KNOW CHRONIC JOINT PAIN

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Learning Objectives

- After completing this module, participants will be able to:
 - Discuss the prevalence of chronic joint pain, including osteoarthritis
 - Understand the impact of chronic joint pain and its comorbidities on patient functioning and quality of life
 - Explain the pathophysiology of chronic joint pain
 - Assess and diagnose patients presenting with chronic joint pain
 - Select appropriate pharmacological and non-pharmacological strategies to manage chronic joint pain
 - Know when to refer patients to specialists

Table of Contents

- What is chronic joint pain?
- How common are the various types of chronic joint pain?
- How can different forms of chronic joint pain, such as osteoarthritis and rheumatoid arthritis, be differentiated from each other in clinical practice?
- How should osteoarthritis, the most common form of chronic joint pain, be treated based on its pathophysiology?

What is chronic joint pain?

- Joint pain that persists beyond the normal expected tissue healing time of 3 months
- A wide variety of conditions can cause chronic joint pain



Davatchi F. In: Kopf A, Patel NB (eds). *Guide to Pain Management in Low-Resource Settings*. IASP Press; Seattle, WA: 2010; International Association for the Study of Pain. *Unrelieved Pain Is a Major Global Healthcare Problem*. Available at: <u>http://www.iasp-pain.org/AM/Template.cfm?Section=Press_Release&Template=/CM/ContentDisplay.cfm&ContentID=2908</u>. Accessed: July 19, 2013; Nielsen GP *et al. Semin Diagn Pathol* 2011; 28(1):37-52.

Discussion Questions

WHAT PROPORTION OF PATIENTS IN YOUR PRACTICE SUFFER FROM JOINT PAIN? WHAT IS THE MOST COMMON CAUSE OF JOINT PAIN AMONG YOUR PATIENTS?

Prevalence of Specific Conditions Associated with Chronic Joint Pain



Mayo Clinic. *Arthritis*. Available at: https://healthletter.mayoclinic.com/secure/pdf/SRAR.pdf. Accessed: August 19, 2013; Wong R *et al. Prevalence of Arthritis and Rheumatic Diseases Around the World: A Growing Burden and Implications for Health Care Needs.* Arthritis Community Research and Evaluation Unit; Toronto, ON: 2010.

Discussion Questions

IN WHAT WAYS DOES JOINT PAIN IMPACT YOUR PATIENTS' QUALITY OF LIFE? HOW DOES THIS INFLUENCE HOW YOU MANAGE THESE PATIENTS?

Impact of Chronic Conditions on Health-Related Quality of Life



Note: a larger negative score indicates a greater impact on health-related quality of life CHD = coronary heart disease; COPD = chronic obstructive pulmonary disease; CPA = chronic polyarthritis Brettschneider C *et al. PLoS One* 2013; 8(6):e66742.

Treating Underlying Causes of Joint Pain

- Many different conditions present with joint pain
 - Understanding clinical, laboratory and radiological features of these diseases can lead to early diagnosis and appropriate therapy
- Prompt recognition of underlying disease and institution of proper therapy can lead to improved prognosis

Polyarticular joint pain. In: *The Merck Manual for Health Care Professionals*. Available at: <u>http://www.merckmanuals.com/professional/</u> musculoskeletal_and_connective_tissue_disorders/symptoms_of_joint_disorders/polyarticular_joint_pain.html. Access: August 9, 2013.

Osteoarthritis: Most Common Form of Chronic Joint Pain

• Affects:

- 13.9% of adults aged 25 years and older
- 33.6% of those 65 years and older
- As the general population ages, the numbers of people affected are likely to increase dramatically

Incidence of Osteoarthritis of the Hand, Hip and Knee



Distinguishing Osteoarthritis from Rheumatoid Arthritis

Characteristic	Osteoarthritis	Rheumatoid arthritis
Pathophysiologic process	Degenerative	Autoimmune
Commonly affected joints	Knees, spine, hips, hands	Fingers, feet
Typically symmetrical involvement	Νο	Yes
Morning stiffness	<30 minutes	>30 minutes
Joint swelling	Hard tissue	Soft tissue
Hand involvement	Distal joints	Proximal joints
Extra-articular involvement	Νο	Yes
Elevated autoimmune markers	No	Yes

Centers for Disease Control. *Osteoarthritis*. Available at: http://www.cdc.gov/arthritis/basics/osteoarthritis.htm. Accessed: August 19, 2013; Centers for Disease Control. *Rheumatoid Arthritis*. Available at: http://www.cdc.gov/arthritis/basics/rheumatoid.htm. Accessed: August 19, 2013; National Institutes of Health. *Osteoporosis and Arthritis: Two Common but Different Conditions*. Available at: http://www.niams.nih.gov/Health_Info/Bone/Osteoporosis/Conditions_Behaviors/osteoporosis_arthritis.asp. Accessed: August 19, 2013; O'Dell JR. In: Goldman L, Ausiello D (eds) *Cecil Textbook of Medicine*. 23rd ed. Saunders Elsevier; Philadelphia, PA: 2007.

Joint Involvement Differentiates Osteoarthritis from Rheumatoid Arthritis



CMC = carpometacarpal; DIP = distal interphalangeal; MCP = metacarpophalangeal; MTP = metatarsophalangeal; PIP = proximal interphalangeal; TMT = tarsometatarsal Lane NE *et al.* In: Goldman L, Ausiello D (eds). *Cecil Textbook of Medicine*. 23rd ed. Saunders Elsevier; Philadelphia, PA: 2007; O'Dell JR. In: Goldman L, Ausiello D (eds). Cecil Textbook of Medicine. 23rd ed. Saunders Elsevier; Philadelphia, PA: 2007;

Commonly Affected Joints: Prevalence of Symptomatic Osteoarthritis



CMC = carpometacarpal; DIP = distal interphalangeal; MTP = metatarsophalangeal; PIP = proximal interphalangeal Centers for Disease Control. *Osteoarthritis*. Available at: <u>http://www.cdc.gov/arthritis/basics/osteoarthritis.htm</u>. Accessed: July 22, 2013.

Factors Contributing to Osteoarthritis Development



Mandelbaum B, Waddell D. Orthopedics 2005; 28(2 Suppl):S207-14.

Discussion Question

WHAT PHYSICAL EXAMINATIONS AND/OR OTHER EXAMINATIONS DO YOU ROUTINELY USE TO EVALUATE OSTEOARTHRITIS?

Radiographic Findings Distinguish Different Types of Joint Pain

Condition	Bone density	Erosions	Cysts	Joint space loss	Distribution	Bone production
Osteo- arthritis	Normal overall	x *	Subchondral	Non- uniform	Unilateral or bilateral Asymmetric	Osteophytes Subchondral sclerosis
Rheumatoid arthritis	Decreased	\checkmark	Synovial	Uniform	Bilateral Symmetric	×
Psoriatic arthritis	Normal	\checkmark	×	\checkmark	Unilateral Asymmetric	\checkmark
CPPD	Normal	×	\checkmark	Uniform	Unilateral Asymmetric	Osteophytes Chondrocalcinosis Subchondral
Ankylosing spondylitis	Early – normal Late – decreased	\checkmark	×	\checkmark	Unilateral Asymmetric	\checkmark
DISH	Normal	×	×	×	Sporadic	Flowing osteophytes Tendon or ligament ossification

*Unless erosive osteoarthritis

CPPD = calcium pyrophosphate deposition disease; DISH = diffuse idiopathic skeletal hyperostosis Adapted from: Swagerty DL Jr, Hellinger D. *Am Fam Physician* 2001; 64(2):279-86.

Radiography: Osteoarthritis vs. Rheumatoid Arthritis of the Hand

Osteoarthritis



Rheumatoid Arthritis



Swagerty DL Jr, Hellinger D. Am Fam Physician 2001; 64(2):279-86.

Radiographic Hallmarks of Osteoarthritis

Gr Subcho scl	ade 1 ndral bone erosis	Grade 2 Decreased joint space	Grade 3 Osteophytes and geodes	Grade 4 Malformation
Grade 1	Grade 1 Doubtful narrowing of joint space and possible osteophytic lipping			
Grade 2	Definite osteophytes and possible narrowing of joint space			
Grade 3	3 Moderate multiple osteophytes, definite narrowing of joint space, and some sclerosis			
Grade 4	Large osteophytes, marked narrowing of joint space, severe sclerosis, and definite deformity of bone end			

Hunter DJ et al. Curr Opin Rheumatol 2009; 21(2):110-7; Swagerty DL Jr, Hellinger D. Am Fam Physician 2001; 64(2):279-86;

Physical Examinations for Osteoarthritis

Knee	Нір
Check alignment	Look for leg length discrepancy
Assess muscle strength (quadriceps atrophy)	Assess muscle strength
Evaluate tenderness/pain	Evaluate tenderness/pain
Assess range of motion	Assess range of motion
Palpate for bony swelling	
Check for crepitus	
Inspect gait	
Look for inflammation	

Note that while instability should be assessed, there there is no physical examination sign for instability. Cibere J *et al.* Arthritis Rheum 2004; 50(2):458-68; Cibere J *et al.* Arthritis Rheum 2008; 59(3):373-81.

EULAR: Major Components in the Diagnosis of Hand Osteoarthritis

Risk Factors

- Female sex
- Age >40 years
- Menopausal status
- Family history of hand osteoarthritis
- Obesity
- Higher bone density
- Greater forearm muscle strength
- Joint laxity
- Prior hand injury
- Occupation- or recreation-related usage

Symptoms

- Pain on usage
- Mild morning or inactivity stiffness affecting one or a few joints at a time
- Symptoms often intermittent
- Symptoms target DIP, PIP, thumb base, index and MCP joints

Clinical Hallmarks

- Heberden's nodes
- Bouchard's nodes
- Bony enlargement without deformity affecting characteristic joints (DIP, PIP, thumb base, index and MCP joints)

Radiographic Features

- Joint space narrowing
- Osteophyte
- Subchondral bone sclerosis
- Subchondral cyst
- Subchondral erosis in erosive hand osteoarthritis

DIP = distal interphalangeal; EULAR = European League Against Rheumatism; MCP = metacarpophalangeal; PIP = proximal interphalangeal Zhang W *et al. Ann Rheum Dis* 2009; 68(1):8-17.

EULAR: Major Components in the Diagnosis of Knee Osteoarthritis



Zhang W et al. Ann. Rheum Dis 2010; 69(3):483-9.

Goals of Osteoarthritis Treatment



Goals in Pain Management

- Involve the patient in the decision-making process
- Agree on realistic treatment goals before starting a treatment plan



Farrar JT et al. Pain 2001; 94(2):149-58; Gilron I et al. CMAJ 2006; 175(3):265-75.

Combining Pharmacological and Non-pharmacological Therapies Is Most Effective in Managing Osteoarthritis



Discussion Question

WHAT NON-PHARMACOLOGICAL THERAPIES HAVE YOU FOUND TO BE HELPFUL IN MANAGING CHRONIC PAIN IN YOUR PATIENTS?

WHICH ONES HAVE YOU FOUND TO BE INEFFECTIVE/UNHELPFUL?

Non-pharmacological Treatment of Osteoarthritis

Core treatment:







Weight reduction

Exercise

Education

Other modalities to potentially consider:

- Acupuncture
- Assisted devices (e.g., splints, insoles)

- Heat and cold therapy
- Transcutaneous electrical nerve stimulation

AAOS: Pharmacological Management of Knee Osteoarthritis

Recommended • Coxibs **Topical nsNSAIDs** • Oral nsNSAIDs Tramadol Not recommended Chondroitin Growth factor injections • Glucosamine Hyaluronic acid • Insufficient evidence Opioids Acetaminophen **Pain patches** Intra-articular corticosteroids

AAOS = American Academy of Orthopaedic Surgeons; coxib = COX-2-selective inhibitor; nsNSAID = non-selective non-steroidal anti-inflammatory drug Jevsevar DS *et al. J Bone Joint Surg Am* 2013; 95(20):1885-6.

Mechanism-Based Treatment of Inflammatory Pain



CNS = central nervous system; coxib = COX-2 inhibitor; nsNSAID = non-specific non-steroidal anti-inflammatory drug Hochberg MC et al. Arthritis Care Res (Hoboken) 2012; 64(4):465-74; Scholz J et al. Nat Neurosci 2002; 5(Suppl):1062-7.

Mechanism-Based Treatment of Chronic Pain in Osteoarthritis



CNS = central nervous system; coxib = COX-2 inhibitor; nsNSAID = non-specific non-steroidal anti-inflammatory drug Hochberg MC et al. Arthritis Care Res (Hoboken) 2012; 64(4):465-74; Scholz J et al. Nat Neurosci 2002; 5(Suppl):1062-7.

What are NSAIDs (nsNSAIDs/coxibs)?

NSAID = Non-Steroidal Anti-Inflammatory Drug

- Analgesic effect via inhibition of prostaglandin production
- Broad class incorporating many different medications:

Examples of nsNSAIDs:

- Diclofenac
- Ibuprofen
- Naproxen

Examples of Coxibs:

- Celecoxib
- Etoricoxib
- Parecoxib

coxib = COX-2-specific inhibitor; nsNSAID = non-specific non-steroidal anti-inflammatory drug

Brune K. In: Kopf A et al (eds). Guide to Pain Management in Low-Resource Settings. International Association for the Study of Pain; Seattle, WA: 2010.

How do nsNSAIDs/coxibs work?



Adverse Effects of nsNSAIDs/Coxibs

All NSAIDs:

- Gastroenteropathy
 - Gastritis, bleeding, ulceration, perforation
- Cardiovascular thrombotic events
- Renovascular effects
 - Decreased renal blood flow
 - Fluid retention/edema
 - Hypertension
- Hypersensitivity

Cox-1-mediated NSAIDs (nsNSAIDs):

Decreased platelet aggregation

Coxib = COX-2-specific inhibitor; NSAID = non-steroidal anti-inflammatory drug; nsNSAID = non-specific non-steroidal anti-inflammatory drug

Clemett D, Goa KL. *Drugs* 2000; 59(4):957-80; Grosser T *et al.* In: Brunton L *et al* (eds.). *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 12th ed. (online version). McGraw-Hill; New York, NY: 2010.

nsNSAIDs/Coxibs and Cardiovascular Risk



Composite includes non-fatal myocardial infarction, non-fatal stroke, or cardiovascular death compared with placebo; chart based on network meta-analysis involving 30 trials and over 100,000 patients. Coxib = COX-2 inhibitor; nsNSAID = non-specific non-steroidal anti-inflammatory drug Trelle S *et al. BMJ* 2011; 342:c7086.

Risk Factors for Gastrointestinal Complications Associated with nsNSAIDs/Coxibs



Odds ratio/relative risk for ulcer complications

ASA = acetylsalicylic acid; coxib = COX-2-specific inhibitor; GI = gastrointestinal; NSAID = non-steroidal anti-inflammatory drug; nsNSAID = non-specific non-steroidal anti-inflammatory drug; SSRI = selective serotonin reuptake inhibitor

1. Garcia Rodriguez LA, Jick H. Lancet 1994; 343(8900):769-72; 2. Gabriel SE et al. Ann Intern Med 1991; 115(10):787-96;

3. Bardou M. Barkun AN. Joint Bone Spine 2010; 77(1):6-12; 4. Garcia Rodríguez LA, Hernández-Díaz S. Arthritis Res 2001; 3(2):98-101.

Gastrointestinal Effects of nsNSAIDs/Coxibs Beyond the Upper Gastrointestinal Tract

- There is strong evidence to suggest that potentially clinically relevant adverse gastrointestinal events are not limited to the upper gastrointestinal tract
- Studies suggest NSAIDs also increase the risk for lower* gastrointestinal clinical events



*Lower gastrointestinal means distal to the ligament of Treitz or fourth segment of the duodenum Coxib = COX-2-specific inhibitor; NSAID = non-steroidal anti-inflammatory drug; nsNSAID = non-specific non-steroidal anti-inflammatory drug

Allison MC et al. N Engl J Med 1992; 327(11):749-54; Chan FK et al. N Engl J Med 2002; 347(26):2104-10; Fujimori S et al. Gastro Endoscopy 2009; 69(7):1339-46; Laine L et al. Gastroenterology 2003; 124(2):288-92; Lanas A, Sopeña F. Gastroenterol Clin N Am 2009; 38(2):333-53.

Guidelines for nsNSAIDs/Coxibs Use Based on Gastrointestinal Risk and ASA Use

	Gastrointestinal risk		
	Not elevated	Elevated	
Not on ASA	nsNSAID along	Coxib	
	IISNJAID alone	nsNSAID + PPI	
On ASA	Coxib + PPI	Coxib + PPI	
	nsNSAID + PPI	nsNSAID + PPI	

ASA = acetylsalicylic acid; coxib = COX-2-specific inhibitor; nsNSAID = non-selective non-steroidal anti-inflammatory drug; PPI = proton pump inhibitor Tannenbaum H *et al. J Rheumatol* 2006; 33(1):140-57.

How Opioids Affect Pain

Brain

Perception

Modify perception, modulate transmission and affect transduction by:

- Altering limbic system activity; modify sensory and affective pain aspects
- Activating descending pathways that modulate -transmission in spinal cord
- Affecting transduction of pain stimuli to nerve impulses



Reisine T, Pasternak G. In: Hardman JG et al (eds). Goodman and Gilman's: The Pharmacological Basics of Therapeutics. 9th ed. McGraw-Hill; New York, NY: 1996; Scholz J, Woolf CJ. Nat Neurosci 2002; 5(Suppl):1062-7; Trescot AM et al. Pain Physician 2008; 11(2 Suppl):S133-53.

Adverse Effects of Opioids

System	Adverse effects
Gastrointestinal	Nausea, vomiting, constipation
CNS	Cognitive impairment, sedation, lightheadedness, dizziness
Respiratory	Respiratory depression
Cardiovascular	Orthostatic hypotension, fainting
Other	Urticaria, miosis, sweating, urinary retention

CNS = central nervous system

Moreland LW, St Clair EW. *Rheum Dis Clin North Am* 1999; 25(1):153-91; Yaksh TL, Wallace MS. In: Brunton L *et al* (eds). *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 12th ed. (online version). McGraw-Hill; New York, NY: 2010.

Management of Osteoarthritis Flowchart



nsNSAID = non-specific non-steroidal anti-inflammatory drug; PPI = proton pump inhibitor; TENS = transcutaneous electrical nerve stimulation Adapted from: Adebajo A. *BMC Fam Pract* 2012; 13:23.

Selected Osteoarthritis Management Guidelines

Organization		Joints		
		Hand	Нір	Knee
ESCEO ¹	2014			Х
OARSI ²	2014			Х
NICE ³	2014	Х	Х	Х
AAOS ⁴	2013			Х
South Africa ⁵	2013	Х	Х	Х
ACR ⁶	2012	Х	Х	Х
Chinese Orthopaedic Association ⁷	2010	Х	Х	Х
Croatian Society for Rheumatology ⁸	2010		Х	Х
EULAR ⁹	2010			Х
Mexico ¹⁰	2008		Х	Х
EULAR ¹¹	2007	Х		
EULAR ¹²	2005		Х	

ACR = American College of Rheumatology; AAOS = American Academy of Orthopaedic Surgeons; NICE = National Institute of Clinical Excellence; ESCEO = European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis; EULAR = European League Against Rheumatism; OARSI = Osteoarthritis Research Society International Bruyère O *et al. Semin Arthritis Rheum* 2014; pii:S0049-0172(14)00108-5; 2. McAlindon TE *et al. Osteoarthritis Cartilage* 2014; 22(3):363-88; 3. National Institute for Health and Care Excellence. 2014; 4. Jevsevar DS *et al. J Bone Joint Surg Am* 2013; 95(20):1885-6; 5. Hodkinson B *et al. S Afr Med J* 2013;103(8 Pt 2):576-85; 6. Hochberg MC *et al. Arthritis Care Res (Hoboken)* 2012; 64(4):465-74; 7. Chinese Orthopaedic Association. *Orthop Surg* 2010; 2(1):1-6; 8. Grazio S *et al. Reumatizam* 2010; 57(1):36-47; 9. Zhang W *et al. Ann Rheum Dis* 2010;69(3):483-9; 10. Secretaria de Salud. 2008; 11. Zhang W *et al. Ann Rheum Dis* 2007;66(3):377-88; 12. Zhang W *et al. Ann Rheum Dis* 2005;64(5):669-81.

But... Patients with Chronic Pain of Just One Type of Pain Pathophysiology May be Rare



Patients with mixed pain may benefit from *combination therapy*

Otori S et al. Yonsei Med J 2012; 53(4):801-5; Vellucci R. Clin Drug Investig 2012; 32(Suppl 1):3-10.

Discussion Question

WHAT TREATMENT APPROACH WOULD YOU TAKE WITH A PATIENT SUFFERING FROM MIXED PAIN?

Neuropathic Pain in Osteoarthritis

- Some osteoarthritis patients may use terms such as "burning" or "numbness" to describe their pain
 - These verbal descriptors are suggestive of a neuropathic component
- Based on mechanism of action and preliminary studies, non-traditional analgesics such as $\alpha_2 \delta$ ligands, TCAs and SNRIs, may be useful for treating this component
 - However, further studies are needed to clarify the role of these drugs in osteoarthritis

When to Refer Patients with Osteoarthritis

Urgency	Hip osteoarthritis	Knee osteoarthritis		
Immediate	Evidence of infection in the joint	Evidence of infection in the joint		
Urgent	Symptoms rapidly deteriorate and are causing severe disability	Evidence of acute inflammation (e.g., hemarthrosis, gout, pseudo-gout)		
Soon	N/A	Joint continues to "give way" (i.e., fails to provide proper support) despite therapy Symptoms rapidly deteriorate and are causing severe disability		
Routine appointment	Symptoms impair the quality of life*	Symptoms impair the quality of life*		

*Referral criteria should take into account the extent to which the condition is causing pain, disability, sleeplessness, loss of independence, inability to undertake normal activities, reduced functional capacity or psychiatric illness N/A = not applicable

National Institute for Clinical Excellence. Referral Advice: A Guide to Appropriate Referral From General to Specialist Services. London, UK: 2001.



- A wide variety of conditions can cause joint pain, but osteoarthritis is the most common cause, affecting >10% of the population
- It is important to assess and treat underlying causes of joint pain to help guide choice of therapy and improve prognosis
- Signs, symptoms and radiographic findings can help distinguish osteoarthritis from other causes of joint pain

Key Messages (cont'd)

- Signs of infection or autoimmune/ inflammatory disease should prompt referral to a specialist
- Core management of osteoarthritis should include education, exercise and weight reduction
- Pharmacological management may include paracetamol, nsNSAIDs/coxibs and/or opioids