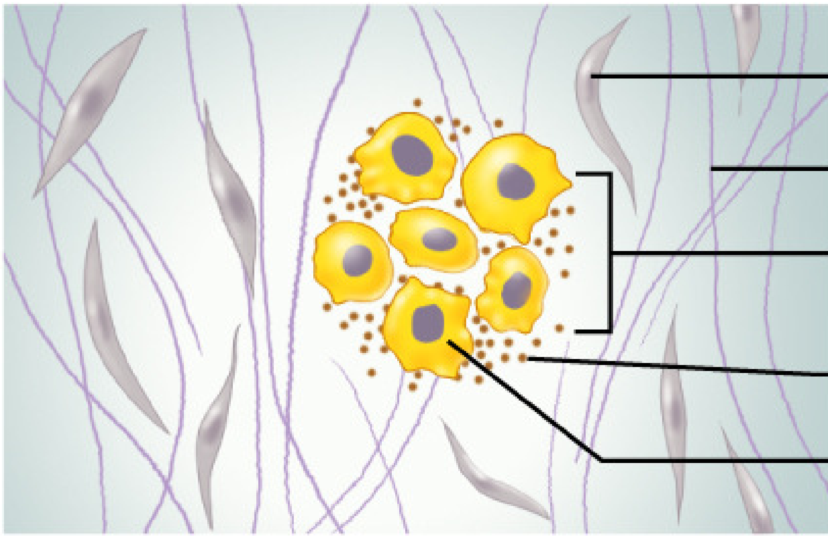
Stages of Intramembranous Ossification

- Results in the formation of cranial bones of the skull (frontal, perietal, occipital, and temporal bones) and the clavicles.
- All bones formed this way are flat bones
- An ossification center appears in the fibrous connective tissue membrane
- Bone matrix is secreted within the fibrous membrane
- Woven bone and periosteum form
- Bone collar of compact bone forms, and red marrow appears

Stages of Intramembranous Ossification

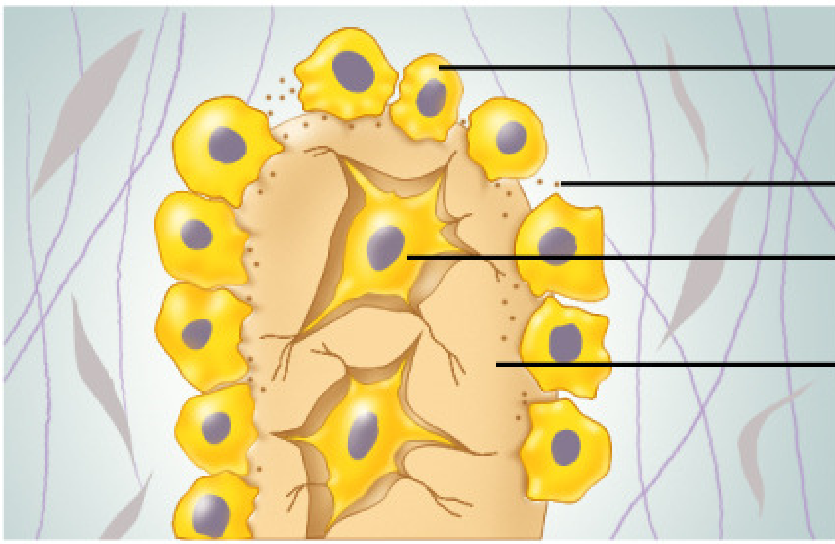


① **An ossification center appears in the fibrous connective tissue membrane.**

- Selected centrally located mesenchymal cells cluster and differentiate into osteoblasts, forming an ossification center.

Figure 6.7.1

Stages of Intramembranous Ossification

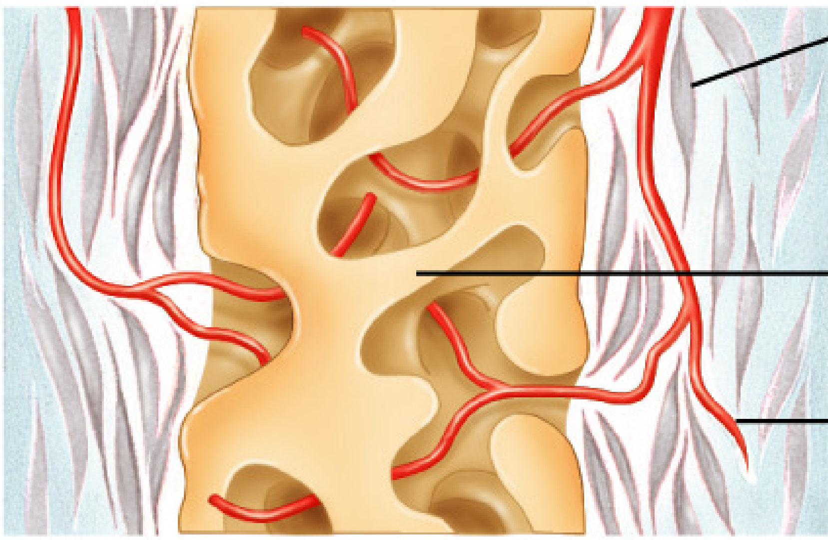


② **Bone matrix (osteoid) is secreted within the fibrous membrane.**

- Osteoblasts begin to secrete osteoid, which is mineralized within a few days.
- Trapped osteoblasts become osteocytes.

Figure 6.7.2

Stages of Intramembranous Ossification

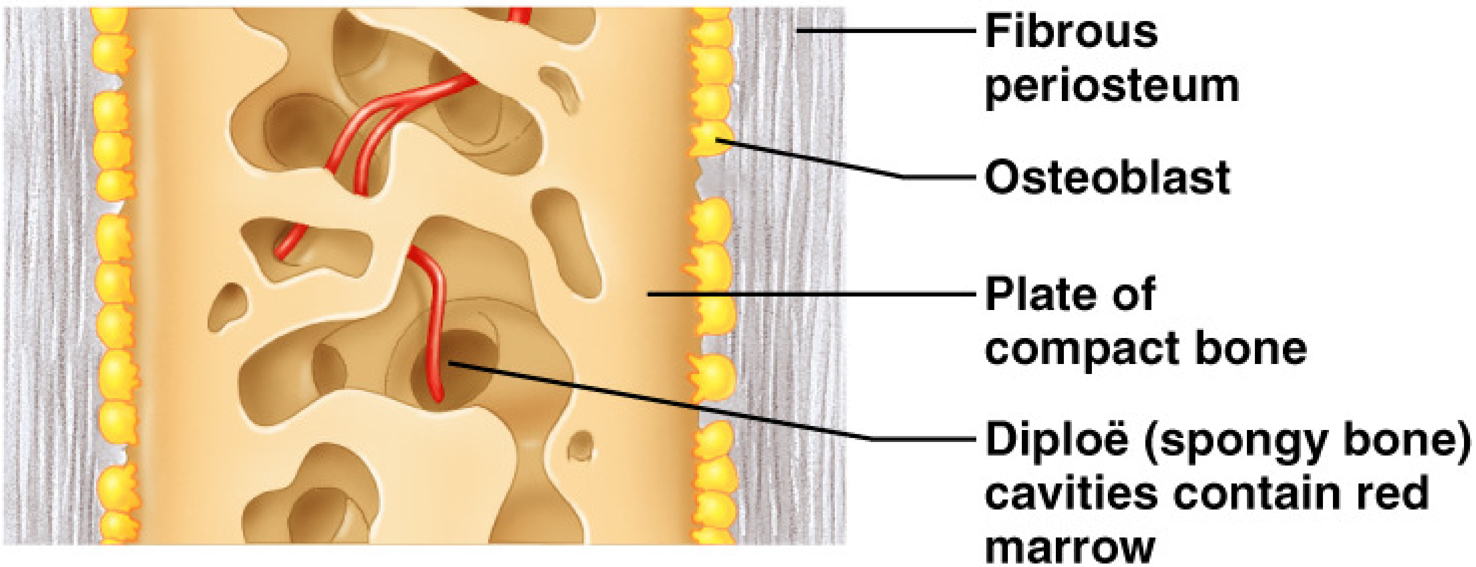


③ **Woven bone and periosteum form.**

- Accumulating osteoid is laid down between embryonic blood vessels, which form a random network. The result is a network (instead of lamellae) of trabeculae.
- Vascularized mesenchyme condenses on the external face of the woven bone and becomes the periosteum.

Figure 6.7.3

Stages of Intramembranous Ossification



④ **Bone collar of compact bone forms and red marrow appears.**

- Trabeculae just deep to the periosteum thicken, forming a woven bone collar that is later replaced with mature lamellar bone.
- Spongy bone (diploë), consisting of distinct trabeculae, persists internally and its vascular tissue becomes red marrow.

Figure 6.7.4

Endochondral Ossification

- Results in the formation of all of the rest of the bones
- Begins in the second month of development
- Uses hyaline cartilage “bones” as models for bone construction
- Requires breakdown of hyaline cartilage prior to ossification
- Formation begins at the primary ossification center

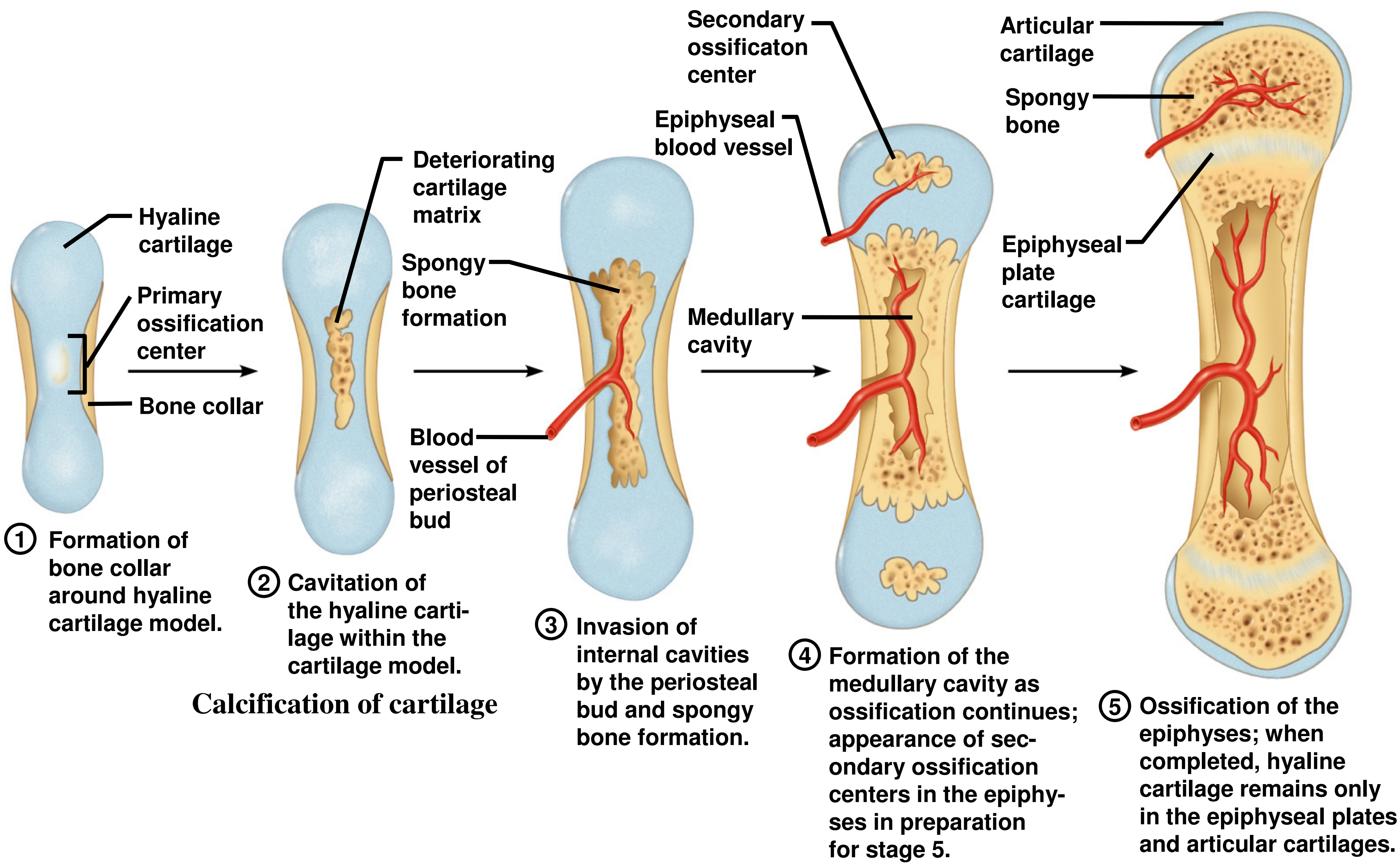
Endochondral Ossification

- The perichondrium covering the hyaline cartilage "bone" is infiltrated with blood vessels converting it to vascularized periosteum.
- This change in nutrition causes the underlying mesenchymal cells to specialize into osteoblasts

Stages of Endochondral Ossification

- Formation of bone collar
- Cavitation of the hyaline cartilage
- Invasion of internal cavities by the periosteal bud, and spongy bone formation
- Formation of the medullary cavity; appearance of secondary ossification centers in the epiphyses
- Ossification of the epiphyses, with hyaline cartilage remaining only in the epiphyseal plates

Stages of Endochondral Ossification



Calcification of cartilage

Postnatal Bone Growth

- Growth in length of long bones
  - Cartilage on the side of the epiphyseal plate closest to the epiphysis is relatively inactive
  - Cartilage abutting the shaft of the bone organizes into a pattern that allows fast, efficient growth
  - Cells of the epiphyseal plate proximal to the resting cartilage form three functionally different zones: growth, transformation, and osteogenic

Details of Stages of Endochondral Ossification

- 1) Bone collar forms around the diaphysis of the hyaline cartilage model
  - Osteoblasts of the converted periosteum secrete osteoid against the hyaline cartilage diaphysis encasing it in a bone collar

Details of Stages of Endochondral Ossification

- 2) cartilage in the center of the diaphysis calcifies and then cavitates
    - Chondrocytes w/I the shaft hypertrophy & signal surrounding cartilage matrix to calcify.
    - Chondrocytes die due to lack of nutrients (impermeability of calcified matrix)
    - Matrix deteriorates thus opening up cavities

Details of Stages of Endochondral Ossification

- 3) Periosteal bud invades the internal cavities and spongy bone forms
    - The forming cavities are invaded by a collection of elements
    - Periosteal bud contains a nutrient artery and vein, lymphatics, nerve fibers, red marrow elements, osteoblasts, and osteoclasts
    - Osteoclasts erode the calcified cartilage matrix & osteoblasts secrete osteoid around the remaining hyaline cartilage forming bone-covered cartilage trabuculae (the formation of spongy bone)

Details of Stages of Endochondral Ossification

- 4) The diaphysis elongates and a medullary cavity forms
    - Osteoclasts open up a medullary cavity by breaking down the newly formed spongy bone
    - Cartilage is growing, bones being calcified and eroded and then replaced by bony spicules on the epiphyseal surfaces facing the medullary cavity

Details of Stages of Endochondral Ossification

- 5) The epiphysis ossify
    - Secondary ossification centers appear in one or both epiphyses.
    - Steps 1-4 occur there <u>except</u> no medullary cavity forms

Details of Stages of Endochondral Ossification

- Finally, hyaline cavity remains at:
    - Epiphyseal surface (articular cartilage)
    - Epiphyseal plates (junction of the diaphysis and the epiphysis)

Functional Zones in Long Bone Growth

- Growth zone – cartilage cells undergo mitosis, pushing the epiphysis away from the diaphysis
- Transformation zone – older cells enlarge, the matrix becomes calcified, cartilage cells die, and the matrix begins to deteriorate
- Osteogenic zone – new bone formation occurs

Postnatal Bone Growth

- Long bones lengthen by interstitial growth of the epiphyseal plates, and increase thickness by appositional growth

Long Bone Growth and Remodeling

- Growth occurs at the epiphyseal plate (the cartilage abutting the diaphysis) called the Growth Zone
- Cartilage cells stack and divide quickly pushing the epiphysis away from the diaphysis causing bone to lengthen
- The older chondrocytes die & deteriorate forming the Calcification Zone
- The resulting calcified spicules become part of the Ossification Zone and are invaded by marrow elements from the medullary cavity

Growth in Length of Long Bone

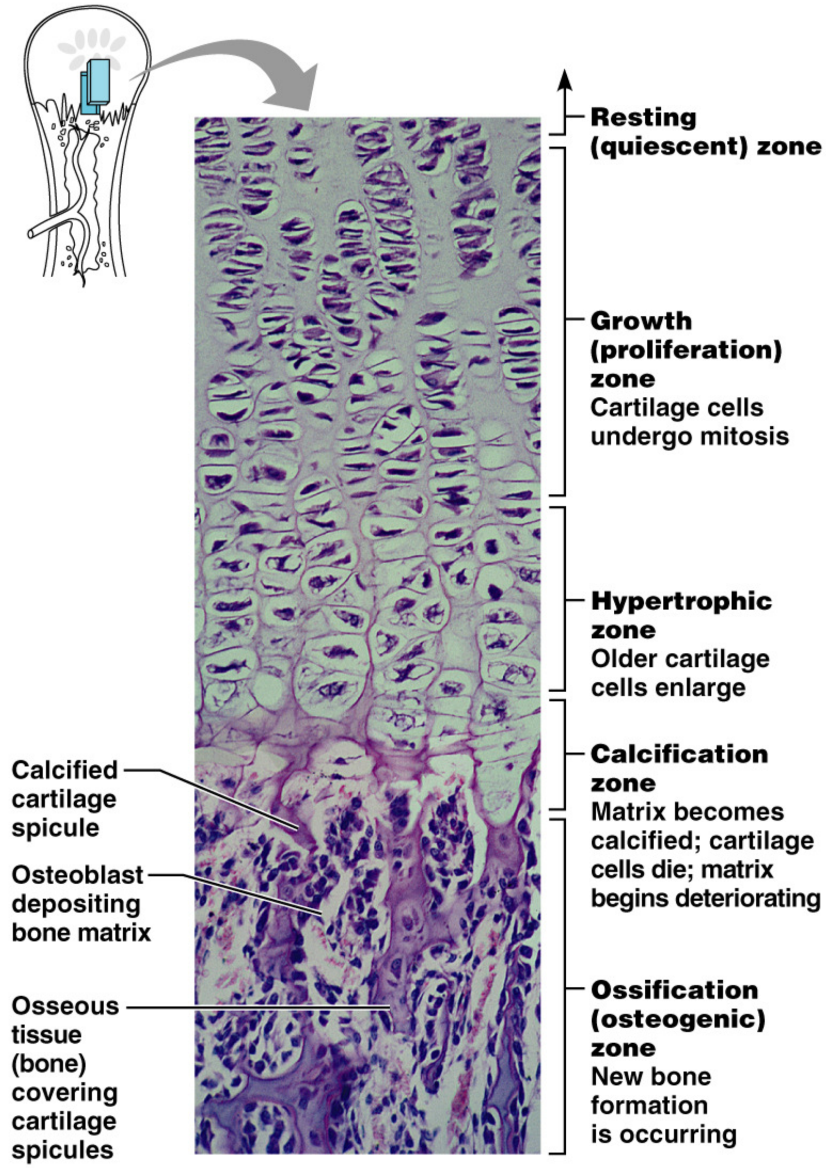


Figure 6.9

Long Bone Growth and Remodeling

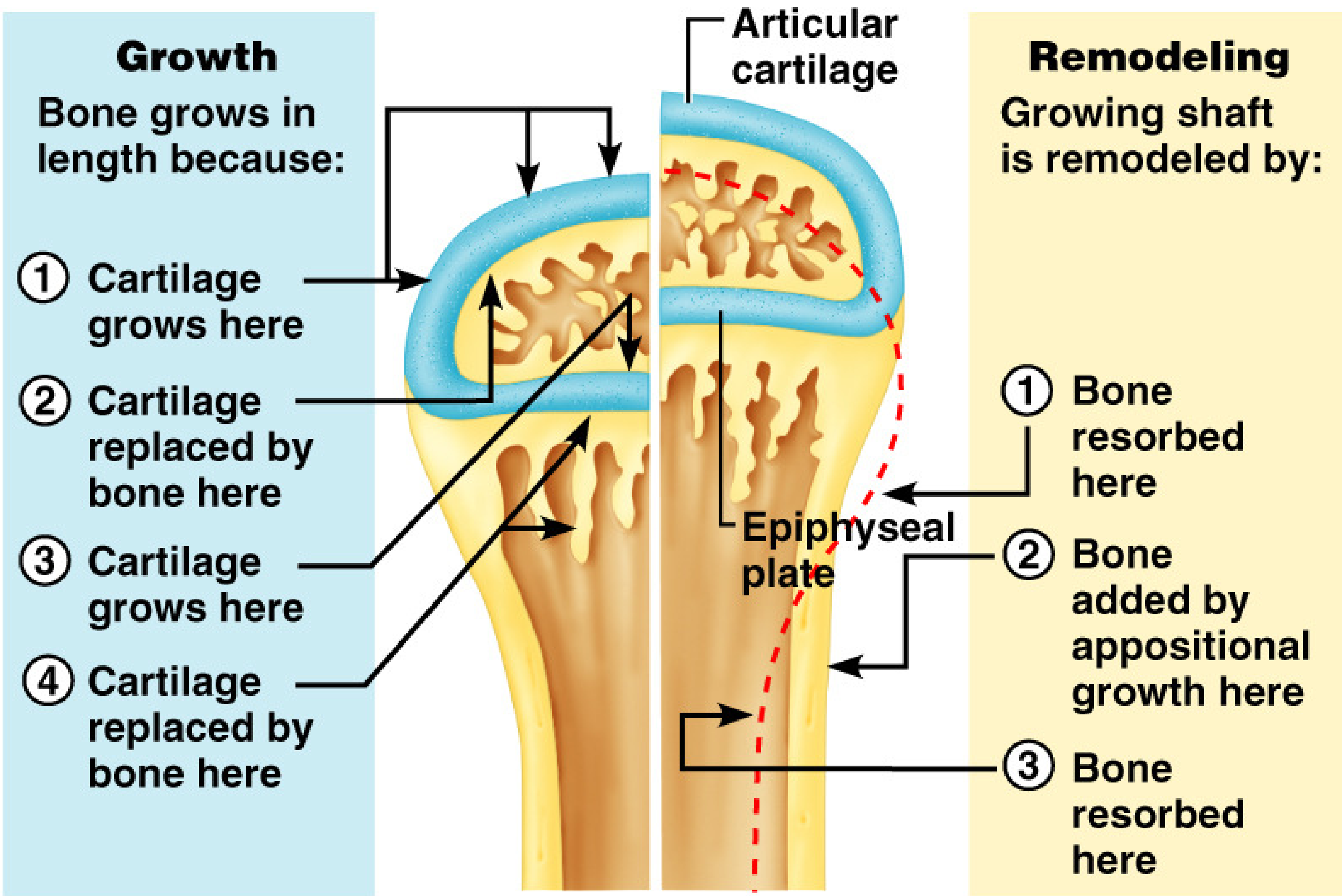


Figure 6.10

Long Bone Growth and Remodeling

- Longitudinal growth is accompanied by remodelling which includes appositional growth to thicken bone
- Includes bone formation & reabsorption
- Bone growth stops around age 21 for males and 18 for females when the epiphysis & diaphysis fuse (epiphyseal plate closure)

Long Bone Growth and Remodeling

- Growth in width (thickness) via appositional growth
- Osteoblasts beneath the periosteum secrete bone matrix on the external bone surface as osteoclasts on the endosteal surface of the dyaphysis remove bone

Hormonal Regulation of Bone Growth During Youth

- During infancy and childhood, epiphyseal plate activity is stimulated by growth hormone (released by the anterior pituitary)
- During puberty, testosterone and estrogens:
  - Initially promote adolescent growth spurts
  - Cause masculinization and feminization of specific parts of the skeleton
  - Later induce epiphyseal plate closure, ending longitudinal bone growth

Bone Remodeling

- Remodeling units – adjacent osteoblasts and osteoclasts deposit and resorb bone at periosteal and endosteal surfaces

Bone Deposition

- Occurs where bone is injured or added strength is needed
- Requires a diet rich in protein, vitamins C, D, and A, calcium, phosphorus, magnesium, and manganese
- Alkaline phosphatase is essential for mineralization of bone

Bone Deposition

- Sites of new matrix deposition are revealed by the:
  - Osteoid seam – unmineralized band of bone matrix
  - Calcification front – abrupt transition zone between the osteoid seam and the older mineralized bone

Bone Resorption

- Accomplished by osteoclasts (giant, multinucleated cells that arise from the same stem cells that produce macrophages)
- Resorption bays – grooves formed by osteoclasts as they break down bone matrix
- The osteoclast membrane seals off the bone that is to be broken down
- Resorption involves osteoclast secretion of:
  - Lysosomal enzymes that digest organic matrix
  - Hydrochloric acid that converts calcium salts into soluble forms
  - The broken down products are endocytosed (transcytosed) and released into the interstitial fluid and blood

Control of Remodeling

- Two control loops regulate bone remodeling
  - Hormonal mechanism maintains calcium homeostasis in the blood (negative feedback)
  - Mechanical and gravitational forces acting on the skeleton

Hormonal Mechanism

- Rising blood Ca^{2+} levels trigger the thyroid to release calcitonin
- Calcitonin inhibits bone resorption and stimulates calcium salt deposit in bone
- Falling blood Ca^{2+} levels signal the parathyroid glands to release parathyroid hormone (PTH)
- PTH signals osteoclasts to degrade bone matrix and release Ca^{2+} into the blood

Hormonal Control of Blood Ca

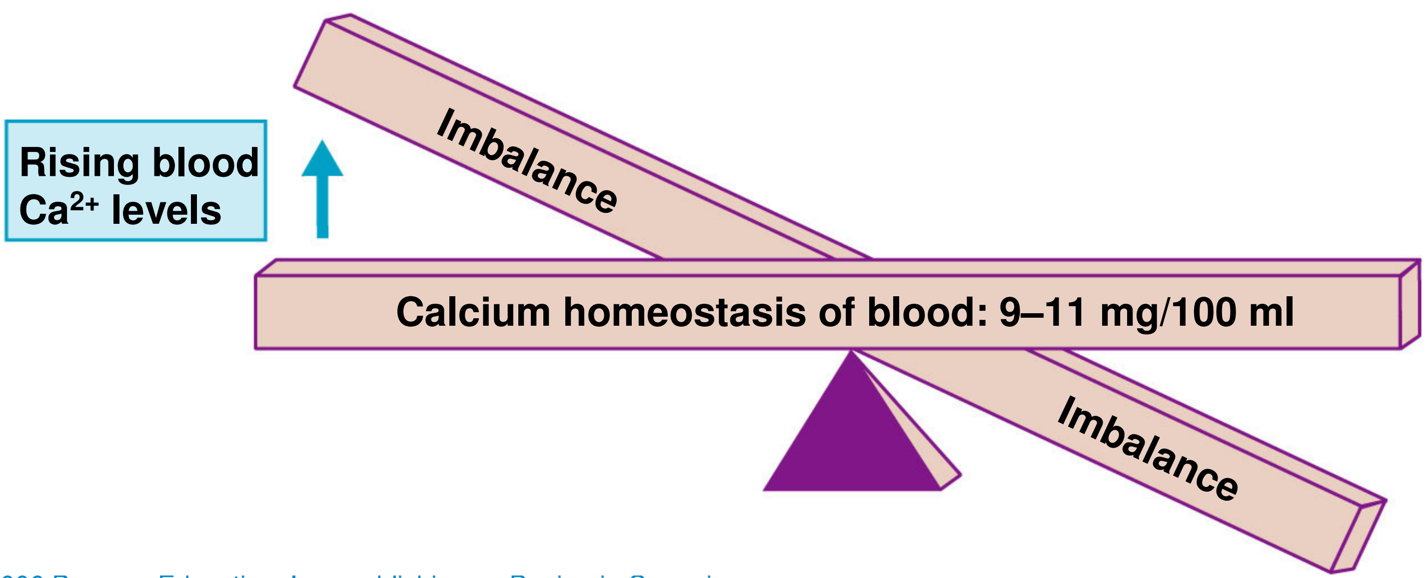


Figure 6.11

Hormonal Control of Blood Ca

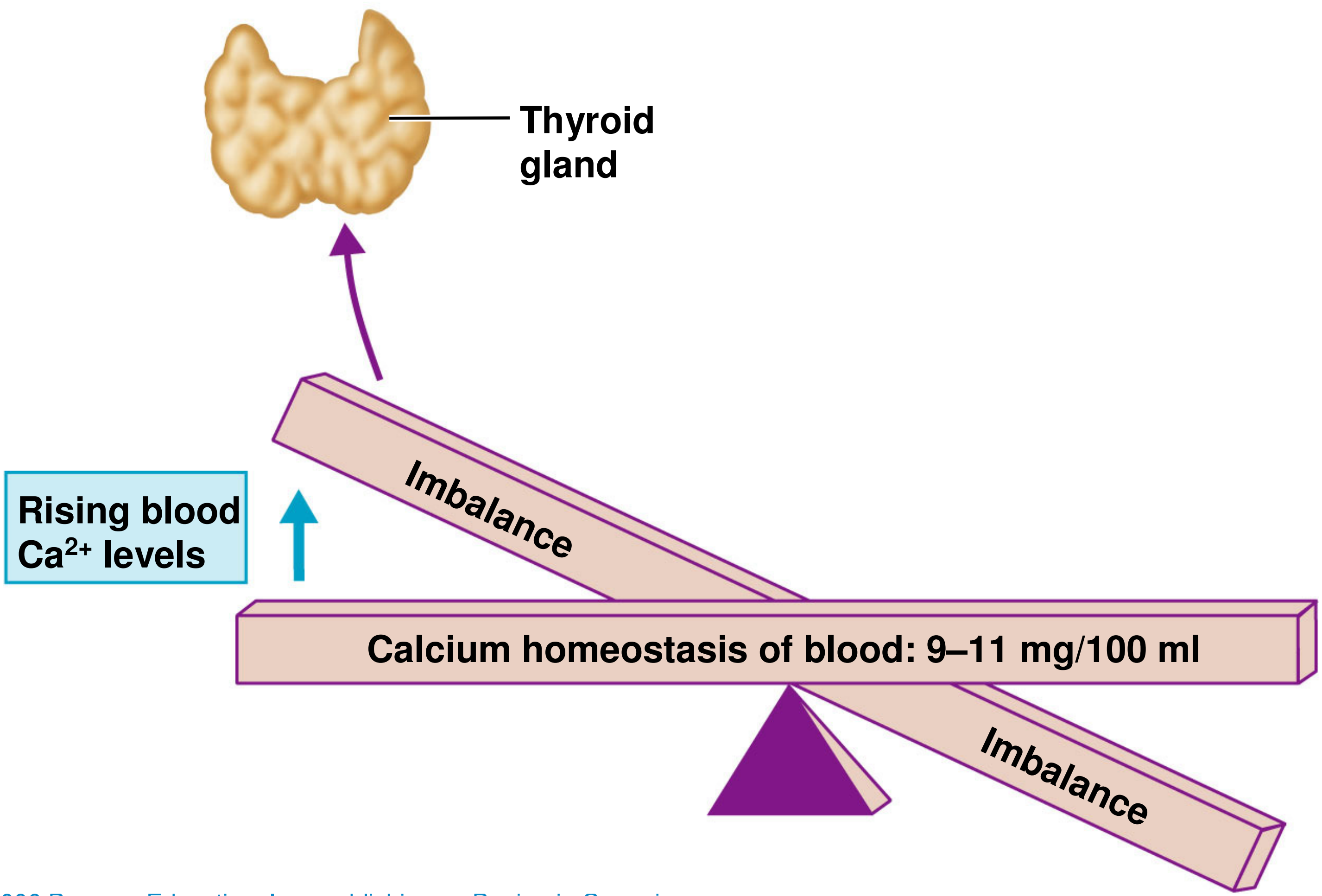
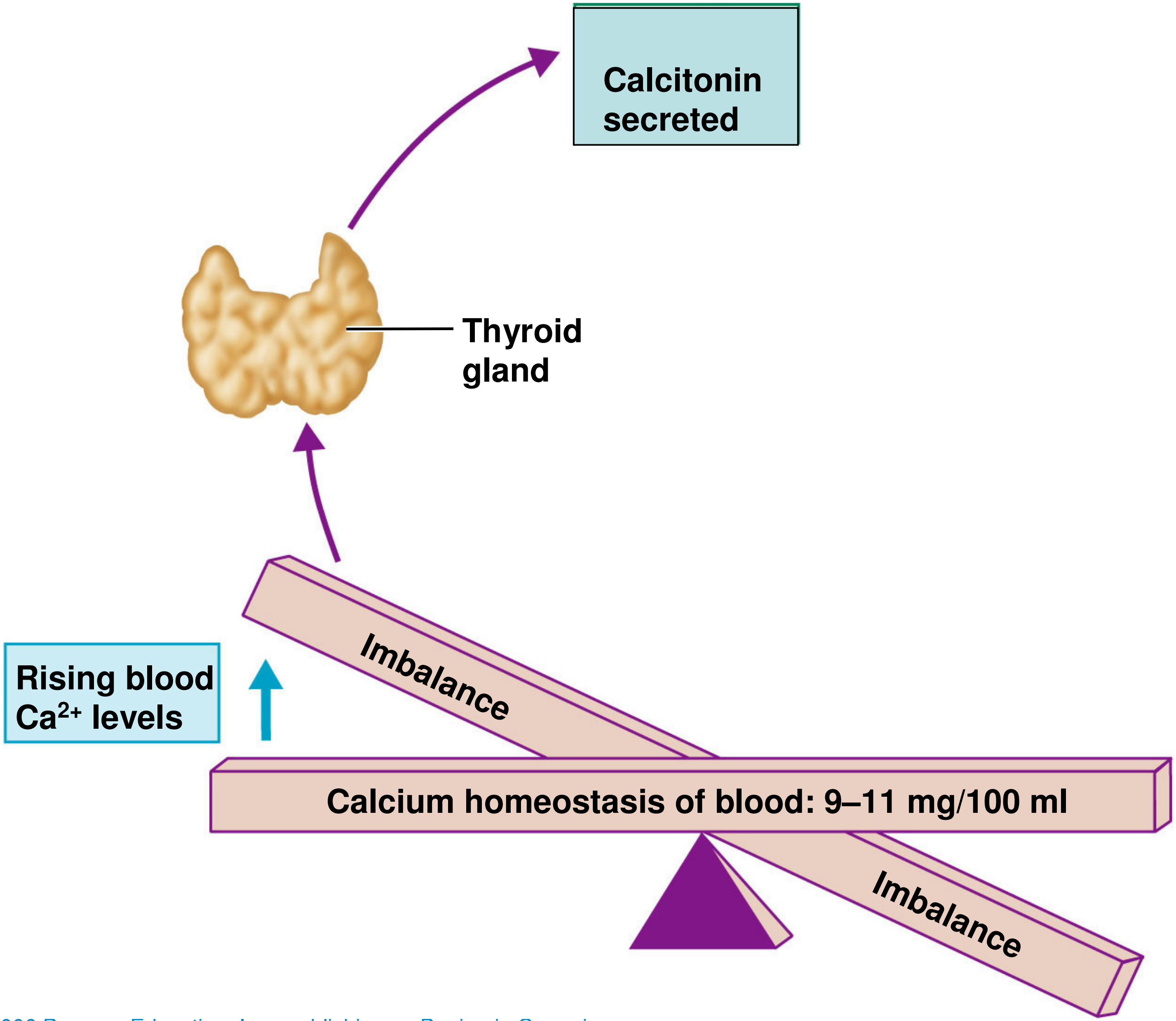


Figure 6.11

Hormonal Control of Blood Ca



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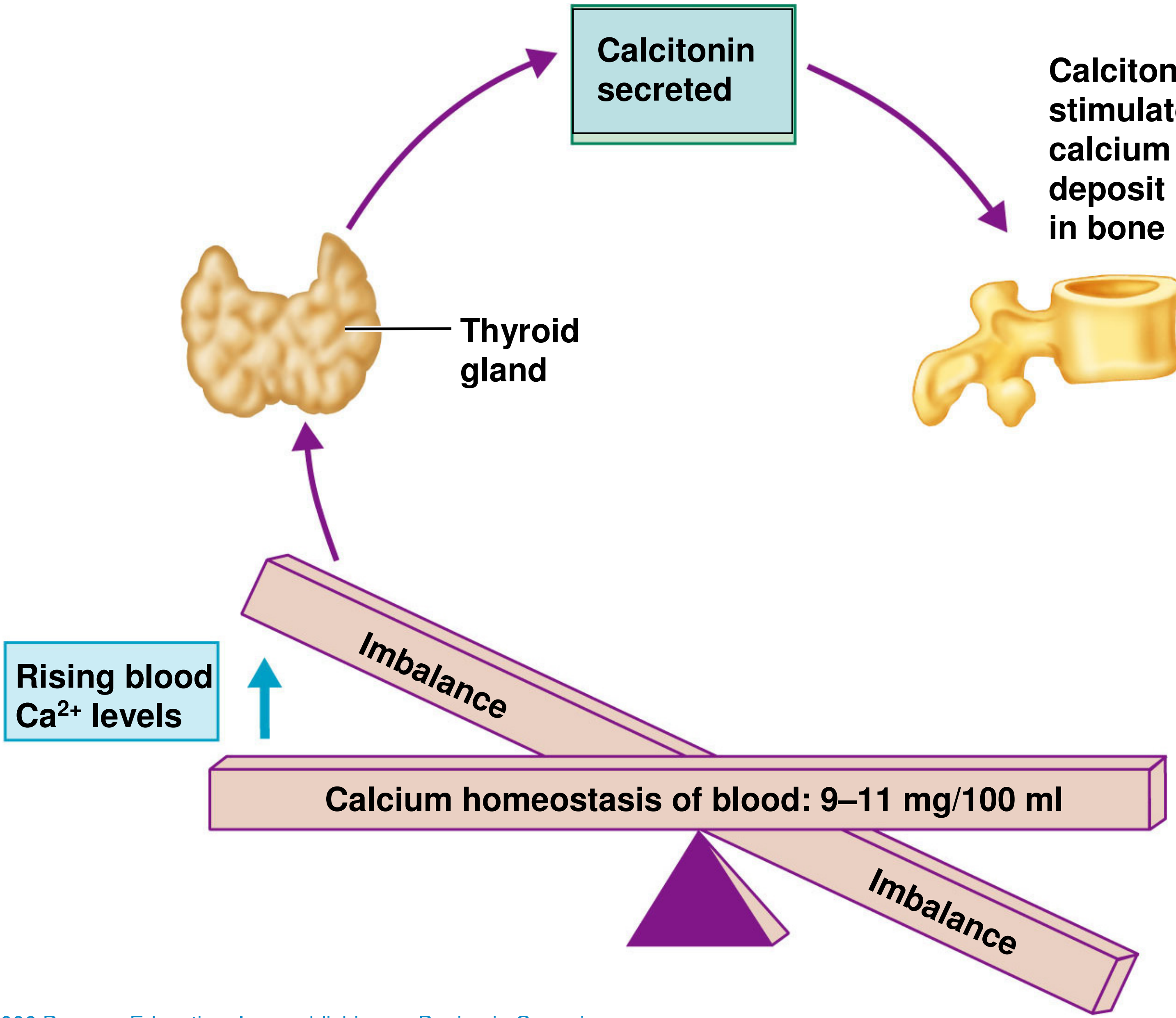
Hormonal Control of Blood Ca



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Hormonal Control of Blood Ca

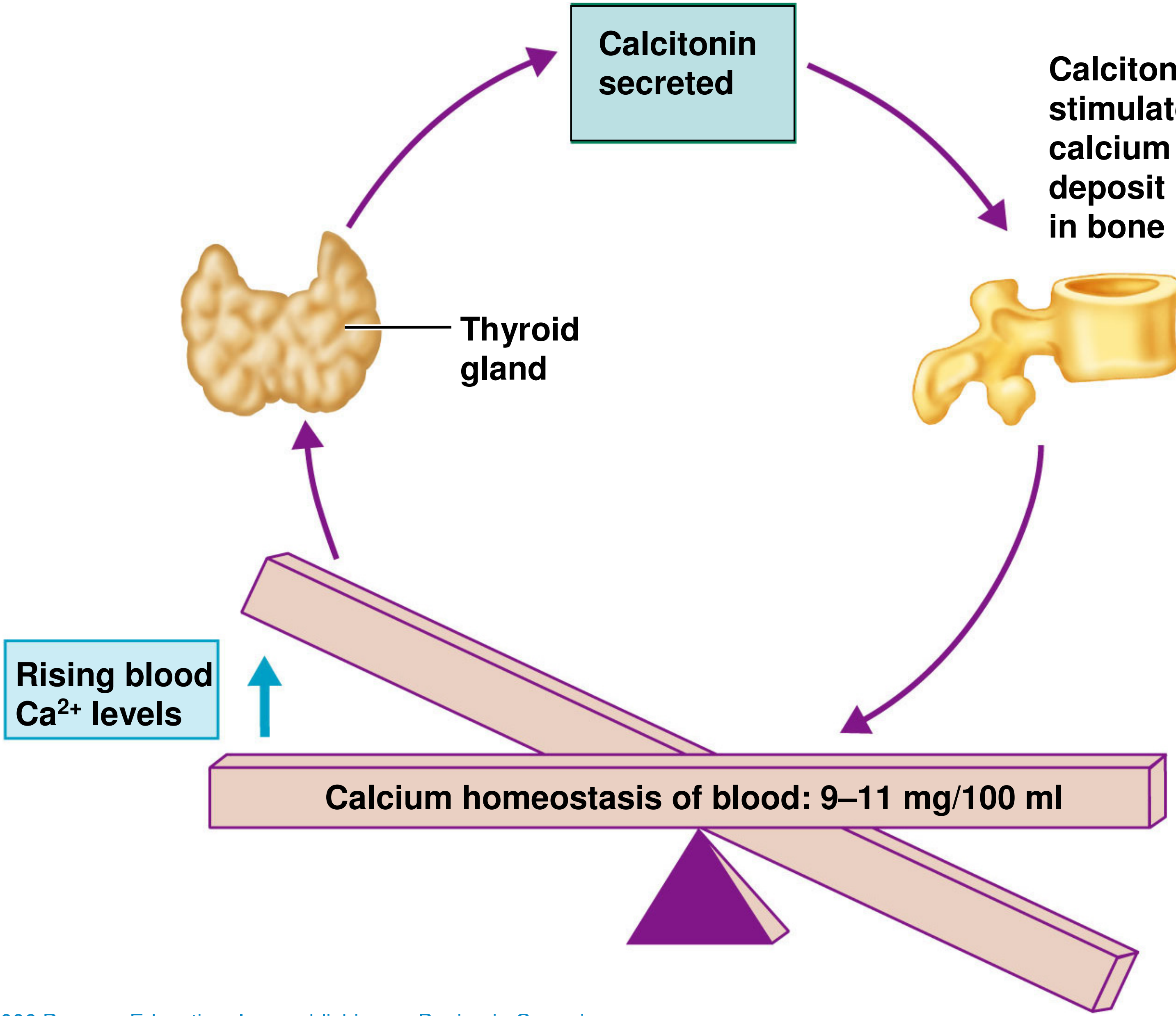
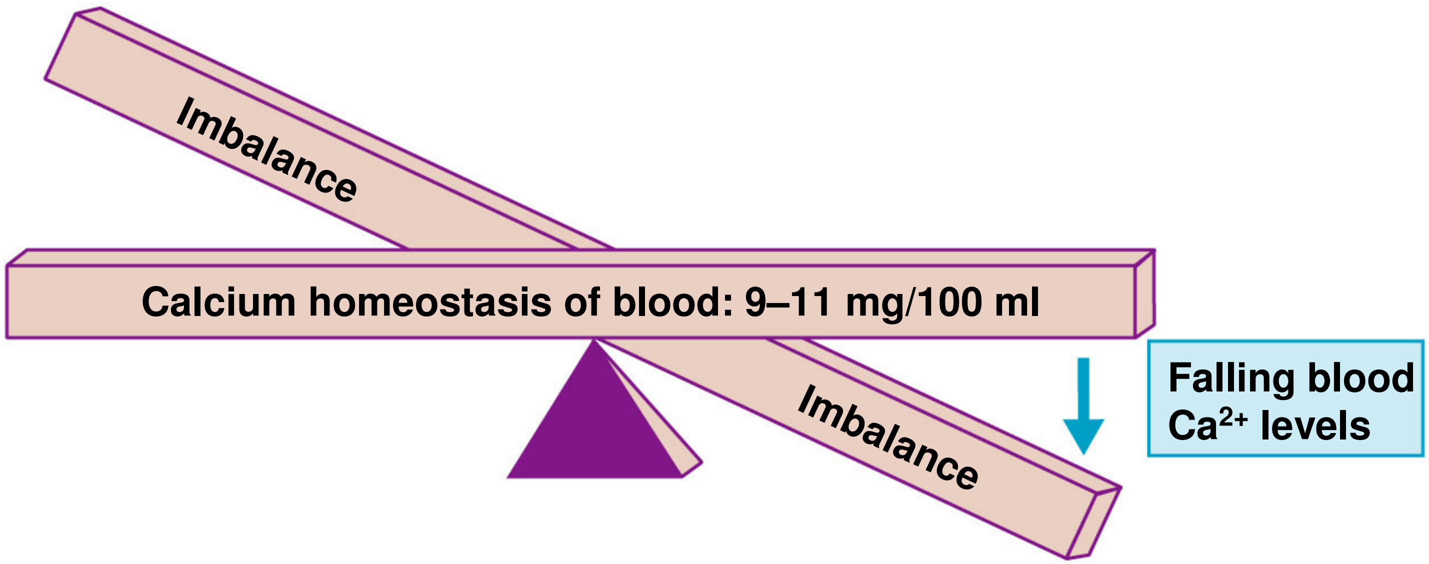


Figure 6.11

Hormonal Control of Blood Ca



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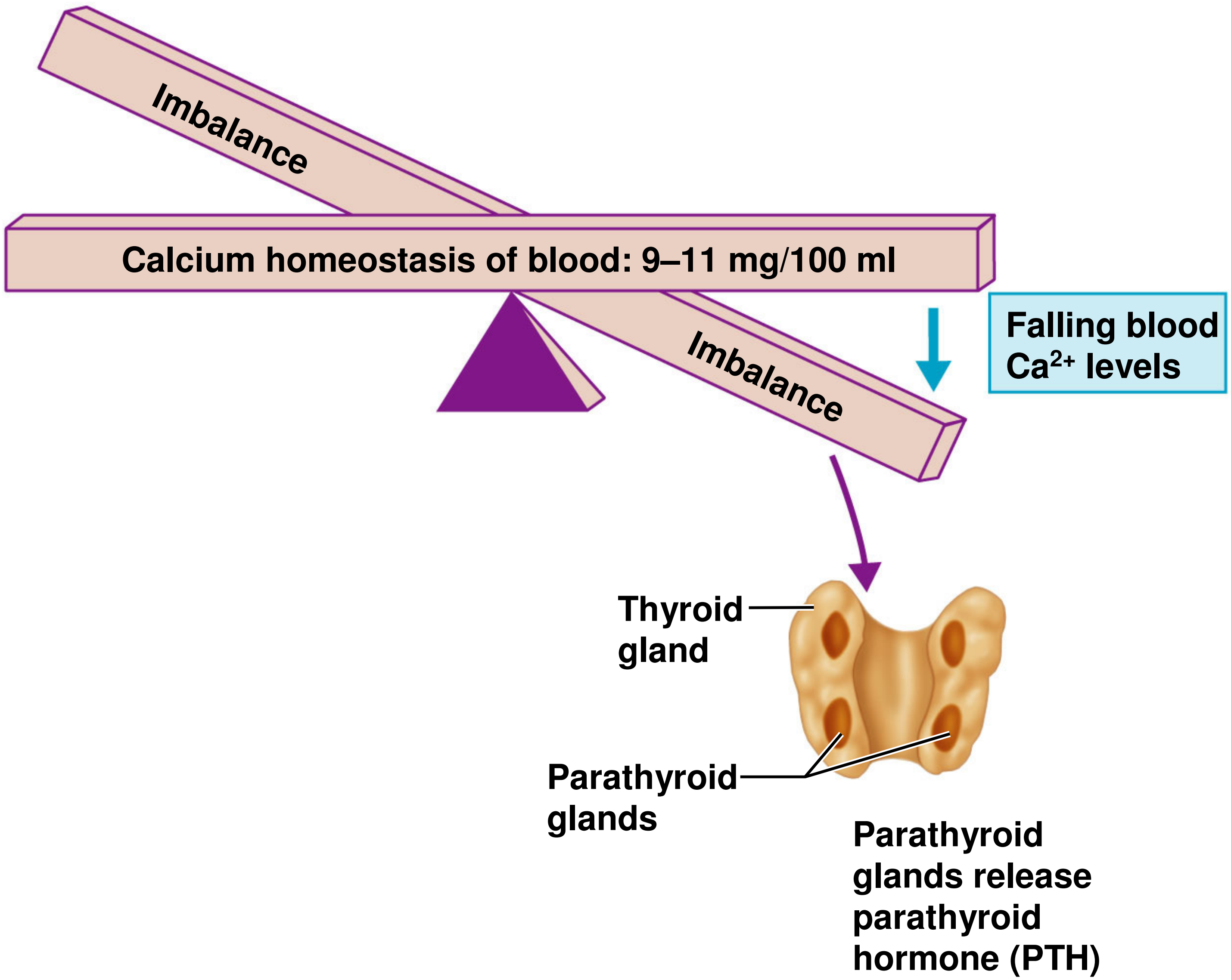
Hormonal Control of Blood Ca



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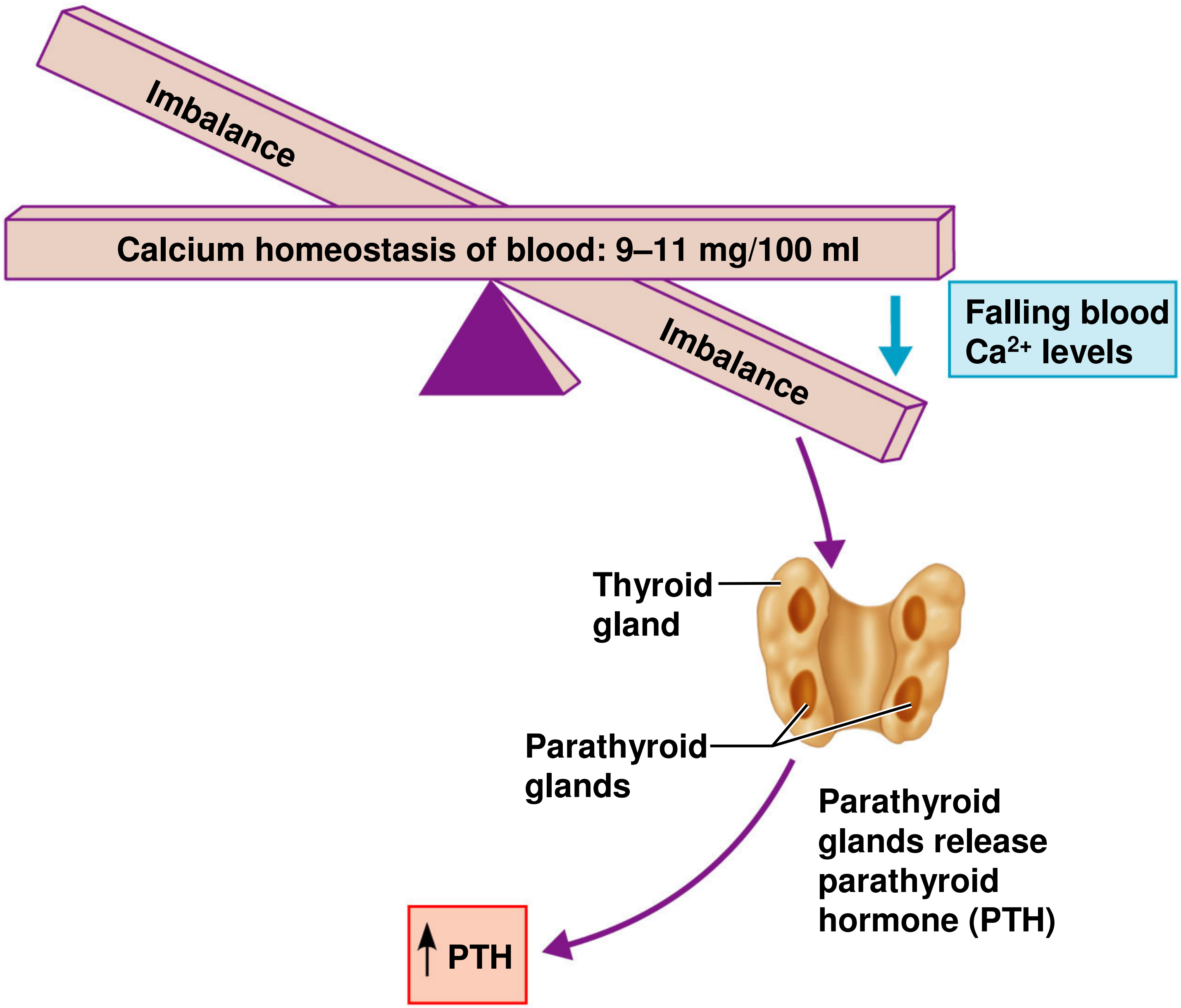
Hormonal Control of Blood Ca



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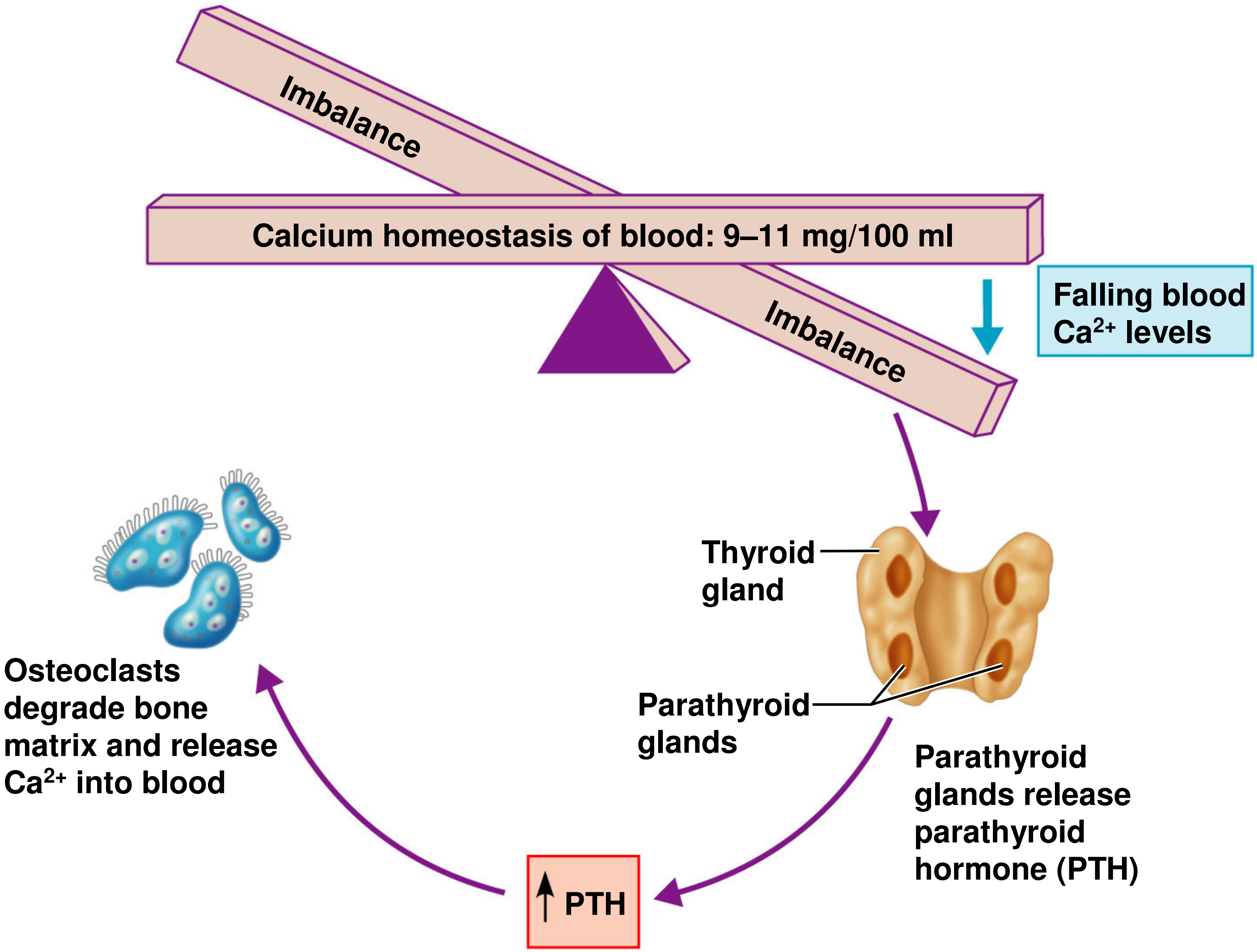
Hormonal Control of Blood Ca



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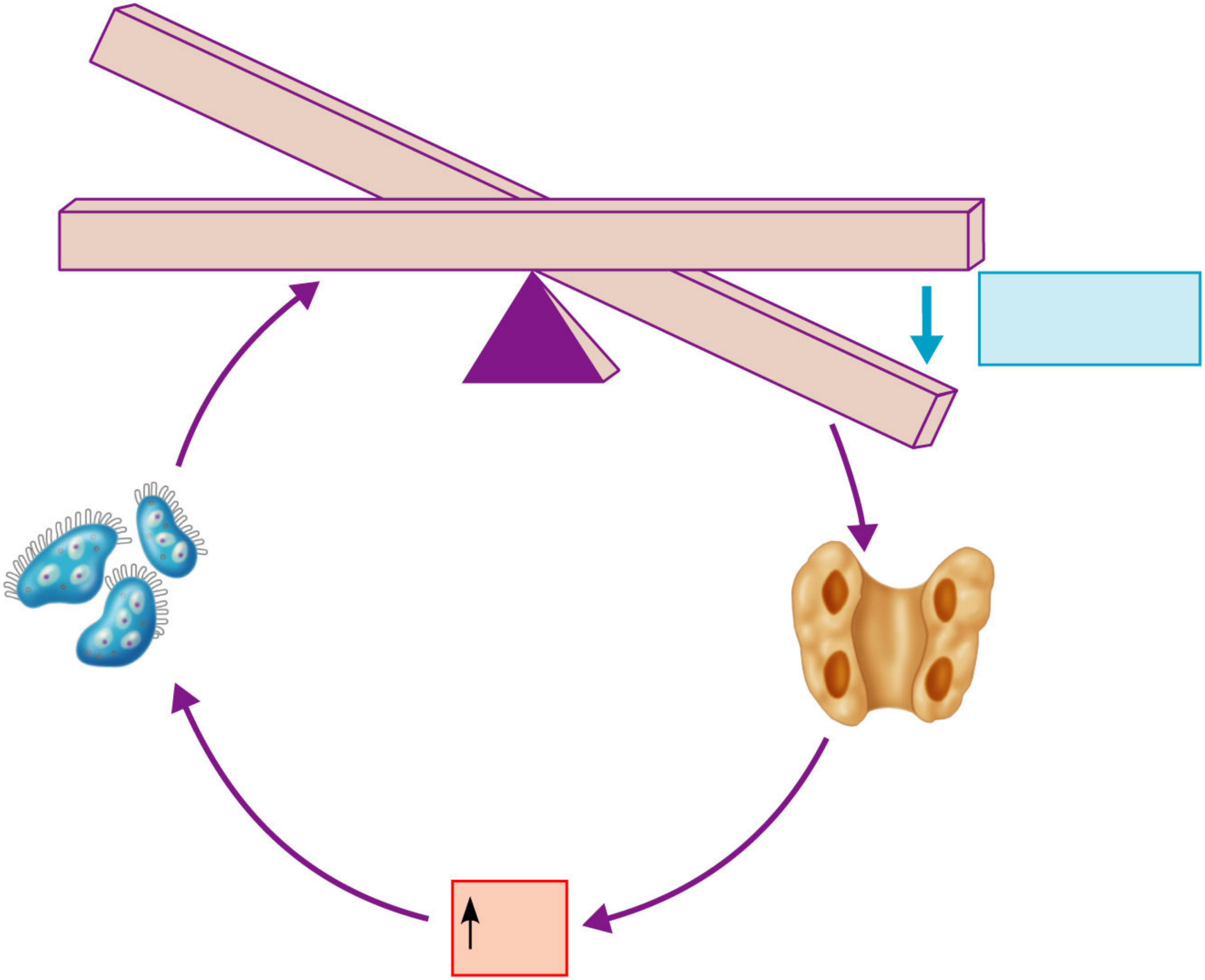
Hormonal Control of Blood Ca



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