Calcium Metabolism physiology of hormone 2007

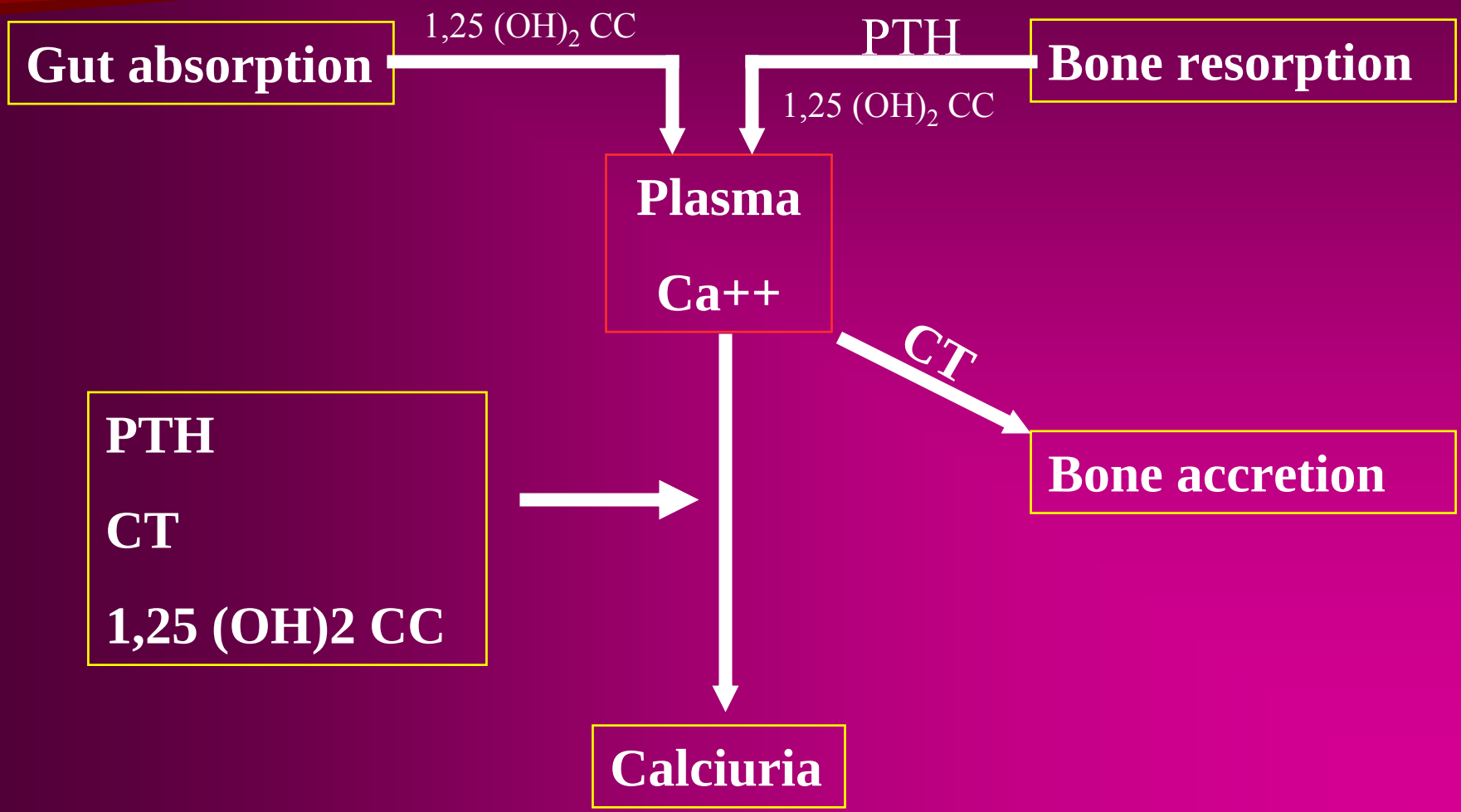
Calcium metabolism

- What is the recommended daily intake?
- 1000mg
- What is the plasma concentration?
- 2.2-2.6mmol/L
- How is calcium excreted?
- Kidneys - 2.5-10mmol/24 hrs
- How are calcium levels regulated?
- PTH and vitamin D (+others)

Calcium homeostasis

- Three Calcitropic hormones
  - PTH
  - 1,25 (OH)2 CC
  - CT
- Three targets
  - Bone
  - Gut
  - Kidney
- Three bone cells
  - Osteoblasts
  - Osteocytes
  - Osteoclasts

Calcium homeostasis



Calcium physiology

- Blood Calcium is tightly regulated by:
  - PRINCIPLE ORGAN SYSTEMS
    - GUT, BONE, KIDNEYS
  - HORMONES
    - PARATHYROID HORMONE (PTH), VITAMIN D,calcetonin
  - INTEGRATED PHYSIOLOGY OF ORGAN SYSTEMS AND HORMONES MAINTAIN BLOOD CALCIUM

CALCIUM PHYSIOLOGY: BLOOD CALCIUM

- Calcium flux into and out of blood
- "IN" FACTORS:

1- intestinal absorption

2- Bone resorption

– "OUT" FACTORS:

1- Renal Excretion

2- Bone formation (Ca INCORPATION INTO BONE)

– BALANCE BETWEEN "IN" AND "OUT" FACTORS

- Organ physiology of Gut, Bone and kidney
- Hormone function of PTH and vitamin D3

CALCIUM HOMEOSTASIS

DIETARY CALCIUM

THE ONLY "IN"

DIETARY HABITS,

SUPPLEMENTS

INTESTINAL ABSORPTION

ORGAN PHYSIOLOGY

ENDOCRINE PHYSIOLOGY

BONE

ORGAN, ENDOCRINE

BLOOD CALCIUM

KIDNEYS

ORGAN PHYS.

ENDOCRINE PHYS.

URINE

THE PRINCIPLE "OUT"

Vitamin D (cholecalciferol)

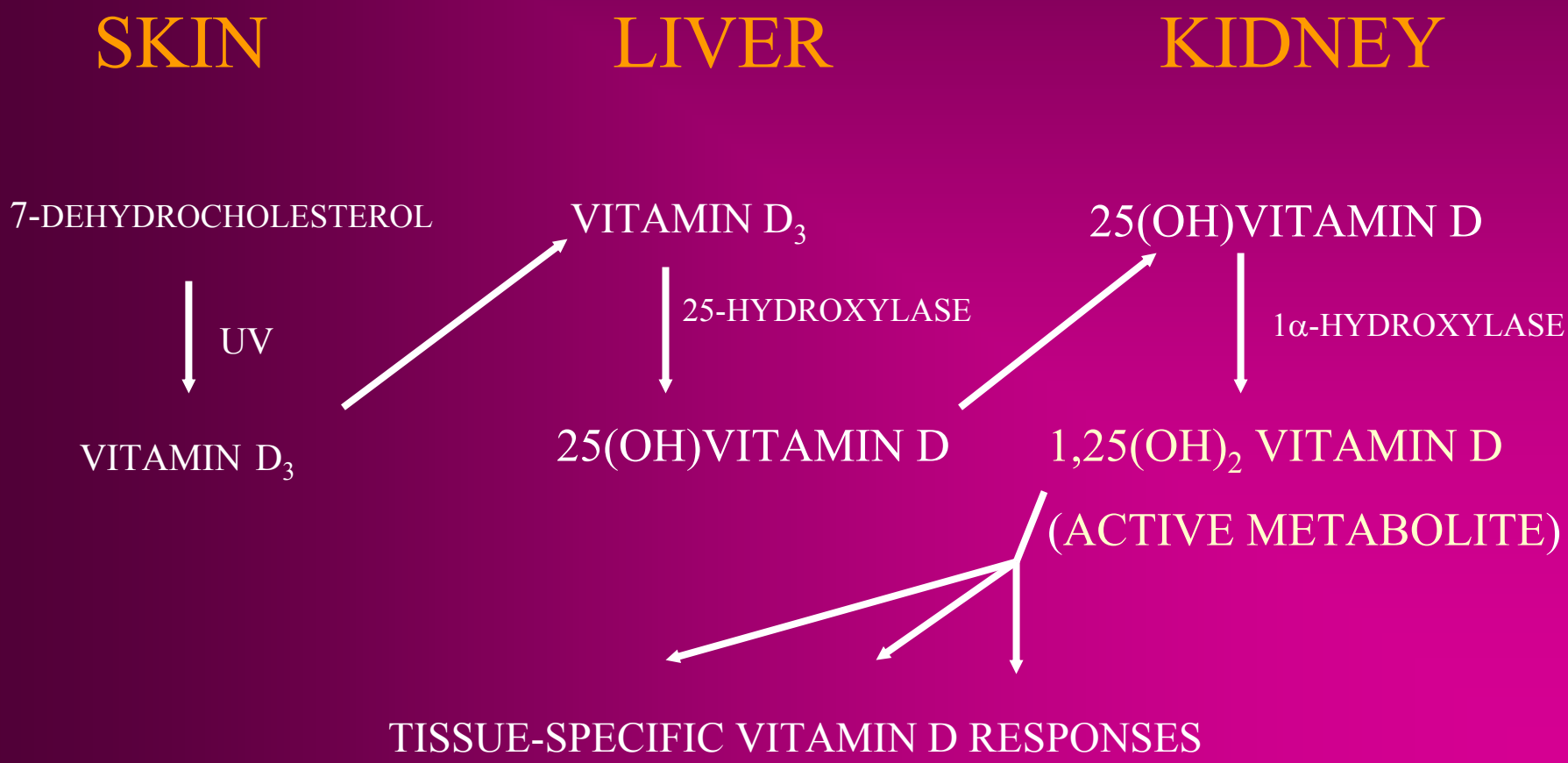
- Sources of vit D
- Diet
- u.v. light on precursors in skin
- Normal daily requirement
- 400IU/day
- Target organs
  - bone - increased Ca release
  - gut - increased Ca absorption

VITAMIN D PHYSIOLOGY

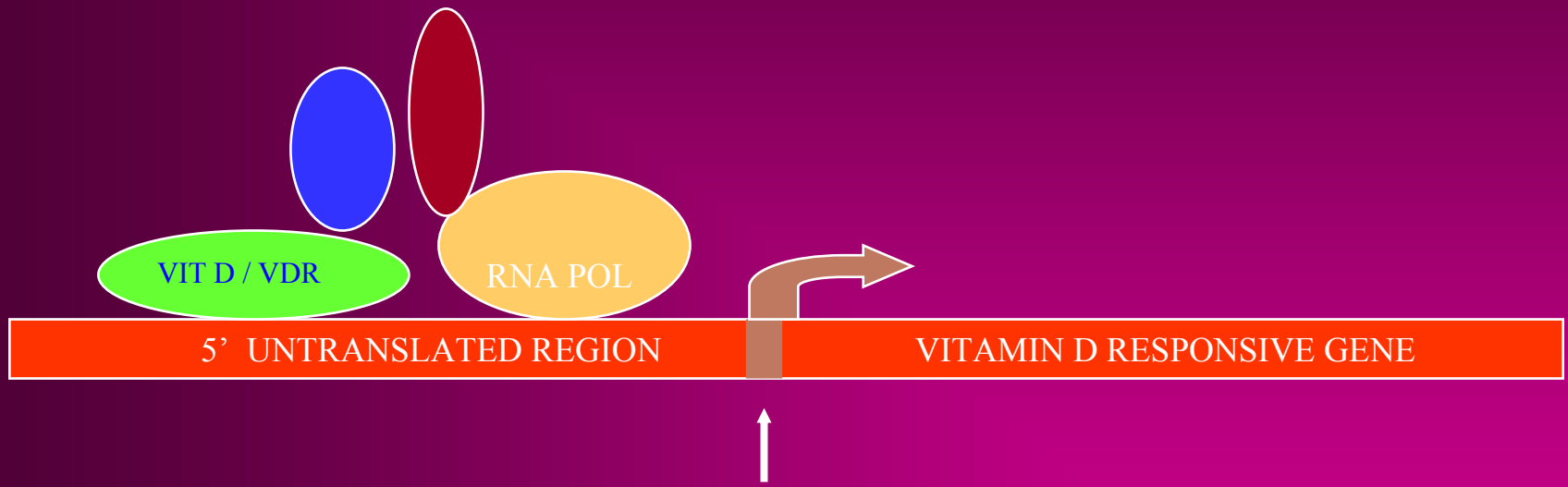
- VITAMIN D IS A HORMONE BY CLASSIC CRITERIA: MADE IN ONE PLACE (OR SEQUENTIALLY SEVERAL PLACES!), AND ACTING IN OTHER PLACES.

THIS DISTINGUISHES IT FROM OTHER "CLASSIC" VITAMINS, SUCH AS VITAMIN C, B VITAMINS, ETC., WHICH ACT AS COFACTORS IN BIOCHEMICAL REACTIONS.

VITAMIN D SYNTHESIS



VITAMIN D MECHANISM OF ACTION

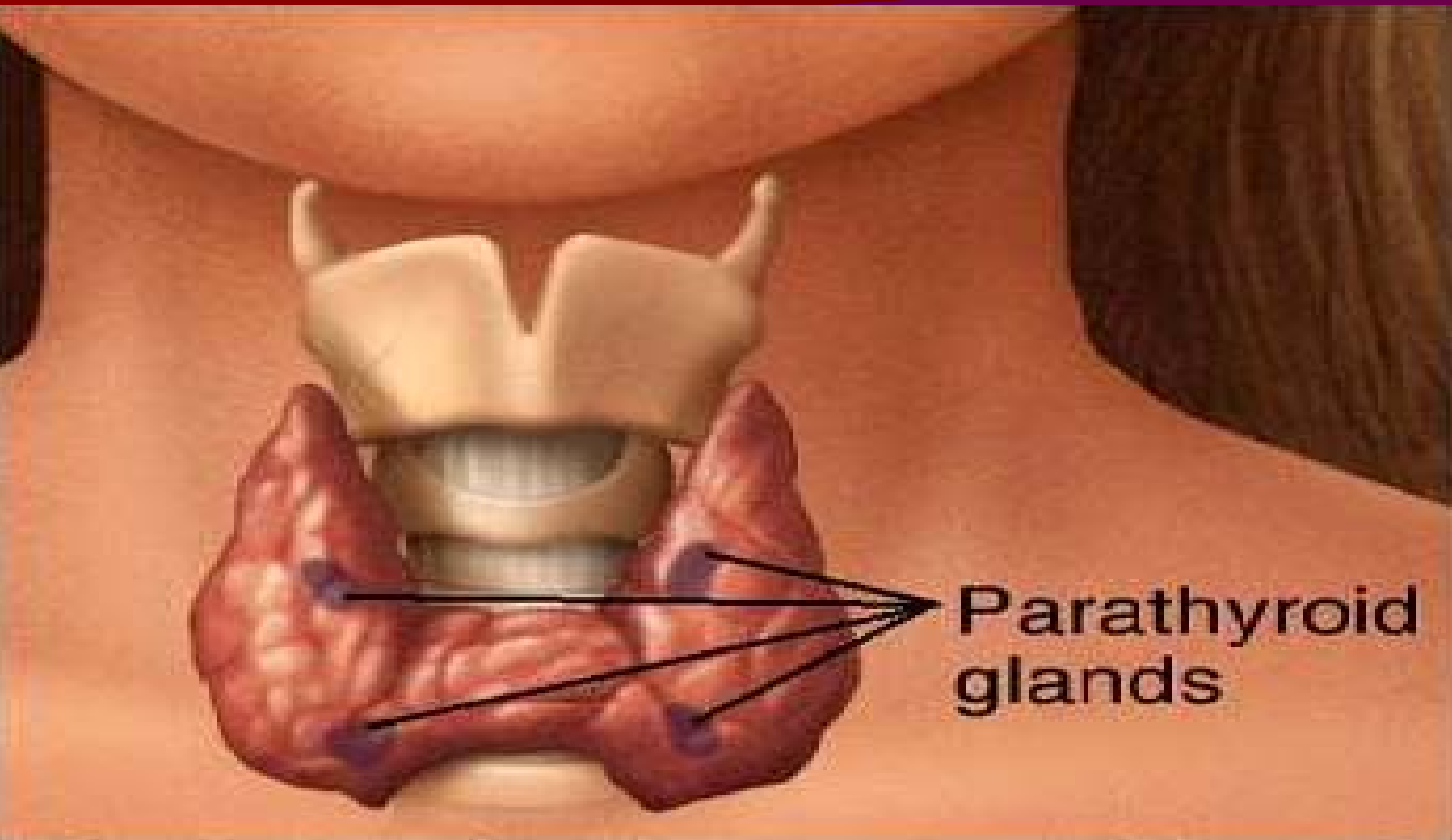


IN THE NUCLEUS

FUNCTION OF VITAMIN D

- TISSUE SPECIFICITY
  - GUT
    - STIMULATE TRANSPORT OF CALCIUM AND PHOSPHATE IN THE SMALL INTESTINE (PRINCIPALLY DUODENUM)
  - BONE
    - STIMULATE TERMINAL DIFFERENTIATION OF OSTEOCLASTS
    - STIMULATE OSTEOBLASTS TO STIMULATE OSTEOCLASTS TO MOBILIZE CALCIUM
  - PARATHYROID
    - INHIBIT TRANSCRIPTION OF THE PTH GENE (FEEDBACK REGULATION)

The **Parathyroids**, associated with the thyroid but comprising separate structures



PTH

- Physiological role
- Production related to plasma calcium levels
- Control of calcium levels
  - target organs
    - bone - increased Ca/PO4 release
    - kidneys
      - increased reabsorption of Ca
      - increased excretion of PO4
    - gut - indirect increase in calcium reabs by stimulting activation of vitamin D metabolism

4. Parathyroid hormone and calcitonin regulate blood calcium level

- The four **parathyroid glands** are embedded in the surface of the thyroid gland.

- They secrete **parathyroid hormone (PTH)**, a peptide:
  - Raises blood calcium levels.
  - Secretion regulated by calcium in the blood.
  - Causes osteoclasts to break down bone, releasing Ca^{2+} into the blood.
  - Stimulates the kidneys to reabsorb Ca^{2+}.
  - Stimulates kidneys to convert **vitamin D** to its active form that to stimulate the uptake of Ca^{2+} from food in the intestine.
  - PTH and calcitonin are **antagonistic** hormones.

- A lack of PTH causes hypoparathyroidism, a **tetany**:
  - Calcium levels in the blood drop.
  - There are convulsive contractions of the skeletal muscles.

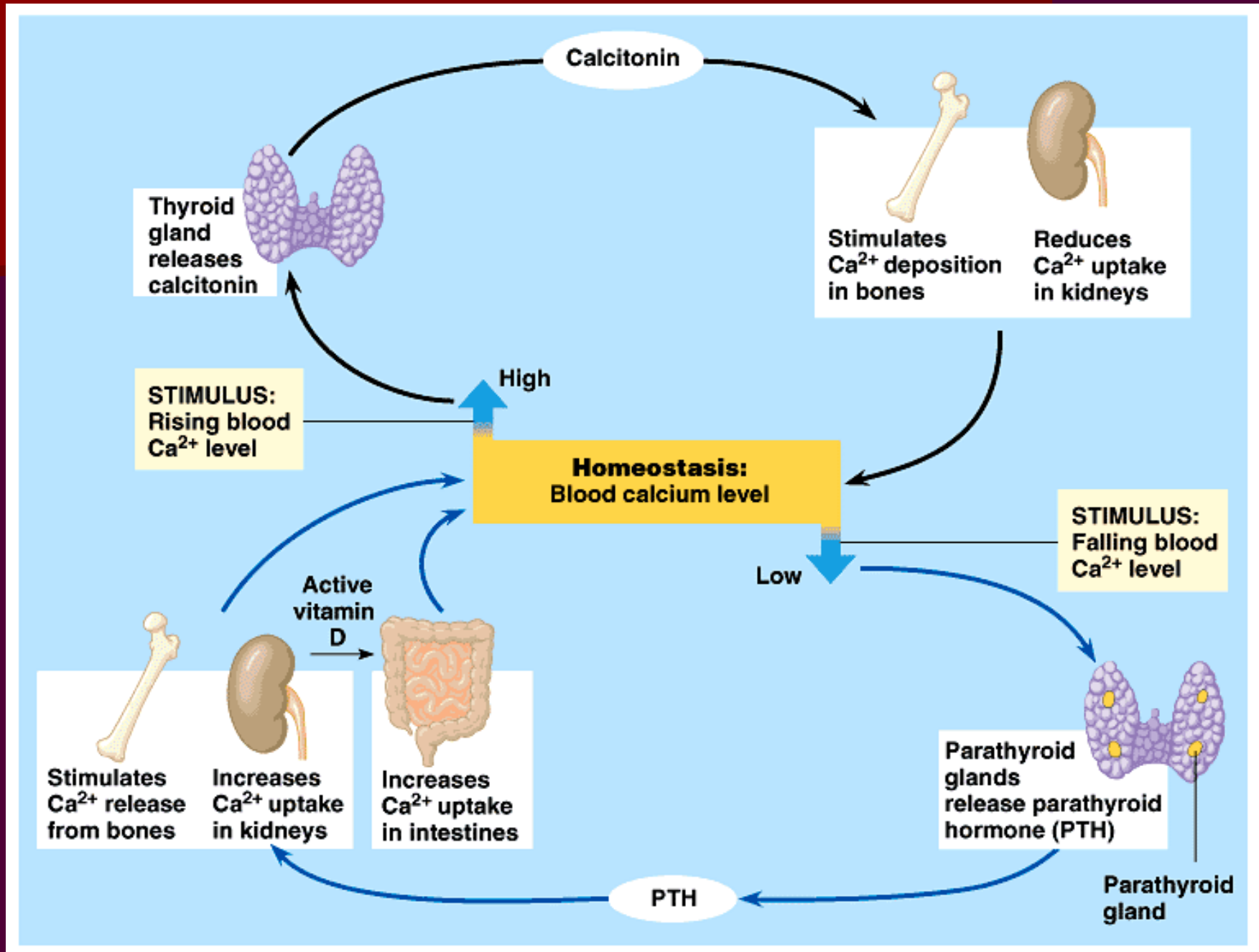
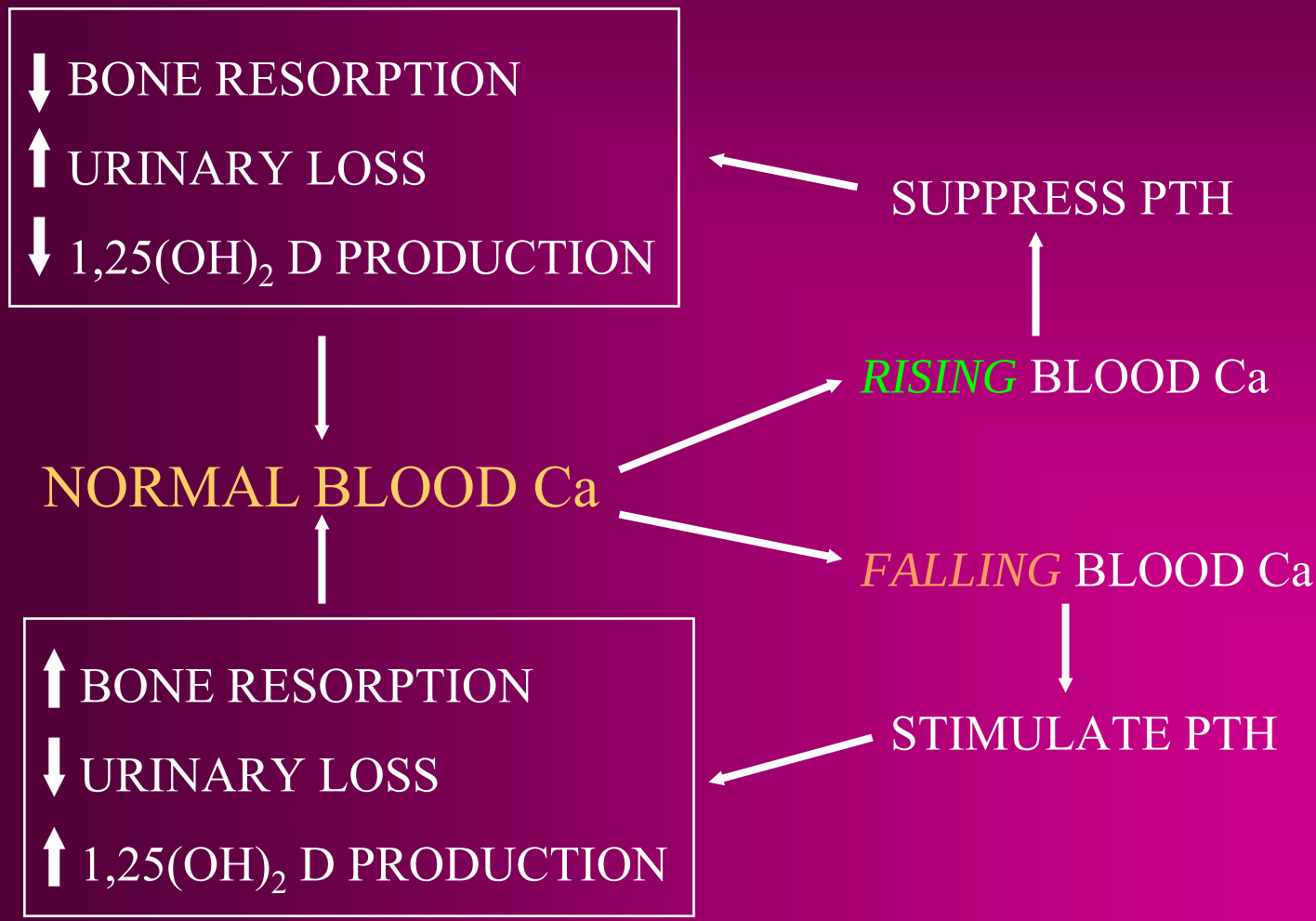

Calcitonin
Thyroid gland releases calcitonin
Stimulates Ca^{2+} deposition in bones
Reduces Ca^{2+} uptake in kidneys
STIMULUS: Rising blood Ca^{2+} level
High
Homeostasis: Blood calcium level
STIMULUS: Falling blood Ca^{2+} level
Low
Active vitamin D
Stimulates Ca^{2+} release from bones
Increases Ca^{2+} uptake in kidneys
Increases Ca^{2+} uptake in intestines
Parathyroid glands release parathyroid hormone (PTH)
Parathyroid gland
PTH

Fig. 45.9

Parathyroid hormone (PTH) Physiology

- PTH FUNCTIONS to preserve normal blood calcium (and phosphate)
  - PTH STIMULATES BONE RESORPTION AND, THUS, INCREASES BLOOD CALCIUM
  - PTH STIMULATES RENAL TUBULAR REABSORPTION OF CALCIUM, AND THUS, INCREASES BLOOD CALCIUM
  - PTH STIMULATES RENAL 1α-HYDROXYLATION OF 25(OH)VITAMIN D, THUS INDIRECTLY STIMULATING INTESTINAL ABSORPTION OF CALCIUM

CALCIUM, PTH, AND VITAMIN D FEEDBACK LOOPS



Calcitonin

- Physiological role

- Levels increased when serum Ca >2.25mmol/L
- Target organs
  - Bone - suppresses resorption
  - Kidney - increases excretion

ORGAN PHYSIOLOGY AND CALCIUM METABOLISM

- THERE ARE 3 PRICIPLE TISSUES THAT FUNCTION PROMINENTLY IN CALCIUM HOMEOSTATIS. DISORDERS OF THESE TISSUES, OR OF THE CALCIOTROPIC FACTORS THAT AFFECT THEIR FUNCTION MAY RESULT IN DISORDERS OF CALCIUM METABOLISM
  - INTESTINES
  - KIDNEYS
  - BONE

Factors affecting bone turnover

- Other hormones
- Oestrogen
  - gut - increased absorption
  - bone - decreased re-absorption
- Glucocorticoids
  - gut - decrease absorption
  - bone - increased re-absorption/decreased formation
- Thyroxine
  - stimulates formation/resorption
  - net resorption

Skeletal System

- Bones are made of several tissues
- Primarily made of collagen and hydroxyapatite - $Ca_{10}(PO_4)_6(OH)_2$
- About 206 bones in the human body

- What is the composition of bone?
- The matrix
  - 40% organic
    - Type 1 collagen (tensile strength)
    - Proteoglycans (compressive strength)
    - Osteocalcin/Osteonectin
    - Growth factors/Cytokines/Osteoid
  - 60% inorganic
    - Calcium hydroxyapatite
- The cells
  - osteo-clast/blast/cyte/progenitor

Functions of Skeletal System

- **SUPPORT:** Hard framework that supports and anchors the soft organs of the body.
- **PROTECTION:** Surrounds organs such as the brain and spinal cord.
- **MOVEMENT:** Allows for muscle attachment therefore the bones are used as levers.
- **STORAGE:** Minerals and lipids are stored within bone material.
- **BLOOD CELL FORMATION:** The bone marrow is responsible for blood cell production.

Rickets

- Disease of children due to a lack of vitamin D.
- Calcium is not deposited in bones.
- Bones become soft.
- Bowing of the bones, and other deformities occur.

Homeostatic Imbalances

Osteomalacia

- "Rickets" of adults.
- Due to a lack of vitamin D.
- Calcium is not deposited in the bones.
- Bones become brittle.

Homeostatic Imbalances

Osteoporosis

- Bone reabsorption is greater than bone deposition.
- Due to any of the following:
  - Lack of estrogen in women.
  - Lack of exercise to stress the bones.
  - Inadequate intake of calcium and phosphorus.
  - Abnormalities of vitamin D metabolism.
  - Loss of muscle mass.

Risk factors for osteoporosis

In-correctable

- Gender
- Race (non-black)
- Genetic predisposition
- Family history

Correctable

- Smoking
- Alcoholism
- Caffeine
- Sedentary lifestyle
- Immobilization
- Excessive exercise
- Low BMI
- Gonadal failure
- Dietary lack
- Indoor life
- Drugs
  - Heparin
  - Corticosteroids

Osteoporosis

Vertebral bone

Vertebral fracture

Normal vertebrae

Osteoporotic fracture of femoral neck

Prevention of osteoporosis

- Diet rich in calcium 1.2 g/d
- Vitamin D 400 IU/d
- Exercise
  - 40 min walk
  - 4 times a week
- Sunshine

Age Related Dysfunctions

Arthritis:

Osteoarthritis- 90% of pop. By age 40

chronic inflammation of articular cartilage

can be normal age-dependent change

can also be pathology due to ?

Age-related changes

decrease blood supply

trauma

Osteoarthritis

CAUSES OF HYPERCALCEMIA

- HORMONAL
  - PRIMARY HYPERPARATHYROIDISM
  - HYPERVITAMINOSIS D
  - PARANEOPLASTIC (e.g., PTHrP, cytokines)
- NON-HORMONAL
  - RENAL FAILURE
- DRUGS
  - THIAZIDES, LITHIUM, OTHERS

Thank you