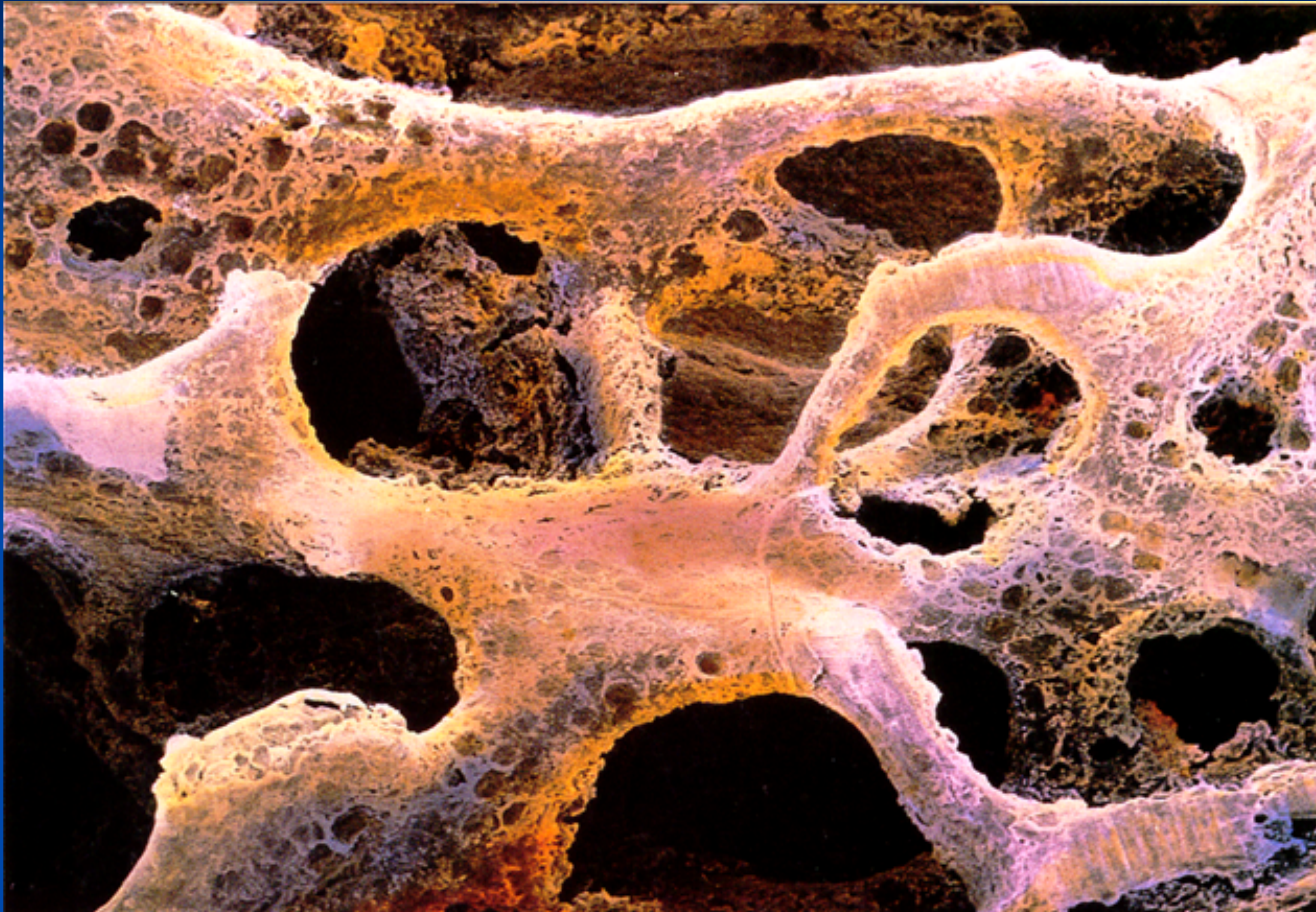
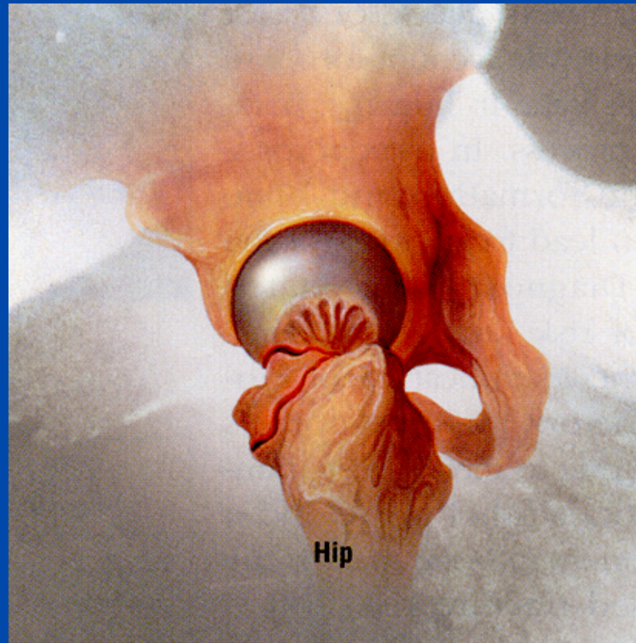
OSTEOPOROSIS

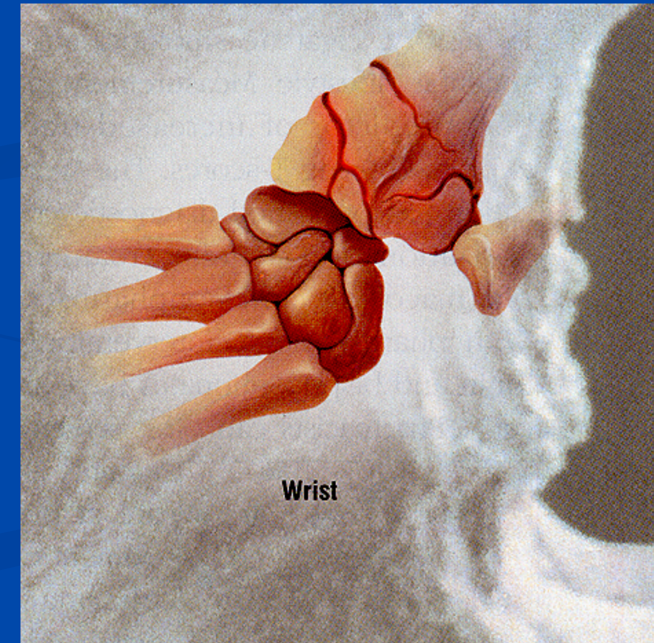
Treatment of Osteoporosis

OSTEOPOROSIS



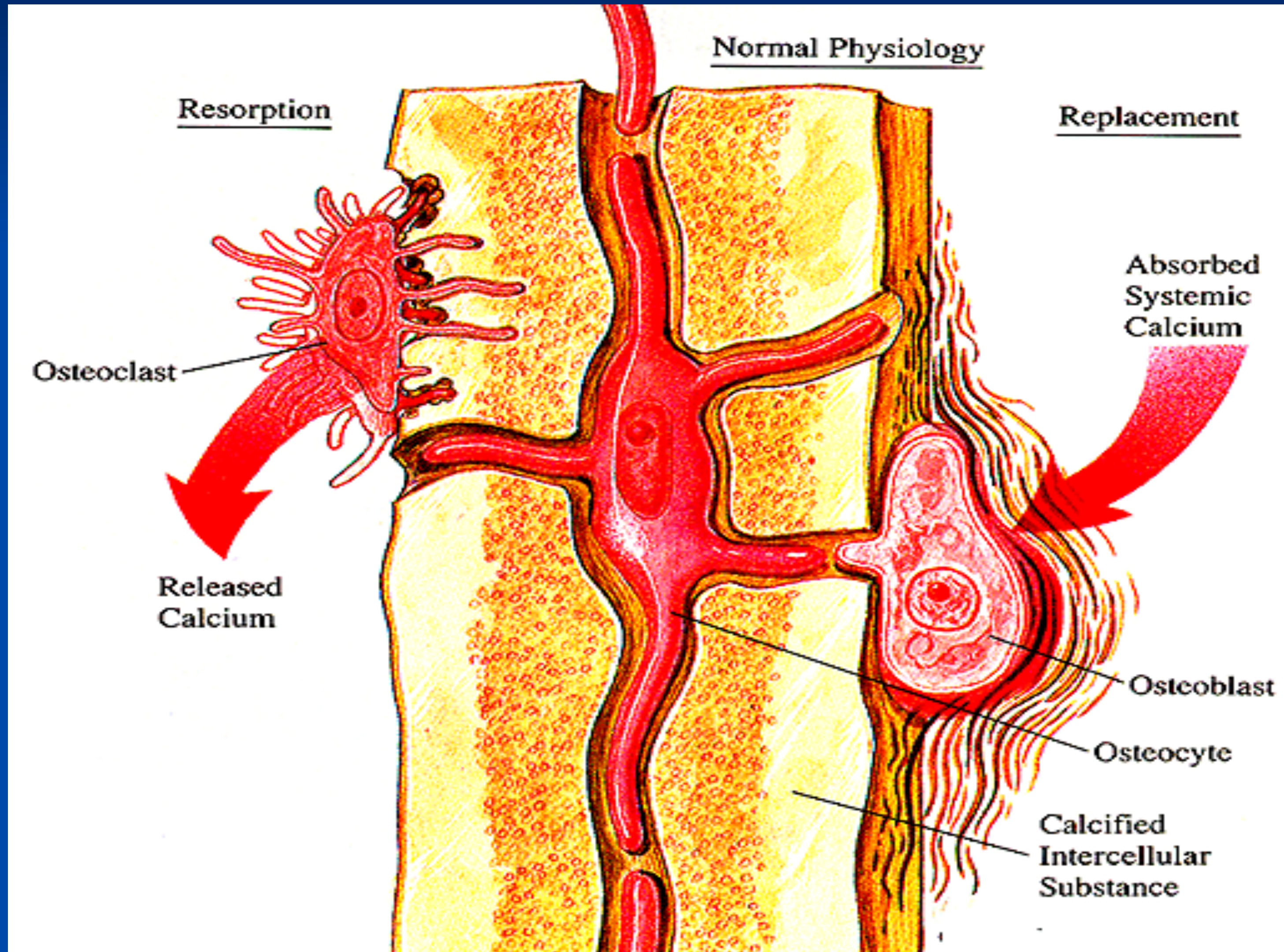
OSTEOPOROSIS accounts for more than 1.3 million fractures annually, affecting more than 25 million Americans. These fractures occur mainly in three areas: the vertebra, the hip, and the wrist.



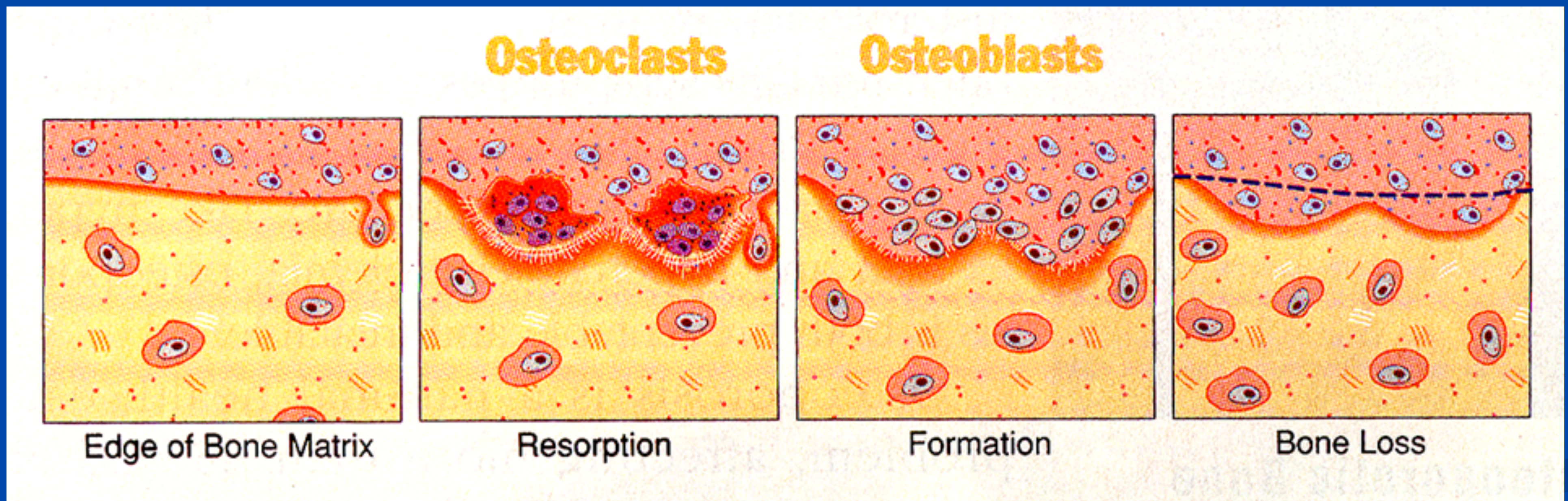


Osteoclasts are responsible for bone resorption.

Osteoblasts are responsible for bone formation.

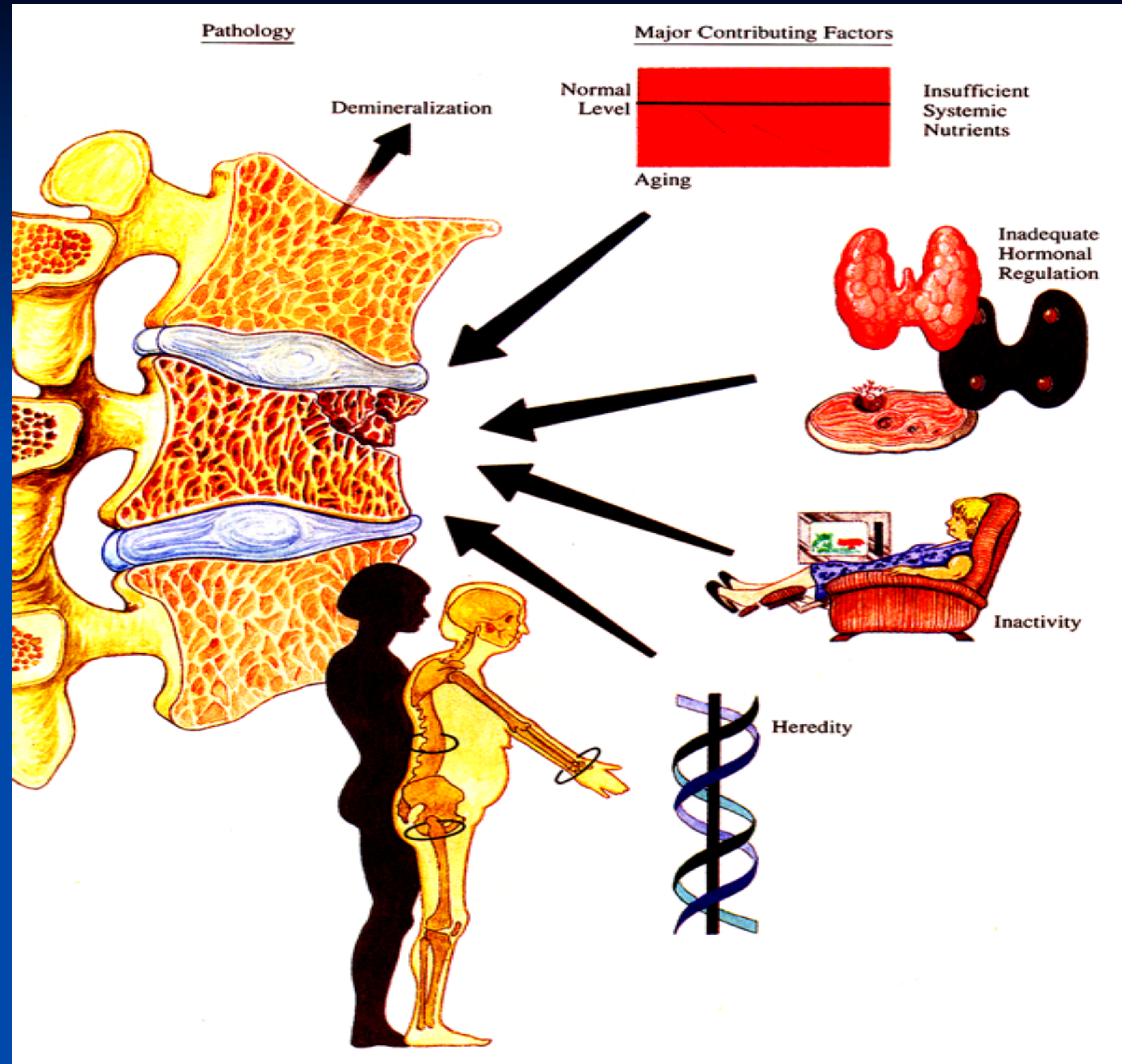


OSTEOPOROSIS is a disorder of the remodeling process in which resorption process exceeds formation → either too much bone is being resorbed or too little is being formed.



RISK FACTORS

- diet: Ca deficiency
- estrogen deficiency
- hyperparathyrodism
- sedentary lifestyle
- alcohol / smoking
- family history
- drugs:
  - glucocorticoids
  - heparin
  - phenobarbital
  - phenytoin

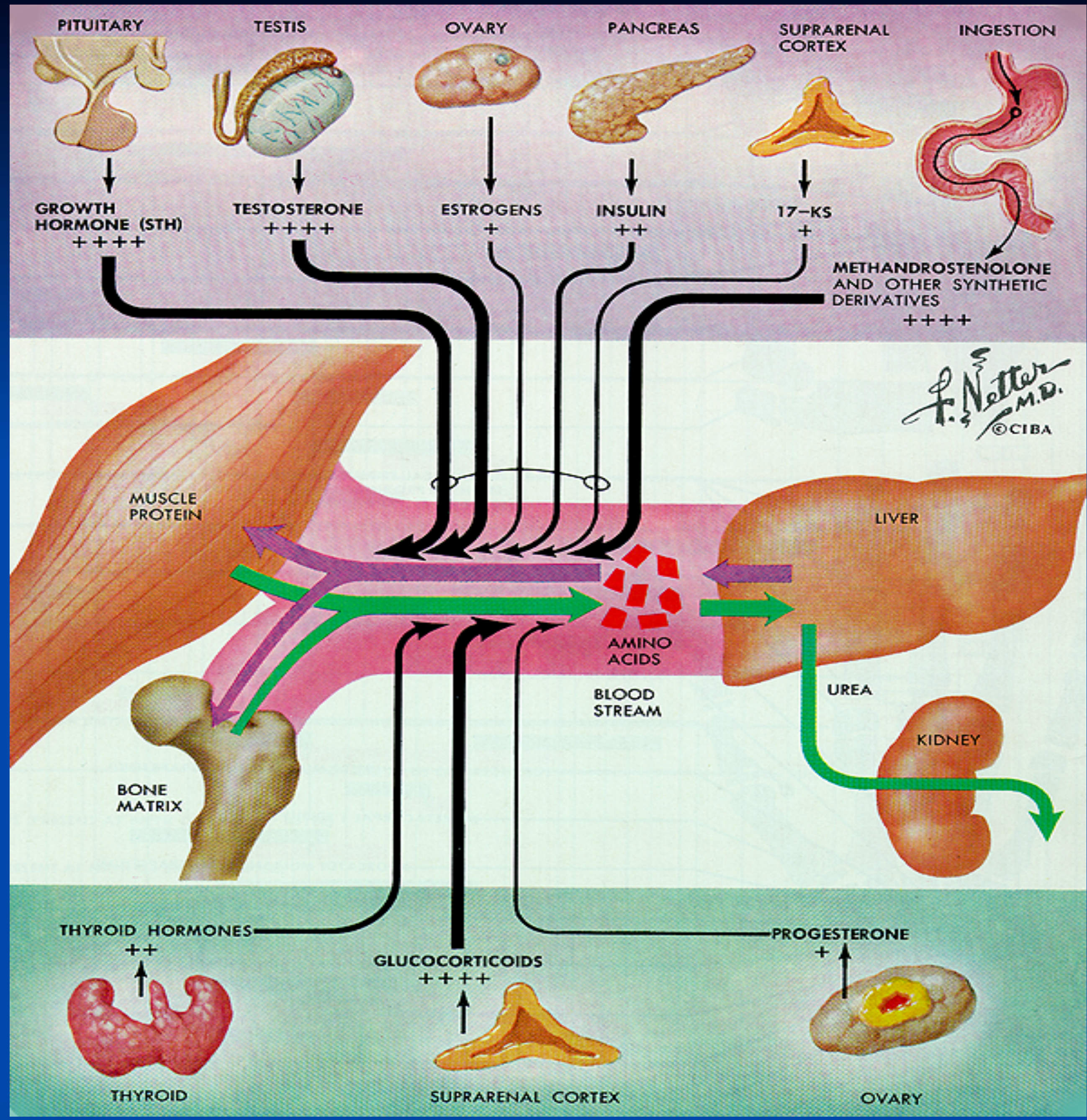


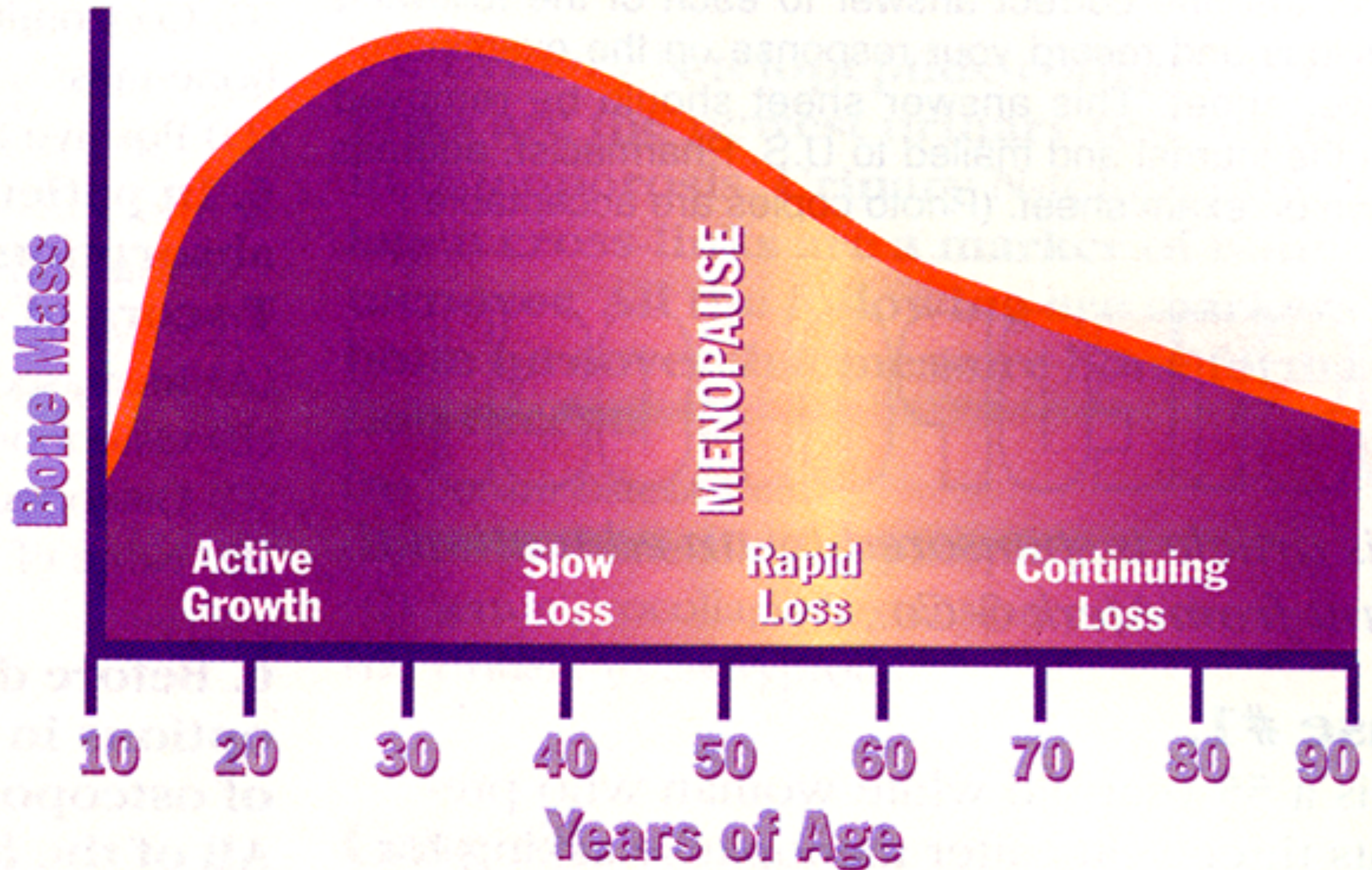
ANABOLIC EFFECTS

versus

CATABOLIC EFFECTS

- GROWTH HORMONE
- TESTOSTERONE
- ESTROGEN
- GLUCOCORTICOIDS
- THYROID HORMONE (LEVOTHYROXINE)
- PARATHYROID HORMONE



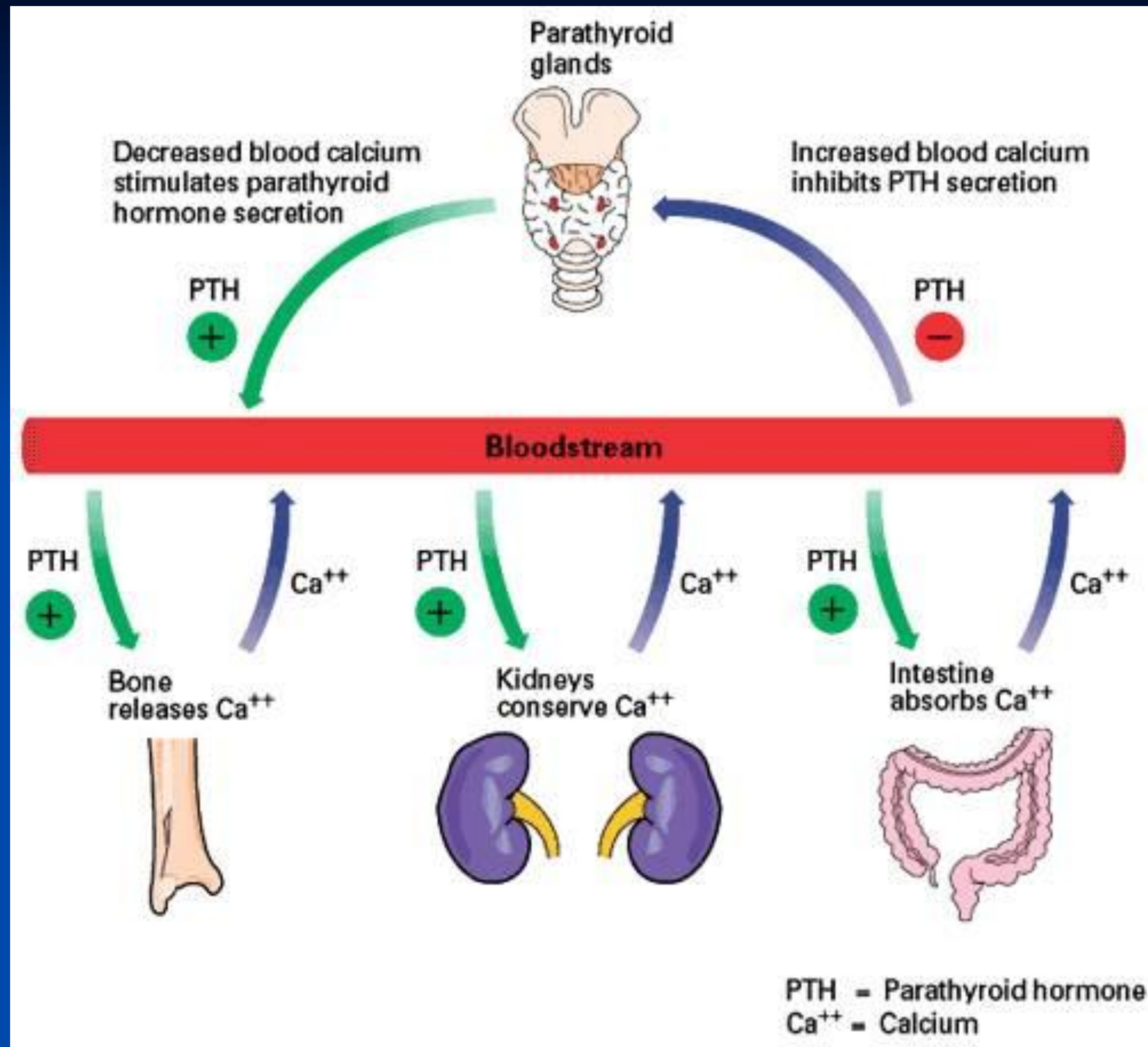


BONE MASS IN WOMEN
Bone Mass
MENOPAUSE
Active Growth
Slow Loss
Rapid Loss
Continuing Loss
10
20
30
40
50
60
70
80
90
Years of Age

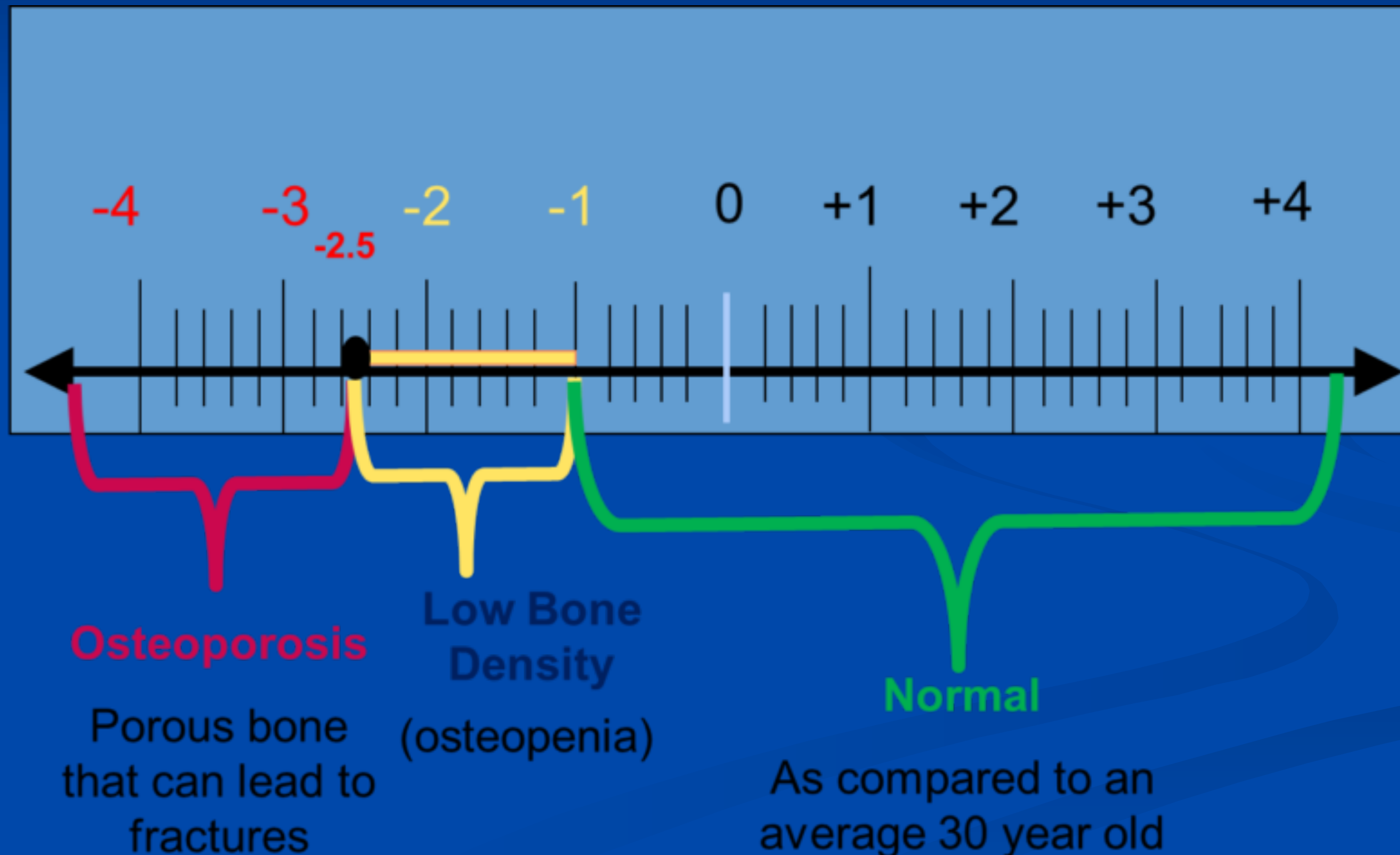
SERUM CALCIUM REGULATED BY:

(1) PARATHYROID HORMONE

(2) CALCITONIN
(PARAFOLLICULAR CELLS IN THYROID GLAND)



A standard method of identifying osteoporosis is measurement of bone density at either the femur neck region of the proximal femur (hip) or the lumbar spine. (as the T-score decreases, risk for fracture increases)



Prevention of Osteoporosis

(1) adequate calcium intake / vitamin D intake

(2) weight-bearing and strengthening exercise

- jogging, walking, running, biking, tennis, weight lifting

(3) reduced alcohol consumption

- excessive alcohol (> 2 drinks/day) → decreased BMD (bone-mineral density) & moderate alcohol → increased BMD

(4) smoking cessation

- smoking impairs absorption of dietary calcium, influences estrogen metabolism

Table 110-2

Dietary Reference Intakes for Calcium and Vitamin D[33]

Life Stage Group	RDA Calcium	RDA Vitamin D
Males		
19–50 years	1,000 mg	600 IU (15 mcg)
51–70 years	1,000 mg	600 IU (15 mcg)
>70 years	1,200 mg	600 IU (15 mcg)
Females (Nonpregnant)		
19–50 years	1,000 mg	600 IU (15 mcg)
51–70 years	1,200 mg	600 IU (15 mcg)[a]
>70 years	1,200 mg	800 IU (20 mcg)[a]

[a]NOF recommends vitamin D 800 to 1,000 IU in patients ≥ 50 years.

IU, International Unit; RDA, Recommended Dietary Allowance.

CALCIUM SUPPLEMENTS

SUPPLEMENT	ELEMENTAL CALCIUM
Calcium Carbonate	40 %
Calcium Lactate	13 %
Calcium Gluconate	9 %
Calcium Citrate	21 %
Calcium Phosphate	39 %
Calcium Glubionate	6.5 %

Vitamin D (25-OHD) Serum Levels

Vitamin D Status	Blood levels (ng/mL)	Blood levels (nmol/L)
Severe deficiency	Less than 10	Less that 25
Deficiency	10-20	25-50
Insufficiency	20-30	50-75
Normal	Above 30	Above 75
Overdose	Over 100	250

(25-OHD = 25-hydroxyvitamin D)

PHARMACOTHERAPY

Pharmacologic treatment is indicated in the following patients:

(1) Patients who have experienced a hip or vertebral fracture

(2) Patients with T-scores < -2.5 at the femoral neck, total hip, or lumbar spine

(3) Postmenopausal women and men age > 50 years-old with low bone mass and high risk of fracture

Agents for Prevention & Treatment of Osteoporosis

(1) Estrogen (Premarin) / Medroxyprogesterone (Provera)

(2) Raloxifene (Avista)

(3) Denosumab (Prolia Injectable)

(4) Biphosphonates: Alendronate (Fosamax)

(5) Calcitonin: Miacalcin Nasal Spray / Calcimar Injectable

ESTROGEN / PROGESTIN THERAPY (EPT)

- An estimated 10-15% of a woman's bone mass is estrogen dependent.

- EPT is approved for the prevention of osteoporosis in postmenopausal women with a uterus
- ET is approved for postmenopausal women without a uterus

- EPT/ET are only prescribed in women who have failed other therapies for osteoporosis after assessing "Risks vs Benefits."

  - Risks: EPT/ET are associated with increased risk of breast & uterine cancers, DVT, PE, coronary heart disease (CHD)

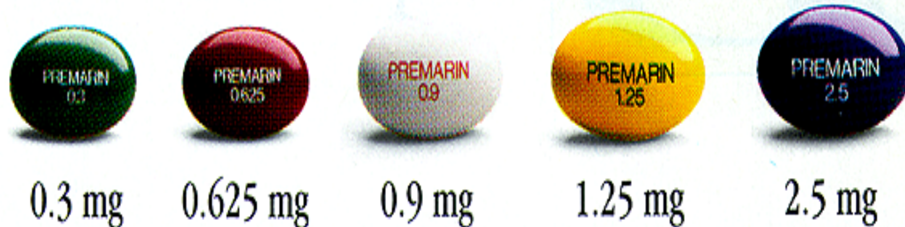
- When prescribed, ET and EPT should be used at the lowest effective doses and the shortest duration indicated

ESTROGEN REPLACEMENT

Nothing else is

PREMARIN®

(conjugated estrogens tablets)



The appearance of these tablets is a trademark of Wyeth-Ayerst Laboratories.

simple as it *looks*.

it's a complex blend of estrogens.

125 steps to ensure

No wonder 25,000,000,000

without a single recall since introduction.

Nothing else is

PREMARIN®

(conjugated estrogens tablets)

Contraindications:
Estrogens should not be used in women (or men) with any of the following conditions: known or suspected 1) pregnancy, 2) breast cancer, 3) estrogen-dependent neoplasia, 4) undiagnosed abnormal genital bleeding, 5) active thrombophlebitis or thromboembolic disorders.

NOTE: Estrogens have been reported to increase the risk of endometrial carcinoma in postmenopausal women.

For nonhysterectomized postmenopausal women

Cyclic HRT* with new convenience

INTRODUCING NEW

PREMPHASE™

(conjugated estrogens tablets/medroxyprogesterone acetate tablets, USP)

The appearance of the Premarin® (conjugated estrogens tablets, USP) tablet is a trademark of Wyeth-Ayerst Laboratories. The appearance of the Cycrin® (medroxyprogesterone acetate tablets, USP) tablet is a registered trademark of Wyeth-Ayerst Laboratories.

PREMARIN
(conjugated estrogens)

+

PROVERA
(medroxy-progesterone)

||

PREMPRO

PREMPRO

PACKAGING

Raloxifene (Avista)

- Raloxifene is a SERM (selective estrogen receptor modulator) with agonist and antagonist properties

- Mechanism of Action:
  1. Raloxifene binds to estrogen receptors as an agonist in bone and lipid metabolism
     → inhibits osteoclasts → decreases bone resorption
     → increases BMD (bone mineral density)

  2. Raloxifene binds to estrogen receptors as an antagonist in breast and endometrial tissue

Raloxifene (Avista)

- Dose: Raloxifene (Avista) 60 mg PO daily.

- Efficacy / Indication: Studies have demonstrated that Raloxifene is not as effective as Alendronate (Fosamax) for increasing BMD (4.8% vs. 2.2%).

Contraindications:

1. Patients with active venous thromboembolism (VTE) or a past medical history of VTE
2. Women who are pregnant, plan to become pregnant, and those nursing (i.e., lactation)

Biphoshonate: Alendronate (Fosamax)

Mechanism of Action: Alendronate concentrates in mineral tissue and interfere with osteoclast-medicated bone resorption → increases BMD

Indication: Alendronate is considered 1st line therapy for prevention and treatment of osteoporosis in postmenopausal women due to its efficacy and low side effect profile

Side Effects: GI symptoms → acid regurgitation

- Alendronate is taken with 6-8 oz of water 30 mins before breakfast, in an upright position

FOSAMAX

(Alendronate)

Prevention:
5 mg PO daily OR 35 mg PO weekly

Treatment:
10 mg PO daily OR 70 mg PO weekly

Postmenopausal Osteoporosis

If you don't treat it, who will?

FOR THE TREATMENT OF OSTEOPOROSIS IN POSTMENOPAUSAL WOMEN

For appropriate postmenopausal patients with osteoporosis...

Help change the future

In clinical studies
FOSAMAX dramatically reduced vertebral fracture incidence** by building healthy bone

Built bone in the overwhelming majority of patients§

Generally well-tolerated nonhormonal therapy

Prescribe FOSAMAX today

(alendronate sodium tablets)

MIACALCIN (calcitonin) NASAL SPRAY

MOA: inhibits osteoclasts → deceases bone resorption

Indications: 3rd line agent, used in women who have been postmenopausal for at least 5 years → fractures reduction has not been shown in clinical trials.

Side Effects: rhinitis, sinusitis nasal irritation

In postmenopausal osteoporosis treatment
MIACALCIN® Nasal Spray:
(calcitonin-salmon)
No Ifs. Just Efficacy.
Absorption, Safety, and Efficacy. Anytime. Anywhere.

MIACALCIN (cont.)

Dosage: 1 spray daily in alternating nostrils

Now, for many postmenopausal osteoporosis patients

NEW

MIACALCIN® *(calcitonin-salmon)* Nasal Spray

Indicated for the treatment of postmenopausal osteoporosis in females greater than 5 years postmenopause with low bone mass who refuse or cannot tolerate estrogens, or in whom estrogens are contraindicated. Patients should ensure adequate calcium and vitamin D intake.

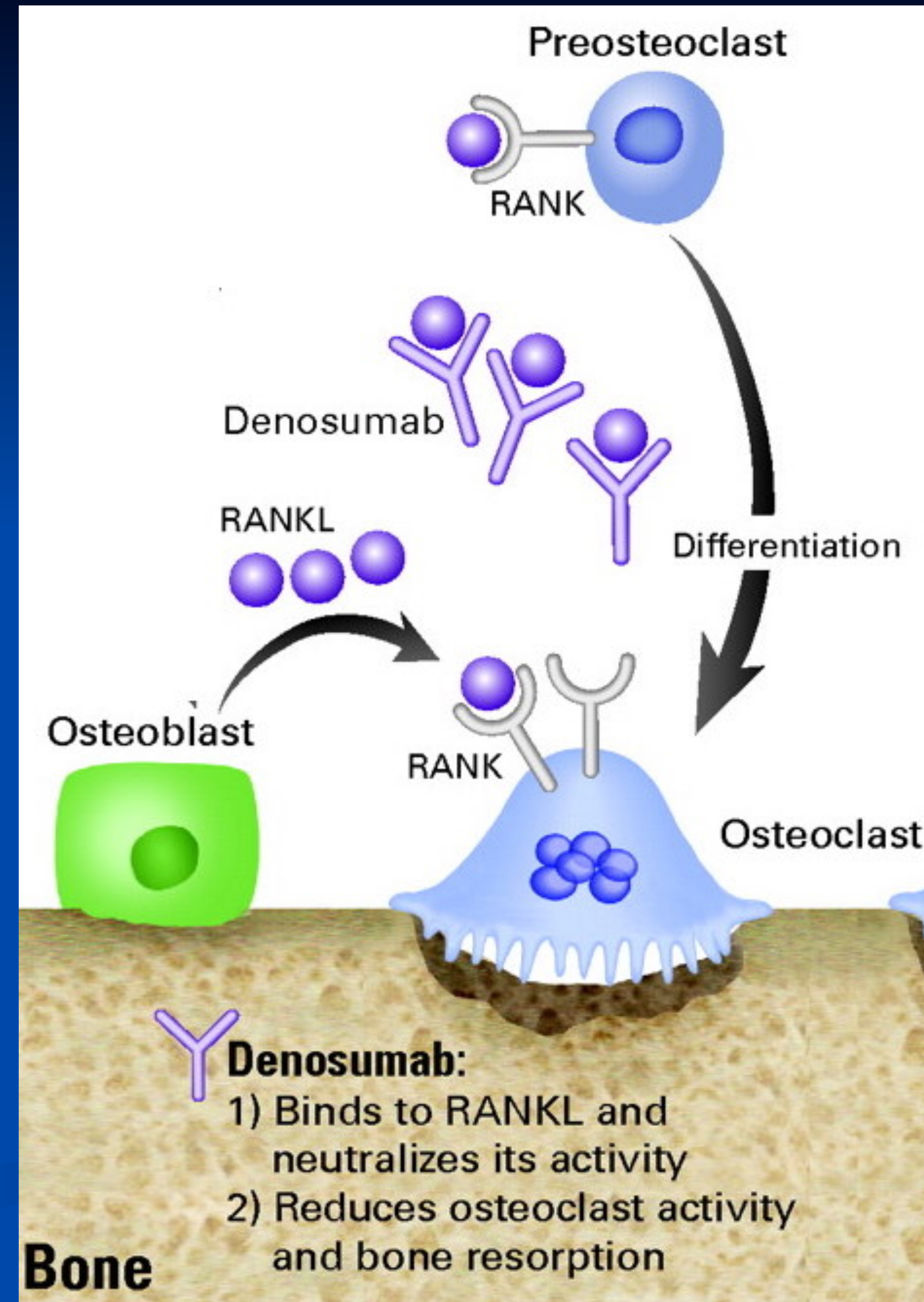
Denosumab (Prolia)

Mechanism of Action:
Denosumab is a human monoclonal antibody that binds to and inhibits RANKL

→ prevents maturation and development of osteoclasts

→ reduces osteoclastic activity

→ reduces bone resorption



Denosumab (Prolia)

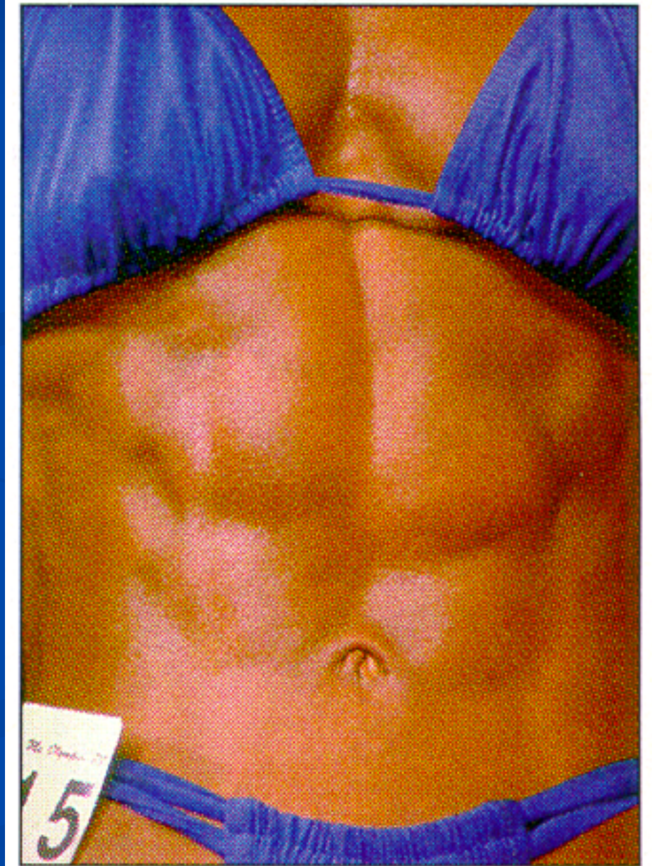
Indication: Denosuman is approved for treatment of postmenopausal women with osteoporosis who are at high risk for fracture

Dosage: Denosuman is admininstered SC every 6 months and inhibits bone turnover with a rapid onset.

Side Effects:, pain in extremity (i.e., arms & legs), hypercholesterolemia, back pain, musculoskeletal pain, and cystitis

You can’t reveal washboard abs except by losing body fat. Rippling women may have as little as 6 % fat; the healthy range is 15 to 23 %. Most women stop menstruating when fat falls below 10 %. The resulting estrogen loss can cause osteoporosis even in 20-year-olds. Is a chic stomach worth a dowager’s hump ?

Rippling Abs Can Be Bad



PHARMACY
CLOSED