

# Aging and the Spectrum of Rheumatic Diseases

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The aged population in India is the second largest in the world. Disorders of the musculoskeletal system including articular and non-articular conditions are a major cause of disability and discomfort in the elderly. Joint pains were noted in 33% of 60-69 year olds and 48.4% of those over 80 years of age in one series while in a hospital based survey of an acute elderly unit, arthritis contributed to loss of function in 48%.<sup>1,2</sup> This emphasizes the importance of identification and management of rheumatic problems in the elderly population as these disorders hamper their ability to live independently.

## Age related changes in the immune system and musculoskeletal tissues

Understanding of the mechanisms underlying the age-related changes in immune function may enhance our ability in identifying sub-populations of the elderly at risk for autoimmune diseases as well as in preventing and treating these disorders. Aging is associated with a decline in immune function with the primary defect being in the T-cells. Lymphocytes derived from the aging population differ those from young individuals by a variable loss of suppressor activity, which may provide an explanation for the increased frequency of autoantibodies in this population.<sup>3, 4</sup>

The age-related changes in the articular cartilage that increase the risk of degeneration include fibrillation of the surface of cartilage, decrease in the size and aggregation of proteoglycan aggregates, increased collagen cross-linking resulting in loss of stiffness and tensile strength. Primarily, aging of the chondrocytes

results in a decrease and modification of their synthetic activity. As a result the aggregates produced are smaller and less uniform, link proteins are less functional and response to anabolic growth factors is decreased. The senescence of these chondrocytes is associated with a decline in their mitotic activity, increased expression of senescence associated enzyme beta-galactosidase and erosion of telomere length.<sup>5</sup>

Alterations in tendons, ligaments and joint capsules result in serious impairment in older persons. The degenerative changes may produce spontaneous or low energy ruptures of these tissues. Skeletal muscle mass decline begins gradually at 25 years of age and the process accelerates after 50 years of age to 10% of muscle mass per decade. Between 30-80 years of age, strength of muscle groups decreases by 60%.<sup>6</sup>

## Principles of evaluation of the elderly patient with rheumatic complaints

In general, the elderly patient is difficult to evaluate due to complexities in presentation as well as communication problems. Vague complaints or functional decline may indicate serious disease. Common diseases present in an atypical manner resulting in missed diagnoses. Co-morbid diseases, polypharmacy, drug interactions and side effects affect the evaluation process.<sup>7</sup> A variety of systemic conditions, some with serious implications, like carcinomas, multiple myeloma, hyperthyroidism, myxoedema and neurological disorders like Parkinson's as well as Alzheimer's disease may present with musculoskeletal complaints; needs to be kept in mind.<sup>8</sup>

Pain is the commonest symptom in rheumatologic diseases but its evaluation and management in the elderly is difficult. There is no difference in the reporting of acute pain across all age groups. In its evaluation, the clinician should avoid the pitfall of attributing the symptom to a flare of pre-existing disease as new-onset articular disorder may be missed. Chronic pain is reported more frequently with advancing age up to the seventh decade after which it reaches a plateau despite

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the increasing load of pain producing disease in this population. This is probably the result of impaired nociceptive function of the nervous system. The various changes described include a combination of age related increased threshold of pain perception, reduced efficacy of endogenous analgesic systems, decreased tolerance of pain and slower resolution of post injury hyperalgesia. Multiple factors that influence the resultant decrease in pain perception and reporting include age, co-morbid disease, biocultural cohort effects or altered psychosocial factors. Visceral disorders like myocardial infarction and acute abdomen may be painless in the elderly resulting in delayed or missed diagnoses. Under reporting of symptoms may be related to reticence on the part of elderly to complain or a decline in cognitive function. Therefore, the physician has to search for alternative clues. Patients may use different terminology to describe pain e.g. hurt, ache, burning or there may be a decline in functional status, altered mental state or recent onset of depression. The intensity of pain should be documented on a variety of validated visual scales. The examination of the part for swelling, inflammation and trigger points help in narrowing the differential diagnosis. Important, but not always reliable are the relatives and caregivers.<sup>9-12</sup>

The practicing clinician must be aware of those rheumatologic diseases that are distinctly uncommon in old age as well as those that predominantly have their onset in old age. Disorders like Reiter's disease, Still's disease, and ankylosing spondylitis are unlikely to have a new onset of disease in old age. Polymyalgia rheumatica, giant cell arteritis (temporal arteritis), calcium pyrophosphate deposition disease (pseudogout) are almost exclusively seen in older individuals. Disorders like rheumatoid arthritis may be seen in all age groups. Gout and osteoarthritis are common in middle age and in the elderly.<sup>8, 13</sup>

The elderly patient with a rheumatologic problem, therefore, may be a person who had onset of disease in youth or middle age and has reached old age with burnt out or active disease, complications of long-standing disease or drugs as well as those who have a disability interfering with their activities of daily living. Of special interest to the geriatric specialist would be those individuals who develop a new onset of arthritis after 60 years of age and its difference in presentation from onset of disease in the younger age groups. In the future, the number of elderly who have undergone surgical procedures or joint replacements with related problems will also be common.

## **Diffuse pain syndromes and predominantly non-articular rheumatic disorders in the elderly**

Diffuse pain syndromes are common in the elderly. Polymyalgia rheumatica and fibromyalgia are common but other inflammatory, endocrine and neoplastic conditions have to be considered in the differential diagnosis.<sup>14</sup>

### ***Polymyalgia rheumatica (PMR)***

The emphasis that this disease affected the elderly was made as early as 1888 when Bruce called it "senile rheumatic gout". The incidence peaks in the 70-80 years age group. It is an acute or slowly progressive, symmetric disorder with severe morning stiffness and aching pain predominantly in cervical, shoulder and pelvic girdles. Fatigue is prominent while weakness is moderate. Physical examination may be unremarkable but edema of the hands, wrists, ankles and feet may be seen. The ESR is usually over 40 mm per hour. MRI shows inflammation of subacromial, subdeltoid and other bursae.

#### Criteria For Polymyalgia Rheumatica

1. Pain persisting for at least 1 month and involving two of the following areas: neck, shoulders and pelvic girdle
2. Morning stiffness > 1 hour
3. Rapid response to prednisone (20 mg/day or less)
4. Absence of other diseases capable of causing musculoskeletal symptoms
5. Age > 50 years
6. ESR > 40 mm / hour

Relief with 10-15mg of prednisone per day is diagnostic. Dose reduction may be considered after 4 weeks of institution of treatment using clinical evaluation and acute phase reactants as indicators. Treatment may be needed for 18 months.<sup>15,16</sup>

### ***Temporal or Giant Cell Arthritis (GCA)***

It is an uncommon but serious disorder, seen in patients over 50 years of age. Many consider GCA and PMR to be different phases of the same disease. Predominant symptom is headache in the distribution of temporal or occipital arteries which may be thick,

nodular, tender or erythematous on examination. Visual disturbances including permanent loss of vision are serious manifestations. Jaw claudication is seen in 50%. Some cases may have constitutional symptoms, arthritis or present as a fever of unknown origin. ESR is usually very high and out of proportion to the musculoskeletal symptoms. Confirmation of the diagnosis requires a biopsy of the temporal artery. The 1990 American College of Rheumatology criteria are outlined below:

Criteria for diagnosis of Giant Cell Arteritis (At least 3 of the 5 criteria should be present)

1. Age at disease onset  $\geq$  50 years
2. New headache
3. Temporal artery abnormality (tenderness on palpation, decreased pulsation unrelated to arteriosclerosis of the cervical arteries)
4. Erythrocyte sedimentation rate by Westergreen method  $\geq$ 50 mm / hour.
5. Temporal Artery biopsy

Early recognition and institution of high dose steroids (Prednisolone 60mg) daily reduces the possibility of serious consequences like blindness. The initial dose of 40-60mg prednisolone should be given for 4-8 weeks followed by a slow taper over months if the clinical features remit. Sometimes intravenous methylprednisolone may need to be given in cases with recent or impending visual loss. Therapy may be needed for 2 years.<sup>15</sup>

### **Inflammatory Myopathies**

Inflammatory myopathies in the elderly carry significance due to their association with malignant disease. The mean age of onset of malignancy associated myositis is 60 years, the highest risk being for dermatomyositis followed by polymyositis and inclusion body myositis. Malignancy may precede, accompany or follow the diagnosis of myositis, usually developing within one year of each other. The site or type of malignancy is that expected for the age group and sex of the individual with the exception of ovarian cancer that is higher in women with dermatomyositis. Inclusion body myositis is exceedingly rare in India but is a common inflammatory myopathy in persons older than 50 years of age. The popular use of HMG CoA inhibitors (statins) alone or in combination with other lipid lowering agents in the elderly has the potential

for producing drug induced myositis.<sup>17-20</sup>

### **Fibromyalgia**

This disorder has an increasing prevalence with age and is predominantly seen in females. It presents with diffuse widespread non articular pain and is diagnosed by characteristic tender points over various parts of the body.<sup>14,21</sup>

1990 American College of Rheumatology Criteria for the diagnosis of Fibromyalgia<sup>21</sup>

3 months of widespread pain defined as:

Bilateral above and below the waist including axial skeletal pain

And

Pain to palpation with 4 kg pressure at a minimum of 11 out of 18 predefined tender points on both sides (the insertion of suboccipital muscles, anterior aspect of intertransverse spaces at C5-C7, midpoint of upper border of the trapezius, origin of the supraspinatus above the scapular spine near the medial border, second rib lateral to the costochondral junction, 2 cm distal to the lateral epicondyle, upper outer quadrant of the buttocks in the anterior fold of muscle, just posterior to the greater trochanteric prominence, the medial fat pad proximal to the knee joint line.

### **Articular disorders in the elderly**

At the outset, it is essential to distinguish an inflammatory disorder from non inflammatory ones. The cardinal signs of inflammation, systemic symptoms and laboratory evidence identify an inflammatory disorder. Classically, morning stiffness precipitated by prolonged rest, of over 60 minutes duration, improvement with activity and non steroidal anti inflammatory drugs would suggest such a disorder. The common disorders in this category are rheumatoid arthritis, gout, pseudogout, inflammatory osteoarthritis and infectious arthritis. The absence of evidence of inflammation would suggest osteoarthritis in which the stiffness is intermittent, precipitated by rest, exacerbated by activity, lasting less than 60 minutes and usually less than 30 minutes. Some cases may be traumatic or rarely some cases may be of pigmented villonodular synovitis. Inflammatory monoarticular disorders in the elderly are likely to be gout, pseudo gout or septic arthritis which are usually acute in onset. Polyarticular disease (>4 joints) may be rheumatoid arthritis or polyarticular gout and are usually chronic. Non inflammatory arthritis is usually

osteoarthritis.<sup>22</sup>

### **Rheumatoid arthritis (RA)**

The typical features of elderly onset rheumatoid arthritis (EORA) are an age of onset >60 years, an equal sex ratio, acute presentation of oligoarticular or polyarticular disease, absence of rheumatoid nodules, high ESR and a negative rheumatoid factor. This form of disease has a good prognosis. On the other hand, seropositive elderly patients with RA have a higher rate of complications and mortality as compared to those who are seronegative. After the age of 85 years, the disease is relatively mild. Early in the disease diagnostic difficulties from PMR can be overcome by assessment of anticyclic citrullinated peptide antibodies, which are positive in EORA. Despite comparable disease severity and activity the use of biologicals and combination disease modifying agents is less in the patients with EORA than in their younger counterparts. Notwithstanding concerns regarding the use of biologicals in the elderly, etanercept therapy has shown improvement in disease activity and function in some elderly populations.<sup>23-28</sup>

### **Osteoarthritis (OA)**

This disorder increases with advancing age and OA of the knee is the most common condition producing functional disability in the elderly. Nodal generalized OA is a polyarticular disease with Heberden's and Bouchard's nodes usually seen in menopausal females with a familial predisposition. Erosive or inflammatory OA may be confused with other inflammatory arthritides like RA as the presentation is sometimes abrupt. The radiologic erosions are central and not marginal as seen in RA. Involvement of the first carpometacarpal joint or metatarsophalangeal joint is common. Elderly people may have a rapidly progressive form of OA of the hip with 50% reduction in joint space width within two years. The ESR is usually less than 20mm per hour (Westergreen) and morning stiffness is <30 minutes except in the inflammatory form. Pain relief with non pharmacological therapy includes local capsaicin or non steroidal creams or gels. Oral Acetaminophen (Paracetamol) is safe while the non steroidal anti-inflammatory agents (NSAID) may have tendency to produce gastrointestinal bleeding in the elderly. Opioids (codeine or tramadol) and intra-articular steroids are also useful in short term. Intra-articular visco supplementation with hyaluronic acid or oral nutraceuticals like glucosamine and

chondroitin sulphates are symptomatic slow acting drugs for OA. Structure modifying or chondro protective drugs are also under evaluation as are stem cell and chondrocyte transplants. Surgery is an option in cases with persistent pain and limitation of activities.<sup>29-32</sup>

### **Crystal arthropathies**

**Gout:** Predominantly a disease of middle aged males; new onset gout is just as common in the elderly females after 60 years of age. Almost all patients over age 80 years with new onset disease are females. Typically, an acute monoarthritis with a classical presentation, this disease occurs in attacks with asymptomatic periods called intercritical gout and later progresses to chronic tophaceous gout. It may be precipitated by low dose salicylates or thiazide diuretics, chemotherapy of malignant disease or onset of renal failure. In the elderly, polyarticular disease sometimes resembling RA is more common as is involvement of the upper extremities and early appearance of tophi often at atypical sites. Joint aspiration in acute arthritis is diagnostic. In the elderly, colchicine and non steroidal anti inflammatory drugs are limited in use by side effects or co-morbid disease. However, if tolerated, the response to colchicine is a useful diagnostic test in the elderly. Systemic or intra-articular steroids may be an alternative in acute attacks while low doses of allopurinol are useful after the acute attack has subsided.<sup>33-35</sup>

**Pseudogout:** Chondrocalcinosis i.e. the deposition of crystals of calcium pyrophosphate dihydrate in the joint tissues increases with age. An acute form of disease producing mono or oligoarticular disease called pseudogout is common in the elderly. Unlike gout, larger joints like knee are involved. Some cases may have additive, symmetric or polyarticular disease. Occasionally, it may be associated with fever, chills, leucocytosis or elevated ESR. Diagnosis is by joint aspiration and evaluation for crystals. Treatment is with NSAIDs or short courses of oral or intra-articular steroids.<sup>33, 36</sup>

**Systemic lupus erythematosus:** It is uncommon in the elderly and the presentation is atypical with the more frequent manifestations being serositis, pneumonitis, neuropathy, myositis and Sjogren's syndrome. Drug induced SLE must also be considered.<sup>33</sup>

**Infectious arthritis:** Various risk factors for the development of infections in the joints include advanced

age (over 80 years), diabetes mellitus, recent joint surgery, prosthetic joint, skin infection, aspiration or injection of steroids, malignancy, immunocompromised state due to steroids or chemotherapy, or a joint replacement.<sup>37</sup>

### **The elderly patient with joint replacement**

Frequently the physician will see elderly patients who have undergone or are planning a joint replacement, usually of the knee or hip. Pre-operatively they may need evaluation of other medical conditions like cardiovascular diseases or diabetes mellitus. Early in the post operative period there may be haemarthrosis and minor wound healing problems. The serious problem is of deep or peri prosthetic infections, which may be of early onset (<3 months of surgery) or late onset (>3 months after surgery). There is a small but definite risk of postoperative deep infections in the knee replacement if the patient had received an intra-articular steroid injection 11 months prior to surgery. There is no consensus on whether antibiotic prophylaxis should be given to patients with prosthetic joints who are undergoing dental or other procedures likely to produce bacteremia. Some experts suggest use of antibiotics similar to those used in prevention of infective endocarditis within 2 years of implant procedure.<sup>37, 38</sup>

**Spinal problems:** Back pain is usually a disorder of middle age but is a common and disabling condition in the elderly also. In this population, its origin may be mechanical (degenerative disc disease with instability of the spine, lumbar spine stenosis and disc displacement), osteoporotic (with or without compression fractures) or systemic disorders (infections, primary or metastatic tumors).<sup>39</sup>

**Reflex sympathetic dystrophy:** This disorder is characterized by regional limb pain, swelling, vasomotor instability and focal osteoporosis. Antecedent factors may include stroke, myocardial infarction, trauma or an underlying malignancy. It is a result of sympathetic dysfunction.<sup>40</sup>

**Remitting seronegative symmetric synovitis with pitting edema (RS3PE):** This disorder seen in the elderly presents as joint swelling (especially of hands and feet), with pitting edema. It may herald the onset of PMR, dermatomyositis/polymyositis or late onset spondyloarthritis. Fever, weight loss and failure to respond to steroids indicate a search for malignancy.<sup>40</sup>

**Falls and injuries in the elderly:** A fall is not a normal part of aging but a sentinel event in the elderly patient's life resulting in injury, with fear of falling again and consequently decreases in activities. As many as 50% of older patients admitted to hospitals with falls die within one year.<sup>7</sup> Of women with inflammatory polyarthritis one in three had a fall in the previous year and these were more frequent in those over 75 years of age.<sup>41</sup> Therefore, joint problems are an important predisposing factor for falls in the elderly and should be addressed early in the evaluation process.

### **General management principles in the older patient:<sup>42</sup>**

1. Patients often belittle their symptoms or conceal their functional limitations.
2. Identify the patient's psychological and socio-economic status.
3. Exercise is of benefit in mild to moderate arthritis.
4. Older arthritis patients have an increased risk of osteoporosis.
5. Older patients may be taking multiple medications including herbal preparations.
6. Non pharmacological treatment has a major role to reduce polypharmacy and side effects of drugs.
7. Avoid drug prescribing cascades i.e. misinterpretation of an adverse drug reaction as a new medical condition and adding new drugs instead of withdrawing the culprit drug.
8. Non steroidal anti inflammatory drugs (NSAIDs) have risks of gastrointestinal bleeding, renal and sometimes hepatic toxicity. Drugs should be prescribed in lowest tolerable doses and NSAIDs preferably given with meals. Regular monitoring with laboratory tests is useful.
9. Long term use of steroids has adverse effects in the elderly. In some situations a short course of low dose steroids in a disease like RA may be appropriate to improve functional status.
10. Paracetamol with or without low dose narcotics is useful. Tramadol provides good analgesia with fewer side effects than codeine.

11. There is not much experience in the use of TNF inhibitors in persons over 70 years of age.

Besides early diagnosis and prompt treatment of disabling rheumatic problems, the goal of the clinician should be to return the patient to the previous level of functional activity in the shortest possible time. Longer periods of disability lead to deterioration in functional status of the elderly with adverse long term consequences.

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