

Pharmacotherapy 2

Osteoarthritis

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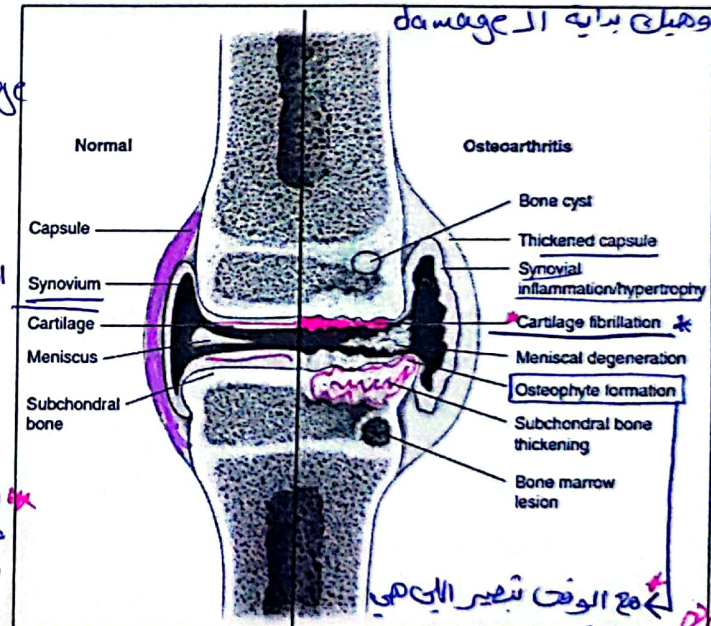
Department of Clinical Pharmacy and Pharmacy Practice

• هي عبارة عن Fibrous capsule تتركب المفصل أو العظامتين ببعض، الـ synovium (سجى الـ synovial fluid)
التي يمنع الـ Friction أنه يسهل المفصل للتحرك مثل lubrication، وعناصير (أس) كالأصفيحة في sponge tissue تقريباً
70-80% منه هو Fluid component و 20-30% هو solid عبارة عن glycosaminoglycans, collagen وعنا 1-2%
هي عبارة عن cell (chondrocyte cell) مسئلة عن الـ synthesis و degradation للـ cartilage لهيك
دائم في balance بين الـ (synthetic enzymes) والـ (degradative enzymes) التي تفرزها خلايا في الـ normal
في الـ osteoarthritis يكون في imbalance بينهم في الـ (يكون في تفرج الـ superficial)
protein تالست تآكل ويغير الـ degradative activity أكثر من الـ synthetic
Osteoarthritis (OA)

General Principles

- or cartilage disease / disease of cartilage
- ✓ OA, or degenerative joint disease, is characterized by deterioration of articular cartilage with subsequent formation of reactive new bone at the articular surface.
- ✓ Risk factors include increasing age, obesity, gender, certain occupations and sports activities, history of joint injury or surgery, and genetic predisposition.

• بعض المهنة يتعرضون المرضين لاستخدام كثير لمفاصل
مخينة ويكون في stress على مفاصل الـ hand
يكون في الـ degenerative أو يغير الـ OA
مثلاً الناس التي تستخدموا الـ wrist, elbow
في ضغط كبير (التي يتغلوا على الـ humerus مثلاً)
أو المزارعين مثلاً



• مع الوقت يتغير إلى هي
• very characteristic (bone manifestation)

OA الـ specific الـ osteoplast activity في المنطقة مونة
تتسبب تآكل حيث هو في bone formation هي نوع من
لنوع الـ adaptation للمفصل لأنه يغير في loss لتبريد
الـ activity الـ osteoplast

يعتبر كل شخص حسب شدة المرض التي يعيقه كثير

② اختلافي عن joints مهم الحركة ممكن بها structural abnormality في المفاصل والسرعة motion
وممكن ال pain هو اللي أثر
③ لما يصحى من النوم لانه يكون في (gelling phenomenon) يكون thickening in synovial fluid لانه لو
اله فرق ما سرك اله فصل

✓ The predominant symptom is deep, aching pain in affected joints. Pain accompanies joint activity and decreases with rest.

① له اي خاصية لـ OA انه مع activity يزيد ومع ال rest يقل
صوت او شعور المفصطة بسبب الاحتكاك

✓ Limitation of motion, stiffness, crepitus, and deformities may occur. Patients with lower extremity involvement may report weakness or instability. => مثلا اذا كانه في ال knee ممكن يحتاج مساعدة حتى يحافظ على ال stability اله

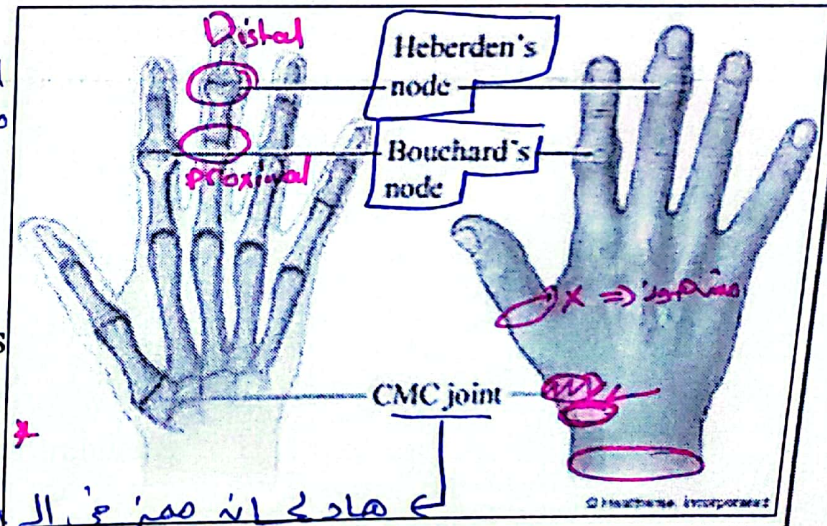
③ ✓ Upon arising, joint stiffness typically lasts less than 30 minutes and resolves with motion.

✓ Presence of warm, red, and tender joints suggests inflammatory synovitis. => لمرض ال inflammation حينا ممكن يصير ال local ولكن ال OA مش inflammatory disease

⑤ ✓ Physical examination of affected joints reveals tenderness, crepitus, and possibly enlargement.

✓ Heberden and Bouchard nodes are bony enlargements (osteophytes) of the DIP and PIP joints, respectively.

ما د معيز يكونه في مفاصل ال المفاصل انتح bone enlargement



هناك انه ممكن في ال OA ال مفاصل الوجود في قاعدة الابهام وهو قريب من ال wrist joint وممكن مرات الواحد يفكر انه ال ال wrist هو ال involve بيها هو قاعدة الابهام

عادة يزيد في الـ cold , humid , يكون احسن في الـ warm والـ dry

CLINICAL PRESENTATION Osteoarthritis

اما هو حينا انه هو degenerative bone disease
repetitive الـ put في كل مكان الواحد اكبر كلما الـ Age الـ risk اكثر

- Usually occurs in older adults (≥ 65 years of age)

Gender

- Age ≤ 45 years more common in men
- Age > 45 years more common in women

Symptoms

- Pain in affected joint
- Deep, aching character
- Pain on motion $\Rightarrow$ مع الحركة يزيد مع نهاية النصف لانه يكون على activity كثير
- Stiffness in affected joints
- Resolves with motion, recurs with rest ("gelling phenomenon")
- Usually duration < 30 minutes
- Often related to weather $\Rightarrow$ مختلف حسب الرطوبة والضغط والحرارة
- Limited joint motion
- May result in limitations of activities of daily living
- Instability of weight bearing joints

Signs, history, and physical examination

- Monoarticular or oligoarticular, asymmetrical involvement يعني عكس الـ RA حينا عنه انه

poly (3 او اكثر) وكانه symmetrical

- Transient joint effusion
- Genu varum ("bow-legged")
- Hips
 - Groin pain during weight bearing exercises
 - Stiffness, especially after activity
 - Limited joint movement
- Spine
 - Lumbar involvement is most common at L3 and L4
 - Paresthesia
 - Loss of reflexes
- Feet
 - Typically involves the first metatarsophalangeal joint
- Shoulder, elbow, acromioclavicular, sternoclavicular, temporomandibular joints may also be affected.

حسب الدكتور
حصول شقوق في
بعض مفاصل
حسب اعراضهم
اي (3)

Observation on joint examination

- Bony proliferation or occasional synovitis $\Rightarrow$ مش بالضرورة مع وجود الـ inflammation ومعنى
- Local tenderness
- Crepitus
- Limited motion with passive/active movement
- Deformity

Radiologic Evaluation

تساعد بتقييم المرفق

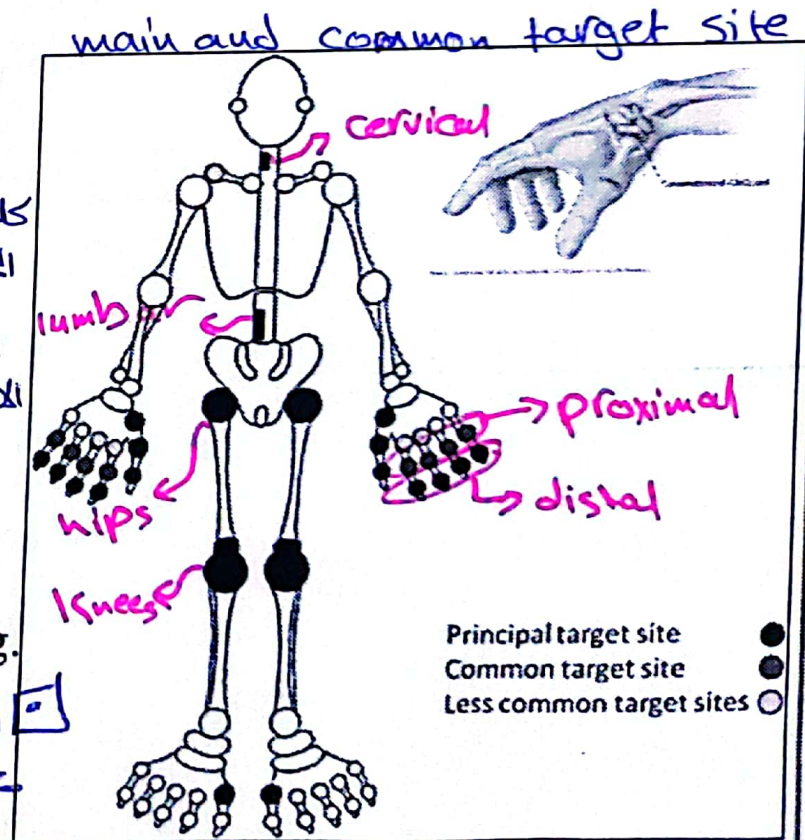
- ✓ The joints most commonly affected are the distal and proximal interphalangeal joints of the hands, the first carpometacarpal joint and joints of the hips, knees, and cervical and lumbar spine.

CMC → base of thumb

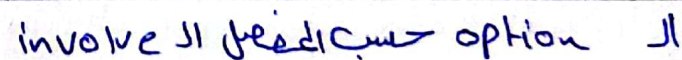
Diagnosis

- ✓ It is made through patient history, physician examination, radiologic findings, and laboratory testing.
كلهم يسأعون في الفحص = المريض
- ✓ American College of Rheumatology criteria for classification of OA of the hips, knees, and hands include: الأشياء التي تصيغها علينا:
 - presence of pain
 - bony changes on examination
 - Normal ESR ⇒ to exclude RA
 - radiographs showing osteophytes or joint space narrowing.

ال ESR في ال RA أو أي other inflammatory condition يكون عالي في ال OA لا يكون عالي يكون Normal هناك فعمل testing lab (عشان نستبعد) other inflammatory conditions



معناها ممكن المرفوع فترة ممارسة exercise مثل او لعب ما، به يقول Taichi ويعود يرجع للممارسين اليه كأنه يقلعها او يركز على الـ weight loss
مثل ما حكيهنا صافي اني الله اولوية على غيره، بمعنى لما واحد احضاني عارف شوييني في فبعل او شوي النسخ لـ exercise او درجة التدريب لكل مرفوع يكون متابع المرفوع



الممسوحة ضوئياً بـ CamScanner

هو elastic tape لاصق يساعد اما بالرياضيين او الناس
 التي عندهم OA هو يزيد الـ circulation في المنطقة يزيد الـ support
 يزيد الـ range of motion يساعد حرية المفاصل ، يساعد تقليل الالام

اذا يدكم اقربا عنه اكثر

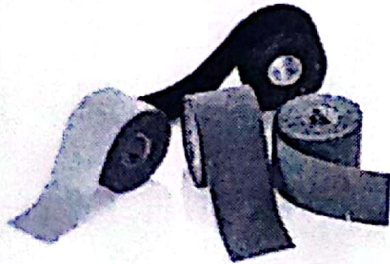


عالم ياباني الي خوره و بليست
 بالفكرة بار 70 وما زال يستخدم
 Hypoallergenic
 and latex free non-pharmacologic

Utilizes a high grade
 cotton for breathability
 and comfort

Can be worn
 continuously for
 3-5 days

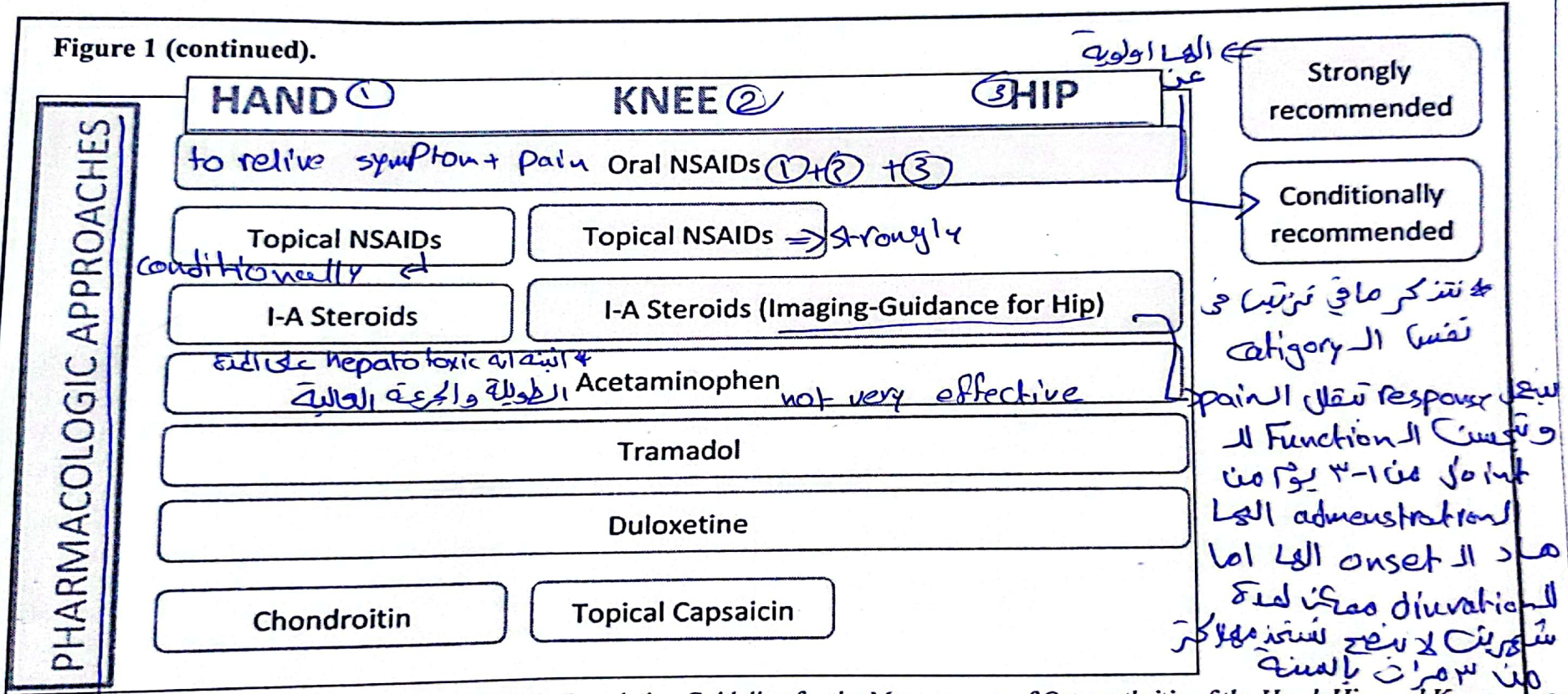
KINESIO



منع استخدام الـ USAID لها مشاكلها ودنا نراجعى الى عنده مثلا مشاكلنا في الـ CV, Kidney, G6PD كلنا دائما انه المريض يستخدم الـ minimum effect dose قدر الامكان

deep & hip location of hip choice with hand evidence topical NSAID
so they suggest no clinically (local) surface of hip of topical NSAID in hip OA
effects oral & topical, effects on hips of topical NSAID in hip OA
local SE, irritations, local SE, systemic SE, irritations, local SE, irritations, local SE, irritations

Figure 1 (continued).



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

Arthritis & Rheumatology, Volume: 72, Issue: 2, Pages: 220-233, First published: 06 January 2020, DOI: (10.1002/art.41142)

Arthritis & Rheumatology, Volume: 72, Issue: 2, February 2020

A

PHYSICAL, PSYCHOSOCIAL, and MIND-BODY APPROACHES

HAND

KNEE

HIP

Iontophoresis

TENS

Manual Therapy (with or without exercise)

Massage Therapy

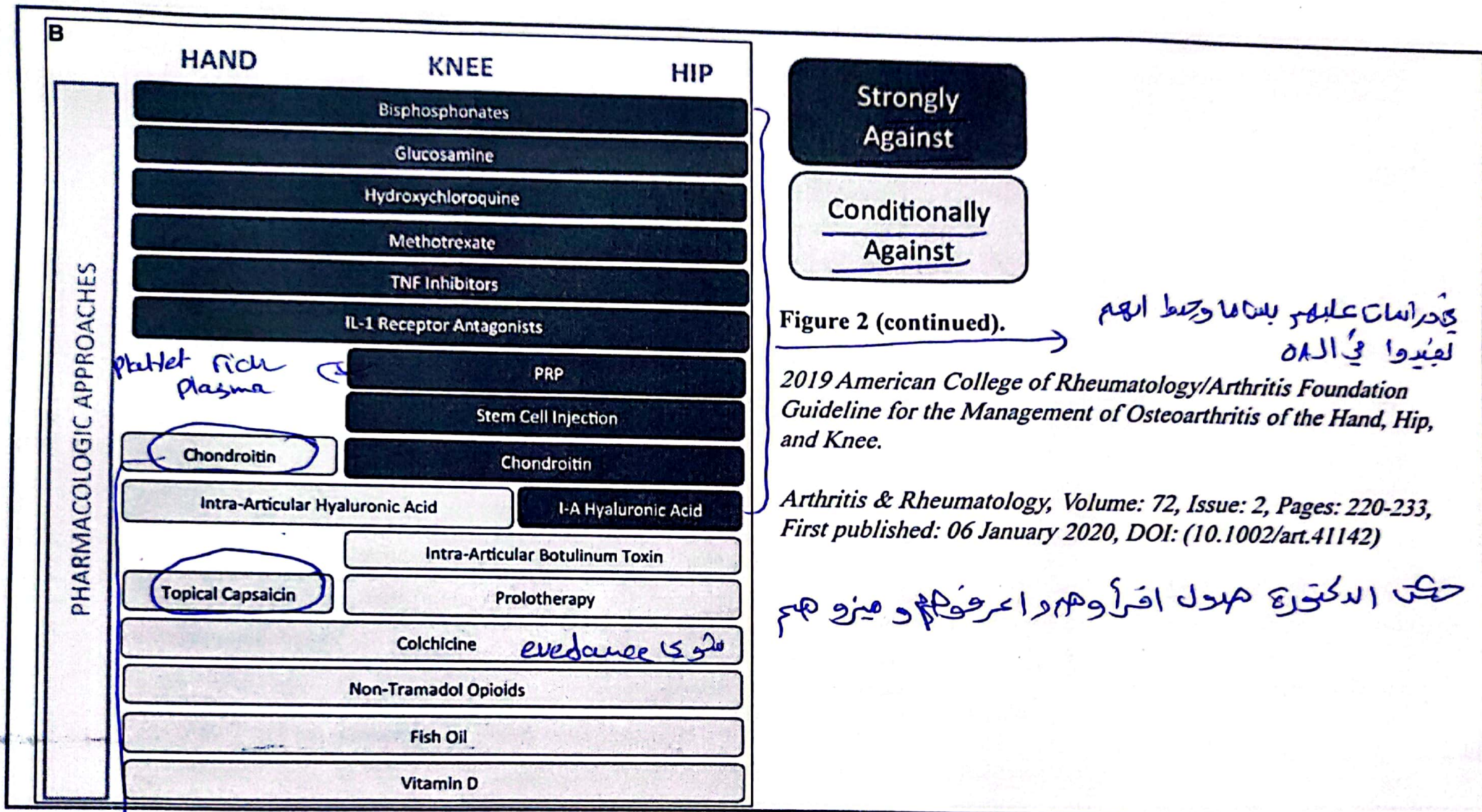
Modified Shoes

Wedged Insoles

Pulsed Vibration
TherapyStrongly
AgainstConditionally
Against

Not recommended

Figure 2. Therapies recommended *against* (physical, psychosocial, and mind-body approaches [A] and pharmacologic approaches [B]) in the management of hand, knee, and/or hip osteoarthritis. No hierarchy within categories is implied in the figure. TENS = transcutaneous electrical nerve stimulation; TNF = tumor necrosis factor; IL-1 = interleukin-1; PRP = platelet-rich plasma; IA = intraarticular.



يُدراسات عليهم بلسا وحيط اهم
لغيروا في الـ ٥٥

حتى الدكتور همدول افروهم و اعرفهم و ميزو هم

الدكتور باعتمادها ان همدول و ميزو بالـ ٥٥
له حثيا عنه قبل كانه
Conditionally effect
ad recommended

⑩ في بعض الأبحاث موجد بأيد والوجه بارع / هود (الوجه في الفترة) (الأيام الموحدة)
عبرهم بالأسفل في أي يوم أنهم استخدموا وانهم effective والتي لكي لا
احتمال أن نرى update (بشيء عن الـ guideline) إلى الـ 2019 فخلال هذا الوقت في بعض
الاختلافات الواضحة مثل كتاب deborah بكي عن الـ capstan لكي أنه
الـ recommended في الـ hand هو not recommended في الـ 2019 لهذا لا
نرى update، مماثلة نوع إلى ما عدا معرفة في، لهذا ضروري
نتائج

لما الشخص الموصوف الدواء يوظف في
 ثاني من اجل يسهل يعني هو الهم مست
 indicated واما يوظف يوظف

TABLE 106-3 Monitoring of Medications Used In Osteoarthritis Treatment

Drug	Adverse Drug Reactions	Monitoring Parameters	Comments
Oral Analgesics			
Acetaminophen	Hepatotoxicity	Total daily dose limits لا تشاركها تجاوز الـ 4g 4g للناس القويين او الـ 3g للناس الهنالك او alcoholic	Use caution with multiple acetaminophen-containing products—total 4 g limit (or less in patients with hepatic dysfunction)
Tramadol	Nausea, vomiting, somnolence	No routine labs recommended	Drug-drug Interaction with other serotonergic medications
Opioids	Sedation, constipation, nausea, dry mouth, hormonal changes	No routine labs recommended	Risks of addiction, dependence, and drug diversion →
NSAIDs	Dyspepsia, CV events, GI bleeding, renal impairment	Kidney BUN/Creatinine, Hgb/Hct, blood pressure	Risks higher in those older than 75 years of age
Topical Analgesics			
Capsaicin	Skin Irritation and burning	Inspection of areas of application نتاج المنطقة التي طبقت عليه	Wash hands thoroughly after application
NSAIDs	Skin itching, rash, irritated Dyspepsia, CV events, GI bleeding, renal impairment هيكلية systemic في حالة مارت absorption و دخل الـ circulation و طوي يترك مع رايانة المصاحبة	Inspection of areas of application. As needed: BUN/Creatinine, Hgb/Hct, blood pressure لا اننا نكتفي انه في مارت systemic	Wash hands thoroughly after application. Avoid oral NSAID or aspirin other than cardioprotective dose. Ensure patient applying gel, solution, or patch correctly
Injectable drugs			
Intra-articular corticosteroids	Hypertension, hyperglycemia (change skin colour) local هيكلية systemic	Glucose, blood pressure	HPA axis suppression if used too frequently
Intra-articular hyaluronates	Local joint swelling, stiffness, pain	No routine labs recommended	Less effective than Intra-articular

→ expensive

لا الـ corticosteroids
 لها اولوية جبرها على
 المريض

TABLE 106-2 Dosing of Medications for Osteoarthritis

multiple acetaminophen product
 للمريض بخلاف ذلك acetaminophen
 product الذي فيه أكثر من acetaminophen

Drug	Brand Name	Starting Dose	Usual Range	Special Population Dose	Other
Oral analgesics					
Acetaminophen	Tylenol	325-500 mg three times a day	325-650 mg every 4-6 hours or <u>1 g 3-4 times/day</u>	Chronic alcohol intake, hepatic disease	Contained in many combination analgesics
Tramadol Tramadol ER	Ultram Ultram ER	25 mg in the morning 100 mg daily	Titrate dose in 25 mg increments to reach a maintenance dose of 50-100 mg three times a day. Titrate to 200-300 mg daily	Creatinine clearance <30 mL/min (0.5 mL/s)—maximum dose is 200 mg daily Do not use if creatinine clearance <30 mL/min (0.5 mL/s)	May need to taper dose upon discontinuation to <u>prevent withdrawal symptoms</u>
Hydrocodone/ acetaminophen	Lortab, Vicodin, Norco	5 mg/325 mg three times daily	2.5-10 mg/325-650 mg 3-5 times daily	Titrate dose slowly in older adults (age >65 years)	Maximum dose limited by total daily dose of acetaminophen
Oxycodone/ acetaminophen	Percocet	5 mg/325mg three times daily	2.5-10 mg/325-650 mg 3-5 times daily	Titrate dose slowly in older adults (age >65 years)	Maximum dose limited by total daily dose of acetaminophen
Topical analgesics					
Capsaicin 0.025% or 0.15%	Capzasin-HP		Apply to affected joint <u>3-4 times per day</u>		
Diclofenac 1% gel	Voltaren		Apply 2 or 4 g per site as prescribed, <u>4 times daily</u>		

Diclofenac 1.3% patch Flector

Apply one patch twice daily to the site to be treated, as directed.

Diclofenac 1.5% solution Pennsald

Apply 40 drops to the affected knee, applying and rubbing in 10 drops at a time. Repeat for a total of four times daily

→ *دوسو التطبيق على مفاصل
joint ال weight drop*

Diclofenac 2% solution Pennsald

Apply 40 mg (two pump actuations) twice daily

Intra-articular Corticosteroids

Triamcinolone Kenalog 5-15 mg/joint

10-40 mg/large-joint (knee, hip, shoulder)

Methylprednisolone acetate Depo-Medrol 10-20 mg/joint

20-80 mg/large-joint (knee, hip, shoulder)

*localy in affected
joint, كذا كان large
joint به جرعة عالية*

*total joint ك
40mg يعني في joint واحدة
اذا عندي 80 maximum*

If multiple joints injected, maximum total dose is usually 80 mg

Often administered concomitantly with a local anesthetic

10-40 mg for medium joints (elbows, wrists)

Nonsteroidal anti-Inflammatory drugs (NSAIDs)

Aspirin, plain, buffered, or enteric-coated	Bayer, Ecotrin, Bufferin	325 mg three times a day	325-650 mg four times a day	Doses of 3,600 mg/day are needed for anti-inflammatory activity
<u>Celecoxib</u>	Celebrex	100 mg daily	100 mg twice daily or 200mg daily	
Diclofenac XR	Voltaren-XR	100 mg daily	100-200 mg daily	Available OTC and Rx
Diclofenac IR	Cataflam	50 mg twice a day	50-75 mg twice a day	
Diflunisal	Dolobid	250 mg twice a day	500-750 mg twice a day	
Etodolac	Lodine	300 mg twice a day	400-500 mg twice a day	
Fenoprofen	Nalfon	400 mg three times a day	400-600 mg 3-4 times a day	
Flurbiprofen	Ansalid	100 mg twice a day	200-300 mg/day 2-4 divided doses	
Ibuprofen	Motrin, Advil	200 mg three times a day	1,200-3,200 mg/day in 3-4 divided doses	
<u>Indomethacin</u>	Indocin	25 mg twice a day	Titrate dose by 25-50 mg/day until pain controlled or maximum dose of 50 mg three times a day	
<u>Indomethacin SR</u>	Indocin SR	75 mg SR once daily	Can titrate to 75 mg SR twice daily if needed	

حسب دواء celecoxib والبرافين انهم على نفس القيمة
(4.7 من الفيدو)

دواء التهاب المفاصل

TABLE 106-2 Dosing of Medications for Osteoarthritis (Continued)

Drug	Brand Name	Starting Dose	Usual Range	Special Population Dose	Other
Ketoprofen	Orudis	50 mg three times a day	50-75 mg 3-4 times a day		
Meclofenamate	Meclomen	50 mg three times a day	50-100 mg three to four times a day		
Mefenamic acid	Ponstel	250 mg three times a day	250 mg four times a day		FDA approval for 1 week of therapy
Meloxicam	Mobic	<u>7.5 mg daily</u>	<u>15 mg daily</u>		
Nabumetone	Relafen	500 mg daily	500-1000 mg 1-2 times a day		
Naproxen	Naprosyn	250 mg twice a day	500 mg twice a day		
Naproxen sodium	Anaprox, Aleve	220 mg twice a day	220-550 mg twice a day		Available OTC and Rx
Naproxen sodium DR	Naprelan		375-750 mg twice a day		
Oxaprozin	Daypro	600 mg daily	600-1200 mg daily		
Piroxicam	Feldene	10 mg daily	20 mg daily		
Salsalate	Disalcid	500 mg twice a day	500-1000 mg 2-3 times a day		

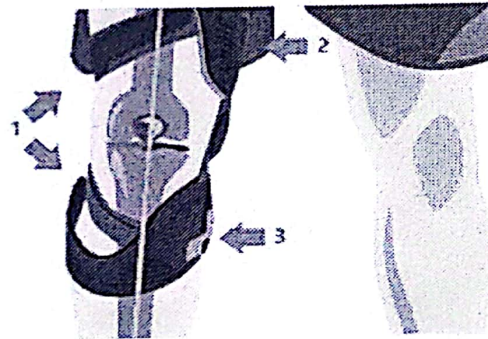
Nonpharmacologic Therapies

بدلاً نعرف مشي الاسي الى رجل الوضع اسوأ ويزيد الألم ، وسو لازم نتجنب

- ✓ Activities that involve excessive use of the joint should be identified and avoided.
- ✓ When ^{Knees, hip} weight-bearing joints are affected, support in the form of a cane, crutches, or a walker can be helpful.
لـ الي روطوا دعامة او لمينوا بالمسي
- ✓ Weight reduction may be of benefit, even for non-weight-bearing joints.
- ✓ Consultation with occupational and physical therapists may be helpful.



Knee OA without bracing
(bone-on-bone contact)



The 3-Point Leverage
System



Knee OA with bracing
(space created between bones)



لـ الدعامة يسهل support و خفف الاحتكاك
لـ تخفف الاحتكاك ويتساعد على الحركة

✓ Physical supports (cervical collar, lumbar corset), local heat, and exercises to strengthen cervical, paravertebral, and abdominal muscles may provide relief in some patients.

✓ النهج الجراحي Surgical Management can be considered when patients suffer from disabling pain or deformity:

للمشت تأثر كبير على (ال) activity Function خلال اليوم

- Joint replacement surgery usually relieves pain and increases function in selected patients.

- Laminectomy and spinal fusion should be reserved for patients who have severe disease with intractable pain or neurologic complications.

ماهي حالة كانه في ال Lumbar
يمكن يستخدم ال Corset مشد

TABLE 106-1 Nonpharmacologic Interventions In the Treatment of OA^{28,29}

Intervention	Strength of Recommendation
Exercise	Strong
Weight loss (If overweight)	Strong
Patient education	Strong
Use of assistive device (Ie, cane)	Moderate
Use of shoe Insoles	Moderate
Application of heat	Moderate
Use of fitted knee braces	Minimal
Lateral patellar <u>taping</u>	Minimal
Passive exercise alone	Minimal

Robustness of recommendation: Strong—fully supported by evidence-based guidelines, Moderate—supported by evidence-based guidelines, Minimal—little support by evidence-based guidelines.

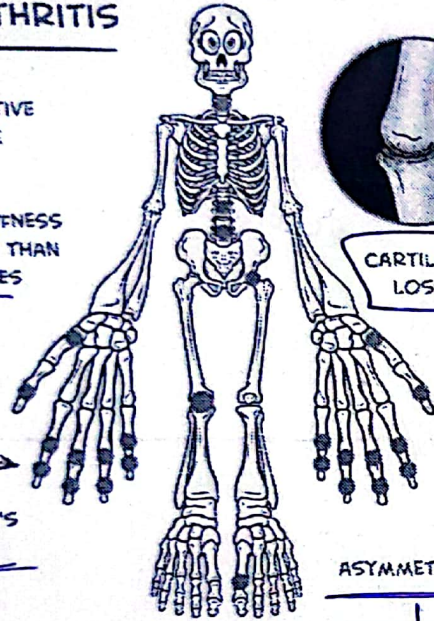
OA versus RA

OSTEOARTHRITIS

✓ DEGENERATIVE DISEASE

MORNING STIFFNESS
LASTING LESS THAN
30 MINUTES

✓
HEBERDEN'S
NODES



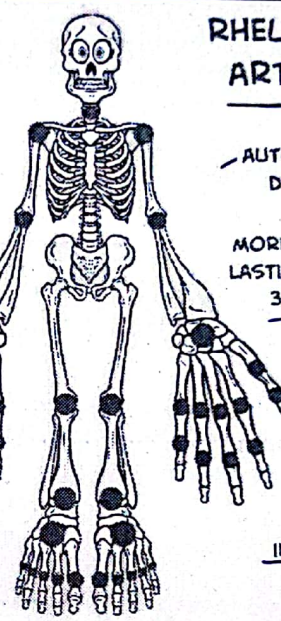
CARTILAGE
LOSS

ASYMMETRICAL



INFLAMED
SYNOVIUM

SYMMETRICAL



RHEUMATOID ARTHRITIS

✓ AUTOIMMUNE
DISEASE

MORNING STIFFNESS
LASTING MORE THAN
30 MINUTES

EXTRA-
ARTICULAR
INVOLVEMENT



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موتور، كتيو
التي هي لـ ١٥

deformities
management ال RA ال
as soon as ال ال
ال ال ال ال
DMARD ال ال ال
كافي

Deemah Santani
دعاء السنتاني

Stages of Knee Osteoarthritis - YouTube

<https://www.youtube.com/watch?v=BBqiltHNOrc>

4:08

Knee Joint Injection - YouTube

<https://www.youtube.com/watch?v=n7BtIHmhOcg>

1:13

Steroid Therapy for Knee Joint Arthritis - Medical Animation by
Watermark - YouTube

<https://www.youtube.com/watch?v=aYjqH9ePIMA>

1:14

Knee joint steroid injection - YouTube

https://www.youtube.com/watch?v=0W3i_fJfa4w

4:53