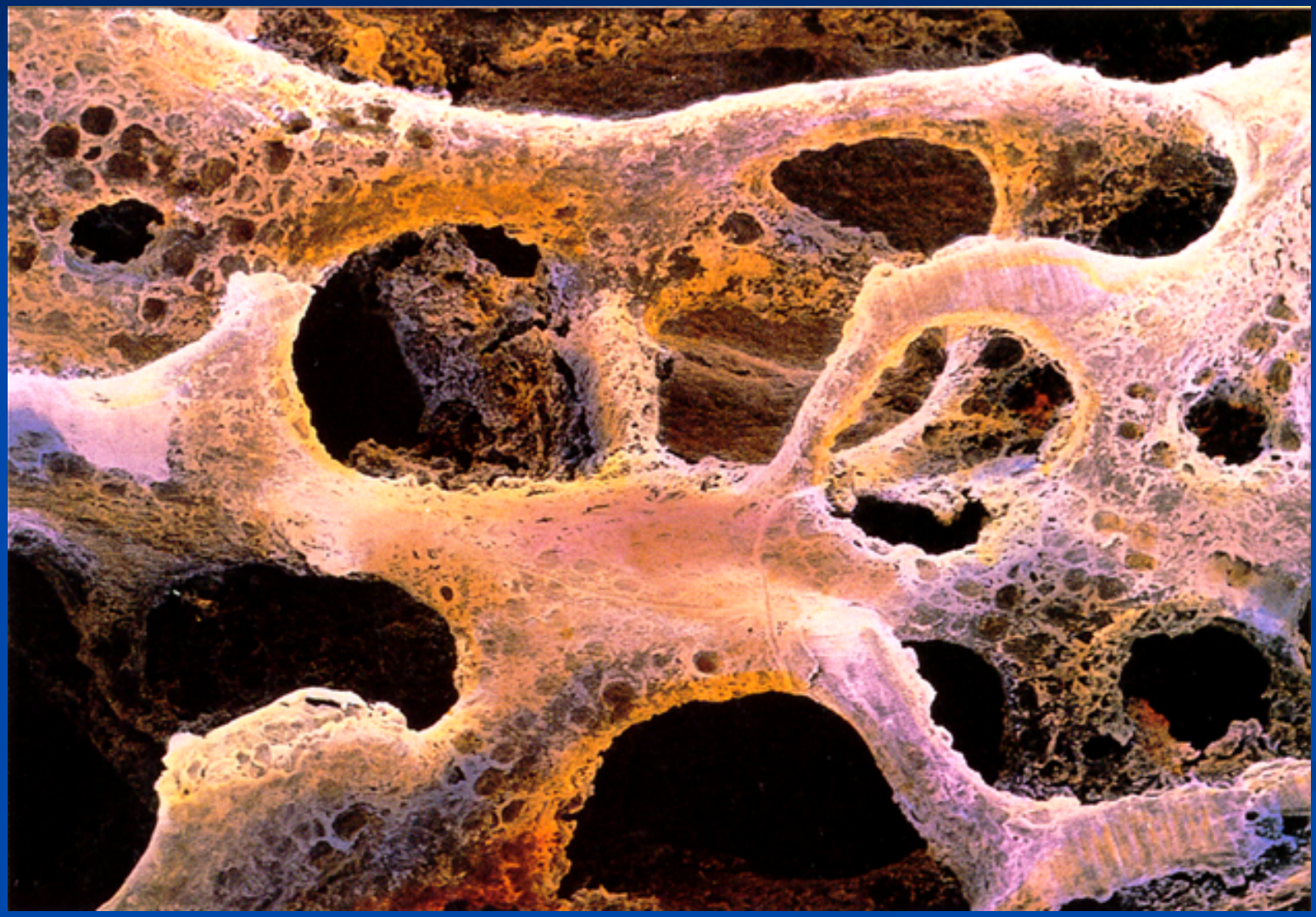
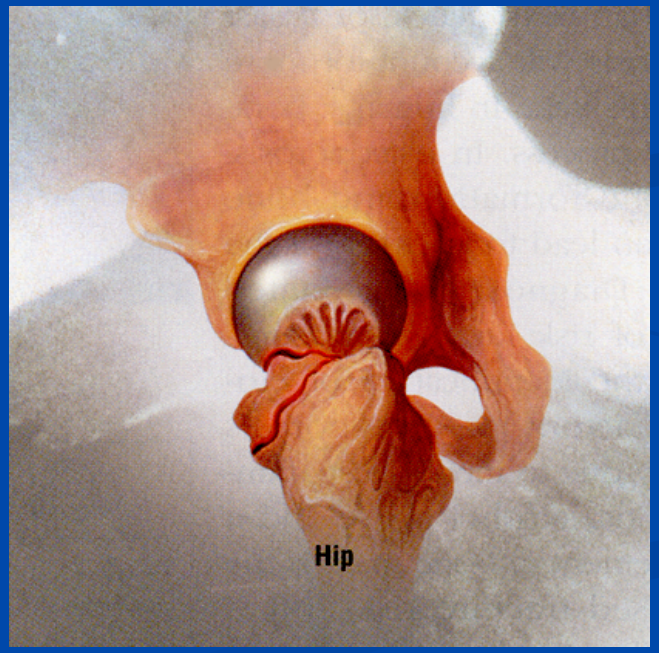
OSTEOPOROSIS

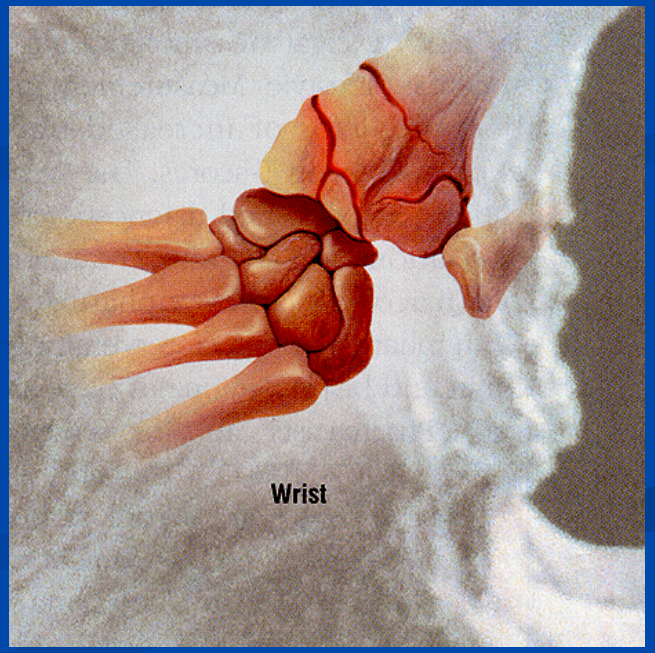
Treatment of Osteoporosis

OSTEOPOROSIS



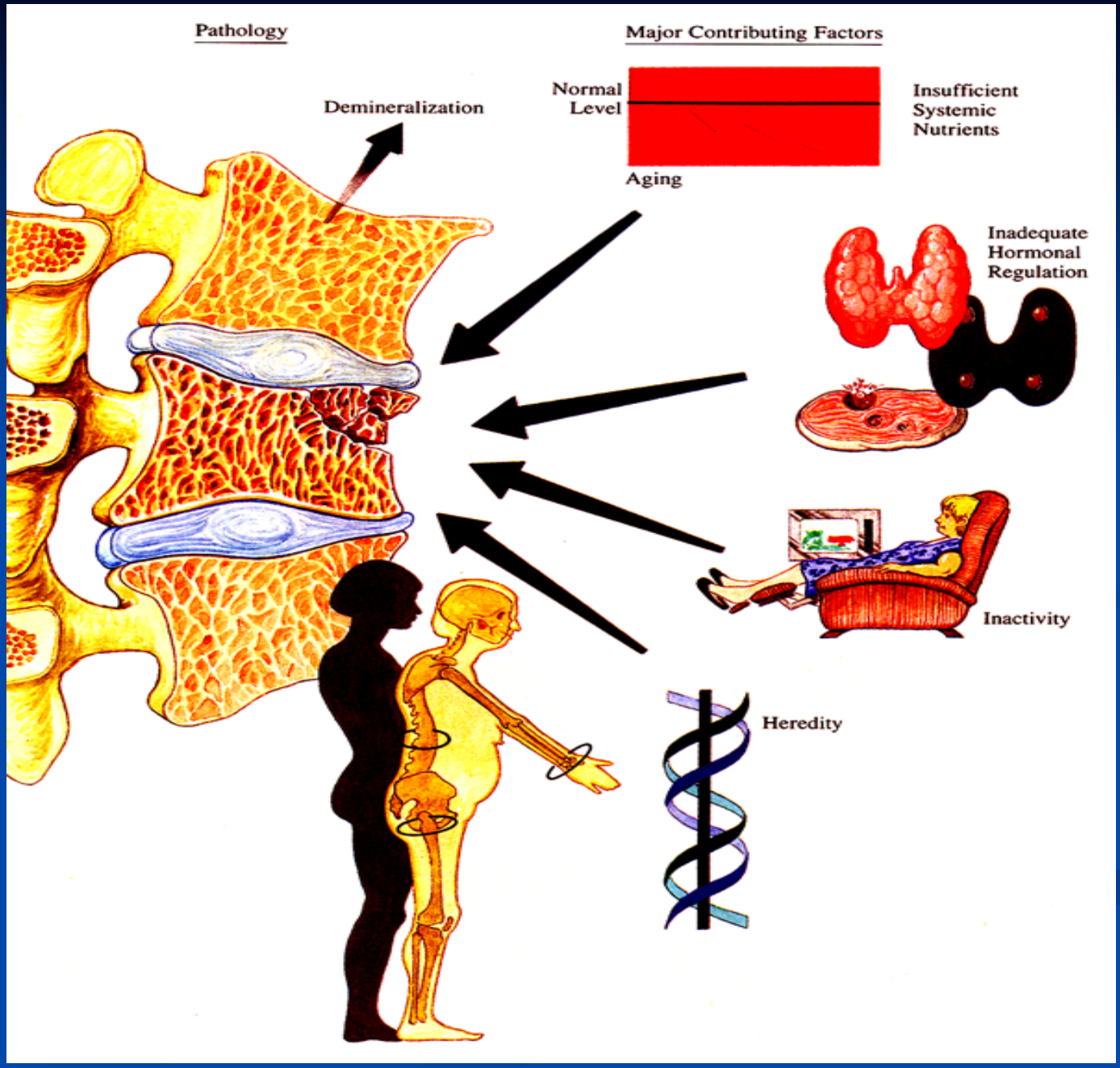
OSTEOPOROSIS accounts for more than 1.3 million fractures annually, affecting more than 25 million Americans. These fractures occur mainly in three areas: the vertebra, the hip, and the wrist.





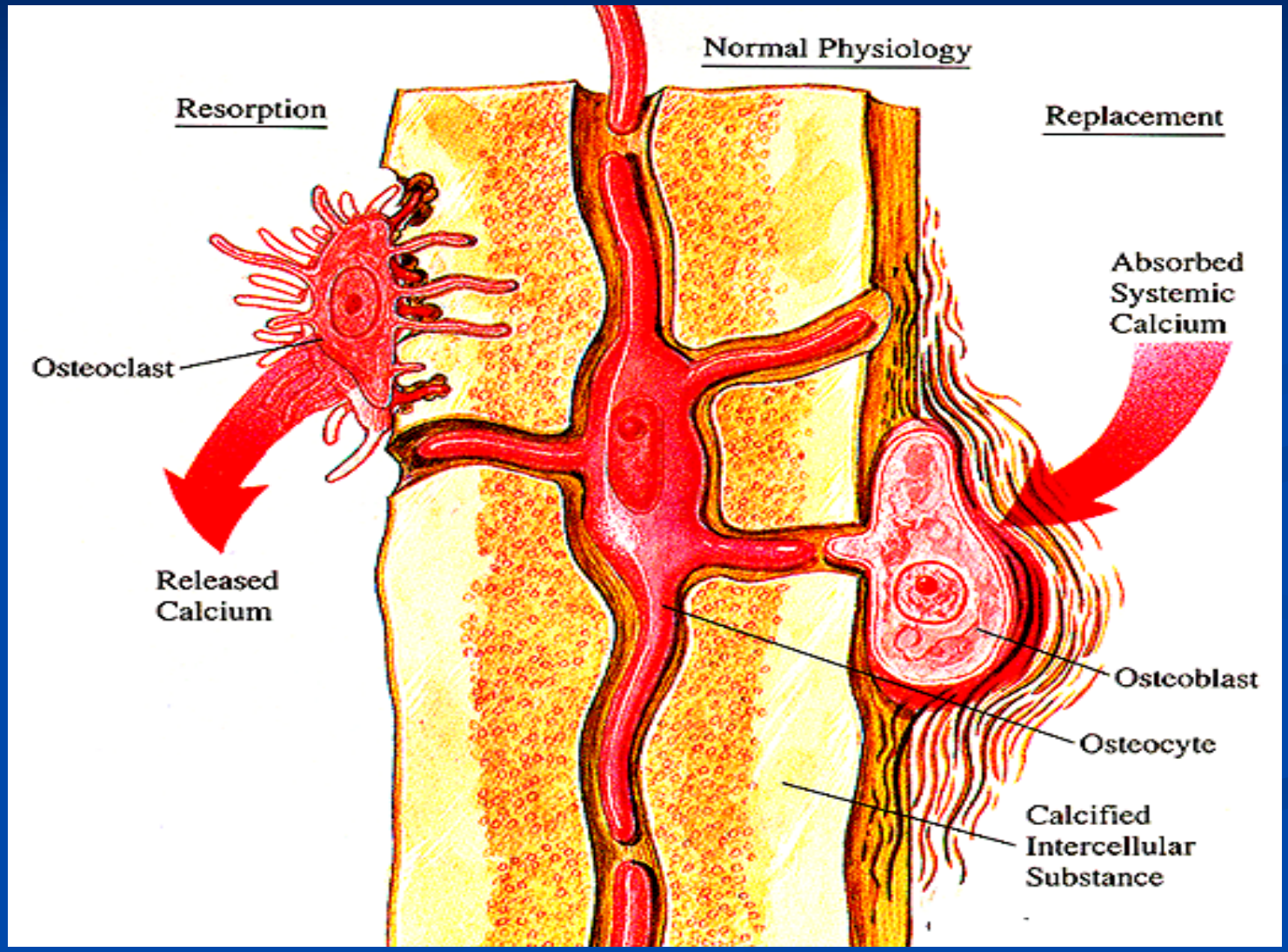
RISK FACTORS

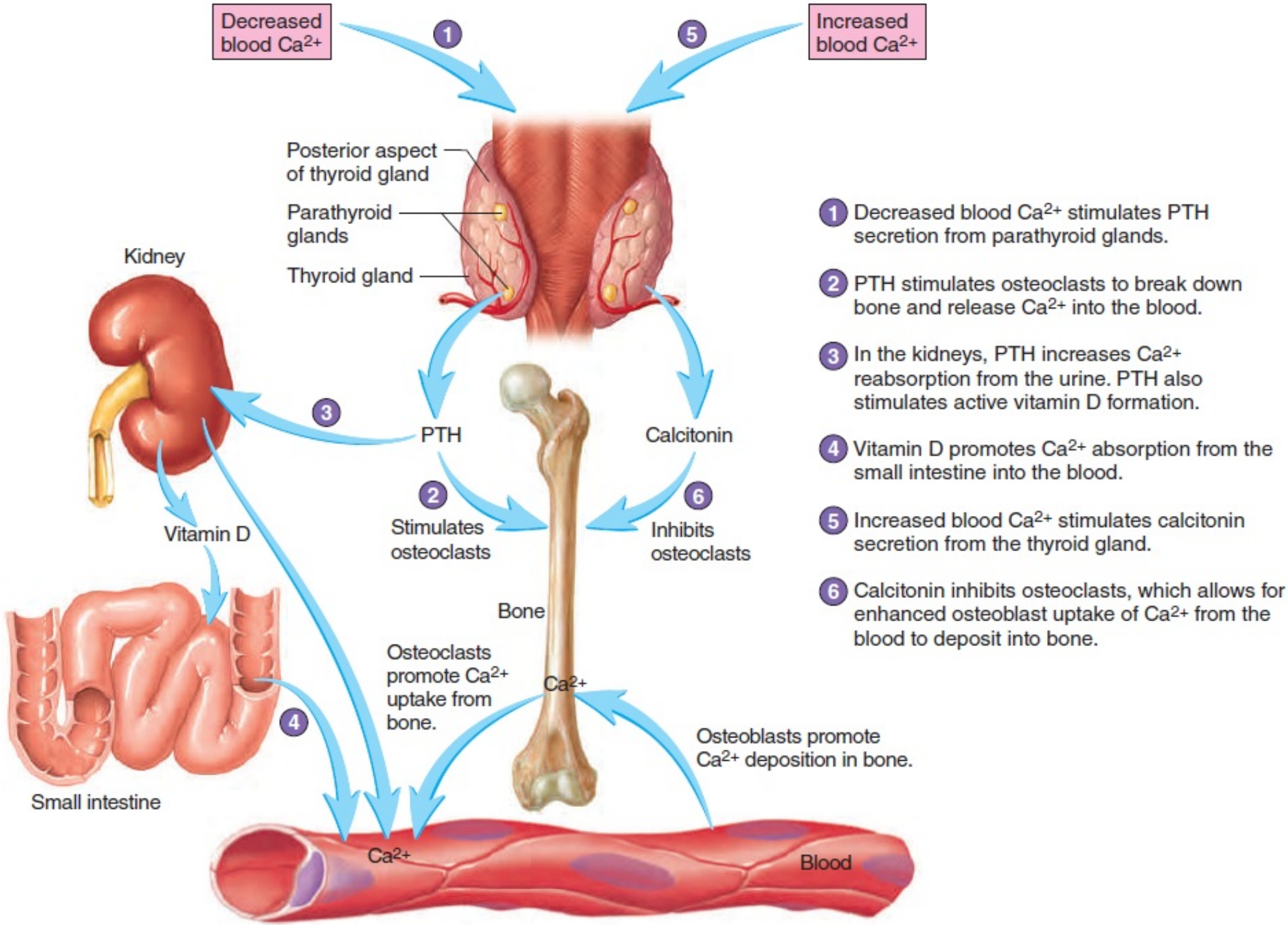
- diet: Ca deficiency
- estrogen deficiency
- hyperparathyrodism
- sedentary lifestyle
- alcohol / smoking
- family history
- drugs:
  - glucocorticoids
  - heparin
  - phenobarbital
  - phenytoin



Osteoclasts are responsible for bone resorption.

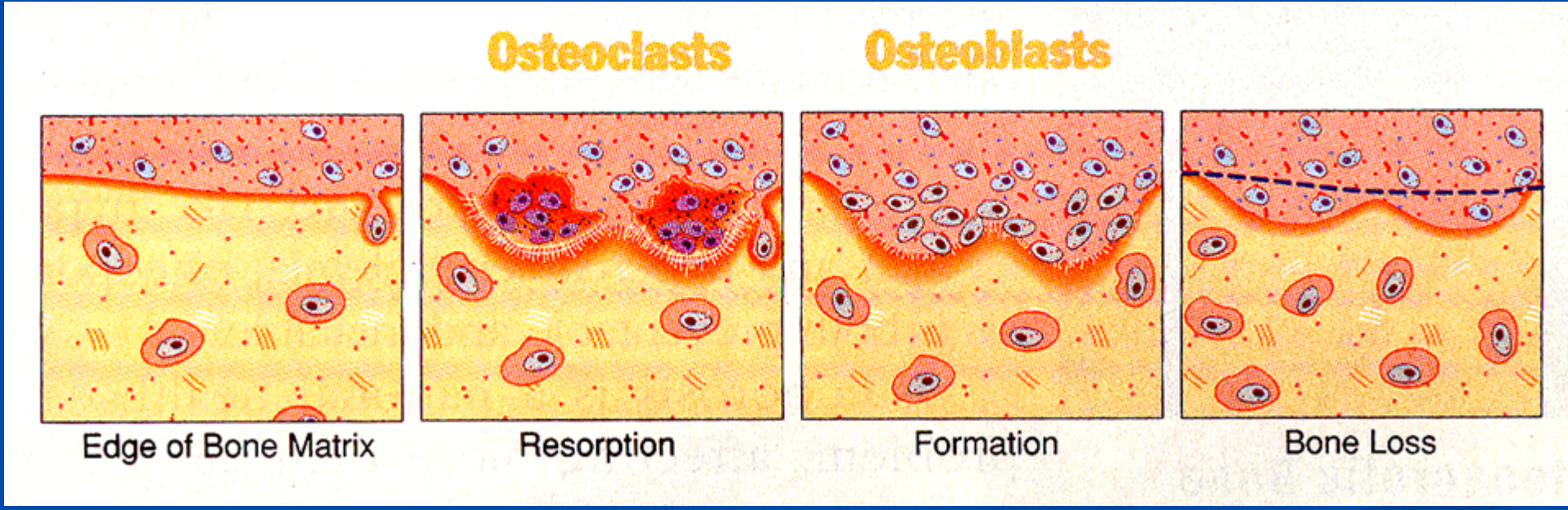
Osteoblasts are responsible for bone formation.





PROCESS Figure 6.9 Calcium Homeostasis

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.

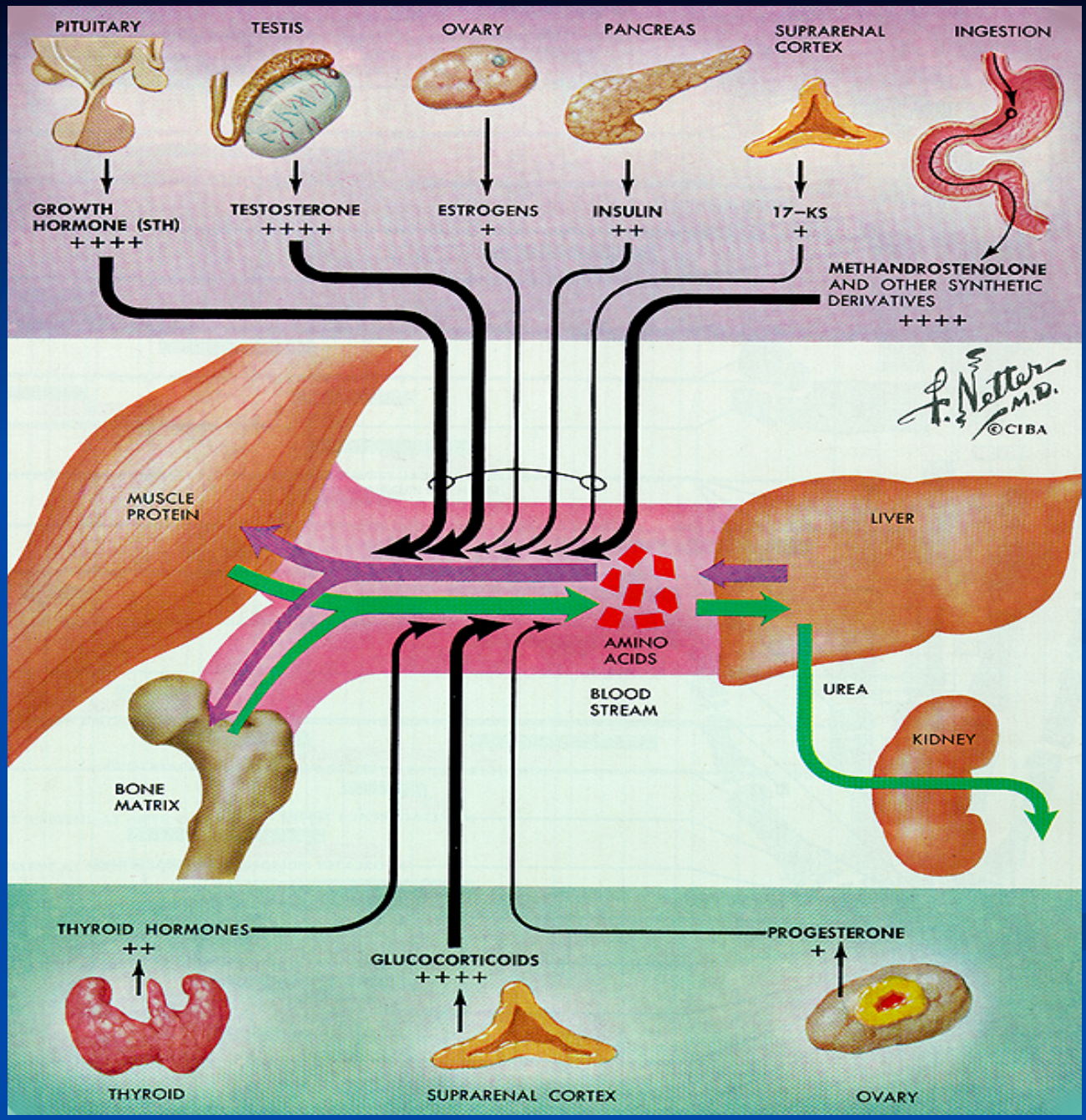


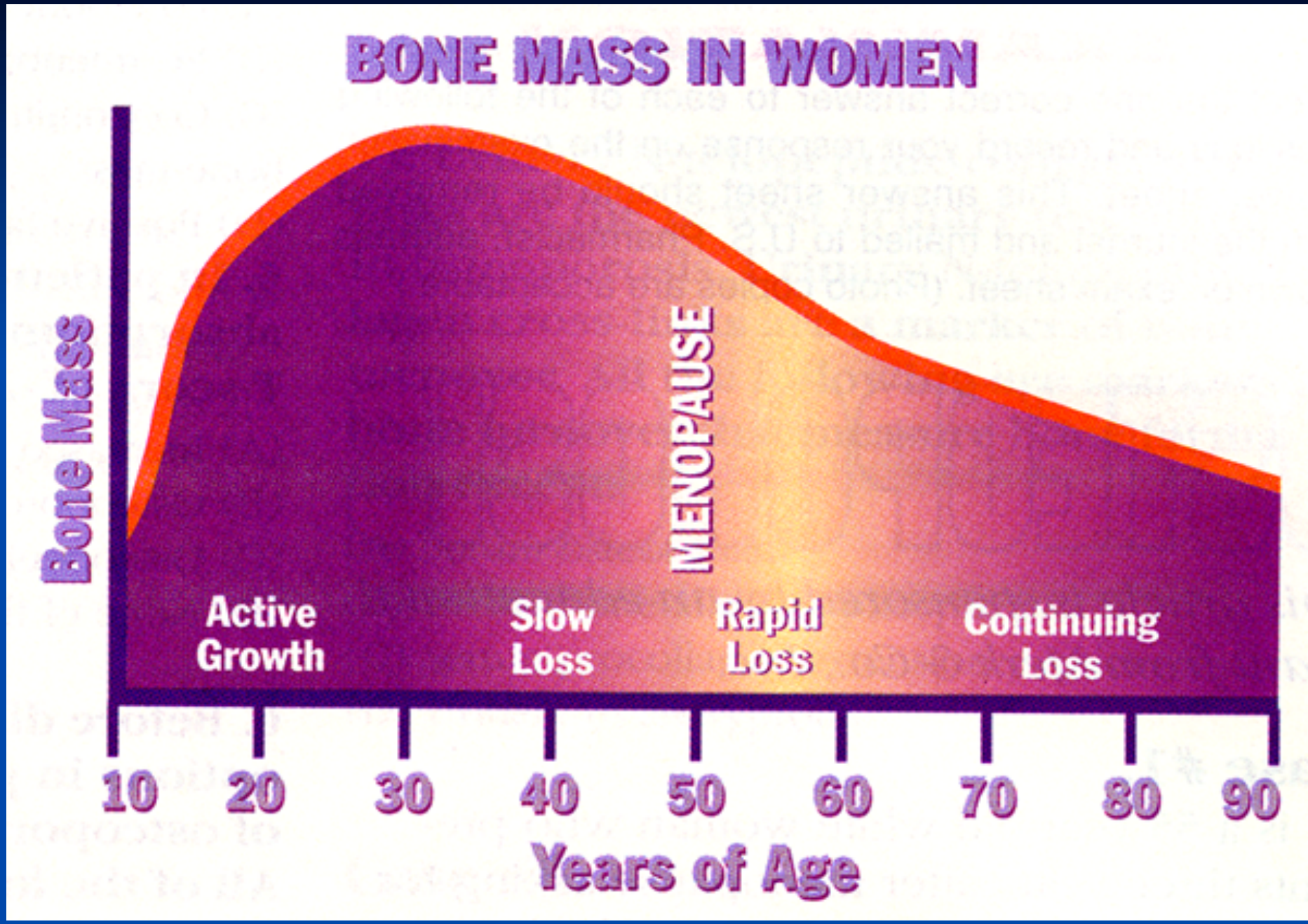
ANABOLIC EFFECTS

versus

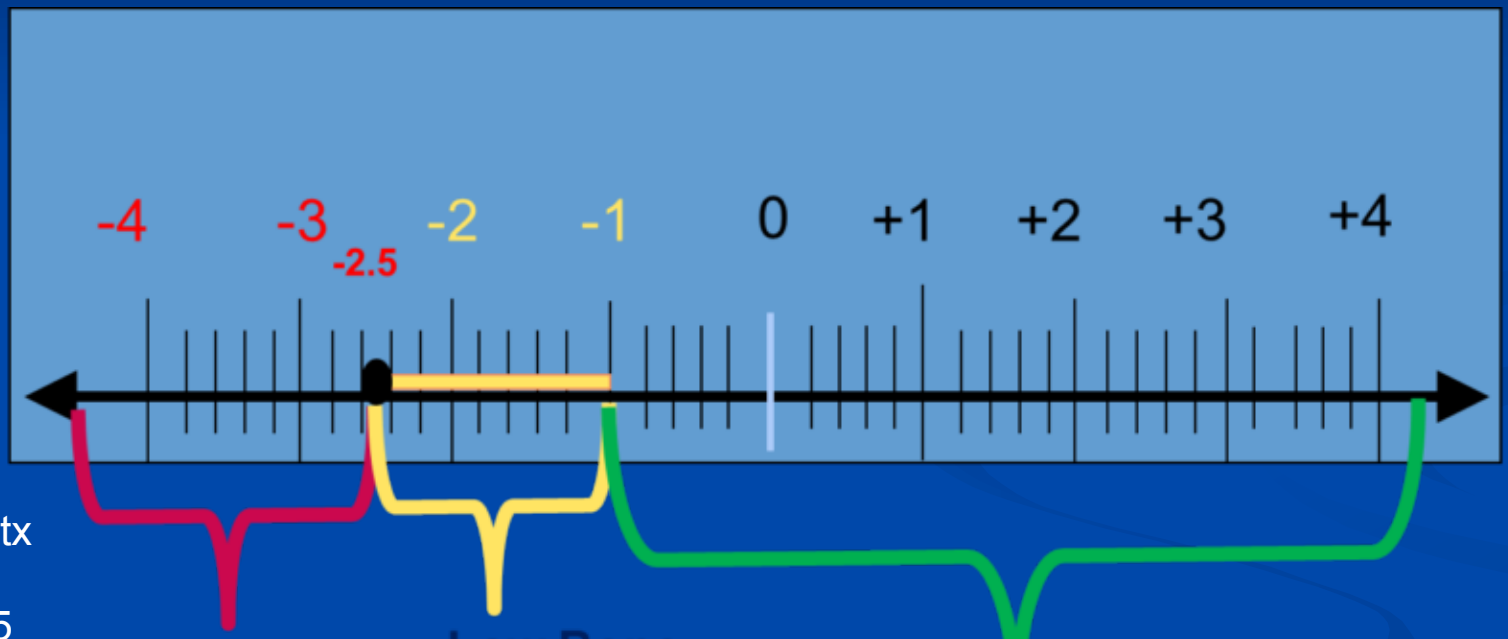
CATABOLIC EFFECTS

- 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

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)



Note: Pharm tx is indicated if T-score < -2.5

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

Alcohol
- decreases intestinal absorption of Ca / Vit D
- decreases estrogen
- increases cortisol / PTH

(4) smoking cessation
- smoking impairs absorption of dietary calcium, influences estrogen metabolism
- increases cortisol levels

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)
    - DVT, PE → estrogen —> increases clotting factors
- 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)

0.3 mg 0.625 mg 0.9 mg 1.25 mg 2.5 mg

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.

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.

Nothing else is

PREMARIN®

(conjugated estrogens tablets)

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.

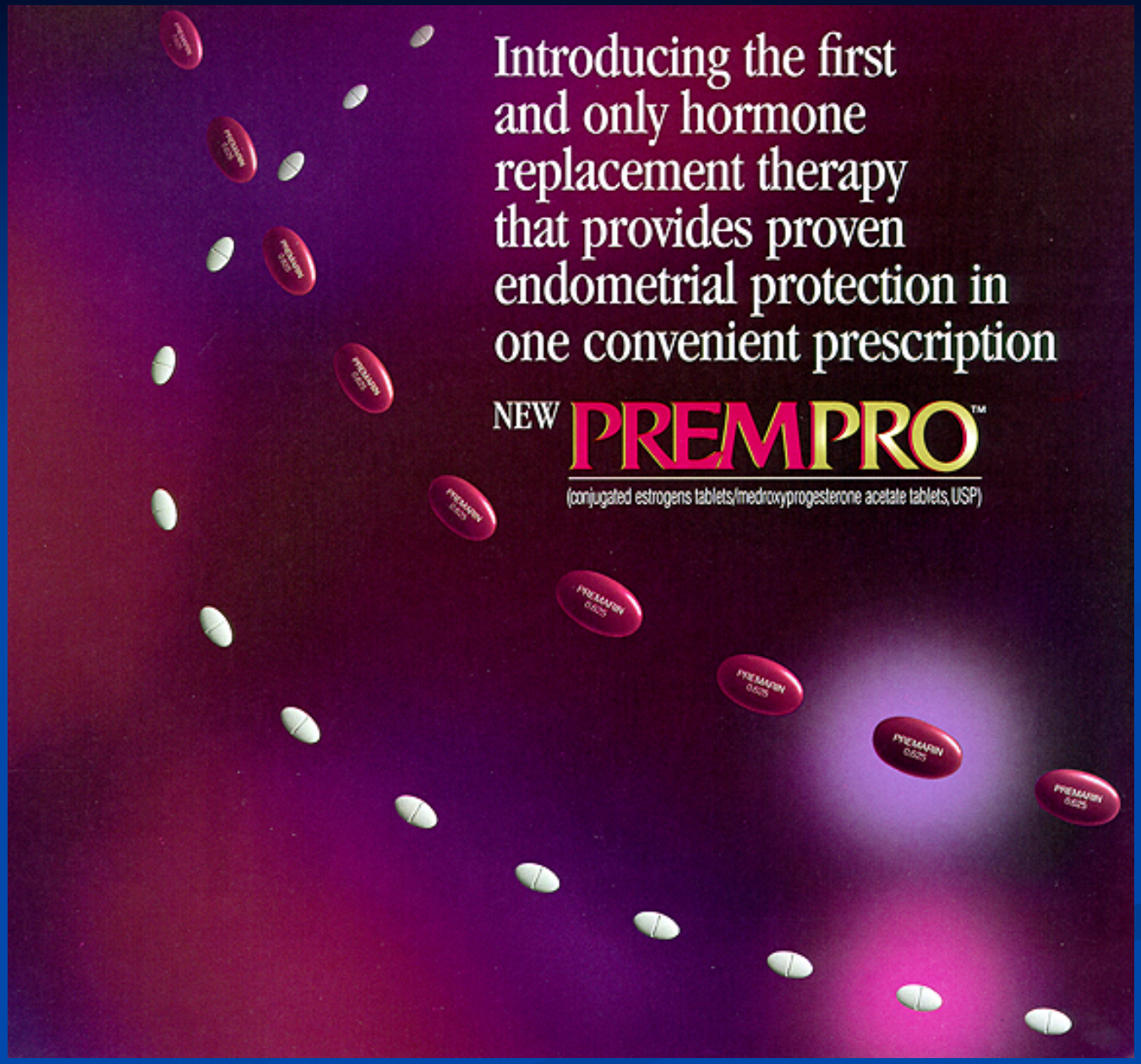
PREMARIN
(conjugated
estrogens)

+

PROVERA
(medroxy-
progesterone)

II

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
     —> decreases risk of breast and uterine cancers

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

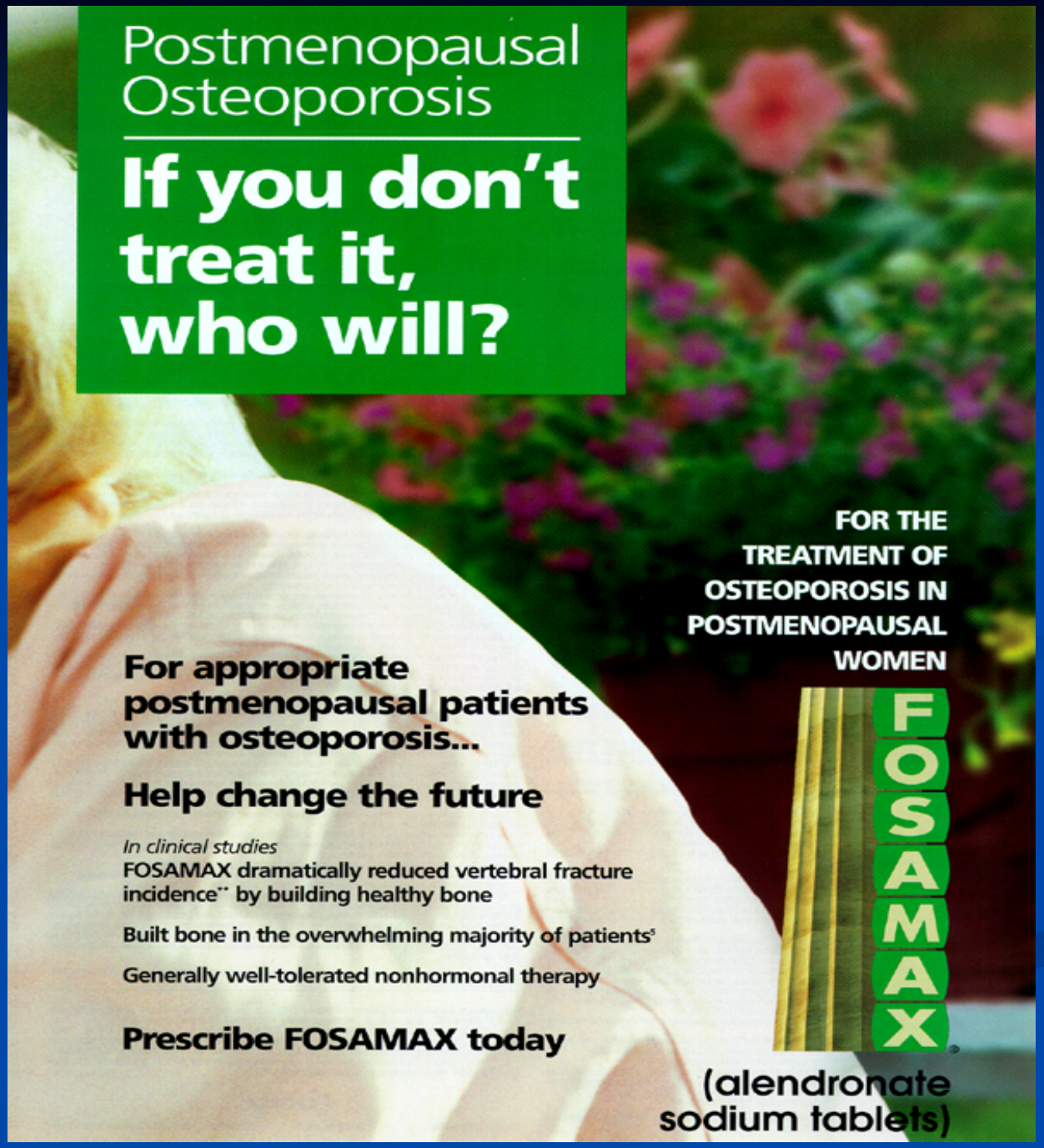
(Alendronate)

Prevention:

5 mg PO daily OR 35 mg PO weekly

Treatment:

10 mg PO daily OR 70 mg PO weekly

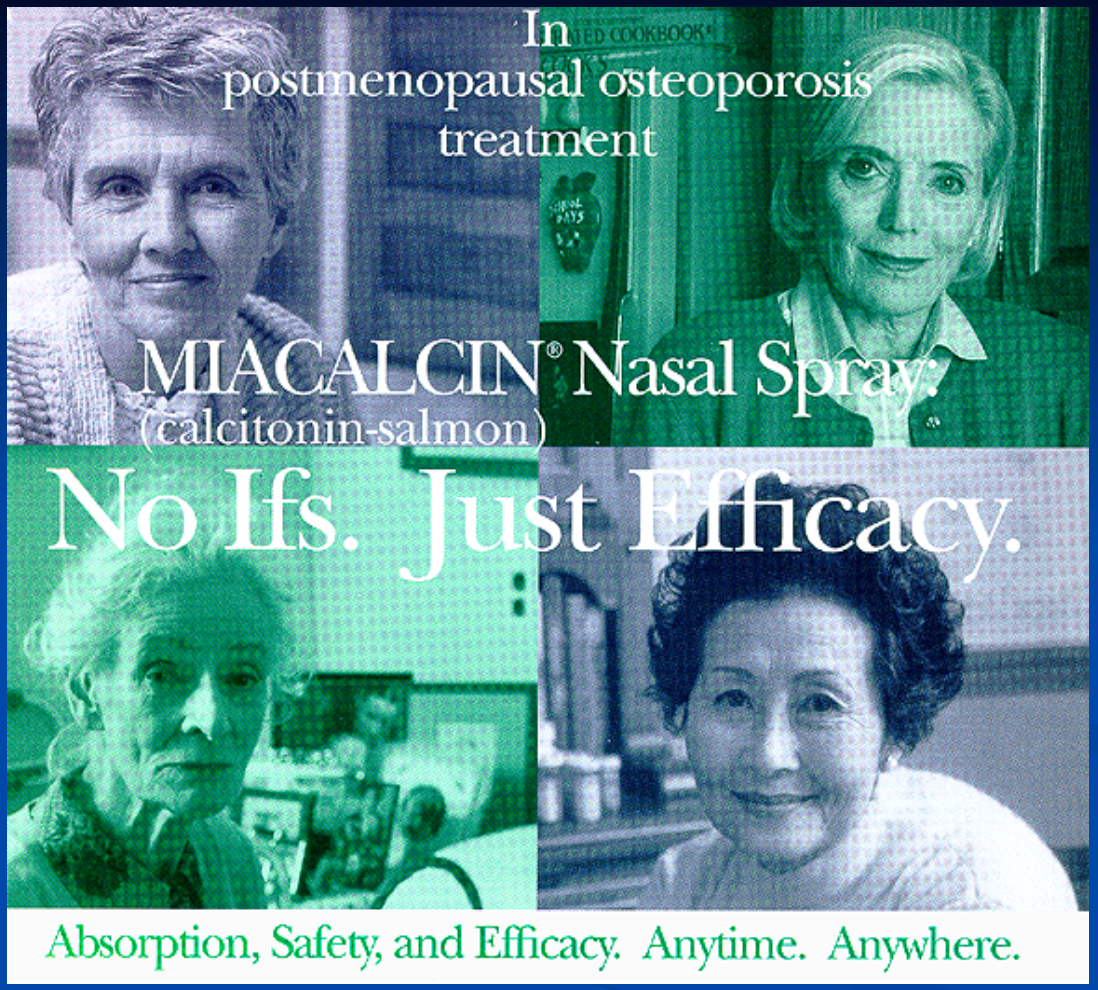


MIACALCIN (calcitonin) NASAL SPRAY

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



MIACALCIN (cont.)

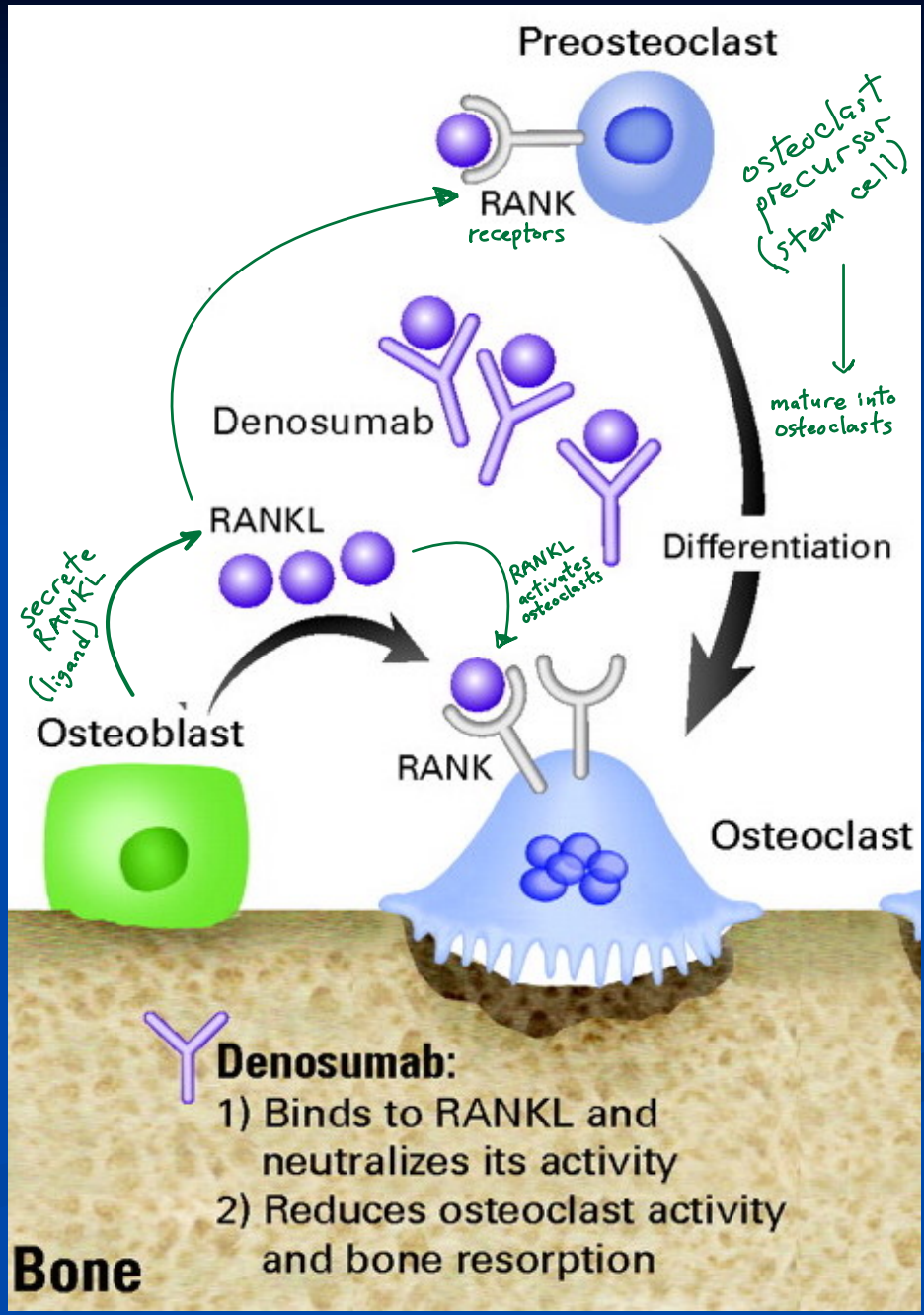
Dosage: 1 spray daily in alternating nostrils

Denosumab (Prolia)

Mechanism of Action:

Denosumab is a human monoclonal antibody that binds to and inhibits RANKL

1. prevents maturation and development of osteoclasts
   - reduces osteoclastic activity
   - reduces bone resorption
2. prevents RANKL from activating osteoclasts
   - decreases osteoclast activity
   - decreases bone resorption



RANKL = receptor activator of nuclear factor "ligand"

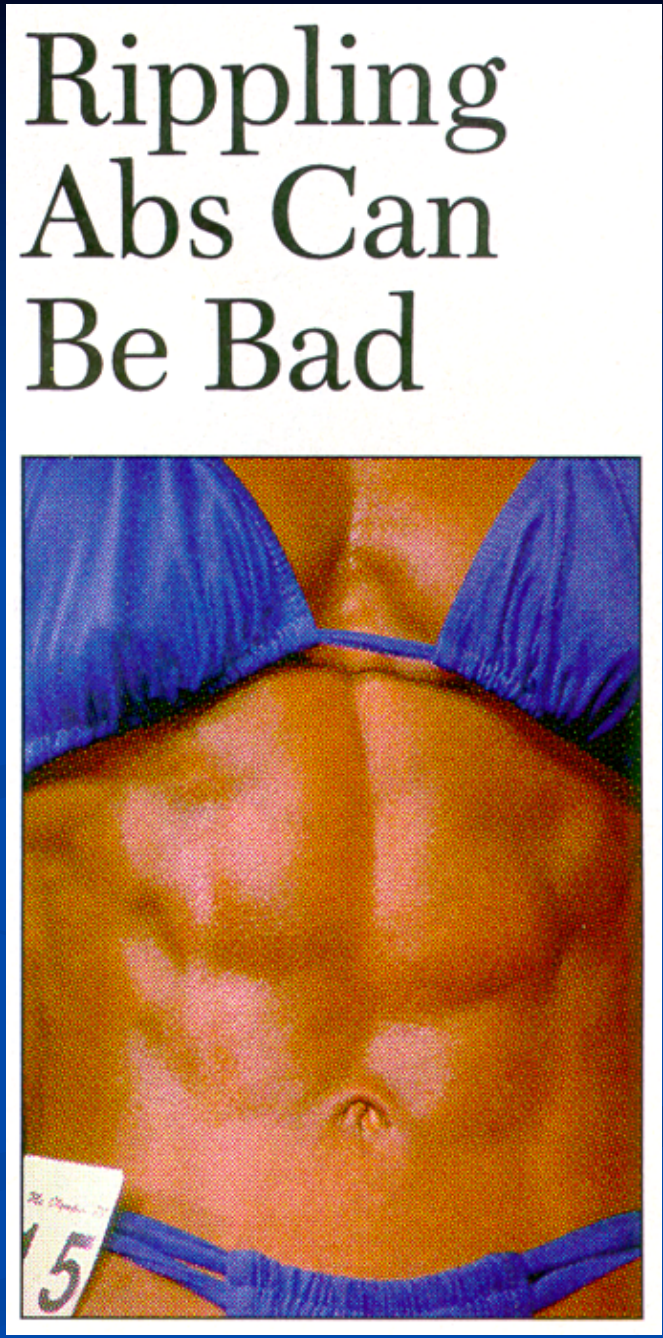
Denosumab (Prolia)

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 ?




PHARMACY
CLOSED