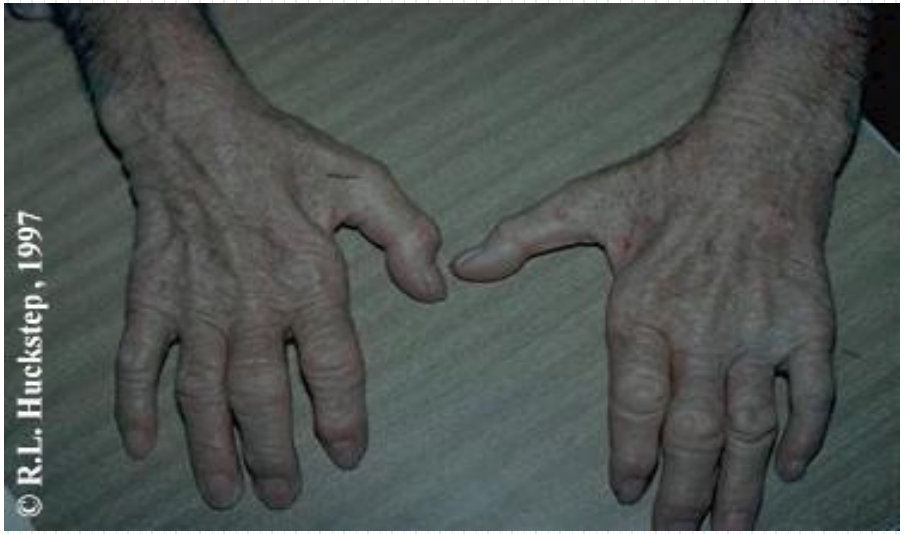
OBAT NYERI SENDI

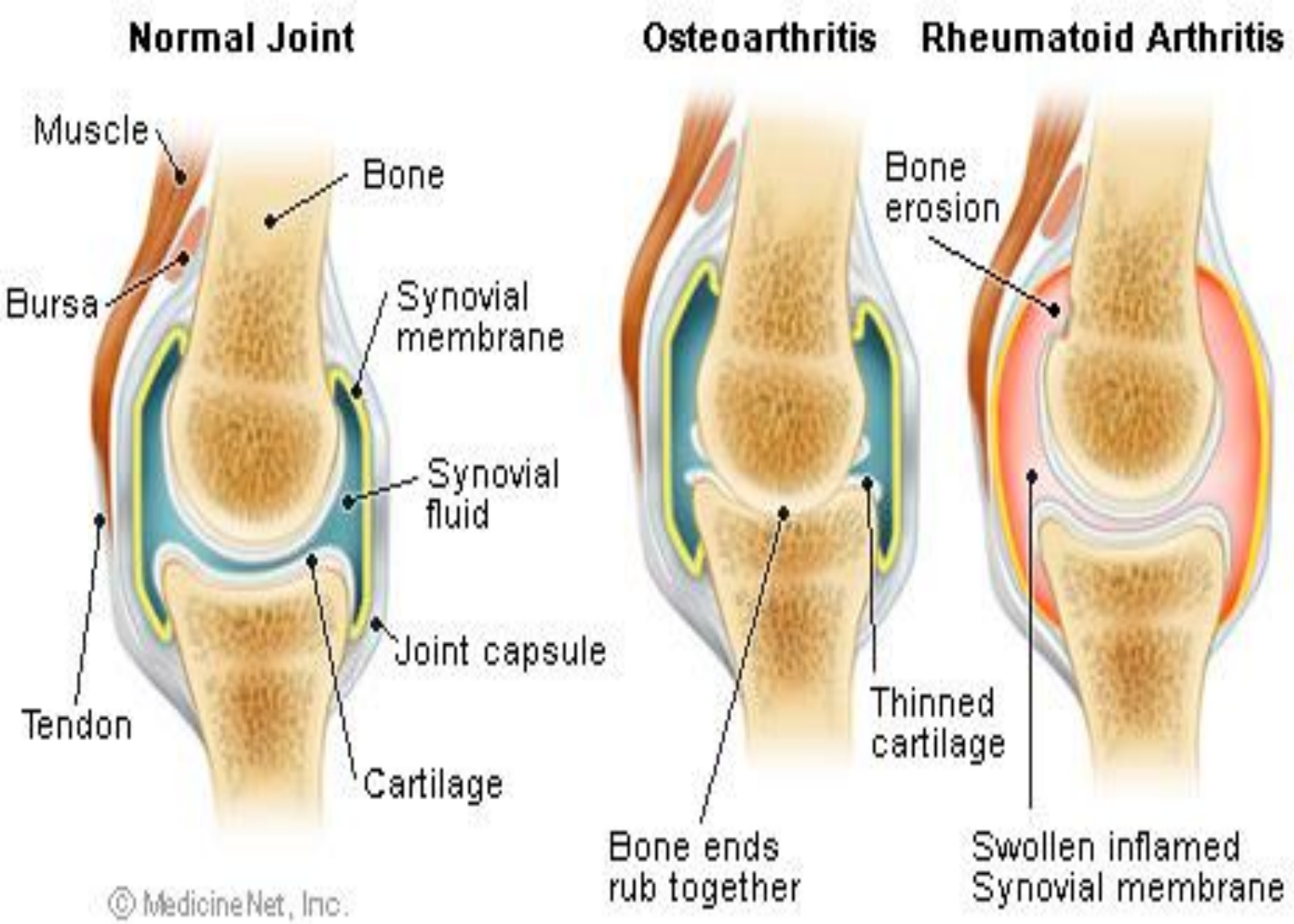
OSTEOARTHRITIS

RHEUMATOID ARTHRITIS

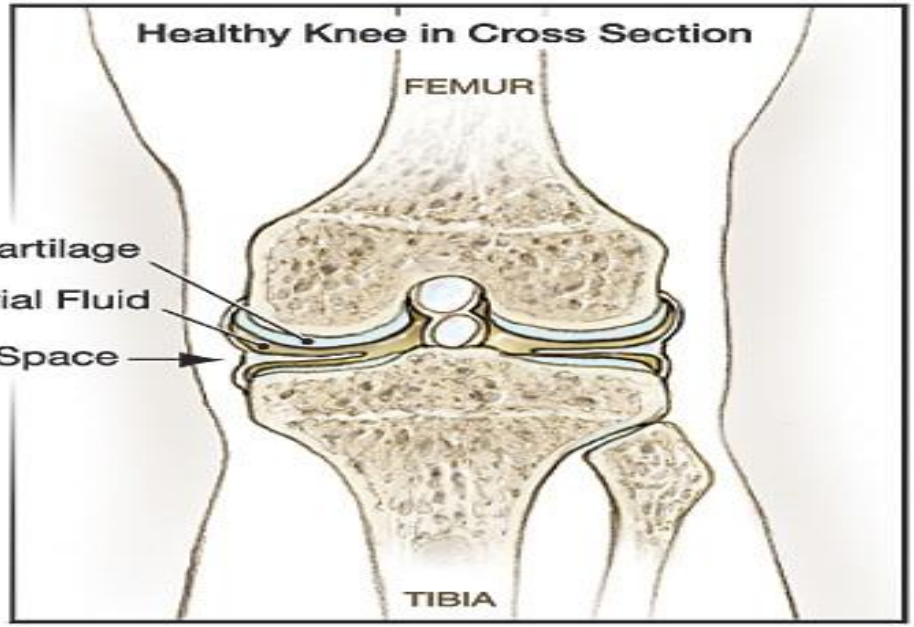
GOUT ARTHRITIS

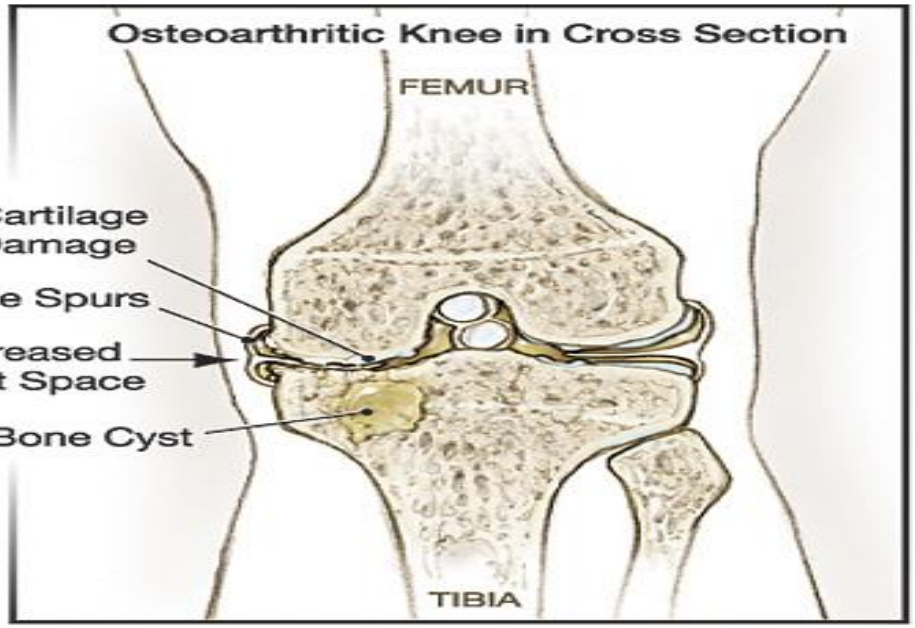
OSTEOARTHRITIS



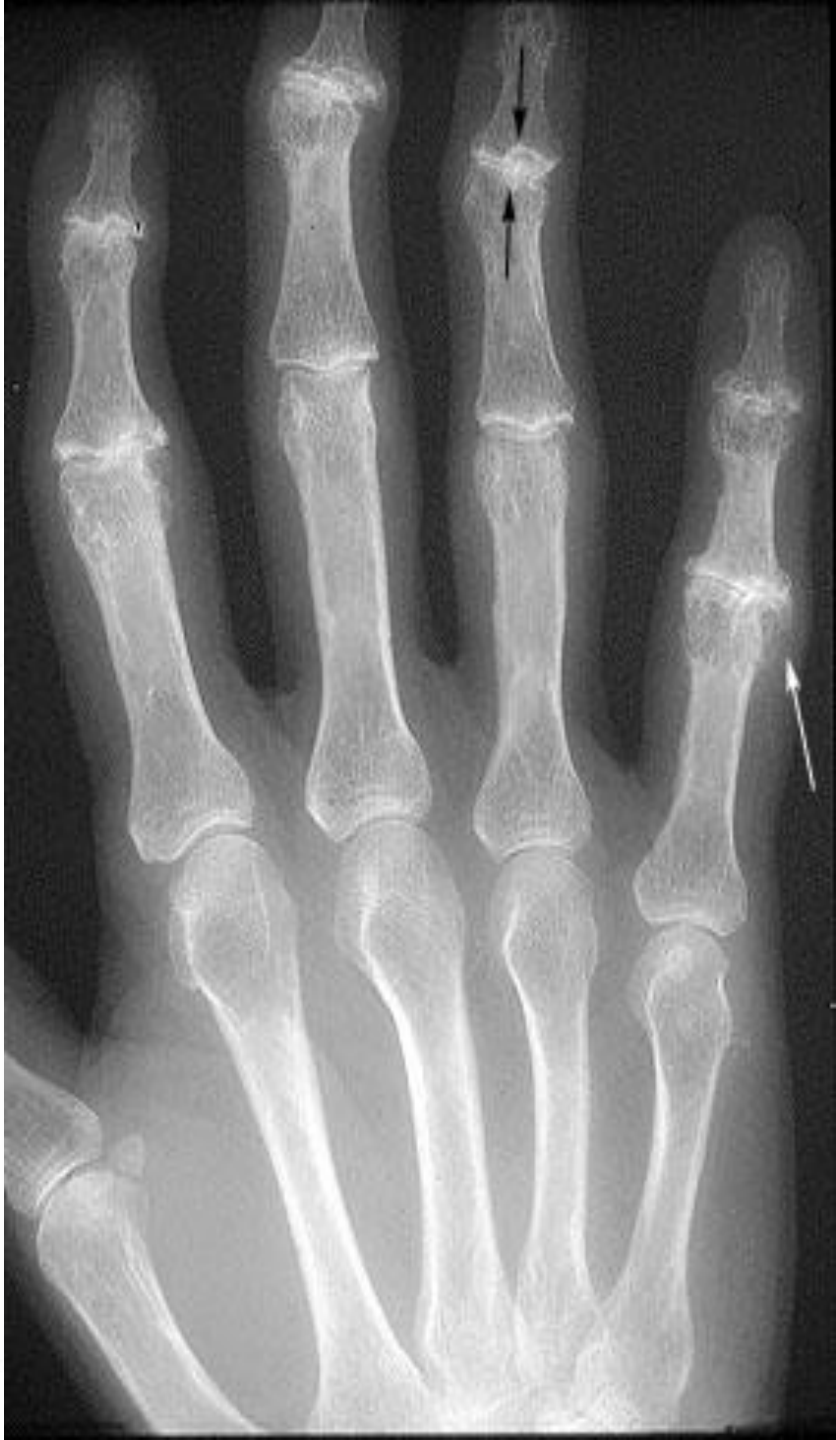


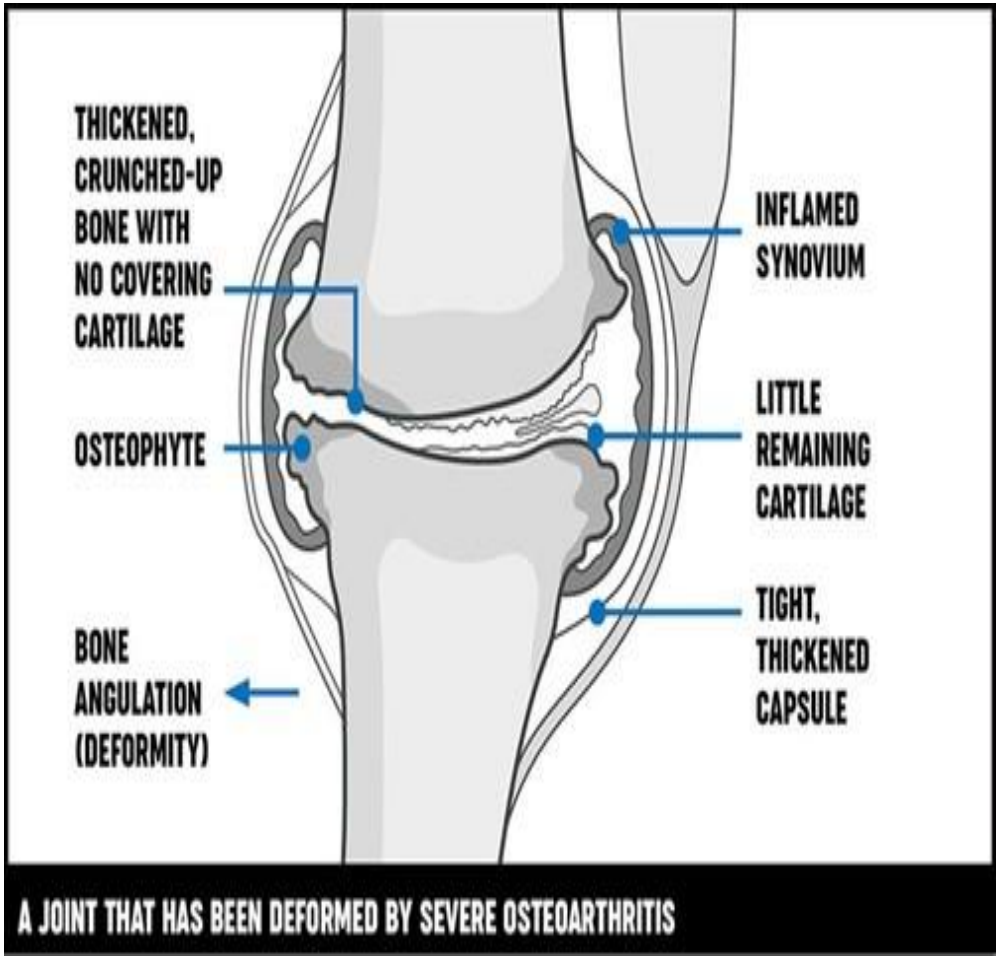
Normal and Arthritic Joints

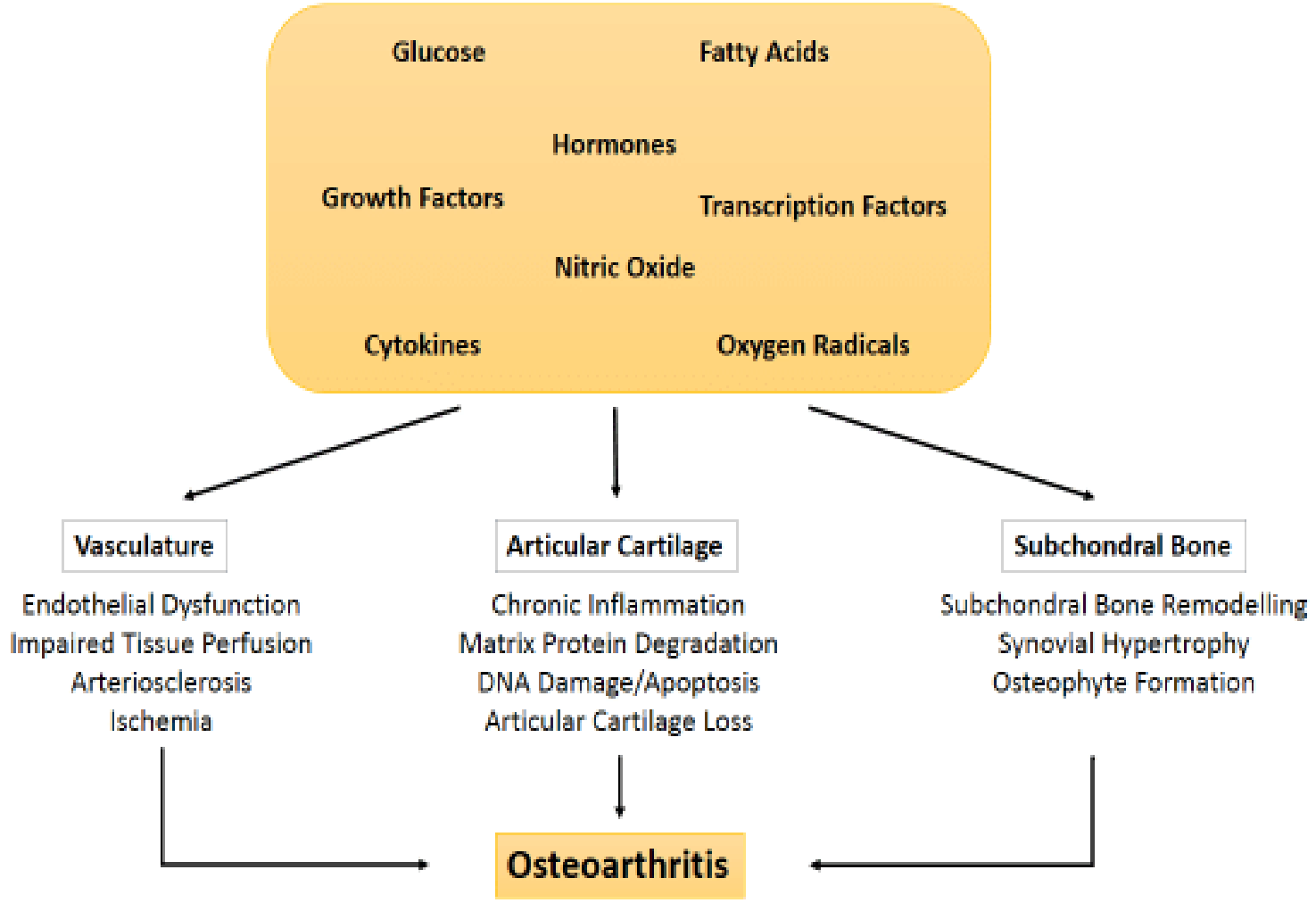

Healthy Knee in Cross Section
FEMUR
Cartilage
Synovial Fluid
Joint Space
TIBIA


Osteoarthritic Knee in Cross Section
FEMUR
Cartilage Damage
Bone Spurs
Decreased Joint Space
Bone Cyst
TIBIA

C. Lynn




THICKENED, CRUNCHED-UP BONE WITH NO COVERING CARTILAGE
OSTEOPHYTE
BONE ANGULATION (DEFORMITY)
INFLAMED SYNOVIUM
LITTLE REMAINING CARTILAGE
TIGHT, THICKENED CAPSULE
A JOINT THAT HAS BEEN DEFORMED BY SEVERE OSTEOARTHRITIS


Glucose
Fatty Acids
Hormones
Growth Factors
Transcription Factors
Nitric Oxide
Cytokines
Oxygen Radicals
Vasculature
Endothelial Dysfunction
Impaired Tissue Perfusion
Arteriosclerosis
Ischemia
Articular Cartilage
Chronic Inflammation
Matrix Protein Degradation
DNA Damage/Apoptosis
Articular Cartilage Loss
Subchondral Bone
Subchondral Bone Remodelling
Synovial Hypertrophy
Osteophyte Formation
Osteoarthritis

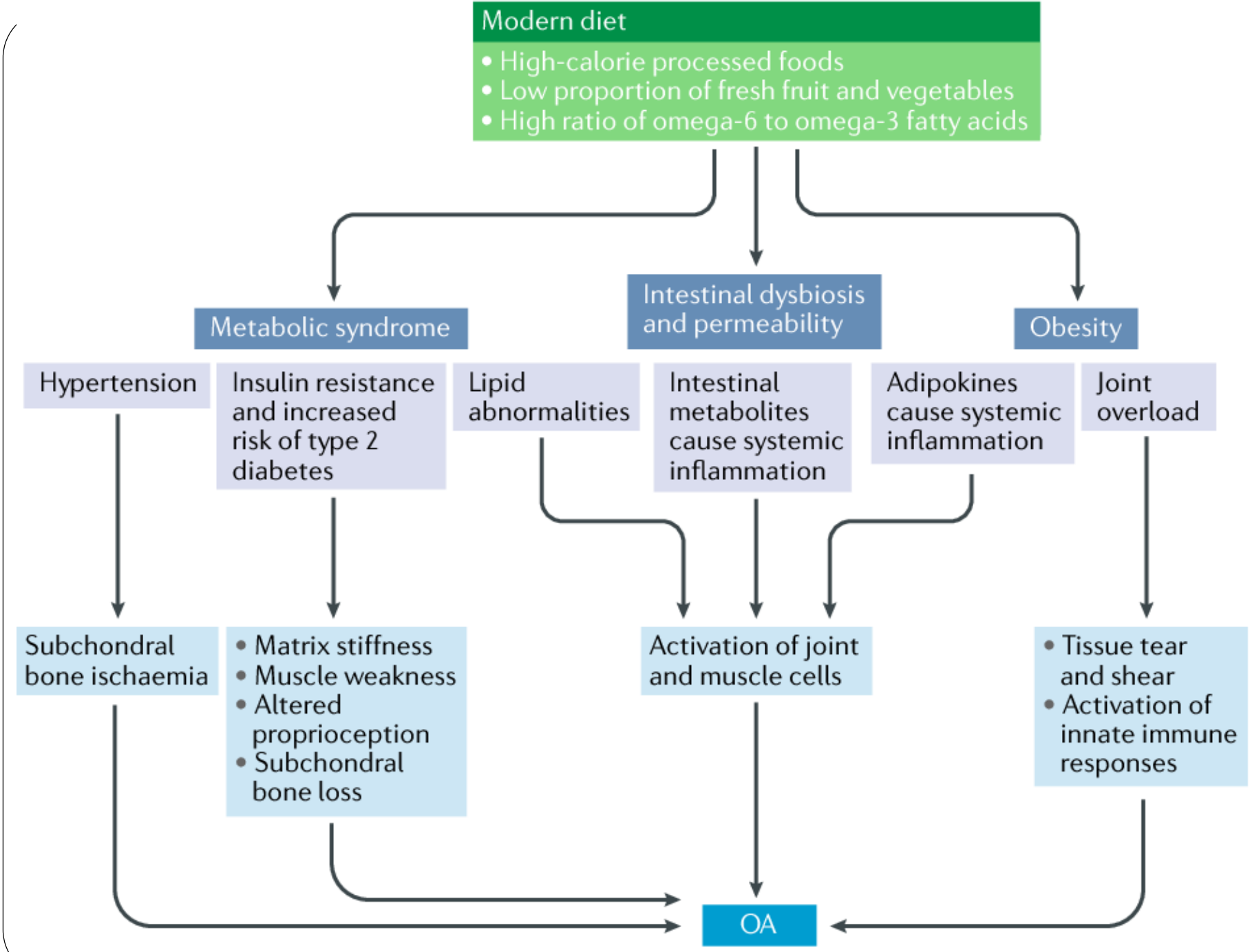


Fig. 3 | **Diet as a mismatch factor.** The deleterious effects of modern diets on osteoarthritis (OA) arise

Treatment of OA

- Rapid acting drugs

1. Analgetic drugs

- Paracetamol, metamizol
- Nonsteroidal antiinflammatory drugs
- Weak opioids – tramadol

2. Topical transdermal treatment

- NSAID (diclofenac, ketoprofen)
- Irritants (capsaicin, menthol)

3. Steroid antiflogistic drugs (corticoids) intra-articular administration

- triamcinolone, betametazone
- avoid frequent administration

- Slowly acting drugs

chondroprotectives

1. Disease modifying drugs (DMOAD)?

- Glucosaminsulphate
- Chondroitinsulphate
- Hyaluronic acid

No proven agents that reverse osteoarthritis (alternative to pharmacotherapy in advanced stages of the disease is surgery).

Osteoarthritis

A chronic degenerative joint disorder with the characteristics of loss of articular cartilage, osteophytes formation, change in the synovium and joint capsule[1]

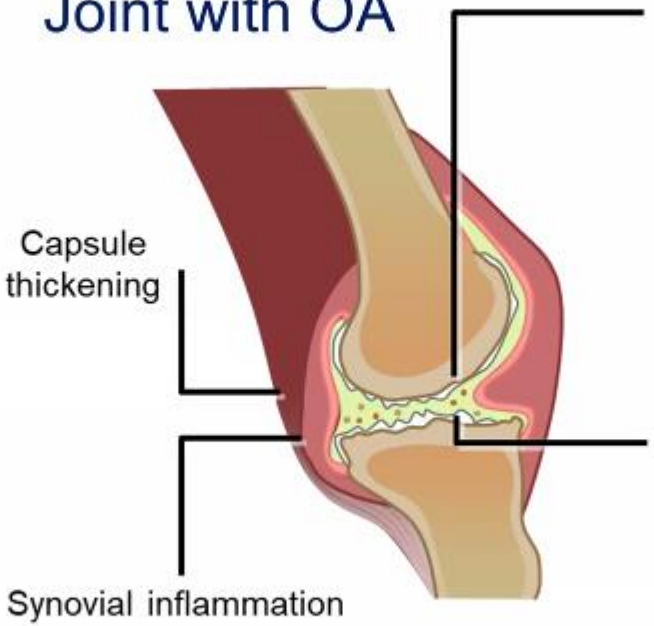
1. No curative treatment has been found yet currently[2]
2. Management consists of non-pharmacological therapy, pharmacological therapy[3] and surgical approach[4]
3. Therapeutic goals are:
   - Pain reduction/management [5,6]
   - Improvement or preservation of mobility[5]
   - Prevention of functional impairment[5,6]
   - Improvement in Quality of Life[5,6]
   - Prevention from toxic effects of medications[6]

1. GS Man et al. *Journal of Medicine and Life. 2014;(7) 1:*37-41
2. Anandacoomarasamy A and March Lyn. Ther Adv Musculoskel Dis. 2010; 2(1) 1728
3. Hochberg MC et al. *Arthritis Care Res* 2012;64:465-74
4. Glyn-Jones S et al. *Lancet* 2015; [Published Online].
5. AHRQ Publication No. 17-EHC011-EF May 2017
6. Coniam Stephen, Mendham Janine. 2016;220/ access online 2 Jul 2020 (https://books.google.com.sg/books?id=JSr5BQAAQBAJ&pg=PA220&lpg=PA220&dq=OA+goals+Avoid+the+toxic+effects+of+the+drug&source=bl&ots=-aXNGaW8ca&sig=ACfU3U0U-GYnuyi_IkmQo8Rxv3PzFRIQNw&hl=en&sa=X&ved=2ahUKEwi1jNPT-63qAhWHYysKHa15C8EQ6AEwDHoECAwQAQ#v=onepage&q&f=true

Characteristics

Normal joint

Joint with OA



Early OA

Articular cartilage surface irregularity

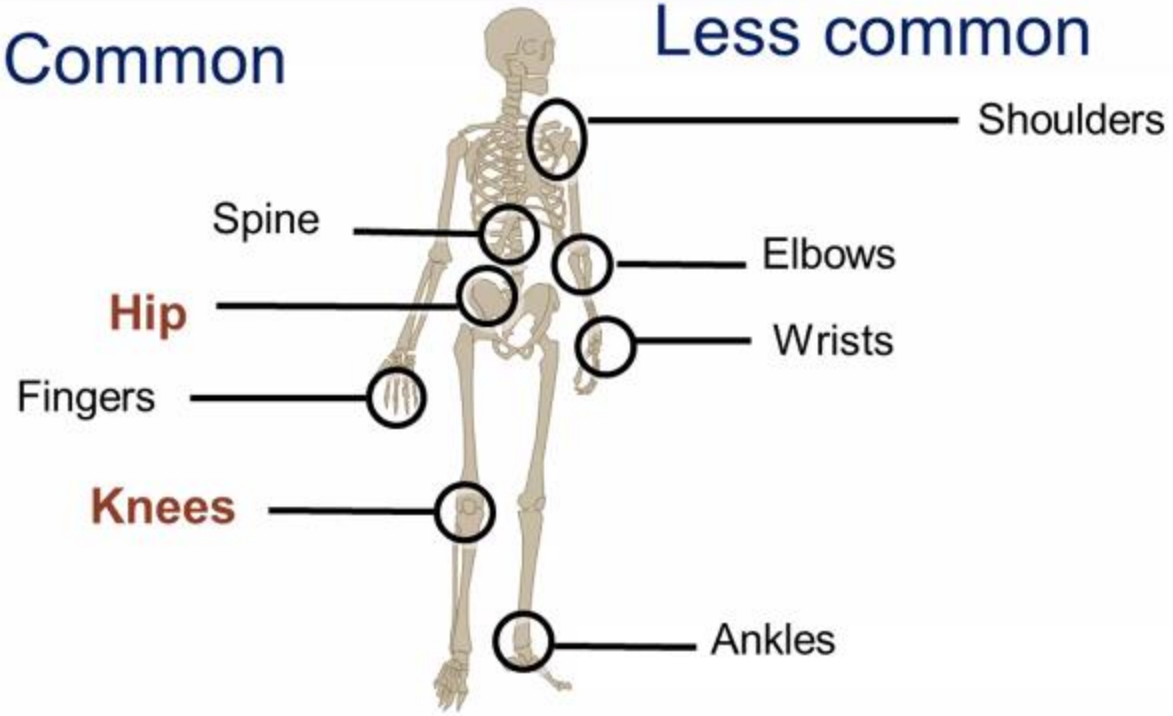
Superficial cleft within tissue

Alter proteoglycan distribution

- Late OA
- Deepened cleft
- Increase in surface irregularities
- Articular cartilage ulseration
- MMP degrades proteoglycans and collagen

1. Dieppe P. Rheumatology. London: Mosby, 1998. 1.1–1.2.
2. Herfindal E, Gourley D. Baltimore: Williams and Wilkins, 1996. 6th ed.

Joint involvement



Knee and hip OA has the most incidence,[1] affecting 10% males and 18% females > 60 years old[2]

DALYs, disability-adjusted life years; OA, osteoarthritis.

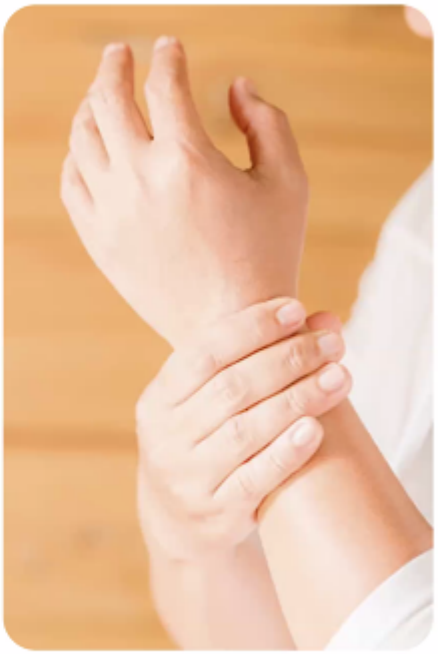
1. Cross M et. al. Ann Rheum Dis 2014;73:1323-30;
2. 2Glyn-Jones S et al. Lancet 2015; [Published Online].

Osteoarthritis of the Hand

Classification Criteria For Osteoarthritis Of The Hand

Hand joint, aching, or stiffness and 3 or 4 following features:

- Hard tissue enlargement of 2 or more of 10 selected joints
- Hard tissue enlargement of 2 or more DIP joints
- Fewer than 3 swollen MCP joints
- Deformity of at least 1 of 10 selected joints



The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hand. Arthritis Rheum 1990;33:1601---10

Symptoms and Signs

SYMPTOMS

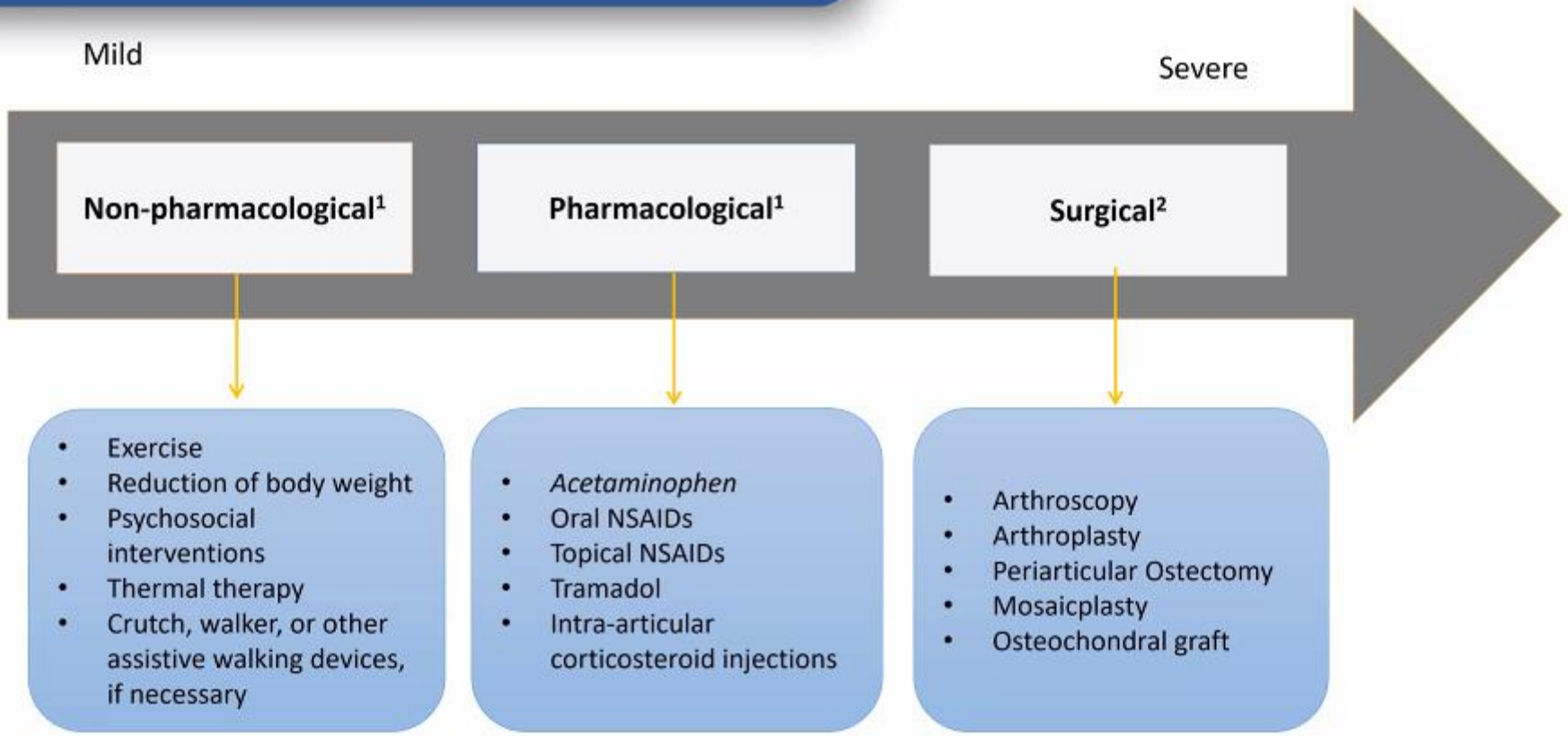
- Joint pain on movement
- Joint stiffness after a period of inactivity
- Decrease in joint function or loss of normal range of movement
- Deformity, swelling, crepitation

SIGNS

- Tenderness on palpation/pressure
- Loss of synovial space
- Bony enlargement/osteophytes
- Crepitation
- Joint deformity (*Heberden's nodes*)

Hunter JD et al. Rheum Dis Clin North Am. 2008; 34(3): 623–643.

Management of osteoarthritis



NSAIDs, non-steroidal anti-inflammatory drugs.

1. Hochberg MC et al. *Arthritis Care Res* 2012;64:465-74
2. Glyn-Jones S et al. *Lancet* 2015; [Published Online].

Osteoarthritis and Cartilage 27 (2019) 1578–1589

Osteoarthritis and Cartilage

OARSI OSTEOARTHRITIS RESEARCH SOCIETY INTERNATIONAL

OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis

R.R. Bannuru † *, M.C. Osani †, E.E. Vaysbrot †, N.K. Arden ‡ §, K. Bennell ‖, S.M.A. Bierma-Zeinstra ¶ #, V.B. Kraus ††, L.S. Lohmander ‡‡, J.H. Abbott §§, M. Bhandari ‖‖, F.J. Blanco ¶¶ ##, R. Espinosa ††† ‡‡‡, I.K. Haugen §§§, J. Lin ‖‖‖, L.A. Mandl ¶¶¶, E. Moilanen ###, N. Nakamura ††††, L. Snyder-Mackler ‡‡‡‡, T. Trojian §§§§, M. Underwood ‖‖‖‖ ¶¶¶¶, T.E. McAlindon †

2019 OARSI Recommendations for Knee OA

OARSI OSTEOARTHRITIS RESEARCH SOCIETY INTERNATIONAL

Table II: Evidence Level-based treatment recommendations for Knee OA

Core (Strong):

Arthritis Education; Exercise Programs with or without Dietary Weight Management.

Level 1A High Consensus (Strong):

Topical NSAID

Level 1B High Consensus (Conditional):

PHARMACOLOGIC

- No comorbidities: Non-selective NSAIDs, Non-selective NSAID + PPI; COX-2 Inhibitors, IACS
- GI comorbidities: COX-2 Inhibitors; IACS, IAHA
- CV comorbidities: IACS, IAHA

NON PHARMACOLOGIC

Aquatic Exercise, Gait Aids, Self-Management Programs

Level 2 Low Consensus (Conditional):

PHARMACOLOGIC

- No comorbidities: IAHA
- GI comorbidities: Non-selective NSAID + PPI

NON PHARMACOLOGIC

Cognitive Behavioral, Therapy with Exercise

GCP Statements (Conditional):

PHARMACOLOGIC

- No comorbidities: IA Treatment
- GI comorbidities: IA treatment, NSAID risk mitigation, pain management program

R.R. Bannuru et al. Osteoarthritis and Cartilage 27 (2019) 1578e1589.

American College of Rheumatology
Empowering Rheumatology Professionals

Arthritis & Rheumatology
Vol. 72, No. 2, February 2020, pp 220–233
DOI 10.1002/art.41142

2019 American College of Rheumatology/Arthritis Foundation Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee

Sharon L. Kolasinski,[1] Tuhina Neogi,[2] Marc C. Hochberg,[3] Carol Oatis,[4] Gordon Guyatt,[5] Joel Block,[6] Leigh Callahan,[7] Cindy Copenhaver,[8] Carole Dodge,[9] David Felson,[2] Kathleen Gellar,[10] William F. Harvey,[11] Gillian Hawker,[12] Edward Herzig,[13] C. Kent Kwoh,[14] Amanda E. Nelson,[7] Jonathan Samuels,[15] Carla Scanzello,[1] Daniel White,[16] Barton Wise,[17] Roy D. Altman,[18] Dana DiRenzo,[19] Joann Fontanarosa,[20] Gina Giradi,[20] Mariko Ishimori,[21] Devyani Misra,[2] Amit Aakash Shah,[22] Anna K. Shmagel,[23] Louise M. Thoma,[7] Marat Turgunbaev,[22] Amy S. Turner,[22] and James Reston[20]

2019 ACR Recommendations for Knee OA

AMERICAN COLLEGE of RHEUMATOLOGY
Empowering Rheumatology Professionals

1. Physical, Psychosocial, And Mind-body Approaches:

- **Strongly recommendation** : Exercise, Self-Efficacy and Self-Management Programs, Weight Loss, Tai Chi, Cane, TF Knee Brace,
- **Conditionally recommendation**: Heat Therapeutic Cooling, Cognitive Behavioral Therapy, Acupuncture; Balance Training, PF Knee Brace, Yoga, RFA

2. Pharmacologic Approaches

- **Strongly recommendation** : Oral NSAIDs, Topical NSAIDs, I-A Steroids (Imaging-Guidance for Hip)
- **Conditionally recommendation :** Acetaminophen, Tramadol, Duloxetine, Topical Capsaicin

Kolasinski SL et al. Arthritis & Rheumatology. 2020; 72(2): 220-233.

Chronic pain as a cause of disability?

- Chronic pain (moderate to severe pain, of 3 or more months duration)[1]
- In the elderly, chronic pain is associated with higher risk of (joint) failure, which may progress to disability[2,3]
- Severity of disability is associated with increase in mortality rate in OA patients[4]

5 of 11 causes of chronic disability (duration → years) worldwide are chronic pain[5]

Condition	Average ranking
Low back pain	1.1
Major depressive disorder	1.9
Iron deficiency anemia	3.3
Neck pain	4.3
COPD	5.8
Other musculoskeletal disorder	5.9
Anxiety disorder	6.4
Migraine	8.9
Diabetes	9.1
Fall	10.1
Osteoarthritis	12.3

COPD, chronic obstructive pulmonary disease.

1. Moore RA et al. Pain Practice. 2014;14:79-94
2. Egermont LH. et al. J Am Geriatr So. 2014;62:1007-16
3. Levelle SG. Et al. JAMA. 2009;302:2214-21
4. Nuesch E et. al. *BMJ* 2011;342:d1165 e91256
5. Vos T et al. *Lancet* 2012;380:2163-96

Benefits and risks of pharmaceutical therapy in pain management

Choice of therapy

Acetaminophen (Paracetamol) – risks exists, but no evidence of benefits[1-3]

- No strong evidence of efficacy in chronic pains
- Higher risk of liver injury compared to NSAIDs

NSAID – risks exists, with few evidence of benefits[4-9]

- Most common risk for "traditional" NSAIDs are GI bleeding
- CV risks are shown to be moderately elevated in RCTs, but otherwise no reports in longitudinal studies
- Other risks, such as kidney failure; therefore, NSAIDs must be avoided in patients with low eGFR
- 49-59% patients who were given NSAIDs reported moderate pain reductions
- 39-44% patients who were given NSAIDs reported substantial benefits

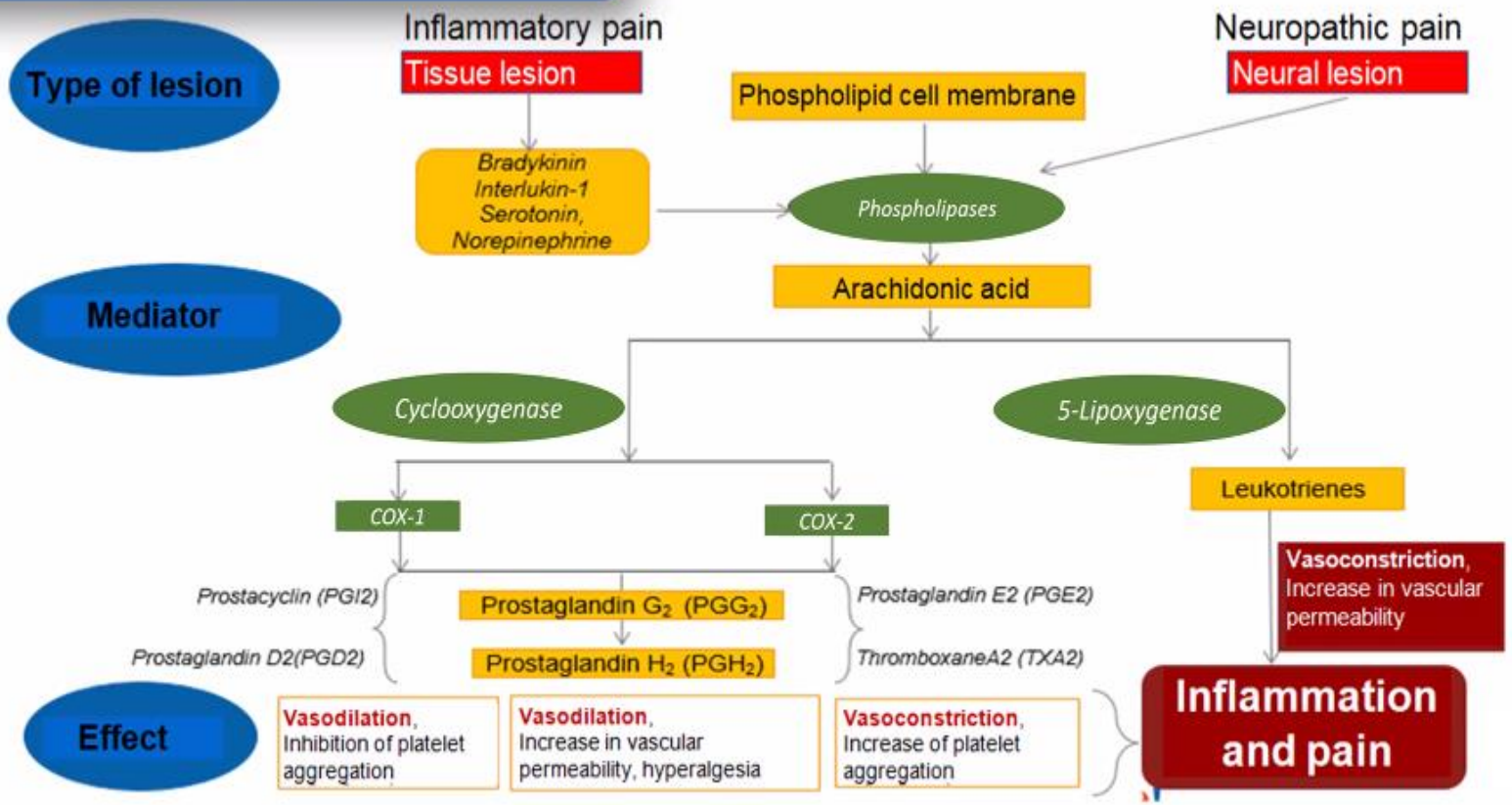
Opioid – risks exists, with inadequate evidence of benefits[10-13]

- Tramadol shown marginal benefits compared to its side effects, making it less commonly used in OA cases
- NSAIDs & coxibs shown lower risks compared to opioids in few large cohort studies
- No studies in "traditional" opioids shown any benefits in chronic cancer pain
- High drop-out ratio, up to 65% in 12-weeks study

eGFR, estimated glomerular filtration rate; NSAIDs, non-steroidal anti-inflammatory drugs; OA, osteoarthritis; RCTs, randomized controlled trials.

[1]Towheed TE et al. *Cochrane Database Syst Rev* 2006;CD004257; [2]Machado GC et al. *BMJ* 2015;350:h1225; [3]Moore RA et al. *Eur J Pain* 2014; [Epub ahead of print]; [4]Moore RA. *BMC Musculoskel Dis* 2007;8:73; [5]Rodriguez LAG et al. *Arthritis Res Ther* 2001;3:98-101; [6]Coxib and traditional NSAID Trialists' (CNT) Collaboration. *Lancet* 2013;382:769-79; [7]Mangoni AA et al. *Br J Clin Pharmacol* 2010;69:689-700; [8]Gutthann SP et al. *Arch Intern Med*1996;156:2433-9; [9]Moore RA et al. *Ann Rheum Dis* 2010;69:374-9; [10]Cepeda MS et al. *Cochrane Database Syst Rev* 2006;CD005522; [11]Solomon DH et al. *Arch Int Med* 2010;70:1968-78; [12]Moore RA et al. *Pain* 2013;154:577-86; [13]Lange B et al. *Adv Ther* 2010;27:381-99.

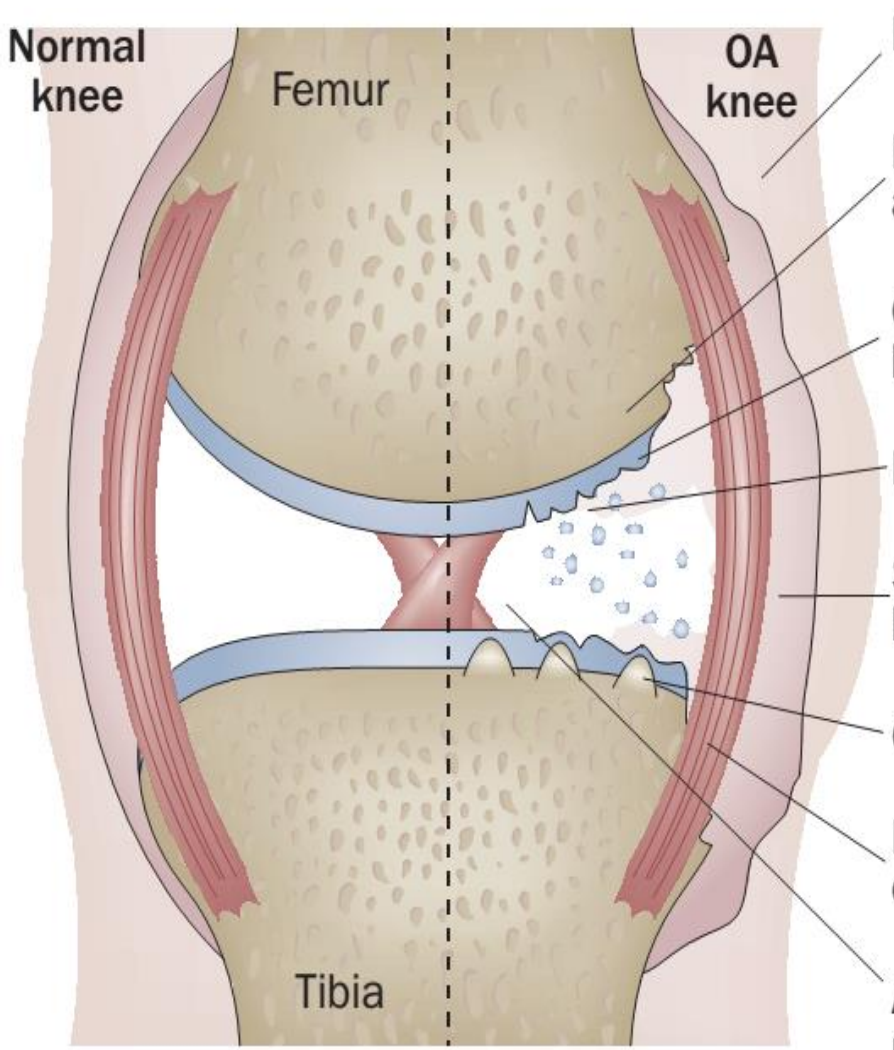
Pathogenesis of Pain



COX, cyclooxygenase; PG, prostaglandin; TxA2, thromboxane A2. *Red text indicates involvement in inflammation.

1. cLain et al. *Spine J* 2005;5:191-201
2. Funk CD. *Science* 2001;294:1871-5
3. Miller SB. *Semin Arthritis Rheum* 2006;36:37-49
4. Khanapure et al. *Curr Top Med Chem* 2007;7:311-40.

Target Terapi DMOAD



Muscle atrophy

Bone remodeling and sclerosis ← Bisphosphonates, Calcitonin, BMP7

Cartilage breaking down ← IL-1β inhibition, MMP inhibition, Cathepsin K inhibition, Aggrecanase inhibitors, BMP7, FGF18

Meniscal damage

Synovial hypertrophy ← TNF inhibitors, IL-1 inhibitors, Bradykinin antagonists

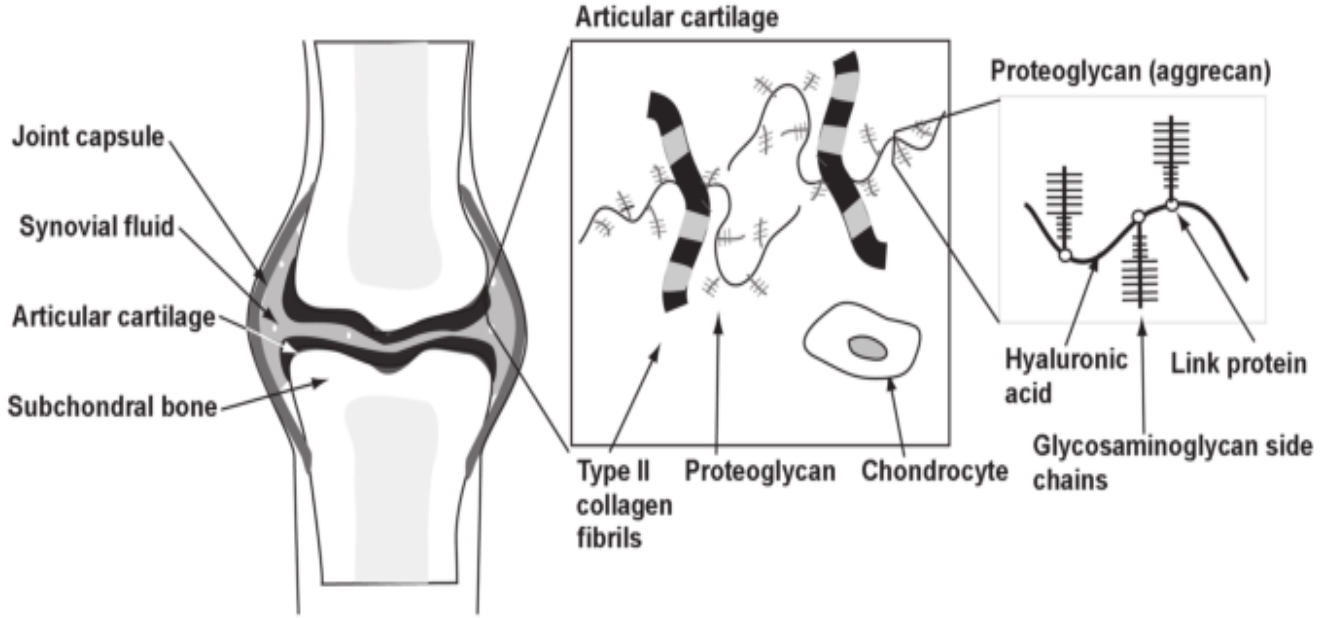
Osteophytes

Ligament dysfunction

Altered fat metabolism ← Leptin

GLUKOSAMIN

- Seny endogen dlm matriks tl rawan sendi dan cairan sendi
- Prekursor utama utk biosintesis asam hiluronat, glikosaminoglikan (GAGs), glikolipod, glikoprotein
- GAGs dpt mengikat air→ usia degeneatif, kemamp mengikatair berkurang
- Mek kerja chondroprotektif :
  - stimulasi langsung kondrosit,
  - memasukkan sulfur ke dalam tulang rawan sendi, dan
  - Perlindungan terhadap proses degenerasi tubuh dengan cara mengubah ekspresi genetik



GLUCOSAMINE SULFATE ACTION MECHANISMS

STIMULATES:

- ↑ proteoglycans

EFFECT:

- Anti-inflammatory activity
- Membrane stabilising activity

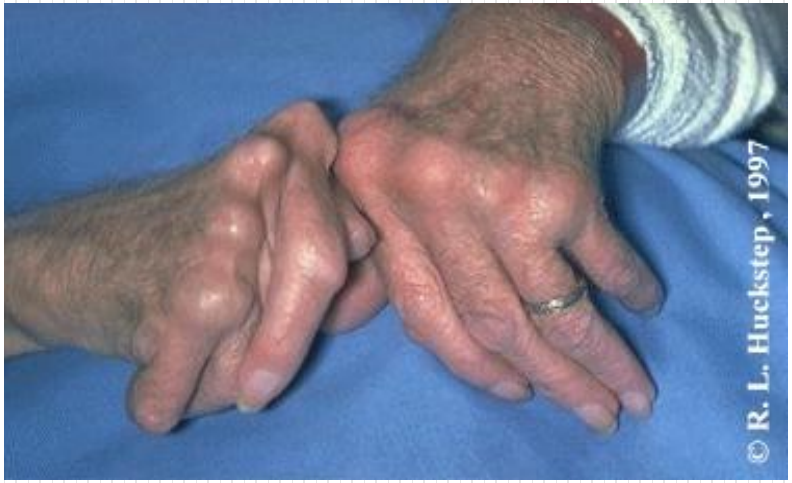
INHIBITS:

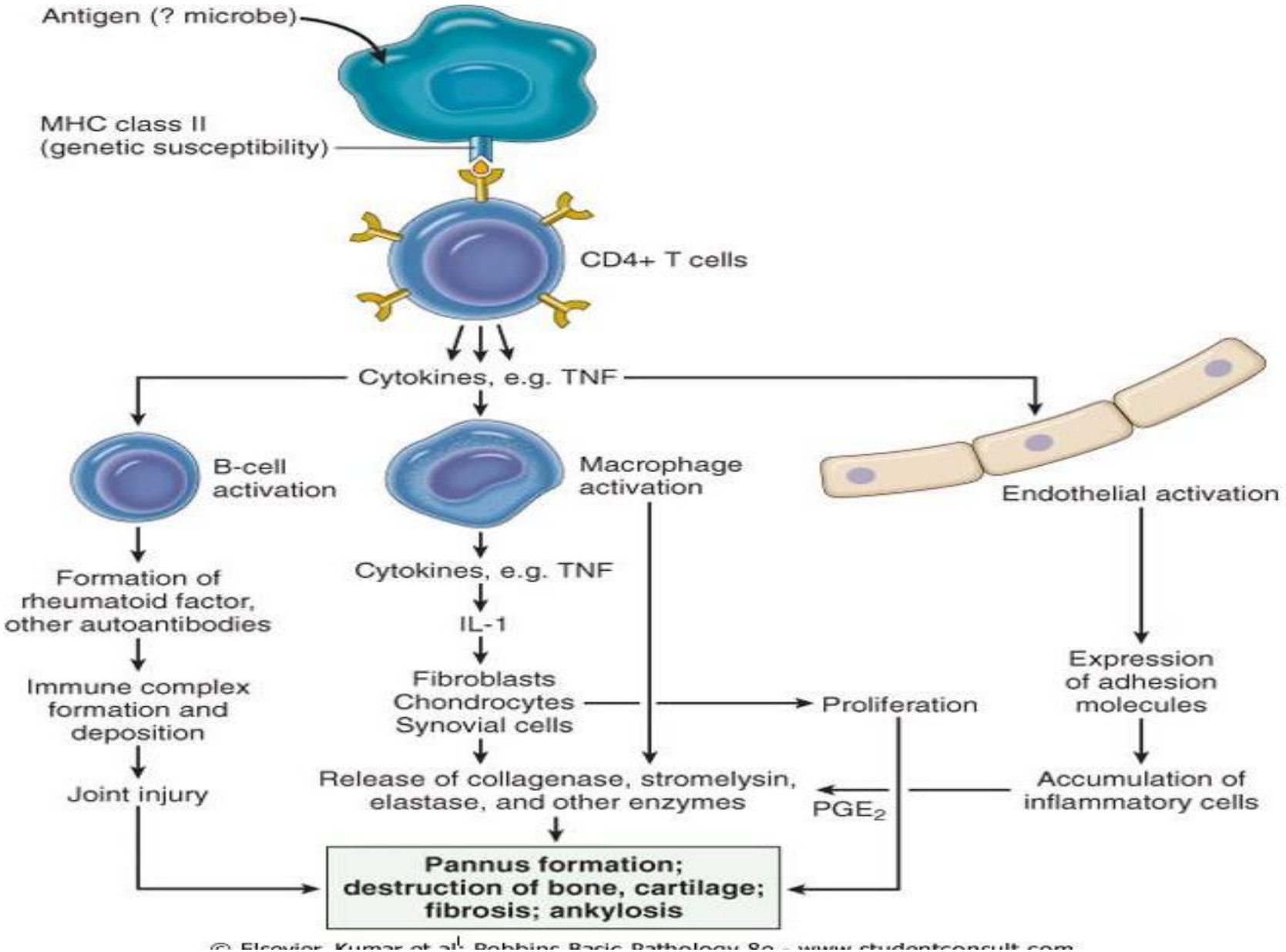
↓ cartilage degradative enzymes (collagenase, aggrecanase, phospholipase A2, etc.)
↓ MMP-3, MMP-2, MMP-9
↓ free radicals
↓ PGE2
↓ IL-1
↓ NF-kB

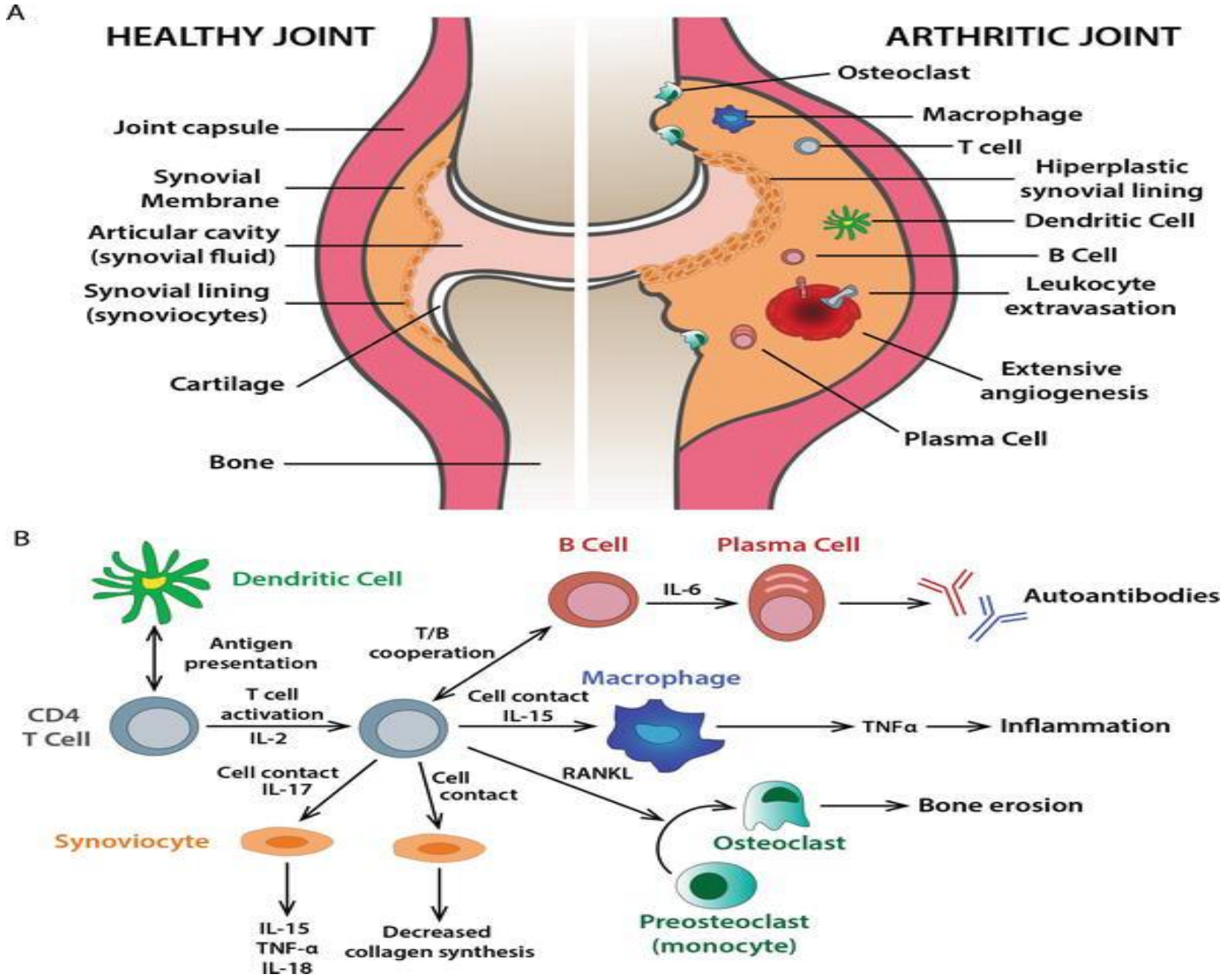
Kondroitin

- GAGs yg diperlukan utk pembent proteoglikan di tl rawan sendi
- Mek kerja
  - memperbaiki fungsi sendi dg meningkatkan sintesis endogen (kondroitin sulfat A dan C) & GAG
  - mencegah degradasi enzimatik GAGs melalui penurunan aktivitas *collagenolitic* dan
    inhibisi enzim seperti *phospholipase* A2 dan *N-asetilglukosamineidas*
  - Meningkatkan viskositas cairan sendi

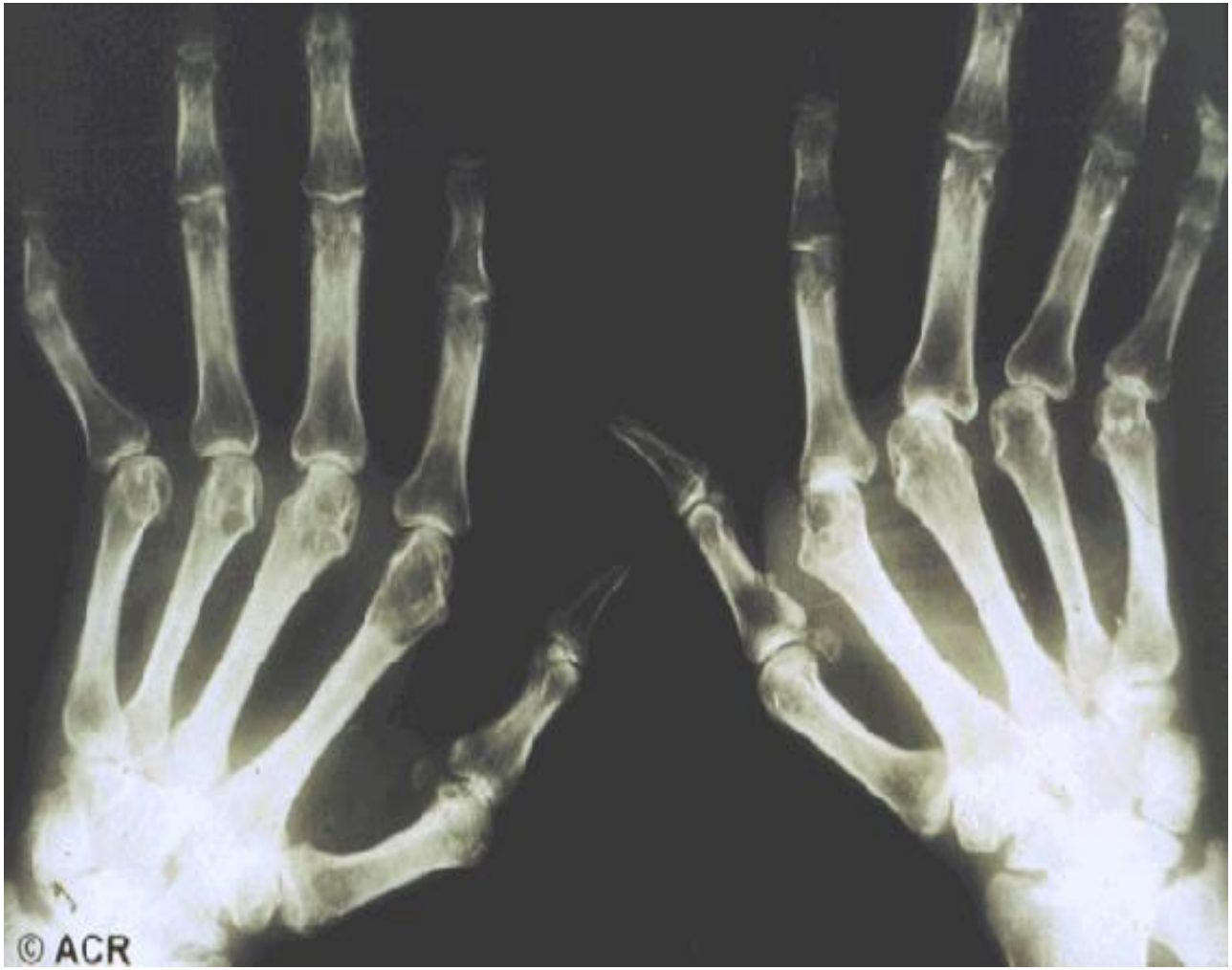
RHEMATOID ARTHRITIS






A
HEALTHY JOINT
ARTHRITIC JOINT
Joint capsule
Synovial Membrane
Articular cavity (synovial fluid)
Synovial lining (synoviocytes)
Cartilage
Bone
Osteoclast
Macrophage
T cell
Hiperplastic synovial lining
Dendritic Cell
B Cell
Leukocyte extravasation
Extensive angiogenesis
Plasma Cell
B
Dendritic Cell
B Cell
Plasma Cell
IL-6
Autoantibodies
Antigen presentation
T/B cooperation
CD4 T Cell
T cell activation
IL-2
Cell contact
IL-15
Macrophage
TNFα
Inflammation
Cell contact
IL-17
Cell contact
RANKL
Bone erosion
Synoviocyte
Osteoclast
IL-15
TNF-α
IL-18
Decreased collagen synthesis
Preosteoclast (monocyte)

Joint Destruction



Modified from Immunex Corporation

Treatment Goals

- Relieve pain
- Reduce inflammation
- Prevent/slow joint damage
- Improve functioning and quality of life

Treatment Approaches

- Lifestyle modifications
- Rest
- Physical and occupational therapy
- Medications
- Surgery

Drug Treatments

- Nonsteroidal anti-inflammatory drugs (NSAIDs)
- Disease-modifying antirheumatic drugs (DMARDs)
- Biologic response modifiers
- Corticosteroids

Current therapies:

NSAIDs (COX2-inhibitor) & Corticosteroid

NSAID- anti-inflammatory & immunosuppressive effcts.

Corticosteroids are primarily used in short courses for flres or during the initiation of DMARD therapy

(GI ulceration & Bleeding. Not DMARD)

Non-biological DMARDs

methotrexate, leflnomide, hydroxychloroquine, sulfasalazine, and minocycline

→ relieving pain and inhibiting the progression of disease

Efficacy (refractory), Safety – Myelosuppression, Hepatic toxicity

Biological DMARDs

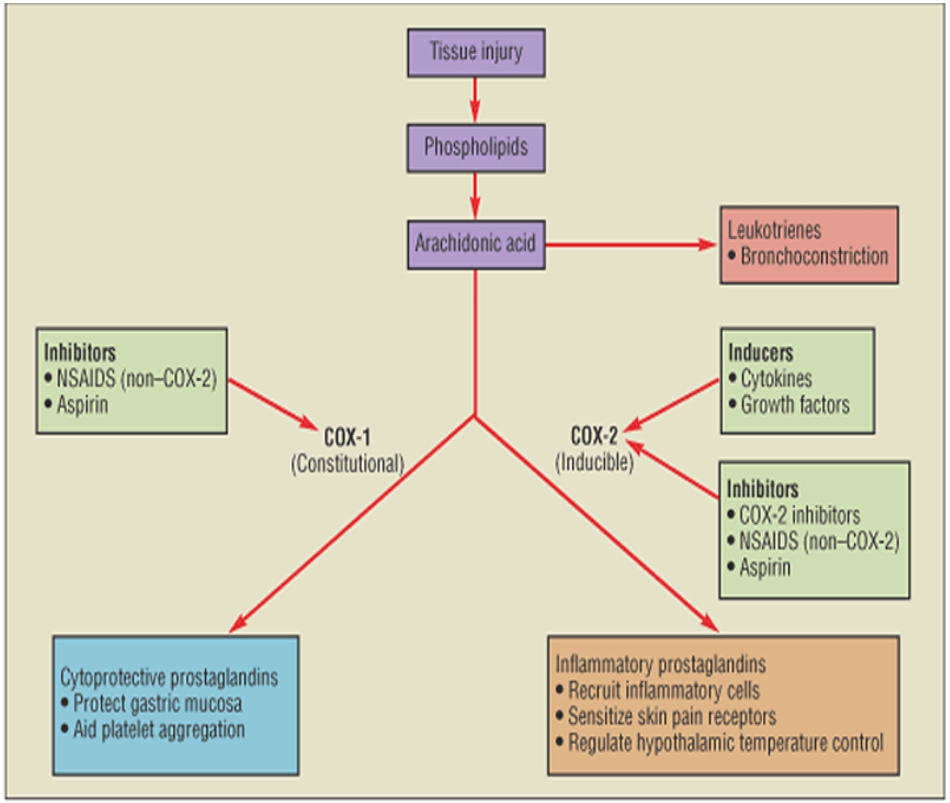
toclizumab, adalimumab, infliximab, golimumab and abatacept

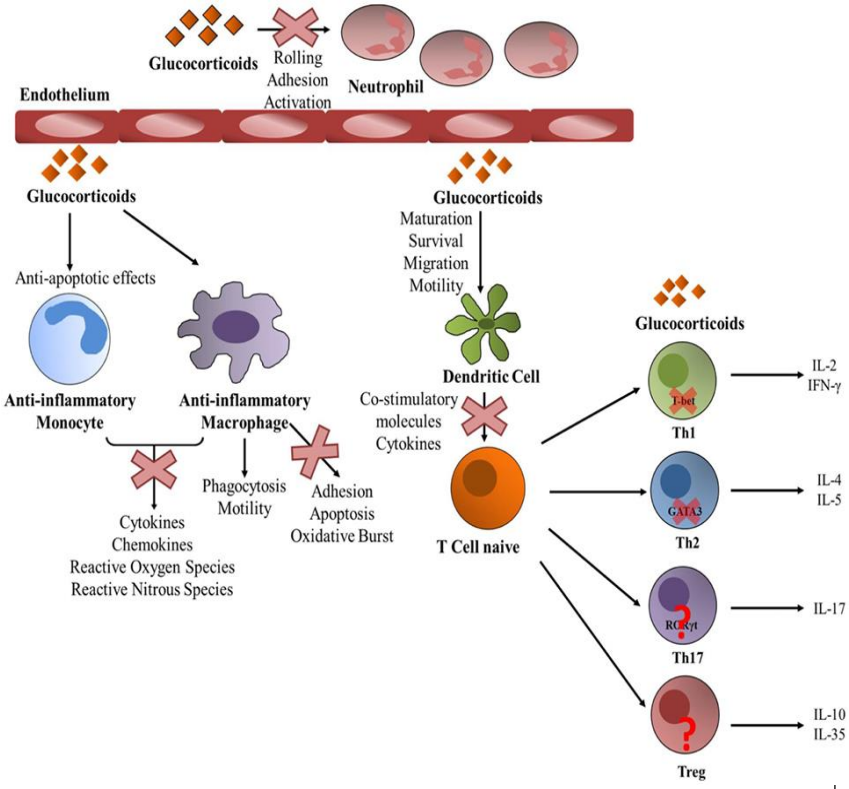
→alter a specific step in the pathogenesis of the inflmmatory response, eg TNFα

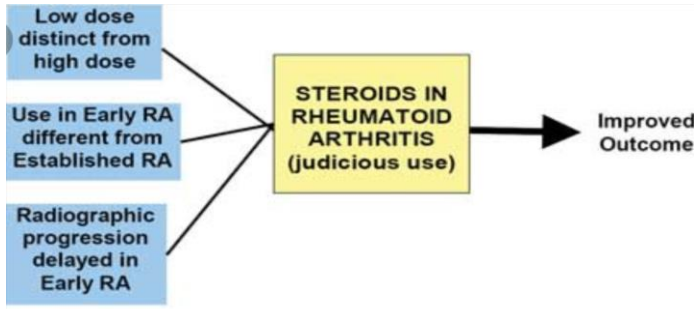
more efficacy, lesser side effects, higher cost as compared to non- biological DMARDs,

Safety – TB, Op infection, CHF, Demyelinating Disease, Lymphoma

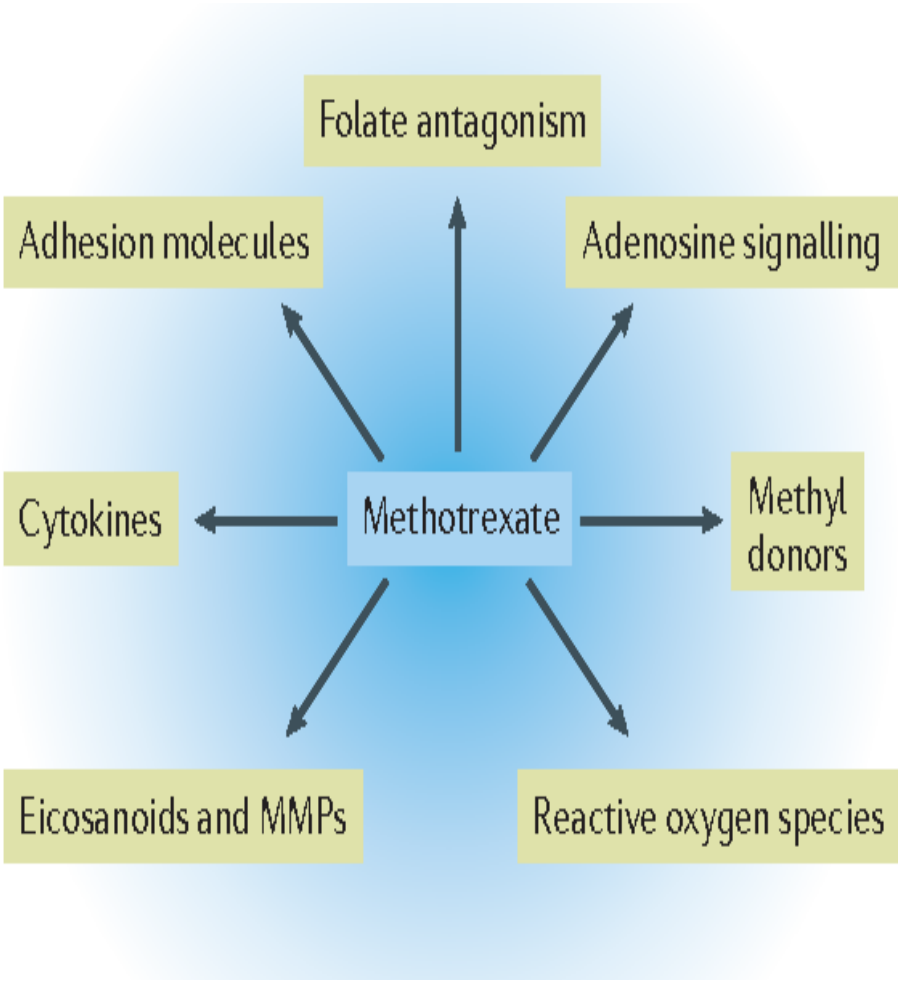
NSAID dan Kortikosteroid







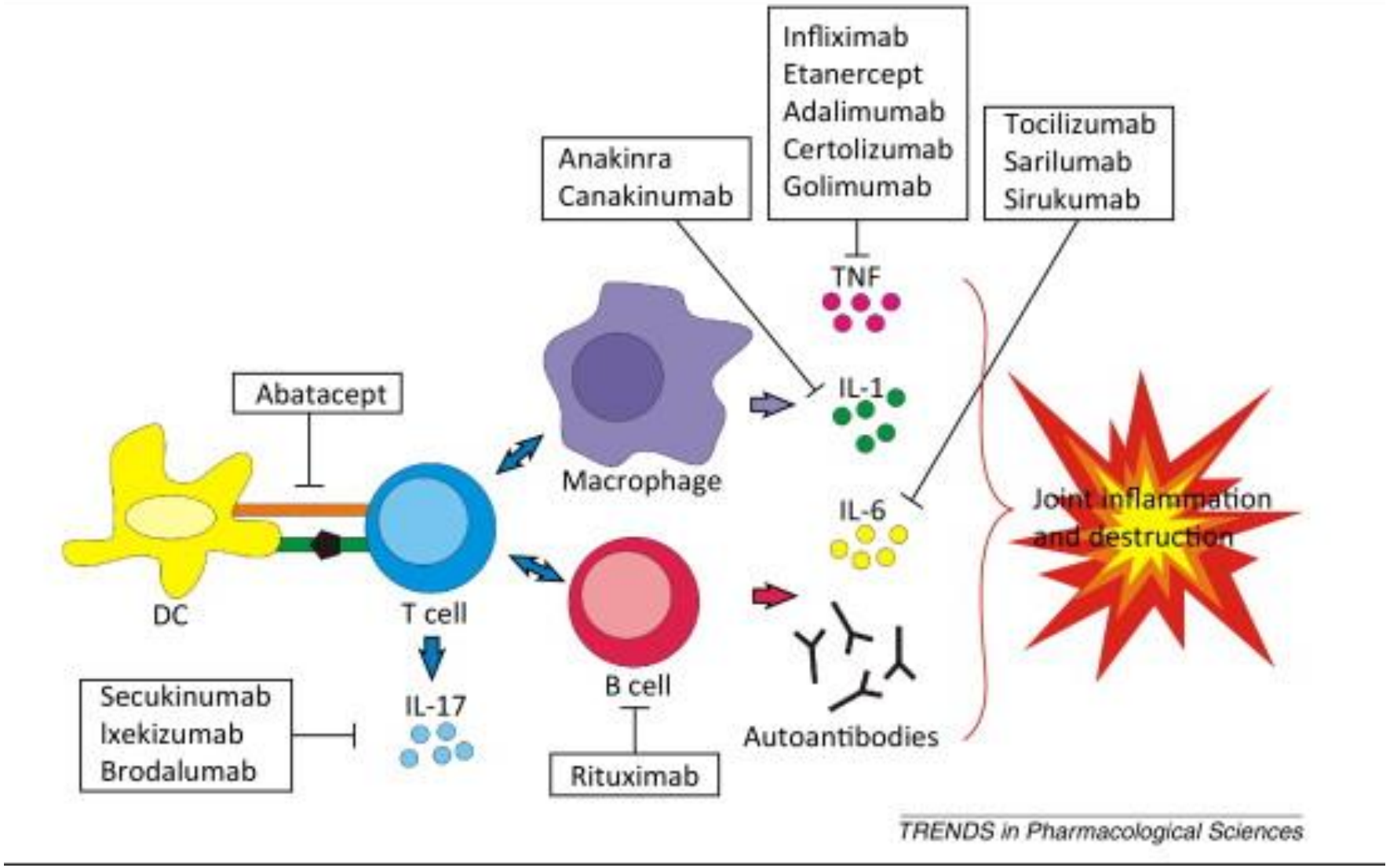
Non Biological DMARDs



- FD : menekan sistem kekebalan tubuh memperlambat laju kerusakan jaringan & progressifitas penyakit.

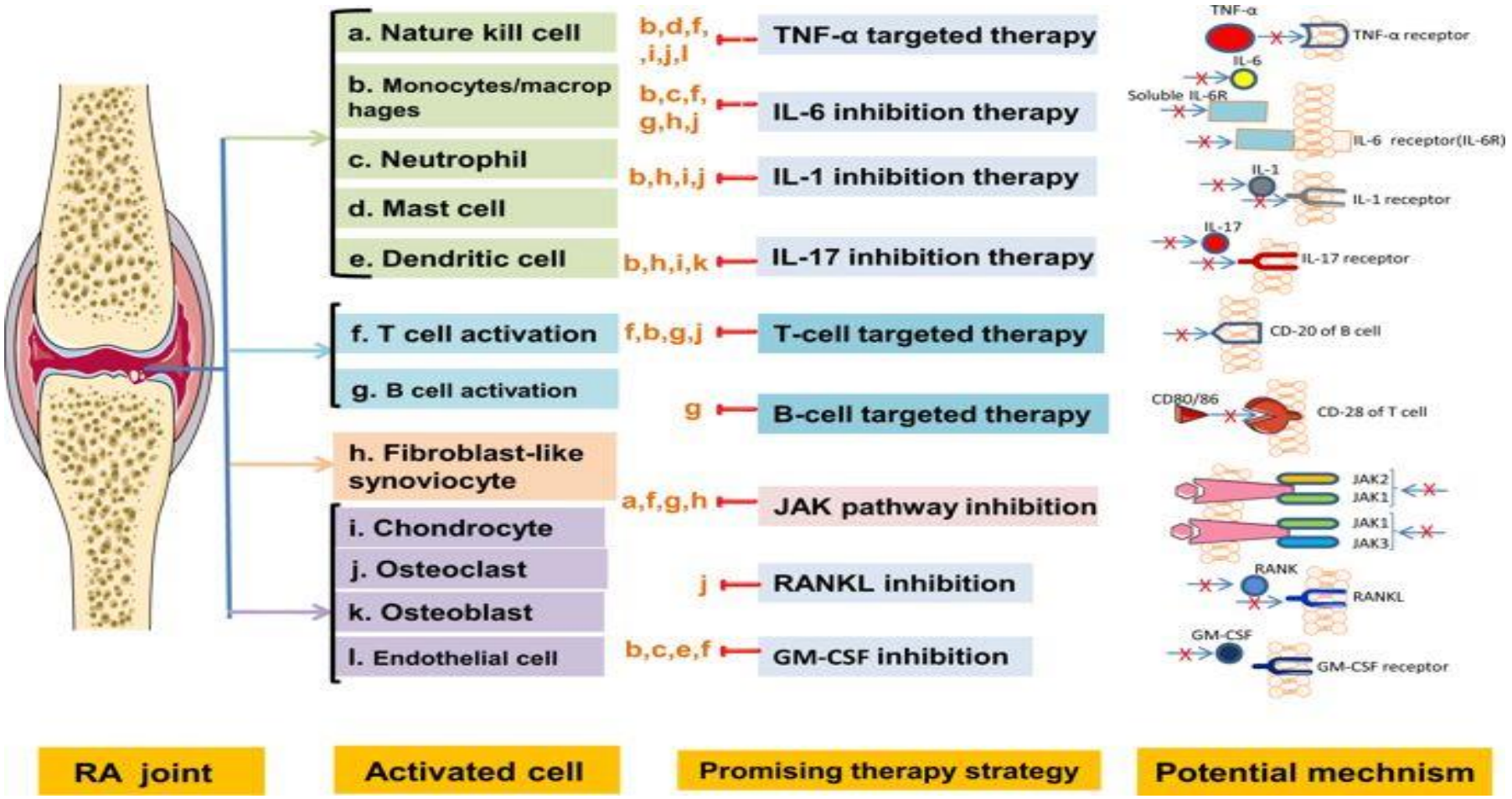
DMARDS	Mekanisme	Dosis	Efektifitas	Efek samping	Persiapan - Pemantauan
Metotreksat	Menurunkan kemotaksis PMN dan mempengaruhi sintesis DNA	7..5 – 25 mg / minggu	+++	Fibrosis hati, pnemonia interstitial dan supresi sumsum tulang	Awal : foto thorax, DPL, TFG, TFH. Selanjutnya DPL dan TFH tiap bulan
Sulfasalasin	Menghambat angiogenesis dan migrasi PMN	2x500 mg/hari ditingkat-kan sampai 3x1000mg	++	Supresi sumsum tulang	Awal pengobatan : G6PD. DPL tiap 4 minggu selama 3 bulan selanjutnya tiap 3 bulan, TFH 1 bulan selanjutnya tiap 3 bulan
Klorokuin basa	Menghambat lisosom dan pelepasan IL-1	6.5 mg/kg bb/ hari (150 mg)	+	Jarang, kerusakan makula.	Pemeriksaan mata pada awal pengobatan, lalu setiap 3-6 bulan
Leflunomide	Menghambat enzim dihidroorotat dehidrogenase sehingga pembelahan sel limfosit T auto reaktif menjadi terhambat	20 mg/hari	+++	Diare, alopecia, rash, sakit kepala, secara teoritis berisiko infeksi karena imunosupresi.	DPL, TFG, TFH
Siklosporin	Memblok sintesis IL-1 dan IL-2	2.5-5mg /kgbb	+++	Gagal ginjal	Awal : kliren kreatinin; DPL, TFG, TFH tiap 2 minggu, 3 minggu dan selanjutnya tiap 4 minggu.

Biological DMARDs



Obat	Mekanisme	Dosis	Waktu Timbulnya Respon	Efek samping	Monitoring
Etanercept	Anti TNF-α	25 mg sc 2x/minggu atau 50 mg sc/minggu	2-12 minggu	Infeksi, TB, demielinisasi saraf	TB, jamur, infeksi lain; TT, DPL, TFH saat awal lalu tiap 2-3 bulan
Infliximab	Anti TNF-α	3 mg/kg iv pada minggu 0,2, & 4, kemudian tiap 8 minggu	2-12 minggu	Infeksi, TB, demielinisasi saraf	TB, demielinisasi saraf TB, jamur, infeksi lain; TT, DPL, TFH saat awal lalu tiap 2-3 bulan
Golimumab	Anti TNF-α	50 mg im tiap 4 minggu	2-12 minggu	Infeksi, TB, demielinisasi saraf	TB, jamur, infeksi lain; TT, DPL, TFH saat awal lalu tiap 2-3 bulan
Rituximab	Anti CD20	1000 mg iv pada hari 0, 15	12 minggu	Reaksi infus, aritmia, HT, infeksi, reaktivasi hepatitis B	TB, jamur, infeksi lain; TT, DPL, TFH saat awal lalu tiap 2-3 bulan
Tocilizumab	Anti Il-6R	8 mg/kg iv tiap 4	2 minggu	Infeksi, TB, HT, gangguan fungsi hati	B, jamur, infeksi lain; TT, DPL, TFH, profil lipid saat awal lalu tiap 2-3 bulan

Promising Theraphy

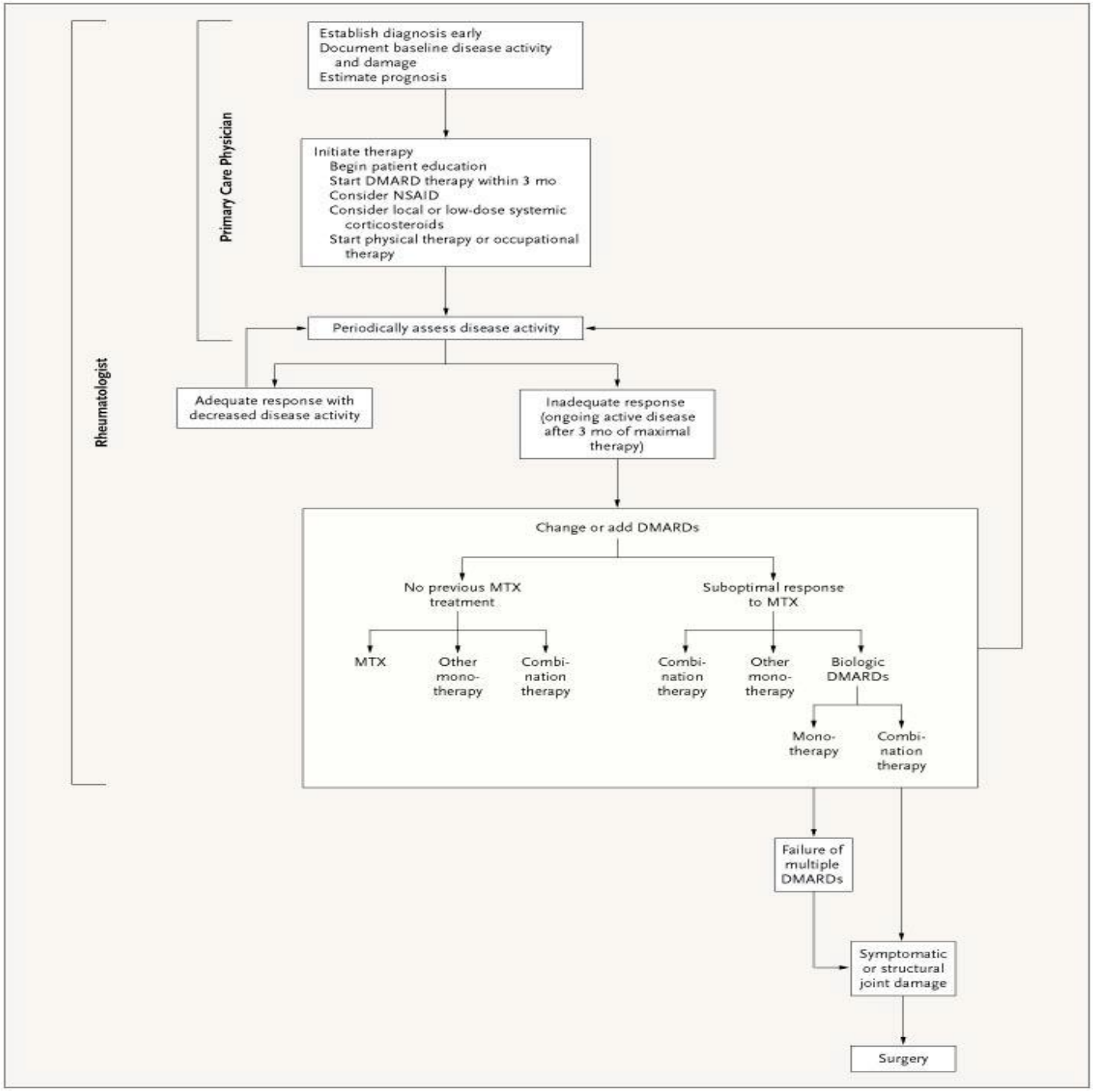


Advantages of DMARDs

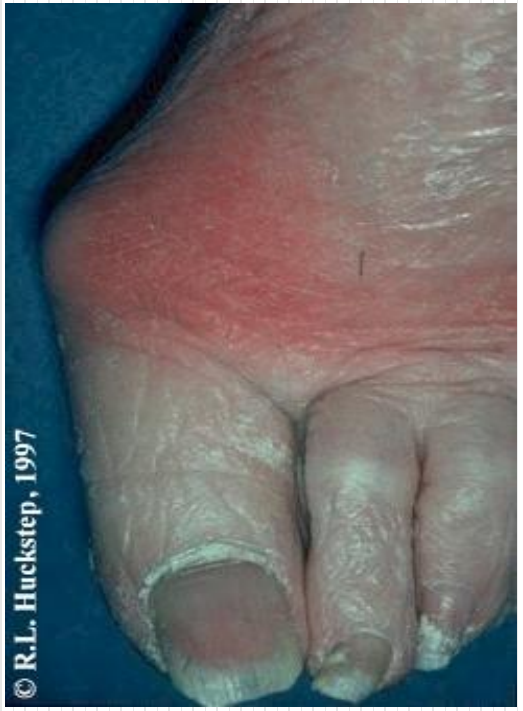
- Slow disease progression
- Improve functional disability
- Decrease pain
- Interfere with inflammatory processes
- Retard development of joint erosions

Selection of an Initial DMARD

Agent	Time to benefit	Potential toxicity	Toxicities to monitor
Azathioprine	2-3 months	Moderate	Myelosuppression, hepatotoxicity, lymphoproliferative
Cyclosporin	4-8 weeks	High	Renal, hyperuricemia
Gold, oral	4-6 months	Low	Myelosuppression, rash, proteinuria, gastrointestinal
Gold, parenteral	3-6 months	Moderate	Myelosuppression, rash proteinuria
Hydroxychloroquine	2-4 months	Low	Macular damage
Leflunomide	4-8 weeks	Low	Hepatotoxicity, gastrointestinal
Methotrexate	1-3 months	Moderate	Hepatotoxicity, pulmonary, myelosuppression
D-Penicillamine	3-6 months	High	Myelosuppression, proteinuria
Sulfasalazine	1-3 months	Low	Myelosuppression, gastrointestinal


Primary Care Physician
Rheumatologist
Establish diagnosis early
Document baseline disease activity and damage
Estimate prognosis
Initiate therapy
Begin patient education
Start DMARD therapy within 3 mo
Consider NSAID
Consider local or low-dose systemic corticosteroids
Start physical therapy or occupational therapy
Periodically assess disease activity
Adequate response with decreased disease activity
Inadequate response (ongoing active disease after 3 mo of maximal therapy)
Change or add DMARDs
No previous MTX treatment
Suboptimal response to MTX
MTX
Other mono-therapy
Combi-nation therapy
Combi-nation therapy
Other mono-therapy
Biologic DMARDs
Mono-therapy
Combi-nation therapy
Failure of multiple DMARDs
Symptomatic or structural joint damage
Surgery

GOUT ARTHRITIS



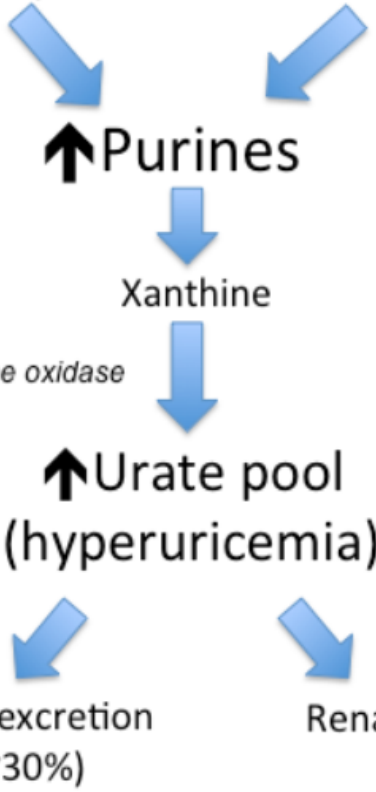
Gout

Elevated Purine Source

- **Catabolism of Purines**
- Tumor lysis syndrome
- **Diet**
  - meat (beef, pork, lamb)
  - seafood (scallops, shrimp, tuna)
  - beer, distilled spirits
  - drinks with fructose

Gout Risk Factors

- **Male gender**
- **Age**
- Obesity
- Ethnicity (Pacific Islanders)
- Polymorphisms (genetics)
- Kidney disease



Hyperuricemia Related Risks

- **Joint inflammation**
- Kidney or bladder stones
- Nephropathy
- CV disease
- Metabolic syndrome

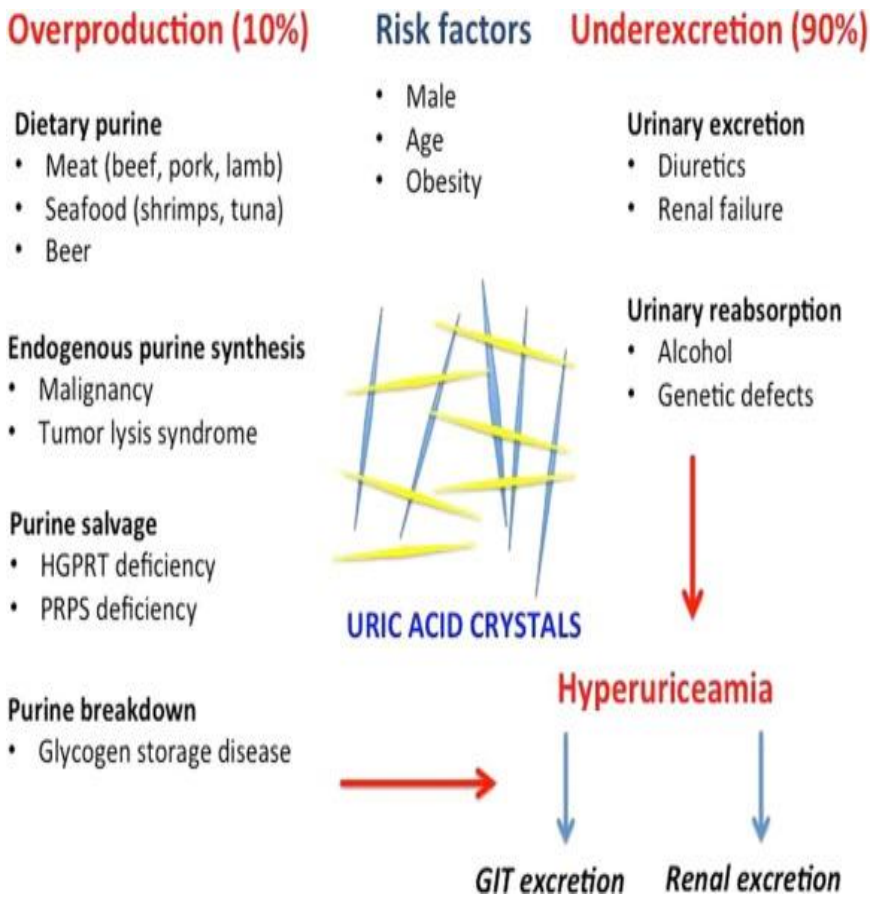
Decreased Renal Clearance *

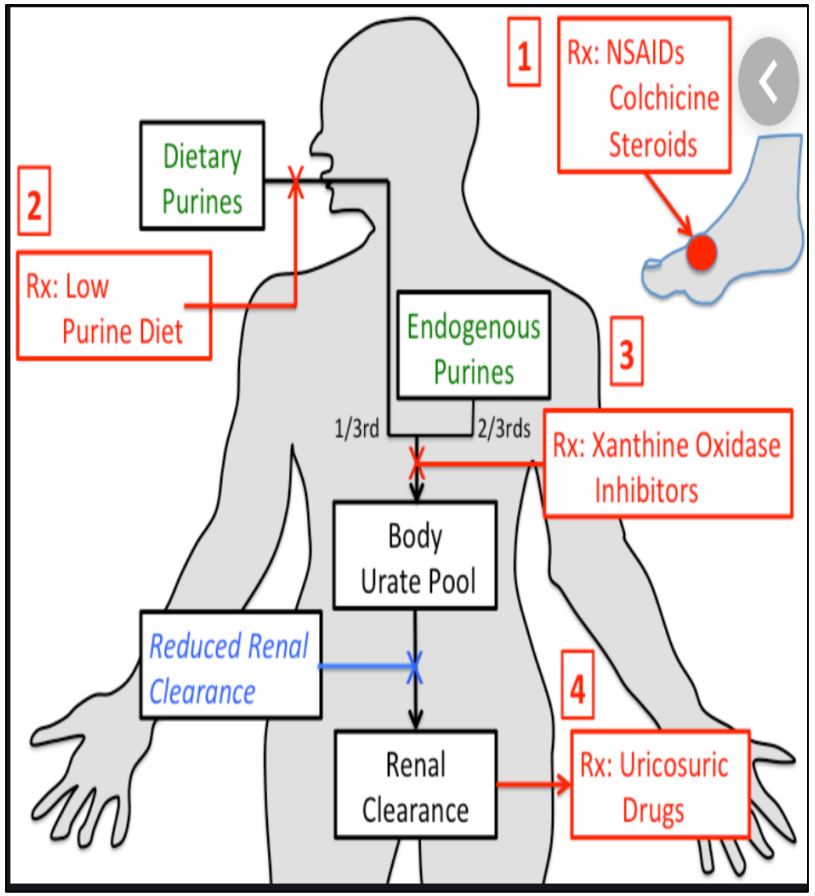
- **Drugs (HTZ, aspirin…)**
- **Fructose**
- Genetic factors
- Kidney disease

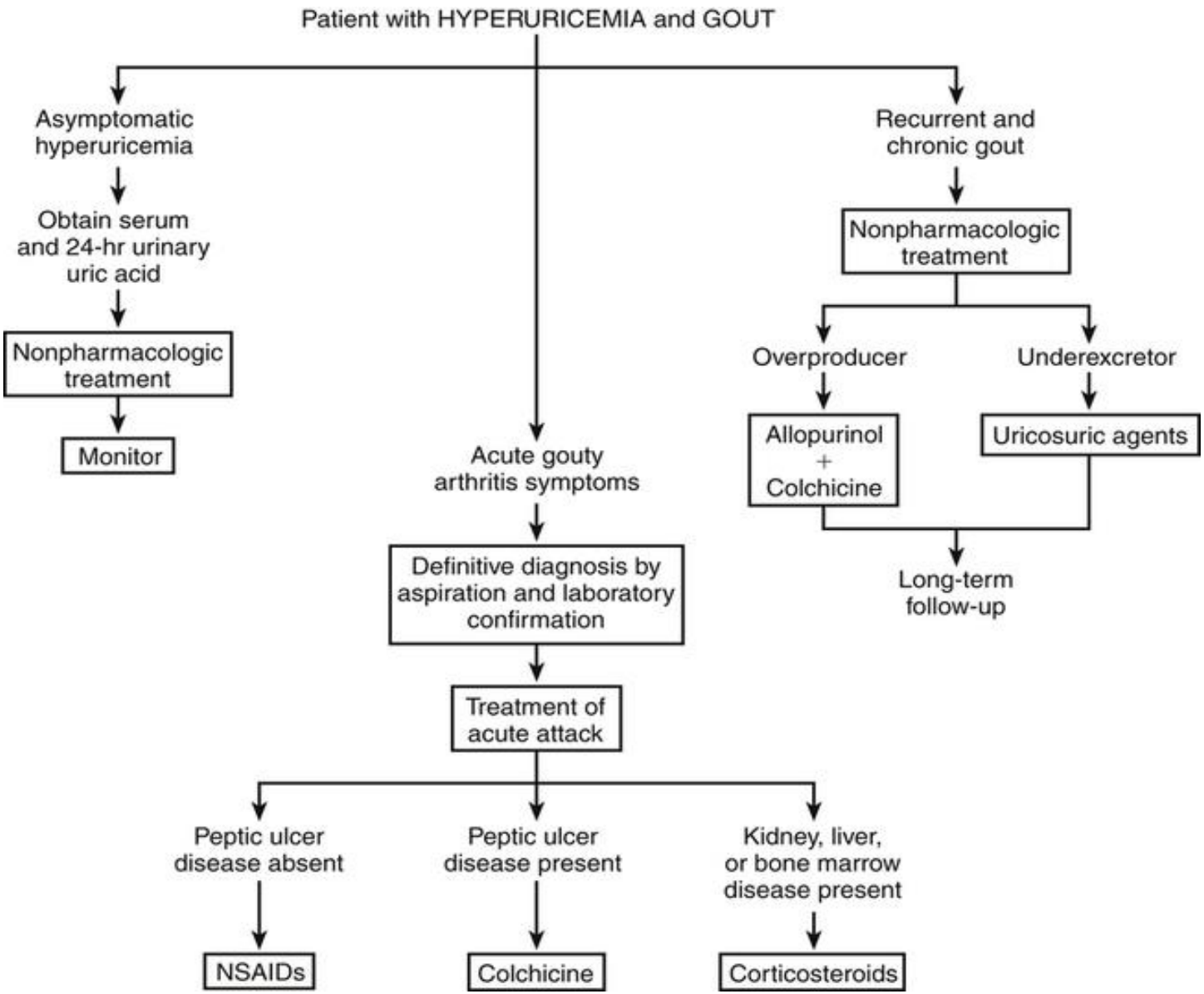
* ~90% of cases of gout are caused by inefficient renal excretion of urate vs. over production.

720 × 540

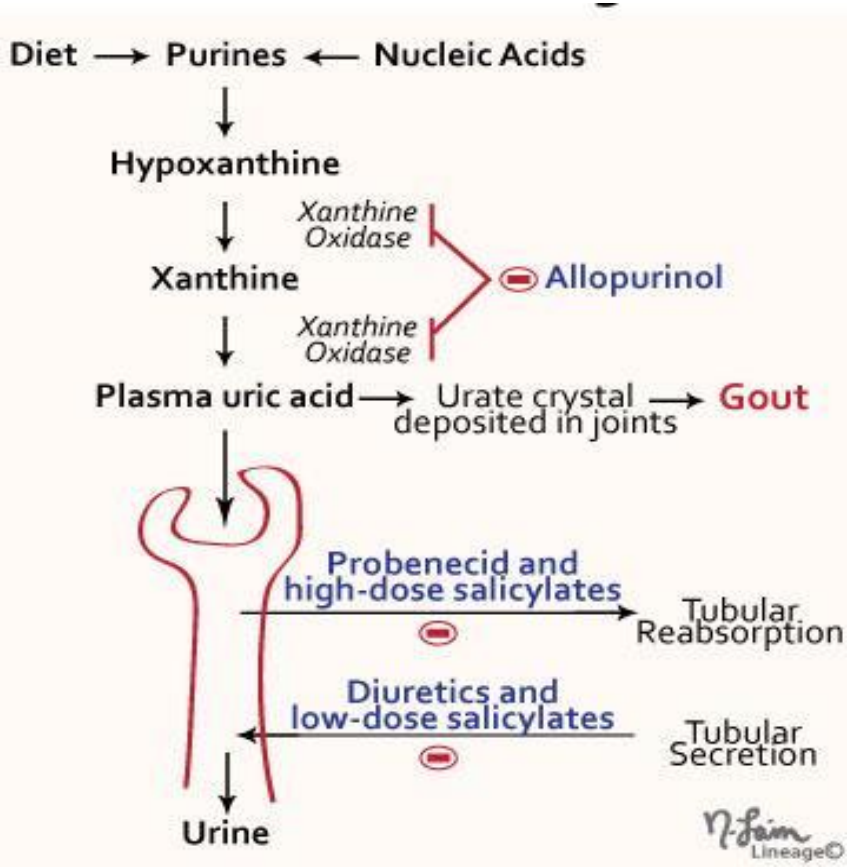
Tata Laksana Hiperurosemia dan Gout





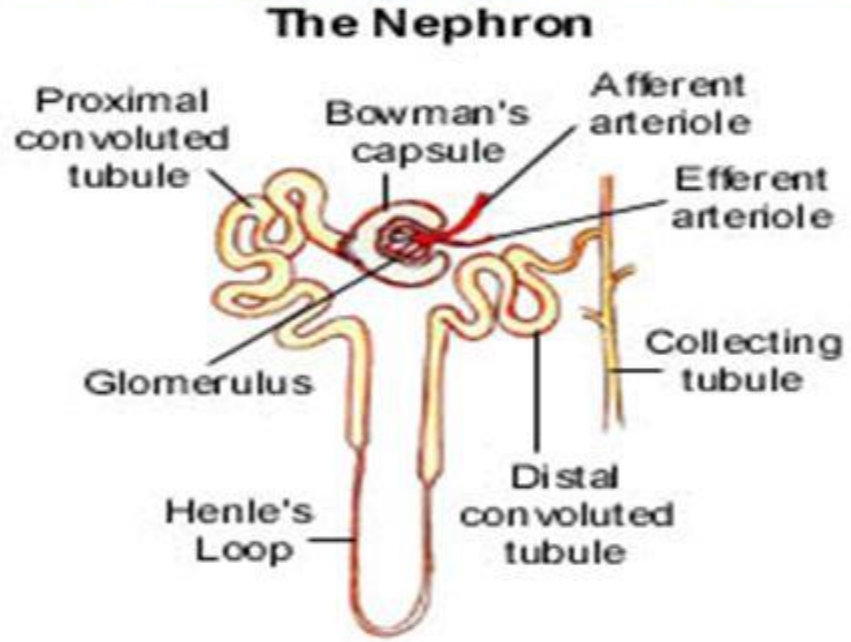

Patient with HYPERURICEMIA and GOUT
Asymptomatic hyperuricemia
Obtain serum and 24-hr urinary uric acid
Nonpharmacologic treatment
Monitor
Acute gouty arthritis symptoms
Definitive diagnosis by aspiration and laboratory confirmation
Treatment of acute attack
Peptic ulcer disease absent
NSAIDs
Peptic ulcer disease present
Colchicine
Kidney, liver, or bone marrow disease present
Corticosteroids
Recurrent and chronic gout
Nonpharmacologic treatment
Overproducer
Allopurinol + Colchicine
Underexcretor
Uricosuric agents
Long-term follow-up

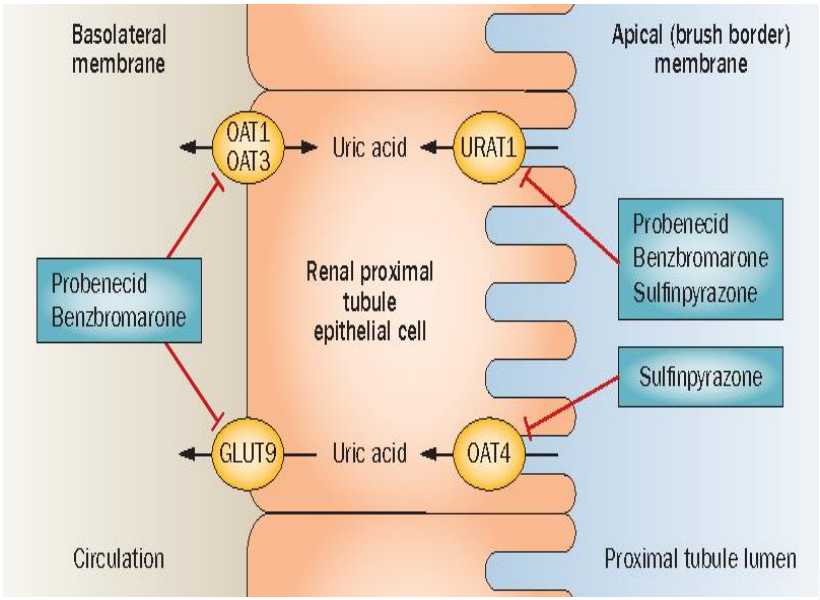
Target kerja Obat Anti-Hiperurisemia

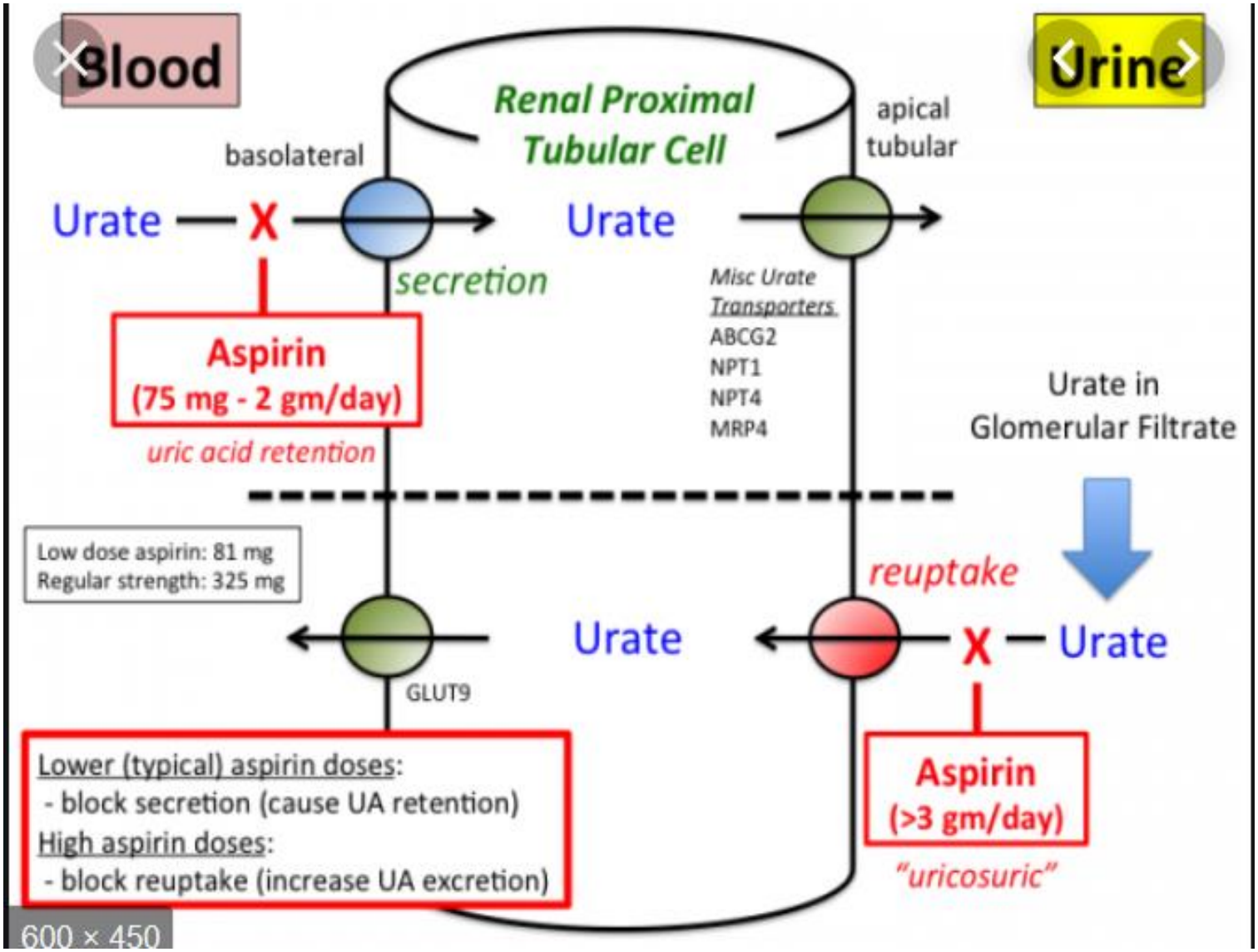


URICOSURIC DRUG

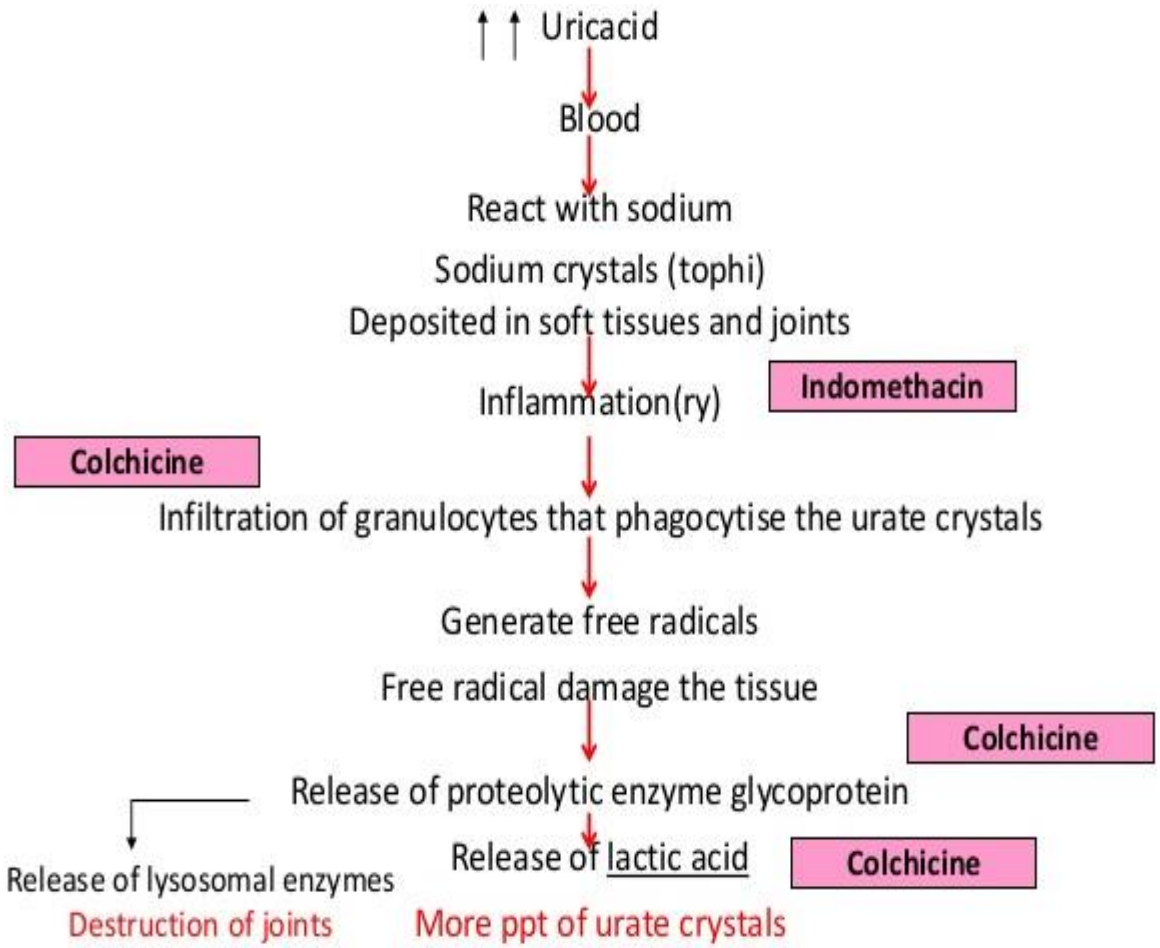
- **Uricosuric drugs** (probenecid, sulfinpyrazone, large dose of aspirin)
- block the active transport sites of the proximal tubules(middle segment , decrease the reabsorption of uric acid & increase the amount excreted



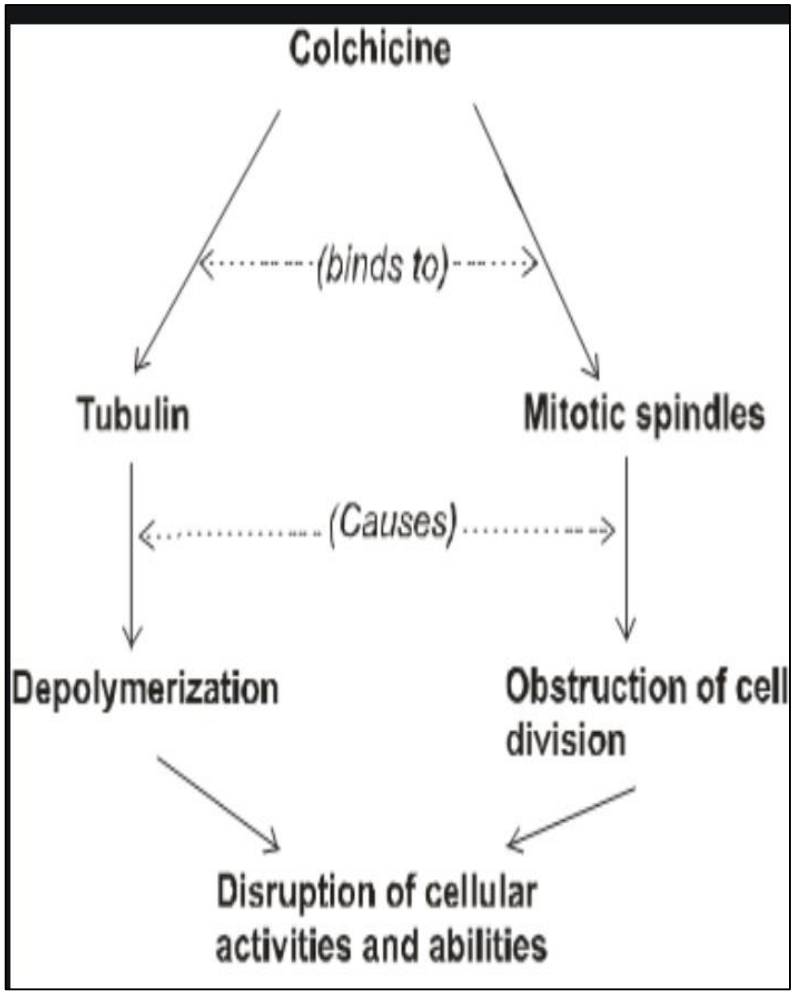



Blood
Urine
Renal Proximal Tubular Cell
basolateral
apical tubular
Urate
X
Urate
secretion
Misc Urate Transporters
ABCG2
NPT1
NPT4
MRP4
Aspirin
(75 mg - 2 gm/day)
uric acid retention
Urate in Glomerular Filtrate
Low dose aspirin: 81 mg
Regular strength: 325 mg
reuptake
Urate
X
Urate
GLUT9
Lower (typical) aspirin doses:
- block secretion (cause UA retention)
High aspirin doses:
- block reuptake (increase UA excretion)
Aspirin
(>3 gm/day)
"uricosuric"
600 × 450

Antiinflamasi pada Gout

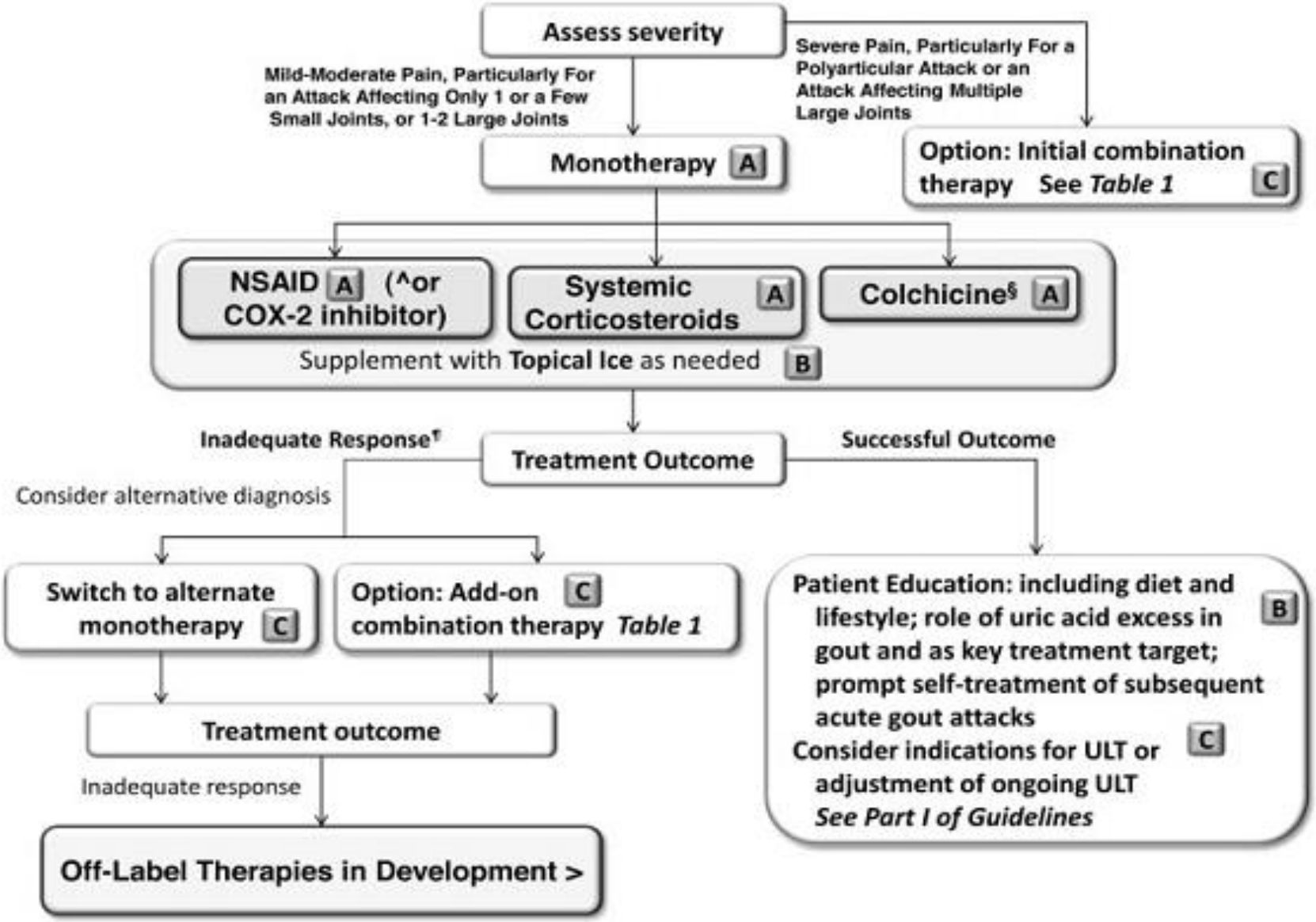


Colchicine

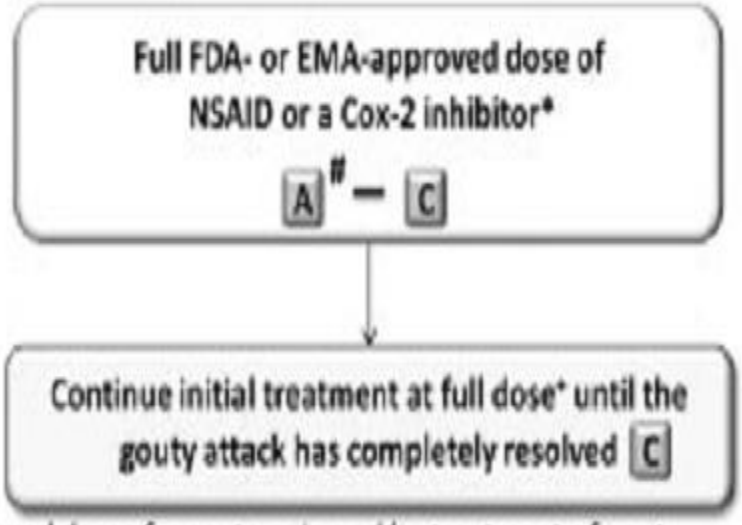


- **Anti-mitotic -** interrupt mitosis is due to its linkage to dimers of tubulin, cause cessation of mitosis in metaphase and interference in cellular mobility.
- **Anti-inflammatory -** Reduces mobility, adhesiveness, and chemotaxis of polymorphonuclear cells.
- Interferes with ICAM, selectins, thus inhibiting T-lymphocyte activation and its adhesion to endothelial cells.
- Impairs cellular secretion of procollagen and increases collagenase production that promotes a larger collagenolytic action.

MANAGEMENT OF ACUTE GOUT



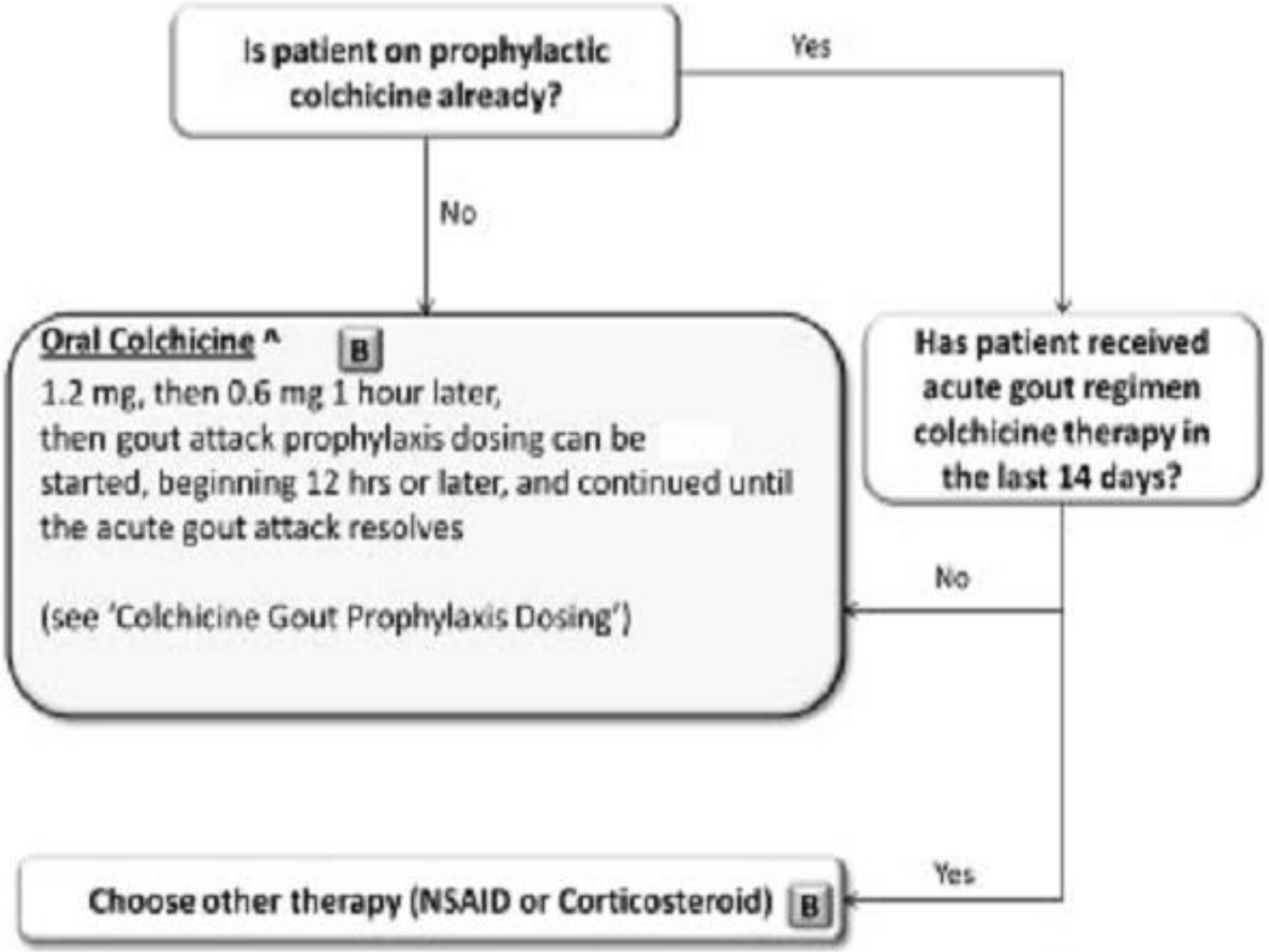
NSAID or selective COX-2 inhibitor



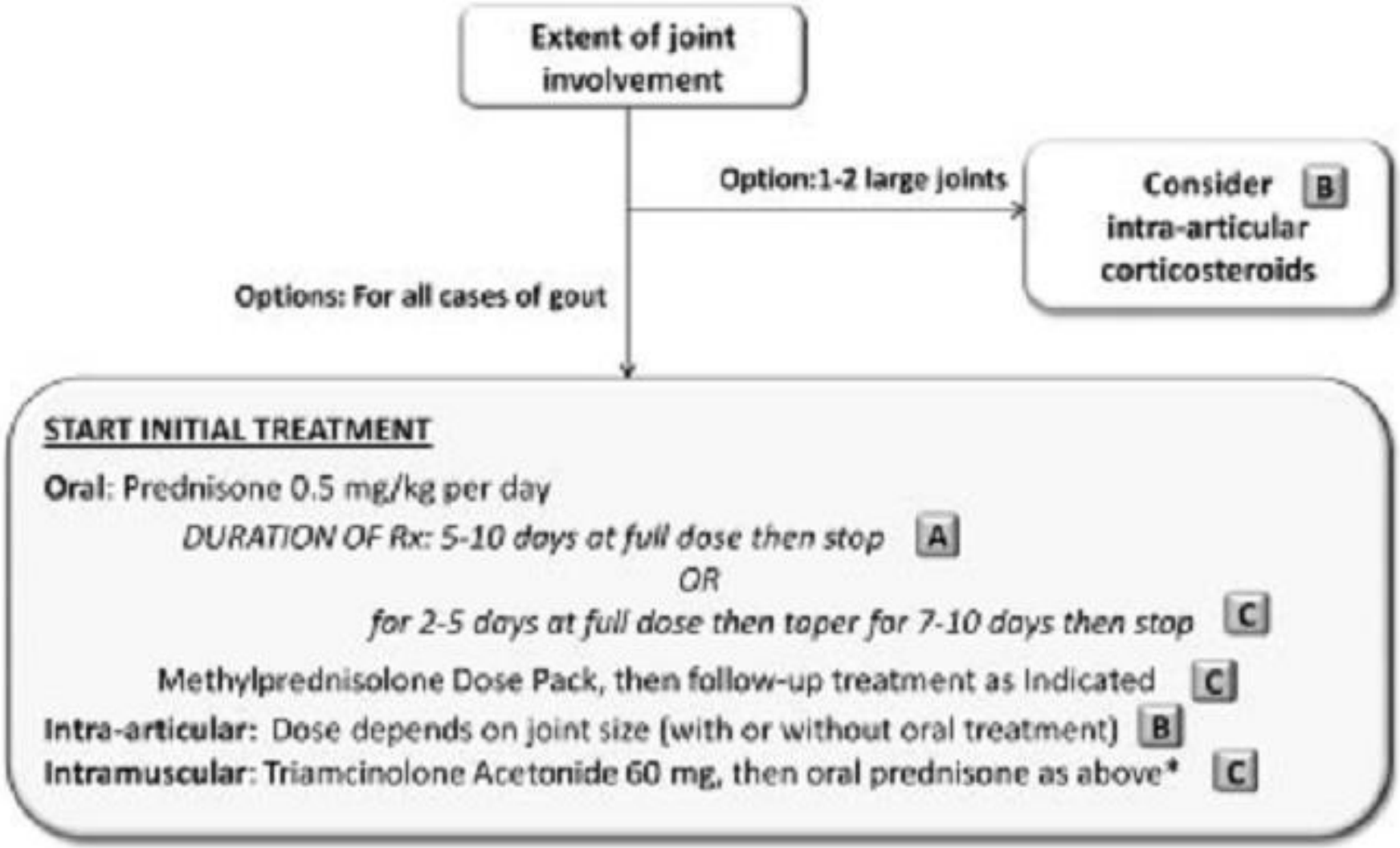
**Regulatory agency approved doses for acute pain and/or treatment of gout*

 # Naproxen, indomethacin, and sulindac are approved by the FDA for the treatment of acute gout, and other NSAIDs also are effective

** The option to taper the dose in patients with multiple comorbidities/hepatic or renal impairment was reinforced by the TFP, without specific TFP voting or more prescriptive guidance.*


Is patient on prophylactic colchicine already?
Yes
No
Oral Colchicine ^
B
1.2 mg, then 0.6 mg 1 hour later,
then gout attack prophylaxis dosing can be started, beginning 12 hrs or later, and continued until the acute gout attack resolves
(see 'Colchicine Gout Prophylaxis Dosing')
Has patient received acute gout regimen colchicine therapy in the last 14 days?
No
Yes
Choose other therapy (NSAID or Corticosteroid)
B

Corticosteroids



MANAGEMENT OF PROPHYLAXIS GOUT