National Cancer Institute

Cairo University

Chronic Musculoskeletal Pain

An Essay by

Dr. Mohamed Younis Hamed Makharita

Lecturer of Anesthesia, Faculty of Medicine,

Mansoura University

Submitted for partial fulfillment of Master Degree in Pain Relief

SUPERVISED BY

Prof. Mohamed Omar Tawfik

Professor of Anesthesia, ICU and Pain Relief

National Cancer Institute

Cairo University

Prof. El Gohary Mousa Tantawy

Professor of Anesthesia, ICU and Pain Relief

National Cancer Institute

Cairo University

Dr. Rada Mohammed Gamal

Fellow of Anesthesia, and Pain Relief

National Cancer Institute

Cairo University

2009

محضر اجتماع لجنة الحكم

على الرسالة المقدمة من الطبيب / محمد يونس حامد مخاريطة
(١) توطئة للحصول على درجة الماجستير فى / علاج الألم

أجتمعت لجنة الحكم على الرسالة المذكورة من السادة /

الاستاذ الدكتور / الجوهرى موسى طنطاوى	(عن المشرفين)
الاستاذ الدكتور / خالد عبدالحميد مصطفى	(ممتحن داخلى)
الاستاذ الدكتور / ماهر فوزى محمود	(ممتحن خارجى)

وذلك فى يوم الخميس ٢٨/٥/٢٠٠٩ فى الساعة العاشرة صباحا
فى جلسة علنية بمدرج / قاعه المؤتمرات بالمعهد

ثم ناقشه السادة أعضاء لجنة الحكم فى

وقررت اللجنة

الاستاذ الدكتور	الاستاذ الدكتور	الاستاذ الدكتور

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Acknowledgement

First and foremost, I thank **ALLAH,** the most Merciful and the most Gracious.

I would like to express my sincere gratitude to ***Prof .Dr. Mohamed Omar Tawfik*** **,**Professor of Anaesthesia , ICU and Pain Relief ,National Cancer Institute, Cairo University, whose guidance and sincere supervision were the cornerstone in the building up of this essay.

I would also like to express my gratitude and sincere thanks to, ***Prof. Dr. El Gohary Mousa Tantawy***, Professor of Anaesthesia , ICU and Pain Relief ,National Cancer Institute, Cairo University, for his keen supervision and advice.

I would like to express my gratitude and sincere thanks to ***Dr. Rada Mohammed Gamal,*** Fellow of Anaesthesia , ICU and Pain Relief ,National Cancer Institute, Cairo University, for her invaluable help, cooperation and encouragement.

Dr. Mohamed Younis Makharita,

Lecturer of Anaesthesia and Surgical Intensive Care,

Faculty of Medicine, Mansoura University

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List of Abbreviations

ACh	: acetylcholine
ADP	: Adenosine diphosphate
ATP	: Adenosine triphosphate
BMI	: body mass index
COX-2 inhibitors	: cyclo-oxygenase -2 inhibitors
ESR	: erythrocyte sedimentation rate
FM	: Fibromyalgia syndrome
LJOA	: Large Joint Osteoarthritis
MEPPs	: miniature end plate potentials
MPS	: Myofascial Pain Syndrom
MRI	: Magnetic Resonance Imaging
NGF	: nerve growth factor
NMDA receptor	: N- methyl- D- aspartate receptor
NMR	: nuclear magnetic resonance
NSAIDs	: nonsteroidal anti-inflammatory drugs
DMARDs	: disease modifying antirheumatic drugs
OA	: Osteoarthritis
PMMA	: polymethylmethacrylate
RA	: Rheumatoid Arthritis
RF	: rheumatoid factor
SLE	: Systemic Lupus Erythematosus
TrPs	: Trigger points

Introduction

The musculoskeletal system consists of the bone and articulations of the skeleton (joints) and the ligaments , muscles, and tendons that connect and manipulate them. There are over 100 acute and chronic musculoskeletal disorders, some with multisystem involvement whilst others affect specific regions only. Musculoskeletal pain is considered any pain emanating from bones, muscles , joints or supporting connective tissue, including ligaments and tendons. Conservative estimates of reported cases indicate that 23 millions of the U.S. population have one or more chronic disorders of the musculoskeletal system .[1]

The vast majority of patients first present for consultation and treatment, it is the complaint of pain, above all other symptoms, that dominates the initial patient–physician encounter. Certainly, the fear of having a potentially crippling disease or of not being able to perform certain tasks because of weakness, stiffness, or loss of dexterity comes to the fore after the impact of the illness is explored. However, it is the worsening of pain or the fear of increased pain that has brought the patient to see the physician at that particular time although other symptoms may have been present for months or even years.

Musculoskeletal disorders are the main cause of disability in the workforce and the leading cause of disability in age-related groups.[2] The spectrum of musculoskeletal disease is vast, pain physician typically treats many types of musculoskeletal diseases. The pain physician encounters patients with inflammatory conditions, such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE) or degenerative joint disease such as osteoarthritis, or other conditions such as myofascial pain syndromes and fibromyalgia.

Aim of the study

This essay reviews the epidemiology, pathophysiologyic mechanisms, clinical picture, and managements of the most common musculoskeletal painful disorders including:-

-Rhomatoid arthritis (RA) and Osteoarthritis (OA) as examples for joint pain.

-Myofacial pain and Fibromyalgia as examples for muscle pain.

-Malignant bone pain as examples for bone pain.

I. Joint Pain

Pain involving joints has many causes which may be due to intrinsic disorders (i.e. those involving the joints and related structures) or extrinsic disorders arising outside the joints(Fig 1)

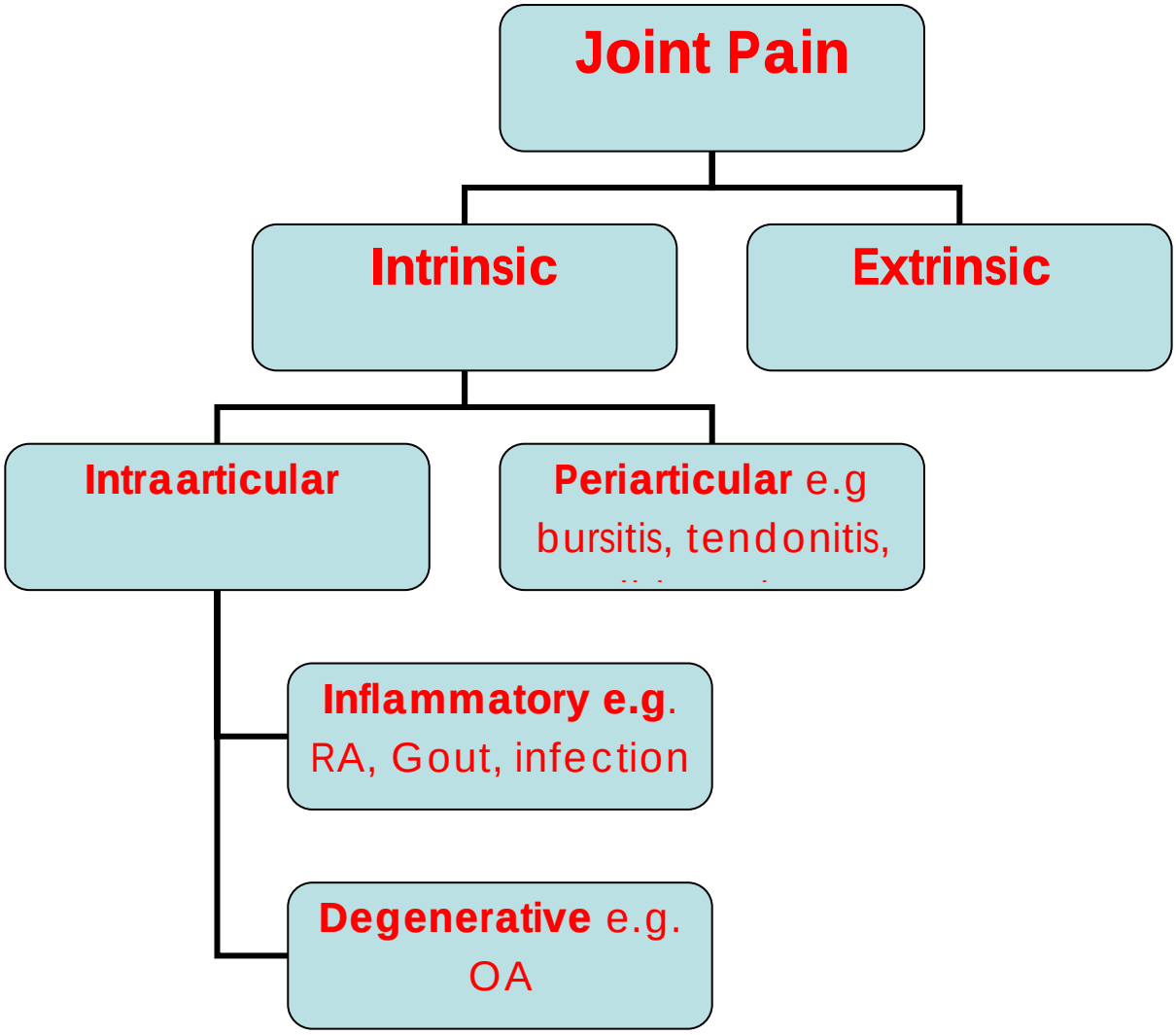

Figure 1: Etiology of joint pain (From: Burton, 1996)[3]

Rheumatoid Arthritis

Rheumatoid arthritis (RA) a chronic systemic inflammatory disease with approximately 0.5- 1.5% of the population affected. It affects more women than men in a ratio of 2.5:1. It can occur at any age but is more common between the age of 40 and 70 years .[4]The cause of RA is unknown but there appears to be a genetic predisposition to the development of this disease. Family studies demonstrate a modest genetic predisposition to the development of RA, with concordance rate for monozygotic twins being in the order of 12-15% and the rate of dizygotic twins being 2-5 %. First degree relatives of patient with RA have a fourfold risk of developing the disorder compared to general population.[5] It seems probable that RA is under the influence of multiple genes. Some studies report a relatively weak association between certain HLA-DRB1 alleles and disease susceptibility. Although there is a much stronger association with HLA alleles and disease severity once the disease becomes established. [6]

The cardinal features of RA are pain and swelling involving many joints. Other symptoms and signs of inflammation include warmth, erythema, and loss of function. The pain is usually more prominent and more persistent than in osteoarthritis, occurring at rest, at night, and on activity. Although the clinical diagnosis of RA is usually obvious in full-blown cases, the variability of presentation, severity, and progression can make the disease more difficult to diagnose. The American College of Rheumatology has promulgated useful guidelines to assist the clinician in its diagnosis.[7]These guidelines are presented in Table1.

Table 1: 1987 Criteria for the Classification of Acute Arthritis of Rheumatoid Arthritis.[7]

Criterion	Definition
1. Morning stiffness	Morning stiffness in and around the joints, lasting at least 1 hour before maximal improvement
2. Arthritis of 3 or more joint areas	At least 3 joint areas simultaneously have had soft tissue swelling or fluid (not bony overgrowth alone) observed by a physician. The 14 possible areas are right or left PIP, MCP, wrist, elbow, knee, ankle, and MTP joints
3. Arthritis of hand joints	At least 1 area swollen (as defined above) in a wrist, MCP, or PIP joint
4. Symmetric arthritis	Simultaneous involvement of the same joint areas (as defined in 2) on both sides for the body (bilateral involvement of PIPs, MCPs, or MTPs is acceptable without absolute symmetry)
5. Rheumatoid nodules	Subcutaneous nodules, over bony prominences, or extensor surfaces, or in juxtaarticular regions, observed by a physician
6. Serum rheumatoid factor	Demonstration of abnormal amounts of serum rheumatoid factor by any method for which the result has been positive in <5% of normal control subjects
7. Radiographic changes	Radiographic changes typical of rheumatoid arthritis on posteroanterior hand and wrist radiographs, which must include erosions or unequivocal bony decalcification localized in or most marked adjacent to the involved joints (osteoarthritis changes alone do not qualify)

* For classification purposes, a patient shall be said to have rheumatoid arthritis if he/she has satisfied at least 4 of these 7 criteria. Criteria 1 through 4 must have been present for at least 6 weeks. Patients with 2 clinical diagnoses are not excluded. Designation as classic, definite, or probable rheumatoid arthritis is *not* to be made.

Signs and Symptoms

The onset of the disease may be subtle with nonspecific early signs and symptoms. Easy fatigability, malaise, myalgias, anorexia, and generalized weakness are often the first symptoms the patient with RA may experience. Ill-define morning stiffness most often will progress to symmetric polyartheritis, affecting small joints of the hand and feet , joint pain with color, tenosynovitis, and fusiform joint effusions. The wrists, knee, ankles, fingers, and bones of the feet are most often affected although any joint can be affected. Untreated, the synovitis becomes worse and joint effusions are common .Tendons may become inflamed and may spontaneously rupture.[8] Ultimately, the destruction of the cartilage and supportive bone will result in severe disability and pain. Deformities of the affected joints, including flexion contractures, ulnar drift of the fingers, and wrist as a result of slippage of the extensor tendons off the metacarpophalangeal joints will ultimately occur with poorly treated or untreated disease (Fig.2).

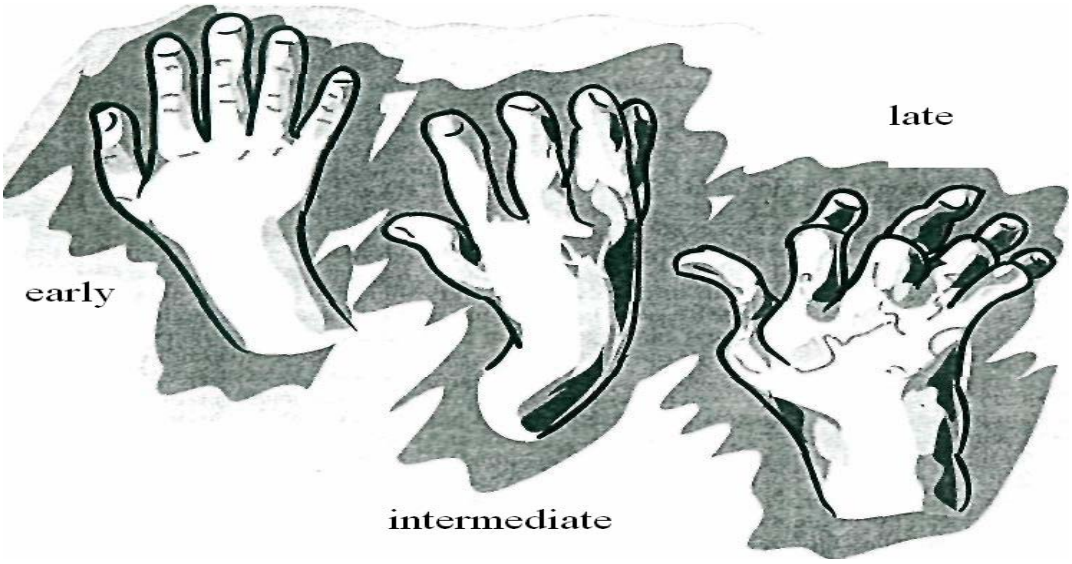

Figure 2: Stages of rheumatoid arthritis

Extra-articular manifestations of RA are common. Carpal tunnel syndrome is frequently associated with RA and, in fact may point to diagnosis if the clinician thinks about it.[9] Carpal tunnel syndrome and the other entrapment neuropathies such as tardy ulnar palsy are the result of proliferation and thickening of the affected connective tissue. Other extra-articular manifestations of RA include rheumatoid nodules, which are painless masses that appear under the skin and around the extensor tendons these nodules can also occur in the lung. Ocular manifestations are common, and uveitis and iritis can be quite severe. Vasculitis and anemia can also occur and if undiagnosed can lead to life-threatening multisystem organ failure. Pericarditis and pleuritis herald significant extra-articular disease and must be treated aggressively.[10]

Pathophysiology

These signs and symptoms of RA are the result of the autoimmune response associated with the disease. Immunologic abnormalities associated with RA include inflammatory immune complexes in the synovial fluid as well as antibodies that are produced by the patient's own plasma cells. Among these antibodies is a substance called RF factor, which also serves as the basis of the serologic test used in the diagnosis of R A. As RA progresses, the patient's own T-helper cell lymphocytes infiltrate the synovial tissue of the joints. These T-helper cells produce cytokines that facilitate the inflammatory response and contribute to ongoing joint damage. Macrophages and their cytokines (e.g., tumor necrosis factor, granulocyte-macrophagc colony-stimulating factor) are also abundant in diseased synovium. Increased adhesion molecules contribute to inflammatory cell migration and retention in the synovial tissue. Increased macrophage-derived lining cells are prominent along with some lymphocytes and vascular changes in early disease.[11]