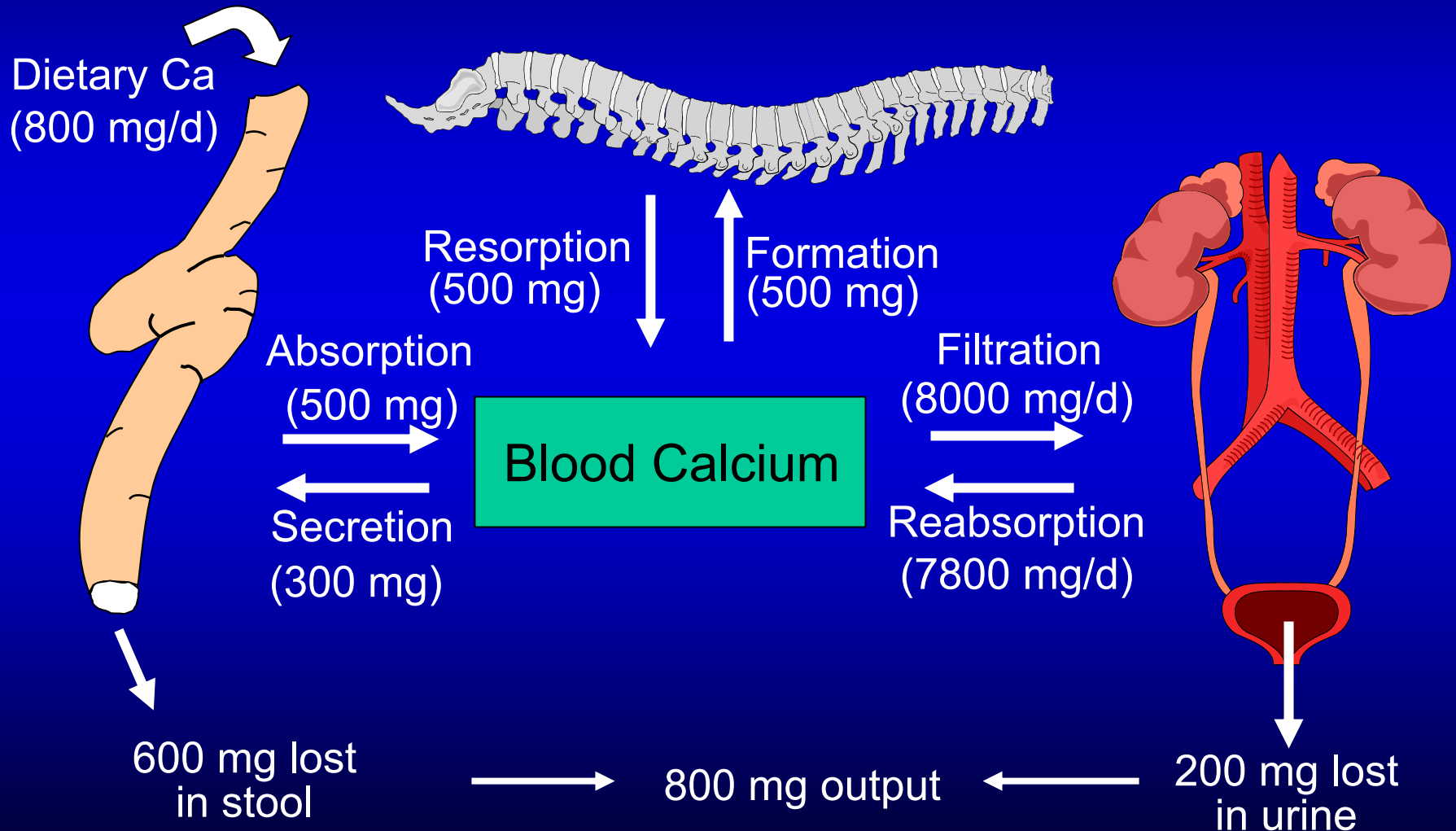


# **The Skeletal Response to Aging: There's No Bones About It!**

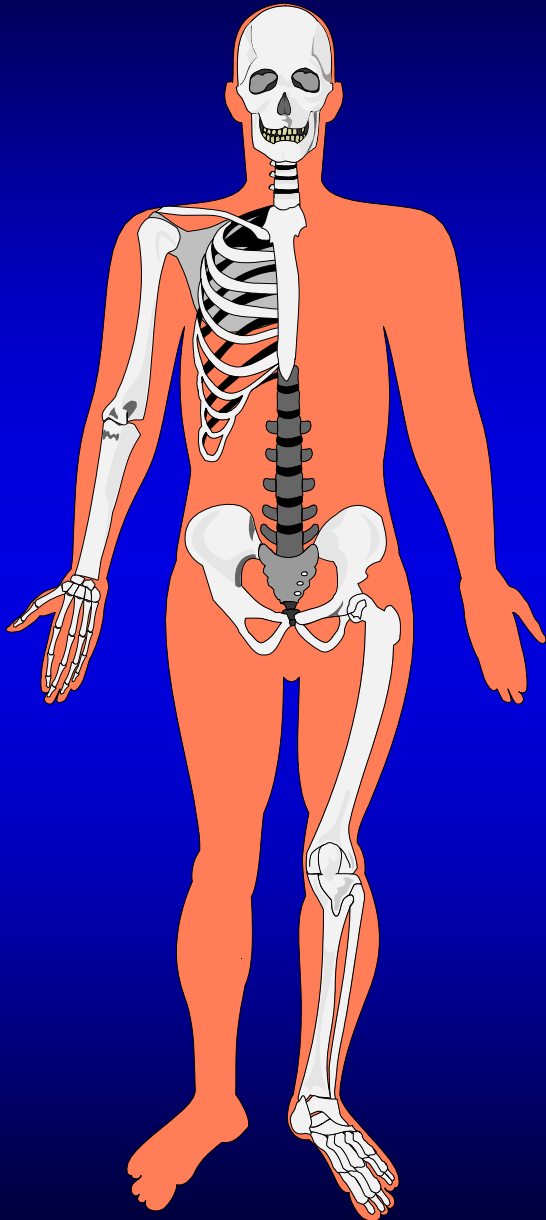
**April 7, 2001**

**Joseph E. Zerwekh, Ph.D.**

# Interrelationship of Intestinal, Skeletal, and Renal Systems to the Overall Maintenance of Normal Calcium Homeostasis

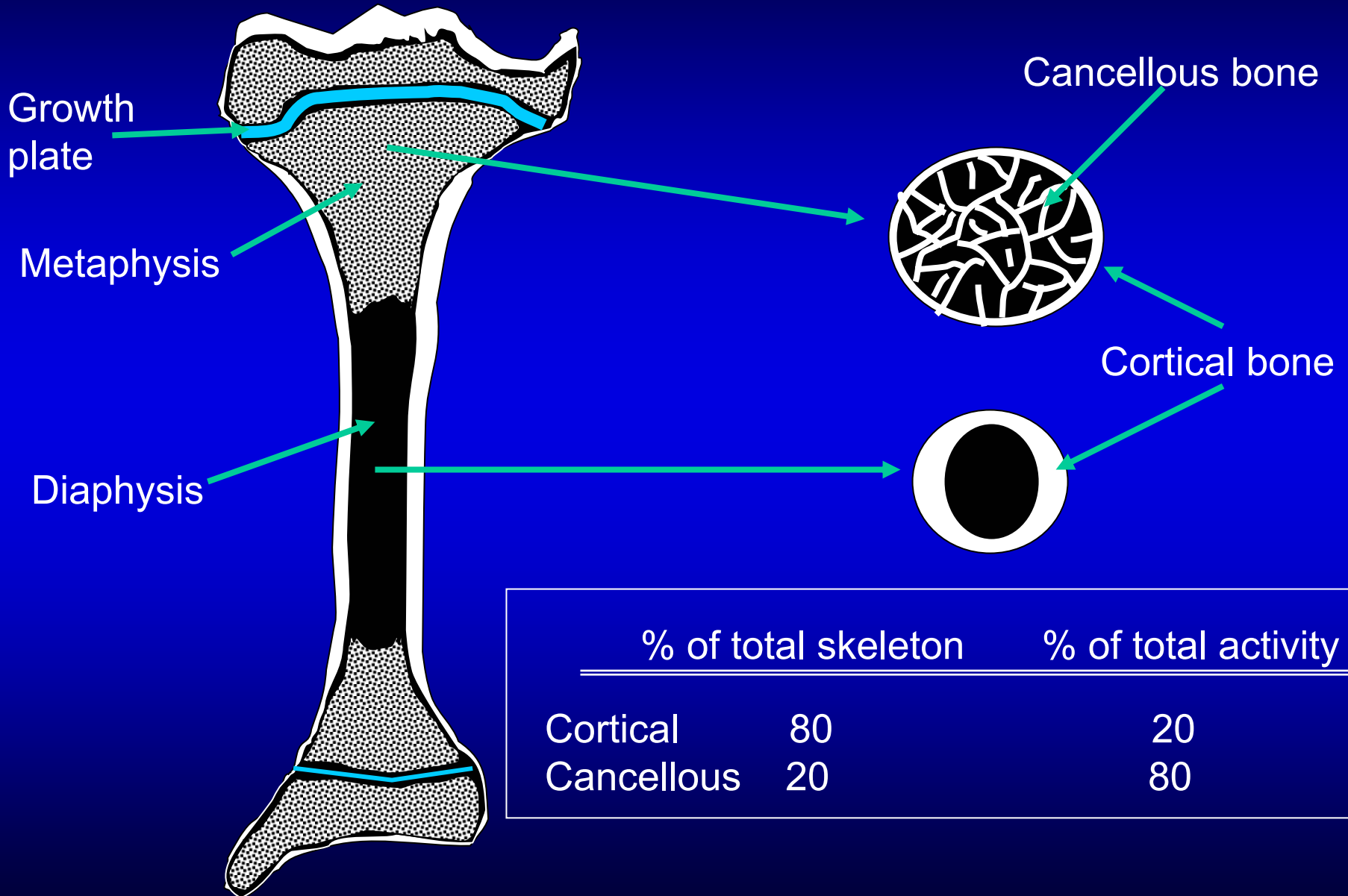


# Functions of the Human Skeleton



- Protects soft tissues and organs from injury
- Provides sites for insertion of muscles
- Capable of repair in response to injury
- Storehouse for 99% of body's calcium, 80% of phosphorus, and substantial amounts of magnesium, sodium, and carbonate
- Third line of defense in maintaining acid-base balance

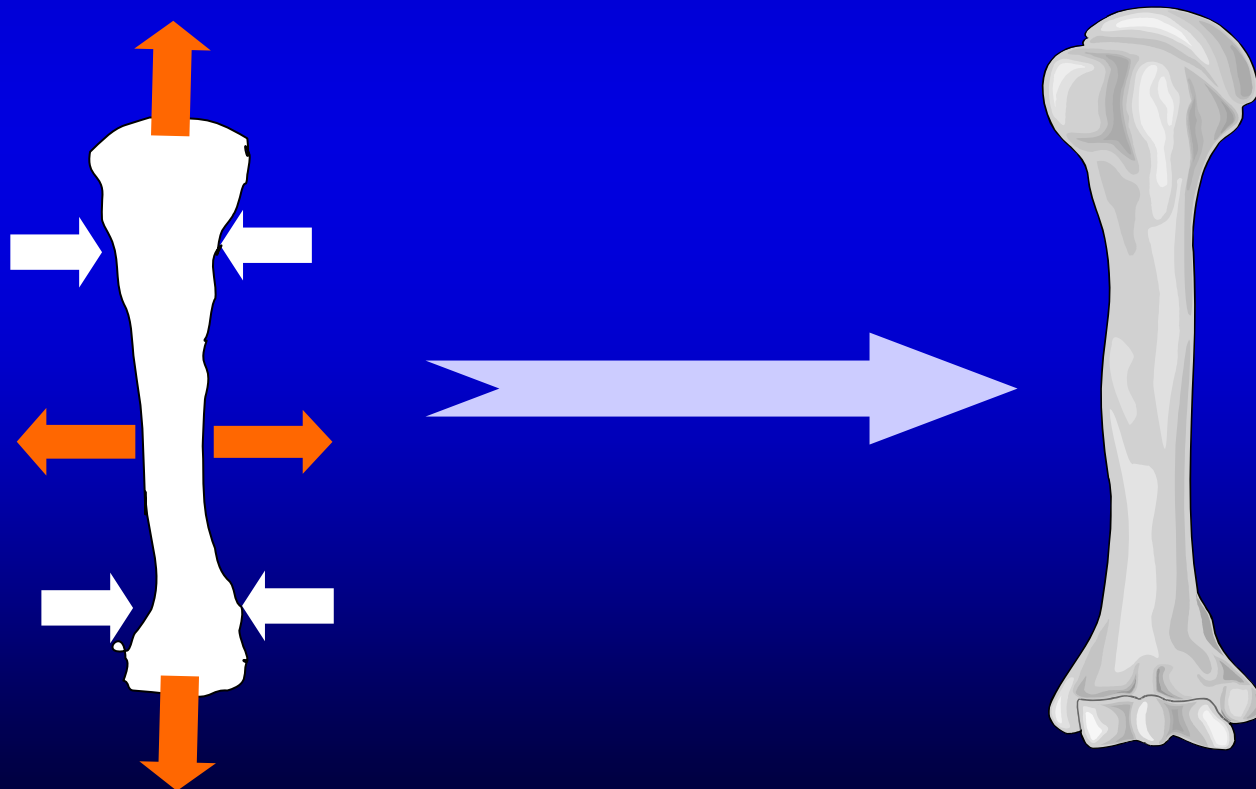
# Distribution of Cortical and Cancellous Bone in a Long Bone

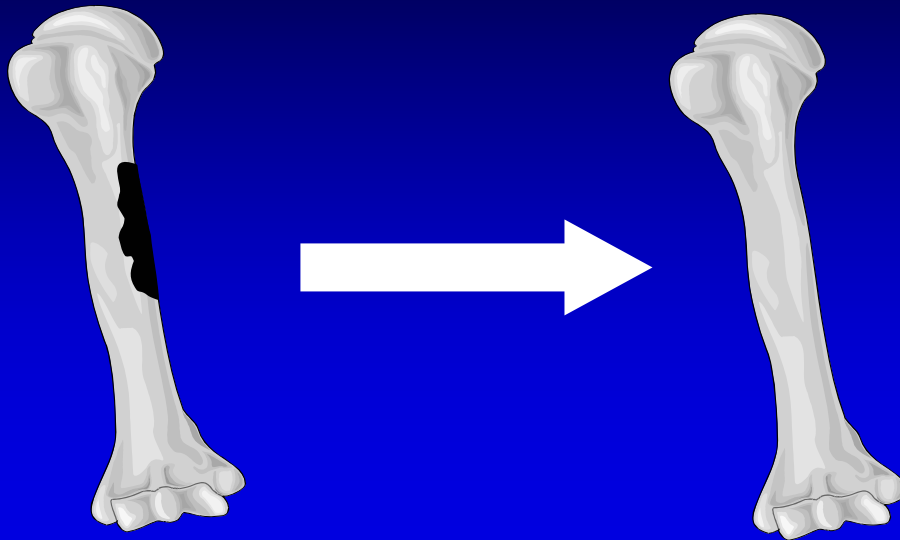


# Bone Modeling

↑ Denotes sites of bone resorption

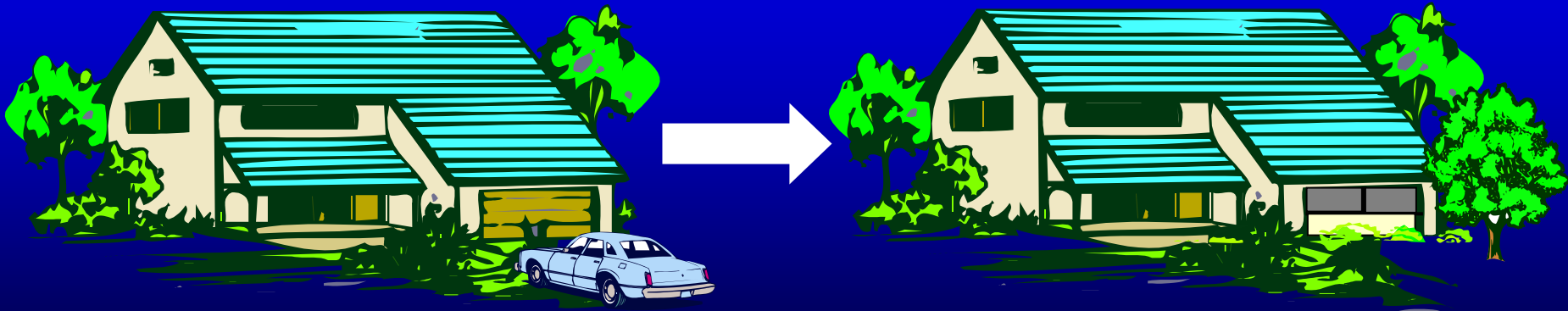
↑ Denotes sites of bone formation



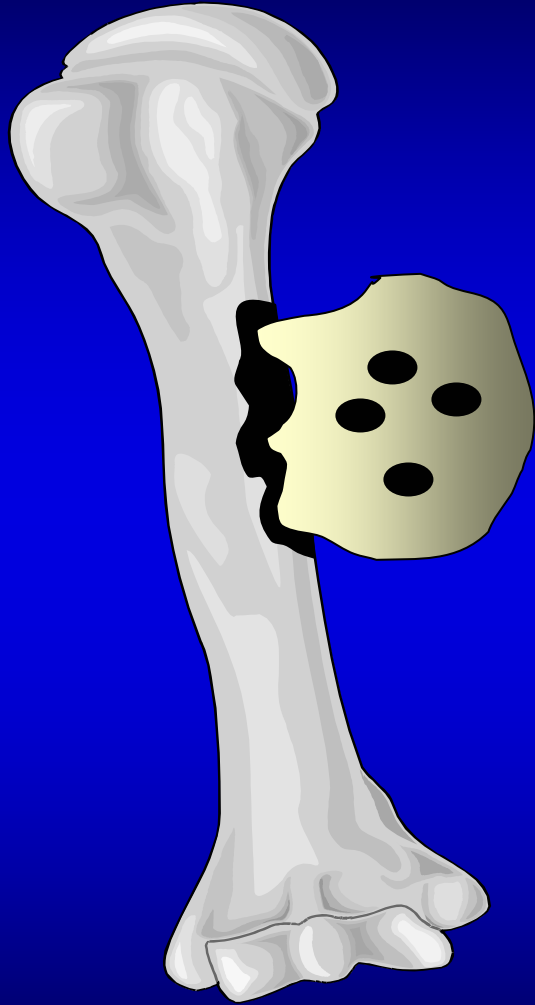


**Bone  
Remodeling**

**Home Remodeling**



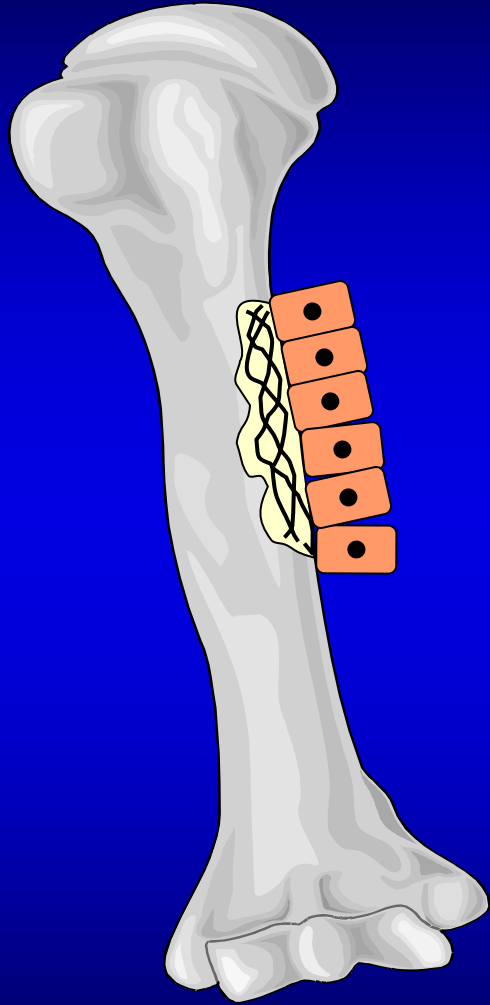
**Garage to Playroom**



**OSTEOCLAST**



**DEMOLITION CREW**

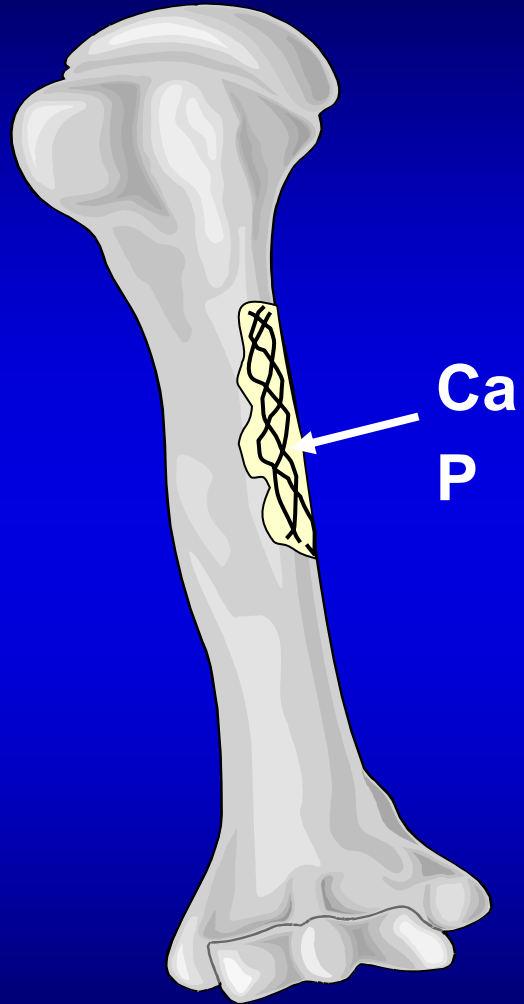


**OSTEOBLASTS**  
(Laying down collagen)



**CARPENTER**





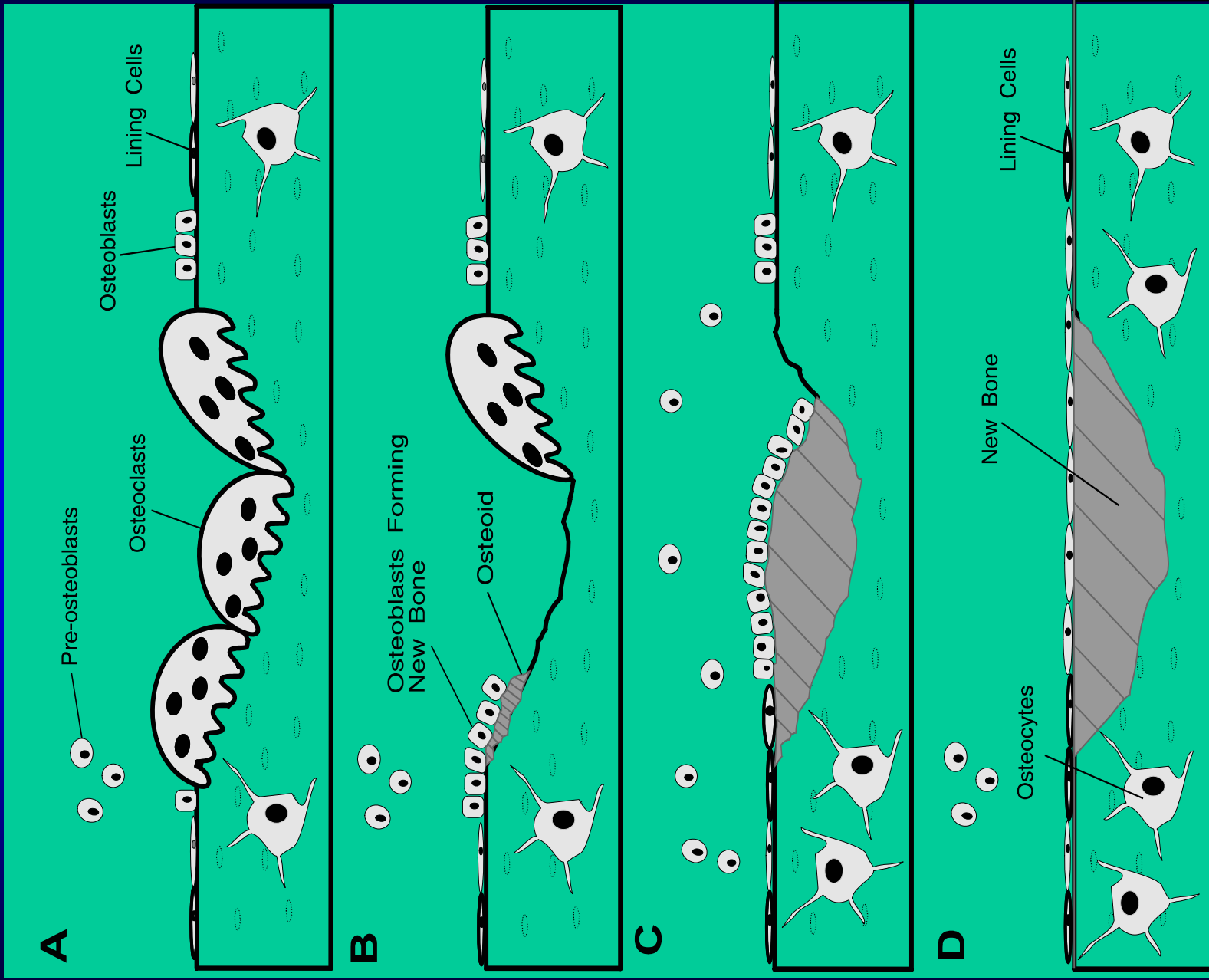
Ca  
P

**MINERALIZATION**

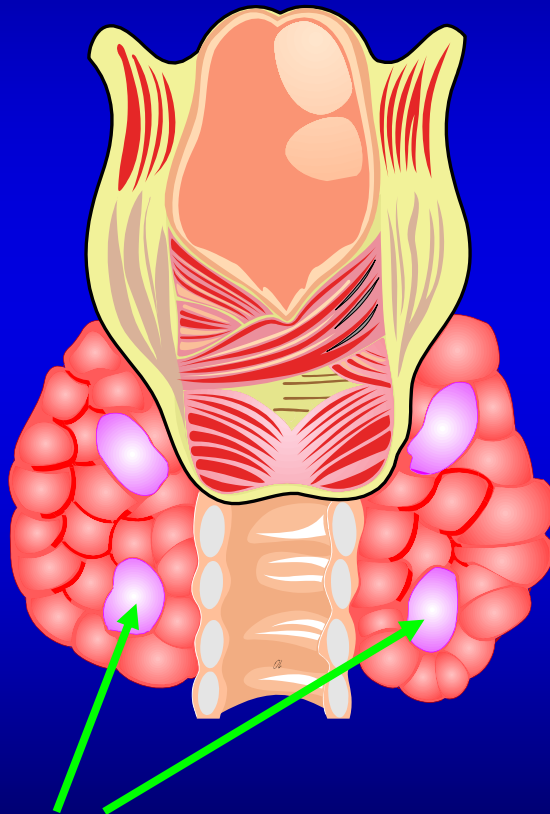


**CEMENT CREW**

# Summary of Bone Remodeling



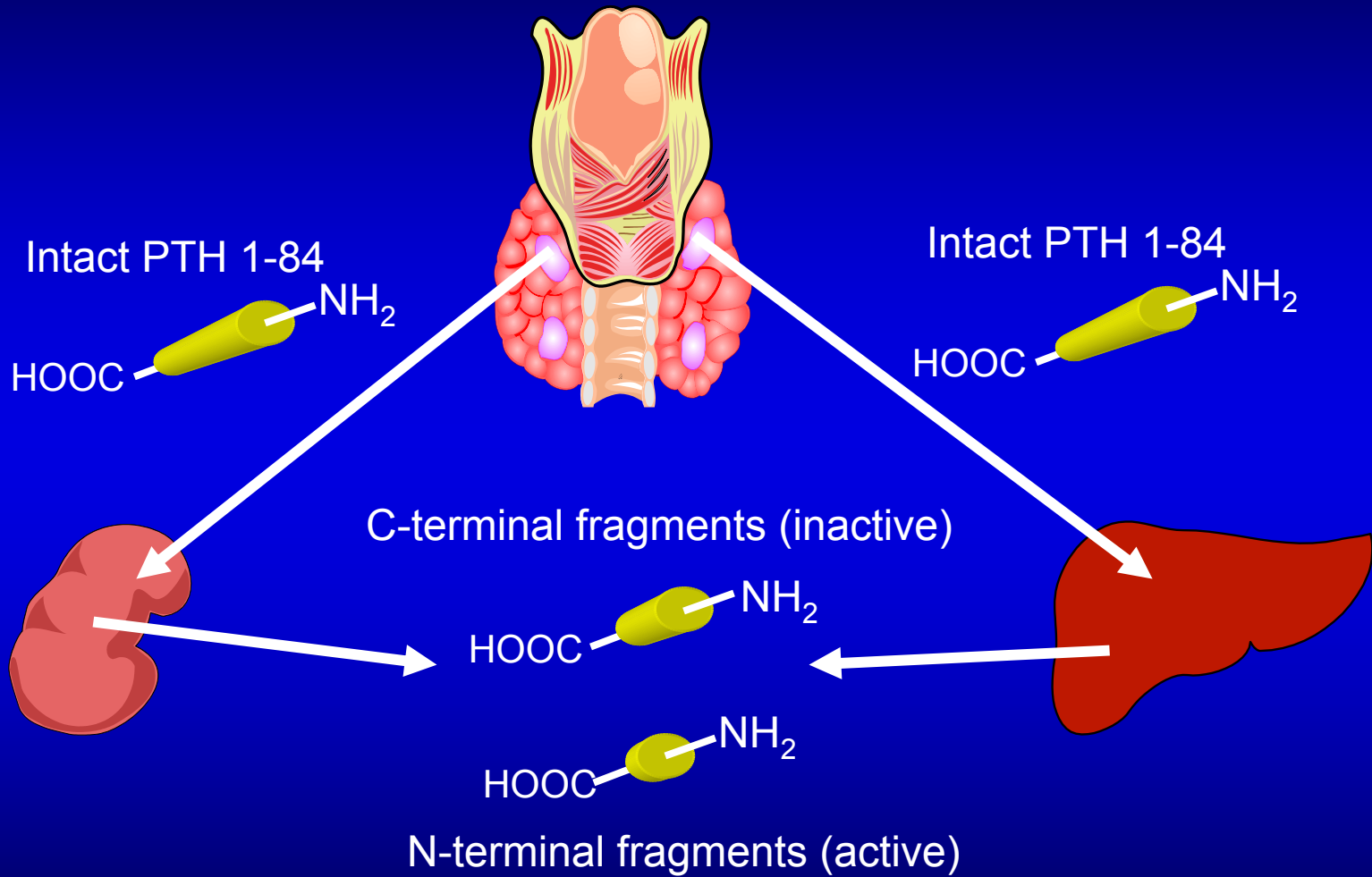
# The Role of Parathyroid Hormone in Normal Calcium Homeostasis



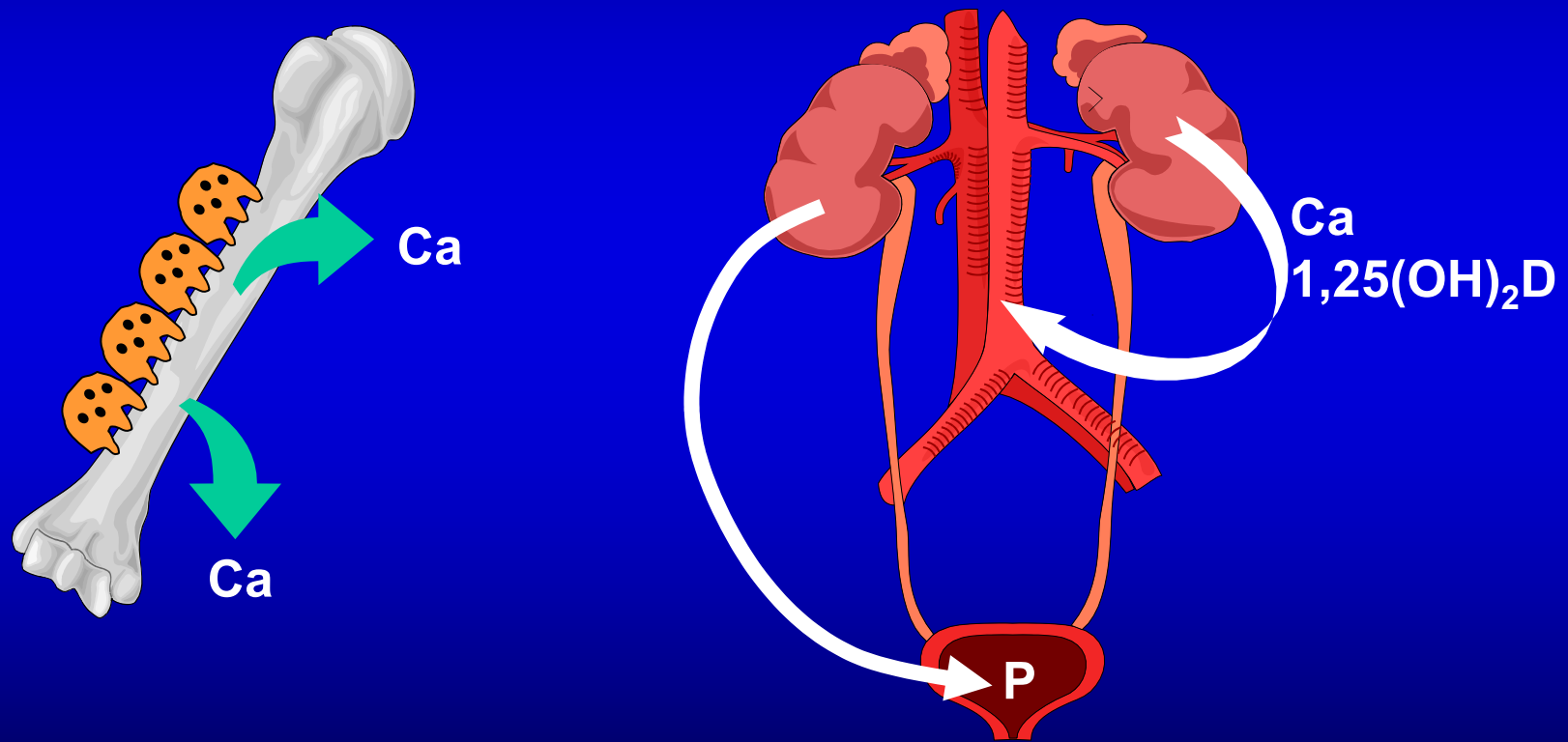
Parathyroid glands

- Major calcium-sensing glands in body
- Secrete parathyroid hormone in response to low circulating calcium
- Parathyroid hormone increases serum calcium by:
  - 1) Promoting bone resorption
  - 2) Diminishing urinary calcium excretion
  - 3) Indirectly promoting increased dietary calcium absorption via increased renal production of  $1,25(\text{OH})_2\text{D}$

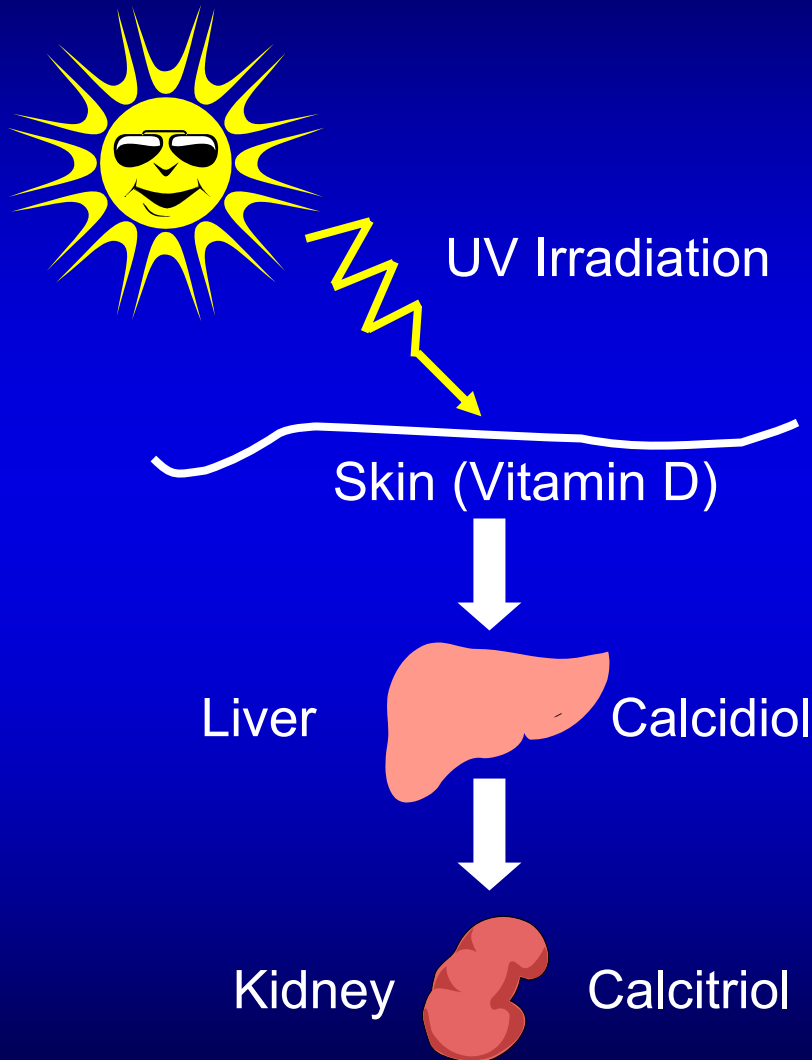
# Secretion and Metabolism of Human PTH



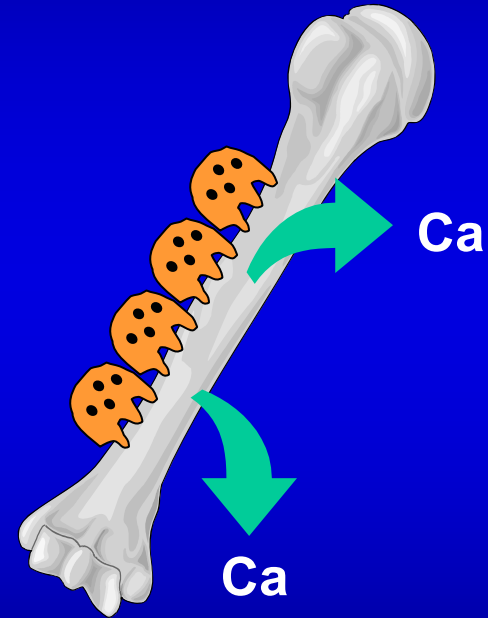
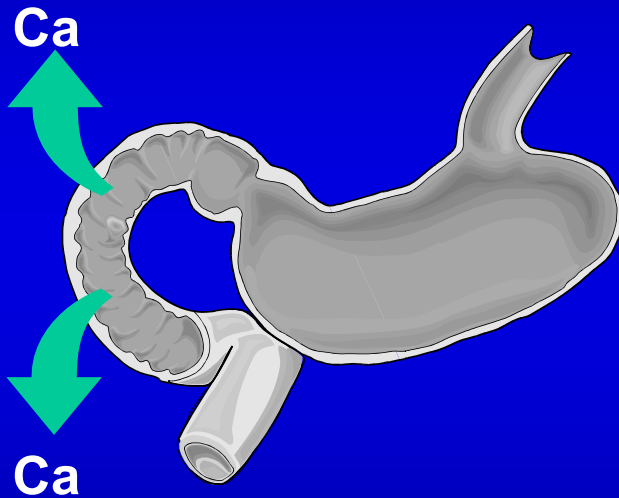
# Physiological Action of Parathyroid Hormone in Raising Blood Calcium Concentration



# Cutaneous Production and Systemic Activation of Vitamin D



# Physiological Action of $1,25(\text{OH})_2\text{D}$ in Raising Blood Calcium Concentration

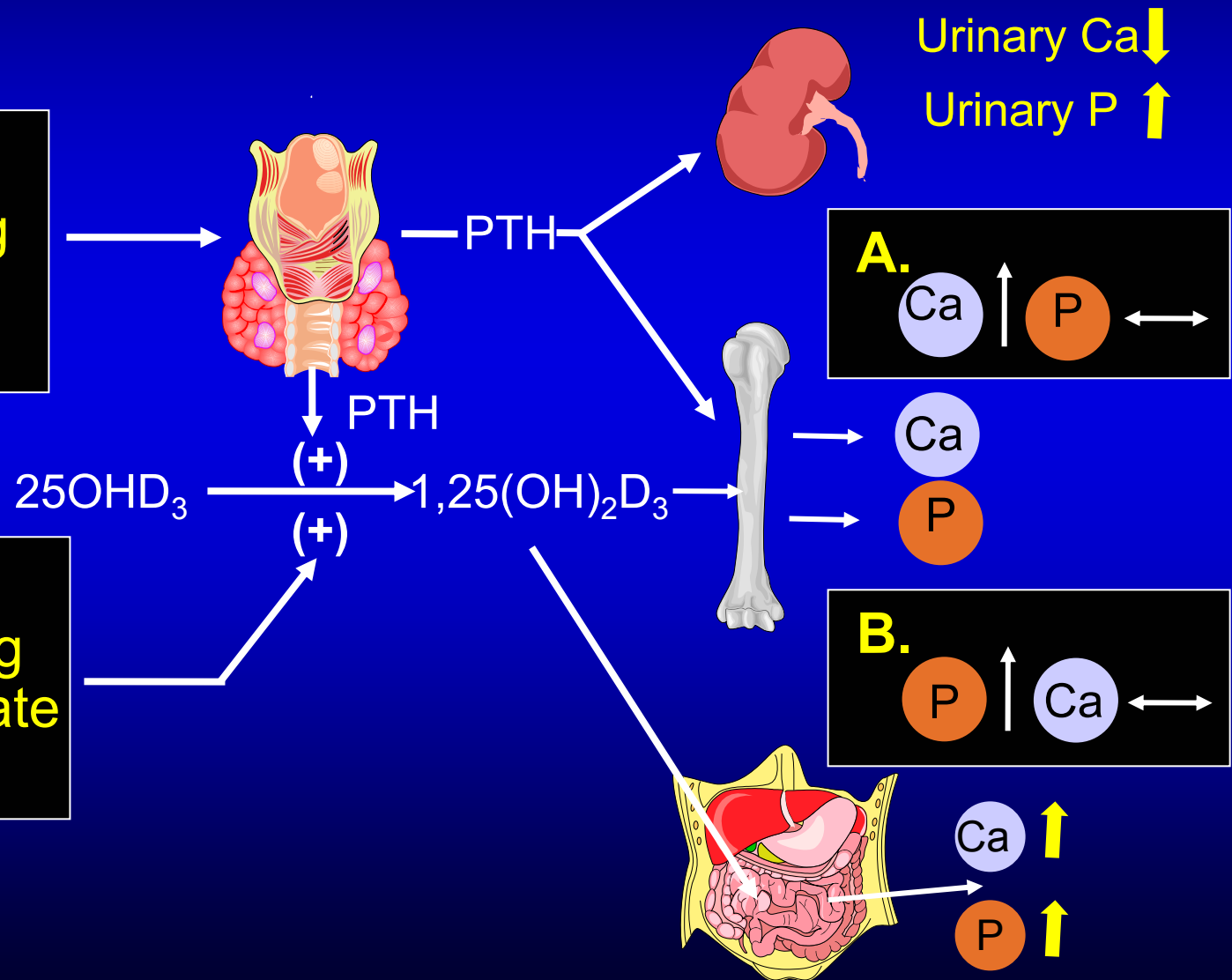


# Central Role of PTH and Vitamin D in the Homeostatic Control of Calcium and Phosphate

**Initial Plasma Condition**                      **Physiological Adjustment**                      **Final Plasma Condition**

**A. Low Circulating Calcium**  
Ca

**B. Low Circulating Phosphate**  
P



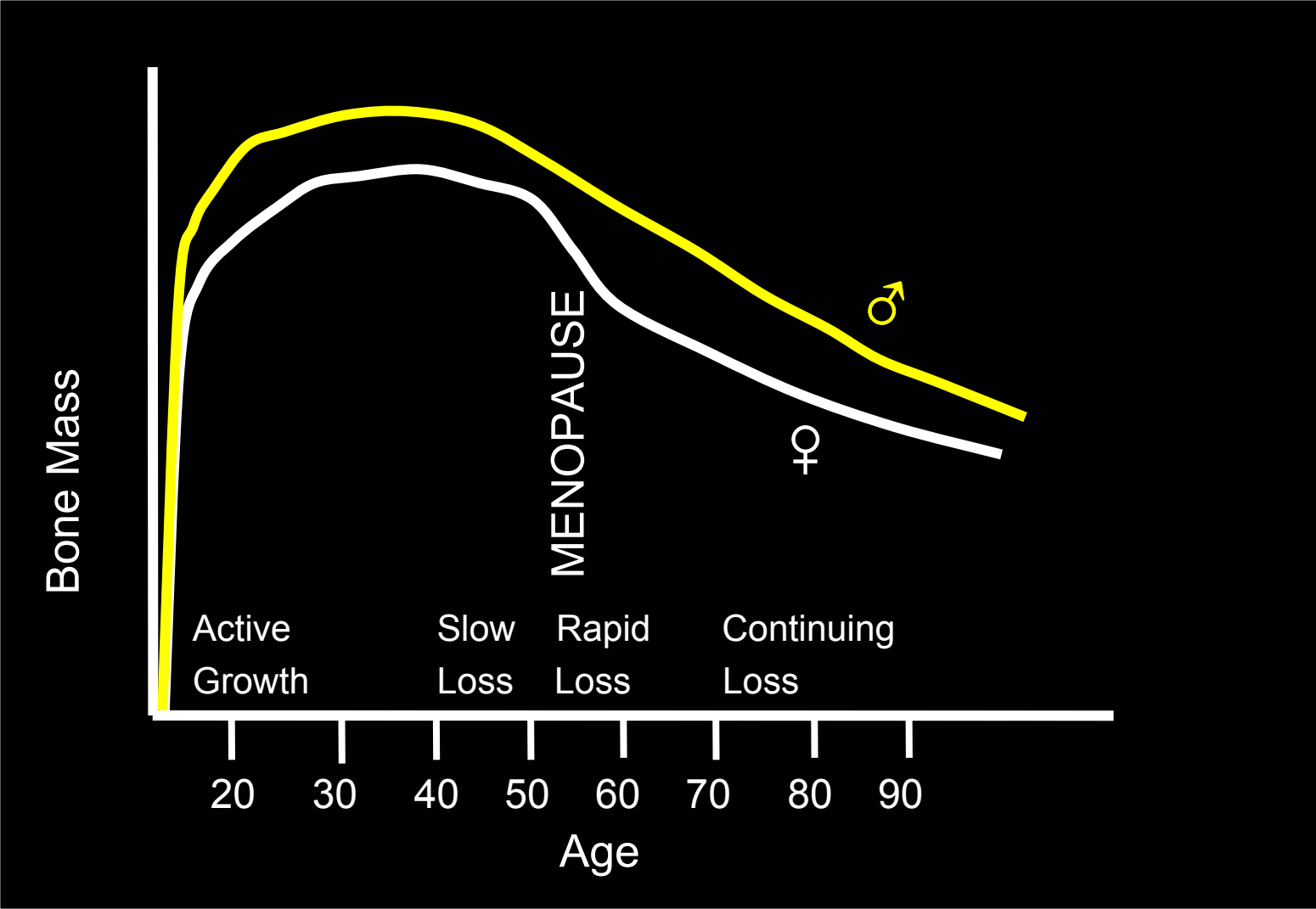
**A.** Ca ↑ P ↔

**B.** P ↑ Ca ↔

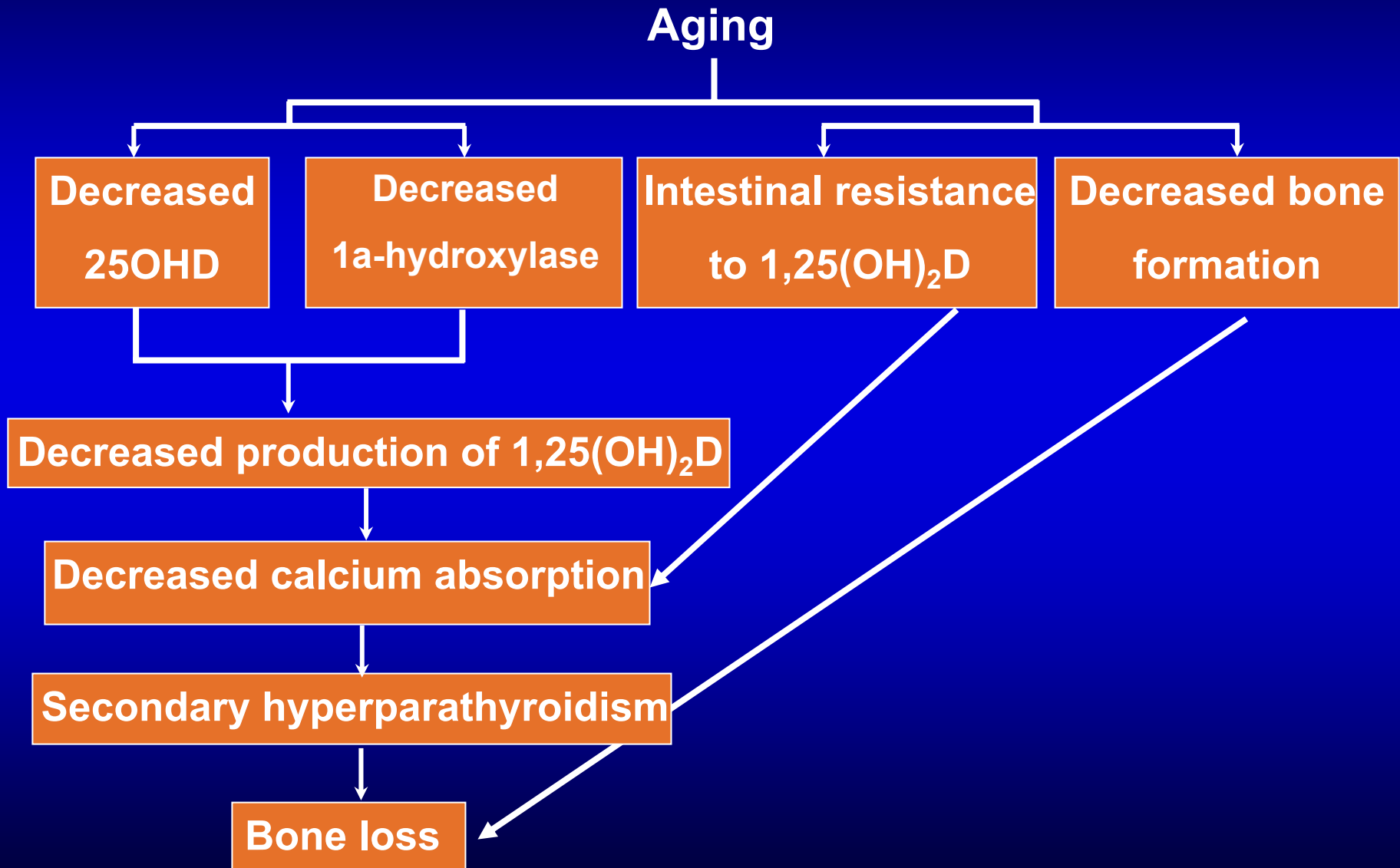
Ca ↑  
P ↑



# Change in Bone Mineral Density versus Age in Normal Men and Women



# Model for the Proposed Changes in Calcium Homeostasis and Bone Turnover with Age

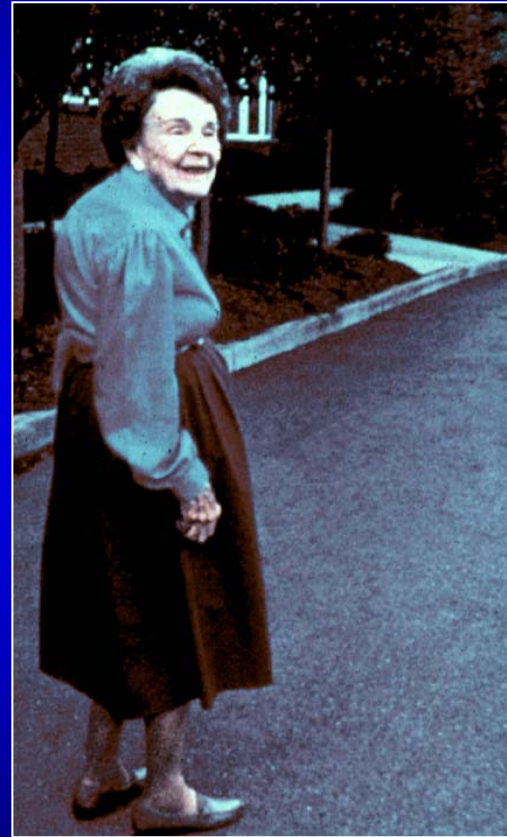


# Osteoporosis

Patient  
at age  
50...



and  
25 years  
later



Used with permission of the National Osteoporosis Foundation. *Osteoporosis: The Silent Disease*. National Osteoporosis Foundation. Partners in Prevention Slide Presentation. 1993

# Definition of Osteoporosis

“A systematic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fractures.”

**Normal Trabecular Bone**



**Osteoporotic Bone**



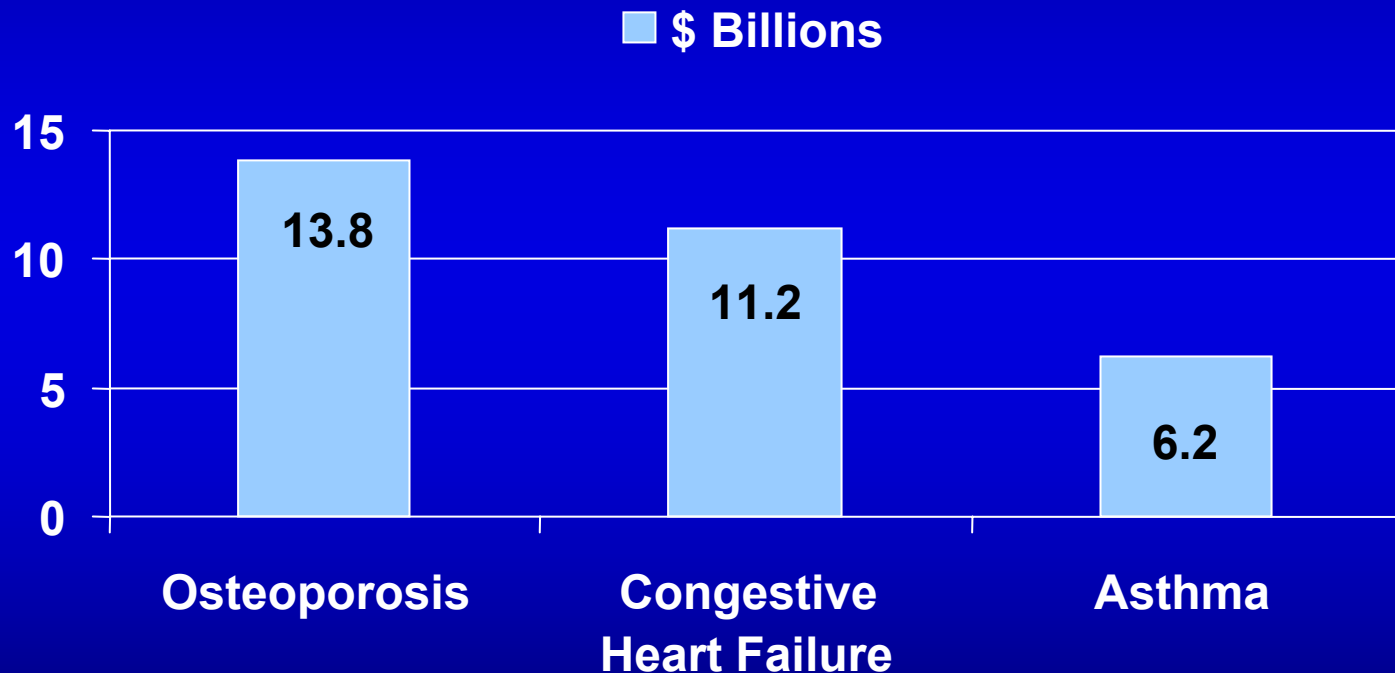
# Comparative Yearly Incidence

	<u>Estimate</u>
Osteoporosis-related fractures	1,500,000
Breast cancer	184,000
Ovarian cancer	26,000
Cervical and endometrial cancer	15,000
Prostate cancer	317,000

# Osteoporosis is Pervasive

- Afflicts 25 million Americans
- 15% of women and 5% of men will experience a hip fracture in their lifetime
- Hip fractures occur as frequently as breast cancer
- Total cost of osteoporosis is estimated at about \$14 billion each year

# Annual Costs of Various Chronic Diseases



Ray NF et al. *J Bone Miner Res* 1997;12:24-35; DHHS pub. No. PHS 92-1774; Irwin et al. *Battelle med Tech Assess Pol Res Cen* 1992; Weiss et al. *N Engl J Med* 1992;326:862



# Medical, Nursing Home and Social Costs of Osteoporotic Fractures



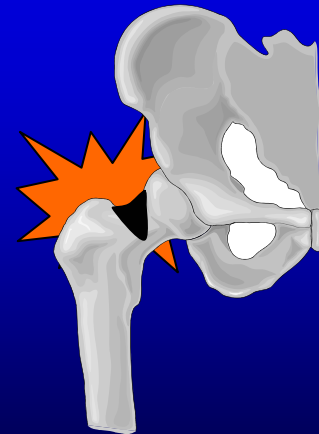
National Osteoporosis Foundation, 1993; Ray NF et al. *J Bone Miner Res* 1997;12:24-35

# Established Risk Factors for Osteoporosis

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## *Genetic*

- Female
- Caucasian or Asian races
- Thin body habitus
- Low peak bone mass
- Family history of fractures

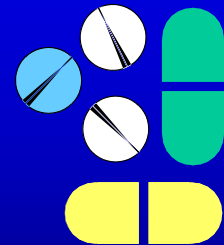


# Established Risk Factors for Osteoporosis

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## *Medical*

- Menopause
- Menstrual dysfunction or early menopause
- Glucocorticoids, thyroid, anticonvulsants, benzodiazepines and GnRH use



# Established Risk Factors for Osteoporosis

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## *Nutritional*

- Low calcium intake
- Vitamin D deficiency
- Excessive caffeine intake
- Excessive dietary sodium
- Reduced alkali intake



# Established Risk Factors for Osteoporosis

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## *Lifestyle*

- Excessive smoking
- Excessive alcohol
- Lack of exercise



- Slipping, falling as a result of loose rugs, cords, etc.