

OSTEOPOROSIS

Treatment of Osteoporosis

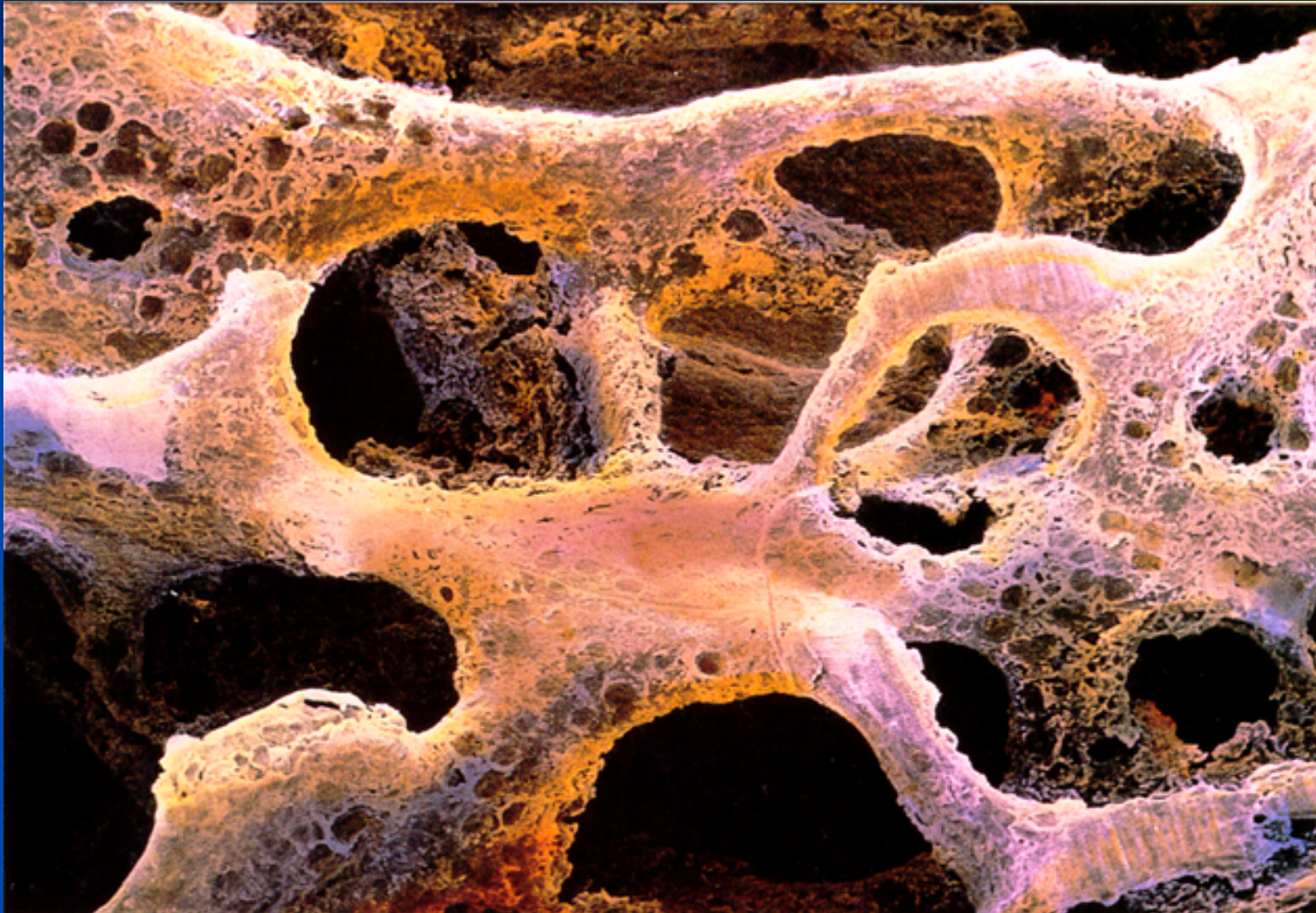


Osteoporotic fractures are
**4 times
more common
than stroke.**^{1,2}

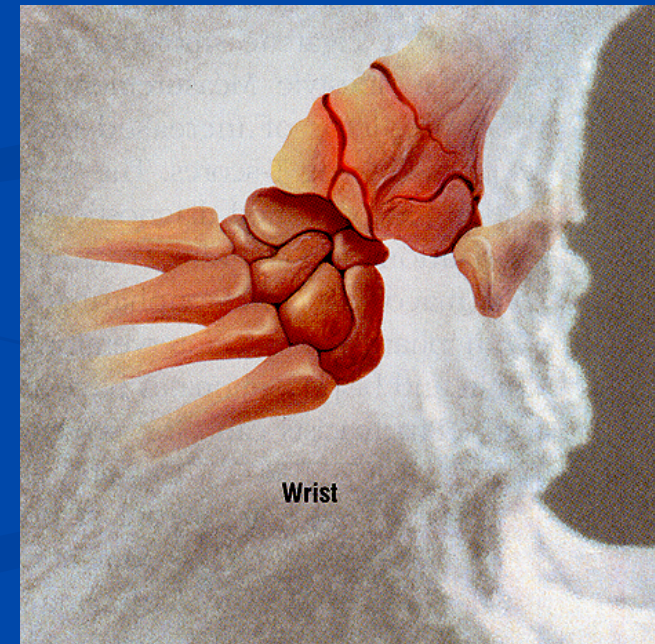
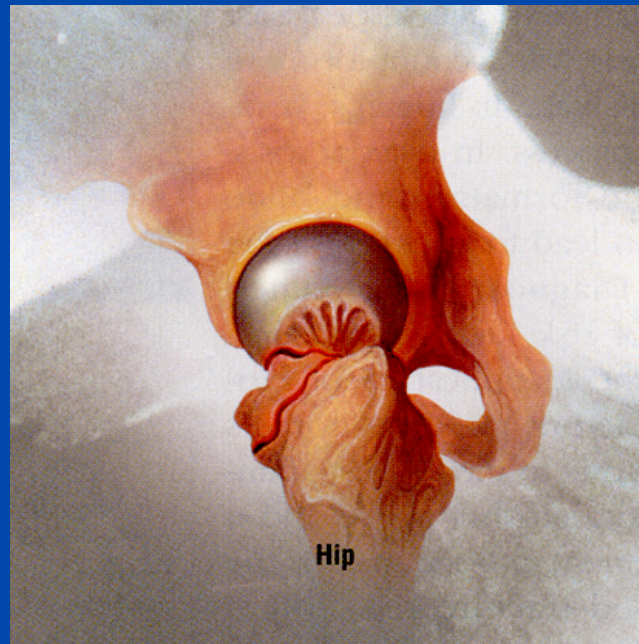
Osteoporotic fractures pose a
**lifetime risk
of death
comparable to
breast cancer.**³

Osteoporosis is still
**undiagnosed and
untreated in over
15 million women.**^{*4}

OSTEOPOROSIS

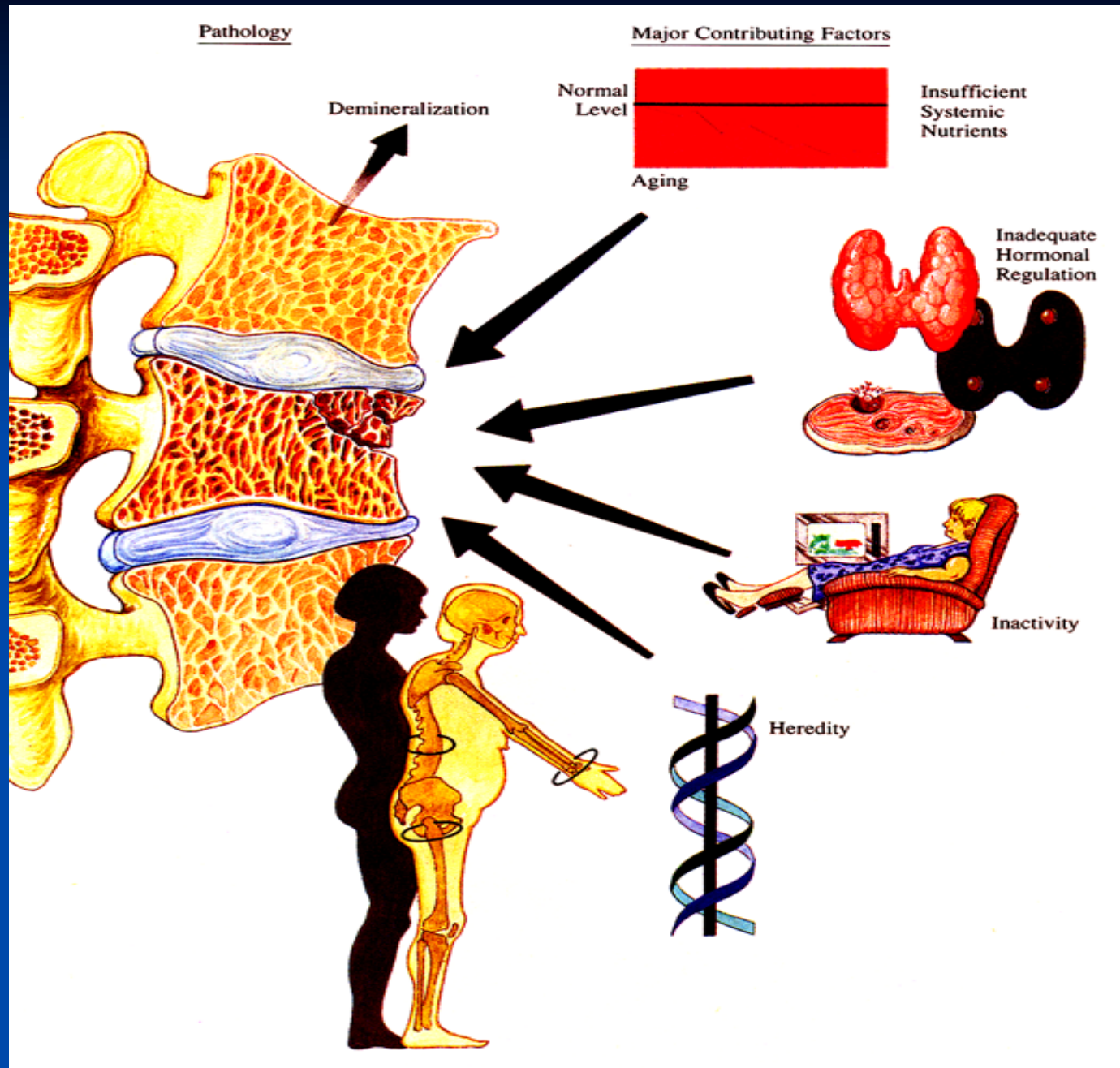


OSTEOPOROSIS accounts for more than 1.3 million fractures annually, affecting more than 25 million Americans. These fractures occur mainly in three areas: the vertebra, the hip, and the wrist.

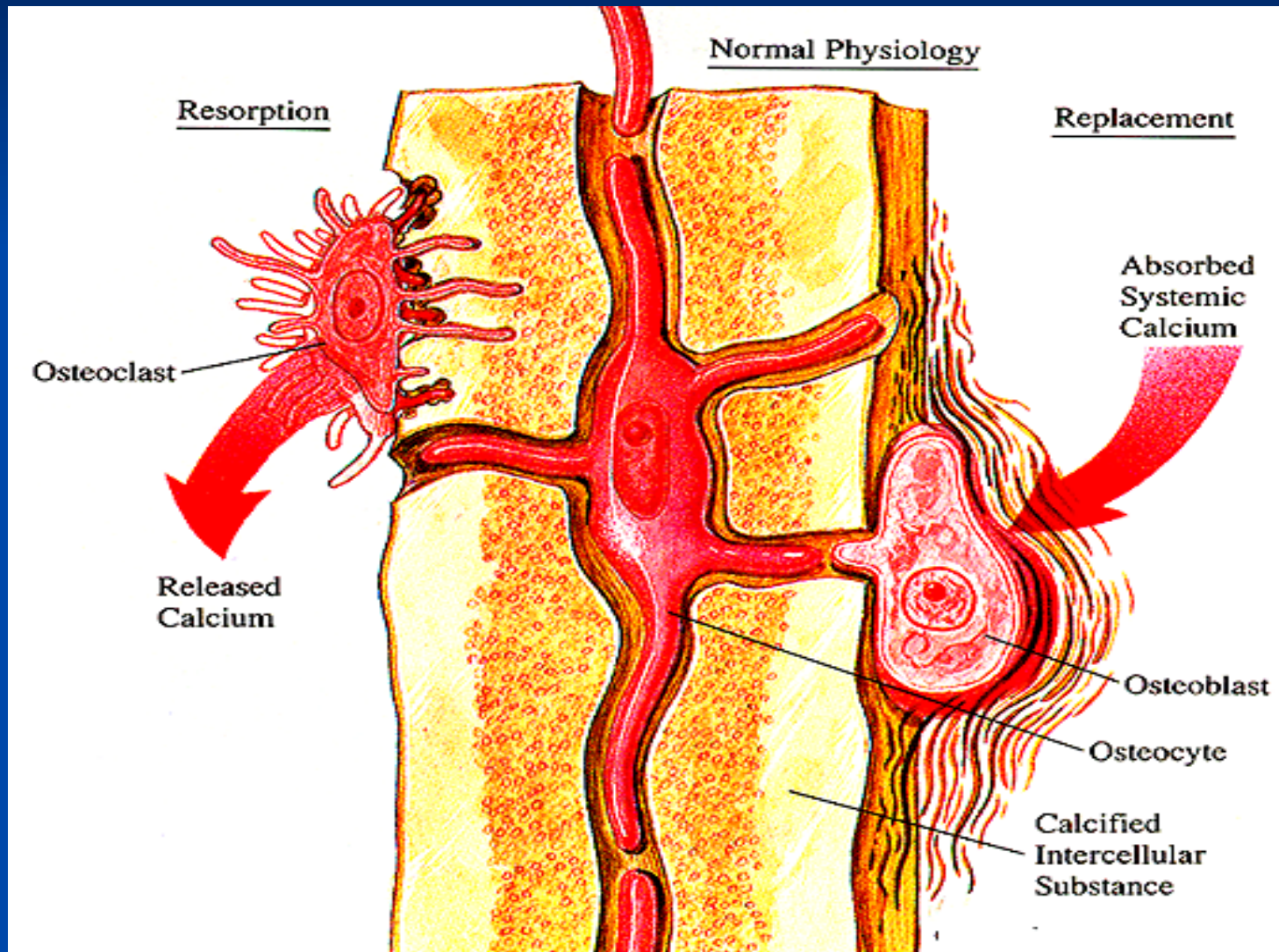


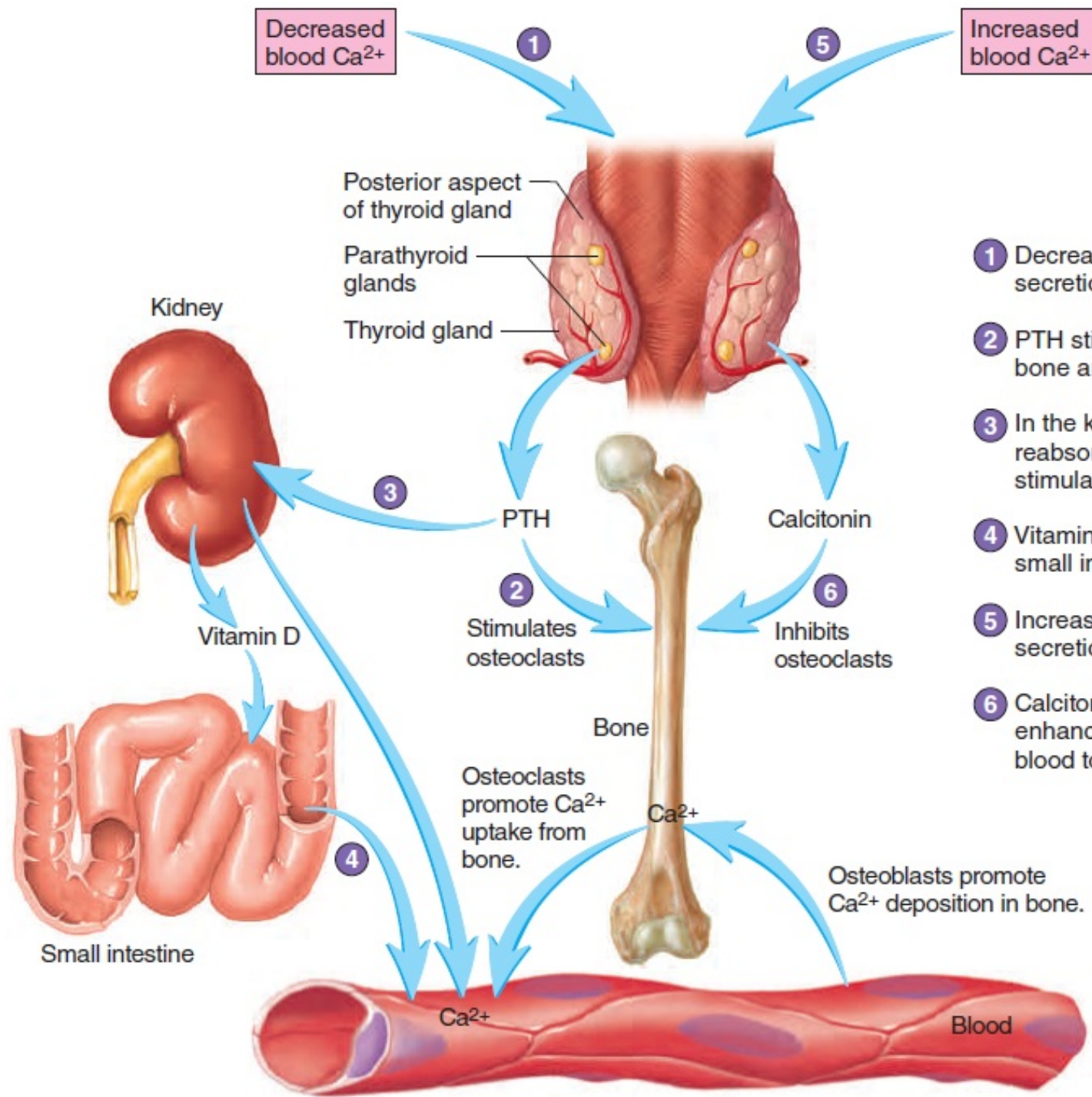
RISK FACTORS

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



Osteoclasts are responsible for bone resorption.
Osteoblasts are responsible for bone formation.

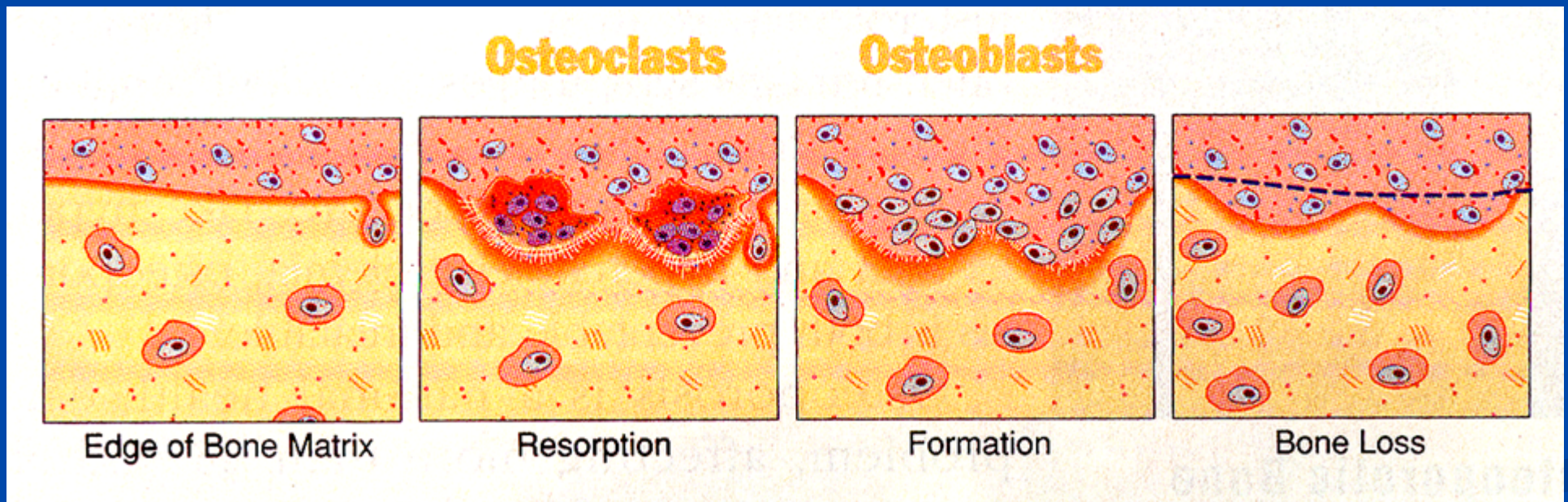




- 1 Decreased blood Ca²⁺ stimulates PTH secretion from parathyroid glands.
- 2 PTH stimulates osteoclasts to break down bone and release Ca²⁺ into the blood.
- 3 In the kidneys, PTH increases Ca²⁺ reabsorption from the urine. PTH also stimulates active vitamin D formation.
- 4 Vitamin D promotes Ca²⁺ absorption from the small intestine into the blood.
- 5 Increased blood Ca²⁺ stimulates calcitonin secretion from the thyroid gland.
- 6 Calcitonin inhibits osteoclasts, which allows for enhanced osteoblast uptake of Ca²⁺ from the blood to deposit into bone.

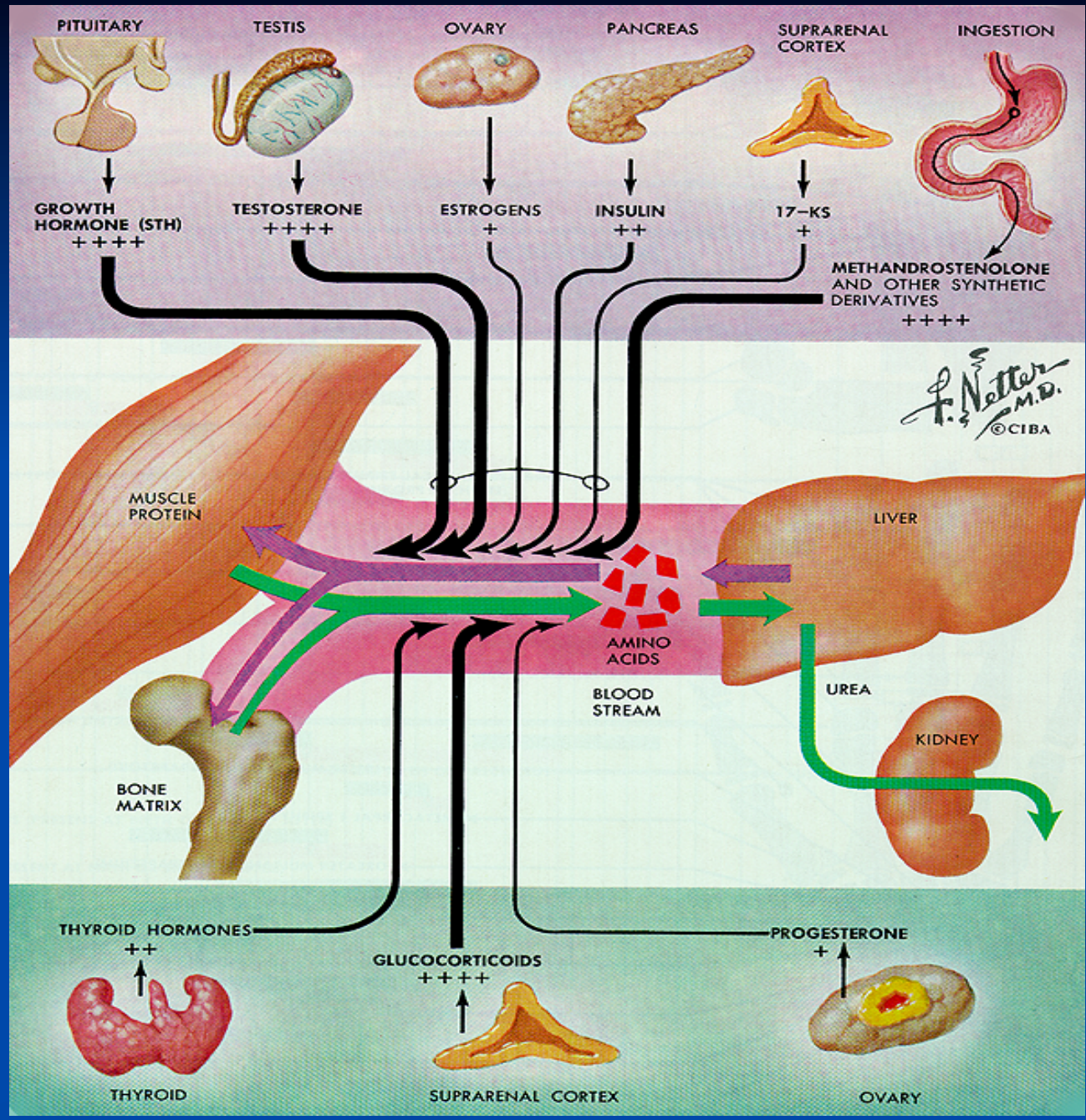
PROCESS Figure 6.9 Calcium Homeostasis

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.

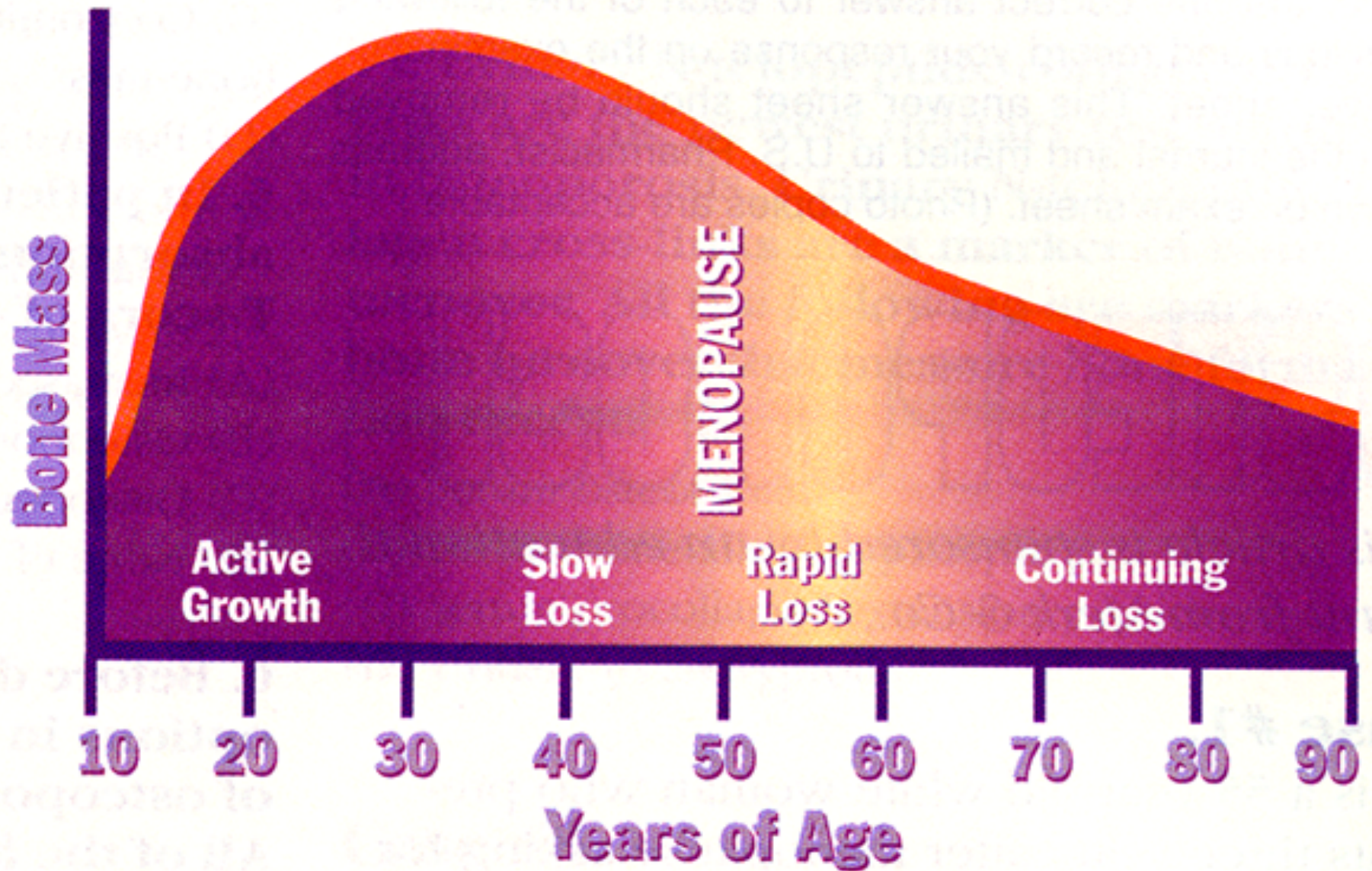


ANABOLIC EFFECTS versus CATABOLIC EFFECTS

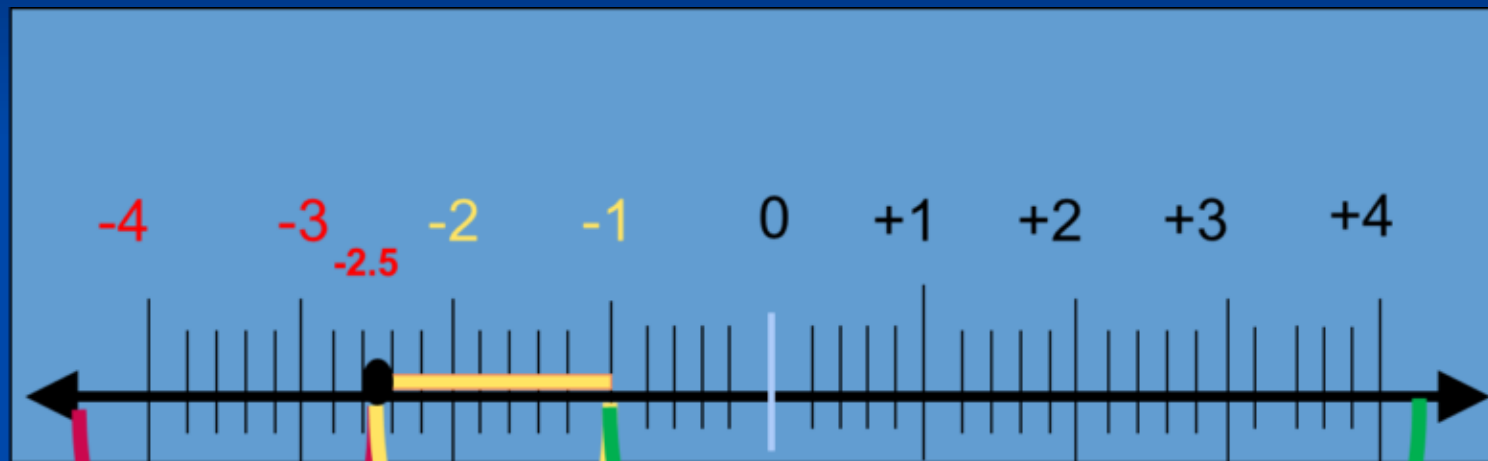
- GROWTH HORMONE
- TESTOSTERONE
- ESTROGEN
- GLUCOCORTICOCIDS
- THYROID HORMONE (LEVOETHYROXINE)
- PARATHYROID HORMONE



BONE MASS IN WOMEN



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

Osteoporosis

Porous bone that can lead to fractures

Low Bone Density (osteopenia)

Normal

As compared to an average 30 year old

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

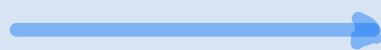
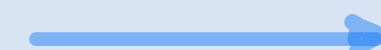
Alcohol

- 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 D³³**

Life Stage Group	RDA Calcium	RDA Vitamin D
Males		
19–50 years	1,000 mg	600 IU (15 mcg)
<u>51–70 years</u> 	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)
<u>51–70 years</u> 	1,200 mg	600 IU (15 mcg) ^a
>70 years	1,200 mg	800 IU (20 mcg) ^a

^aNOF recommends vitamin D 800 to 1,000 IU in patients \geq 50 years.

IU, International Unit; RDA, Recommended Dietary Allowance.

CALCIUM SUPPLEMENTS

<u>SUPPLEMENT</u>	<u>ELEMENTAL CALCIUM</u>
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 than 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

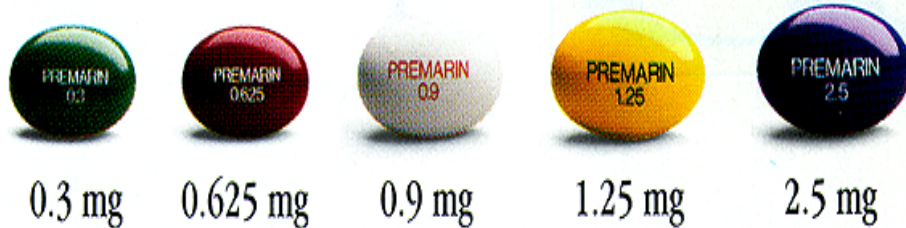
ESTROGEN / PROGESTIN THERAPY (EPT)

- 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)
 - ↳ 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)



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)

||

PREMPRO



Introducing the first
and only hormone
replacement therapy
that provides proven
endometrial protection in
one convenient prescription

NEW **PREMPRO**[™]
(conjugated estrogens tablets/medroxyprogesterone acetate tablets, USP)

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)

Biphosphonate: Alendronate (Fosamax)

Mechanism of Action: Alendronate concentrates in mineral tissue and interfere with osteoclast-mediated 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 → decreases 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 *THE GREAT COOKBOOK*
postmenopausal osteoporosis
treatment

MIACALCIN[®] Nasal Spray:
(calcitonin-salmon)

No Ifs. Just Efficacy.

Absorption, Safety, and Efficacy. Anytime. Anywhere.

The advertisement features four elderly women in a collage. The top-left woman is in a kitchen with a book titled 'THE GREAT COOKBOOK' on the wall. The top-right woman is smiling. The bottom-left woman is looking slightly to the side. The bottom-right woman is smiling. The text is overlaid on the images in a serif font.

MIACALCIN (cont.)

Dosage: 1 spray daily
in alternating nostrils



Now, for many postmenopausal osteoporosis patients

NEW MIACALCIN[®] (*calcitonin-salmon*)
Nasal Spray

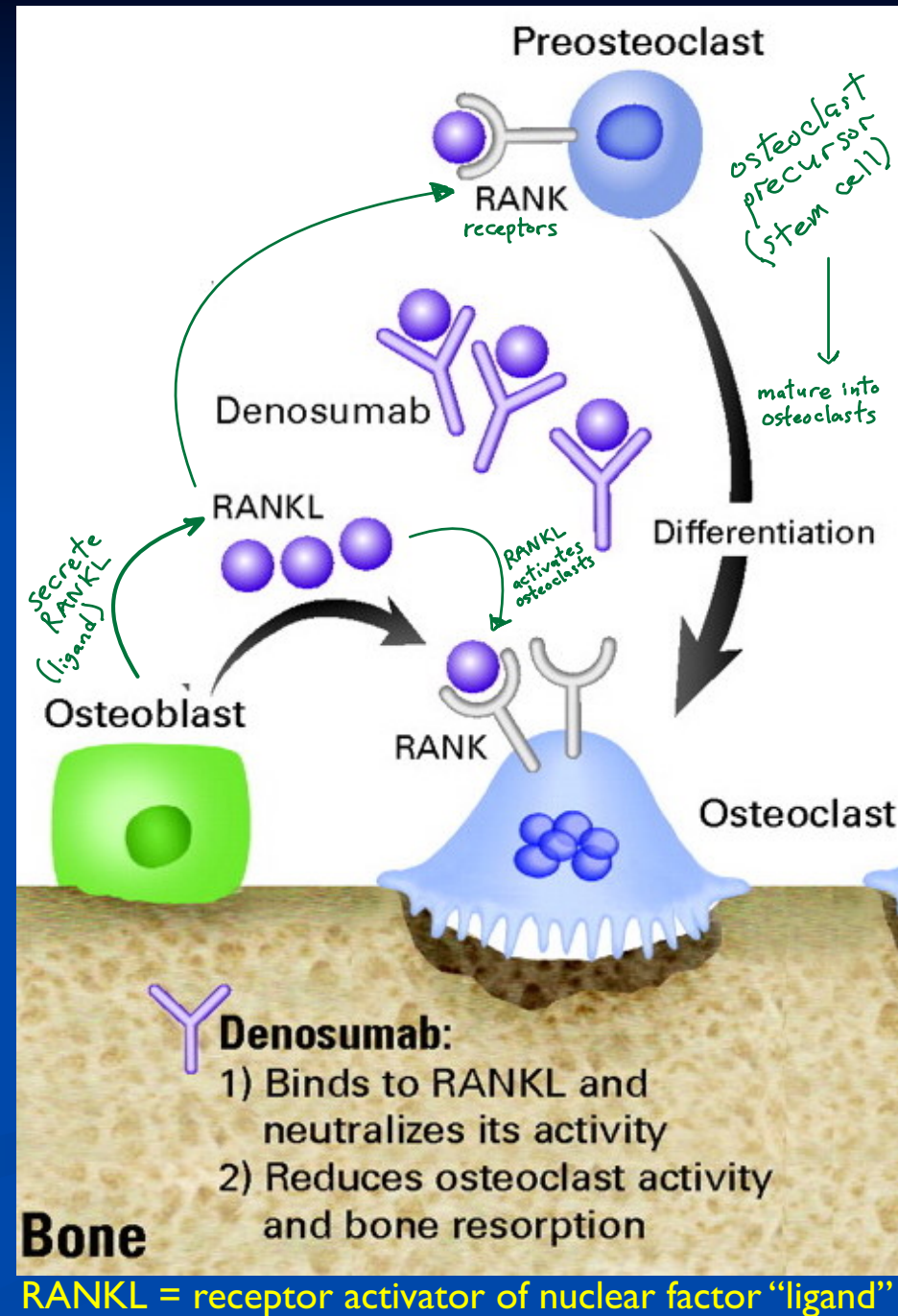
Indicated for the treatment of postmenopausal osteoporosis in females greater than 5 years postmenopause with low bone mass who refuse or cannot tolerate estrogens, or in whom estrogens are contraindicated. Patients should ensure adequate calcium and vitamin D intake.

Denosumab (Prolia)

Mechanism of Action:

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

- 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



Denosumab (Prolia)

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

Dosage: Denosumab is administered 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

