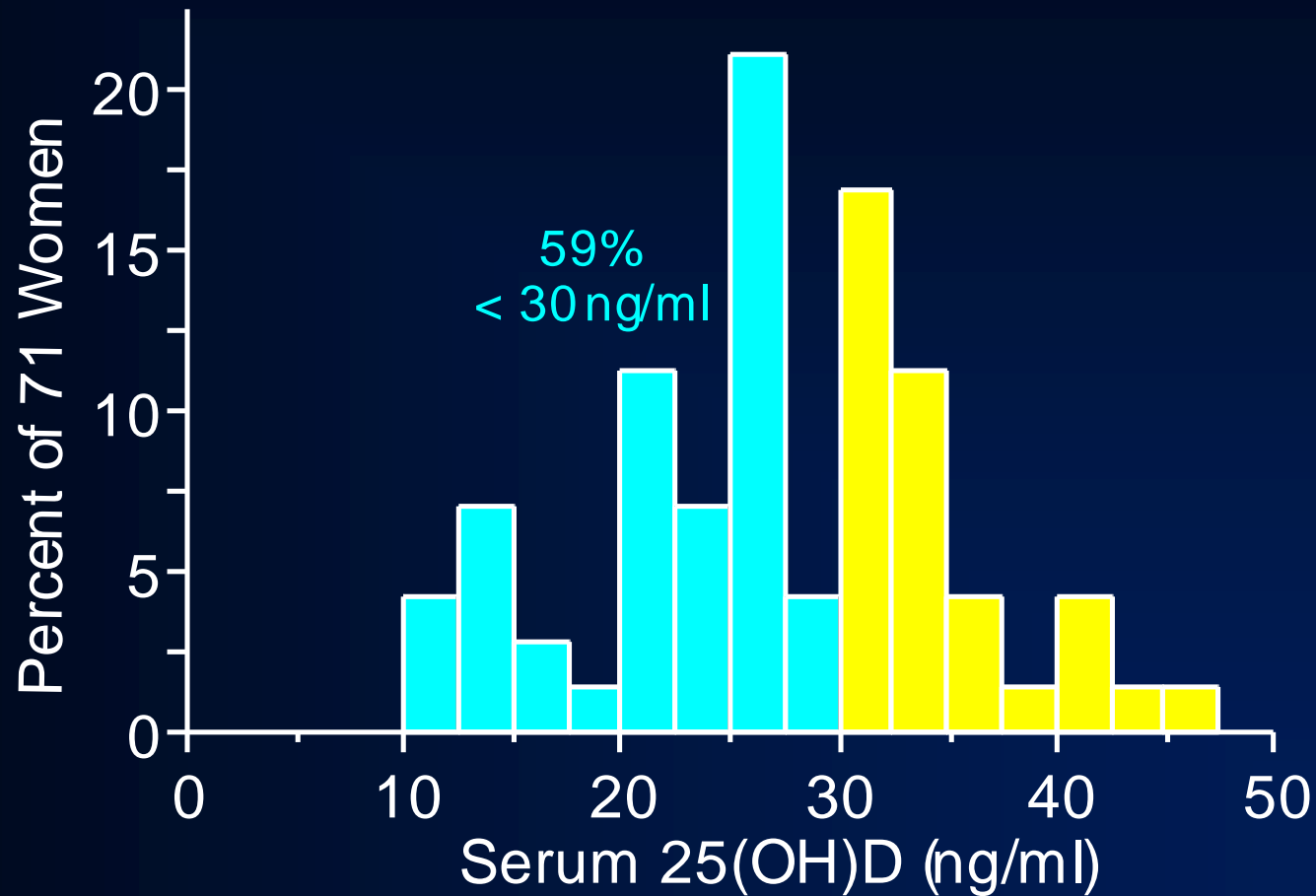


NHANES III data; mean vitamin D intake from food plus supplements

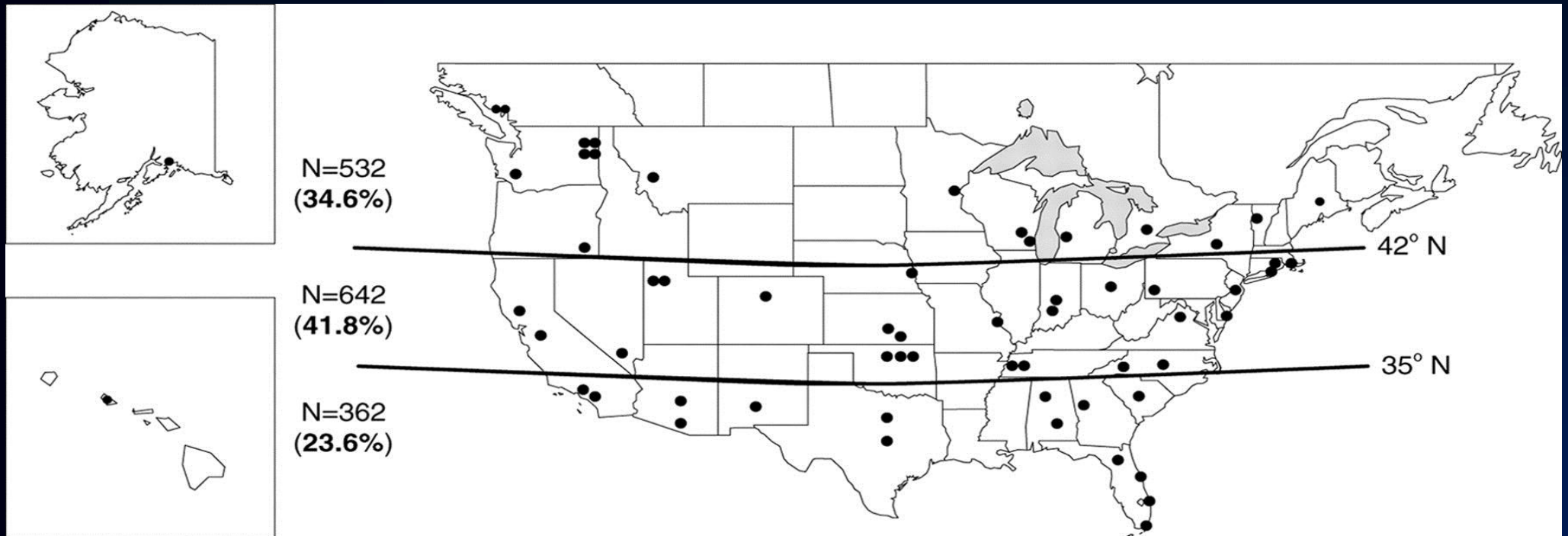
**Without sunlight as a source
Without food as a source...**

**We are all likely to be
deficient in Vitamin D**

Low Vitamin D Status is Endemic

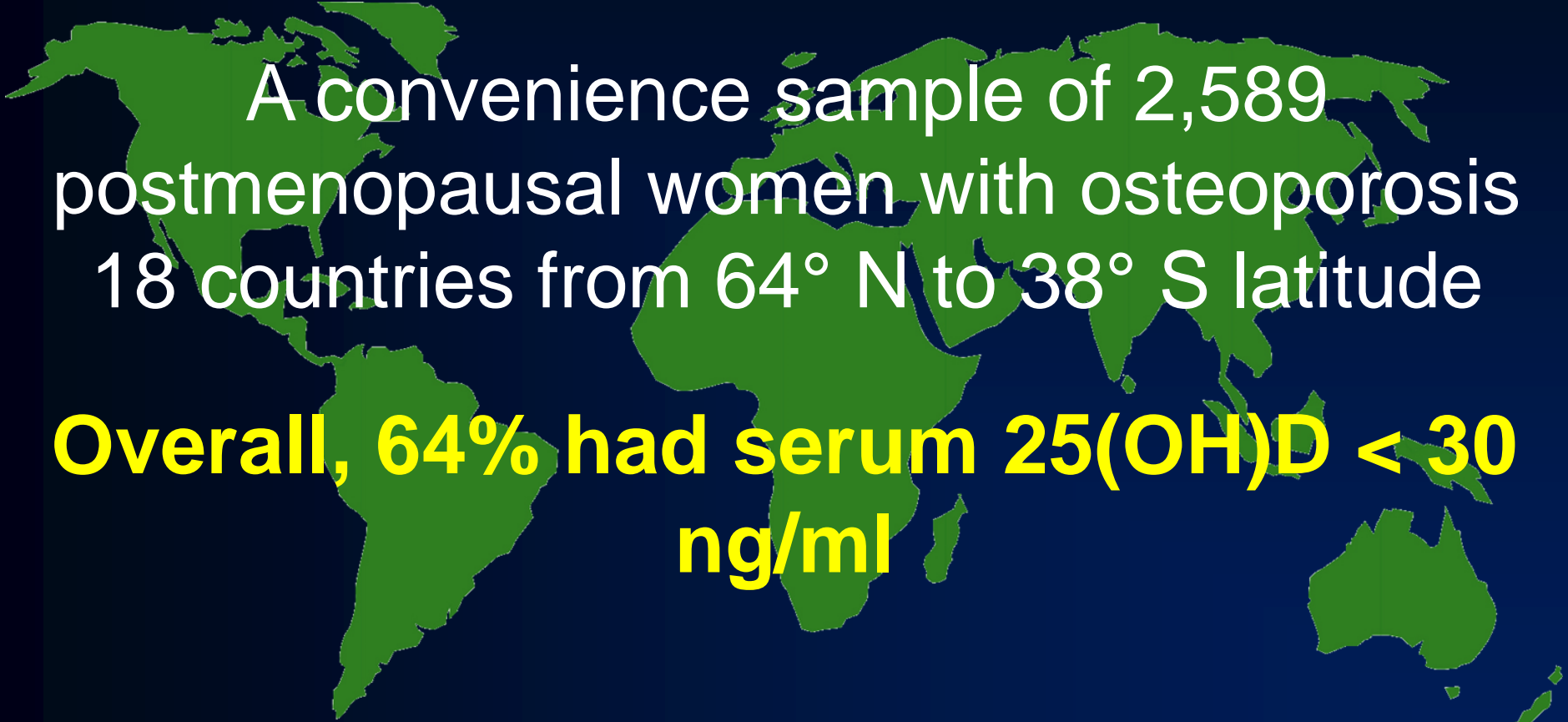


In the United States, 25-40% of the population is deficient in vitamin D



Holick, M. F. et al. J Clin Endocrinol Metab 2005;90:3215-3224

Vitamin D Inadequacy is Common Worldwide



A convenience sample of 2,589 postmenopausal women with osteoporosis from 18 countries from 64° N to 38° S latitude

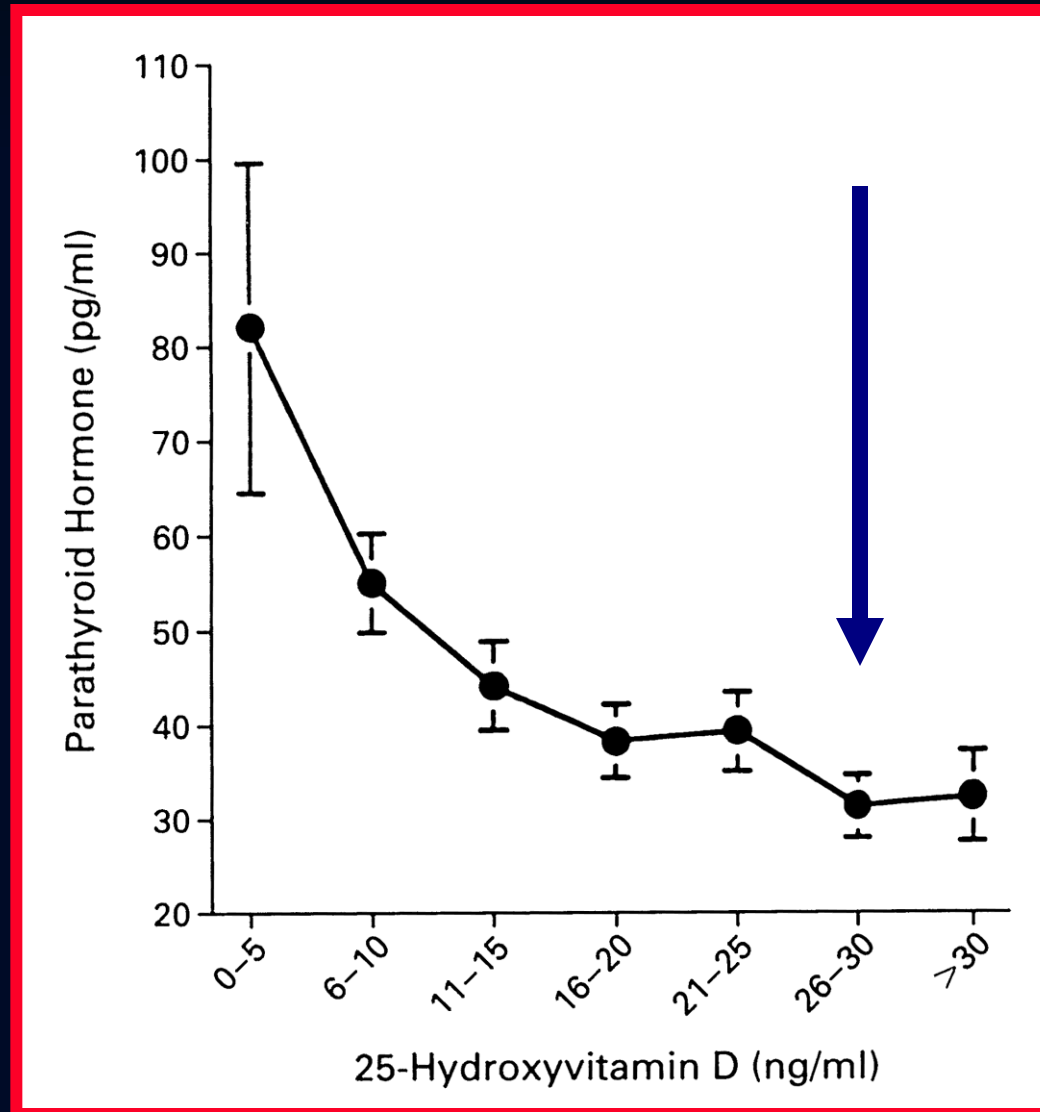
Overall, 64% had serum 25(OH)D < 30 ng/ml

How does one determine what is a normal and what is abnormal re 25-hydroxyvitamin D?

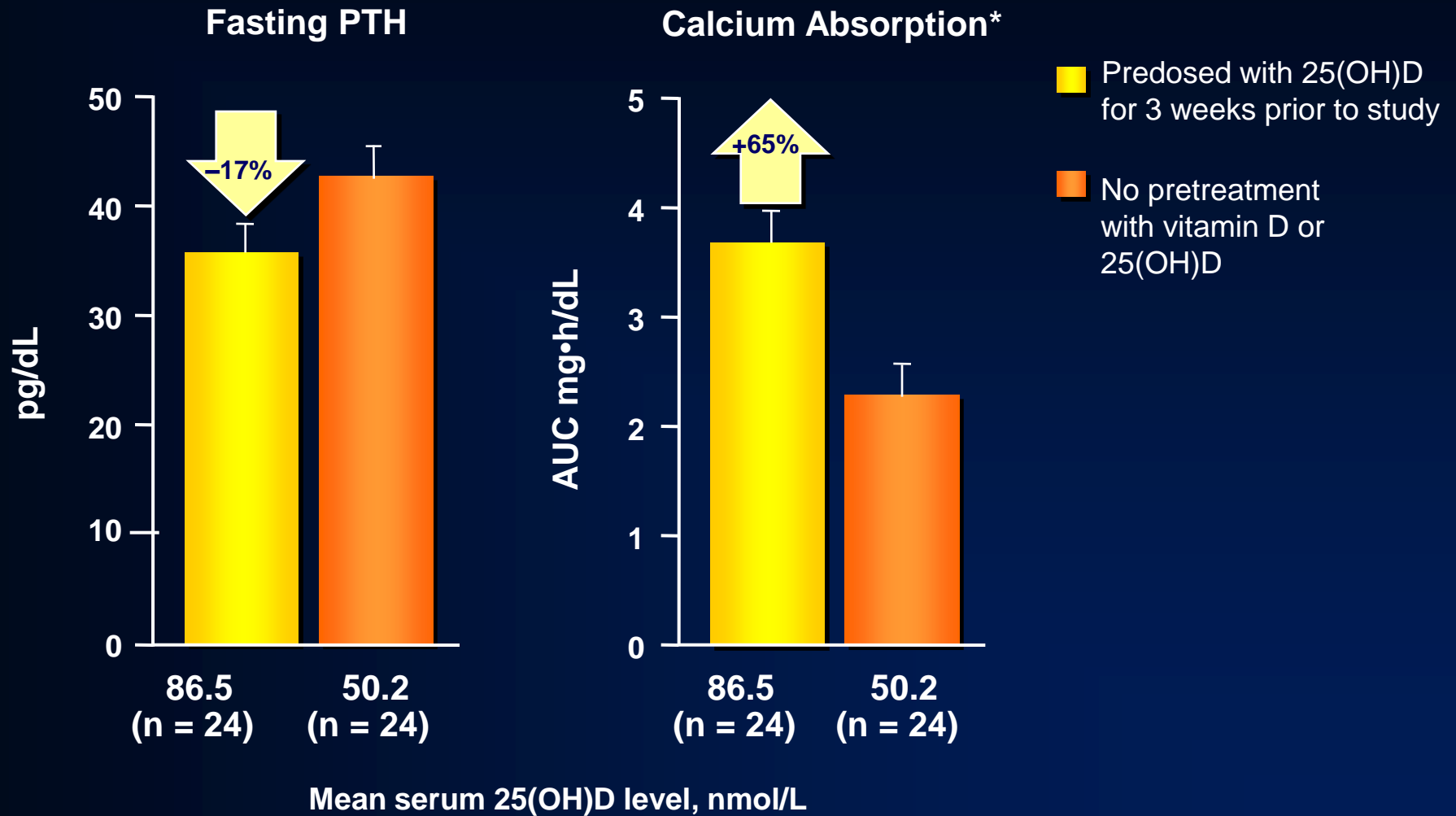
What value of circulating 25-hydroxyvitamin D should we aim for?

- **>20 ng/ml?**
- **>30 ng/ml?**

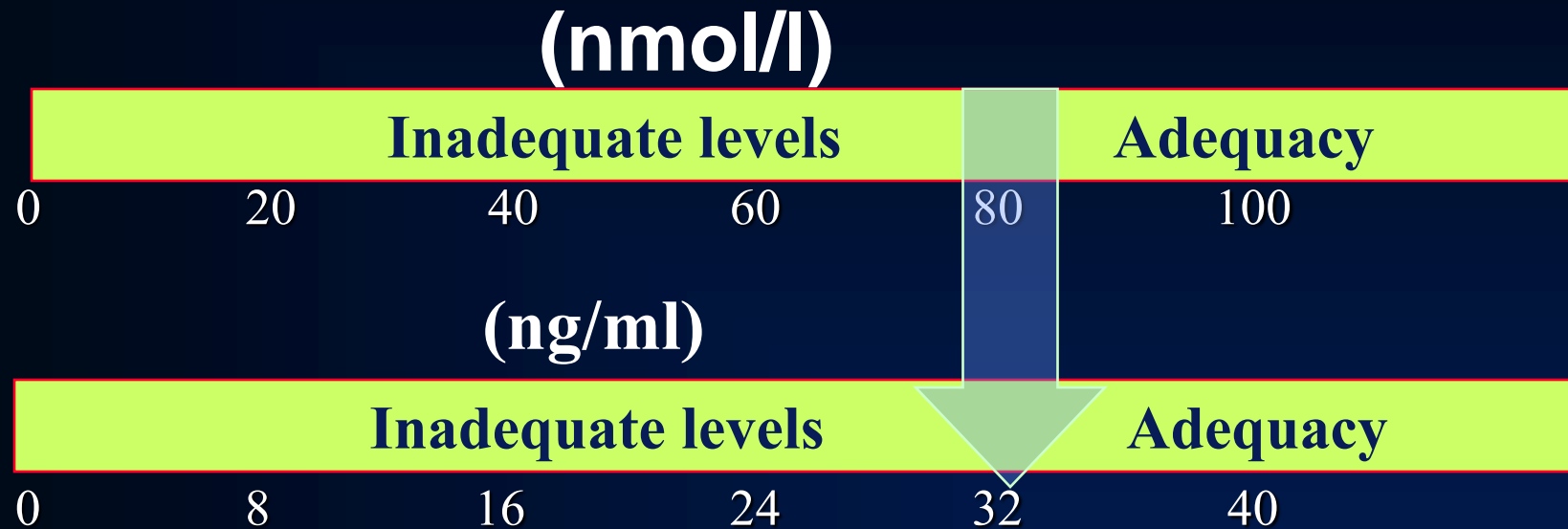
VITAMIN D DEFICIENCY IN MEDICAL INPATIENTS



Vitamin D Status: Impact on Calcium Absorption and PTH



25-Hydroxyvitamin D: Threshold values for adequacy

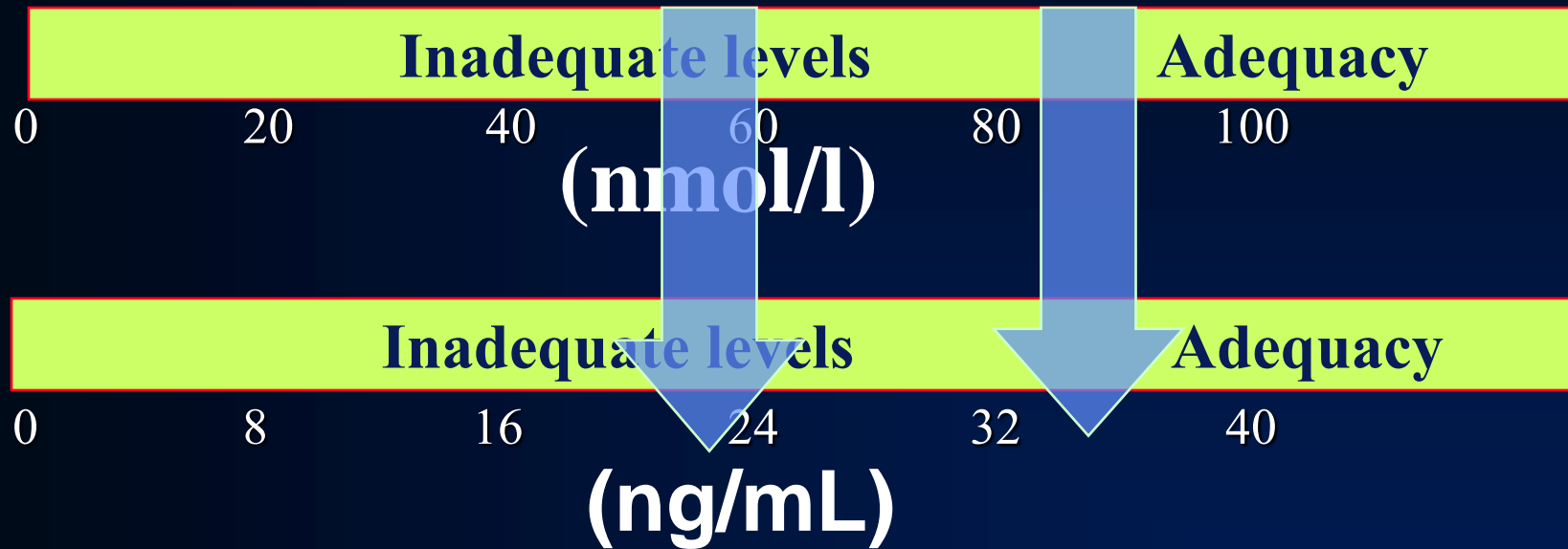


25-HydroxyVitamin D:

Why 20 ng/mL and not 30 ng/mL?

- The IOM says:
 - No convincing evidence that PTH levels rise consistently when the 25 OH D level falls < 30 ng/mL
 - No convincing evidence that optimal calcium balance requires a 25-OH D level > 30 ng/mL
 - No convincing evidence that skeletal health requires levels > 30 ng/mL.
 - No convincing evidence that putative non-skeletal effects of vitamin D are
 - substantiated
 - associated with 25-OH D levels > 30 ng/mL
 - More consistent negative effects of Vitamin D deficiency are seen when levels are < 20 ng/mL

25-Hydroxyvitamin D: Threshold values for adequacy*



The threshold value for adequacy > 30 ng/mL

**Institute of Medicine (11-10) suggests that adequacy in healthy people might be as low as 20 ng/mL, but this is controversial*

The Controversy* **

*Counterpoint: "Why the IOM recommendations for Vitamin D are deficient" (Heaney and Holick, JBMR, 2011)

**Many groups such as The Endocrine Society have not changed their recommendations of 30-80 ng/mL

25-hydroxyvitamin D: what is recommended by most professional societies?

- Lower limit: 30 ng/mL (75 nmol/l)
- Upper limit: 50-80 ng/mL (125-200 nmol/l)

In Armenia

Since Vitamin D measurements are not practical because of expense, how should we ensure vitamin D adequacy in the population?

The IOM Report (November 2010)*

- Recommended daily intake: 600 IU (under 70 yrs); 800 IU (over 70 yrs old)
- Maximal daily intake: 4,000 IU

In Armenia- a suggestion

- Perhaps larger doses 2,000 IU per day for 2 months is advisable
- Then nutritional intake according to the Institute of Medicine guidelines is reasonable

Vitamin D Supplementation and Fracture Risk

- Some studies have found a reduction in fractures with supplementation
- Others have not seen an effect
- Conflicting results may relate to differences in baseline vitamin D status of participants, range of doses used, and compliance

Principle #4

- Calcium and vitamin D sufficiency, along with an appropriate exercise regimen, are always recommended for everyone, particularly those with osteoporosis
- Treatment for osteoporosis alone with calcium, vitamin D and an exercise regimen are rarely sufficient
- Pharmacological agents are typically needed in these situations

Vitamin D has been claimed to be influential in all of the following:

Deficiency

Elevated BP

MI risk

PVD

Sudden death

CVD mortality

Overall mortality

Adequacy

Fall protection

Muscle strength

Cancer protection

Immune competence

– Infectious disease protection

Cardiovascular health

Vision

Cognition

Kelepouris et al Ann Intern Med 1995

Orwoll, 2002, 2008

Finkelstein 2004

Major points

- Calcium homeostasis is exquisitely controlled
- The body protects itself from serum calcium levels becoming abnormal in most situations
- PTH and Vitamin D are key elements to this control
- There is an epidemic of vitamin D deficiency throughout the world
- Good calcium and vitamin D nutrition are keys to good skeletal health



Shnorhagalutyun!