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THERAPY

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MAIN CLINICAL SYNDROMES AND DIAGNOSTIC PROCEDURES IN RHEUMATOLOGY

Rheumatic diseases cause a large burden on society in terms of direct costs and indirect cost from psychosocial and economic factors. Understanding immune pathways have enabled therapies to intervene at cellular and receptor level. By treating inflammatory arthropathy, early, we are able to influence long-term outcome. Without a diagnosis, no treatment is possible.

Examination techniques are universally recognized as a sensitive detector of disease. New imaging techniques enable a specific diagnosis. Magnetic resonance imaging is able to demonstrate joint erosions well before conventional X-ray. However they do not replace the basic clinical examination. It is not uncommon for X-rays and blood tests to be reported as normal in the presence of disease. False positive tests are entirely possible. Interpretation of all investigations MUST be taken in the clinical context.

There are well over a hundred musculoskeletal related conditions. The starting point is to determine the difference between inflammatory and mechanical or degenerative process. Thereafter one can make an anatomical diagnosis of the precise articular or extraarticular structures involved and finally a pathological diagnosis.

The History. A comprehensive history of the presenting complaint, the general medical and systematic history is obtained. Past history and family history should be obtained, as well as a list of medications and allergies.

Pain. Pain is the most common presenting complaint. Chronology of the pain and aggravating factors provide clues to origin. These include prior trauma for example, or even preceding infections causing reactive arthritis. Pain can be acute, for example, as in gout where the onset may be almost instantaneous or over hours, compared to pseudogout, which may occur over weeks and osteoarthritis, which can be gradual over years. Thirty percent of rheumatoid patients present with acute onset. Pain may wax and wane over days in cycles over months as in palindromic rheumatism.

Inflammatory pain is usually maximal in the morning and increases again at the end of the day. Mechanical pain is maximal with use, and activity. Night pain and rest pain may be frequently seen with bone diseases such as Pagets, but also is seen with malignancy. Neuralgic pain is usually diffuse in a dermatomal distribution worsened by specific activity, whereas referred pain is unaffected by local movement. Diffuse unrelenting pain described as constant and «all over» is often associated with

Fibromyalgia. The description of pain may be very subjective. Joint pain is often described as aching, whilst nerve entrapment is frequently associated with shooting pain or like an electric shock.

Ask the Following Questions:

Is the joint pain localized to a single joint? Localization to a single joint should suggest a septic arthritis, gout, tuberculosis, hemophilia, sickle cell disease, trauma, avascular necrosis, and pseudogout.

Is there fever? The presence of fever should make one think of septic arthritis, rheumatic fever, gonococcal arthritis, ReiterV syndrome, lupus erythematosus, Lyme arthritis, polymyalgia rheumatica, Still's disease,»apd rheumatoid arthritis.

Is there a urethral discharge? The presence of a urethral discharge should make one think of Reiter's syndrome or gonococcal arthritis.

Is there low back pain? The presence of low back pain should suggest rheumatoid spondylitis, ochronosis, and gout.

Is the arthritis migratory? The presence of migratory arthritis should make one think of rheumatic fever and rat-bite fever.

What is the age of the patient? Younger patients may have sickle cell disease, hemophilia, trauma, rheumatic fever, Still's disease, and gonococcal arthritis. Older patients are more likely to have osteoarthritis, polymyalgia rheumatica, and gout. It should be noted that there is considerable overlap here.

Stiffness. The duration of the stiffness, especially morning stiffness is proportional to the amount of inflammation. Degenerative process results in short duration morning or post rest stiffness. The stiffening of the joints is called «gelling». Inflammatory disease causes prolonged morning stiffness. In the case of Rheumatoid arthritis this usually exceeds an hour. In Polymyalgia, the stiffness is also typical in the morning and is usually proximal in the shoulder girdle, neck and thigh region.

Locking. Locking implies mechanical derangement of a joint or tendon. In the case of the flexor tendons of the hands, irregularity of the tendons within the tendon sheath may cause tendon entrapment and locking of the fingers. Joint locking occurs most classically in the knee, due to meniscus injury, and in the spine with disk or apophyseal joint disease.

Swelling. Subjective complaints of swelling are common and should be differentiated from the objective finding of swelling in joints or soft tissues on examination.

Ask the Following Questions:

Is it painless? The presence of joint swelling without pain, especially on motion, would suggest Charcot's disease.

Is the involvement primarily in small or large joints? Involvement of the small joints is characteristic of rheumatoid arthritis, gonococcal arthritis, and Reiter's syndrome. Involvement of the larger joints is more characteristic of gout and osteoarthritis. However, osteoarthritis and rheumatoid arthritis may involve both.

Is the involvement symmetrical or asymmetrical? Asymmetrical involvement is more typical of gout, rheumatic fever, hemophilia, neoplasm, septic arthritis, and trauma. Symmetrical involvement is more characteristic of rheumatoid arthritis and osteoarthritis.

Is there fever? The presence of fever should make one think of rheumatic fever, gonococcal arthritis or other types of septic arthritis, Reiter's syndrome, rheumatoid arthritis, and lupus erythematosus.

What is the age of the patient? The younger patients with joint swelling most likely have gonococcal arthritis, lupus erythematosus, rheumatoid arthritis, and hemophilia. Gout, osteoarthritis, and neoplasm are more common in older patients. However, there is considerable overlap here.

Fatigue. Midday fatigue is a frequent complaint in inflammatory arthritis. Depression is also a frequent cause of fatigue. Exercise may well aggravate the fatigue of inflammation whils making that of depression better. The presence of overwhelming fatigue is also extremely common with Fibromyalgia.

Cracking and clicking of joints. Cracking of the joints is known to be related to nitrogen bubbles «popping» into synovia] fluid with negative pressure. This is usually a benign phenomenon and does not aggravate disease or progressive degeneration. Crepitus, however may be felt especially with mechanical change or cartilage irregularity.

Constitutional symptoms. This includes fever sweats and loss of appetite and weight as seen in inflammatory arthritis. The practitioner should also be alert to other systemic diseases including underlying malignancy.

Systematic inquiry. Inquire about skin rashes, especially psoriasis, photosensitivity or raynauds. Mouth and genital ulcers, diarrhoeas or genitourinary infections may provide clues to spondyloarthropathy. Inquire about ophthalmologic problems such as red or dry eye as there is a close relationship between several rheumatic diseases and the eye, including Sjogrens or inflammatory eye involvement.

Impact on Daily life. Inquire about the effect on daily life and other psycho-social effects. An American College of Rheumatology (ACR) functional assessment classification is used to assess function. Various scales are derived for different illnesses including the health assessment questionnaire (HAQ), for rheumatoid and the WOMAC score for Osteoarthritis. Occupational history or repetitive strain activity may cause aggravating factors for the complaint and should be documented.

The Examination. The initial goal is to establish the anatomical source of pain. This requires differentiating between articular versus extraarticular source. Every joint should be assessed individually, and the soft tissue, contractile structures around the joint appropriately examined. The technique requires the classical «look – feel – move» approach ofApley and application of the concept of the capsular pattern of Cyriax.

Look:

- Gait
- Swelling
- Redness in joints or tendons
- Skin changes. Examine for psoriasis, raynauds phenomenon, ulceration of skin and rashes.
- Wasting of regional muscles
- Deformity or contracture

Feel. Palpate the margins of each joint. Synovial thickening is felt as a «soft spongy» texture with the additional prejice of fluid identified by fluctuant swelling. Each joint is palpated in turn and presence or absence of synovial thickening is recorded.

Assessment of function. This technique is the most useful in localizing the pathology. There are three techniques of movement in the joint examination.

Active movement: The patient utilizes his own muscles and contractile structures to move a particular joint through its range of movement. This tests the joint as well as the contractile structures.

Passive movement: Here the patient is encouraged to relax and the examiner moves the joint through its accepted range of movement. By ensuring that the joint muscles are relaxed, this checks the actual joint capsule itself. The joint range of movement may be found to be reduced. This suggests age-indeterminate involvement of the joint. Reproduction of the pain on passive movement confirms the joint as source of the complaint. If the pain is not reproduced by movement within the capsular pattern, then the cause lies elsewhere.

Resisted movement: This isolates the cause to a particular tendon or bursa. The joint is made to relax then force is applied by the patient against resistance of the examiner. Reproduction of the pain confirms the source to be the contractile soft tissue structure.

The capsular pattern is a range of movement that is affected by disease of the joint. In the case of active joint inflammation, passive movement in the capsular pattern will be tender. Should the complaint be reproduced in this manner, then the joint itself is the source of the pain.

Restriction in the capsular pattern suggests age indeterminate disease of that joint.

The Hand. Each individual joint is examined, including DIP'S, PIP's and the MCP's as well as joints of the thumb. Swelling is recorded. The range of movement of the fingers is noted. The finger flexor tendons are then examined by feeling the tension in the pulps at the base of each finger. Tightness suggests tenosynovitis. (Saville sign). The flexors are then palpated for nodules in the palm whilst flexing and extending the fingers. These nodules may be a cause of locking.

The Wrists. The wrists are palpated as a single bony unit for signs of swelling. Range of movement is tested. Flexion should be between 60-90 degrees and extension 60-90 degrees Restriction suggests an inflammatory arthritis.

Hypermobility may be examined by extending the 5th finger to more than 90 degrees and moving the thumb against the volar aspect of the wrist. Tendonitis of the Abductor pollicislongus and Extensor pollicisbrcvis; De Quervain syndrome, which presents as thumb wrist and forearm pain, is checked by holding the thumb in a closed hand and stretching the tendon by adducting the wrist (Finkelstein's test). Check for sensory signs in the hand and for tap tenderness over the median nerve, (lateral to Palmaris longus tendon whilst extending the wrist-Tinel sign). Phalens test with flexion of the wrists produces aggravation of carpal tunnel symptoms.

The Elbow. Palpate the radial and ulnar margins for synovial thickening. Palpate for nodules or tophi on the extensor surface of the elbows. Contracture or deformity is noted. Extension should be 0 degrees whilst hypermdbility will allow more than 10 degrees of extension. Flexion of 145 degrees is normal. Movement at the elbow should be checked especially flexion and extension. Passive flexion and extension pain suggests elbowjoint involvement.

The Shoulder. Painful passive movement in the capsular pattern – abduction and external rotation with or without restriction at the joint suggests shoulder joint as a cause of the pain. Restriction of abduction and external rotation suggests age indeterminate involvement. The shoulder movement is glenohumeral up to 90 degrees and scapulothoracic from 90- 150 degrees and glenohumeral from 150-180 degrees. The shoulder and scapula should be steadied when examining, to ensure movement tested is glenohumeral.

Thoracic Spine. The thoracic spine allows 45-75 degrees of rotation. Chest expansion should be greater than 4 cm.

Pain in the thoracic spine should always be properly assessed for cause. Feel for bony tenderness and pain on active and passive movement, including extension, lateral flexion and rotation.

Lumbar spine. Check for lordosis or loss of lordosis and scoliosis.

Pelvic tilt may be noted and leg lengths should be measured from the anterior superior iliac spine to the medial malleolus at the ankle. A difference of one centimetre is acceptable.

Lumbar root symptoms will radiate to the appropriate dermatome and will have a sharp burning or electricity sensation with or without neurological signs. Forward flexion and lateral flexion may aggravate root symptoms, whilst extension will often aggravate symptoms of spinal stenosis. A positive straight leg-raising test suggests root entrapment.

Capsular joint problems, seen in inflammatory arthritis, produce symmetrical pain and restriction to all ranges of motion, flexion, lateral flexion, rotation and extension. The forward flexion is measured by the Shobertest.A line is measured 10 cm above and 5 cm below the «dimples of venus» and then remeasured after the patient is flexed fully. The increase should be at least 5 cm. Lateral flexion should be 30 degrees. Extension should be 30 degrees and rotation 45 degrees.

The sacroiliac joint. Palpate the joint itself, or apply lateral compression of the pelvis.

The knee. The knee is inspected for swelling, deformity and posteriorly for popliteal (Bakers) cyst. Regional muscle atrophy of quadriceps is common in derangement of the knee. Feel for heat or swelling in the joint. Swelling can be bony or soft with synovitis. Foreign bodies may be felt. Knee extension should be 0 degrees, flexion 120-150.

Toes. Inspect for deformity, nodules or bony or soft tissue swelling. The capsular pattern consists of flexion and extension. Extcnsiorvis the most sensitive. The metatarsals are examined, successively for callous, synovial thickening or tenderness. The metatarsals can be tested by squeezing them together to elicit pain. The great toe can usually flex 30 degrees and extend 90 degrees. Bonny swelling or bunions are noted.

Presenting symptoms.

Articular:

- Joint pain

Osteoarthritis: pain is typically worse at the end of the day and after activity, and may be relieved by rest.

Pain in inflammatory arthritis, e.g., rheumatoid arthritis, tends to be worse after rest, particularly in the mornings.

Rheumatic disease affecting joints often causes referred pain, e.g., cervical spondylosis presenting as shoulder pain.

Pattern of distribution:

Symptoms tend to be bilateral in inflammatory arthritis with smaller joints, such as those of the hands and feet, being affected first.

- Stiffness

May be due to mechanical dysfunction or local inflammation of a joint, or a c mbination of both.

Early morning stiffness is characteristic of inflammatory arthritis.

An elderly patient complaining of severe pain in both shoulders or stiffness of the pelvic girdle in the early morning suggests polymyalgia rheumatica.

Joint stiffness after rest may indicate osteoarthritis.

- Swelling

Joint swelling may be due to inflammation of the synovial lining, increase in synovial fluid, hypertrophy of the bone or swelling of the structures surrounding the joint.

Heberden's nodes are hard swellings caused by formation of calcific spurs of the articular cartilage which can develop in the distal interphalangeal joints of patients with osteoarthritis.

Bouchard's nodes are hard swellings caused by formation of calcific spurs of the articular cartilage which can develop in the proximal interphalangeal joints of fingers or toes of patients with osteoarthritis). Bouchard's nodes are much less common than Heberden's nodes.

- Hand deformities

The characteristic features of the hands in patients with rheumatoid arthritis are subluxation of the metacarpophalangeal joints, radial deviation of the wrist joint and ulnar deviation of the fingers.

Swan-neck deformity (proximal interphalangeal joint hyperextension with concurrent distal interphalangeal joint flexion) occurs in patients with rheumatoid arthritis, but may also follow trauma or be congenital.

Boutonniere deformity (flexion of the proximal interphalangeal joint accompanied by hyperextension of the distal interphalangeal joint) can result from tendon laceration, dislocation, fracture, osteoarthritis or rheumatoid arthritis.

Mallet finger (flexion deformity of the distal interphalangeal joint preventing extension) results from an extensor tendon rupture or an avulsion fracture of the distal phalanx.

Dupuytren's contracture is a progressive contracture of the palmar fascial bands causing flexion deformities of the fingers. Dupuytren's contracture is more common in men and increases after age 45. The cause is unknown but it is more common in patients with diabetes, alcoholism or epilepsy.

- Loss of function

This is often caused by a combination of muscle weakness, pain, mechanical factors such as tendon and joint impairment and damage to the nerve supply.

From the patient's point of view, they may describe a joint as «giving way» or simply «feeling weak».

It may be useful to gain some idea of the patient's disabilities by asking about mobility including stairs, personal care such as feeding, washing and dressing, shopping and cooking.

Extra-articular:

- Rheumatoid nodules:

Rheumatoid nodules are subcutaneous soft tissue swellings most often seen in patients with rheumatoid arthritis, but also with other diseases, e.g., rheumatic fever, connective tissue diseases, sarcoidosis, Weber Christian disease, gout and xanthomatosis.

Nodules are the most common extra-articular feature of rheumatoid arthritis and are present in up to 30 % of patients.

In rheumatoid arthritis the nodules are usually located between the skin and a bony prominence (especially the elbow).

Rheumatoid nodules may be freely mobile or attached to deep tissues.

- Skin rash:

Intermittent rashes appear with rheumatic fever, rheumatoid arthritis, chronic juvenile arthritis, and connective tissue diseases such as systemic lupus erythematosus (SLE).

Check for psoriasis, which may be hidden from view.

Circinatebalanitis in Reiter's disease may be asymptomatic and is not always admitted, so a specific examination is therefore important.

Oral ulceration may be a feature of Reiter's and Behcet's disease as well as connective tissue disorders.

Sjogren's syndrome will cause a dry mouth (xerostomia).

Raynaud's syndrome: usually bilateral and affects fingers more often than toes.

- Diarrhoea

Transient mild diarrhoea may precipitate a reactive arthritis.

It may also be indicative of enteropathic arthritis secondary to ulcerative colitis, Crohn's disease, coeliac disease or Whipple's disease.

- Urethritis: may indicate Reiter's disease.
- Red, gritty eyes: Conjunctivitis or iritis may occur in Reiter's syndrome.
- Uveitis may occur in other spondyloarthropathies.
- Episcleritis (painless), scleritis (painful), and keratoconjunctivitissicca may occur in rheumatoid and related diseases.
- Cardio-respiratory

Episodes of pericardial or pleuritic chest painmay indicate connective tissue disease.

Musculoskeletal chest pain is a common feature of the spondyloarthropathies.

Breathlessness may indicate associated pulmonary fibrosis or a cardiac defect such as aortic regurgitation in the spondyloarthropathies.

- Neurological

Peripheral neuropathies, e.g., entrapment neuropathy (e.g., carpal tunnel syndrome) may be an early feature of inflammatory synovitis.

Migraine, depression, dementia or stroke may point to SLE, vasculitis or antiphospholipid syndrome.

- Systemic symptoms: weight loss, fever and anorexia are present in many types of inflammatory arthritis.

Other relevant history

Prodromal symptoms and events. Acute rheumatic disease may follow events such as upper respiratory tract infections, diarrhoea, genitourinary infection, insect bites (e.g., Lyme disease) and vaccinations. Medication: Some drugs, e.g., hydralazine, are a potential cause of joint problems. A good response to non-steroidal anti-inflammatory drugs (NSAIDs) may be indicative of inflammatory arthritis, e.g., rheumatoid arthritis.

Past history. Have there been any previous attacks of the symptoms diagnosed in the past.

Is there any other relevant past history, e.g., psoriasis, inflammatory bowel disease or any history or risk of sexually transmitted infection.

Family history, e.g., inflammatory arthritis, psoriasis.

Mental health. Many ill effects are aggravated by anxiety or depression.

Disability, pain and social isolation may well lead to depression.

Investigations.

Blood tests Full blood count

Anaemia may be due to chronic disease or blood loss from gastric irritation secondary to NSAIDs.

White cells: possible changes include neutrophilia in septic arthritis, eosinophilia in polyarteritisnodosa, neutropenia in Felty's syndrome and leucopenia in SLE.

Platelets may be increased in rheumatoid arthritis and may be decreased in SLE.

Acute phase proteins: ESR and CRP are non-specific indicators of inflammatoiy activit

Erythrocyte sedimentation rate (ESR) Nonspecific test for inflammatory process anticoagulated blood in calibrated tube; rate of sedimentation of RBCs in 1 hour. Normal <15m;<20f; add 10 past age 60y.

C-reactive protein (CRP)

Uric acid: may be raised in gout.

Renal function: may be renal dysfunction in chronic disease such as gout or connective tissue disorders.

Autoantibodies:

1. Rheumatoid factor may support the diagnosis of rheumatoid arthritis. An antibody to a substance called cyclic citrullinated peptide (CCP) has been found to be more specific than rheumatoid factor in rheumatoid arthritis and may be more sensitive in erosive disease.

- (RF)RF is an IgM antibody directed against IgG
- Present in the sera of 75 % of patients with Rheumatoid Arthritis
- Higher titer of RF are commonly associated with severe RA
- High titers also seen in syphyllis, sarcoid; infective endocarditis; TB; leprosy; parasitic infections; old age.
- Presence of RF does NOT rule in RA. Absence of RF does NOT rule out RA
- It the pretest probability of RA is high, the presence of RF is supportive ofthe diagnosis
- If the pretest probability of RA is high, the absence of RF should not change your clinical diagnosis
- Anti-CCP: Citrulline antibody

An antibody (an immune protein) directed against a circular peptide (a ring of amino acids) containing an unusual («non-standard») amino acid called citrulline that is not normally present in peptides or proteins. (Citrulline is formed by the body as an intermediary in the conversion of the amino acid orthithine to arginine). The citrulline antibody provides the basis for a test of importance in rheumatoid arthritis.

2. Antinuclear antibodies may suggest systemic lupus erythematosus or other connective tissue disorders.

Table 1.

Antinuclear Antibody (ANA) Patterns and Clinical Associations

ANA Pattern	Antigen Identified	Clinical Correlate
Diffuse	Deoxyribonucleoprotein	Nonspecific
	Histones	Drug-induced lupus, lupus
Peripheral (rim)	ds-DNA	50 % of SLE (specific)
Speckled	U1-RNP	>90 % of MCTD
	Sm	30 % of SLE (specific)
	Ro (SS-A)	Sjogrens 60 %, SCLE, neonatal lupus, ANA(-) lupus
	La(SS-B)	50 % of Sjogrens, 15 % lupus
	Scl-70	40 % of diffuse scleroderma
	PM-I	Polymyositis (PM), dermatomyositis
	Jo-1	PM w/ pneumonitis + arthritis
Nucleolar	RNA polymerase I, others	40 % of PSS
Centromere	Kinetochore	75 % CREST (limited scleroderma)

3. Anticardiolipin (ACLA) – Antiphospholipid Syndrome

4. HLA B27: increased positivity in ankylosing spondylitis and other spondyloarthropathies.

5. Serology, e.g., HIV, may be appropriate

6. Tests suggesting necrotizing vasculitis without immune complex deposition

a. Antineutrophil cytoplasmic antibodies (ANCA)

b. ANCA by immunofluorescence methods

c. c-ANCA = Wegener's disease (60 % to 90 %)

d. p-ANCA = microscopic polyangiitis (MPA) (50 % to 80 %).

Other investigations.

Urine: proteinuria may be due to nephrotic syndrome associated with connective tissue disease.

Synovial fluid: White cell count raised in infection. Gram stain (tuberculosis), culture and sensitivities. Crystal identification: urate, calcium pyrophosphate.

Imaging:

X-rays: may show distinctive changes, such as in rheumatoid arthritis, osteoarthritis.

Chest X-ray may be indicated for lung involvement in rheumatoid arthritis, SLE, vasculitis and tuberculosis.

Ultrasound: soft tissue abnormalities, e.g., synovial cysts.

CT scan, MRI: much greater information of bone, joint and soft tissue.

Arthroscopy: Direct view of joint and synovial fluid. Potential for biopsy and therapeutic procedures.

Biopsy.

Routine tests include a CBC, sedimentation rate, ASO titer, CRP, ANA, urinalysis, chemistry panel, arthritis panel (RF, Anti-CCP)

Other tests that may be done include.

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