

GOUT AND OTHER CRYSTAL ARTHROPATHIES

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Gout:

- Common metabolic disorder characterised by hyperuricaemia:
 - Urate level $\geq 0,360$ mmol/l = the level above which the physiological saturation threshold is exceeded
 - Microscopic and macroscopic soft tissue deposits of monosodium urate monohydrate crystals (tophi)
 - Crystals trigger intense but self-limited bouts of acute arthritis
 - Tophi promote chronic inflammatory and erosive arthritis

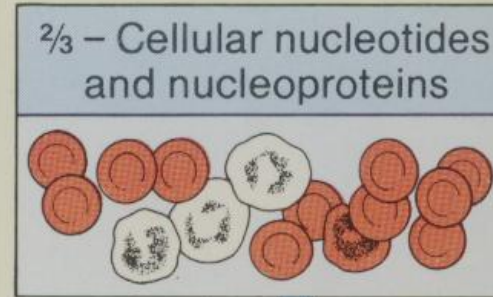
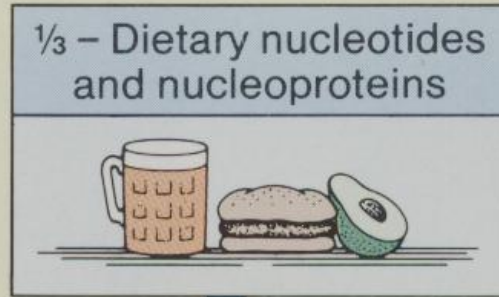
Epidemiology:

- Incidence is increasing
- 1- 3 % of population – most common inflammatory arthritis
- Hyperuricaemia correlated with:
 - Serum creatinine
 - Body weight
 - Age
 - Alcohol intake: beer contains high guanosine
 - Dietary factors:
 - Meat
 - Seafood
 - Fructose
 - Negative correlation with low-fat dairy products, coffee and ascorbate
 - Increased cell turnover
 - Mutations involved in purine metabolism

Pathogenesis and pathology of gout

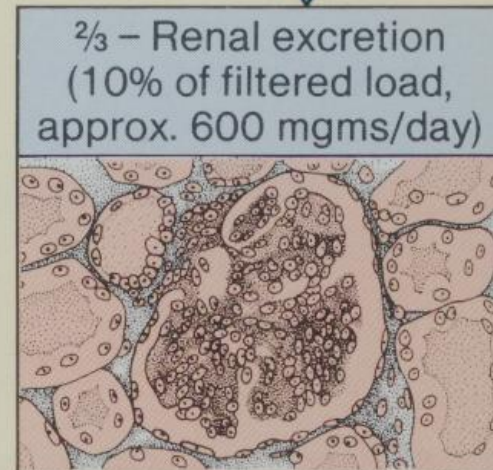
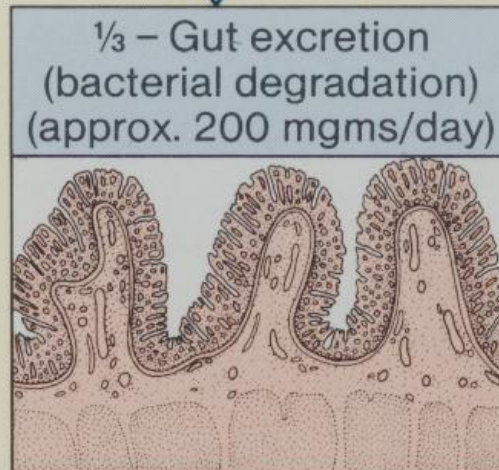
Monosodium urate monohydrate

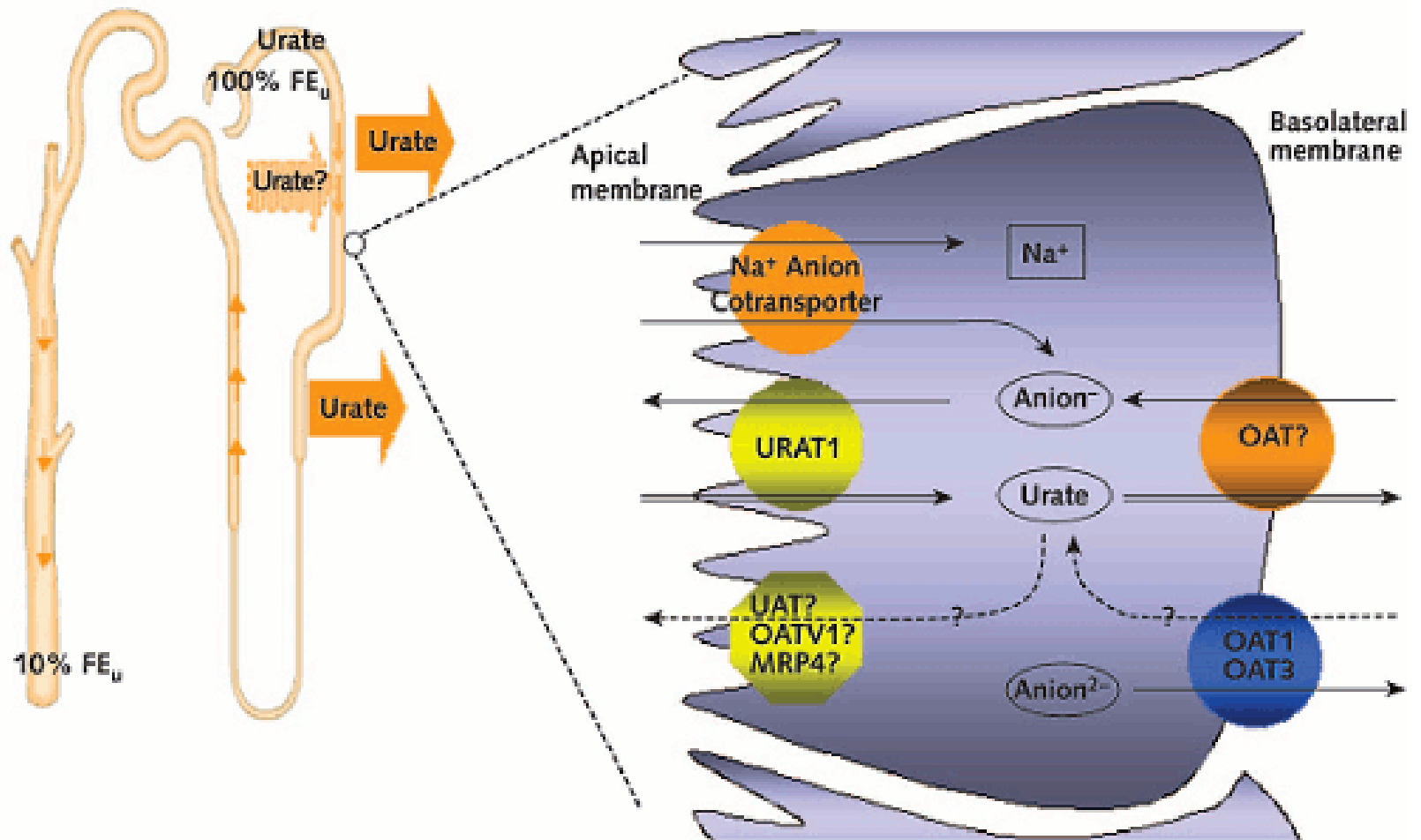


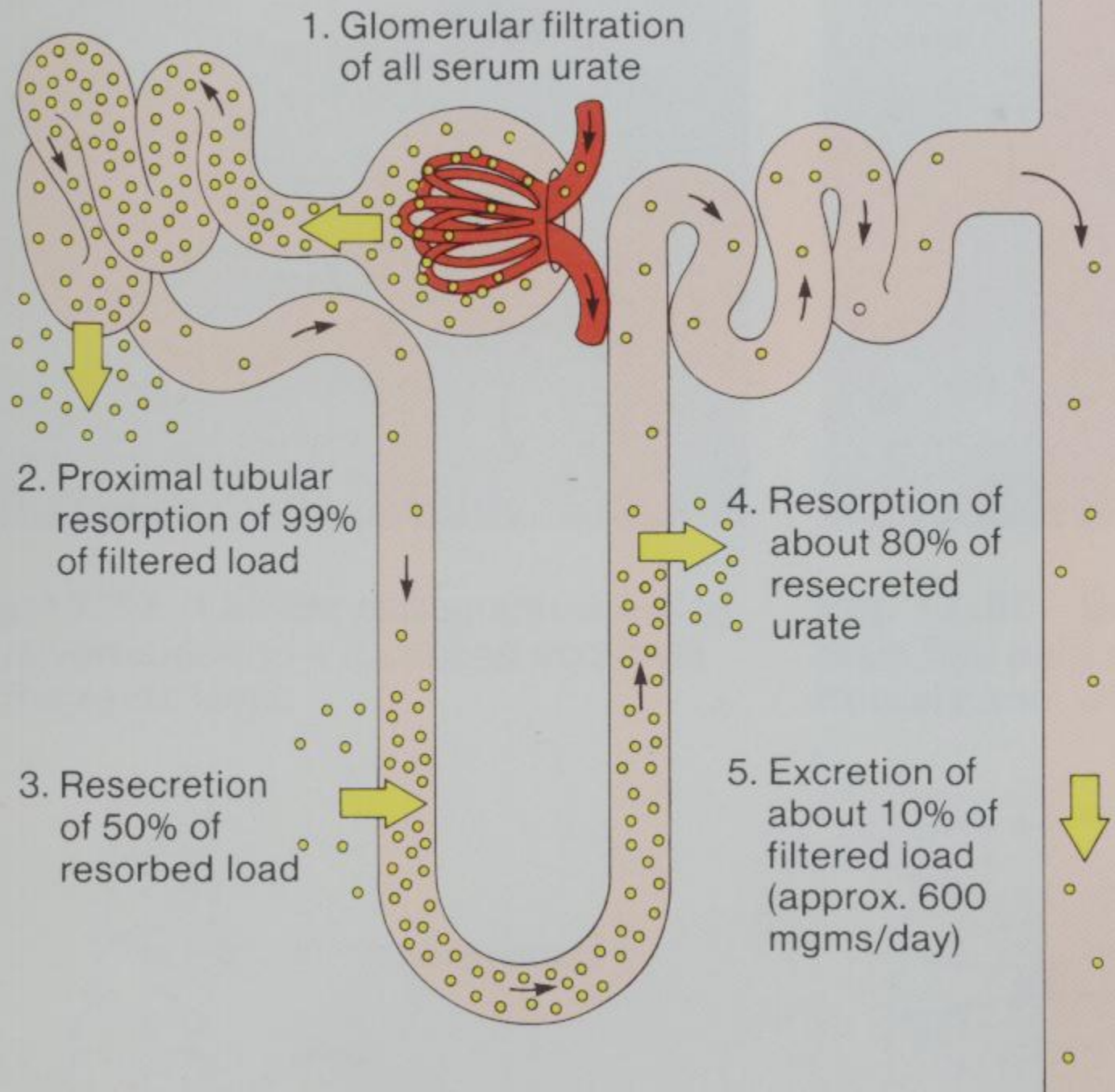


Adenine and Guanine

Uric acid pool
(approx. 1000 mgms)







1. Glomerular filtration of all serum urate

2. Proximal tubular resorption of 99% of filtered load

3. Resecretion of 50% of resorbed load

4. Resorption of about 80% of resecreted urate

5. Excretion of about 10% of filtered load (approx. 600 mgms/day)

Renal factors:

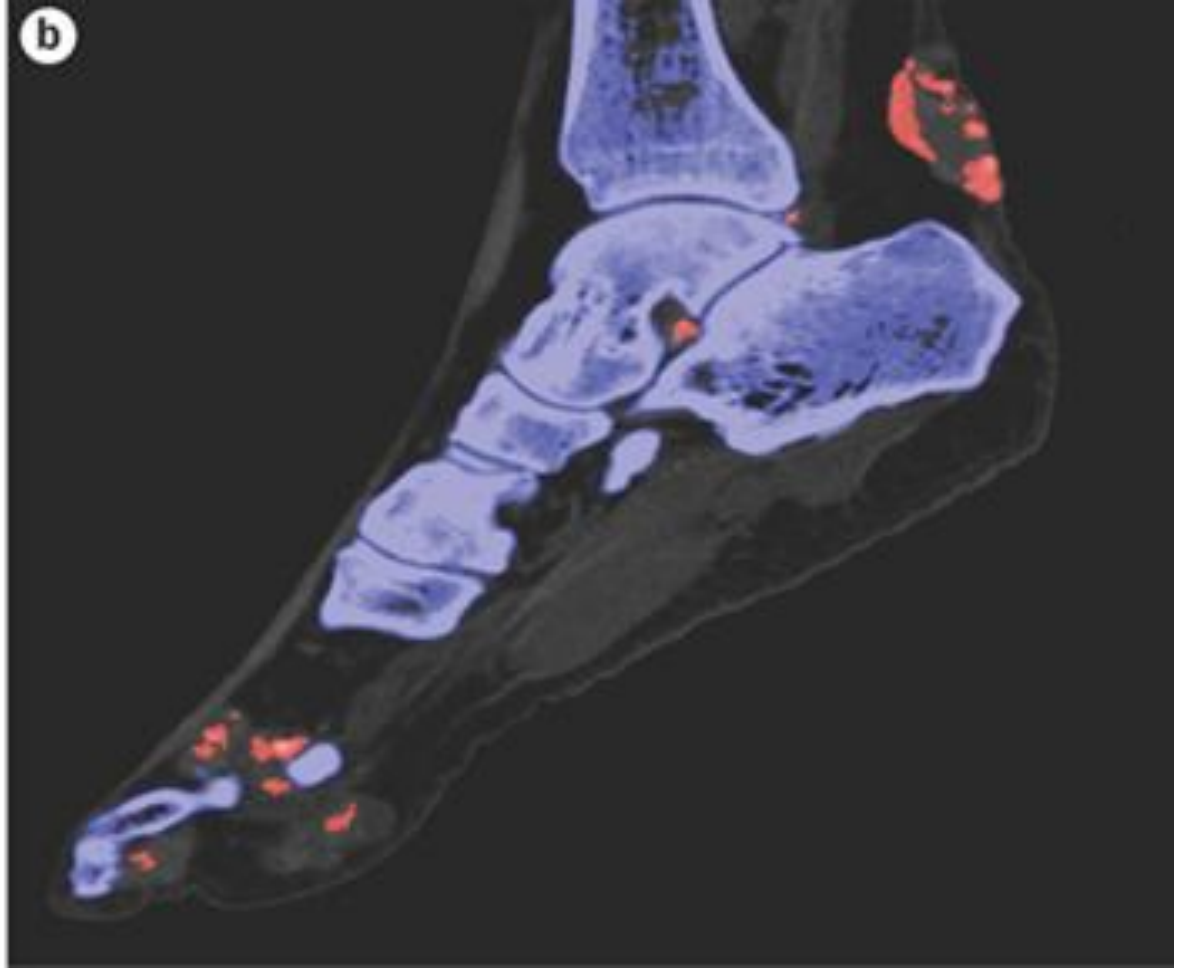
- Renal uric acid hypoexcretion:
 - Multifactorial
 - Genetics
 - Mutations in genes that encode ion transporters
 - Role in urate transport in kidney
 - High alcohol consumption
 - Decreased glomerular filtration rate
 - Medications
 - Diuretics
 - Low-dose aspirin

Crystal formation:

- Urate concentration increases as there is an imbalance between production and excretion
- Saturation level in serum
 - Crystals form above serum urate level of 0,425 mmol/l
- Crystal growth is promoted by macromolecules, such as collagen and proteoglycans

Tophus formation

- Cooler temperature than surrounding tissue
- Undervascularised tissue in synovial joints
- Early tophus development can be seen by dual-energy CT



Spectrum of clinical pictures in gout

Asymptomatic hyperuricaemia:

- Elevate urate, without gout
- Risk of developing gout increases with increasing urate levels
- Minority hyperuricaemics develop gout

Asymptomatic hyperuricaemia

- ↑ s-urate concentrations without symptoms
- Crystals found in joints without symptoms

Acute gouty arthritis:

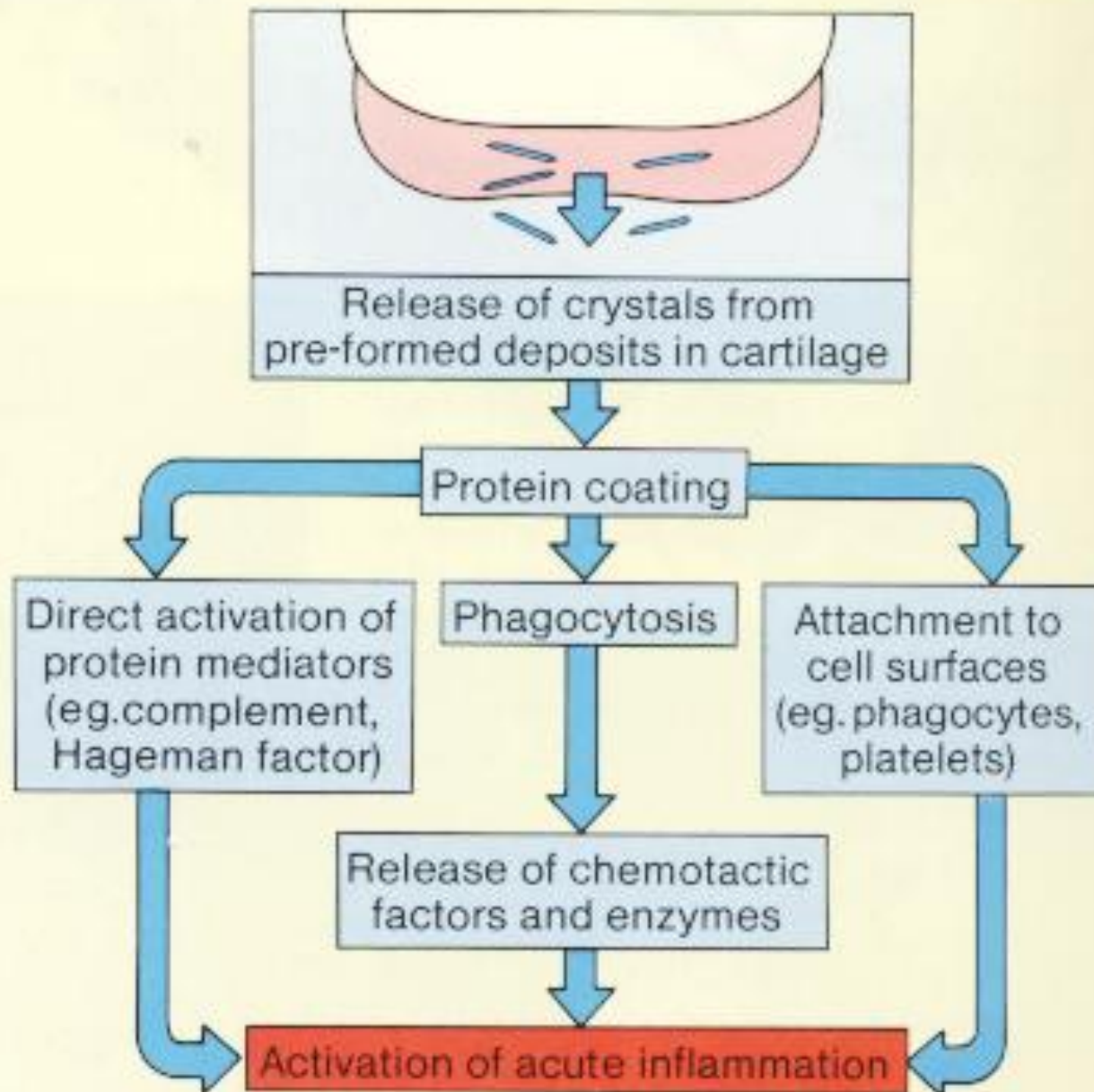
- Recurrent attacks of a severe, acute arthritis associated with monosodium urate monohydrate (MSU) crystals in the synovial fluid
- Usually monoarticular, later in the course of the disease can be polyarticular
- Joints of the lower body: 90% will have attack in 1st MTP joint
- In previously damaged joints
- Attacks initially infrequently, later more frequent and severe

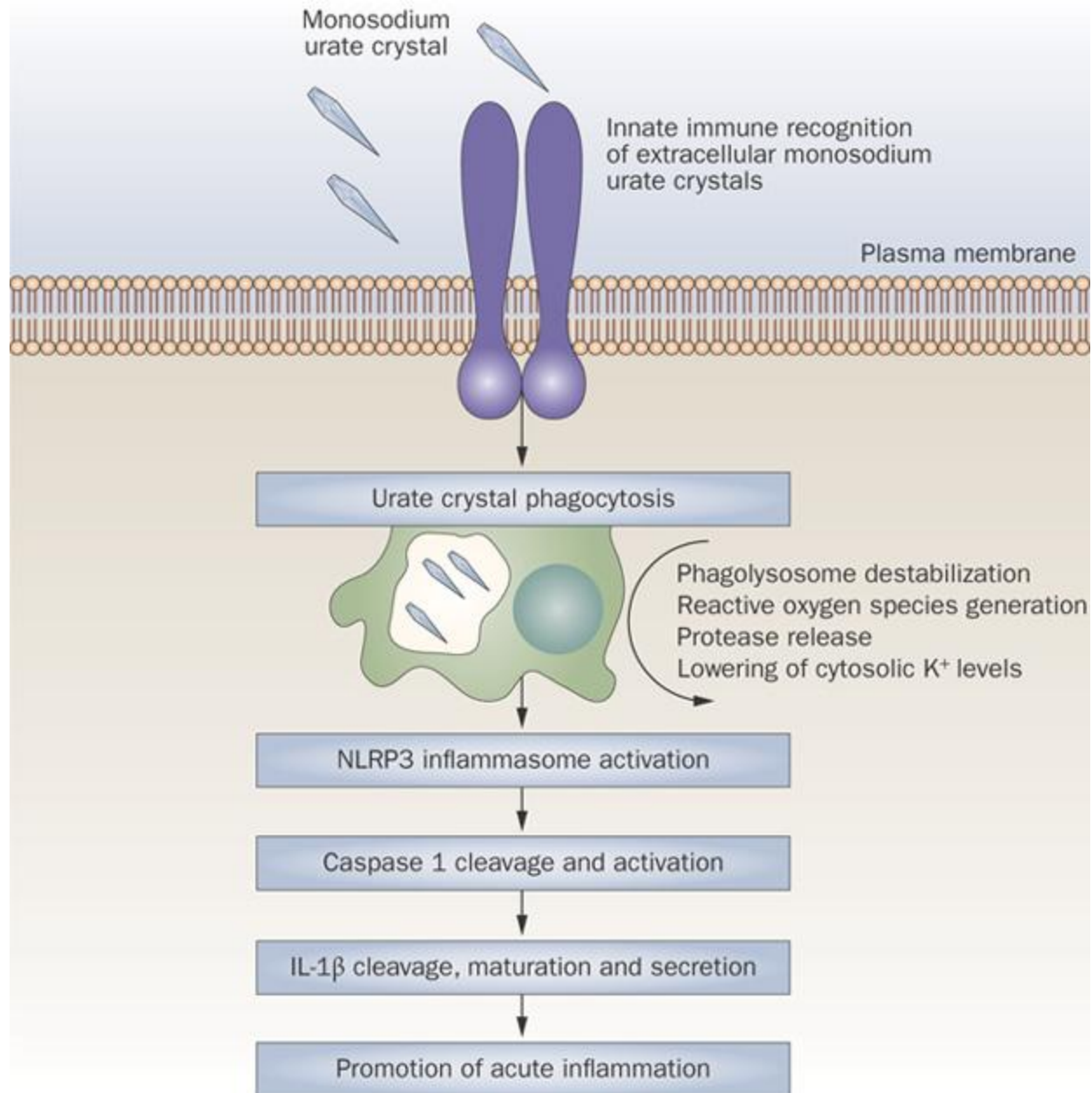
Precipitating factors:

- Trauma
- Alcohol excess
- Surgery
- Dietary excess
- Hemorrhage
- Venisection
- Infections
- Radio- and chemotherapy
- Certain drugs:
 - Diuretics, IV heparin, Cyclosporin

Acute arthritis

- Crystals are liberated into a joint
- Interact with complement components and bind messenger proteins
- Chemotaxis of polymorphs
- Phagocytosis of the crystals
- IgG coat is removed and lysis of the cell occurs
- Inflammatory mediators are released:
 - Prostaglandins
 - Leukotriene B4
 - Oxygen radicals
 - Hageman factor
 - Classical Complement pathway: C3a and C5a





Clinical picture: Acute Gout



The end of the attack:

- Increased vascular permeability
- Larger protein molecules, esp apo- β -containing lipoproteins enter the synovial fluid
- Forms an additional protein coat
- Inhibits phagocytosis

Diagnosis

- Serum urate unreliable during acute attack
- Intracellular urate
- Rule out sepsis



After the acute attack:

- Intercritical gout:
 - Asymptomatic

Gout arthritis

- Most joints can be involved including SI and manubriosternal joint
- Tophi in surface of the cartilage, deeper layers and synovium
- Cartilage breaks away from bone
- Secondary osteoarthritis







Chronic tophaceous gout:

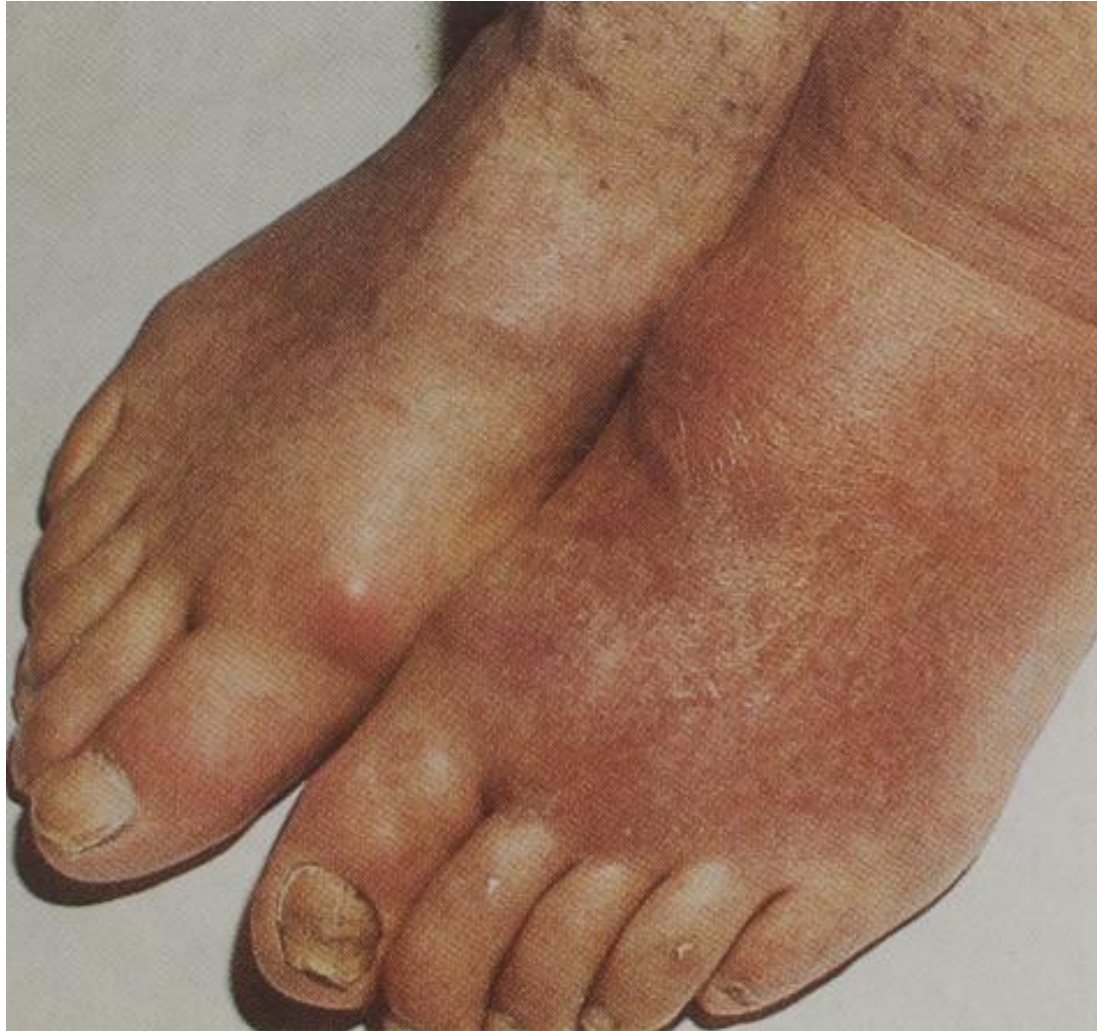
- Collections of MSU crystals or tophi in the tissues
- Fibrous tissue and fibrocartilage
 - Helix of ear, Overlying elbows or fingers, tendons, skin
- Stellate bundle of crystal deposit in tissues
 - Surrounded by histiocytes and multinucleated giant cells
 - Peripheral proliferation of fibroblasts
- Multicentric
- Dystrophic calcification

Gout tofi





Gout cellulitis



Renal disease

- Gouty nephropathy:
 - renal disease due to crystal deposition in the kidney.
- Uric acid urolithiasis or kidney stones.

The
Gout Remedy
Report

Cure
Your
Gout
Using a
**Natural
Home
Remedy...**



www.CureYourGout.com

Treatment of Gout

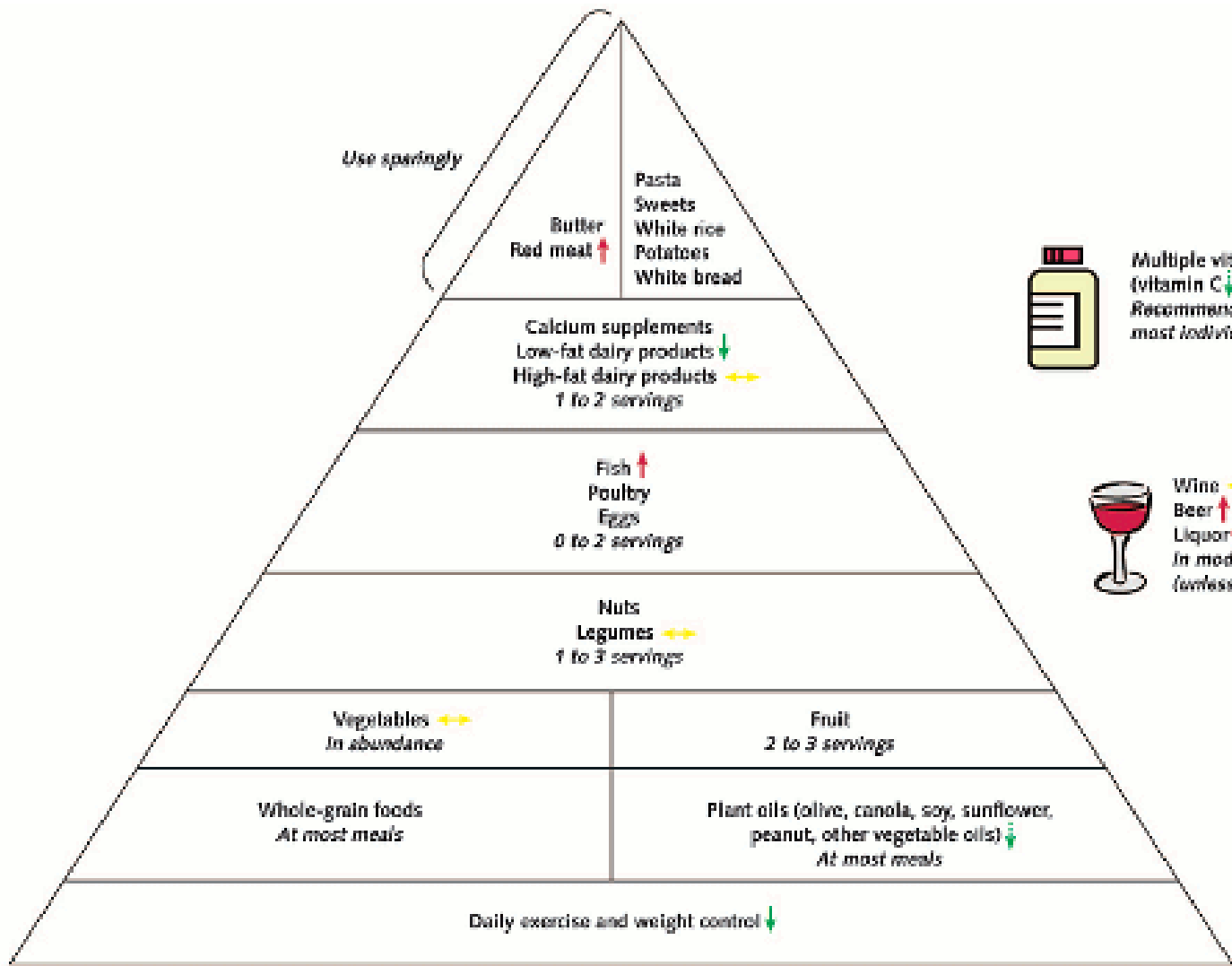
- Control the acute attack
- Decrease urate

Acute attack

- Treat symptoms
 - Colchicine
 - NSAIDs
 - Corticosteroids?

Further management

- Lifestyle change
 - Purine free diet lowers urate by 10%
 - Treat metabolic syndrome



Use sparingly

Butter
Red meat ↑

Pasta
Sweets
White rice
Potatoes
White bread

Calcium supplements ↓
Low-fat dairy products ↓
High-fat dairy products ↔
1 to 2 servings

Fish ↑
Poultry
Eggs
0 to 2 servings

Nuts
Legumes ↔
1 to 3 servings

Vegetables ↔
In abundance

Fruit
2 to 3 servings

Whole-grain foods
At most meals

Plant oils (olive, canola, soy, sunflower,
peanut, other vegetable oils) ↓
At most meals

Daily exercise and weight control ↓



Multiple vitamins
(vitamin C) ↓
Recommended for most individuals



Wine ↔
Beer ↑↑
Liquor ↑
*In moderation
(unless contraindicated)*

Urate lowering treatment

- Reduce crystal load
- Not during the acute attack
- Keep serum concentration constant
- Serum urate below level of crystal formation

Urate lowering treatment

- Allopurinol
- Probenecid

- Must prevent acute attacks:
 - NSAIDs
 - Colchicine

Treat urate to target:

- < 0.36mmol/l
- Dose of allopurinol/ probenecid adjusted to achieve urate target
- Reasons for treat to target
 - Reduce acute attacks
 - Reduce tophus size
 - Depletes crystal stores in synovium
 - Improves renal function
 - Slows down progression of renal disease

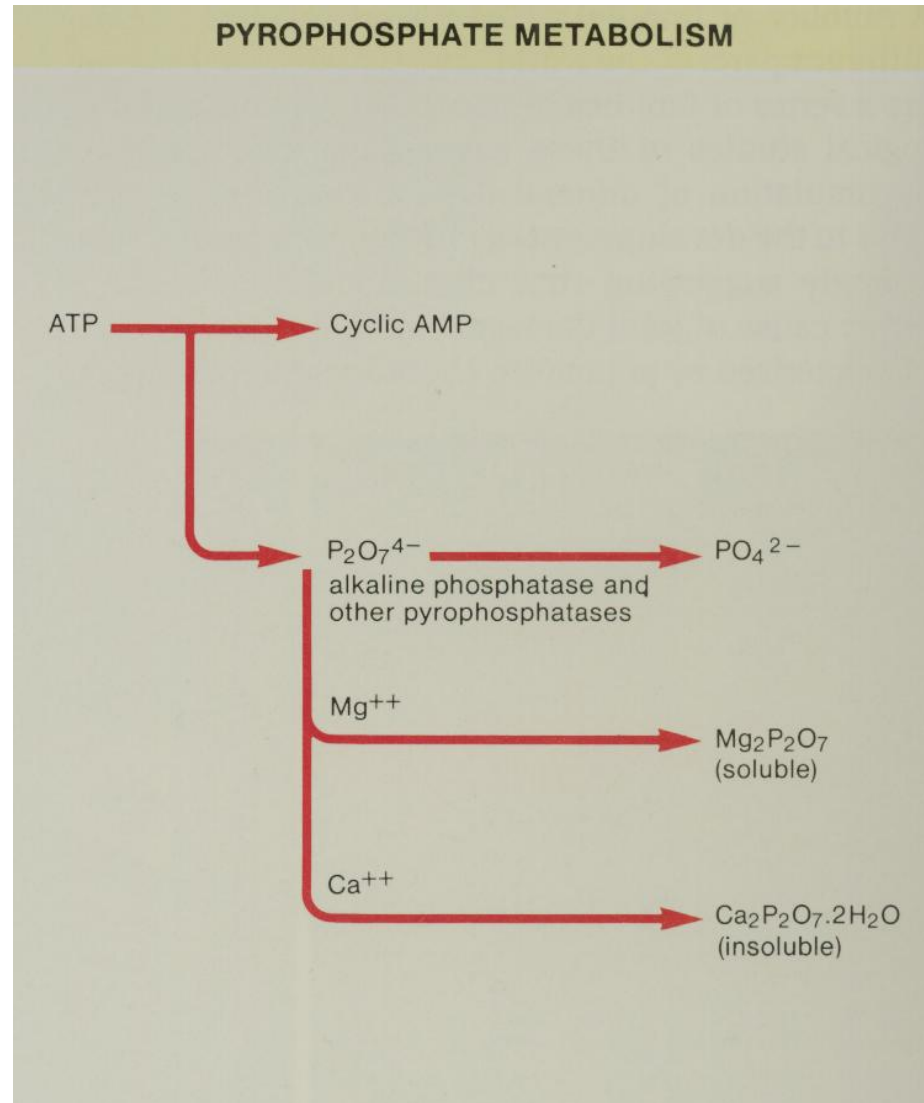
New treatments for gout

- Febuxostat
 - Selective xanthine oxidase inhibitor
- Pegloticase
 - Pegylated uricase
 - Very rapid reduction of tophi

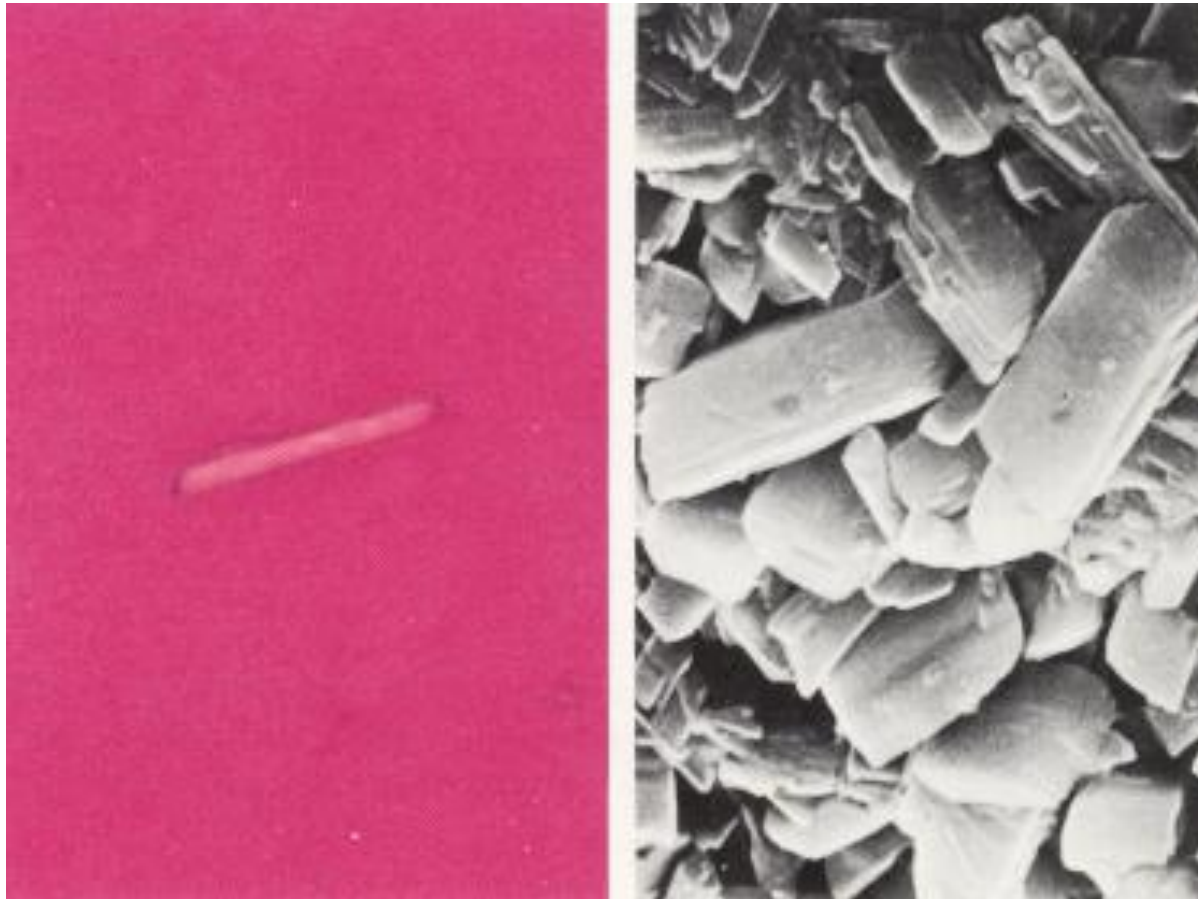
Crystals found in joint tissues

- Monosodium urate monohydrate
- Calcium Pyrophosphate dihydrate
- Basic Calcium Phosphates
- Corticosteroid esters
- Cholesterol crystals

Calcium pyrophosphate deposition (CPPD) disease



Calcium Pyrophosphate Dihydrate (CPPD) Crystals



Classification of CPPDD:

- **Familial in 1%**
- **Sporadic and related to aging**
- **Secondary 10%**

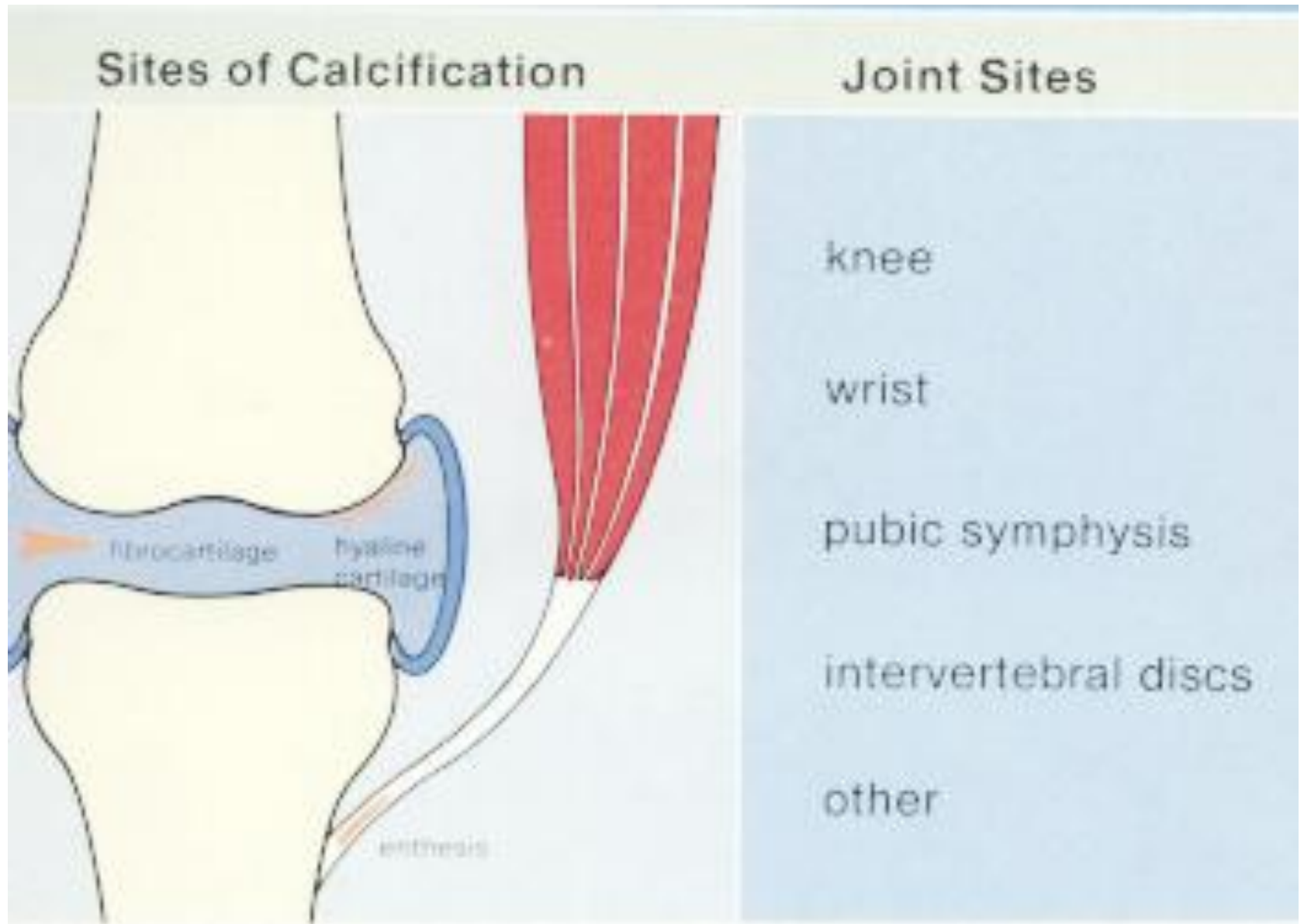
Secondary

- Association strong:
 - Hyperparathyroidism
 - Hemochromatosis
 - Hypomagnisaemia
- Association weaker
 - OA
 - Hypermobility
 - Hypophosphatasia
 - Ochronosis
 - Hypothyroidism
 - Pagets's
 - Acromegaly
 - Diabetes mellitus
 - Gout
 - Amyloid

Spectrum of disease:

- Acute arthritis
- Chronic inflammatory joint disease
- Osteoarthritic and RA-like disease
- Chondrocalcinosis of the spinal joints, ligaments, tendons and minisci

Chondrocalcinosis



Diagnosis of CPPDD

- Demonstration of crystals by definitive means
- Presence of typical calcifications in X-rays
- Acute arthritis, especially of the knees or other large joints, with or without hyperuricaemia

Diagnosis continued:

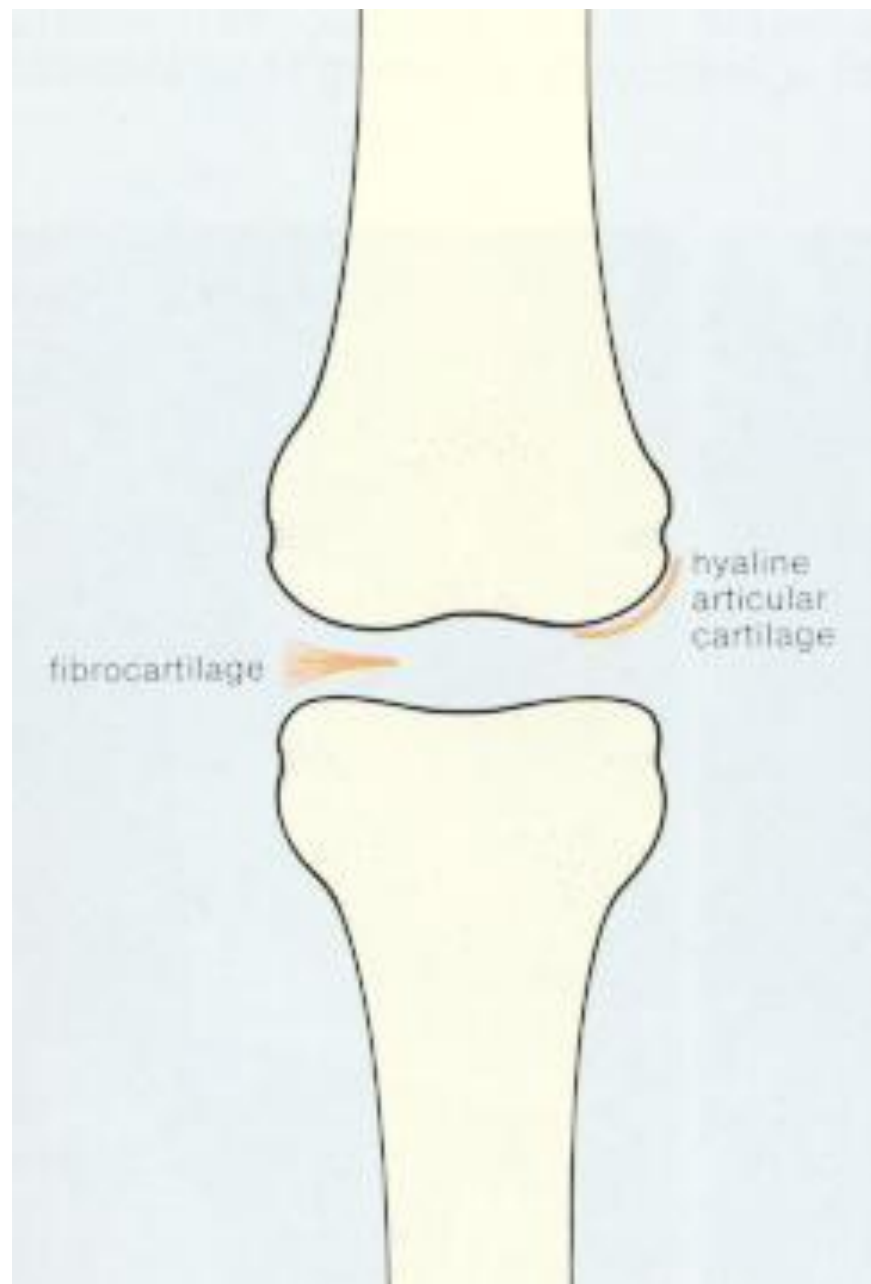
- Chronic arthritis, especially with acute exacerbations with the following features:
 - Uncommon site for primary osteoarthritis- wrist, MCP, elbow, shoulder
 - Radiological: radiocarpal or patellofemoral joint space narrowing, especially if isolated (patella wrapped around femur)
 - Subchondral cysts
 - Severe degeneration – progressive, with subchondral bony collapse and fragmentation and intraarticular radiodense bodies
 - Osteophyte formation- variable and inconstant
 - Tendon calcification
 - Axial skeleton involvement

Clinical picture

- Type A: Pseudogout
- Type B: Pseudorheumatoid arthritis
- Type C and D: Pseudo-osteoarthritis
- Type E: Lanthanic (Asymptomatic)
- Type F: Pseudoneuropathic joints
- Monoarthropathy
- Traumatic arthritis
- Pseudoankylosing spondylitis
- Solitary tophaceous deposit

Clinical picture of CPPDD

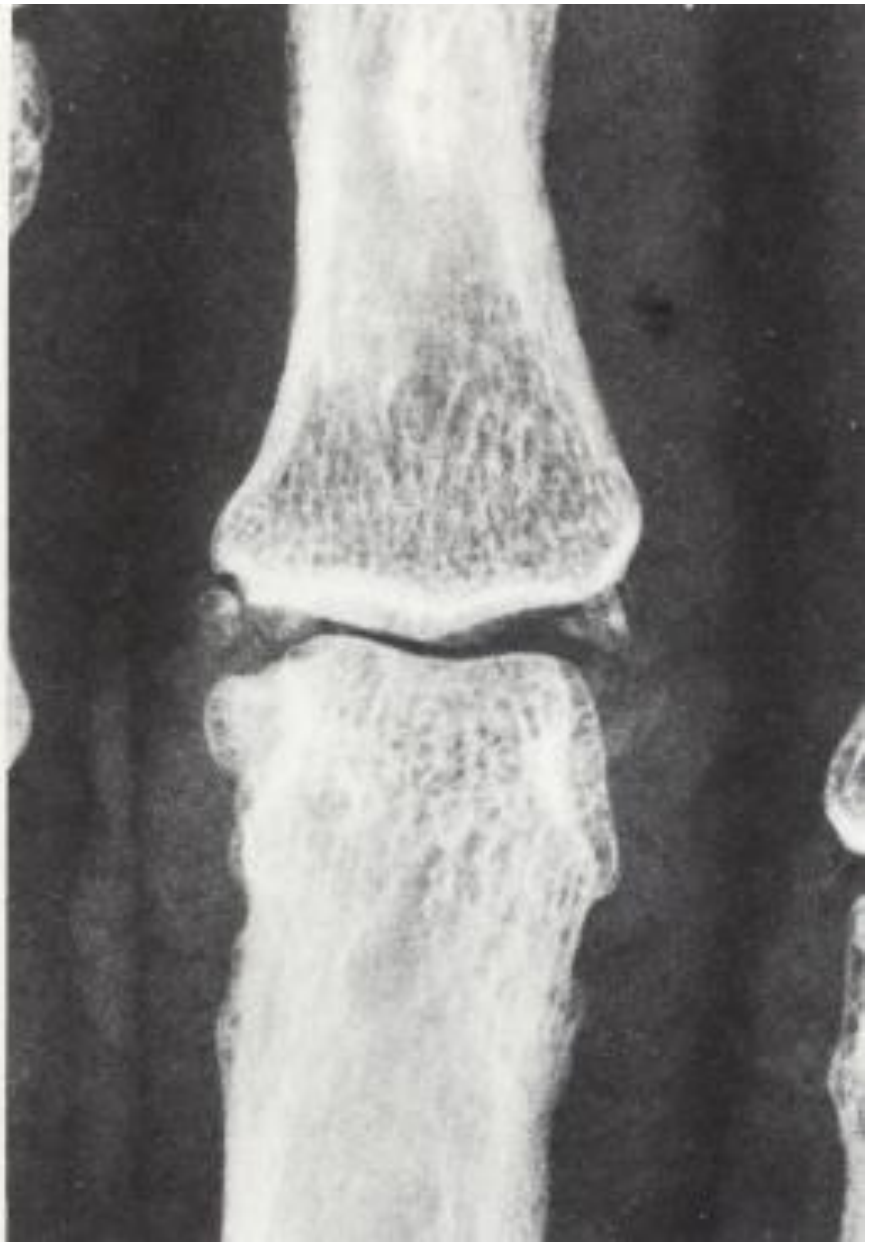






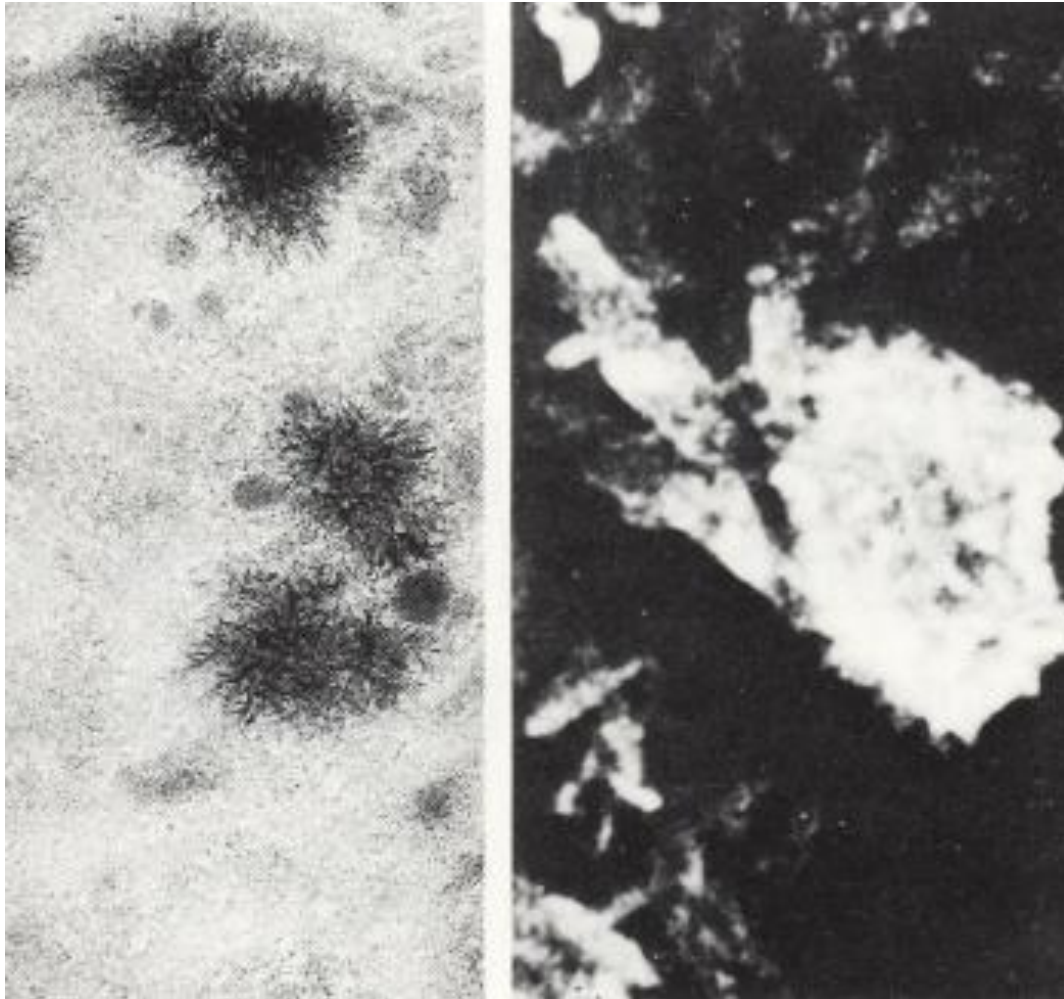








Basic Calcium Phosphate crystals



Basic Calcium Phosphate crystal deposition disease (Hydroxyapatite)

- Apatite
- Octacalcium phosphate
- Tricalcium phosphate
- Several patterns of disease in joints and periarticular structures
- Acute, subacute and chronic conditions
- Common areas of involvement:
 - Shoulder
 - Greater trochanter of the hip
 - Lateral epicondyle of the elbow
 - Tendons around the wrist
 - Tendons at the lateral and medial aspects of the knee

Patterns of disease

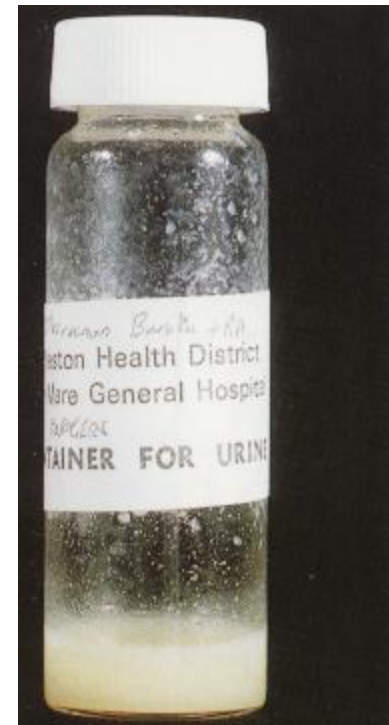
- Calcific periarthrititis
 - Unifocal, multifocal, familial
- Calcific tendonitis and Bursitis
- Intra-articular BCP Arthropathies
 - Acute (gout-like) attacks
 - Milwaukee shoulder/knee syndrome
 - Erosive polyarticular disease
 - Mixed crystal deposition disease (BCP & CPPD)

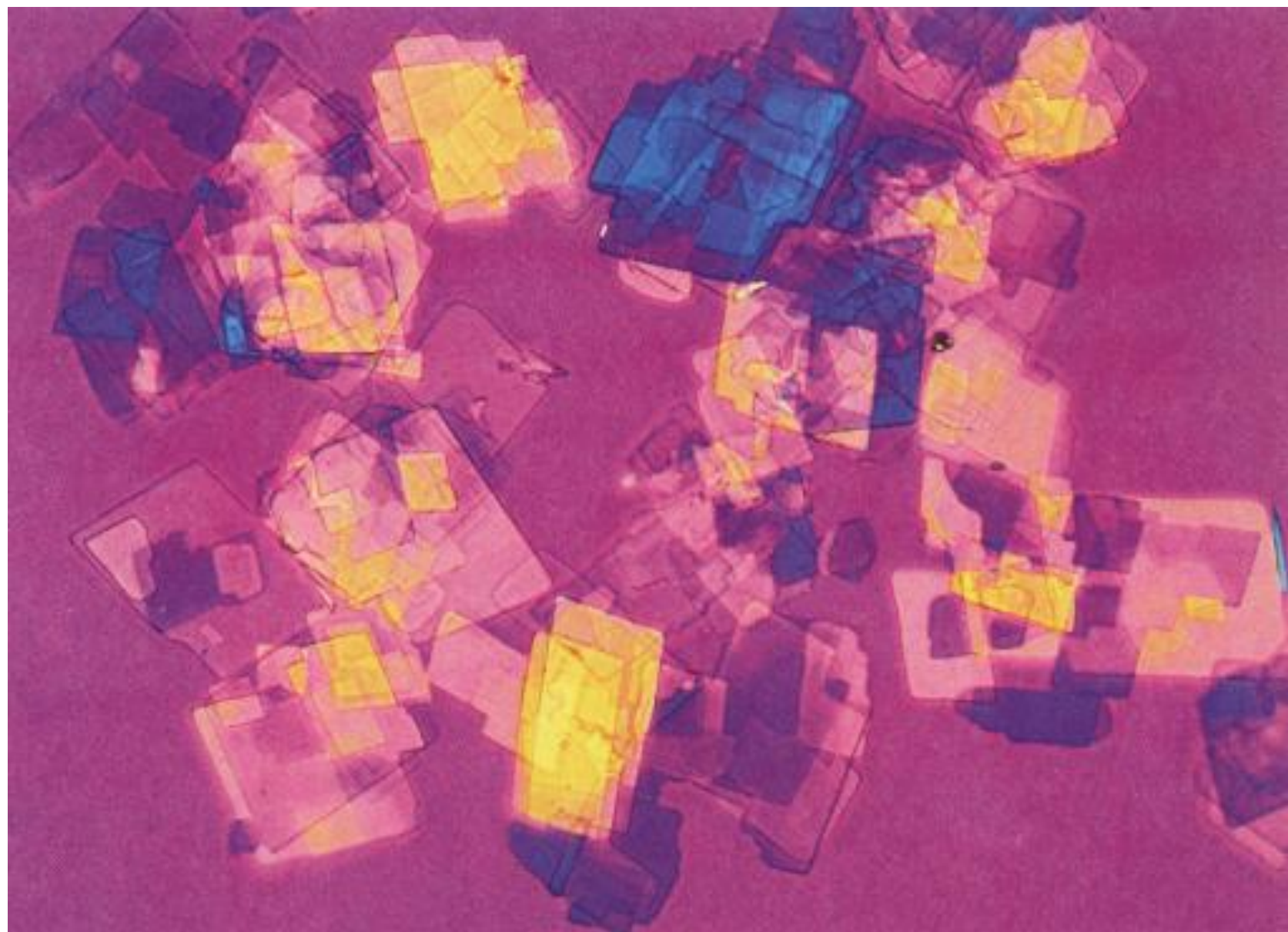
Patterns of BCP disease II

- Secondary BCP Crystal arthropathy/
periarthropathy
 - Chronic renal failure
 - Collagen diseases with calcinosis
 - Post local corticosteroid injection
- Tumoral Calcinosis
 - Hyperphosphatemic
 - Nonhyperphosphatemic

Other crystals

Cholesterol crystals





Treatment of other crystal arthropathies:

- Symptomatic

