CONTENTS

FOREWORD

The purpose of this handbook is to provide easy reference to subjects in Rheumatology. It has been designed to be carried in the Student's coat pocket and has been deliberately limited in its content.

The information is presented in telegraphic format. The details should be filled in during the Seminars and reading should be supplemented by referring to more comprehensive texts, as described at the back of the book.

You are encouraged to read these notes in conjunction with *A Primer of the Rheumalic Diseases* as well as *An Atlas of Clinical Rheumatology* by P Dieppe et al.

A CD-ROM of Clinical Rheumatology is available at the Princess Alice Orthopaedic Hospital. It is a complete multimedia programme with text, videos and slides on a wide range of subjects including joint injections, x-rays and several clinical pictures.

The Medical Library also has the following Rheumatology Journals, which regularly feature Editorials dealing with controversial issues in Rheumatology Practice: *Arthritis Rheumatism, Journal of Rheumatology, British Journal of Rheumatology, Seminars in Arthritis & Rheumatism, Scandinavian Journal of Rheumatology, North American Clinics in Rheumatology and Bailliere's Clinical Rheumatology.*

Hope you enjoy the course.

Asgar Ali Kalla.

Head-Rheumatology

THE SCOPE OF THE RHEUMATIC DISEASES

Arthritis implies inflammation of a joint- term currently used by lay people to describe any joint disease of whatever cause.

Rheumatism was used to describe acute rheumatic fever. It is now used by lay people to describe any pain/discomfort in the musculoskeletal system.

Rheumatology is that branch of internal medicine which deals with:

1. Disorders of the musculo-skeletal/connective tissue.
2. Those medical conditions presenting with bone or joint pain.

It shares interests with Orthopeadic surgery. Young discipline – 25 years in South Africa.

Classification of Rheumatic disorders.

f. Inflammatory	Rheumatoid Arthritis Seronegative Arthritis Juvenile Chronic Arthritis.
2. Connective Tissue Diseases/Vascutitis	Systemic Lupus Erythematosus Progressive Systemic Sclerosis Polymyositis/Dermatomyositis Polyarteritis Nodosa
3. Degenerative	Osteoarthritis
4. Crystal Synovitis	Gout Pyrophosphate/apatite deposition disease.
5. Infectious/Post· Infectious (reactive) Arthritis	Acute Rheumatic Fever Septic Arthritis Tuberculous Arthritis
6. Associated with a Medical Disorder	Endocrine Haematological Sarcoidosis. ·
7. Metabolic Bone Disease	Osteoporosis Osteomalacia
8. Non-Articular Rheumatism	Tendinitis/Bursitis Disc Protrusion Low back syndromes Fibromyalgia
9. Miscellaneous	Inherited Connective Tissue Disorders.

SYMPTOMS AND SIGNS IN THE RHEUMATIC.DISEASES

1. **PAIN** Most important symptom of all. (Definition of rheumatic diseases = painful disabilities of movement).

   Characteristics:

   (1) *Site* (Where do you feel the pain?)

   Two types of pain -local and referred; Segmental (dermatone) Extrasegmental (nondermatone)

   The more distal the lesion, the more local the perception of pain.

   Referred pain from a joint to another joint can fool the unwary doctor! (Hip to knee)

   (2) Severity (How bad is the pain? -try to use common reference experience, e.g. uterine contraction).

   (3) Nature (How do you describe the pain?)

   (4) Radiation (Does it stay in one place or does it move?)

   (5) Aggravating/relieving factors (What makes it worse/better?)

   (6) Temporal relationships (When does it occur? e.g. carpal tunnel symptoms are often worse at night)

   (7) Associated features (Does anything else happen to you when you get the pain?)

A. *Referred Pain* -pain perceived elsewhere than the site of its production (an error of perception)

   1. Pain is referred segmentally (except from the dura mater.)
      Cervical dural pain = whole neck, occiput and midthoracic region.
      Thoracic dura = thorax, mid neck, mid lumbar
      Lumbar dura= lumbar, mid thorax to back of leg, ankle.
      The above are nordermatomal or extra segmental dural references
   2. Pain is referred distally.
   3. Never crosses the midline.
   4. Extent of reference is determined by:
      the strength of the stimulus·
      the size of the dermatone
      the depth of the tissue causing the pain (Deeper = more widespread)

B. *Symptoms referred from the nervous system*

   Spinal cord compression = no pain. Paraesthesiae are the rule.

   Dural sleeve of nerve root compression = Pain in a dermatone
   Paraesthesia
   Numbness

   Nerve trunk compression = no pain, weakness, paraesthesia

   Small nerve compression = no pain, numbness, weakness

C. *Measurement of pain* -Difficult because pain is a unique personal experience. Influenced by many factors, e.g. temperature, mood, culture, pain threshold.

   Complex questionnaires eg McGill pain questionnaire may be used, but in a clinic a simpler measuring scale is needed.

Visual analogue scales PAIN VAS (A lOcm vertical or horizontal line.)

I have _____ my pain could
no pain not be worse

I have _____ my pain could
no pain mild moderate severe not be worse

Uses (1) Provides a record of pain
(2) Can be used to assess response to treatment

Problems (1) Difficult for some patients to understand. May have to use sonie other method, e.g. a series of faces etc.
(2) Should the patient see their previous records?
(3) More useful for followup to assess an analgesic (for example)

2. **JOINT STIFFNESS**- 3 varieties
   (a) *Early Morning stiffness*- an important symptom of inflammatory joint disease, especially RA. (Duration reflects activity of inflammation)
   (b) *Inactivity stiffness*- an important symptom of OA (shortlived < 15 minutes) ·
   (c) *Permanent stiffness*- end result of several joint diseases. Some patients find it hard to distinguish *a* from *c*.
3. **PATTERN OF JOINT INVOLVEMENT.**
4. **SWELLING.**
5. **DEFORMITY.**

The Clinical Examination (Look, Feel, Move)

A systematic approach is essential.

LOOK

1. **Redness -usually a sign of acute inflammation.**
2. **Wasting of muscle**
3. **Abnormal shape of joint (deformities, swelling)**

FEEL

1. Swelling- 2 types:
   soft, elastic, compressible -synovial membrane
   -synovial effusion
   Hard incompressible- bone.
2. Heat- back of hand. Not very reliable except where it is marked.
3. Feel the outline of the joint.
4. Feel for tenderness:
   Press firmly over the joint margin.

MOVE

Loss of function -several causes/combinations:

(i) Muscle spasm
(ii) Contraction of soft tissues
(iii) Joint damage

The examination of the musculo skeletal system, like all other systems, relies on an assessment of FUNCTION for a diagnosis. Meticulous physical examination is the key -healthy structures function painlessly- faulty structures will not. The whole principle is to put manual tension on all tissues around a joint. ie. selected tension also called differentiated tension.

Measuring loss of function

Since one is interested in pain/limitation of movement, all that is required is to ask the patient to perform active movements at all the joints to establish which area is painful/limited or both. Once this has been established the local area may be examined in greater detail.

A basic distinction must be drawn between inert and contractile structures.

(i) Inert structures are incapable of any capacity to contract/relax; they include the joint capsule, ligaments, bursae, fasciae and the dura mater and Dural sleeve around the emerging nerve roots. These structures will be moved at the end of the range of movement of a joint ie. if you apply passive movement to the joint and there is pain at the end of the range, an inert structure is at fault.

(ii) Contractile structures such as muscles and tendons can be tested by resisted movement. Provided you isolate the muscle you can define which contractile structure is at fault.

1.1 ***Testing the range of motion of a joint*** (Visual estimate= inaccurate; Goniometer= accurate)

Neutral zero- Cadaveric position is the starting point for measuring the range of movement (ROM) for each joint, e.g. flexion, extension, rotation. ROM is expressed in degrees of motion. Joint range is tested by active, and by passive movement. First ask the patient to move all the joints actively. It helps to define the area of disease but gives no idea of what the cause is.

Importance of measuring range of motion.

A. Characteristic impairment of ROM for inflammatory/other joint disease.
B. Provides a record of the progress of a joint disease.

1.2 Passive movement

If there is a limitation of passive movement, then *an inert structure must he at fault.* (One exception is partial rupture of a muscle). If you find such a limitation, then you must decide whether it is a capsular or noncapsular structure.

All inflamed joints have a characteristic reduction in their range of motion.

a) *Capsular lesions*

If an entire joint capsule becomes inflamed then all movements of the joint will

be painful. In practice, the presence of capsular inflammation produces a characteristic limitation of passive movement called the capsular pattern. Every joint has its own capsular pattern.

Table 1
Capsular patterns

Shoulder= ER > Abd > IR (lR).	Hip flex= IR > Abd. > ER
Elbow = Flex > Ext.	Knee= Flex > Ext.
Wrist= Flex = Ext.	Ankle= Plantar flex > dors flex
Trapezes MCP = Abd only	Talocalcaneal= increasing valgus
Spine= flex/ext./rotation/side flexion all equally reduced	Middorsal = Addling rot >others
	Big toe MTP =All except flexion Other toes MTP flex > ext.

The pattern remains the same no matter what the cause. In the early stages, it is due to muscle spasm. Much later when there is disorganization of the joint the capsular pattern may disappear.

b) If the impaired passive movement is noncapsular, i.e. not an arthritis, then other structures capable of limiting passive movement must be considered.

(i) Internal derangements

(ii) Ligamentous sprains

are both capable of producing a noncapsular limitation of movement.

Note that extra-articular structures may limit passive movement. e.g.. a fixed flexion deformity of one joint may influence the joint above and below by limiting their movements.

1.3 Resisted movement is now tested.

You are resisting the initiation of movement and measuring muscle power.

SUMMARY

Preliminary examination	**Passive movement for Inert structures**	**Resisted movement for contractile structures**
Begin with active movement at all the major joints then proceed to detailed examination	Examine for pain, limitation, end feel	Examine for pain and weakness
	Principal findings	***Principal findings***
	a) Capsular lesions	a) Pain lessening appropriate structures
	b) Noncapsular pattern	b) Painless weakness
	c) Extra-articular	c) Shrug/painless = normal

On passive movement elicit the •end feel'-
e.g. normal elbow – extension = hard
– flexion = soft
– pronation/supination = rubbery
Crepitus - soft tissue is fine, bone on bone is hard and grating.

Patterns and an algorithm for a patient with shoulder pain
Active movement hurts – **l**ocalises the problem to the joint area but tells you nothing about the source.
Passive movement limited in one direction = ligament
Passive movement limited in several directions =joint capsule

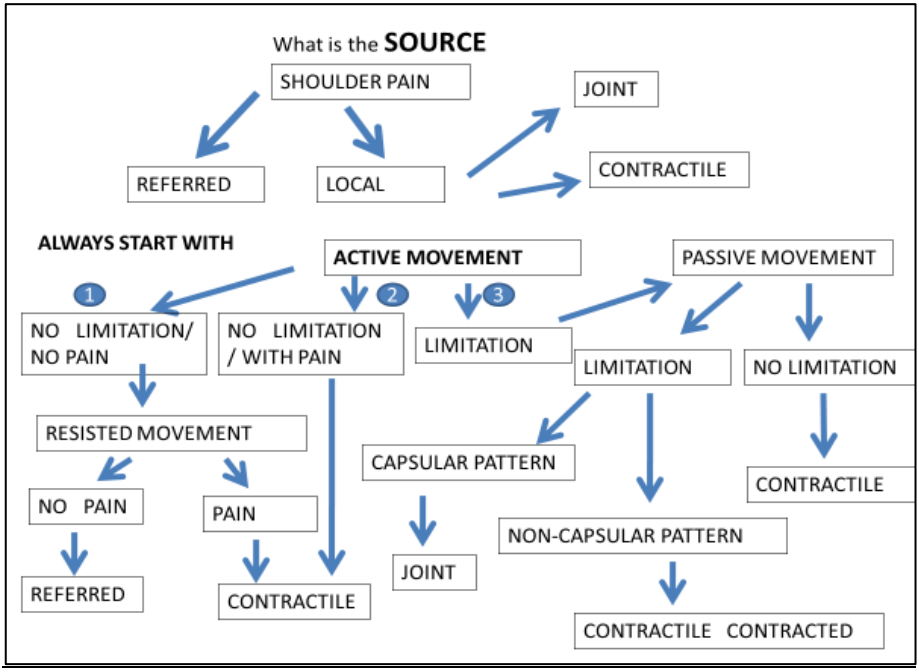


Figure 1

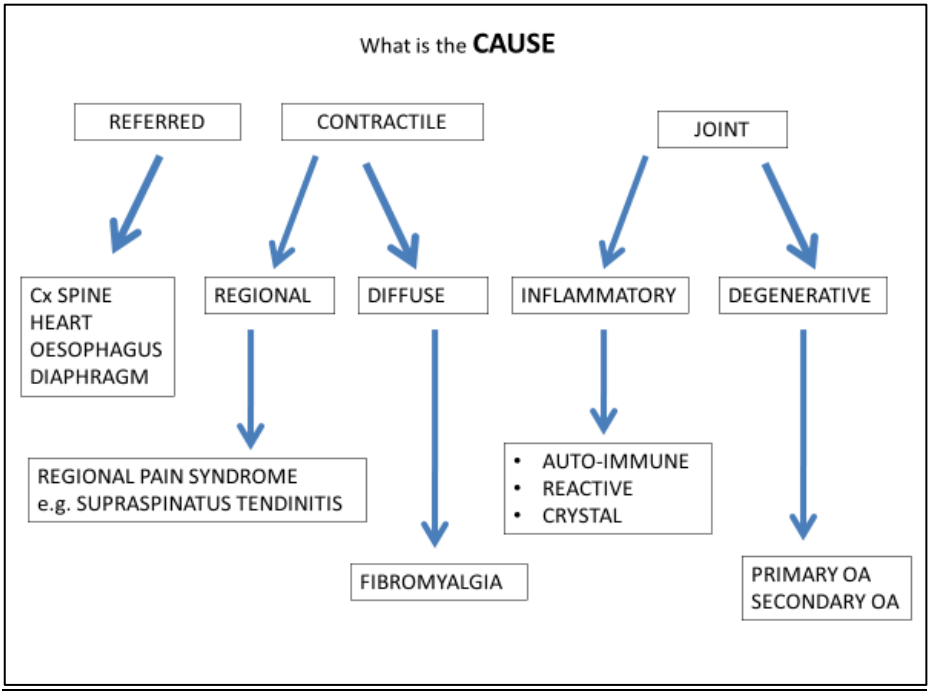


Figure 2

Resisted movement hurts= tendon/muscle disease (few exceptions)

1.4 Test the integrity of the ligaments around the joint: e.g. knee/ankle.

1.5 **Testing for hyper mobility.**

Joints may also exhibit an excessive range of movement especially inherited disorders of connective tissue – Marfan, Ehlers-Danlos. and the hypermobility syndrome

Scoring for excessive joint mobility

	R	L	
Little finger MCP extends to 90° or more	1	1	=2
Thumb can be passively opposed to forearm	1	1	=2
Elbow extension greater than 10°	1	1	=2
Knee extension greater than 10°	1	1	=2
Palms flat on the ground in front of the feet with knees, straight		1	=1
		Score	9

A score of 2/4 Hypermobility.

See page 32.

2.0 **Other measures of function**- walking time, stair-climbing etc.

. 2.1 **Measuring functional capacity**- not satisfactory but use revised ACR criteria.

See page 45.

3. *Deformity* describes an abnormal position of a joint – fixed
– not fixed.

It is also described with reference to neutral zero.

Types of deformity

Flexion
Varus/valgus (adduction/abduction)
Ulna deviation of the fingers
'Swan-neck' deformity
Buttonhole deformity
Equinus deformity
Scoliosis.

EXAMINATION OF THE MUSCULOSKELETAL SYSTEM

THE NECK

Anatomy and Biomechanics

The head balances on 7 cervical vertebrae in a flexible chain held together by 14 apophyseal joints, 5 intervertebral discs, 12 joints of Luschka and a system of muscles and ligaments.

The head and atlas move together around the odontoid peg and the upper articular facets of the axle.

Range of movement in sagittal plane (flexion, extension) is 90 degrees, (3/4 due to extension).

Age in years	Flex/Ext	Lat Rotat	Lat flex
<30	90	90	45
30-50	70	90	45
>50	60	90	30

About half of flexion/extension occurs at occiput Cl level, and about half of rotation occurs at atlantoaxial joint. With degenerative changes the disc space narrows and the spinal canal shortens. The intervertebral foramina become narrowed, movements become restricted, and unusual mechanical strains on the synovial joints result. The formation of osteophytes leads to encroachment on the spinal canal and intervertebral foramina. The canal may also be further narrowed by bulging of the ligamenta flava.

Pain sensitive structures

1. ligament
2. nerve roots (dural sleeve)
3. articular facets and capsules
4. muscles
5. dura

Examination of Range of Movement

1. ACTIVE- to assess muscle function and strength
2. PASSIVE- to assess non-mobile structures, ligaments, fascia, capsules.
3. Against resistance- to study origin and insertions of tendons and ligaments, and muscle power.

The reduction of movement is either capsular or non-capsular. A capsular pattern is an equal and painful limitation of all movements except flexion. A non-capsular pattern is one of pain and limitation of either 2, 3 or 4 neck movements.

Cervical Spine facet joints
IV disc

Inspection

1. Torticollis
   - i) muscular spasm of sternomastoid
   - ii) muscle weakness (head being displaced to the healthy side)

2. Flexed and stiff neck
   i) RA
   ii) AS
   iii) degenerative disease of the cervical discs
3. Patients holds his head when turning it- severe involvement of atlanto-occipital and atlanto axial region due to
   i) osteomyelitis
   ii) RA
   iii) TB
   iv) neoplasm

Palpation

First identify the following anatomical landmarks:

a) occiput
b) inion
c) mastoid process
d) spinous processes of C7 and T1

Facet joints lie along lines through the mastoid processes parallel to the midline.

Pain over the occiput- consider atlanto axial dislocation.

Basilar settling – when the dens appears to travel up through the foramen magnum, especially when there is collapse of the lateral masses of Ct. The pain in the occiput is due to tension in the transverse ligament, and radiation over the skull follows the distribution of the 2nd cervical nerve.

May also experience frontal and retro orbital pain when there is an anastamosis between C2 and ophthalmic branch of the trigeminal nerve.

Movements

Tested either sitting up or recumbent. It is important to fix the trunk. When one considers that the symptoms may be those of cervical nerve root involvement one should carry out compression and elevation tests. May provoke root pain when the cervical spine is compressed or by lateral flexion of the head towards the affected side.

Always examine for cervial ribs when there are symptoms of a thoracic outlet syndrome.

Structures causing neck pain

1. acromioclavicular joint
2. temperomandibular joint
3. fibromyalgic syndrome
4. cervial spine disorders
   localised neck disorders:
   4.1 OA (apophyseal joints)
   4.2 RA (atlanto axial)
   4.3 JRA
   4.4 osteomyelitis
   4.5 ankylosing spondylitis

4.6 Paget's
4.7 Torticollis
4.8 Neoplasms
4.9 Occipital neuralgia (greater and lesser occipital nerves)
4.10 Diffuse Idiopathic Skeletal Hyperostosis (DISH)

Capsular pattern seen in:

1. Fractures
2. Ankylosing spondylitis
3. Cervial myeloma
4. Chordoma
5. RA
6. Ageing (most common)
7. Very advanced OA

Lesions producing neck and shoulder pain

1. RA
2. Fibromyalgia
3. OA (apophyseal and Luschka)
4. Cervical spondylosis
5. Intervertebral OA

Neck and head pain with ra diation

1. Cervical spondylosis
2. RA
3. OA (apophyseal and Luschka joints, intervertebral discs)
4. Spinal cord tumors
5. Cervical neurovascular syndronie

Routine X-rays Include

1. AP views of the atlas and axis through the open mouth to assess the status of the dens.
2. AP views of lower 5 cervical vertebrae to assess Luschka'sjoint.
3. Lateral views of flexion, neutral, extension looking for atalanto axial subluxation and to assess the width of the spinal canal.
4. (R) and (L) oblique to assess formainal narrowing.

SHOULDER

The shoulder girdle is composed of three joints and one articulation.

1. Sternoclavicular joint
2. Acromioclavicular joint (C4 structure)
3. Glenohumeral joint
4. Scapulothoracic articulation

The humerus is suspended from the scapula by soft tissue, muscles, ligaments, and a joint capsule and has minimal osseus support.

Bony palpation

Suprasternal notch
sternoclavicular joint
Clavicle
Coracoid Process
Acromioclavicular articulation
Acromion
Greater tuberosity
Bicipital groove with tendon of long head of the biceps
Spine of scapula

Soft tissue palpation by clinical zones

I. Rotator cuff
2. Axilla
3. Prominent muscles of the shoulder girdle

Rotator cuff

Undergoes degeneration and subsequent. tearing of its tendon of insertion. This results in restriction of shoulder movement, especially ABDUCTION.

Cuff is composed of four muscles, three of which are palpable at their insertion into the greater tuberosity. These 3 are Supraspinatus, Infraspinatus and Teres minor, called the SIT muscles. The fourth muscle is the subscapularis. The rotator cuff lies directly below the acromion. Of these muscles the supraspinatus is the most commonly ruptured.

Subacromial and Subdeltoid Buna

Bursitis is a frequent pathological finding which can cause much tenderness and restriction of shoulder motion.

Muscles of the Shoulder Girdle

Rupture/tear of long head of biceps causing it to curl like a ball at midpoint of humerus Deltoid
Trapezius
Rhomboids
Latissimus dorsi
Serratus Anterior

6 Motions of the Shoulder Girdle

ABDUCTION
ADDUCTION
EXTENSION
FLEXION
INTERNAL ROTATION
EXTERNAL ROTATION

1. Apley "scratch test" – Abduction
   External rotation
2. Internal rotation and adduction
3. Abduction of arms *to* 90° elbows extended and *turn* palms up in supination and continue abduction until hands touch over head. Place hands behind neck, push elbows out posteriorly - a *test* of abduction and external rotation.

   Place hands behind back as high as they will go as if scratching the inferior scapula angle- adduction and internal rotation.

Range of Motion

Active and Passive testing

If a patient has difficulty performing active movements, then carry out passive movements. As a general rule, if able to perform a complete range of active movement without pain or discomfort, there is no need to conduct passive tests.

Passive Range of Motion tests

If active range is incomplete or painful then do passive testing. Causes of reduced active movements:

1. Pain
2. Muscle weakness
3. Soft tissue contracture (in the joint capsule or ligaments)
4. Bony blockages

If passive movement is full, but active is restricted then pain or muscle weakness is the cause.

If passive movement is restricted, then cause is either bony (intra-articular) or soft tissue (extra-articular).

To distinguish between intra-articular and extra-articular blockage check the Quality and Feel of the blockage within the joint. If blockage feels rubbery and gives slightly under pressure, the blockage is probably extra-articular (soft tissue). If blockage seems inflexible and range of movement ends abruptly, there is probably an intra-articular (bony) blockage.

Capsular pattern

Is designated by a hard end-feel and limitation of all three passive movements in fixed proportions. Limitation of Internal Rotation is slight. There is greater restriction of glenohumeral abduction, but it is the impairment of external rotation that is the most marked.

ABDUCTION

1. pure glenohumeral (1st 90°)
2. scapulothoracic
3. combination of 1 and 2.

Ratio of 1:2 is 2:1 ie for every 3° of abduction. 2° occur in the glenohumeral joint. After the first 20° the humerus and scapula move together. in a ratio of 2:1 to complete abduction. Pure glenohumeral abduction is about 90°.

Abduction then continues to 120° and then full abduction can only be completed if the humerus is externally rotated.

ADDUCTION - normally about 45°
FLEXION - about 90°
EXTENSION – about 45°

Reduced flexion/extension- Bicipital tendinitis or bursitis in shoulder

EXTERNAL ROTATION (40°-450) or (0- 90°)

Hold elbow against waist, and with the patients wrist in your hand, externally rotate the arm, using the shoulder as the point and the forearm as the indicator of motion; or when the shoulder is in a position of 90° of abduction, the range of external rotation is from 0-90°. Similarly, for internal rotation i.e. 0-90°.

INTERNAL ROTATION (55°)

As above but rotate internally.

NEUROLOGIC EXAMINATION

Assesses muscle strength, and integrity of nerve supply to the shoulder.

Muscles of:

ABDUCTION	ADDUCTION	EXT ROTATION	INT ROTATION
Deltoid·	Pec major	Infraspinatus	Subscapularis
Supraspinatus	Lat dorsi	Teres minor	Pec maj
			Lat dorsi
			Teres major

Scapular elevation

Trapezius
Levator Scapulae

Special Tests

1. Yergason test - a test of stability of biceps tendon
   fully flex elbow
   – grasp elbow in one hand while holding the wrist with the other hand
   externally rotate arm against resistance pulling down on the elbow at the same time
   When positive the tendon will pop out of the groove and the patient will experience pain.
2. Drop arm test - to detect tears in rotator cuff.

Get patient to abduct arm to 90°. Then ask to lower arm slowly. The arm will drop to the side if there are tears in the rotator cuff, especially supraspinatus.

Physical signs

1. Acromioclavicular joint (ACJ)

   The acromioclavicular ligaments are derived from C4 segment, the pain is localised to the point of the shoulder and cannot radiate to the ann.

   Painful arc is uncommon, if present it indicates that the inferior.ligament is tender. Resisted movements are painless. If tender, then the lesion is the superior ligament. If non-tender, then the lesion is the inferior ligament.

Glenohumeral joint

Limitation of Ext Rotation, then abduction and least of alllnt Rotation. In the earliest stage, there may only be limitation of external rotation.

Subdeltoid bursitis

Acute

Passive scapulohumeral abduction is grossly restricted by severe pain. Ext rotation is little diminished (non capsular pattern).

Chronic

Usually a full range of movement
Painful arc
Resisted movements are painless

Long head of Bieeps

Pain on resisted flexion and supination at the elbow causes pain under acromion.

Supraspinatus Tendinitis

Pain on abduction (also seen in subdeltoid bursitis) and also on resisted abduction (not seen in subdelt bursitis). Sometimes coupled by painful resisted external rotation.

Middle arc syndrome (30°- 70°) pain starts at 30° of abduction and disappears at 70°.

Infraspinatus Tendinitis

Pain on resisted ext rotation

Subscapularis Tendinitis
Pain on resisted int rotation

Frozen shoulder -Adhesive capsulitis

The end resull of chronic pain in the shoulder, regardless of cause. It is characterised by chronic limitation of both active and passive motion in the shoulder. Patients with adhesive capsulitis may substitute scapular swing with elevation and depression of the shoulder girdle for true range of motion in the glenohumeral joint. This condition is caused by fibrosis and tightening of the joint capsule and periarticular ligaments and soft tissues. It is frequently associated with a variety of systemic or localised disorders, including coronary artery disease, cerebrovascular accidents, injury to the upper extremity, rotator cuff tears, calcific tendinitis, or post-thracotomy syndromes. Itmay also occur gradually without any obvious underlying disease and may be difficult to distinguish from rheumatoid arthritis involving the shoulders.

THE ELBOW

Complex joint but lesions are relatively few. Like the shoulder the history does not help much in the diagnosis but the clinical findings are easy to interpret because they are clear cut.

Lesions of the elbow usually cause local pain.

Examination (10 movements -4 passive 6 resisted)

Primary movements are flexion and extension.

The capsular pattern limits flexion more than extension.

Pronation/supination are then tested (remember passive pronation which is painful can be elbow arthritis or biceps enthesitis.)

Resisted movement:

Flexion	Biceps or brachialis (rare)
Extension	Triceps (rare)
Pronation	Pronator teres but may he accessory sign of medial epicondylitis
Supination	Supinator brevis (rare), biceps (common)

Wrist extension with elbow in full extension- tennis elbow

Wrist flexors with elbow in full extension- golfer's elbow.

HANDS, WRISTS AND ELBOWS

Function of the hands is important formost of the activities of daily living. In addition to the musculoskeletal components (bones, muscles, ligaments and joints) dysfunction of nerves and blood vessels may also impair hand function. Careful history and examination of the hands often allows the physician to differentiate between osteoarthritis, rheumatoid arthritis, systemic lupus erythen1atosus, scleroderma, psoriasis and crystal synovitis. It is important to note the distribution of joint involvement, the nature of the swelling, the type of deformity and the relationship to active and passive motion.

The posture of the hand is the result of forces acting within it A knowledge of the dynamic anatomy of the hand is fundamental in the recognition of factors that upset the normal muscle balance, produce deformities and thereby destroy function.

BONES AND JOINTS OF THE HAND

Structurally, the hand consists of a linked system of longitudinal bony segments that are arranged in a series of integrated arches (1, 2 and 3), the concavities of which face toward the palm, forming the hand into a cup (Figure 1). The depth of the cup is varied by the controlled mobility of the fingers and the two borders of the hand. The thumb contributes the greater part of the border mobility because it can separate widely from the palm and swing around in front of, and oppose, any of the fingers. Although the extrinsic flexor and extensor muscles are largely responsible for altering the shape of the working hand, it is the intrinsic muscles that are responsible for maintaining the integrity of the arch system.

Movement of the borders of the hand passes through the mobile transverse arch at the level of the metacarpal heads (MP joint). It is the mobility of this arch which allows the palm to adapt to objects of various sizes. A more proximal transverse arch is present in the carpus arid is permanent in shape (carpal joints). The mobile longitudinal arches are made up of all the digital rays (IP joints- proximal and distal). The longitudinal arches are more mobile than the transverse arches and can individually alter their shape in response to the demands of grasp. Disturbance of this arch leads to severe impairment of function.

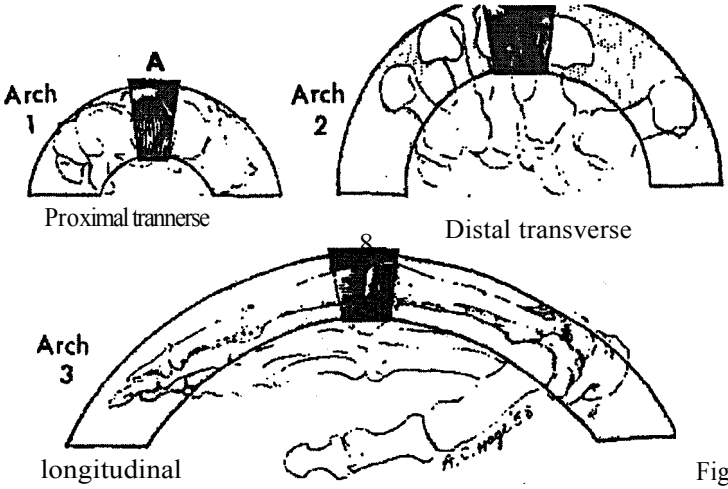
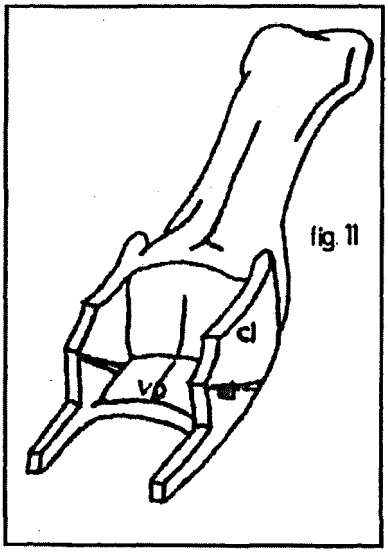


Figure 1

LIGAMENTS

The flexor tendon sheath extends from the head of the metacarpals to the insertion of the flexor tendon at the distal phalanx. The transverse carpal ligament spans the volar aspect of the proximal palm to form the roof of the carpal tunnel. It traverses from the scaphoid tubercle and crest of the trapezium on the radial side to the pisiform and hamate on the ulnar side. Also on the ulnar side of the wrist, the canal of Guyon, or ulnar tunnel, is formed by the transverse carpal ligament on the floor, the volar carpal ligament along the roof, and the pisiform along the ulnar wall.



TENDONS

The digital flexor tendons at the wrist, as they enter the carpal tunnel, are arranged with the deep flexors lying side by side along the floor.

The superficial flexors are arranged volar to these in two layers. In the palm, each of the flexor digitorum superficialis (FDS) lies superficial to the flexor digitorum profundus (FDP) of the corresponding finger. As this pair of tendons enter the fibro-osseous tunnel of each finger, the FDS divides into two slips, allowing the FDP to pass through and lie more superficial, distal to the base of the proximal phalanx. As the FDS moves distally it re-decussates and splays out to insert at the middle portion of the middle phalanx. The FDP continues distally to insert along the volar aspect of the midportion of the distal phalanx. The digital extensor mechanism is a conjoined tendinous structure made up of the extrinsic long extensor tendon and the tendinous insertions of the intrinsic muscles. The intrinsic muscular portion has tendinous extensions from the volar and dorsal interossei to the radial and ulnar lateral slips of the extrinsic portion, and extensions of lumbrical muscles to the radial lateral slips of the extrinsic portion. On flexion of the MP joint, the sagittal bands slide forward to apply the extensor forces along the central slip and extend the middle phalanx. On flexion of the PIP joint, the lateral slips slide volar to the axis of rotation to lose and allow flexion of the DIP joint. Otherwise, it would be taut and extend the DIP by a tenodesis effect. The extensor mechanism of the thumb is a modified form of the digital mechanism, since there is no middle phalanx.

INTRINSIC MUSCLES

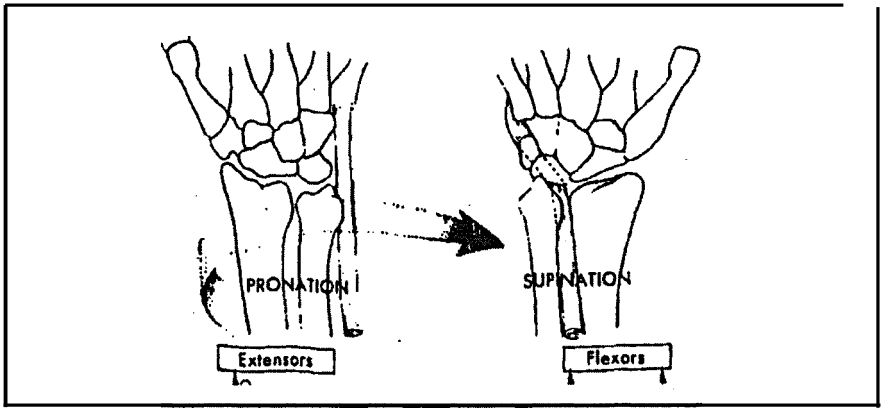
Dorsal interossei: 4 in number, arising from the adjacent surfaces of the shafts of the metacarpals (I-IV) and insert on the lateral slips of the extensor hood of MII-IV. They move Mil radialward (abduct), MJV ulnarward and Mlll both radial and ulnarward.

Volar Interossei: 3 in number, arising from Mll,IV,V and inserting on the lateral slip of their respeCtive extensor hood mechanisms. They move MIV, V radial ward. (adduct), and Mil ulnarward.

Lumbrical: 4 in number. The first and second lumbricals arise from the radial side of theirrespective FDP tendons. The third arises from·the adjacent sides ofthe 2nd and 3rd FDP, and the fourth arises from the adjacent sides ofthe 3rd and 4th FDP. They all insert on the radial aspect of the lateral slips of their respective extensor hood mechanisms.

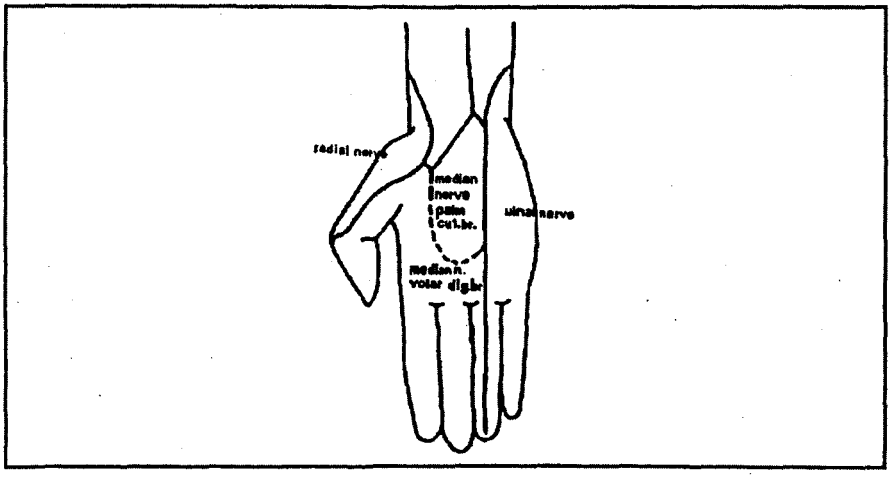
THE WRIST JOINT

The wrist includes 8 carpal bones, the radiocarpal, intercarpal and the carpo-metacarpal articulations, ligaments and soft-tissue structures. It transmits forces between the forearm and the hand, providing stability through the five primary extrinsic flexors and extensors passing over the carpus and inserting into the base of the metacarpals. The wrist is the key joint in placing the hand in a working position and when its movement is considered in relation to finger movement, two independent actions are possible. When the extrinsic wrist muscles stabilise the joint, the extrinsic and intrinsic finger muscles can alter the finger position. Conversely, when the finger is stabilised the wrist can be moved in a variety of directions. Anatomical deformity of any of the constituent parts of the wrist leads to instability and significant alteration of digital function. Synovitis at the ulna styloid may be associated with rupture of the extensor digiti minimi, resulting in an inability to extend the little finger and ring fingers.



MEDIAN NERVE

Compression of this nerve by the thickening of the synovium around the flexor tendons can be due to a number of pathological conditions. There is a close association between RA and carpal tunnel syndrome. The pain is characteristically troublesome at night, waking the patient and can be relieved only by vigorous movement of the hands for a considerable time. During the day, it is brought on by any activity that involves persistent grasping, particularly of small objects. Tingling and numbness occur in the thumb, index and middle fingers. Symptoms can also be induced by tapping the median nerve on the volar aspect of the wrist (Tinel sign). In patients with clinical features of median nerve compression but absence of these 2 signs, consider median nerve entrapment in the forearm (pronator syndrome). The symptoms can be reproduced by asking the patient to flex the wrist by pressing the backs of the two hands against each other for about one minute (Phalen sign). The symptoms are probably due to anoxia of the nerve secondary to the effects of venous stasis. Surgical decompression leads to prompt relief of the signs and symptoms.



ULNAR NERVE

Entrapment of the ulnar nerve at the wrist is much less common than median nerve involvement because there are no tendons and therefore no expanding diseased synovium in Guyon's canal. There can, however, be a spillover effect from severe synovitis of the carpal tunnel. Ulnar nerve entrapment is much more common at the elbow and is usually associated with degenerative changes at the elbow joint. Electromyography is sometimes necessary to locate the exact site of entrapment.

RADIAL NERVE

Radial nerve palsy may result in an inability to extend the MCP joints. The differential diagnosis of dropped fingers is between posterior interosseous nerve compression and tendon rupture. Simultaneous rupture of all the extensor tendons of the wrist is extremely uncommon and should raise the suspicion of a radial nerve lesion. To test:
i) passively push the wrist into flexion; if the fingers extend slightly then their tendons are intact because of a tendosis effect; ii) passive full extension of the fingers that can be maintained by the patient shows that the muscles are not paralyzed but that the extrinsic extensor tendons had been dislocated below the axis of flexion of the MCP joints; iii) if direct electrical stimulation of the muscle produces extension of the fingers then their tendons are intact and the nerve supply to the muscle is at fault. In all cases the nerve is compressed between an extending synovitis of the elbow joint and the deep surface of the supinator muscle. Inability to extend the wrist may be the first sign of mononeuritis multiplex due to rheumatoid vasculitis.

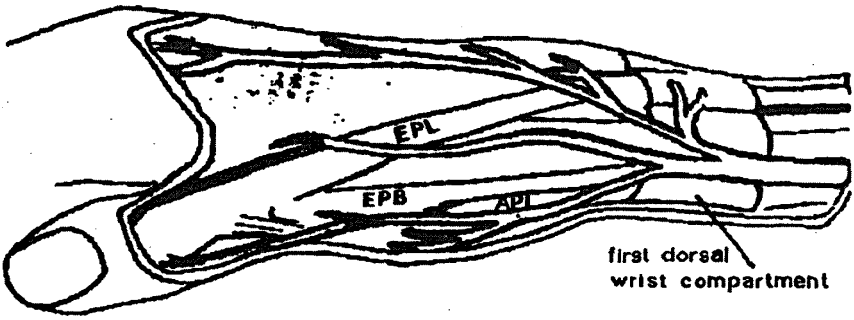
VASCULAR

Many of the rheumatic diseases cause vascular changes resulting in ischaemia and gangrene to soft-tissue structures. This may manifest in mild cases with patchy or diffuse palmar erythema, nail fold infarcts, splinter haemorrhages or frank gangrene of the digits. The pathogenesis may be due to inflammation of the vessel wall or obstruction to flow from an embolus. Rarely, compression may result in Volkmann's contracture.

Vasculopathies are probably the underlying mechanism of many of the clinical features of rheumatic disease. The skin is enriched with superficial and deep blood vessels and is often the first organ to show signs of vasculitis. Dermatomyositis, scleroderma and SLE have characteristic distributions of involvement of the hand.

IMPORTANT PHYSICAL SIGNS

Hand Joints- Several joints can be tested simultaneously by asking the patient to make a fist. If active movement is limited, passive movement should be carried out. This helps one differentiate between disease of the joints compared with that of the soft tissues in the palm. The bony outline at the PIP and MCP joints is easily fell Any bogginess or difficulty in feeling the outline should raise the suspicion of synovitis. Synovitis of the MCP joints is best assessed with the MCP joint flexed. Early synovitis of the PIP joint may be missed by a cursory examination. Compression of the PIP joint on the sides with vertical pressure on the dorsal surface may reveal this early feature. Passive flexion while pressing the sides may produce pain in early cases.



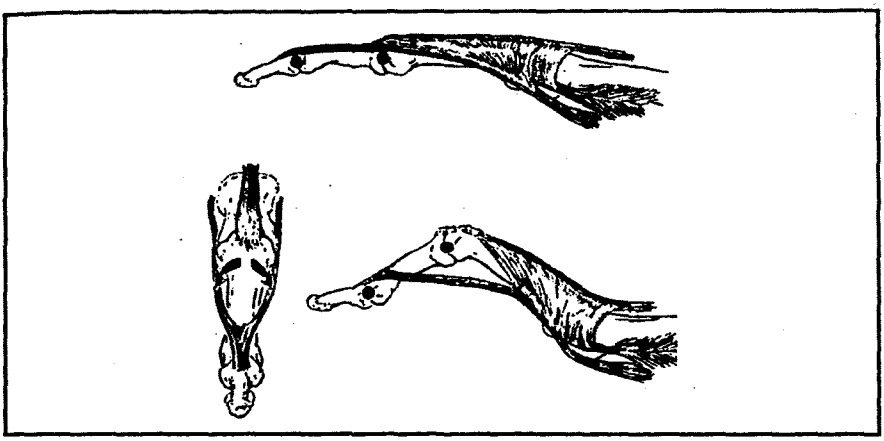
Finkelstein -with thumb flexed into palm of fist, actively or passively deviate wrist ulnarward with wrist in neutral. Stenosing tenovaginitis (DeQuergvain' s) of first dorsal compartment of wrist (APL and EPB) will cause pain.

Tinel – Tapping along a nerve will cause distal pamesthesiae over areas of nerve regeneration. Useful in carpal tunnel syndrome. Very subjective!

Saville- inability to compress soft-tissue at the base of the finger (volar aspect). Useful early sign of flexor tenosynovitis, which may be the cause of a painful hand in the absence of PIP or MCP synovitis. With your thumb on the palm, ask the patient to move each finger. Feel for crepitus in the tendon sheath as well as nodules along the sheath, which indicate more extensive flexor tenosynovitis. Treatment is difficult, sometimes requiring surgical removal of excess synovium.

Swan-neck- shortening of the intrinsic muscles eventually collapses the beam system of the fingers by pulling the MCP joint into flexion and hyperextending the PIP joint. The head and beak of a swan are formed by secondary flexion of the DIP joint. All degrees of this exaggerated action of the intrinsic muscles are shown by an inability to flex the IP joints when the MCP joints are held extended. The test for this condition is carried out in 2 stages. The first stage applies passive flexion to all3 digital joints. If flexion is possible, it establishes that there is no restriction to motion caused by pathological conditions of the extrinsic extensor tendon or the digital joints. In the second stage of the test the intrinsic muscles are tensed by pushing the MCP joint into full extension and then applying dorsal pressure to the tip of the finger in an attempt to produce passive flexion. In the normal hand, passive flexion is still possible in this position. If rheumatoid disease is affecting the intrinsic muscles, the degree of resistance to passive flexion is directly proportional to the severity of disease.

Boutonniere – this is caused by tendon imbalance over the PIP joint. The fully developed deformity has 3 components: flexion of the PIP joint, hyperextension of the DIP joint and secondary changes in the joints on either side. The expanding synovium weakens the terminal portion of the central slip of the extrinsic extensor tendon and of the lateral fibres that normally retain the lateral bands in place, causing them to dislocate in a palmar direction. During this dislocation, the lateml bands cross the axis of the joint and, instead of being extensors they become flexors of the joint.



Piano-key sign -the ulna styloid may be prominent and unstable. Vertical compression produces immediate return (like a piano key). Remember also that disease of the ulnar styloid may cause rupture of the extensor digiti minimi tendon. Extensor lag may be the earliest sign of impending rupture of the tendon. Sometimes the tendons slip in the valleys at the MCP and may be mistaken for tendon rupture. Passive extension of the fingers, with the patient able to keep the fingers extended excludes tendon rupture.

Clubbing – alerts the physician to the possibility of hypertrophic pulmonary osteo athropathy.

Nail changes -important in Psoriasis. Nailfold capillary abnormalities may help to classify undifferentiated connective tissue syndromes.

Raynaud's phenomenon – 3 colour change triggered by cold-exposure. Numerous causes. Rare in seronegative spondarthropathies

Tennis elbow- lateral epicondylitis associated with inflammation of the common wrist extensor origin.

Golfer's elbow- medical epicondylitis associated with inflammation of the common
·wrist flexor origin.

THE SACROILIAC/BUTTOCK/HIP

Most pain felt in the buttock is referred from the spine (rarely the sacroiliac joint but remember Ank. Spondylitis).

Referred pain: extra-segmental dural reference from a disc may cause pain in the buttock, iliacfossa, groin, thigh or leg.

Approach

Pain in the buttock/thigh. You must first decide whether it is referred from the spine (detailed history and examination of the spine.) If this is normal, then pass to examine sacroiliac joint/buttock/hip.

Sacroiliac Joint

All the manoevres depend on exerting tension on the joint. All are poor tests and do not really help when one most needs them.

i) Patient prone -firm pressure on the sacrum
ii) Patient supine- press firmly downward and laterally on the ilium
iii) Patient on side -press upper part of iliac crest downwards

There are many others.

Hip

The state of the capsule is assessed by four movements: flexion, internal rotation, external rotation, extension.

Thomas Test

Flex both hips fully. Hold the one hip in flexion, extend the other. Repeat with opposite side. If the extending hip does not come to rest on the couch, this will tell you that there is a flexion deformity present.

Pain on hip flexion can be caused by a hip capsular pattern, a psoas bursitis, it is part of the sign of the buttock!

The straight leg raise test stretches the duramater via the sciatic nerve. If this causes pain, then you mist look at hip flexion with knee flexed. If this produces more pain than the straight leg test, this points to a buttock lesion (the sign of the buttock).

Resisted movements – only resisted adduction/flexion are tests for muscular lesions around the hip (resisted flexion also loads the hip joint!) All the other resisted movements are accessory signs for bursitis (psoas trochanteric), e.g. resisted int/ext rotation/extension/abduction = accessory signs for gluteal bursitis.

Resisted adduction = adductors -riders sprain
Resisted extension of knee in prone position tests quadriceps
Resisted flexion of knee tests hamstrings

Buttock Lesions (the sign of the buttock)

(Remember pressure on any nerve root below L3 may give rise to buttock pain). The signs are produced by a lesion of the buttock i.e. something is stretched/squeezed.

Major lesions

Osteitis or neoplasma upper femur
Ischiorectal abcess
Fractures sacrum

Minor lesions

1. Psoas Bursitis- uncommon. Most painful is passive adduction in flexion. All the resisted movements are painless.
2. Gluteal Bursitis- pain in full passive flexion/lateral rotation with or without pain on resisted abduction.
3. Rarer causes -ischial bursitis
   -haemorrhaigic psoas bursitis

Hip lesions

(Derived from L3 therefore pain referral is anterior thigh to the knee).

Causes

1. Osteoarthritis
2. Rheumatoid arthritis
3. Lesions in childhood- nearly all serious
   Dislocation
   Perthers disease
   Tuberculosis
   Slipped upper femoral epiphysis
   Irritable hip of childhood

THE KNEE

History- First exclude other causes for pain in the 'knee. When this is done, the primary distinction is between disorders of spontaneous origin and those of traumatic origin.

In the event of injury, a detailed history is required.

(i) To assess the type of strain imposed on the joint at the time of injury eg a valgus strain will damage the medial collateral ligament.

(ii) Many traumatic disorders can be distinguished by their typical history and progression.

Examination

Preliminary examination must exclude the spine/hip as the cause of knee pain.

Passive Movement

Patient lies on his back- the first two movements passive flexion and extension evaluate the state of the joint capsule.

The capsular pattern of the knee is- marked limitation of flexion, less of extension.

Now 7 other movements are tested for the ligaments:

1. Valgus strain with knee flexed -medial collateral ligament.
2. Varus strain.
3. Passive lateral rotation (knee flexed)

4. Passive medial rotation (knee flexed)
5. Passive forward shearing (knee flexed)
6. Passive backward shearing (knee flexed)
7. Passive lateral shearing of tibia and femur.

Resisted Movement (Patient prone)

1. Resisted flexion = hamstrings
   - painful resisted medial rotation =semimembranosus
   - painful resisted lateral rotation =biceps femoris
2. Resisted extension = quadriceps

(Note painless weakness -look for L3 lesion or muscle disease)

Accessory Signs

1. Check for fluid
2. Check for Baker's cyst- popliteal fossa
3. Check for warmth
4. Check for synovial thickening by rolling finger up/downwards at the reflexion of synovial membrane over the femoral condyle.

Types of Findings

Capsular lesions -arthritis of the knee- search for cause

Noncapsular lesions

Ligamentous lesions

Pain =strain

Pain and laxity= severe strain

Laxity =past sprain or rupture

Medial collateral ligament sprain- very

common 3 classic sites-joint line the most

common

Lateral collateral- rare

Coronary ligaments- medial more common than lateral

Cruciate ligaments

Contractile Structures

Supra patellar tendon- rare

Infra patellar tendon -common

THE LEG/ANKLE

Easy, most of the causes are local muscular lesions. Rarely referred pain (but when it does occur it is a 5th lumbar disc compressing 1/2 sacral roots).

Examination

Resisted Movement- Patient upright. Patient stands on ball of foot on one leg then the other.

Now test resisted

1. Dorsiflexion of the ankle
2. Plantar flexion
3. Medial (inversion)
4. Lateral (eversion)

Findings

1. **Strain of gastrocnemius** -common. Called tennis leg. Suspect when pain on resisted plantar flexion (= gastrocnemius + soleus) Now flex the knee (relaxes gastrocnemius) If pain disappears= gastrocnemius strain.
2. **Tendo Achilles**

   Pain is felt at the back of heel- standing on tiptoe= pain. Resisted plantar flexion hurts as wen.
3. **Everton of the Ankle**
4. **Invertors**

   Tibialis anterior= pain on resisted dorsiflexion and inversion.

   Posterior tibial =pain on resisted inversion.
5. **Dorsiflexions**

   Tibialis anterior usually at musculo-tendinous junction approx. 10 cm. above the ankle.

   Ankle joint permits only two movements- dorsi/plantar flexion.

   Examine while standing and supine.

   Standing will bring out strains which may be missed by supine examination.

   Passive dorsiflexion/plantar flexion evaluate the capsule of the joint.

   Next test ligaments.

   Put ankle into plantar flexion.

   Now apply passive inversion (talo-fibula, calcaneofibular, lateral midtarsal ligaments)

   Now apply passive eversion.

Midtarsal Joint (Sub talar and mid tarsal joints) Passive dorsiflexion

Passive plantar flexion

Passive adduction: Hold calcaneous steady

Passive abduction Passive
medial rotation Passive
lateral rotation

Findings

Ankle

Capsular pattern- unusual. Some limitation of dorsiflexion with more limitations of plantar flexion.

Ligamentous sprains - very common

Talocalcaneal Joint

Capsular pattern -limitation of varus

Plantar fasciitis

Midtanal Joint (Talonavicular, calcaneo-cuboid)

Capsular pattern -limitation of adduction and medial rotation.

Metatarsophalangeal J o i n t s

Test with passive plantar dorsif

IMMUNOLOGY IN THE RHEUMATIC DISEASES

Immunity refers to the reaction of the immune system to foreign substances, including microbes as well as macro-molecules such as proteins and polysaccharides.

Innate Immunity {natural or native immunity) refers to the mechanisms designed largely for protection from microbes and includes:

1) physical/ chemical barriers e.g.: epithelia *I* defensins.
2) blood proteins e.g.: complement
3) phagocytic cells e.g.: neutrophils and macrophages

Specific Immunity (adaptive immunity) refers to the immune response normally stimulated when an individual is exposed to a foreign antigen. Depending on the components of the immune system which are engaged, two types of specific immune responses may occur:

1) Humoral immunity- mediated by antibodies (produced by B lymphocytes)
2) Cellular immunity- mediated by T lymphocytes

Tolerance: refers to immunologic unresponsiveness to self (autologous) antigens and is mediated by the following mechanisms:

1) Elimination of lymphocytes reactive to self-antigens (usually by apoptosis)
2) Functional inactivation of self-reactive lymphocytes (anergy)

Autoimmune disease: refers to abnormalities in induction or maintenance of self-tolerance which leads to immune responses against self (autologous) antigens.

Principal **cellular constituents of the immune system** are lymphocytes, mononuclear phagocytes and related accessory cells (e.g. dendritic cells). Lymphocytes are capable of specific antigen recognition and are classified into subsets depending on function and phenotype; thus:

- B cells produce antibodies,
- CD4 T cells help to stimulate Bcell antibody Production and activate macrophages
- CDS T cells kill target cells expressing foreign antigen (cytotoxic cells)
- NK cells lyse viral-infected cells and tumour cells

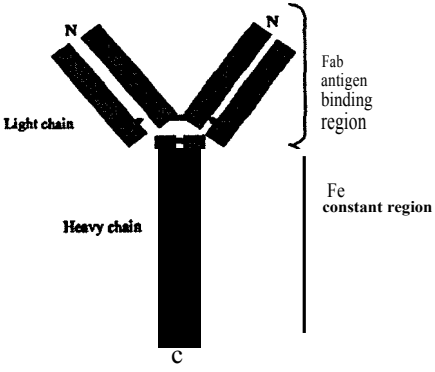


Figure 1: Outline of the structure of an antibody.
Specific antigen binding occurs via the Fab region whilst antibody binding to Fe receptors on macrophages and B cells occur via the constant region.

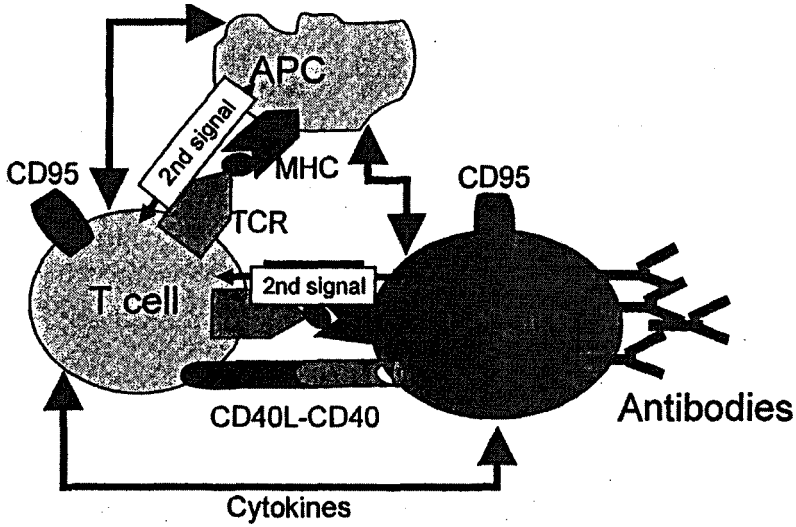


Figure 2: Cellular interaction in the immune system.
Antibody production depends on complex interactions between a variety of immune cells. Some of the cell surface molecules which play a role in the regulation of cell-cell interactions are shown.

Antibodies are a family of structurally related glycoproteins produced by B cells and function as mediators of humoral immunity. The diagram (figure l) shows the variable (antigen-binding sites) and constant regions of antibodies. The production of antibodies depends on a complex interaction of cellular reactions as shown in figure 2. Any of a number of these interactions may break down in autoimmune diseases to result in the production of autoantibodies. Antibodies directed at self antigens are known as autoantibodies and these are useful in the characterization of autoimmune connective tissue diseases. Table 2 shows some of the well characterized autoantibody associations with connective tissue diseases.

Major Histocompatibility Complex (MHC)

A region of highly polymorphic genes whose products are expressed on the surfaces of a variety of cells. MHC genes play a central role in immune responses to protein antigens because antigen-specific T lymphocytes only recognize portions of protein antigens (peptides) that are non-covalently bound to MHC gene products. There are two types of MHC gene products, called class I and class II MHC molecules (also known as HLA molecules representing the Human leucocyte antigen based on original serological markers). In general, antigens associated with class I molecules are recognized by CDS+ cytolytic T cells, whereas class 11-associated antigens are recognized by CD4+ helper T cells. As a result of this central role in antigen presentation, MHC associations with autoimmune diseases were sought. Table 1 shows some frequent associations of diseases with MHC patterns.

Table I: Association of MHC with disease

Disease	HLA allele	Relative risk*
Rheumatoid arthritis	DR4	6
Ankylosing spondylitis	827	90-100
Sjogren"s syndrome	DR3	10
Dermatitis herpetiform is	DR3	50
IDDM	DR3	*5*
IDDM	DR4	5-6
IDDM	DR3/DR4	20
SLE	88, DR2/3, C4AQO	?

• relative risk= probability of individuals with a HLA allele/s to develop a . disease compared with individuals lacking that HLA allele/s.? = unknown.

Cytokines

The effector phases of both innate and specific immunity are mediated by protein hormones called cytokines. Cytokines belong to a family of proteins, the same cytokines often being made by many cell types, and individual cytokines can often act on many cell types (pleiotropic). In general, cytokines are synthesized in response to inflammatory or antigenic stimuli and act locally, in an autocrine or paracrine fashion, by binding to high affinity receptors on target cells. Cytokines are classified into a number of protein families according to their functions. Thus TNF (tumour necrosis factor) constitutes a prototypic member of a family of proteins which are now known to mediate critical cellular functions in a variety of inflammatory diseases like Rheumatoid arthritis and Crohn's disease. Similarly, J nterteukin-1 (IL-l) plays a role in inflammatory *I* erosive disease in RA. Other cytokines like IL-10 may play an anti-inflammatory function and regulate the effects of the pro-inflammatory cytokines.

Complement

The complement system comprises a group of more than 30 serum and cell surface proteins that interact with other immune system molecules in a highly-regulated manner to provide many of the effector functions of humoral immunity and inflammation. Complement proteins usually function in a cascade of reactions in one of two converging pathways – alternative pathway and classical pathway. The classical pathway is usually initiated by the binding of complement proteins to antibody-antigen complexes, hence explaining the reduction of complement proteins in immune-complex-mediated conditions like SLE, and occasionally in RA associated with vasculitis. A full review of complement proteins and their functions can be found in any immunology textbook.

Mechanisms of Autoimmunity

Autoimmunity results from the failure or breakdown of the mechanisms normally responsible for maintaining self-tolerance. Loss of self-tolerance may result from abnormal selection or regulation of self-reactive lymphocytes, and from abnormalities

in the way, self-antigens are presented to the immune system. Whilst every individual has the potential to develop autoimmunity, the intricate regulation of the immune response protects the majority of us from disease. Thus, a number of factors may play a role in determining susceptibility to autoimmunity:

I) Immune abnormalities of lymphocyte or APC (antigen presenting cell) function.

2) Genetic background (i.e., MHC and other candidate genes)

3) Gender (autoimmune diseases commoner in females)

4) Tissue injury (NBI Apoptosis)

5) Microbial infections (molecular mimicry)

Autoimmune diseases may be organ-specific or systemic, and these may be caused by different antigens and different immune abnormalities. For instance, the immune complex-mediated diseases are typically systemic (e.g., SLE) whilst the organ-specific diseases are usually mediated by antibody or T cell responses to antigens restricted to certain tissue types (e.g., Anti-acetylcholine receptor antibody and Myasthenia gravis).

Examples of systemic autoimmune diseases in Rheumatology include Rheumatoid arthritis, Systemic Lupus Erythematosus, Scleroderma, Sjogren's syndrome, Psoriatic arthritis, Inflammatory myopathies, and some vasculitides. The immune dysfunction in these disorders are too complex to discuss in detail here but include a variety of defects described in T cell, B cell and macrophage function.

Autoantibodies are generated in a number of these conditions and may serve not only to characterize/classify these diseases but may also have a significant role in pathogenesis. The target antigens of autoantibodies associated with the Connective tissue diseases are known to include major components of cellular function, such as DNA, RNA, transcription mechanisms etc. Table 2 shows some of the more clearly defined associations of autoantibodies with Connective tissue diseases.

Table 2: Autoantibody associations with disease.

Disease	Autoantibody	Target antigen
SLE	ANA, dsDNA, Sm	Nucleoproteins
Scleroderma	ANA, centromere, topoisomerase	Nucleoproteins
Sjogren's syndrome	Ro, La	Ro, La (spliceosome)
Anti-phospholipid	ACL, B2GPI	Phospholipids
Wegener's granulomatosis	c-ANCA	Proteinase-3
Polymyositis	Jo-t	tRNA synthetase
Dermatomyositis	Mi-2	?
Rheumatoid arthritis	Rheumatoid factor	lgG, lgM, lgA

ANA= antinuclear antibody, dsDNA =double stranded DNA, ACL = anticardiolipin antibody, B2GPI = Beta-2 glycoprotein I, c-ANCA = anti-neutrophil cytoplasmic antibody, tRNA =transfer RNA, Ig = immunoglobulin, =target antigen not clearly defined.

It is important to note that the autoantibodies help in characterizing *I* classifying subsets of connective tissue diseases, but should not be used in isolation for the diagnosis of these disorders. A percentage of normal people may have low titre autoantibodies, hence the emphasis still rests on a thorough clinical assessment of the problem, with the use of autoantibody measurements as supportive tools in arriving at a diagnosis.

Autoimmune diseases clearly can result following dysfunction at a variety of levels within the immune system. Current immunotherapy directed at the autoimmune disorders is relatively non-specific although they do influence a number of the aforementioned mechanisms (e.g., azathioprine, cyclophosphamide, methotrexate, chloroquine etc.). However, with a better understanding of the immune processes more specific immunotherapy is being developed (e.g., cyclosporine which specifically influences T cell function, anti-CD4, anti-TNF etc.). A good marriage between immunology and rheumatology will hopefully lead to a better understanding of these disorders and subsequently to more specific and targeted therapy.

NON-ARTICULAR RHEUMATISM

Recognition important because: -

1. Common
2. Often misdiagnosed as arthritis
3. Response to therapy usually excellent

TENOSYNOVITIS

=Inflammation of the synovial membrane of the tendon sheath

Causes: Rheumatoid arthritis
Gout
Gonorrhea
Trauma – acute
– chronic (overuse)
Xanthomatosis
Idiopathic

Clinical: Pain on active/resisted movements, swelling tenderness, crepitus, nodules.

Treatment: Rest- immobilization, physiotherapy, NSAIDs, steroid injection and splints, surgical decompression.

Common forms of tenosynovitis:

THE HAND

Flexor tenosynovitis: common in RA, some normal individuals diabetics.
Saville sign
Stenosing tenovaginitis- constriction of tendon sheath with 2° changes in tendon, usually enlargement distal to constriction.
Trigger finger- snapping sensation or "locking"- tendon pulled through constriction by flexor nodule

Extensor tenosynovitis Common at the wrist and it may cause rupture 4th and 5th extensors.
Treatment- surgery.

De Quervain's tenosynovitis stenosing tenosynovitis of abductor pollicis longus and extensor pollicis brevis
- Cause: occupational; overuse
Clinical: pain, tenderness, swelling- along course of tendons
Finkelstein's test

THE FOOT

1. **Achilles tendinitis** -painful heel; worse on resisted plantar flexion.
2. **Tibialis posterior** - swelling in region of medial malleolus; pain on resisted inversion.
3. **Peroneus**- swelling in region of lateral malleolus; pain on resisted eversion.

THESHOULDER

Anatomy of rotator cuff

Rotator cuff syndromes
- Supraspinatus tendinitis
- Subacromial bursitis
- Acute calcific tendinitis
- Rupture of supraspinatus tendon – partial
  complete
- Bicipital tendinitis
- Adhesive pericapsulitis (frozen shoulder).

A Supraspinatus tendinitis

Pathogenesis: attrition, degeneration and reactive inflammation with trauma leading to swelling of tendons and interference with movement at coraco-acromial arch.

Age: 40-60years

Clinical: pain at deltoid insertion or poorly defined over deltoid.
Worse on – active/resisted movement
– sleeping on involved side
Tenderness
Painful arc 60°- 110°
Unilateral/bilateral- dominant side commonest.

X-Ray nil, or calcification in the tendon, and after many years erosion of greater tuberosity is seen.

Course: Self-limiting

Treatment: Rest
NSAIDs
Physiotherapy
Steroid injection.

B Acute calcific tendinitis

Clinical: – acute onset. Symptoms, signs and treatment as for supraspinatus tendinitis. May resolve spontaneously.

Pathogenesis: Rupture of inflamed calcific deposit into subacromial bursa or glenohumeral joint with resultant severe acute inflammation.

C Rotator cuff tears

>45 years. Underlying degeneration. May follow trauma.

a) **Partial:** – inability to initiate abduction.
– painful arc.
Treatment: Rest
NSAIDs
Steroid injection.

b) **Complete:** Persistent inability to initiate abduction.
Treatment: -surgical repair

D **Bicipital tendinitis**

I$_o$ or associated with rotator cuff degeneration

Clinical: Tender over bicipital groove (take care this is 'normally' a sensitive area!)
Pain on resisted flexion of elbow
Pain on resisted supination of flexed pronated forearm ("palm-up" sign).

Treatment: As for supraspinatus tendinitis

E **Frozen shoulder** (Adhesive pericapsulitis)

? Auto-immune response to local tissue breakdown
"Periarthritic personality"

Pathology: thickening of joint capsule with decrease in volume of glenohumeral joint cavity.
Mild synovial cell proliferation and inflammatory reaction.

Associations: – local – shoulder injury, rotator cuff injury, or any intrinsic shoulder disease causing pain or immobility

general - IHD)
– chronic lung disease) Common denominator
– breast Sx)
– hemiplegia) is pain/immobility
– herpes zoster)
– diabetes mellitus

Females> Male- 50+ years usually

Clinical: - Night pain/stiffness gross movements
– Unilateral/bilateral
– Ann held in internal rotation
Occasionally there is an associated painful bluish-red swelling of the ipsilateral hand or both hands (often called Charcot's blue oedema). Fingers become flexed and skin is tightly bound down when oedema disappears. This combination is called the hand-shoulder syndrome. This is classified as an algodystrophy (reflex sympathetic dystrophy).

Course: 3 phases:
i) pain and increased stiffness 2-9 months
ii) less pain, more movement/stiffness 4-12 months
iii) gradual recovery (thawing) additional 5-26 months

Treatment: Prophylaxis -active mobilization
Established- NSAIDs, analgesic and steroid injections may be tried.
Calcitonin claimed to be effective.
Regular exercise to maintain mobility.
Manipulation under anaesthesia+ PT may be used.

THE WRIST

Ganglion

Cystic swelling near or attached to tendon sheath derived from sheath or capsule, containing thick, mucoid, hyaluronic acid-rich material.

Sites: dorsum wrist/foot, fingers.

Clinical: Swelling

Treatment: Nil {may resolve spontaneously).

THE ELBOW

Epicondylitis

1. ***Lateral epicondylitis*** **(Tennis elbow)**

Adults usually 40-50- not confined to tennis players.

Pathogenesis: Minor tears of common extensor origin with periositis

Clinical: Unilateral/bilateral, usually dominant side.
Ache – localised over epicondyle or referred behind it
– wide radiation (forearm)
-full movements of the elbow
- localised tenderness is present
-aggravated by resisted active dorsiflexion of the wrist of the pronated extended forearm.
-Self-limiting

Treatment: Rest
NSAIDs
Physiotherapy
Steroid injection
Surgery

2. ***Medial epicondylitis*** **(Golfer's elbow)**
Pain/tenderness distal to medial epicondyle
Pain on resisted active flexion of wrist.

Treatment: as for tennis elbow.

3. ***Biceps tendinitis***
Pain on resisted supination (palms up sign).

THE ANKLE

Plantar fasciitis (**Policeman's heel)**

? Bursitis: Trauma in some. Many, no cause found but NB ankylosing spondylitis is a common cause. Pain on walking especially on starting. Very incapacitating. Tenderness localised to insertion of plantar fascia to calcaneus.

Treatment shoe insert {excavated heel)
local steroid injection.

BURSITIS

Bursa =closed sac lined by synovium which facilitates motion of tendons/ muscles/skin over another structure e.g. bone.

Causes: RA, gout sepsis, "traumatic," idiopathic.

Examples: Sub-deltoid.
Gluteus medius — painful hip, local tenderness
pain on resisted abduction.
Olecranon — – RA, gout, trauma
– swelling± painless. Full movements.
·Achilles Tendon
Calcaneal
.Bunion- painful bursa over medial aspect of 1st MTP
Prepatella (housemaid's knee)
Ischial (weaver's bottom)
Anserine- sartorius bursa (medial tibia).

Treatment: Protection from irritation
NSAIDs
Physiotherapy
Local steroid injection
Excision if refractory

NERVEENTRAPMENTSYNDROMES

·Carpal tunnel syndrome:

Mechanism: Tenosynovitis in flexor compartment of wrist where tendons are enclosed in bony canal, roofed by rigid transverse carpal ligament increasing compression and degeneration of median nerve.

Causes: tenosynovitis, trauma, RA, pregnancy, Colles' fracture, hypothyroidism, amyloidosis, acromegaly, diabetes mellitus.

Clinical: Pain, paraesthesia 1st $3^{1}1_{2}$ fingers, worse at night which may radiate up to the shoulder.
Unilateral/bilateral (usually dominant side).
Tine! sign, Phalen sign.
Sensory loss median nerve distribution.
Weakness, abduction/apposition thumb and wasting thenar eminence are late signs.

Diagnosis: Characteristic symptoms; nerve conduction studies (sensory more sensitive than motor).

Treatment: Night splint in neutral position.
Local steroid injection may help. Diuretics claimed to be beneficial.
Surgical decompression.

Ulnar nerve entrapment

Site: Elbow/wrist (Guyon's canal}

Causes: Post-fracture, RA, Hypermobility

Clinical: Pain, paresthesia medial 1.5 fingers, weakness

Treatment: Surgery.

Other entrapments
Tarsal tunnel, lateral cutaneous nerve of thigh (meralgia paraesthetica).

HYPERMOBILITY SYNDROME

Arthropathy associated with joint laxity. Hypermobility is a common finding in children, but seldom persists into adult life: Itis a feature of some congenital conditions *(see* p. 7) and may also be acquired in rheumatoid arthritis and other chronic inflammatory arthropathies, neuropathic joints, acromegaly, rheumatic fever, and neurological diseases associated with hypotonicity. The hypermobility syndrome (without other abnormalities) is inherited as an autosomal dominant disorder.

Incidence
M.=F.
Onset in children or young adults with traumatic synovitis or unexplained effusion; or later with premature osteoarthrosis.

Joint affected
Knee common
Often hands
Occasionally ankles, cervical or lumbar spine, and feet.
One or many joints affected.

Symptoms
Joint and muscle pains.
Sometimes related to trauma.
Joint swelling.

Signs
Hypermobility (p. 7)
Joint effusions; later bony swelling and crepitus. '
Billowing mitral valve leaflet in some.

Course
Osteo-arthritic changes progress to moderate disability at older ages.

Associations
Dislocation of shoulder or patella.
Congenital dislocation of hip.

XR
Early: normal.
Later: degenerative changes (loss of joint space, sclerosis, osteophytes, subarticular cysts).

Laboratory
Normal E.S.R.
Synovial fluid: non-inflammatory.

Treatment
1. Analgesics as required.
2. Avoid trauma.

3. Physiotherapy.
4. Reassurance.

CONDITIONS ASSOCIATED WITH HYPERMOBILITY

1. ***Marfan 'sSyndrome***
   Autosomal dominant inheritance of tall, slender build, long fingers and toes (arachnodactyly), high arched palate, and often other skeletal deformities such as pigeon chest, flat feet, and kyphoscoliosis.
   Eye defects, most commonly ectopia lentis (50%); cardiovascular defects (20%); septal defects, conduction defects, and aneurysms. Later manifestations are aortic incompetence and dissecting aneurysm particularly in males; back-ache (30%); arthritis (20%).
2. ***Marfonoid Hypermobility Syndrome***
   Arachnodactyly and skeletal features of Marfan's syndrome with skin hyper-extensibility without ocular or cardiovascular abnormalities.
3. ***Ehlers-Danlos Syndrome***
   Autosomal dominant inheritance of velvety, fragile, hyper extensible skin (poor healing – tissue-paper scars), easy bruising, and sometimes other congenital abnormalities. Several types are described.
4. ***Osteogenesis Imperfecta***
   Autosomal dominant inheritance of bone fragility resulting in recurrent fractures and severe deformities.
5. ***Down's Syndrome (mongolism).***
   Trisomy 21 with dwarfism, mental retardation characteristic facies, and other limb and heart abnormalities.

Generalised Pain Syndromes

Dr MTL NYO

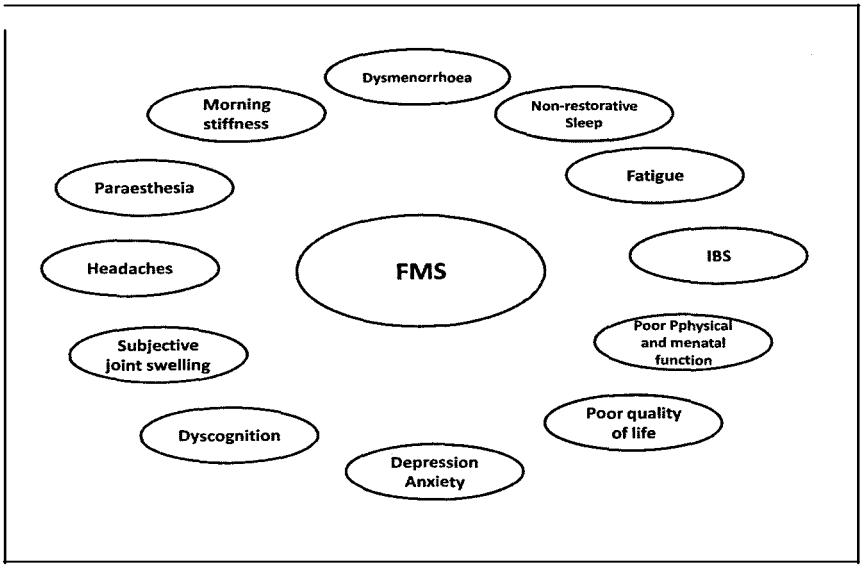
Pain has been shown to be the most frequent reason for medical consultations in the general population. At least 50% of these patients suffer from musculoskeletal pain. Among these patients with musculoskeletal diseases, non-articular rheumatic pain syndromes are a major component. TI1ese conditions can be regional or generalized.

Regional pain syndromes: tendonitis and bursitis, neurovascular entrapment, flatfoot and regional myofascial pain syndrome

Generalized pain syndromes: Fibromyalgia syndrome, chronic fatigue syndrome and multiple bursitis-tendinitis syndrome

Firomyalgia Syndrome (FMS)

FMS is one of the most common causes of chronic widespread pain. It is characterized by reduced pain thresholds (hyperalgesia) and pain with normally innocuous stimuli (allodynia). Diffuse pain is often accompanied by a wide range of symptoms including fatigue, non-restorative sleep, functional impairment, cognitive dysfunction, variable bowel habits, depression, stiffness, paranesthesia, and many more.

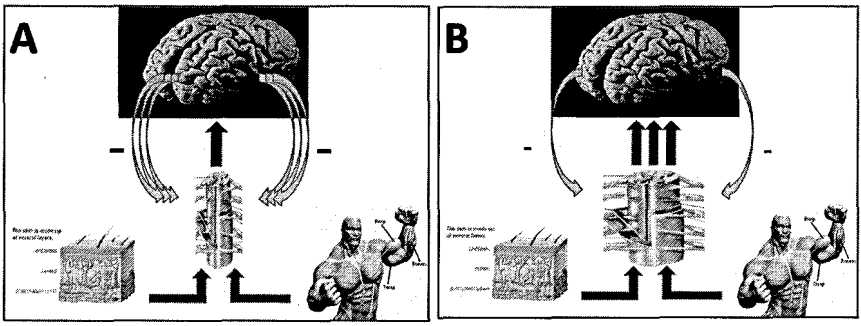


In general, FMS is a long term chronic illness. Prospective long-term outcome studies based in tertiary hospitals in America and Europe found no significant change in disease over a 6-8-year period. Severity of pain, fatigue, disability and quality of life remains unchanged. Furthermore, they found little improvement in health status, health service utilisation, and costs, with approximately 25% of patients with FMS receiving disability or other compensation payments. Health status as measured by short form 36 in patients with FMS is at least as poor, if not worse, than those with other musculoskeletal diseases such as rheumatoid arthritis and osteoarthritis.

Pathophysiology

Hyperalgesia and allodynia result from peripheral and central sensitisation. Peripheral sensitisation is a reduction in threshold and an increase in responsiveness of the peripheral ends of nociceptors. Central sensitisatiou refers to mechanisms that lead to an increase in the neuronal excitability in the central nervous system (esp dorsal horn cells).

Although the pathogenesis of FMS remains unclear, the currently known abnormalities support the hypothesis that FMS is not a subjective pain condition. Somatosensory abnormalities, cerebrospinal fluid and functional neuroimaging studies all suggest that abnormal pain processing is the central pathophysiological process in FMS.



Normally, as in figure A, a potential pain stimulus is transmitted from periphery such as muscles or skin to the spinal cord where it is processed and modulated by spinal inter-neorones and central inhibition from higher brain centers. In FMS, as depicted in figure B, transmission of the pain signal at the spinal cord level is increased and central inhibition is decreased, resulting in a much more pronounced perception of pain.

Diagnosis

The diagnosis of fibromyalgia, similar to other functional disorders, requires that organic diseases are not causing the symptoms. Systemic and rheumatic diseases can be ruled out by a patient history, physical examination, and laboratory investigations. Because there are no specific laboratory tests for fibromyalgia, the 1990 American College of Rheumatology (ACR) classification criteria have been used in clinical settings; however, they are not ideal for individual patient diagnosis.

ACR 1990 Classification Criteria (FMS)

History of widespread pain for at least 3 months
Widespread Pain: includes pain

- On both sides of the body
- **Above and below the waist**
- **Axial skeletal pain (cervical spine, anterior chest,** thoracic spine or low back pain)

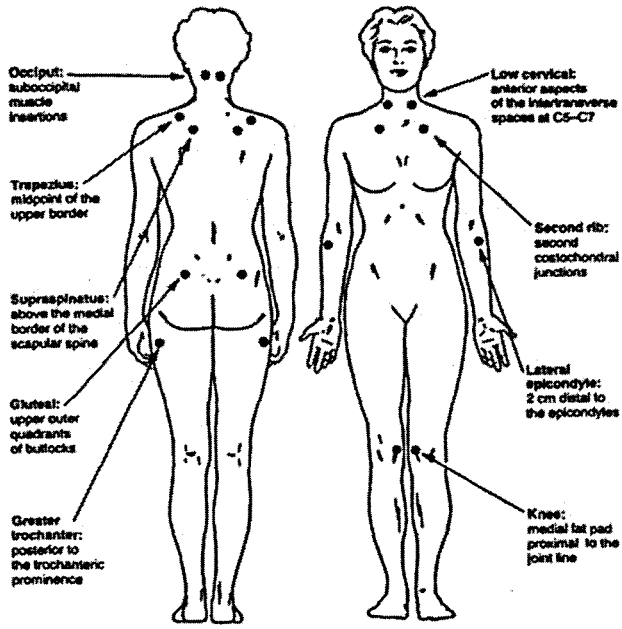
Pain In 11of 18tender point sites on digital palpation

Digital palpation should be performed with an approximate force of4 kg/cm2. A tender point has to be painful at palpation, not just "tender."

No pain at control points

Limitations of 1990 ACR Diagnostic Criteria

-Tender counts are usually subjective --
-The importance of symptoms was not considered
-Not all patients with FMS have ≥11 tender points
-63% of patients with FMS report pain at control points
- Women are more likely to have tender points than men



fibromyalgia Tender Points
General locations of the 18 tender points that make up the criteria for identifying fibromyalgia.

Causes of generalized aches and pain and stiffness which should be considered and excluded before the diagnosis of FMS is ascertained are as follows

- •. Hypothyroidism
- Hyperparathyroidism
- Polymyalgia rheumatica
- Early inflammatory arthritis (RA, SLE, Spondyloarthritis)
- Parkinsonism (mainly stiffness)
- Myositis
- Malignancies

2010 ACR Preliminary Diagnostic Criteria for FMS

Criteria

A patient satisfies diagnostic criteria for fibromyalgia **if the** following 3 conditions are met:

1) Widespread pain index(WPI≥) 7 and symptom severity (SS) scale score ≥.5 or WPI 3-6 and SS scale score >:9.
2) Symptoms have been present at a similar level for at least 3 months.
3) The patient does not have a disorder that would otherwise explain the pain.

Ascertainment

1) WPI: note the number areas in which the patient has had pain over the last week. In how many areas has the patient had pain? Score will be between 0 and 19.

Shoulder girdle, left	Hip (buttock, trochanter), left	Jaw, left	Upper back
Shoulder girdle, right	Hip (buttock, trochanter), right	Jaw, right	Lower back
Upper arm, left	Upper leg. left	Chest	Neck
Upper arm, right	Upper leg. right	Abdomen	
Lower arm, left	Lower leg, left		
Lower arm, right	Lower leg, right		

2) SS scale score:

Fatigue
Waking unrefreshed
Cognitive symptoms

For the each of the 3 symptoms above, indicate the level of severity over the past week using the following scale:

0 = no problem
1= slight or mild problems, generally mild or intermittent
2 = moderate, considerable problems, often present and/or at a moderate level
3 = severe: pervasive, continuous, life-disturbing problems

Considering somatic symptoms in general, indicate whether the patient has:

0 = no symptoms
1= few symptoms
2 = a moderate number of symptoms
3 = a great deal of symptoms

The SS scale score is the sum of the severity of the 3 symptoms (fatigue. waking unrefreshed, cognitive symptoms) plus the extent (severity) of somatic symptoms in general. The final score is between 0 and 12.

Somatic symptoms that might be considered: muscle pain, irritable bowel syndrome. fatigue/tiredness, thinking or remembering problem, muscle weakness, headache, pain/cramps in the abdomen, numbness/tingling, dizziness, insomnia, depression, constipation. pain in the upper abdomen, nausea, nervousness, chest pain. blurred vision. fever, diarrhea a. dry mouth, itching, wheezing. Raynaud's phenomenon, hives/welts, ringing in ears. vomiting. heartburn, oral ulcers, loss of/change in taste, seizures, dry eyes, shortness of breath, loss of appetite, rash, sun sensitivity, hearing difficulties, easy bruising, hair loss, frequent urination. painful urination. and bladder spasms.

Laboratory Tests

No laboratory tests exist for confirming the diagnosis of FMS.
ESR, CRP, TSH, (? RF, ANF) are usually requested to exclude inflammatory diseases especially early inflammatory arthritis and hypothyroidism.

Treatment of FMS

Non-pharmacological

1. Education
2. Regular aerobic exercise
3. Cognitive behavioral therapy

Pharmacological Treatment:

1. Tricyclic Antidepressants (Amytryptylline)
2. Serotonin-Norepnephrine Reuptake Inhibitors (Duloxetine, Milnacipran)
3. Alpha 2 delta ligands (Pregabalin Gabapentin)
4. Tramadol +Paracetamol

Chronic Fatigue Sydrome (CFS)

Medical opinions are split on the relationship between FMS and CFS. They are similar, and share many clinical features. Some believe the two conditions are the same, while others view them as different CFS may be viewed by some authorities as FMS with fatigue being a more prominent symptom than pain. Differentiating the two can be difficult in some patients but the following are helpful:

- First, pain is the predominant problem in people with fibromyalgia, whereas fatigue is the major complaint in people with CFS. Fatigue is usually severe and often completely incapacitating.
- Second, an abrupt onset preceded by a viral infection is more typical of CFS than FM.
- TI1ird, the presence of sore throat or enlarged or tender lymph nodes would also suggest CFS.

The management of FMS and CFS is similar. Education, exercise and low-dose antidepressant drugs are used to treat both conditions.

Prognosis in CFS is similar to FMS. Less than I0% of patients experience full remission. Most cases are chronic although in some there is some improvement over time.

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RHEUMATOID ARTHRITIS

Dr. N Abrahams, Dr. A Gcelu

RA affects an estimated 0.5- I% of the general population with twice as many women as men. The usual age of onset is between the third and fifth decade of life.

RA is the most common and most serious inflammatory arthritis that, if left untreated, will lead to irreversible joint damage, functional impairment and increased mortality. The outcome of the disease has improved considerably in recent years with the availability of effective therapies and the recognition that early intensive treatment strategies result in better outcomes.

Patients with inflammatory arthritis should be seen early and treated at the earliest opportunity. The initial aim should be to differentiate features of early RA from other diseases with similar presentations, such as psoriatic arthritis (PsA) or systemic lupus erythematosus (SLE) and from those that will remit spontaneously.

Patients with RA requiring therapy should be treated with the target being to induce remission in order to prevent joint damage, disability and long-term complications of the disease.

What is early RA?

There is no clear definition of early RA, but some authors refer to early RA as a disease with duration of I year or less, others up to 2 years.

Why treat early?
The evidence is that 70% of patients with recent-onset RA develop bony erosions within the first 3 years and 25% develop erosions within 3 months of disease onset. Therefore, early rather than delayed start of treatment results in less radiological damage and improves long-term functional outcome and mortality.

There appears to exist a window of opportunity where the disease process can be effectively suppressed or reversed, resulting in prevention of dan1age progression and even a return to an asymptomatic state. This window may be an immunopathologic ally distinct phase compared with later disease, and may last as little as 12 weeks from initial presentation. The American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) task force has developed new classification criteria to focus on features at earlier stages of disease that are associated with persistent and/or erosive disease, rather than defining the disease by its late-stage features, as was the case with the 1987 ACR classification criteria for RA. The new classification criteria are outlined in Table I.

Approach to early arthritis
Recognize features of inflammatory arthritis:
- Early-morning stiffness >60 minutes
- Pain worse at rest, relieved by activity
- swelling of joints.

Identify the pattern of the disease

- Peripheral v. axial
- Symmetrical v. asymmetrical
- Small v. large joints.

Exclude other inflammatory arthritides (e.g. SLE, PsA, gout, infection).

Table I. The 2010 American College of Rheumatology/European League Against Rheumatism classification criteria for rheumatoid arthritis4

Target population (who should be tested?)

Patients who have at least one joint with definite clinical synovitis (swelling) and those in whom the synovitis is not better explained by another disease

Classification criteria for RA

This is a score-based algorithm: add score of categories A-D: a score of ≥6/10 is needed to classify a patient as having definite RA

A. Joint involvement Score	
1 large joint	0
2 - 10 large joints	1
I - 3 small joints (with or "without involvement of large joints)	2
4- 10 small joints (with or without involvement of large joints)	3
>10 joints (at least I small joint)	5
B. Serology (at least 1 test result is needed for classification)	
Negative RF and negative ACPA	0
Low-positive RF or low positive ACPA	2
High-positive RF or high-positive ACPA	3
C. Acute-phase reactants (at least 1 test result is needed for classification c	
Normal CRP and normal ESR	0
Abnormal CRP or abnormal ESR	1
D. Duration of symptoms	
< 6 weeks	0
2: 6 weeks	1

A SCORE OF 6 OR MORE CONFIRMS THE DIAGNOSIS

Treatment

Non-pharmacological (lifestyle)

- Cessation of smoking
- Maintenance of physical activity
- Healthy diet
- Maintenance of appropriate body weight.

Recommended interventions

- Dynamic exercises
- Occupational therapy

Pharmacological treatment

Symptom-modifying anti-rheumamatic drugs (SMARDs)

- Simple analgesics
- NSAIDs (classic and COX-2, more effective than analgesics in active disease).

Glucocorticoids
In very early inflammatory arthritis steroids may be given as a single dose, either intramuscularly or intra-articularly to induce remission. Low-dose prednisone can be used to relieve short-term symptoms and signs of disease.

Disease-modifying anti-rheumatic drugs (D.MARDs)
• Synthetic DMARDs- there is strong evidence that early treatment with synthetic DMARDs retards radiographic progression, and therefore DMARD therapy should not be delayed. In patients with early inflammatory arthritis before the stage of fulfilling ACR criteria for RA, treating with DMARDs (MTX) reduces progression of radiographic damage.

• Methotrexate (anchor drug)
• Salazopyrine
• Chloroquine is a weaker DMARD
• Leflunomide - similar efficacy to MTX and therefore best alternative.

Biological DMARD therapy
Biological DMARDs provide rapid control of inflammation and have proven efficacy both in terms of clinical outcomes and structural damage in early disease. However, they are more expensive than traditional DMARDs, and this limits their use in early disease. They may also predispose to reactivation of TB and cause deep fungal infections.

Tumour necrosis factor inhibitors

• Infliximab- chimeric monoclonal antibody
• Etanercept- soluble fusion protein to TNF
• Adalimumab - fully human monoclonal antibody

IL-6 inllihitor
IL6 receptor blocker (tociluzimab)

B-cell depletion
B-cell therapy (rituximab)

Co-stimulation modulator
T-cell co-stimulation modulation (abatacept).

Monitor disease activity
The objective of treatment is to achieve a state of low disease activity (LDA), and ideally remission, in order to prevent structural damage and long-term disability. This can be achieved by regularly monitoring disease activity at 1-3-month intervals as long as remission is not achieved, using different indices of disease activity, e.g. DAS 28
The predictors of disease severity in RA are listed below

• Female gender
• High tender and swollen joint count
• HAQ score
• Acute phase reactants
• Rheumatoid factor
• Anti-CCP antibodies
• Erosive disease

Extra articular manifestations of RA

Ophthalmic
- Keratoconjunctivitis sicca
- Scleritis and Episcleritis
- Keratitis
- Retinal Vasculitis
- Scleromalacia

Pulmonary
- Pulmonary nodules
- Interstitial lung disease
- Pleural effusion

Cardiac
- Pericarditis
- Heart block- due to nodules in the conduction system

Major Cutaneous Vasculitis

Amyloidosis

Felty's Syndrome
Splenomegaly
- Neutropenia
- Leg ulcers

Neuropathy
- Peripheral neuropathy
- Mononeuritis multiples

Complications of RA
- Accelerated atherosclerosis
- Lymphoma
Related to medication
- Fibromyalgia

Spondyloarthritis (SpA)

Dr.MTLNYO

The Concept of spondyloarthritides

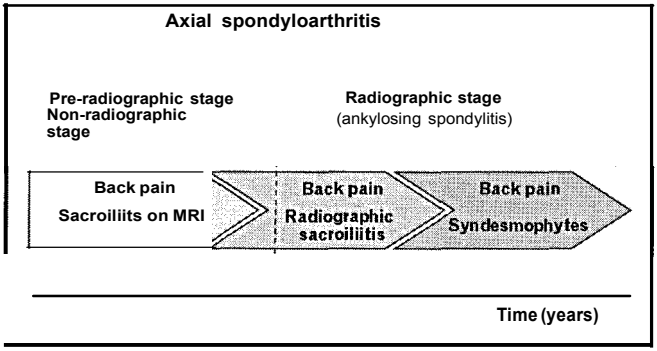
TI1e group of diseases collectively labeled spondyloarthritides consists of several disorders:

I. Ankylosing spondylitis (AS)
2. Psoriatic arthritis (PsA)
3. Reactive arthritis (ReA)
4. IBD related arthritis (IBDRA)
5. Undifferentiated SpA

The main links between these conditions are the association with HLA-827, the same pattern of peripheral joint involvement with an asymmetric oligo-articular arthritis predominantly of the lower limbs, and the possible occurrence of sacroiliitis, spondylitis, enthesitis, dactylitis, and uveitis. 1l1e serological tests for rheumatoid arthritis, i.e RF and ACPA/ACCP, are usually negative in these conditions. It can be difficult to differentiate these disorders, because they may occur simultaneously or sequentially. The monitoring, and to a lesser degree, the diagnosis and treatment of these diseases are related more to their clinical presentation than to the precise diagnosis.

The major advantage of the concept of SpA is that it allows a diagnosis before a patient has enough clinical and radiological features to allow a more specific diagnosis such as AS, PsA, ReA or JBDRA. It makes early diagnosis and treatment possible especially in the pre-radiographic phase of SpA i.e in the absence of sacroilitis on X-rays.

The introduction of MRI has improved dramatically the imaging of sacroilitis. On MRI, active inflammation of the sacroiliac joints with or without signs of structural damage can be anatomically accurately visualized. MRI can detect sacroilitis several years before X-ray changes are evident.



*Reproduced from Martin Rudwaleit et al (4).

Diagnosis of SpA and classification Criteria

"AMOR criteria" were published in 1990 by Amor which aimed to embrace all SpA subgroups.

SpA can also be divided into patients with predominantly axial and predominantly peripheral SpA. The ESSG (European Spondyloarthropathy Study Group) proposed "ESSG Criteria" in 1991. The concept of predominant symptoms (axial or peripheral) has been taken into consideration by the ESSG criteria.

In 2009, the Assessment of Spondyloarthritis International Society (ASAS) published new criteria for axial - "ASAS criteria" incorporated MRI and radiographic features. Separate new ASAS criteria for peripheral were also published in 2010.

The Clinical Features of SpA

1. Axial Arthritis / Axial Features

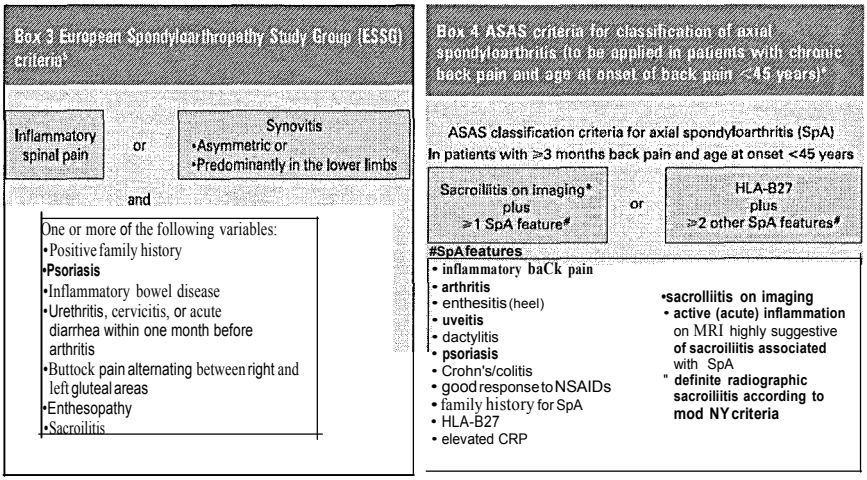
- Inflammatory Back Pain (IBP): Morning stiffness of at least 30 minutes, Improvement with exercise but not with rest, Awakening due to back pain during the second half of the night, Alternating buttock pain, Onset before the age of 40 years, At least 3 months' duration
- Ankylosis of the spine, vertebro-costal and sterno-costal joints-+ limited range of movement in cervico-thoraco-lumbar spine and limited chest wall expansion
- Abnormal postures: Loss of lumbar lordosis -+ thoracic kyphosis -+ forward stooping of the neck ultimately so-called "question mark posture"
  Spinal osteoporosis + ankylosed spine -+ increased risk of fracture
- Sacroilitis: Sacroiliac joint tenderness
- Arthritis of hip and shoulder joints

2. Peripheral Arthritis

- Oligo-articular, asymmetric, transient and migratory, predominantly in the lower limbs
- Bilateral symmetric poly-articular presentation is possible but distal inter-phalangeal joints are often involved, unlike rheumatoid arthritis

3. Extra-articular features

- Enthesitis: The most typical enthesitis is inflammation of the Achilles tendon or the plantar fascia insertion. Pain appears in the morning, as soon as the patient sets his or her foot on the floor and disappears after a few hours. Iliac crest, anterior tibial tuberosity or anterior chest wall may be involved.
- Dactylitis (Sausage digit): Tenosynovitis± synovitis of PIPs and DIPs resulting in edema of the digits.
- Acute anterior uveitis: Unilateral eye pain and redness, photophobia and increased lacrimation -more likely to occur in patients who are positive for HLA-B27
- Diarrhoea: Inflammatory lesions in the gut are common in ankylosing spondylitis. Inflammatory bowel disease may or may not have already been diagnosed in these patients.
- Psoriasis, Nail Dystrophy
- Keratoderma Blenorrhagicum; Circinate balanitis; Conjunctivitis; Uveitis



Investigations

1. Imaging: X-rays, MRI, Musculoskeletal ultrasound, Nuclear Scintigraphy
2. Bloods: HLA-B27, ESR, CRP

Management of SpA

Non-pharmacological

1. Exercise
2. Physiotherapy
3. Occupational therapy

Pharmacological

Analgesics

Intra-articular corticosteroid injections

Axial arthritis: 1st line - NSAIDs

2nd line- Biologic DMARDs (TNF antagonists, IL-6 antagonists, etc)

Peripheral Arthritis: 1st line - NSAIDs (Systemic corticosteroids may be used for short-term)

2nd line- Conventional DMARDs (Methotrexate, Salfasalazine, Leflunomide, etc)

3rd line- Biologic DMARDS

Ankylosing Apondylitis (AS)

Ankylosing Spondylitis is the prototype of the disease belonging to the concept of SpA. It is defined by the presence of axial symptoms resulting in both spinal mobility limitation and radiological evidence of sacroiliitis. Nevertheless, other manifestations can obviously be observed, in particular in enthesopathy (40 to 60%), acute anterior uveitis (30 to 50%) and asymmetric oligo-articular predominantly lower limb peripheral arthritis.

Box 1 Modified New York criteria for ankylosing spondylitis (1984)[1]

- Clinical criteria:
  - low back pain and stiffness for more than 3 months that improves with exercise, but is not relieved by rest.
    Limitation of motion of the lumbar spine in the sagittal and frontal planes.
    Limitation of chest expansion relative to normal values correlated for age and sex.
- Radiological criterion:
  - Sacroiliitis grade ≥2 bilaterally or grade 3-4 unilaterally.

Definite AS if the radiological criterion is associated with at least one clinical criterion

The modified New York criteria are widely used both in clinical practice and in clinical trials to classify ankylosing spondylitis patients. TI1ey are often used as an aid for diagnosis even though they were not designed as such and do not perform well in early disease. Although the criteria are sensitive, they are unable to select mild, undifferentiated or early forms of the disease.

Radiographic features of sacroilitis may sometimes take 3-7 years after disease onset and extra-spinal and extra-articular features are more common at an early stage of the disease. For these purposes, SpA classification criteria can be used (Amor, ASAS or ESSG criteria).

Psoriatic Arthritis (PsA)

Approximately I0% of patients with psoriasis have associated PsA. Psoriasis usually antedates the appearance of arthritis, but the onset is simultaneous in I5% of patients, and in up to 15% the arthritis may precede the onset or diagnosis of psoriasis. The arthritis usually starts between the ages of 30 and 50 years, but can also begin in childhood. In the majority of patients, exacerbations and remissions of skin and joint involvement occur with little or no apparent relationship to arthritis.

There is a poly-articular or oligo-articular pattern of joint involvement in 90% of patients. About 5% present with predominant spondylitis. A few patients present with a mutilating type of disease known as "arthritis mutilans". The typical pattern of joint involvement is an as}1nmetrical distribution with distal inter-phalangeal involvement and dactylitis. **PsA** is a chronic erosive disease and treatments resemble those of rheumatoid arthritis. Since the publication in 1996, the CASPAR (Classification Criteria for Psoriatic Arthritis) criteria are increasingly used in both clinical practice and in clinical trials to diagnose and classify patients with PsA.

CASPAR Criteria	
To meet CASPAR criteria, a patient must have inflammatory articular disease (joint, spine or entheseal) with 3 points from the following 5 categories.	
1. Psoriasis	
• Current psoriasis	2
• History of psoriasis	1
• Family history of psoriasis (1st and 2nd degree relatives)	1
2. Typical psoriatic nail dystrophy (pitting, onycholysis, subungual hyperkeratosis)	1
3. Negative rheumatoid factor	1
4. Dactylitis (now or previously diagnosed by a rheumatologist)	1
5. Juxtaarticular new bone formation on X-rays	1

IBD-related/Enteropathic Arthritis

IBD-related arthritis describes the occurrence of inflammatory arthritis in patients with ulcerative colitis or Crohn's disease. The frequency of arthritis in inflammatory bowel disease ranges from 17 to 20%, with a higher prevalence in patients with Crohn's disease.

The most common manifestation of IBD-related arthritis is inflammation of the peripheral (limb)joints. Axial involvement and enthesitis may also be encountered. The peripheral arthritis is usually transient, migratory and non-defom1ing. The inflammatory episodes are generally self-limiting, often subsiding within 6 weeks, but recurrences are common. In some cases, the arthritis may become chronic and destructive. Intestinal symptoms usually antedate or coincide with joint manifestations, but arthritis may precede the intestinal symptoms by years.

Reactive Arthritis {ReA)

ReA describes an episode of aseptic peripheral arthritis that occurs within 6 weeks (usually 2 weeks) of a primary infection elsewhere in the body, usually:

- genito-urinary infection with *Chlamydia trachomatis* or

  enteritis due to Gram-negative enterobacteria such as *Shigella, Salmonella, Yersinia* or *Campylobacter* species. In about 10-25% of cases, however, the triggering organism can be asymptomatic.

The patients are usually young adults, with a mean age of about 30-40 years.

There is no universal agreement of classification and diagnostic criteria for ReA.

Clinical Features

- typically, an acute, asymmetric oligo-arthritis
- frequently associated with one or more characteristic extra-articular features such as

  ocular inflammation (conjunctivitis or acute anterior uveitis)

  enthesitis

  dactylitis

  - muscocutaneous lesions (keratoderma blenorrhagicum and circinate balanitis)

  urethritis

  on rare occasions, carditis

About 30% of the patients have acute inflammatory low back pain.

The triad of arthritis, conjunctivitis and urethritis is called classical reactive artllritis or **Reiter's syndrome** although most patients with ReA do not present with this triad.

Diagnosis

The diagnosis of reactive arthritis relies on the typical clinical picture and on demonstration of the triggering infection, such as isolation of the microbe or demonstration of elevated antibodies. During the acute phase of enteric infections isolation is usually possible from the stools. However, by the time arthritic complications

appear, the patient may have already recovered from the gastroenteritis and the microbe is often no longer detectable. Therefore, the laboratory diagnosis is often dependent on the serological tests.

Treatment

1. High dose NSAIDs
2. Intra-articular corticosteroid injection
3. Moderate to high dose of systemic prednisone may be needed to control the symptoms in the short term
4. Antibiotics during acute phase of infection (often it is too late once arthritis has developed)
5. Salfasalazine in chronic form of ReA
6. Physiotherapy

Natural History and outcome

The average duration of arthritis is 4-5 months with 50% of the patients recovering from arthritis in the first 6 months. Recurrent attacks are more common in patients with *Chlamydia-induced* reactive arthritis. Approximately 15-30% of patients develop chronic or recurrent peripheral arthritis, sacroiliitis or spondylitis. The presence ofHLA-B27 is associated with a more severe arthritis, chronicity of arthritis and extra-articular features.

Undifferentiated SpA

Undifferentiated SpA are frequently under-diagnosed and include isolated clinical syndromes, such as HLA-B27-associated sero-negative oligo-arthritis or poly-arthritis, mostly of the lower limbs.

This arthritis has no recognizable preceding bacterial infectious trigger, nor associated inflammatory bowel disease or psoriasis.

Patients with undifferentiated SpA may have dactylitis, enthesitis, anterior uveitis (acute iritis) or a syndrome of aortic insufficiency plus heart block. The cardiac syndrome or the acute iritis may occur in patients who never develop signs of arthritis, and may sometimes accompany or precede the onset of SpA.

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Crystal Induced Arthritis

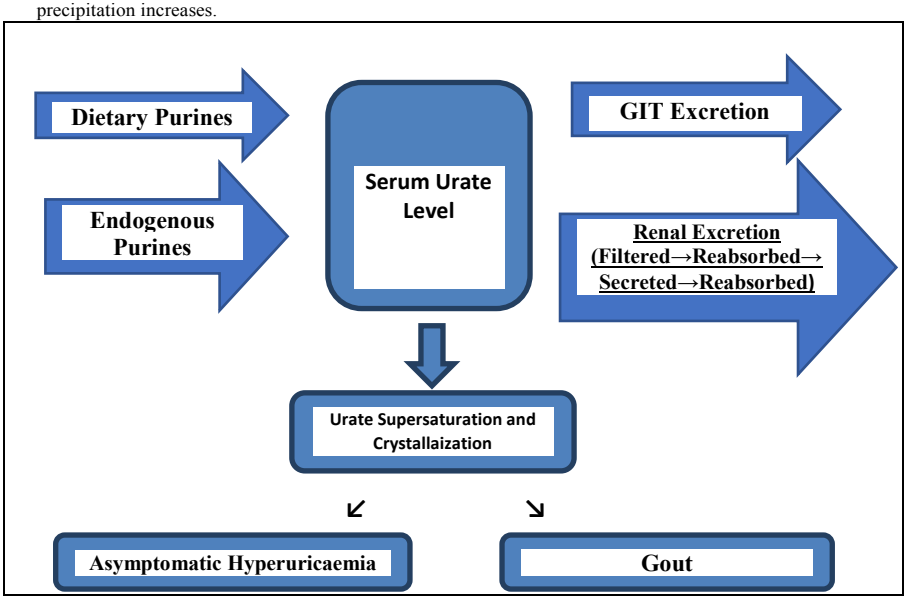
Dr.MTLNYO

There are 3 main types:

1. Gout
2. Calcium Pyrophosphate Dihydrate **(CPPD)** deposition disease
3. Basic Calcium Phosphate **(BCP)** deposition disease

Gout

Gout is a common form of arthritis caused by deposition of monosodium urate (MSU) crystals within joints associated with chronic hyperuricaemia. Uric acid is the final metabolite of endogenous and dietary purine metabolism. When urate concentrations exceed 0.38 mmol/L, risk of MSU.crystal formation and precipitation increases.



MSU crystals are pro-inflamatory stimuli that can initiate, amplify, and sustain an intense inflammatory response. They can be phagoc)'tosed by monocytes thus triggering a typical inflammatory response through release of pro-inflammatory mediators such as interleukin Ip, tumour necrosis factor *a,* and interleukin 8.

Uric acid production depends on the balance between purine ingestion, de-novo synthesis of purines in cells, recycling, and the degradation function of xanthine oxidase at the distal end of the purine pathway.

See Figure 5 (Overleal)

About 90% of the daily load of urate filtered by the kidneys is reabsorbed, and this process is mediated by specitic anion transporters, particularly **"URAT1**".

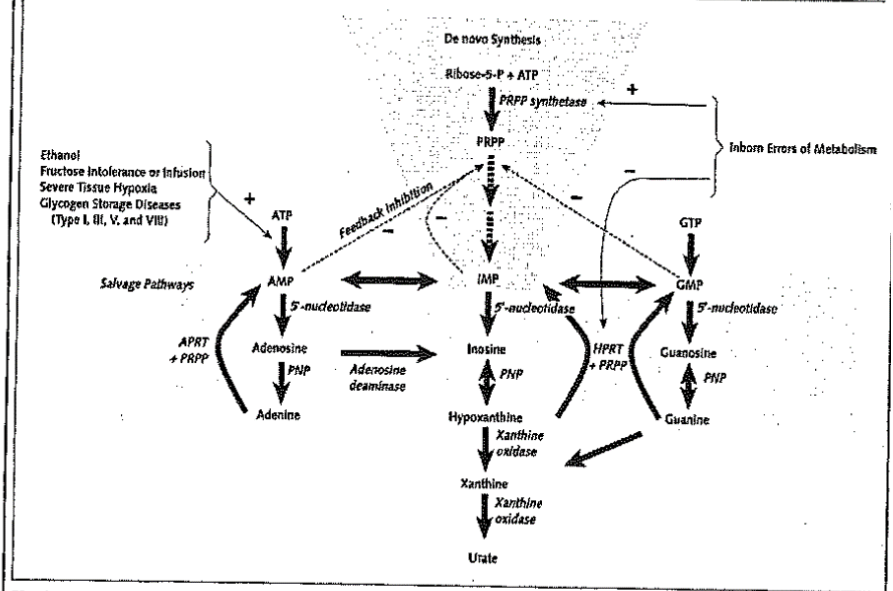
Risk Factors

The prevalence of gout is much higher in men than in women and rises with age. In women, it mainly develops after menopause possibly because of the fall in oestrogen; oestrogen is uricosuric.

The prevalence of gout in men and increases with high consumption of meat, seafood, fructose, beer and spirits. However, consumption of vegetables with a high purine content and moderate wine consumption have no effect. Consumption of dairy products, vitamin C, and coffee, including decaffeinated coffee, is associated with decreased uric acid level or prevalence of gout, or both.

90% of gout is due to under-excretion of uric acid whereas 10% is due to overproduction of uric acid. Hyperuricaemia is the most important risk factor for gout but most people with hyperuricaemia remain asymptomatic throughout their lives.

Figure 5. **Urate production pathways implicated in the pathogenesis of gout.**



The de novo synthesis starts with 5'-phosphoribosyl 1-pyrophosphate (*PRPP*), which is produced by addition of a further phosphate group from adenosine triphosphate (*ATP*) to the modified sugar ribose-5-phosphate. This step is performed by the family of PRPP synthetase (PRS) enzymes. In addition, purine bases derived from tissue nucleic acids are reutilized through the salvage pathway. The enzyme hypoxanthine–guanine phosphoribosyl transferase (*HPRT*) salvages hypoxanthine to inosine monophosphate (*IMP*) and guanine to guanosine monophosphate (*GMP*). Only a small proportion of patients with urate overproduction have the well-characterized inborn errors of metabolism, such as superactivity of PRS and deficiency of HPRT. Furthermore, conditions associated with net ATP degradation lead to the accumulation of adenosine diphosphate (*ADP*) and adenosine monophosphate (*AMP*), which can be rapidly degraded to uric acid. These conditions are displayed in left upper corner. Plus sign denotes stimulation, and minus sign denotes inhibition. APRT = adenine phosphoribosyl transferase; PNP = purine nucleotide phosphorylase.

*Reproduced from Hyon K. Choi et al (3).

Clinical Features

Acute gouty arthritis often begins with monoarthritis involving lower limbs most commonly affecting the first metatarsophalangeal joint (Podagra) although anyjoint can be affected. The initial attack is sometimes polyarticular (3-14%). Untreated gout mostly resolves within 7-10 days due to innate anti-inflammatory mechanisms.

Subsequent attacks frequently last longer than does the first attack, may affect several joints, and may spread to the upper limbs, especially the arms and hands.
Several factors that might trigger acute attacks include alcohol intake, meat and seafood consumption, fasting, trauma, surgery and certain drugs.

When left untreated acute attacks of gout can lead to chronic gout, which is characterized by chronic destructive polyarticular involvement with low-grade joint inflammation, joint deformity, and tophi.

Cause of Hyeruricaemia		
	Urate Undersecretion (90%)	**Urate Overproduction (10%)**
Primary Hyperuricaemia	URAT – 1 polymorphisms SLC2A9 (GLUT9) polymorphisms	HPR deficiency Increased PRPP synthetase Glycogen storage disease
Secondary Hyperuricaemia	Renal impairment Hypertension Drugas Low-dose aspirin Diuretics Cyclosporin Alcohol Lead nephropathy Hypothyroidism	Excessive dietary Purine intake Haematologicsl disorder Myoproliferative disorder Lymphoproliferative disorder Leukaemia Psoriasis Drugs Cytotoxics Alcohol Vit B12

Diagnosis

Analysis of synovial fluid or tophus aspirate is a key method for making a diagnosis of gout, by demonstrating MSU crystals under polarised microscopy. Under direct polarised light, they are strongly birefringent and appear very bright against the black background. Under compensated polarised light, they are yellow when aligned parallel to the slow vibration and blue when aligned perpendicular to the slow vibration of a compensator (negatively biregringent). They appear as needle-shaped crystals under ordinary light microscopy.

A third of patients have normal semm uric acid concentrations during an acute attack of gout.

Hyperuricaemia, gout and chronic diseases

The presence of kidney stones is the most frequent type of gout-related nephropathy. The presence of uric acid stones can precede onset of gouty arthritis.
TI1e prevalence of metabolic syndrome in patients with gout has been reported to be as high as 62%. Results from animal studies suggest that hyperuricaemia might play a part in development of metabolic syndrome.

Growing experimental and clinical evidence suggests that hyperuricaemia might lead to hypertension.

Hyperuricaemia and gouty arthritis are associated with a heightened risk of myocardial infarction, peripheral arterial disease, and a raised risk of death mainly because of an increased risk of cardiovascular diseases.

The data regarding the association between asymptomatic hyperuricaemia (i.e without gout) and cardiovascular diseases are currently inconclusive.

Treatment

Treatment of acute gout attacks

1. NSAIDs - high dose
2. Colchicine - 0.5mg 2-4 times a day
3. Corticosteriods- intraarticularly or systemically if the first 2 options are contraindicated or ineffective

Treatment of hyperuricaemia (Urate lowering therapy)

The current evidence does not support treating asymptomatic hyperuricaemia, although lifestyle advice should be offered.

Urate lowering therapy (ULT) is indicated to treat recurrent attacks, arthropathy, tophi, UA renal lithiasis and radiographic evidence of gout.ULT should not be started during an acute attack in order to avoid worsening of acute arthritis. However, if the patient is already on ULT, it should be continued during an acute attack. The target blood uric acid level is 0.36 mmol/1 or less and the dose of ULT needs be titrated frequently to reach this target as quickly as possible. The lower the uric acid level, the quicker is resolution of MSU crystals in the joints. A joint free of MSU crystals cannot have gouty arthritis.

1. Uricostatic drugs (XO inhibitors) -Allopurinol, Febuxostat
2. Uricosuric drugs (URATI inhibitors)- Probenecid, Sulphinp)Tazone, Benzbromarone, Losartan
3. Uricol)1ic drugs (Recombinant uricase)- Pegloticase

Prophylaxis

ULT can precipitate acute gouty attacks especially in the first 3-6 months which often lead to non-compliance of treatment. Prophylaxis should therefore be given for 3-6 months in patients with non-tophaceous gout but perhaps for a longer period in patients with tophaceous gout.

1. Colchicine 0.5mg 2 times a day for 3-6 months
2. Low dose NSAIDs for 6-12 weeks (not evidence-based)

Life style advice

1. Weight loss if obese
2. Avoid high alcohol intake (esp beer), fructose, meat (esp red meat) and seafood.

CPPD Deposition Disease

Prevalence of Calcium Pyrophosphate Dihydrate (CPPD) deposition disease is unknown and is dependent on the definition. It can be: - familial

- sporadic or
- secondary to **another** disease

Age is the most common risk factor for sporadic CPPD deposition disease (rare under age 60).

CPPD disease was originally described in 1960s as 6 groups of clinical sy11dromes

1. Acute monoarticular or oligoarticular inflammatory arthritis (Pauedogout)
2. OA like presentation (Pseudo-OA)
3. OA like presentation with discrete acute attacks
4. RA like presentation- chronic inflammatory polyarthritis (Psuedo-RA)
5. Neuropathic type arthritis despite nom1al sensation (Psuedo-Charcot)
6. Asymptomatic chondrocalcinosis on X-rays (Most common)

However, CPPD deposition disease can also present as pseudo-Ankylosing Spondylitis, crowned dens syndrome, tenosynovitis, peripheral nerve and spinal cord compression and pseudotumoral deposition.

Chondrocalcinosis is the radiological finding of deposition of CPPD on joint cartilage which may be present in several kinds of joints, but is especially seen in the knee, the wrist and the symphysis pubis. CPPD can also develop at tendon insertions and ligaments. Chondrocalcinosis is a frequent finding in elderly healthy individuals (36% in those aged 75-84 years and 44% in those aged 85 years or more). This deposition is often asymptomatic and thus should not be considered as a certain cause of joint symptoms.

Chondrocalcinosis, especially if present in young patients and associated with acute CPP crystal arthritis, warrants screening for associated conditions such as:

Hyperparathyroidism

Haemochromatosis

Hypophospahtasia

Hypomagnesemia

? Gout, Ochronosis or Wilson's disease

Diagnostic Tests

1. CPPD crystals (positively birefringent rhomboid-shaped crystals) in synovial fluid
2. Plain radiographs (finely stippled linear densities in hyaline or fibro-cartilage) i.e chondrocalcinosis
3. Ultrasound
4. CTscan
5. New MRI modalities
6. Electron Microscopy and X-ray diffraction

Treatment of CPPD Deposition Disease

1. Resting the joint
2. NSAIDS
3. Intra-articular steroid injections
4. Colchicine may be beneficial in Pseudogout
5. Systemic corticosteroids if other modalities cannot be used
6. Hydroxychloroquine for chronic arthritis

BCP Deposition Disease

Basic Calcium Phosphate (BCP) crystals are:

- Carbonate-substituted hydroxyapatite
- Tricalcium phosphate
- Otacalcium phosphate and others

Less popular than CPPD but may be more common in osteoarthritic synovial fluid

Not easily detectable and special stains are necessary

Associated with a variety of clinical syndromes including

- Milwaukee Shoulder syndrome
- OA (BCP Arthropathy)
- Calcific periarthritis, bursitis and tendinitis
- Limited systemic sclerosis
- Dermatomyositis
- Mixed crystal deposition disease
- Chronic renal failure
- Hypercalcaemia

Treatment of BCP Arthropathy

Symptomatic treatment

NSAIDs

Intra-articular steroid injections

Physiotherapy

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JUVENILE IDIOPATIC ARTHRITIS/ARTHRITIS IN CHILDREN

C Rainier-Pope, C Scott

May be: Acute or Chronic:

1 Acute arthritis:

Most forms of arthritis in children are acute and self-limiting (often reactive arthritis following a minor infection).
Other important causes that must be excluded and that may require urgent treatment include septic arthritis, TB arthritis, HIV arthropathy, malignancies (such as leukemia) and other causes.
In addition, other causes for limb or joint pain, such as hypermobility, mechanical causes, non-accidental injury, sickle cell disease, benign nocturnal pain of childhood (growing pains) and bone pain from malignancies need to be excluded.

The following flow diagram may aid in the approach to excluding these conditions:

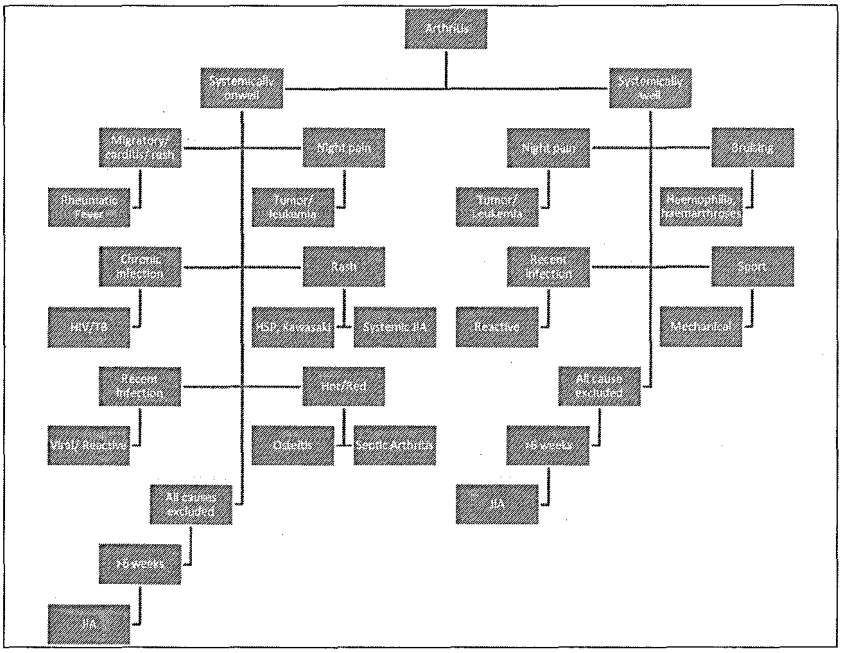


fig 1

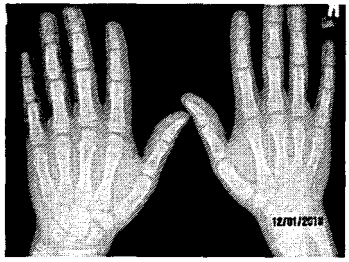
2 Chronic Arthritis:

The most common cuase of Chronic arthritis in Children is JIA.
Other causes for arthritis must be excluded before JIA can be diagnosed and in addition to the causes of acute arthritis given above, other connective tissue diseases such as SLE, Mixed Connective Tissue disease, Juvenile Dennatomyositis and Sarcoidosis must be considered.

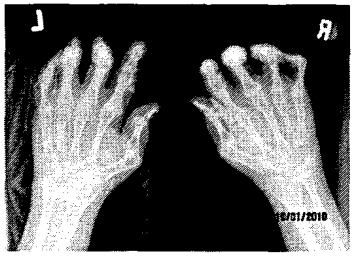
Juvenile Idiopathic Arthritis (JIA)

Definition: JIA is an umbrella term for a group of persistent arthritis in children under the age of 16 years, of unknown cause and lasting more than 6 weeks. (International League of Associations for Rheumatology, ILAR).

This definition is very important as if strictly applied, rules out a number of conditions in the differential diagnosis.



Early



Late Destruction

CLASSIFICATION

This is important for treatment options and prognosis.

1. Oligoarticular JIA
    a. Persistent
    b. Extended
2. Polyarticular JIA
    a. Rheumatoid factor negative
    b. Rheumatoid factor positive.
3. Systemic JIA (sJIA)
4. Enthesitis related Arthritis (ERA)
5. Psoriatic Arthritis
6. Unclassified: arthritis in childhood not fitting into the above criteria

N.B. There is no specific diagnostic blood test for JIA.

1.OLIGOARTHRITIS

50-60% of patients
Most frequently seen in girls I to 3 years of age.
Girls> boys 4:1
Incidence: 60/100,000
70% ANA positive
50% have only one joint (monarticular), usually the knee. Next most frequent is the ankle, then small joints of the hand. Can affect any joint.
If more than 4 joints are affected after 6 months of the disease the patient is classified as extended oligoarticular arthritis.

Symptoms:
Pain in the joints, morning stiffness and gelling. Parents may note a limp or swelling of the joint.
About \4 have no pain only stiffness and joint swelling. Frequently causes overgrowth of the affected limb.
Iridocyclitis occurs in 20%, usually asymptomatic and may cause permanent visual impairment.
Important to rule out TB monoarthritis.

Special investigations: (This applies for all JIA)
1. FBC, ESR, CRP, Rheumatoid factor (or anti-CCP). Acute phage reagents and platelets may be raised (frequently normal or only mildly elevated); mild anaemia., ANA, HIV status, Mantoux and liver enzymes for base line evaluation before therapy is started.
2. X-ray chest and affected joints,
3. Ultrasound, MRI of affected joints.

Treatment
I. Non-steroidal anti inflammatory dmgs (NSAID): Ibuprofen, Diclofenac, initially for relief of pain but does not stop the inflammatory process.
2. Intra articular injections of steroid. (JAI) Patient may need twilight sedation for this.
3. Oral steroid lmgfkg daily. Taper off the steroids to a minimum as rapidly as possible
4. If not satisfactory in 3 months repeat IAI and consider starting immediately with Disease modifYing dmgs (DMARD), Methotrexate (Mtx) 0.4 mg/kg as an oral or *SCI* 1M weekly pulse.
If this does not control the process, consider the biologicals e.g. anti-Tumor necrosis factor (aTNF). Very expensive.

Assess progress
Childhood quality of life questionnaire, Joint counts, visual analogue scale. Repeat blood tests and if on Mtx, include liver enzyme for liver toxicity. Uveitis (iridocyclitis) may occur in up to 20% so routine screening by ophthalmologist every every 3- 4 months is essential.

Additional therapy
Counselling, parent education, teacher education, including appropriate literature, physiotherapy, occupational therapy.

Outcome
Up to 60% of children with persistent oligoarthritis will remit within 20 years.

2a POLYARTHRITIS, RHEUMATOID FACTOR NEGATIVE

Five or more joints in the first 6 months of the disease.
Occurs in all races and usually afflicts girls 1-3 years old and 3 times more frequent in girls than boys.

Symptoms:
Insidious onset of widespread joint symptoms, frequently starting with the small joints of the hands including the distal interphalangeal joints (DIP). Iridocyclitis occurs in 5%. Without treatment, severe joint damage can occur.

Laboratory findings. Acute phase reactants are elevated, mild anaemia and elevated platelet counts. By definition rheumatoid factor is negative but ANA may be positive in 40%.

Treatment:
Start DMARD as soon as diagnosis is made and include NSAID. If no improvement within 3 to 6 months consider adding additional DlVIARD e.g. sulfasalazine and chloroquine. If these don't control, should use of anti-TNF biological drugs. Anti-TNF can prevent erosion and joint destruction. Some children may require multiple joint injections. Physiotherapy, occupational therapy and co-operation with parents and teachers.

Outcome:
There can be significant physical and emotional problems with disablement and requiring joint surgery after many years and when epiphyses are closed. Less than 40% may ultimately go into remission.

2b. POLYARTHRITIS,RHEUMATOID FACTOR POSITIVE

Insidious onset of5 or more joints in the first 6 months and often very widespread joint involvement (>30 joints). More frequent in older and adolescent girls and have a positive rheumatoid factor on 2 occasions at least 3 months apart. Usually symmetrical, involving small joints of the hands but sparing the metacarpophalangeals (MCP) Iridocyclitis is not a feature.

Laboratorv
Elevated a ute phase reactants and anaemia. Rheumatoid factor needs to be positive on 2 occasions and a positive anti-cyclic citrullinated peptide (anti-CCP) may be more specific

Treatment
Prolonged disability and joint destruction can occur and aggressive treatment should be started at the time of diagnosis as this is the window of opportunity. The treatment is similar to polyarthritis. If joint destruction has started, treatment is less effective. Immediate NSAID and DMARD must be commenced and if no improvement within 3 months may need anti-TNF blockers. May require additional bioligics if not responsive to Anti-TNF inhibitors.

Outcome
Generally bad and require treatment for many years often requiring surgical joint replacement in late adolescence and adulthood. Disability can be profound and avoid wheel chairs as it can be difficult to get the patient mobile again.

3. SYSTEMIC J1A (sJIA)

This form of JIA is the least common and commences with a spiking quotidian fever and skin rash, often preceding the joint symptoms by some weeks. There is no age or sex preference.

Criteria: In addition to the fever, at least one of the following:

I. Evanescent rash
2. Lymphadenopathy
3. Serositis.
4. Hepatosplenomegally
5. Negative Rheumatoid factor.

Clinical features
These children are ill, irritable with the very typical quotidian fever. Headaches, myalgias, arthritis, abdominal pain and breathlessness on lying down due to pericarditis. Early in the illness the picture can be very confusing.

Laboratorv.
No specific- rest for sJIA. Acute phase reactants are all very elevated, neutrophilia and thrombocytosis and anaemia. Ferritin is usually highly elevated. There are no autoantibodies.
Aneamia, thrombocytopaenia, leucopenia, clotting abnormalities, hepatitis, falling ESR and rising ferritin indicate the presence of Macrophage Activation syndrome, a potentially fatal complication.

Treatment
Usually requires high dosage steroids (1-2 mg /kg per day). NSAIDS useful to contra fever and arthritis symptoms. Response to other DMARD and TNF-inhibitors is often poor but response toIL 6 blockers (Tocilizumab) and IL I blockers (Anakinra) is frequently dranmtic.

Outcome
Varies with the severity and the treatment. The joint symptoms can persist for a long time and there can be significant joint destruction. Relapses are frequent.

4. ENTHESITIS RELATED ARTHRITIS(ERA)

Arthritis and or enthesitis *with at least 2 of the following: -

1. Onset of arthritis in older boys usually >6 years and early adolescence.
2. Sacro-iliiatis or lumbosacral pain.
3. HLA-827 positive.
4. First degree relative with ERA or ankylosing spondylitis.
5. Anterior iridocyclitis.

- inflammation of the tendons and ligaments where they are attached to the bone (the enthesis) Frequent sites are SIjoint, inferior pole of the patella, the Achilles tendon and plantar fascia insertion into the calcaneus. Heel pain is a frequent early symptom. Early morning stiffness improves with activity

ERA overlaps with Ankylosing Spondylitis {AS). Symptoms in the early stages may be vague and ill-defined. Usually characterized by early morning symptoms and

Laboratory
No definite test but HLA-827 helps to confirm the diagnosis. High ESR and anaemia can occur. X-rays and MRl of the lumbo-sacral spine and sacro-iliac joints can be helpful in long standing older patients.

Treatment
Similar to Polyarticular JIA. Sulphasalazine is sometimes helpful. Patients may respond well to anti-TNF therapy.

5. PSORIATIC ARTHRITIS

This is the least common form of JIA. A picture similar to oligoarthritis and often diagnosed as such until they develop or are found to have psoriasis as well.
In addition, they must have at least 2 of the following:
!. Dactylitis
2. Nail abnormalities
2. Family history of psoriasis

Girls >boys and mostly in the 7 to I 0-year age group. A number develop iridocyclitis and children with HLA-827 develop AS.
In adults, psoriatic arthritis can be very destructive causing arthritis mutilans but this is rare in children.

Laboratory
No specific test. RF negative and about half are ANA positive.

Treatment
Mild disease: similar to oligoarthritis.
Aggressive disease: treat like polyarthritis using methotrexate (sulphasalazine) and anti-TNF therapy in non responsive cases.

Outcome
Tend to have long lasting disease, often with severe joint destruction.

Further reading

Extensive use was made of: - Pediatric Rheumatology in Clinical Practice, Patricia Woo. Ronald M. Laxter, David D. Sherry. Springer-Verlag, London, 2009

SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

Dr. MTL NYO

SLE is the prototypic autoimmune disease characterized by the production of autoantibodies to components of the cell nucleus in association with diverse clinical manifestations encompassing almost all organ systems.

Pathogenesis

As in other autoimmune diseases the triad of genetic predisposition, environmental factors and immune dysregulation seems to underlie the pathogenesis of SLE. Additionally, hormonal factors are also implicated and they may explain why SLE is far more common in younger females of reproductive age.

Several genes are associated with SLE including some MHC class 11 genes and non-HLA genes such as IRF5, ITGAM, STAT4, BLK, BANK1, PDCD 1, PTPN22, TNFSF4, TNFA1P3, SPP 1.

The most important environmental factor that is known to exacerbate SLE is sunlight exposure.

Other implicated environmental factors are exposure to mercury, crystalline silica or EBY.

SLE is a classic immune complex mediated disease. B cell over-activity is a hallmark of SLE and B cells produce a plethora of autoantibodies mostly directed against intracellular antigens while T cells provide excessive help to B cells. The role of ineffective clearance of apoptotic cells are now increasingly recognized. Nuclear components from this defective apoptosis are sensed by plasmacytoid dentritic cells either via toll-like receptors (TLR) or independent of TLRs which then leads to production of several antinuclear antibodies by B-cells (Plasma cells).

Clinical Features

SLE has a protean manifestation and virtually any organ system can be involved in this systemic inflammato1y disease.

Joints : Arthralgia, arthritis, Jaccoud arthropathy
Muscles : Myalgia, myositis (5%)
Skin -Acute : Malar rash, intera1iicular rash
- Subacute : Annular rash, psoriasiform rash
-Chronic : Discoid rash, Chilblain, Lupus tumidus, Lupus profundus (panniculitis)
-Vascular : Raynaud, livedo reticularis, splinter haemorrhages
-Photosensitivity

Kidney :Lupus nephritis class 1-VI
Lungs : Lung infections, ILD, pulmonaiy hypertension, pleural effusion, rarely pulmonary haemotThage
Heart : Pericardia! effusion, ?myocarditis, Libman-Sacks endocarditis, CAD
CNS : Aseptic meningitis, CVA, demyelinating syndrome, headache, chorea, myelopathy, seizure disorders, acute confusional state, anxiety disorder, cognitive dysfunction, mood disorder, psychosis
PNS : Autonomic disorder, mononeuropathy (single/multiplex), myasthenia gravis, cranial neuropathy, plexopathy, polyneuropathy, Guillain-Barre syndrome
GIT : Ascites, dysphagia and pancreatitis, GIT vascilitis

Blood : Anaemia, haemolysis, leukopenia, thrombocytopenia, lymphopenia, neutropenia

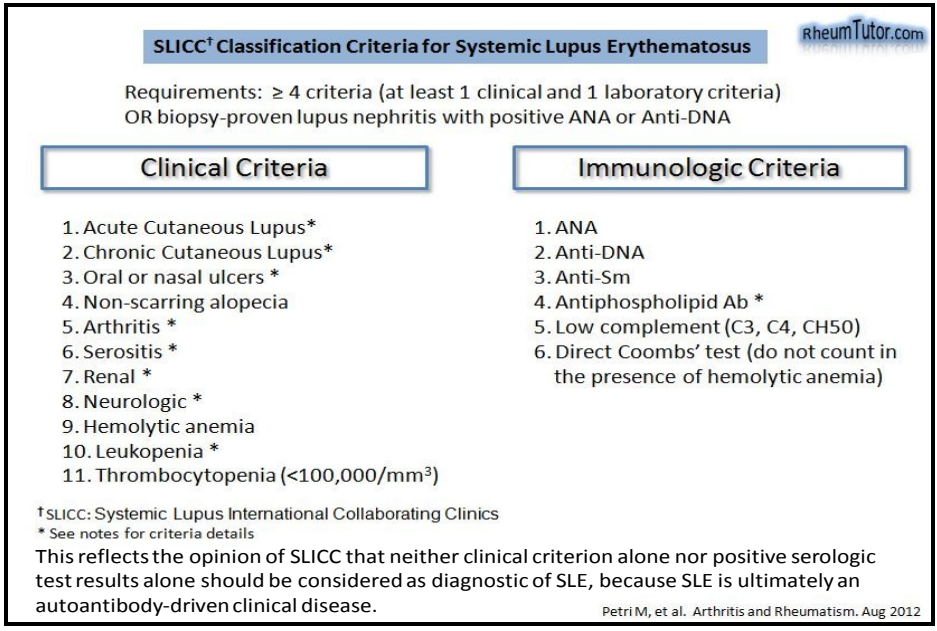
Others : Fever, lymphadenopathy, oral and occasionally genital ulceration, alopecia

Diagnosis of SLE

The diagnosis of SLE depends on thorough clinical assessment and careful investigation. There are no diagnostic criteria. Until recently 1997 modified ACR classification criteria for SLE were extensively used by clinicians and researchers despite the fact that these criteria were meant for identifying a homogeneous group of patients for experimental and clinical trials. In the absence of diagnostic criteria and a specific confirmatory test or feature, it has been the common practice that the classification criteria are misused as diagnostic criteria for many autoimmune rheumatologic conditions although this can lead to missed diagnosis and under-treatment especially in early stages of the disease.

1997 ACR classification requires 4 out of 11 criteria commonly known by a mnemonic "MD **SOAP BRAIN"** (***M***alar rash, ***D***iscoid rash, ***S***erositis, ***O***ral ulcers, ***A***rthritis, ***B***lood disorder, ***R***enal disorder, **A**NA, ***I***mmunological disorder, ***N***eurologic disorder).

The new SLICC classification criteria for SLE that was published in 2012 overcome a number of limitations seen in 1997 ACR classification criteria. The SLICC classification criteria require the presence of 4 out of 16 criteria with at least one clinical and immunological criteria being present (See overleaf). The SLICC criteria are more sensitive compared to 1997 ACR criteria.



However it is important to emphasize that an experienced clinician may make the diagnosis of SLE and institute treatment accordingly even if the classification criteria are not fulfilled.

Diagnostic Tests

ANA (anti nuclear antibodies) : Immunofluorescence is the standard approach for detecting ANAs, and the staining patterns (i.e., homogeneous or diffuse, speckled, rim, nucleolar, or centromere) correspond to the presence of autoantibodies against different nuclear antigens. The ANA assay is an ideal screening test because of its high sensitivity of 95%. The specificity of ANAs for SLE however is low because multiple other conditions are associated with a positive ANA (i.e., scleroderma, polymyositis, dermatomyositis, rheumatoid arthritis, autoimmune thyroiditis, autoimmune hepatitis, infections, neoplasms, and many drugs). Also, some healthy individuals test positive for ANAs.

Anti ENA (antibodies to extractable nuclear antigens) : Antibodies to double stranded DNA (**Anti-dsDNA**) are found in 70% of SLE patients at some point during the course of their disease and are 95% specific for SLE. **Anti-Sm** (Smith) antibodies are detected in 10% to 30% of SLE patients, and their presence is pathognomonic for SLE. **Anti-Ro** (SS-A) and **anti-La** (SS-B) antibodies are detected in 10% to 50% and 10% to 20% of SLE patients, but are not disease specific. Their presence has been associated with the development of secondary Sjögren's syndrome, photosensitivity, CNS disease, neonatal lupus, and development of congenital heart block in the children of mothers who carry these antibodies. **Antiribosomal antibodies** are highly specific for the diagnosis of SLE and **anti–ribosomal P antibodies** have been linked retrospectively with neuropsychiatric manifestations of SLE, especially lupus psychosis.

Prognosis

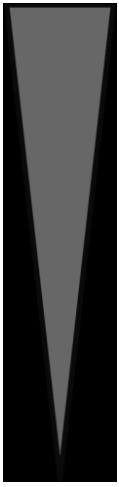
The natural history of SLE is characterized by episodes of relapses or flares, interchanging with remissions, and the outcome is highly variable ranging from prolonged remission to death. Morbidity and mortality have improved over the years due to a number of reasons, including the more conservative use of corticosteroids and of modified immunosuppressive regimens. Factors contributing to mortality include major organ involvement, especially nephropathy, thrombosis, accelerated atherosclerosis and an increased risk of cancer. The antiphospholipid syndrome commonly co-exists with SLE and contributes to morbidity and mortality.

A number of composite indexes have been developed to measure the disease activity in SLE. The most commonly used indexes are BILAG (Britis Isles Lupus Assessment Group), SLEDAI (SLE Disease Activity Index) and several SLEDAI derivatives such as SELENA-SLEDAI, SLEDAI-2k, Hybrid SLEDAI, etc. As for the measurement of SLE-related damage, SLICC/ACR damage is most commonly used.

Treatment of SLE

Treatment of SLE, like in all connective tissue diseases, is organ-based and depends on the type and severity of the organ involved.

As such the treatment may range from a mere symptomatic treatment with NSAIDs for pleuritis or arthritis to an intense immunosuppressive therapy with high dose steroid and cyclophosphamide for lupus nephritis or transverse myelitis. Various pharmacological agents used in the treatment of SLE are shown in the figure below (See overleaf).



Various topical agents (& Dapsone, Thalidomide)

Antimalarials (HCQ, CQ, Quinacrine)

NSAIDs

Steroids (Prednisone, Methyl-prednisone)

Immunosuppressants

- CYC, MMF, AZA, MTX & CSA

IVIG and Plasma Exchange

Biologicals

- Belimumab, Rituximab, Epratuzumab, Sifalimumab, Rontalizumab

Haematopoietic Stem Cell Transplantation (HSCT)

Antimalarials such as chloroquine (CQ) and hydroxychloroquine (HCQ), in addition to their efficacy in skin and joint manifestations of SLE, have also been shown to prevent SLE flares, improve lipid profile, reduce anticardiolipin antibody production and reverse platelet activation induced by anti-phospholipid antibodies. As such many authors nowadays recommend antimalarial therapy with HCQ or CQ in all patients with SLE even in the absence of overt active clinical manifestations.

SLE is associated with increased cardiovascular morbidity and mortality and therefore it is important to identify and treat conventional risk factors for accelerated atherosclerosis while controlling SLE disease activity adequately. Prevention, early diagnosis and treatment of osteoporosis in patients with SLE is also important.

References

1. EULAR Compendium on Rheumatic Diseases
2. Kelly's textbook of rheumatology, 8th edition

IDIOPATHIC INFLAMMATORY MYOPATHY

Dr. A Gcelu

Idiopathic inflammatory myopathies (liM) encompass a group of heterogeneous muscle disorders which share the common clinical features of slowly progressive, symmetric muscle weakness, decreased endurance and fatigue. One of the characteristic features of these disorders is the presence of mononuclear inflammatory cell infiltrates in muscle tissue in all forms of inflanmmtory arthritis.

Idiopathic intlammatory myopathies can be classified into three major groups:

- Pol)myositis (PM)
- Dennatomyositis (DM)
  Inclusion body myositis (IBM)

Cutaneous manifestations of classical DM occurring for 6 months or longer in the absence of clinical and laboratory evidence of myositis with histopathological features of classical DM is well described and is called amyopathic DM.

EPIDEMIOLOGY

The IIM are rare disorders. Both DM and PM are more frequent in women than in men (women: men, 3:1) whereas IBM is more frequent in men than in women. DM affects both children and adults. PM is commonly seen after the second decade of life and IBM is more common in those over the age of 50. The course in IBM is a slowly progressive one for up to I0 years before diagnosis.

ETIOLOGY

liM are considered to he autoimmune diseases. The mechanisms that cause autoimmune reactions are not known but both genetic and environmental factors are likely to confer risk factors to develop chronic inflammatory myopathies. The strongest genetic association is to human leucocyte antigen (HLA) class 2 alleles. The most frequently associated environmental factors are viral infections such as coxsackie which causes acute and self-limiting forms of myositis but their role in chronic myositis is uncertain. PM is seen in patients with retroviral infections e.g. HIV, with the same clinical and histopathological features resembling polymyositis.

There is a close relationship between DM particularly the subset with anti-Mi-2 and UV-light exposure.

There is an increased frequency of cancer in DM. The increased risk is both at the time ofDM diagnosis and up to I0 years after diagnosis, with haematological and solid malignancies.

CLINICAL FEATURES

Constitutional

- Fatigue
- Fever- common with Juvenile Dematomyositis (DM)
- Weight loss - malignancy associated myositis
  poor caloric intake associated with pharyngeal muscle dysfunction

Skeletal muscle

The predominant symptoms in patients with all subsets of myositis are muscle weakness involving striated muscle.

Limb muscle weakness

Insidious bilateral, symmetrical usually painless and proximal muscle weakness in patients with DM and PM; and prominent distal weakness and atrophy of muscles in patients with IBM.

Presentation

Difficulty walking up the stairs or arising from a chair. If untreated the muscle weakness may progress slowly and in severe cases patients may become wheelchair dependent.
Difficulty raising arms e.g. when combing hair or hanging washing.
Frequent falls which are more frequent in IBM due to weakness in knee extensor muscles.

Neck Fle:rors

Unable to raise neck from a pillow

Pharyngeal muscle weakness
Proximal dysphagia with nasal regurgitation of liquids that may result in aspiration pneumonia.
Hoarseness / dysphonia resulting in nasal voice.

NB: Ocular and facial muscle weakness is a very uncommon presentation of liM
Muscle pain is more common in DM
Muscle atrophy is common with IBM

Skin
The cutaneous manifestations ofDM may be mild or severe and may dominate the clinical symptoms. The skin rash may precede the muscle symptoms by months or even years. In some patients, the skin manifestations may be the only clinical sign of DM termed AMYOPATIIIC DM or DM SINE MYOSITIS. Several skin manifestations may occur with OM:

- Gottron's papules
  -considered pathognomic ofDM
  - violacceous, pink or dusky red papules over the dorsal side of metarcarpal or interphalangeal joints. These papules may occur over the extensor surfaces of the wrist, elbow or knee joints.
  - Gottron's sign are macular e1')1hemas with same distribution.
- Heliotrope rash
  - a periorbital violaceous erythema of one or both eyelids with edema

Red or violaceous erythemas may be located over different areas:

V-sign- over anterior chest and neck in the shape ofV.
Shawl sign- over the nape of the neck, upper back and across both shoulders.
Holster sign- on the lateral surface of the thigh and hip.

Other characteristic skin lesions:
Mechanic's hand -consists of hyperkeratosis, scaling, fissuring of the fingers esp on the radial side of the index finger {associated with anti-Jo 1).
Cutaneous calcinosis -mainly in JDM and occasionally seen in adults.
- may be located to the skin, subcutaneous fat, fascia and muscle.

Nailfold abnommlities with periungual erythema, cuticular overgrowth and nail fold telangiectasia.

Ervthrodenna - generalised, widespread contluent erythema involving both sun exposed and non-sun exposed areas.

Joints
Polyarthralgia or polyarthritis affecting small joints of hands and feet that is usually non-erosive is common in myositis patients. A chronic erosive and defonning arthropathy in association with anti Jo-1 autontibodies or overlap syndromes may occur.

Lung
Dyspnoea and cough are the most common pulmonary symptoms. The lung is the most common extramuscular target in DM and PM with a prevalence between 5 and 65%. The most common pulmonary complications are interstitial lung disease and restrictive lung disease due to weakness of respiratory muscles. There are many causes of dyspnoea in patients with JIM:

Non pulmonary etiology
- Respiratory muscle weakness
- Cardiac involvement

Pulmonary etiology
- Interstitial lung disease in up to 70% at the time of diagnosis
- Infection secondary to:
  Aspiration pneumonia
  lmmunosuppresants

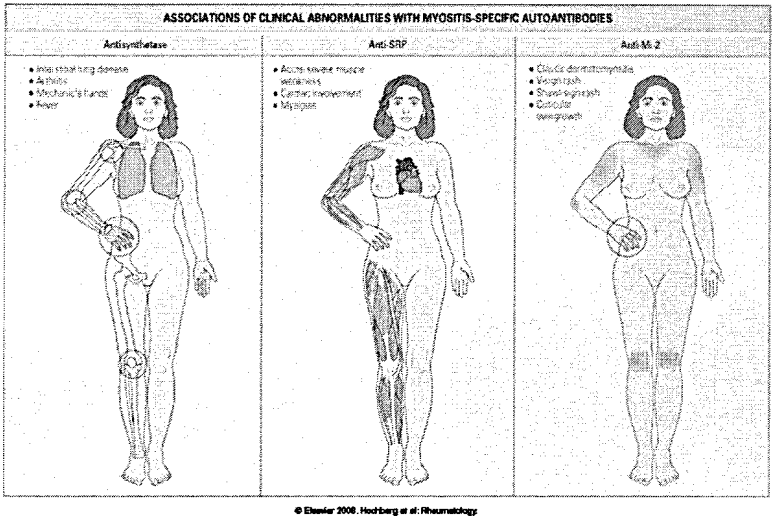
- Drug induced e.g.
  Methotrexate Pulmonary
  hypertension

Heart
Heart involvement is common but seldom symptomatic.
The most common manifestation is a **rhythm disturbance** from inflammation of the conducting system. **Congestive cardiac failure** due to: myocarditis and myocardial infarction (accelerated atherosclerosis secondary to prolonged corticosteroid use or coronary arteritis) are very unusual.

Gastrointestinal Svstem
Pharyngeal muscle weakness is more common in IBM.
Involvement of the smooth muscle of any portion of the intestinal tract is possible and may result in GORD and malabsorption syndrome.

AUTOANTIBODIES

Autoantibodies are present in 55-80% of myositis patients. It has not been elicited whether they have a role in disease mechanisms or are an epiphenomenon. There are myositis associated (MAA) and myositis specific autoantibodies (MSA). The MSAs are found almost exclusively in patients with myositis and are associated with distinct clinical features and distinct genotypes. Certain antibodies are associated with distinct extramuscular clinical subgroups.
There are three main groups of MSAs- antisynthetase, antisignal recognition particle (SRP) and antiMi-2.



DIAGNOSIS

- When evaluating a patient complaining of "weakness" it is important to differentiate between weakness and fatigue of muscle.
- Weakness implies primary disease of muscle or the neuromuscular unit, and fatigue include cardiovascular, metabolic, endocrine and psychiatric disorders, for example, hypotension hypoglycaemia, anemia and infection.

  It is imperative that with suspicion of muscle weakness a **detailed history** is taken to exclude potential causes of proximal muscle weakness listed in **table 1.**

Table 1: Potential causes of proximal muscle weakness

A) Genetic muscle disorders
Muscle dystrophies: limb girdle, Beckers Emery-Dreifuss, facioscapulohumeral (FSH), dyspherlinopathy, distal muscle dystrophy and ocular muscle dystrophy.
Congenital myopathies: mitochondria myopathy, Nemaline myopathy and central core myopathy
B) Neuropathies
Denervation: Spinal muscle atrophy, amyotrophic lateral sclerosis (ALS)
Others: Eaton -Lambert syndrome, myasthenia gravis, Guillain- Barre, chronic demyelinating neuropathy
C) Metabolic myopathies
a) Glycogen storage disease: Me Ardle, acid maltase deliciency
b) lipid storage disease
D) Endocrine disorders
E) Infections
F) Toxic agents and drugs
G) Others: Granulomatous disease

- **Detailed clinical examination** is important especially to distinguish neurologic vs myopathic process. Presence of neurological abnormalities e.g. sensory symptoms will favour a neurological pathology and so will absent tendon reflexes. It is vital to look out for evidence of other causes of muscle weakness e.g. signs of thyroid disease or myasthenia gravis.
- **Diagnostic tests:** A diagnosis of myositis is supported by elevation of serum levels of skeletal- muscle enzymes including creatinine kinase, AST and lactate dehydrogenase. Electromyography (EMG) will assist in distinguishing between a myopathic and a neurologic process and therefore a vital diagnostic test.

Muscle biopsy is the only specific diagnostic test and is always indicated for a definitive diagnosis of polymyositis. A definite diagnosis of dermatomyosits however can be made without muscle biopsy if there are typical skin rashes, muscle weakness, raised muscle enzymes and compatible EMG changes.

The search for an occult malignancy should be done in all those at risk and should include the cancer screening tests that would be routine for that patient based on gender, age and special risk factors.

Laboratory tests to exclude other causes of myopathy and conditions associated with myositis should be done including TSH, electrolytes, HIV and connective tissue disease screen.

MANAGEMENT

Corticosteroids are the mainstay of therapy for DM and PM.

Immunosuppressive agents are used mostly when the disease is resistant to steroid therapy and in those with poor prognostic sign. The most often used agents are methotrexate, azathioprine and rarely cyclosporine.

Intravenous immune globulin (IVIG) has also shown to be effective for resistant cases. Newer biologic therapy especially B cell therapy has shown to be effective.

SYSTEMIC SCLEROSIS

Dr.AGcelu

Systemic sclerosis (SSe) is an uncommon connective tissue disease that is characterised by fibrosis of the skin and internal organs, pronounced alterations in the microvasculature and frequent cellular and humoral abnormalities.

SSe is part of a more extensive group of diseases called scleroderma.

Scleroderma is classified into two major categories defined by the extension of skin sclerosis:

I. **Localised scleroderma** -fibrotic involvement confined to the skin and subcutaneous tissues with no involvement of internal organs
   - Morphea
   - Linear
   - En coup de sabre

2. **Systemic sclerosis** - can be divided into two subsets:
   - Limited systemic sclerosis (JeSSc)- skin involvement distal to elbows and knees and face.
   - Diffuse systemic sclerosis (dcSSc)- skin involvement proximal to the knees and elbows.

The important features which differentiate between limited and diffuse **SSc** are the **extent of skin thickening** and **the pace of their disease.**

Raynaud's is almost always the first symptom in lcSSc and it is present for many years up to 10 years before any other manifestation occur. In dcSSc there is a much more acute onset of symptoms including Raynaud's with rapid progression to a full blown disease.

The pattern of organ involvement is different in these subsets. In the pulmonary system, JeSSc tends to favour vascular involvement and deSSe involves the parenchyma. Sclerodenna autoantibodies are associated with very specific patterns of disease within these two major subsets. Classically, the anti-centromereantibody is seen almost exclusively in JeSSe and anti-topoisomerase antibody is only found in those with dcSSc.

LIMITED SYSTEMIC SCLEROSIS	DIFFUSE SYSTEMIC SCLEROSIS
Limited skin involvement	Diffuse skin involvement
Isolated pulmonary HPT	Severe interstitial lung disease
No kidney involvement	Kidney involvement (SRC)
Anti-centromere antibody	Anti-topoisomerase antibody
Long duration of Raynaud's	Short duration ofRaynaud's

SSc sine scleroderma refers to the small number of patients who demonstrate vascular and serological features of SSe without any skin involvement. CREST (Calcinosis, Raynauds, Esophageal dysmotility, Sclerodactyly and Telangiectasia) is an outdated term for JeSSc and should not be used as a synonym for JeSSc because CREST describes only a narrow part of the spectrum of limited systemic sclerosis, does not recognise important complications of this subset including pulmonary arterial hypertension and mid gut disease, and many patients with JeSSc do not develop all features of CREST. SSe can also overlap with other autoimmune diseases such as dermatomyositis, systemic lupus erythematosus and rheumatoid arthritis and this is termed **Overlap syndromes.**

EPIDEMIOLOGY

The incidence and prevalence of SSc varies in different populations suggesting a role for genetic predisposition and/or exposure to environmental trigger factors. Systemic sclerosis has a female predominance with an age of onset usually in the 30-50 range.

ETIOLOGY

Unknown but genetic predisposition and environmental factors have been proposed as possible causative factors. The role of genetic factors is supported by the observation of familiar clustering of the disease, the high frequency of occurrence of other autoimmune disease, differences in SSc prevalence and clinical manifestations among different ethnic groups and the increased prevalence of certain HLA and MHC in various ethnic populations in SSc. Proposed environmental factors include exposure to silica, metal dust, vinyl chloride, organic solvents, hair dyes and certain pesticides. Infections like CMV has been implicated as playing a role in the pathogenesis of SSc.

PATHOGENESIS

Whatever the cause is, events lead to endothelial cell apoptosis and dysfunction and immune activation. There is release of pro-fibrotic cytokines resulting in cytokine activation of fibroblasts to increase extracellular matrix production resulting in deposition of excess fibrosis on the extracellular matrix.

CLINICAL FEATURES

SSe has various clinical characteristics because it involves the skin, visceral organs and vascular structures. At onset, some patients present with few changes and without significant laboratory abnormalities, making the diagnosis difncult to establish.

Vascular abnormalities

Raynaud's phenomenon (RP) is the earliest symptom and is present in greater than 95% of patients with SSc. Complicated RP can result in:

- Fingertip pits and digital ulcers due to chronic ischemia and these occur in up to 50% of patients with SSc. Digital ulcers may occur at sites of trauma and over bony prominences. Digital ulcers may heal slowly and become portal for infections.
- Gangrene due to total lack of blood supply.
- Osteomyelitis and secondary infection.
- Digital amputation in refractory cases.

SSc patients have characteristic microvascular changes that may be observed with a widefield microscope. The widefield microscope magnifies the nailfold capillaries 12-15 times and visualisation of the capillaries is improved using immersion oil on the skin over the nail told. Patients with SSc typically demonstrate nailtold abnormalities of capillary dilatation, avascularity or 'drop-out'
Nailfold capillaroscopy is useful in assisting with the diagnosis and prognosis of patients with new onsctRP.

Cutaneous abnormalities
Three stages of skin changes may occur:

1) The initial stage is an **inflammatory**, edematous stage that may last for months. The hands and fingers appear puffy with loss of skin crease on the fingers and there is decreased sweat and oil production resulting in dry cracky skin.
2) The longer phase of **progressive skin fibrosis.** Skin thickening usually begins with acral involvement, distal to MCP joints, and may progress proximally. Involvement of the skin of the face

does not distinguish between patients with lcSSc and dcSSc. Facial scleroderma results in microstomia and there is usually furrowing around the mouth.
Changes in pigmentation occur during the first two phases with areas of hypo- or hyperpigmentation causing the skin to have a 'salt and pepper' rash due to perifollicular sparing of pigment loss.

3) Tite final stage of **skin softening** occurs most commonly on the trunk and upper arms.

Visceral involvement

GASTROINTESTINAL FEATURES

GI involvement is almost universal and often manifest as the first non-RP symptom.
Motility abnormalities on functional testing are present even in the absence of symptoms.
The entire GIT may be involved from the mouth to the anus.
The etiology of GI involvement relates to a combination of factors including smooth muscle atrophy which is affected by both microvascular insufficiency and neurogenic factors. Smooth muscle atrophy and fibrosis within the Gl mucosa play a role in Gl dysmotility and vascular intimal proliferation occuring elsewhere, also occurs in the Gl tract.

Oropharynx

- Microstomia
- Xerostomia due to submucosal fibrosis of salivary glands or secondary Sjogren's.

Eosophagus

Eosophageal involvement is present in nearly every patient with SSe.

- Dysphagia as a result of involvement of the distal two-thirds of the eosophagus, the portion composed of smooth muscle. This may result in severe weight loss.
- Gastroesophageal reflux and eosophagitis due to the reduced lower eosophageal sphincter (LES) pressure.
- Barrett's eosophagus due to chronic injury of oesophageal mucosa from reflux disease.
- Gastrointestinal bleeding from erosive eosophagitis or mucosal telangiectasia.

Stomach

- Delayed gastric emptying which can exarcebate symptoms of ofGORD.
- Gl blood loss from gastric antral venous ectasia (GAVE) described as a watermelon stomach on endoscopy.

Small and large intestine

- Intestinal bacterial overgrowth due to stasis as a result of diminished peristalsis.
- Pseudo-obstruction as a result of intestinal dysmotility.
- Occult GI blood loss from mucosal telangiectasia.
- Malabsorption.
- Rectal prolapse and/or rectal incontinence as a result of decreased compliance and reduced anal sphincter.

PULMONARY FEATURES

Lung disease is the most common cause of morbidity and mortality in SSe patients. Pulmonary disease most typically includes:

- Interstitial lung disease and/ or
- Pulmonary hypertension.

Less common:

- Aspiration pneumonia as a result of GORD and this can develop into bronchiectasis.
- Endobronchial telangiectasia with hemoptysis.

CARDIAC INVOLVEMENT

- Pericardia! disease
- Left or right ventricular systolic dysfunction
- Arrhythmias as a result of fibrosis along the conduction pathways.

RENAL SYSTEM

Kidney involvement is usually silent and may progress slowly toward renal failure. In some cases, renal failure may be abrupt without any prior symptoms. Sudden onset of high blood pressure and kidney failure in a patient known with scleroderma is known as sclerodem1a renal crisis (SRC). Sclerodemm renal crisis is a vascular manifestation of SSe.

Risk factors for SRC: patients with diffuse cutaneous involvement especially those with early, rapidly progressive skin thickening, serum anti-RNA polymerase antibody and those treated with corticosteroids which are often used to treat complications of Sse.

MUSCULOSKELETAL INVOLVEMENT

- Arthralgia and/or arthritis of small joints of the hands- usually non erosive.
- Tendon friction rubs
- Proximal muscle weakness
- Joint flexion contractures.

TREATMENT OF SSc

Overall

- No effective therapy exists to prevent disease progression
  Cyclophosphamide- improves skin thickening and stabilises pulmonary function
- Autologous stem cells transplantation- clinical studies still underway but results promising.

Organ specific

GIT

Oesophagus dysmotility- prokinetic drugs
GORD- proton pump inhibitors and/or H2 blockers
Gut- broad spectrum antibiotics for bacterial overgrowth and octreotide to stimulate small bowel function

PULMONARY ARTERIAL HYPERTENSION

- Calcium channel blockers
- Endothelin receptor antagonist e.g. bosentan
- Phosphodiesterase 5 inhibitor e.g. sildenafil
- Prostacylin analogoues inhalers for early disease and intravenously e.g. iloprost for severe cases

KIDNEY

- ACE inhibitors effective in SRC to control BP and improves prognosis but no data for use to prevent SRC

DIGITAL VASCULOPATHY

- Calcium channel blockers e.g. nifedipine 1st line therapy
- Iloprost I.V. for severe SSc related RP
  Nifedipine and iloprost have been shown to reduce the frequency and severity of SSe related RP attacks
- Boseman effective to prevent development of new digital ulcers.

Systemic Vasculitis

Dr. H ABDELRAHMAN, Dr. MIL NYO

The vasculitides are a heterogeneous group of relatively rare conditions that can occur independently (Eg. Wegener's granulomatosis) or as a secondary feature of an established disease such as rheumatoid arthritis.

The word vasculitis means inflammation of blood vessels and the blood vessel is the primary site of inflammation. The pathological consequence of such inflammation is destruction of the vessel wall, seen histologically as fibrinoid necrosis, hence the term "necrotising vasculitis".

Vasculitis may be localised to a single organ or vascular bed and be clinically insignificant but more commonly is generalised. Muscular arteries (large and medium sized arteries) may develop focal or segmental lesions and these may be life threatening. Focal lesions (affecting part of the vessel wall) may lead to aneurysm formation and possible vessel rupture; segntentallesions (affecting the whole circumference) are more common and lead to stenosis or occlusion with distal infarction. Small-vessel vasculitis, by contrast, most commonly affects the skin and dysfunction ofintemal organs is much less common.

Systemic inflammatory response resulting from release of chemical mediators from inflamed blood vessels gives rise to **various non-specific systemic manifestations:**

- Fever, night sweats, malaise, weight loss, arthralgia, myalgia
- Normocytic and normochromic anaemia, leucoc)tosis, thromboc)tosis, and raised ESR and CRP

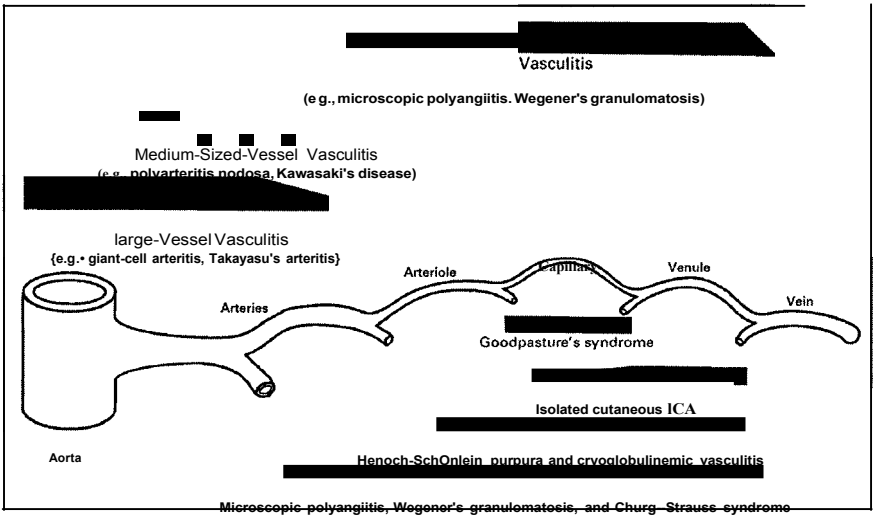
Organ specific manifestations vary depending on the organ that is affected as well as the type of vascular lesion i.e haemorrhage versus ischaemia.

The aetiology of vasculitis is unknown but is clearly multifactorial (ethnicity, genes, gender and environmental factors such as ultraviolet light, infections, toxins, drugs, allergy, smoking, etc).

Classification of the vasculitides

Dominant vessels	Primary	Secondary
Large arteries	- Giant cell arteritis - Takayasu 's arteritis	- Aortitis associated with RA -Infection (Eg. Syphilis, TB)
Medium arteries	- Classic PAN - Kawasaki disease	- Hepatitis B associated PAN
Small Vessels and medium arteries	**ANCA-associated v a s c u l i t i d e s** -Wegener's granulomatosis - Churg-Strauss syndrome -Microscopic polyangiitis	Vasculitis due to - RA, SLE, Sjogrens -Drugs - Infections (Eg. HIV)
Small vessels	- Henoch-Schonlein purpura(HSP) - Croglobulinaemia - Cutaneous leucocytoclastic angiitis - Good pasture syndrome	HSP secondary to drugs Hepatitis C associated cyroglobulinaemia Infections

ANCA = Antt-neutrophtl cytoplasmtc antibody



*Reproduced from J. CHARLES JENNETTE et al (3).

Diagnostic Approach to Patients with Suspected Vasculitis

Vasculitis presents several diagnostic challenges.

- Firstly, patients could present with protean clinical manifestations with a wide spectrum ranging from isolated cutaneous vasculitis to multisystem involvement.
- Secondly, there are several medical conditions that could mimic the presentation of vasculitis. The range of differential diagnosis is therefore broad.
- Thirdly, vasculitis could occur as a primary disorder or be secondary to various medical conditions. It becomes important to differentiate them, as treatment of some forms of vasculitis such as those that are secondary to infection or drugs, is different from that of primary vasculitis.

A primary systemic vasculitis should be suspected in the presence of a systemic inflammatory illness not due to infections, malignancies or systemic autoimmune inflammatory diseases.

Vasculitis "mimics" and **secondary causes of vasculitis** must be excluded and primary vasculitis should always be confirmed with biopsy whenever possible.

To exdud$ vos(ulitis mimics,. ond secondary causes
- Blood <:ultures
- Echoc:ardiogram
- Hepatitis screen (B and C)
- HIV test
- Antiglomerular basement membrane antibody
- Antiphospholipid antibodies
- Antinuclear antibody

To assess extent of vasculitis
- Urine dipstick and microscopy {all patients)
- Chest radiography (all potientsl
- Nerve conduction studies/electromyography/CK

To confirm diagnosis of vasculitis
- Biopsy and/or angiogram

To identify the specific type of vasculitis
- ANCA
- Cryoglobulin
- Complement levels
- Eosinophil counls/lgE levels
- Sf>ocilic findings on biopsy (necrotising granulomatous inRammation, presence of lgA deposils, evidence of immune complex formation (or its absen<:e))

Secondary causes of vasculitis	
Infections	Tuberculosis Hepatitis B & C HIV Parvovirus Cystic fibrosis
Malignancy	Lymphoma Solid malignancy
Connective tissue disorders	RA,SLE Scleroderma Sjogren's syndrome
Dmgs	Penicillamine Propylthiouracil Hydralazine Minocycline Cocaine
Environmental exposure	Dusts Silica

Mimics of Vasculitis

- Atheroembolic disease
- Atheromatous vascular disease
- Anti-phospholipid syndrome
- Multiple myeloma
- Infective endocarditis
- Other chronic infection
- Paraneoplastic syndromes
- Hypersensitivity reactions
- Genetic vascular disorders (Eg. Marfan's syndrome)

Autoiflantmatory syndromes

- Cocaine and amphetamine abuse

Treatment of Primary Vasculitides

Treatment is individualised depending on the specific type of primary vasculitis, extent of the disease and the type of organ involvement. Generally, immunosuppressive treatment is indicated for the inflammatory component and revascularisation is indicated for chronic occlusive vascular lesions.

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POLYMYALGIA RHEUMATICA AND GIANTCELL ARTERTIS

Dr N Abrahams

Polymyalgia Rheumatica (PMR)

PMR is an inflammatory condition of unknown aetiology which is characterised by severe bilateral pain and morning stiffness of the shoulder, neck and pelvic girdle. There is an association with Giant Cell Arteritis (GCA) and these diseases may represent different manifestations of the same disease process.

Epidemiology

PMR is a common condition of older age. It is rare under the age of 50, but the incidence rises with age with a peak between the ages of 70-80. The incidence of disease in patients over 50 is about 100 per 100 1. There is an increased incidence of the disorder at higher latitudes. Women are more frequently affected than men with a ratio of approximately 1:3.

Clinical features

PMR may present with a variety of signs and symptoms, however the most common presenting symptoms include bilateral, severe, persistent pain in the neck, shoulders and pelvic girdle. Pain on active and passive movement of joints (shoulders 70-95%, hips and neck 50-70%)

Other symptoms and signs may include:

Morning stiffness of more than one hour and also after periods of rest.

- Myositis
- Lethargy Loss of weight
- Depression
- Fever
- Joint effusions

Diagnosis

We use the presence of each of the following three criteria for the clinical diagnosis ofPMR

- Age 50 years or older at disease onset
- Bilateral aching and morning stiffness (lasting 30 minutes or more) persisting for at least one month. The stiffness should involve at least two of the following three areas: neck or torso, shoulders or proximal regions of the arms, and hips or proximal aspects of the thighs
- Erythrocyte sedimentation rate 2:40 mmlh
- Some experts add a prompt response of symptoms to glucocorticoids as an additional criterion

Differentiai·ofagnosls

- Rheumatoid Arthritis
- Connective Tissue disease
- Chronic infection- Endocarditis
- Malignancy- Paraneoplastic phenomenon
- Myeloma

Giant Cell Arteritis (GCA)

GCA is a large vessel vasculitis affecting mostly the cranial arteries but can affect the aorta. 30% of patients with PMR will have GCA. Temporal artery biopsy in symptomatic individuals is the gold standard for making the diagnosis.

The main symptoms are new onset headache, jaw claudication and visual loss (due to vasculitis of the posterior ciliary arteries).

Clinical features

Fever, new onset headaches, jaw claudication and visual loss are the main features. There may be bruits over the large vessels and tenderness over the temporal arteries. The pulses may be absent or reduced.

Temporal ArteryBi psy

This should be done when the diagnosis is suspected. The histology shows Giant cell infiltrating to tissues. The biopsy should be l-3cm in length and is 90% sensitive in making the diagnosis.

Radiology

Contrasted CT or MRl is usually negative for GCA but ultrasound of the temporal artery has a characteristic appearance called the "halo sign".

Management

PMR -low dose corticosteroids up to 20mg per day is associated with a dramatic response in symptoms. The disease is usually self limiting and the duration of steroid therapy should be 2 years. Patients who are resistant to treatment may benefit from Methotrexate.

GCA- High dose corticosteroids (lmg/kg) should be used as soon as the diagnosis is suspected. The temporal artery biopsy must be performed soon after starting the steroids. Steroids must not be delayed to make the diagnosis by biopsy as visual loss may develop quickly and is may be permanent. Steroids are tapered over 9 months.

Osteoarthritis (Primary OA)

Dr.MTLNYO

OA is a disease characterised by decoupling of normal degenerative and regenerative/repair processes, which ultimately leads to overall degeneration. OA is currently detined by the American College of Rheumatology (ACR) as a heterogeneous group of conditions that leads to joint signs and S)'mptoms which are associated with defective integrity of articular cartilage, in addition to related changes in the underlying bone at the joint margins.

OA is the most common arthritic disease. The prevalence of OA increases substantially after the age of 40 years in women and 50 years in men. It affects about 50% of people aged?:65 years, and this increases to 85% in the group aged ?:75 years. The incidence of osteoarthritis is rising because of the ageing population and the epidemic of obesity.

Major risk factors for OA are age, female sex, obesity, geographic factors, occupational knee-bending, physical labour, genetic factors and race, joint trauma, vitamin D deticiency, and chondrocalcinosis.

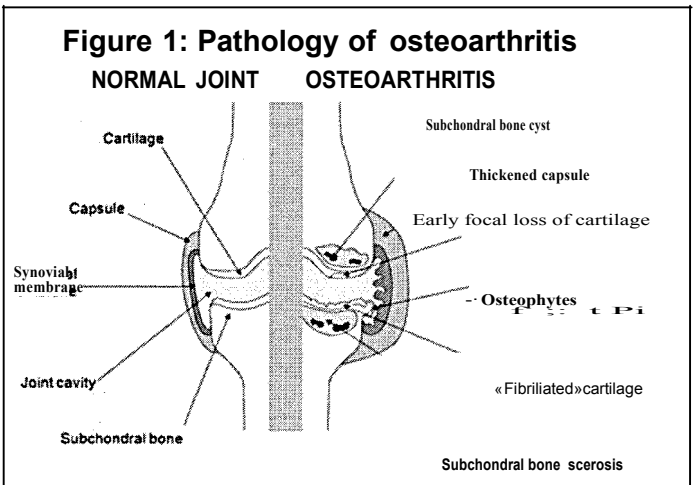
Pathophysiology

The etiology of OA is multifactorial and a combination of mechanical load, metabolic abnormalities, genetic predisposition and inflammation underlies the pathogenesis of OA.

In OA, the degradation of the extracellular matrix exceeds its synthesis, leading to a net decrease in the amount of cartilage matrix or even the complete erosion of the cartilage overlying the bone at the joint surface. This occurs due to a complex interplay between chondrocytes, subchondral bone osteoblasts, synovium and immune cells leading to production of multiple catabolic mediators such as various matrix metalloproteinases, prointlammatory cytokines, cathepsins, prostaglandins E2, nitiric oxide, etc.

The pathological characteristics of OA are loss of cartilage with associated underlying bony changes consisting of sclerosis, subchondral bone collapse, bone cysts, and osteophyte fommtion.

Figure 1: Pathology of osteoarthritis



Inspired from Osteoarthritis;Diagnosis, Medical/Surgical Management 4th edition, Moskowitz, et Al, Lippincott editor

*Reproduced from EULAR compendium

Symptoms and signs

Osteoarthritis causesjoint pain, stiffness, and limitation ofjoint function.
The pain typically is worse with weight-bearing and activity. Morning stiffuess is usually less than 30 minutes. Limited motion develops as the disease progresses because ofjoint-surface incongmity, muscle spasm and contracture, capsular contracture, and mechanical block due to osteophytes or loose bodies.

There is no strict correlation between joint symptoms and the extent or degree of pathological or radiographic changes. Nearly half of patients with radiological features of osteoarthritis have no S)'111ptoms and vice versa. Crepitus may be due to cartilage loss and joint surface irregularity.

Joint enlargement may be caused by secondary synovitis with an increase in synovial fluid or synovial hypertrophy, or marginal osteophytes.
Varus deformities frequently develop in knee OA.
Heberden's nodes, Bouchard's nodes and squaring of hand are commonly seen in hand OA.

Diagnosis

Clinical and/or radiological
ESR is normal and CRP is usually normal
Radiographic findings: Joint space narrowing, osteophytes, subchondral cysts and subchondral sclerosis Ultrasound and MRI are increasingly being used in OA.
Biomarkers (eg. uCTX II, sCOMP, sHyaluronic acid, uC2C, sKS-5D4, etc) are still experimental.

Primary OA most frequently affects the hands, 1^{51} carpometacarpal joints, spine, knees and hips. Involvement of the metacarpophalangeal joints, wTists, elbows, and shoulders is uncommon and secondary causes of OA should be looked for in such cases.

Etiologies of Secondary OA	
Metabolic	**Crystal-associated arthritis (gout, chondrocalcinosis)** Acromegaly Ochronosis **Haemachromatosis** Wilson's disease
Anatomic	Slipped femoral epiphysis Epiphyseal dysplasias Blount's disease Legg-Perthe disease Congenital dislocation of the hip Unequal leg lengths Hypermobility syndromes
Traumatic	Major joint trauma Fracture through a joint or osteonecrosis Joint surgery (e.g. meniscectomy) Chronic injury (occupational arthropathy)
Inflammatory	Any inflammatory arthropathy Septic arthritis

Treatment

Management needs to be individualised and patient centered. There is a wide selection of treatment options for OA. Unfortunately, except for intra-articular corticosteroid or surgery, the effect size of the majority ofOA treatments is only modest.

Non-surgical Treatment

1. Education and information access
2. Exercise (aerobic, strengthening and range of motion exercises)
3. Correction of mechanical factors (weight loss if overweight, appropriate footwear, wedged insoles)
4. Analgesics

   1st line: Paracetarnol, topical NSATDs

   2nd line: NSA!Ds, topical capsaicin, weak opiods

   3rd line: anti-depressants
5. Intra-articular corticosteroid (considered to be very effective for short-term pain relief)
6. Neutaceuticals (Glucosamine, Chondroitin, Avocado soybean unsaponitiables, Diacerein)

   Weak evidence for pain relief exists with virtually no side effects.
7. Intra-articular hyaluronan (inconclusive evidence of efficacy)
8. Sticks, walking aids, braces, splints
9. Acupuncture, thermotherapy (heat or cold), TENS (trancutaneous electrical nerve stimulation)

   No evidence of efficacy but individual patients may experience some symptomatic relief.
10. DMOADs (Disease modifying OA drugs)

    Currently there is no recommended DMOAD. Neutraceuticals, hyaluronan, doxycycline, residronate and Vitamin D may prevent radiological progression of the disease although evidence is inconclusive.

Surgical Treatment

All guidelines agree that referral for consideration of"Total Hip Replacement" or "Total Knee Replacement" should be considered in patients with hip or knee OA who experience persistent pain, stiffness and reduced function that are refractory to non-surgical treatments and which impact significantly on their quality of life. The decision to refer for surgery is individual and ultimately it is the patient who must decide on their own risk/benefit calculation based upon their symptom severity, their general health, their expectations of lifestyle and activity, and the effectiveness of the non-surgical treatments they have tried.

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Osteoporosis and Fragility Fracture

Dr.MTLNYO

Physiology of Healthy Bone

TI1ere are: types of bone, cortical (80% of adult bone) and trabecular (20%). Some bones such as the shafts of long bones (eg. Femur) contain predominantly cortical bone whereas other bones such as ribs or vertebrae contain predominantly trabecular bone.

Bone is composed of

1. Bone cells (Osteocytes, osteoblasts, osteoclasis and lining cells)
2. Organic bone matrix (mainly Type I collagen but also proteoglycan, osteocalcin and osteonectin)
3. Bone minerals (mainly calcium hydroxyapatite)

Osteocytes are resident cells (as are lining and periosteal cells) and present in the entire bone volume. Osteoclasis and osteoblasts are present only at locations with active bone turnover (remodeling), and are present in low number.

Osteoclasts are giant multi-nucleated cells that are able to resorb mineralised bone tissue. The key stimulator of osteoclastogenesis is RANKL (receptor activator of the nuclear factor KB ligand). OPG (Osteoprotegrin) inhibits RANKL. Therefore, RANKUOPG ratio determines the extent of bone resorption. The factors increasing RANKUOPG ratio are parath)Toid hormone, estrogen deficiency, inflammatory cytokines, glucocorticoids, **"vitamin D", etc.**

Osteoblasts are responsible for the fornmtion and mineralisation of bone matrix.

Osteoc)tes are important in guarding the integrity of the material and structural strength of bone. They presumably sense mechanical strain thereby signaling the need for adaptive remodeling and distribution to accommodate prevailing loads.

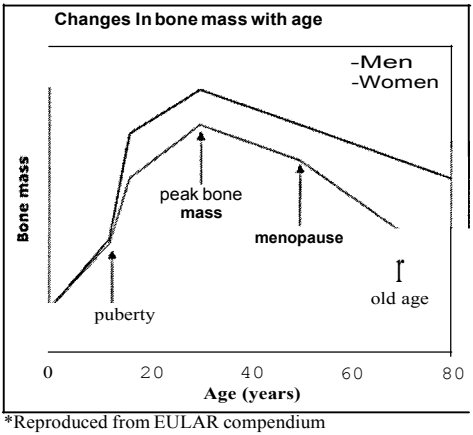
The strength of bone, i.e. the ability of bone to resist fracturing, is determined by its structural and material composition, and by the activities of bone cells that determine the level and balance of bone turnover and ability to repair damage. Bone must be stiff and able to resist deformation, making loading possible. Bone must also be flexible to absorb energy by deforming: to shorten and widen when compressed, and to lengthen and narrow in tension without cracking. If bone is too brittle or flexible, it will crack and fracture.

The optimal state of bone is achieved by modeling (construction) and constant lifelong remodeling (reconstruction). During childhood and adolescence both processes (modeling and remodeling) are involved to establish the peak bone strength. Bone mass and strength achieved at the end of the growth period, simply designated as 'peak bone mass', plays an essential role in the risk of osteoporotic fractures occurring in adulthood.

In young healthy adults. the resorptive phase of the remodeling cycle removes damaged bone, and the formation phase restores the structure. Each cycle is balanced and lasts 90-130 days. Bone resorption and fornmtion are tightly coupled in time, location and quantity. After the remodeling cycle, has completed, mineralisation of new bone will continue.

Bone loss is an inevitable consequence of ageing, roughly starting when the 'peak bone mass' is reached, accelerating at the time ofthe menopause and continuing throughout life in both men and women, and is the result of persistent hypogonadism in women. emerging hypogonadism in some men and secondary hyperparath}TOidism in elderly of both sexes associated with calcium and vitamin deficiency and immobility.

At the cellular level, there are two fonns of bone loss. First, there is an increase in the number of bone remodeling units on the bone surface, which are undergoing resorption at any time. More densely mineralised bone is removed and replaced with younger, less densely mineralised bone, reducing material stiffness. Excavated resorption sites remain temporarily unfilled and there is altering of cross-linking between adjacent collagen fibers. Secondly, there is a remodeling imbalance in which bone fonnation is reduced compared with resorption within each remodeling unit. Since there are more remodeling sites per unit volume of trabecular bone than in cortical bone, a greater portion of trabecular bone is turned over and lost (trabecular thinning).



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Osteoporosis

WHO defines osteoporosis as a generalised bone disease characterised by a decreased bone mass and a **deterioration of bone microarchitecture resulting in an increased fracture risk.**
Since there is no current direct and accurate measure for bone strength, bone mineral density (BMD) which accounts for- 70% of bone strength is the standard to measure osteoporosis. Dual energy X-ray absorptiometry (DEXA) is the most commonly used investigation for measuring BMD.

For epidemiological purposes, osteoporosis is defined by the WHO as a BMD >2.5 standard deviations(SD) below the mean peak BMD in young healthy adults of the same gender, also known and expressed as the T-score as measured by DEXA. Normal bone density is defined as aT-score above -1 SD, and osteopenia as aT-score between -I and -2.5 SD.

Primary osteoporosis is the result of bone loss related to the decline in gonadal function associated with aging. Secondary osteoporosis may result from a variety of conditions that adversely impact bone metabolism. Glucocorticoid-induced osteoporosis is the most common form of secondary osteoporosis.

Causes of secondary osteoporosis	
Endocrine	Thyrotoxicosis, Hyperparathyroidism, Cushing's syndrome, IDDM, Acromegaly
Hypogonadal	Anorexia nervosa, Hyperprolactinaemia, Turner and Klinefelter, Bilater oophorectomy and orchidectomY
Dmgs	Glucorticoids, Aromatase inhibitors
Hematologic malignancies	Multiple myeloma, Mastocytosis, Hemophilia, Thalassaemia
Nutritional and G!"f	Inflammatory bowel disease, Malabsortion syndromes, Malnutrition, Gastrectomy
Neurological	Parkinson's disease, Stroke, Muscular dvstrophy
Other disorders	RA, Ankylosing spondylitis, SLE, Chronic renal failure, Immobilization, Sarcoidosis, Amyloidosis, Organ transplantation

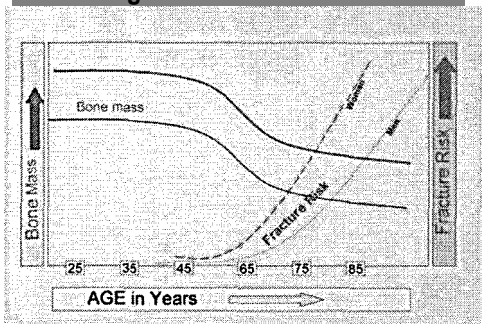
Fragility Fracture

Fragility fracture is a type of pathologic fracture that occurs as result of normal activities, such as a fall from standing height or less. The most common fragility fractures occur in the spine, wrist, and hip.

Factors which are independently associated with increased risk of fragility fracture are as follows:

- LowBMD
- Increasing age
- Gender (female)
  Low body weight
- History of fracture after age of 45-50 years
- Family history of osteoporotic fracture
  Severe immobility
- Current smoking and excessive alcohol use
- Glucocorticoid use
- RA, SLE

Effect of age on Bone Mass & Fractures



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Diagnosis of Osteoporosis

Osteoporosis is diagnosed clinically (fragility fractures) or radiographically (T-score on DEXA).
If clinical evaluation does not raise suspicion of a secondary cause, there is currently little evidence to warrant additional testing in postmenopausal women. In contrast, approximately 50 percent of pre- and perimenopausal women with osteoporosis have an associated underlying cause. There are no evidence-based guidelines to direct the evaluation of a suspected secondary cause of osteoporosis. h1men as well as pre- and peri-menopausal women, a basic laboratory evaluation should be considered if there is no clear etiology evident by history and physical examination.

Evaluation for Suspected Secondary Osteoporosis in Selected Patients	
Test	**Possible Etiology**
Initial screening tests	
Alkaline Phosphatase	High levels in Paget disease, immobilization
Calcium	Low levels in vitamin D deficiency, malabsorption
	High levels in hyperparathyroidism
Liver or kidney function	Liver or kidney disease
FBC	Bone marrow malignancy
TSH	Hyperth)Toidism
Total testosterone (men)	Hypogonadism
25-hydroxy vitamin D (men)	Vitamin D deficiency
Additional Tests (as indicated)	
Estradiol (non-post menopausal women)	Hypogonadism
Intact parailiyroid hormone	Hyperparathyroidism
Serum protein electrophoresis	Multiple myeloma
25-hydroxy vitamin D (women)	Vitamin D defficiecy

Treatment of Osteoporosis /.FragilitY Fractures

The NOF (National Osteoporosis Foundation) recommends treatment of postmenopausal women and men with a personal history of hip or vertebral fracture,T-score of -2.5 or below, or low bone mass (T-score between -I and -2.5) and a I0-year probability of hip fracture of at least 3 percent or any major fracture of at least 20 percent. The I0-year probability of fracture is calculated using the WHO fracture risk assessment tool. The WHO recommends treating persons with or at risk of osteoporosis.

Non-phannacological treatment

I. Prevention of falls
2. Calcium supplements
3. VitaminD

Current Phannacological treatment

I. Bisphosphonates (anti-resmptive)
2. Calcitonin (anti-resorptive)
3. Strontium ranalate (anti-resorptive and anabolic)
4. Teriparatide- recombinant PTII (anabolic)
5. Hormone replacement therapy
6. Selective estrogen receptor modulator (SERM) Eg. Raloxifene

Future Pharmacological treatment

I. Denosumab- anti RANKL antibody (anti-resorptive)
2. Odanacatib- anti Cathepsin K inhibitor (anti-resorptive)
3. Saracatinib- anti c-src kinase inhibitor (anti-resorptive)
4. AMG 785-antibody against sclerostin (anabolic)

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Low Back Pain and Sciatica

Dr.MTLNYO

Low Back Pain (LBP)

Low back pain is defined as pain and discomfort, localised below the costal margin and above the inferior gluteal folds, with or without leg pain.

Non-specific low back pain is defined as low back pain not attributed to recognisable, known specific pathology (e.g. **infection, tumour, osteoporosis, spondyloarthritis, fracture, inflammatory process, radicular syndrome or cauda equine** syndrome).

Acute LBP :< 6 weeks.
Subacute LBP :6- 12 weeks.
Chronic LBP :;, 12 weeks.
Recurrent LBP :Aa new episode after a symptom free period of 6 months

The lifetime prevalence of low back pain is up to 84%. Peak prevalence occurs between ages 35 and 55 years old. Acute LBP is usually self-limiting (recovery rate 90% within 6 weeks). The best estimated lifetime prevalence of chronic non-specific LBP is approximately 23%. Specific causes of low back pain are uncommon (<15% all back pain).

Diagnostic Triage

For most patients with acute low back pain a thorough history and brief clinical examination is sufficient. The primary purpose of the initial examination is to attempt to identify any "red flags" that may suggest a specific diagnosis. However, it is not possible to give a diagnosis based on detectable pathological changes in most cases of acute LBP. A simple and practical classification, the so-called "diagnostic triage", considers three categories of acute LBP-:

1. Suspected or confirmed serious pathology ("red flag" conditions such as malignancy, infection, fracture or spondyloarthritis)
2. Radicular syndromes
3. Non-specific L B P

Red Flags

Age of onset< 20 years or> 55 years
Recent history of violent trauma.
Constant progressive, non mechanical pain (no relief with best rest).
Thoracic pain.
Past medical history of malignant tumour.
Prolonged use of corticosteroids.
Drug abuse, immune-suppression, HIV.
Systemically unwell.
Unexplained weight loss or night sweats.
Widespread neurological symptoms (including cauda equine syndrome).
Structural deformity (eg. Gibbus).
Fever

Individual red flags may indicate a higher probability of a serious underlying condition that may require further investigation. Multiple "red flags" need further investigation.
A properly conducted passive straight leg raising test (Lasegue test) is the most accurate test to identify nerve root pain.
If serious spinal pathology and nerve root pain are excluded, manage the low back pain as non-specific.
Diagnostic triage should be carried out at the first assessment and patients with **chronic LBP** should be reassessed, to exclude specific spinal pathology and nerve root pain.

Predictive factors of Chronicity/disability

Low workplace social support.

Low job satisfaction (e.g. heavier occupation with no modified duty, shorter job tenure).

Psychological distress.

Depressive mood.

Somatisation.

Prior episode of LBP.

Poor perceived general health status.

Imaging in LBP

Diagnostic imaging tests (including X-rays, CT and MRI) are not routinely indicated for non-specific LBP. They serve two purposes: to evaluate patients with red flags or radicular pain; and to plan surgical techniques in those for whom surgery is being considered. The diagnostic imaging does not improve treatment of LBP.
Further, there is no association between degenerative imaging signs at the acute stage and the transition to chronic symptoms.

Treatment

Treatment of acute low back pain in primary care aims at:

1. providing adequate information and reassuring the patient that low back pain is usually not a serious disease and that rapid recovery is expected in most patients
2. providing adequate symptom control
3. early and gradual mobilisation of patients
4. recommending the patient to stay as active as possible and return early to normal activities, including work

Passive treatment modalities (eg, best rest, massage, ultrasound, electrotherapy, laser and traction) should be avoided as mono-therapy and not be used routinely, because they may increase the risk of illness behaviour and chronicity.

For chronic low back pain, consistent features include:

1. **supervised exercises**
2. cognitive behavioural therapy
3. **multidisciplinary treatment**

Pharmacological Treatment

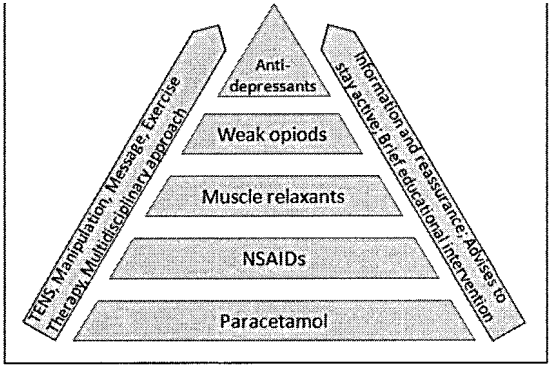
Simple analgesic
NSAIDs and Cox 2 inhibitors
Muscle relaxants
Antidepressants eg. Amytryptyline
Opioids eg. Tramadol, codeine

Pharmacological Treatment of Acute LBP

1st line	**-Paracetamol**
2nd line	-NSAIDs
3rd line	-NSAIDs +weak opiods
	-Paracetamol +weak opiods
4"1ine	-NSAIDs + muscle relaxants

Aim: To restore normal daily activities

Treatment of chronic LBP



Sciatica

Sciatic neuralgia is defined as "pain in the distribution of the sciatic nerve due to pathology of the nerve itself'. Radicular pain is defined as "pain perceived as arising in a limb or the trunk caused by ectopic activation of nociceptive afferent fibres in a spinal nerve or its roots or other neuropathic mechanisms". The incidence of sciatica is related to age. Incidence peaks in the 45-64 years' age group.

Pathophysiology

In about 90% of cases, sciatica is caused by a herniated disc with nerve root irritation. The intervertebral disc has been implicated in the pathophysiology of sciatica through different mechanisms.

At first, the assumption that the protruded disc exerted pressure on the sciatic nerve root was commonly accepted. Therefore, treatment was surgical removal of the disc.
However, as early as the mid 20tncentury, it was suggested that pressure on a nerve results in loss offunction and is rarely associated with pain. Several lines of evidence support this hypothesis:

a) Disc herniation with apparent neural compromise are common findings in asymptomatic patients;
b) Symptomatic patients with disc herniation may experience improvement without any alteration of the original pathology;
c) Removal of herniated disc material does not always relieve pain;
d) Chymopapain, a substance used for chemonucleolysis of herniated discs, may lead to rapid relief of leg pain preceding changes in the size of the disc herniation.

These observations suggest that mechanisms other than pressure on nerve roots are involved in sciatica.
On the other hand, there is evidence suggesting that sciatica or radicular pain arises from an interaction between **inflammatory, immune, and pressure related processes.**

Non-discogenic causes of sciatica probably represent less than 10% of cases, but any new presentation with pain in a nerve root distribution, or change in a previously stable pain state, should be investigated to exclude infective or malignant causes of pain. Red flags for sciatica do not differ from those individualised for low back pain.

Non-discogenic causes of sciatica	
Malignancy	**Metastatic, Sarcoma, Sciatic neuroma, Haemangioblastoma**
Infection	Abscess, Caseating disease(TB), Discitis
Vascular compression	Pseudoaneurysm
Bony compression	Psteophytes, Spondylolisthesis, Spinal stenosis
Muscular compression	Piriformis syndrome
Epidural adhesions	
Gynaecological	**Uterine fibroid, Pelvic endometriosis**

Diagnosis

Pain radiating in the leg which follows a dermatomal pattern
Associated LBP (usually less severe than the leg pain)
Straight leg raising test
Crossed straight let raising test is more specific but less sensitive

Imaging

Imaging is indicated only if non-discogenic causes of sciatica are suspected (red flags).
In patients with severe pain and disability who fail to respond to conservative treatments for 6-8weeks, surgery might be considered and imaging is then used to determine if a herniated disc is present with location corresponding to the pain distribution. Agreement between pain distribution and imaging findings is important because this is part of the decision to consider surgery.

However, disc herniations detected by MRI or CT scan are highly prevalent in the general population (20%-30%) without sciatica. Furthermore, in many patients with sciatica no lumbar disc herniation is identified on MRI or CT scan.

Plain radiography for the diagnosis of lumbar disc herniation is not recommended because disc tissue is not visualized by x-rays, but is still useful as first line exploration if an underlying disease is suspected.

Prognosis /Natural history

Most patients with acute sciatica respond to conservative symptomatic management and resolve over a period of weeks to months (50% of patients improve within 10 days and 75% within 4 weeks). However, up to 30% of patients continue to have pain for one year or longer, with some of them requiring surgery. Among patients undergoing surgery, approximately 10-40% evolved into chronic pain syndrome, sometimes called "failed back surgery".

Non·surgical treatments

Conservative treatments for sciatica are primarily aimed at the reduction of pain and nerve irritation, either by analgesics, non steroidal anti-inflammatory drugs, muscle-relaxants, or corticosteroid epidural injections.
Using the evidence based medicine approach, a recent systematic review found that conservative treatments do not clearly improve the natural history or reduce symptoms of sciatica in most patients. Bed rest or physical therapy (exercises) proved not to be effective.
However, in real life conditions, patients with sciatica should be treated and the most widely used treatments remain analgesics, NSAIDs, and epidural injections of steroid.

Surgical treatments

Removal of disc herniation and eventually part of the disc, or correction of foramina! stenosis are the main objectives of surgical procedures for sciatica. Treatment is aimed at decreasing the leg pain and corresponding symptoms but not at reducing the back pain.
Consensual indications for immediate surgery include:

1) Cauda equina syndrome
2) progressive motor loss
3) hyperalgesia despite maximum conservative treatment

Based on available evidence, patients and doctors should weigh the benefits and harms of surgical and conservative medical treatment options to make individual choices because patients' preference for treatment may have a direct positive influence on the magnitude of the treatment effect.

References

1. EULAR Compendium on Rheumatic Diseases

NONSTEROIDAL ANTI-INFLAMMATORY DRUGS

Introduction

In 1971 John Vane won the Nobel Prize for demonstrating anti prostaglandin mechanisms of action of NSAID.

NSAIDs act non-selectively and therefore accomplish modest palliation of pain and inflammation. Only when significant inflammation is present do the NSAIDs provide better analgesia than do simple analgesics.

Classification

Divided into 2 broad groups:

Acidic agents
Non-acidic agents

Acidic agents

a) *Arylcarboxlyic acids*
   i) Salicyic acids- Aspirin in its various forms
   ii) Anthranilic acids (fenamates)- Flufenamic, Mefenamic, Meclofenamic acids
b) *Arykanoic acids*
   i) Arylacetic acids- Diclofenac Fenclofenac
   ii) Arylpropionic acids - Ibuprofen, fluriprofen, ketoprofen, naproxen, tiaprofenic acid
   iii) Heteroaryl acetic acids- Tolmetin
   iv) Indole and lndene acetic acids - Indomethacin, Sulindac
c) *Enolic Acids*
   i) Pyrazolinediones- phynylbutazone, azapropazone
   ii) Oxicam- Piroxicam

Non-Acidic Agents

Bufexamac, tinoridine

Indications

Inflammatory pain as in RA

Crystal-induced arthritis

Analylosing spondylitis and related conditions and occasionally in osteoarthritis when there is an inflammatory component

Guidelines for prescribing

1. Get to know a few agents well, particularly their dosage and side effects.
2. Initially choose one of the established drugs.
3. No science involved in selection.
4. Route of administration
   i) Usually orally with meals; antacids may be co-administered.

ii) Rectal administration

Indicated in patients with nocturnal and early morning pain and stiffness as occurs in active RA and AS. Gastric side effects may be less compared with oral agents.

iii) Intramuscular injection of Dicofenac or equivalent agents is very effective for:

a) rapid control of severe pain

b) acutcdlare ofRA or AS

c) acute gout

5. Avoid polyphannacy- prescribe one drug at a time. Exception is active RA with significant early morning stiffness.
6. Individualise therapy
   - establish pain pattern for each patient
   - chronophannacology
7. Allow 2-3 weeks' treatment before deciding that it is ineffective.
8. Phenylbutazone and related pyrazolones to be avoided.
   - only indication is acute AS in which it may be used for one week (MCC recommendation).
9. Low dose salicylates (300-600mg) are antipyretic and analgesic only. For anti-inflammatory effect need dose of 4-4 grams/day.

SPECIAL SITUATIONS

1. *Anaplylactic!Anaphylactoid reactions*
   - avoid all NSAIDs in persons who react idiosyncraticaUy to aspirin.
   - Beware patient with triad of vasbmotor rhinitis, asthma, nasal problems.
2. *Sodium and Water retention*

   All NSAIDs can cause this

   Can aggravate or precipitate cardiac failure, angina, hypertension.
3. *Pregnancy*

   Early: conflicting reports of teratogenicity of salicylates and other NSAIDs.

   Late: Prolonged gestation, prolonged labour, greater blood loss at delivery, neona- tal anaemia, intracranial haemorrhage. Premature narrowing of ductus arteriosus. As a general rule "Avoid NSAIDs if at all possible".
4. *Lactation -generally folt to be safe.*
5. *Peptic ulceration*

   Aspirin + Indomethacin are probably the least safe

   In active peptic ulcer "avoid all NSAIDs if at all possible".

   a) Concomitant antacid therapy

   b) Concomitant cimetidine, ranitidine

   c) Enteric coated NSAIDs or NSAIDs which are of the slow release type eg Ketoprofen or using a prodrug like Sulindac.

d) Use of suppositaries

6. *Elderly- Constitute a large proportion of NSAJD users*

Particularly prone to water retention, gastric irritation, CNS effects, hepato, oto and nephro-toxicity.

Keep doses to a minimum, and monitor for side effects.

7. *Hepatic or renal insufficiency*

either avoid or reduce dose of

NSAID Viral illness

Reyes syndrome-linked only with Aspirin. Avoid Aspirin during or after viral illness in children, teenagers.

Drug interaction- With oral anticoagulants, suphonylureas.

- counteract benefits of diuretics, anti-hypertensives, anti-anginal, and anti-heart failure agents

Spectrum of adverse effects of the NSAIDs includes:

GIT: Dyspepsia, nausea, peptic ulcer, occult bleeding, stomatitis, haematemesis, malaena, diarrhoea, aggravation of distal bowel pathologies such as Crohn's and diverticular disease; proctitis, frank bleeding and necrosis may occur with suppositaries, pancreatitis has been reported with sulindac.

CNS: Dizziness, vertigo, tinnitus, deafness, aseptic meningitis, nausea, ataxia, insomnia, somnolence, headache, confusion, hallucinations, psychosis, muscle weakness, tremor (especially liable are elderly people), blurred vision, diplopia, photophobia, mydriasis, conjunctivitis, visual loss.

CVS: salt and fluid retention and consequent provocation or aggravation of hypertension, angina, cardiac failure, oedema, arrhythmias, palpitation.

Idiosyncratic: anaphylaxis/anaphylactoid reaction most likely to occur in persons with history of asthma, hayfever and nasal polyps. Cross-reactivity among the NSAIDs is highly likely. Such reactions may vary from milfto life threatening. Also skin rashes-maculopapular morbilliform, urticarial and even toxic epidermal necrolysis and Stevens-Johnson syndrome.

. Resp System: bronchospasm, laryngospasm, alone or as part of a more generalised anaphylactic/anaphylactoid reaction, pneumonitis.

Immunologic: masking of the infective process may occur; alterations of the immune response.

Hepatic: elevations (usually slight and evanescent) of transaminases may occur, hepatotoxicity very rarely may progress to necrosis, cholestatic jaundice.

Renal: celluria, proteinuria, haematuria, increased likelihood of urinary tract infections, interstitial nephritis, acute renal failure. Analgesic nephropathy is unusual with single analgesic or NSAID exposure; it is usually the consequence of chronic, high dose plycomponent analgesic exposure.

Haematologic: anaemia due to blood loss from the GIT, clotting disturbances due to inhibition of platelet aggregation, blood dyscrasias of any type may occur, rarely.

Endocrine: cortiocotropin production may decrease, thyroid disturbances – chiefly

pyrazolones, ascorbic acid levels in the body may decrease. Salicylates may alter carbohydrate/glucose metabolism – particularly in diabetics which may become markedly hypoglycaemic.

Newer NSAIDs.

Prostaglandins are derived from arachidonic acid metabolism and is dependent on cyclo-oxygenase (COX) activity. Two isoforms of the COX enzyme are found. COX II is induced under inflammatory conditions, while COX I is the enzyme involved in producing "useful" prostaglandins. The recent development of NSAIDs which specifically inhibit COX II have been a major advance in the use of these agents in arthritis. These drugs are not yet registered for clinical use, but will have a major impact on the side-effects experienced with the current NSAIDs, which inhibit COX I activity, predominantly. These newere NSAIDs will have the advantage of being anti-inflammatory/analgesic without the common side-effects of NSAIDs, especially gastroduodenal toxicity. These newer agents have minimal GIT, renal and haematological side-effects and have shown a great therapeutic benefit in osteo-arthritis.

ABBREVIA TIONS

ACJ	Acromio Clavicular Joint
ACR	American College of Rheumatology
ARA	American Rheumatism Association
ARF	Acute Rheumatic Fever
ASOT	Anti-streptolysin "0" titre
CCF	Congestive Cardiac Failure
CCJ	Costo-chondral junction
CIC	Circulating Immune Complexes
CRP	C reactive protein
CPK	Creatine phospho-kinase
CSS	Churg-Strauss Syndrome
DISH	Diffuse Idiopathic Skeletal Hyperostosis
DM	Dermatomyositis
EMG	Electromyogram
EMS	Early Morning Stiffness
ER	External Rotation
ESR	Erythrocyte Sedimentation Rate
HAQ	Health Assessment Questionnaire
IBD	Inflammatory Bowel Disease
IHD	Ischaemic Heart Disease
IR	Internal Rotation
IV	Intervertebral
JAS	Juvenile Ankylosing
JCA	Spondylitis Juvenile Chronic
KFT	Arthritis
MCPJ	Keitel Function Test
MCTD	Metacarpophalangeal Joint
MTPJ	Mixed Connective Tissue Disease
NOMID	Metatarsophalangeal Joint
NSAID	Neonatal Onset Multisystem Inflammatory Disease
OA	Non-steriodal Anti-inflammatory Drugs
PAN	Osteoarthritis
PIPJ	Polyarteritis Nodosa
PM	Proximal Interphalangeal Joint
PSS	Polymyositis
PV	Progressive Systemic Sclerosis
SAARD	Plasma Viscosity
SCJ	Slow Acting Anti-rheumatic Drug
SEA syndrome	Sternoclavicular Joint
SUFE	Seronegative, Enthesopathy, Arthropathy
TMJ	Slipped Upper Femoral Epiphysis
wee	Temperomandibular Joint
	White Cell Count

RECOMMENDED BOOKS

1. Currey HLF: Essentials of Rheumatology, Pitman London 1983.
2. Grennan DM: Rheumatology. BailliereTindall London 1984.
3. Primer in the Rheumatic Diseases.
4. Atlas of Rheumatology- Dieppe, et al.

These texts contain the basic knowledge, especially Currey's Essentials of Rheumatology. One of these should be bought

Reference

1. Textbook of Rheumatology. Kelly, Harris, Ruddy, Sledge. 2 vols in Reference Section of the Library.
2. Rheumatology. JH Klippel and PA Dieppe. 1995.

For the more adventurous

Clinics in the Rheumatic Diseases, Seminars in Arthritis and Rheumatism- housed in the Medical Library on the gallery. Ref. 616.99105.

Both these provide reviews, in depth, of several aspects of the rheumatic diseases.

Essential links to information on rheumatology:

Societies and foundations:

1. American college of rheumatology http://www.rheumatology.org
2. Arthritis foundation USA http://www.arthritis.org
3. Arthritis Society Canada http://www.arthritis.ca
4. Ankylosing spondylitis society http://www.spondylitis.org
5. Osteoporosis foundation http://www.nof.org
6. Lupus association http://www .lupus.org
7. Psoriasis association http://www.psoriasis.org
8. SARAA website http://www.rheumatologysa.com

Patient based websites / Public arthritis websites:

1. The arthritis pages of drdoc on-line http://www.arthritis.co.za
2. Arthritis at about.com http://www.arthritis.about.com/healtblarthritis/

Other interesting resources

1. The arthritis better living spa http://www.arthritisconnection.com
2. National institute of health USA http://www.nih.gov/healthl
3. lnt'lleague of association of rheumatology http://www.ilar.org

Newsgroups

1. Misc.health.arthritis
2. Alt.support.arthritis