

Arthritis: Rheumatoid Arthritis, Osteoarthritis and Gout

OBJECTIVES:

At the conclusion of this course, the learner will be able to:

1. List several types of arthritis.
2. Briefly describe rheumatoid arthritis and gout.
3. Detail rheumatoid arthritis, osteoarthritis and gout in terms of their etiology, prevalence, pathophysiology, signs and symptoms, complications, diagnosis, prevention and treatment, including pharmacological interventions and the latest research about hormone replacement therapy and the cardiovascular side effects of the COX-2 inhibitors and the effect of this research on the withdrawal some medications from the market and stronger warnings.
4. Describe some arthritis resources and associations and the services that they provide.

INTRODUCTION

Arthritis is an inflammatory disease of the bone joints that is marked with a limitation of movement, swelling and pain. It can be caused by an infection in the joint, a buildup of uric acid or simply with the degeneration of a joint or joints as an individual grows older.

Arthritis is the number one chronic disorder that leads to disability in our country among people 15 years of age and older. In 2005, it was estimated that 66 million people, that is, one out of every 3 adults in our nation is affected by arthritis. Nationally, it affects about 300,000 children and it is estimated that it costs the United States in excess of \$86.2 billion every year. Women are more affected than males. (Arthritis Foundation, 2004)

TYPES OF ARTHRITIS

There are more than 100 different types of arthritis. Some of these types include the below.

- *Osteoarthritis*- is the most common form of arthritis. It is a degenerative joint disease in which the cartilage that covers the ends of bones in the joint deteriorates, causing pain and a loss of movement as a result of the bone rubbing against bone rather than cartilage.
- *Rheumatoid arthritis*- is one of the most disabling forms of arthritis. It affects primarily women. This form is an autoimmune disease where the joint lining becomes inflamed as a result of the person's immune system.
- *Gout*- primarily affects mostly men. This form of arthritis affects small joints, specifically the great toe. A defect in body chemistry, that is, a buildup of uric acid leads to gout. This form can be successfully controlled with dietary changes and medications.
- *Ankylosing spondylitis*- when the bones of the spine become inflamed they fuse together, thus leading to ankylosing spondylitis which affects the spine.
- *Juvenile arthritis*- this term encompasses all types of arthritis that can occur among the pediatric population. Some of these types are ankylosing spondylitis, juvenile rheumatoid arthritis and juvenile lupus among other types.
- *Systemic lupus erythematosus (lupus)*- is serious systemic disorder that inflames and damages joints as well as other connective tissue throughout the entire body.
- *Scleroderma*- is a disease that attacks the body's connective tissue. It causes a hardening and thickening of the skin.
- *Fibromyalgia*- affects primarily women. It leads to widespread pain that affects muscles and their attachments to the bone. (Arthritis Foundation, 2004)
- *Septic arthritis*- develops when a bacteria such as streptococcus (pneumoniae), staphylococcus, group B streptococcus, Mycobacterium tuberculosis and candida albicans. It occurs most often among children less than 3 years of age and primarily affects the hip. The onset is generally quite rapid with a low grade fever, severe joint pain and joint swelling.
- *Psoriatic arthritis*- can be mild affecting only a couple of joints or it can be more severe affecting the spine. Genetics may play a role in this form of arthritis. Generally, people with psoriasis

have a greater incidence of arthritis than those without this skin disorder.

- *Fungal arthritis*- this rare form of arthritis is also referred to as mycotic arthritis. Fungi that lead to this form include blastomycosis, histoplasmosis, candidiasis, coccidioidomycosis, sporotrichosis, and cryptococcosis. The infection typically begins in the lungs and then progresses. The knees are most often affected. Immunocompromised patients are at greatest risk. (MDchoice, Inc., 2005)

OSTEOARTHRITIS, RHEUMATOID ARTHRITIS AND GOUT

Osteoarthritis, known as degenerative joint disease, is the most commonly seen form of arthritis among the elderly population. Osteoarthritis results from the wearing out or deterioration of the smooth cartilage lining of the joint. This loss of cartilage makes the joints rougher than they had been when the cartilage was in place. Although it can also affect the hands, degenerative osteoarthritis is most often seen in the knees, spine and hips, the weight bearing joints of the body. This form of arthritis cannot be cured but those that suffer from it rarely become bedridden or crippled as a result of it. Post menopausal osteoarthritis is the result of the depletion of hormonal estrogen after menopause. It is a variation of the larger diagnosis of osteoarthritis from other causes.

Rheumatoid arthritis also involves painful swelling of the joints but it is usually associated with the smaller, non weight bearing joints of the body. Also, it is not usually associated with old age onset, but instead, it primarily begins in the young adult from ages 30 to 40 from unknown causes. It can also develop in young child. This form of rheumatoid arthritis is referred to as Still's disease or juvenile rheumatoid arthritis. Unlike osteoarthritis, rheumatoid arthritis is associated with physical deformities and crippling.

Gout is quite different from osteoarthritis and rheumatoid arthritis. Gout is a disease or disorder that occurs when the body cannot excrete the uric acid it produces because the body is overproducing it or the kidneys have a diminished ability to filter it out and excrete it. When uric acid builds up in the body the joints, as well as soft tissues, become affected by it. The buildup of uric acid in gout causes very painful attacks of arthritis and it is accompanied by a high concentration of uric acid in the bloodstream and the formation of uric acid crystals in the affected joints.

RHEUMATOID ARTHRITIS

Sadly, rheumatoid arthritis is a destructive and chronic inflammation of the joints that affects young adults and children, most commonly occurring in females. It is marked with symmetrical swelling in the smaller joints of the body such as the ankle, hand and wrist. The onset of the deforming and crippling disease can be sudden and unexpected but most often it is somewhat gradual. This disorder is progressive and often without a hoped for remission despite treatment.

About 6.5 million people in the United States are affected with rheumatoid arthritis. Women are affected up to three times more than men. Although the onset can occur at any age, the onset is most frequent among those between 25 and 50 years of age.

Although the cause of this form of arthritis is largely unknown, there appears to be a genetic basis among the white race in that pentapeptide in the HLA-DR and locus of class II histocompatibility genes have been identified. (Langford & Thompson, 2000; Merck & Co., 2005)

PATHOPHYSIOLOGY

This disease progresses from joint inflammation to edema and congestion in the joint's capsule and the synovial membrane. Later, granulation tissue develops and destroys the capsule and cartilage. This fibrous granulation leads to the deformity and immobilization of the affected joint(s). This degenerative process can also affect major bodily organs such as the kidneys, eyes, lungs and the heart. (Langford & Thompson, 2000; Merck & Co., 2005)

SIGNS AND SYMPTOMS

Some of the *early* signs may include:

- a low grade fever,
- malaise,
- fatigue,
- weight loss and
- anorexia.

The *middle stage* signs and symptoms are:

- tenderness in affected joints,
- joint pain and stiffness lasting 30 minutes or more after awakening and/or after a period of immobility,
- bilateral, symmetrical involvement of the small joints of the hands and/or foot, the elbows, wrists and/or the ankles,
- afternoon malaise and fatigue,
- decreasing joint function,
- contractures, especially flexion contractures,
- deformities such as those of the fingers, and
- carpal tunnel syndrome,

The *late* signs and symptoms of rheumatoid arthritis are:

- tenderness in affected joints,
- joint pain,
- subcutaneous and visceral nodules,
- fever that is typically low grade,
- vasculitis leading to leg ulcers,
- dryness of the mucus membranes,
- pericarditis,
- splenomegaly,
- pneumonitis,
- episcleritis, and
- lymphadenopathy. (Langford & Thompson, 2000; Merck & Co., 2005)

DIAGNOSIS

The American Rheumatoid Association (ARA) has established diagnostic criteria. They are as follows:

- 1) morning stiffness in and around joints lasting at least 1 hour before maximal improvement;
- 2) soft tissue swelling (arthritis) of 3 or more joint areas observed by a physician;
- 3) swelling (arthritis) of the proximal interphalangeal, metacarpophalangeal, or wrist joints;
- 4) symmetric swelling (arthritis);
- 5) rheumatoid nodules;

6) the presence of rheumatoid factor; and

7) radiographic erosions and/or periarticular osteopenia in hand and/or wrist joints.

Criteria 1 through 4 must have been present for at least 6 weeks. Rheumatoid arthritis is defined by the presence of 4 or more criteria, and no further qualifications (classic, definite, or probable) or list of exclusions are required." (Arnett FC, Edworthy SM, Bloch DA, McShane DJ, Fries JF, Cooper NS, Healey LA, Kaplan SR, Liang MH, Luthra HS, et al., 1988)

In addition to a complete physical exam and medical history, the following diagnostic tests can be done to facilitate the diagnosis of rheumatoid arthritis.

- *Blood tests* may reveal elevated white blood cells (WBCs), hypochromic [anemia](#), thrombocytosis, polyclonal hypergammaglobulinemia, the presence of γ -globulin antibodies (the "rheumatoid factors") which is positive in 95% of the cases, and an elevated erythrocyte sedimentation rate which occurs in 90% of the cases.
- *Synovial fluid* takes on an opaque color with decreased viscosity. The WBCs are between 3,000 and 50,000/ μ L.
- Initially the *x-ray* may only reveal soft tissue swelling. Later, marginal erosions and narrowing of the joint space's articular cartilage may be seen. (Langford & Thompson, 2000; Merck & Co., 2005)

TREATMENT

The goals of treatment for rheumatoid arthritis aim to control the inflammatory process and to relieve the troublesome and painful symptoms. Currently, there is no treatment available to repair any existing damage to the joints.

Treatment consists of one or more of the following modalities, as based on the unique needs of the patient.

Rest

During the active painful stages of the disease, complete bed rest is necessary. Otherwise, regular rest and sleep is recommended.

Nutrition

A regular, nutritious diet is necessary. Plant oil and/or fish oil supplements may be helpful to some because they decrease the production of prostaglandins.

Exercise

Range of motion and active exercise (ambulation and other exercises) should be done after the inflammation has subsided in order to prevent flexion contractions. Serial splinting, orthopedic interventions and intensive exercise are necessary once flexion contractures become established so prevention is vitally important. Passive range of motion should be done during episodes of acute inflammation to prevent contractures, again, within the limits of pain. These exercises preserve and restore normal or near normal range of motion, muscle mass and muscular strength.

- *Physical therapy* is often indicated and ordered. Some of the treatments that are used include, cool, moist compresses; paraffin treatments and paraffin gloves to reduce the swelling and pain; and endurance and strength exercises. Ambulatory assistive devices, such as a walker, and splints may also be incorporated into the plan of care. Orthopedic shoes with special inserts, including bars, may help to increase mobility and decrease pain. Splints are also used to decrease inflammation and pain.
- *Occupational therapy* may also be incorporated in the plan of care to enable the patient to better perform the activities of daily living. Self help device, such as grasping tools, may be used.

Medications

- *Salicylates and nonsteroidal anti-inflammatory medications (NSAIDs)*. These medications serve as both anti-inflammatory agents and analgesics. Examples are aspirin, ibuprofen, diclofenac, fenoprofen, flurbiprofen, indomethacin, ketoprofen, meclofenamate, nabumetone, naproxen, oxaprofen, piroxicam, sulindac and tolmetin.

Some of the side effects and adverse drug reactions to the NSAIDs are GI irritation, cardiovascular complications, blood dyscrasias, nephrotoxicity (oliguria, azotemia, hematuria and dysuria), abdominal pain, cholestatic hepatitis, anorexia, dizziness and drowsiness. Antacids, H₂ blockers and sucralfate can be given between meals for mild GI side effects of aspirin. 100 to 200 µg bid to qid of misoprostol or a proton pump

inhibitor can be used with aspirin and other NSAIDs to reduce the risk of GI bleeding among high risk patients.

The NSAIDs are contraindicated among patients with asthma, severe liver and/or renal disease, and hypersensitivity. They can be used with caution among the elderly and children, during lactation and pregnancy and for patients with GI, cardiac and/or bleeding disorders.

The patient's blood, renal and hepatic function must be monitored when NSAIDs are used. Baseline hearing and eye exams are also recommended so that changes can be identified. Toxicity may be signaled with tinnitus and/or blurred vision. Current concerns about COX-2 inhibitors and NSAIDs are described below.

- *Gold compounds.* When the NSAIDs have not effectively reduced the pain and swelling after 2 to 4 months, gold or methotrexate is generally considered to relieve the pain, reduce the inflammation, decrease further bony erosion, and to modify the progression of the disease to a clinical remission.

Auranofin is the oral preparation of gold. Parenteral gold preparations include gold thioglucose and gold sodium thiomalate. These preparations are given IM every week, starting with 10 mg for the first week which is increased to 25 mg the next week and then increased to 50mg a week or more until the therapeutic effect is achieved. Prolonged maintenance therapy can sustain an improvement for several years, however, a relapse can be expected in 3 to 6 months if and when the medication is stopped,.

A baseline Hb level, platelet count, total and differential WBC count as well as a urinalysis should be done prior to the administration of gold, Thereafter, these diagnostic tests should be repeated every week for the first month and then two times a month.

Gold is contraindicated among patients who have significant renal disease, hepatic disease and/or blood dyscrasias.

Some of the toxic reactions to gold include stomatitis, albuminuria, pruritus, dermatitis, agranulocytosis, aplastic anemia, and thrombocytopenic purpura. Hepatitis, diarrhea, neuropathy and pneumoniti are less common side effects. Pruritis and eosinphilia (more than 5%) can be the precursor of

a rash and a red flag of impending danger - a rash and dermatitis that can lead to deadly exfoliation. The gold should be held temporarily if these side effects occur and the patient should be given prednisone orally or a topical corticosteroid if the reaction is mild. Dimercaprol, a gold chelating medication, should be given for severe reactions.

Auranofin, which is an oral gold compound, can also be administered for rheumatoid arthritis although it is not as effective as parenteral gold compounds. A baseline Hb level, platelet count, total and differential WBC count and a urinalysis should also be done. Thereafter, these diagnostic tests should be minimally repeated every month. The side effects oral gold are GI symptoms and diarrhea. Mucocutaneous and renal side effects are less than parenteral gold, however, they can still occur.

The usual dosage is 6 mg orally once a day or 3 mg bid. This dosage can be increased to 3 mg three times a day for 3 months, if, after 6 months, the 6 mg daily dosage does not achieve the desired therapeutic effect.

- Oral penicillamine produces many of the benefits that gold does, in fact, it is often used when gold fails to produce its desired effects or the patient is experiencing toxic side effects to the gold. However, penicillamine has to be discontinued more often than gold because of its side effects.

The side effects of this medication include proteinuria, bone marrow suppression, nephrosis, polymyositis, Goodpasture's syndrome, myasthenia gravis, a lupus type syndrome, a foul taste and a rash. The risk of side effects can be decreased if the dosage is started low and kept as low as possible as long as the desired effects have been realized.

The initial daily dosage of penicillamine is 250 mg. This dose should be continued for 1 to 3 months after which the dosage is 500 mg a day for another 1 to 3 months. The dosage can be increased to 750 mg a day if these recommended dosages do not produce and maintain the desired effect. Again, the lowest possible dose should be used.

- *Hydroxychloroquine* is another medication that can be used to treat rheumatoid arthritis. Its toxic side effects include myopathy, dermatitis and retinal degeneration, which is usually reversible. These side effects are generally not as pronounced as

they can be with gold and penicillamine, nonetheless, irreversible retinal degeneration can occur. Visual field testing is done before the therapy begins and then every 6 months as long as the hydroxychloroquine is being taken.

The initial dosage of hydroxychloroquine 200 mg orally with breakfast and dinner (bid). If, after 6 to 9 months of treatment, the patient does not favorably respond to the medication, this dosage should be decreased to 200 mg a day.

- *Sulfasalazine*, a medication that has and continues to be used for colitis, is now being used for rheumatoid arthritis. The initial dosage of this enteric coated tablet is 500 mg a day with an increasing dosage of 500 mg every week until the dosage is 3 to 3 g per day. Serum chemistries and CBC must be monitored throughout the course of this therapy.

The toxic side effects of this medication are neutropenia, hemolysis, rash, gastric symptoms and hepatitis.

- *Corticosteroids* are, at least during the initial phases of therapy, highly effective. Unfortunately, their usefulness and benefits decrease over time and a rebound back to active disease occurs when the corticosteroid therapy is ceased. These medications should only be used when others fail because their long term side effects are quite serious.

Corticosteroids are contraindicated and/or used with caution among patients who have diabetes, untreated or untreatable infections, peptic ulcer, TB, fungal infections, amebiasis, hypersensitivity, seizures, glaucoma, CHF, hypertension, impaired renal function, myasthenia gravis and ulcerative colitis. Cautious use is also recommended with the elderly, children, lactation and pregnancy.

Some of the adverse reactions and side effects associated with corticosteroids include insomnia, euphoria, behavioral changes, peptic ulcer (GI irritation), sodium and fluid retention, hypokalemia, hyperglycemia, and carbohydrate intolerance (metabolic reactions). GI symptoms can be prevented when the dose is administered or taken with food or milk. Monitor blood sugar, potassium, weight, I & O, plasma cortisol levels, adrenal insufficiency and for any signs of infection. The patient must also be assessed for mood changes, particularly depression.

The recommended adult dosage of prednisone should not exceed 7.5 mg per day unless the patient has severe and systemic symptoms, such as pericarditis or vasculitis.

- *Intra-articular injections* of corticosteroid esters offer some the temporary relief of local synovitis. Among the preparations used are triamcinolone hexacetonide and prednisolone tertiary-butylacetate. Soluble 21-phosphate preparations of prednisolone and dexamethasone are not recommended. These medications have a very short term of actions
- *Immunosuppressive/cytotoxic agents* decrease inflammation and they also allow a reduced dosage of a corticosteroid. Some of the side effects include bone marrow suppression, liver disease, azathioprine, malignancy and pneumonitis.

The dosage of methotrexate is 2.5 to 20 mg in a single dose once weekly, starting at 7.5 mg a week with gradual increases as needed in order to achieve the desired dosage. Liver function must be monitored throughout the course of therapy. A liver biopsy should also be done when the liver function test is not normal and the patient needs to continue the methotrexate. This medication is contraindicated among heavy drinkers and diabetics.

The initial dosage of azathioprine is 1 mg/kg/day or 50 to 100 mg per day that can be given bid or once a day. The dosage can be increased by 0.5 mg/kg/day after 6 to 8 weeks for every 4 week interval until a maximum of 2.5 mg/kg/day or when the therapeutic effect is achieved. Again, the lowest dosage possible should be used.

Cyclosporine is effective in treatment of rheumatoid arthritis and may be especially useful in combination with other slow-acting drugs. Dosages generally should not exceed 5 mg/kg/day to minimize toxic effects on blood pressure and renal function.

Etanercept, which is a tissue necrosis factor antagonist, is given with a dosage of 25 mg subcutaneously two times a week. This medication is reconstituted. Do not shake the bottle, swirl it or gently rotate it. Additionally, the injection sites must be rotated at least 1 inch away from a previous site.

Some of the side effects include dyspepsia, abdominal pain, rash, cough, an injection site reaction, headache, dizziness,

pharyngitis, sinusitis, rhinitis, sepsis, and hypersensitivity. It should be used cautiously with pregnant women.

- *Surgery.* A synovectomy may be done to maintain joint function and to relieve some of the pain and inflammation; the excision of subluxations of the metatarsophalangeal joints or the neck may be done in the presence of severe pain; and an osteotomy may help to change the patient's weight bearing surfaces.

(Langford & Thompson, 2000; Merck & Co., 2005)

RECENT NEWS ABOUT COX-2 INHIBITORS AND NSAIDS

In 2005, research indicated that some popularly used and intensely marketed COX-2 inhibitors, used for arthritis, increased the risk of cardiovascular events. On April 7, 2004 the U.S. Food and Drug Administration (FDA) asked Pfizer Inc. to voluntarily take Bextra off the market and to place strong warnings on Celebrex as a result of this research. This advice news lead to the withdrawal of Bextra (valdecoxib) from the market and to the strong warning that Celebrex (celecoxib), too, is associated with cardiovascular complications. Vioxx (rofecoxib) had been previously taken off the market by Merck because of its cardiovascular disease risk as well.

The FDA has also asked the numerous manufacturers of over the counter NSAIDs, other than aspirin and acetaminophen, to include additional information about the potential for gastrointestinal and cardiovascular side effects and risks.

At the current time it appears that the cardiovascular side effects are dose dependent, therefore, decisions about whether or not to take available NSAIDs and Celebrex should be up to the patient and their physician. Additionally, if the decision is to use or continue to use one of these medication, the dosage should be the lowest possible to achieve the desired effect. (Arthritis Foundation, 2005)

OSTEOARTHRITIS

Osteoporosis is a "generalized, progressive diminution of bone density (bone mass per unit volume), causing skeletal weakness, although the ratio of mineral to organic elements is unchanged." (Merck, 2005)

There are three types of osteoporosis:

- Primary osteoporosis Type 1
- Primary osteoporosis Type 2
- Secondary osteoporosis

Type 1 primary osteoporosis is six times more prevalent in women than in men. This type typically appears between the ages of 51 and 75 years of age. It is associated with distal radius fractures (Colles' fractures) and vertebral crush fractures.

Type 2 primary osteoporosis is twice as common in women than men and its onset is generally after 60 years of age. This type is a part of the normal aging process in that it results from decreasing numbers and activity levels of osteoblasts, rather than an increase of osteoclast activity. It is associated with femoral neck fractures, fractures of the pelvis, humerus, vertebrae and tibia. Some people, particularly women, can have type 1 primary osteoporosis and type 2 primary osteoporosis simultaneously.

Secondary osteoporosis can be caused by a number of diseases, medications, and other conditions, such as prolonged space flight weightlessness. It accounts for about 5% of all osteoporosis cases. (Langford & Thompson, 2000; Merck & Co., 2005)

ETIOLOGY AND PREVALENCE

The cause of primary osteoporosis is not known. The possible causes of secondary osteoporosis and osteoarthritis are:

- An endocrine disorder (diabetes mellitus, hypogonadism, hyperthyroidism, hyperparathyroidism, hypogonadism, hyperprolactinemia, and an excess of glucocorticoids)
- Some medications (diltiazem, heparin, glucocorticosteroids, barbiturates and ethanol),
- Some diseases (rheumatoid arthritis, renal or liver disease, malabsorption syndrome, malabsorption syndromes, sarcoidosis malignancies, chronic obstructive pulmonary disease, and sarcoidosis), and
- Long periods of immobility and weightlessness (calcium leaves the bones).

Women are affected with osteoporosis more than men. About 50% of postmenopausal women have osteoporosis. Of these women, 33% will have an osteoporotic fracture during their lifetime. (Langford & Thompson, 2000; Merck & Co., 2005)

Some of the risk factors associated with primary osteoporosis include:

- A sedentary lifestyle

- Prolonged periods of immobility
- Menopause (surgical or natural)
- Late menarche
- Early menopause
- A loss of ovarian function
- Gender (women are at greater risk than men)
- Race (the white and Asian race are at greatest risk)
- A family history of osteoporosis
- Malnutrition
- Lack of calcium
- Lack of sufficient vitamin D
- High dietary sugar and/or red meat
- Anorexia
- Intense exercisers, particularly when the person is also underweight
- Cigarette smoking
- Coffee and alcohol use and abuse (Langford & Thompson, 2000; Merck & Co., 2005)

PATHOPHYSIOLOGY

The resorption of bone exceeds the rate of bone formation when osteoporosis occurs. The bone mass declines, cortical thickness diminishes and the size and number of trabeculae decline. (Merck & Co., 2005)

SIGNS AND SYMPTOMS

Individuals are typically asymptomatic early in the disease. The first symptom is usually a dull, aching, constant pain in the bones, particularly the back and chest. The pain may radiate down the leg, and muscle spasms may be present. Later in the disease, the back pain may become chronic, unrelenting, dull and aching. As the spinal column mass diminishes, dorsal kyphosis and cervical lordosis (dowager's hump) increase, which can lead to one or more compression fractures of the spine and a reduction in height. The most common affected vertebrae are those at the T-8 level and below. Other fractures may also occur with minimal or no trauma, particularly the hip and the wrist in an attempt to break a fall.

Other *early signs* and symptoms are:

- aching joint pain that can get worse with exercise or as the day and its normal activities progress and

- stiffness after a period of immobility

Some of the *middle stage* signs and symptoms include lessening joint motion as well as joint:

- crepitus,
- tenderness,
- grating,
- flexion contractures, and
- enlargement.

The *late* signs and symptoms are:

- an increase in the duration and extent of pain,
- joint tenderness upon palpation,
- pain with passive range of motion, and
- joint deformity and subluxation. (Langford & Thompson, 2000; Merck & Co., 2005)

THE COMPLICATIONS OF OSTEOPOROSIS

The complications of osteoporosis include:

- deformities,
- immobility,
- spinal damage,
- fractures (Langford & Thompson, 2000; Merck & Co., 2005)

DIAGNOSIS

Osteoporosis is diagnosed with a clinical assessment, the presence of bone and/or joint pain, laboratory findings, x-ray, photon absorptiometry and CT scans.

Laboratory findings

- normal PTH levels or low levels with type I patients and high with type II patients when calcium absorption is low or when hypercalciuria is present
- urinary excretion of pyridinium peptide, hydroxyproline-containing peptides (signs of increased bone destruction)
- uptake of technetium-99m methylene diphosphonate

X-Ray

- decreased radiodensity as the result of trabecular loss
- decreased bone density is visible when more than 30% of the bone is lost

Photon absorptiometry and CT scans

- decreased bone density (Langford & Thompson, 2000; Merck & Co., 2005)

PREVENTION

Some of the things that can be done to prevent osteoporosis and osteoarthritis include:

- regular exercise,
- sufficient intake of calcium and vitamin D (women should take or consume a prophylactic daily 1000 mg of calcium and 1500 mg per day after osteoporosis is diagnosed,
- take or consume 400 international units (IU) of vitamin D and
- bone density tests every 1 to 3 years after age 49 for early detection, especially for women. (Langford & Thompson, 2000; Merck & Co., 2005)

TREATMENT

Exercise

A regular exercise routine, as approved by the physician, as well as the following is recommended to strengthen the muscles, maintain joint mobility, and to decrease the rate of calcium loss.

- weight bearing exercises
- hyperextension exercises
- resistance exercises
- range of motion (active, passive and/or active assistive), as indicated by the patient's condition,
- isometric exercises, and
- general conditioning exercises. (Langford & Thompson, 2000; Merck & Co., 2005)

Physical Therapy Interventions

These treatment interventions aim to prevent deformity, increase joint mobility, decrease pain, restore lost function, in some cases, and to

maximize the patient's ability to perform their activities of daily living. Some patients can also benefit from assistive devices, such as a grasper. Most of these interventions can be independently done in the home without the services of a physical therapist:

- heat and massage for muscle spasms
- ambulation assistance with a walker or cane
- transcutaneous electrical nerve stimulation (TENS) (Langford & Thompson, 2000; Merck & Co., 2005)

Nutrition

A regular, nutritious diet that is high in protein is recommended. Women should take or consume 1500 mg of calcium a day and men should take or consume 1,000 to 3,500 mg of calcium a day if they are not absorbing calcium in a normal manner.

Vitamin D should be taken concurrent with calcium. The dosage can range from 400 or 800 IU per day and up to 50,000 IU once or twice a week, as based on the patient's 25 hydroxy vitamin D and 1,25 dihydroxy vitamin D level. Serum and urinary calcium levels should be monitored when high doses are given since hypercalcemia, hypercalciuria, and renal failure can occur. (Langford & Thompson, 2000; Merck & Co., 2005)

Medications

- *Hormone Replacement Therapy.* Estrogen supplements can be considered for postmenopausal women without a uterus and estrogen-progesterone combinations can be considered for postmenopausal women with an intact uterus. Testosterone replacement therapy is an option for older men at risk for primary osteoporosis type 2.

Raloxifene, an estrogen-like drug, can also be considered. (Merck & Co., 2005)

- Salicylates and nonsteroidal anti-inflammatory medications (NSAIDs). These medications were detailed above.
- *Bisphosphonates* inhibit bone resorption. Fosamax (alendronate) is a bisphosphonate that is used for osteoarthritis among

postmenopausal women as well as for those with Paget's disease. The dosage for postmenopausal women is 10 mg every day orally. This medication must be taken with a full glass of water on an empty stomach. Additionally, the patient should be instructed to remain upright for at least 30 minutes after taking dose in order to prevent esophageal irritation.

Some of the side effects associated with bisphosphonate medications include:

- anemia
- hypomagnesemia
- hypophosphatemia
- hypokalemia
- anorexia
- nausea and vomiting
- abdominal pain
- headache
- constipation
- bone pain
- esophageal ulceration
- hypertension and fluid overload

It is contraindicated with hypocalcemia and hypersensitivity. It can be used with caution among children and those that are lactating or pregnant. Cautious use is also recommended if the patient has ulcers, gastritis and/or esophageal disease. Electrolytes and renal function must be assessed throughout the course of therapy. (Merck, 2005; Skidmore-Roth, 2004)

- *Selective estrogen receptor modulator (Evista)*. This medication decreases the resorption of bone and decreases bone turnover. The dosage is 60 mg a day. Some of the side effects include nausea, vomiting, anorexia, diarrhea, hot flashes, depression, migraine headaches, insomnia, vaginitis, weight gain, peripheral edema, leg cramps, sinusitis, pharyngitis, laryngitis, and others. It is contraindicated during pregnancy and lactation as well as for those with a hypersensitivity to it. Cautious use is necessary if the patient is affected with hepatic disease and/or venous thrombosis. It is recommended that daily weights, blood pressure and hepatic function tests be monitored throughout the course of therapy. (Skidmore-Roth, 2004)

- *Salmon calcitonin* can be an alternative when estrogen therapy is contraindicated or refused. It is available in 2 forms, that is, nasally and parenterally. The nasal dosage is one spray (200 U) per day in alternating nostrils. The parenteral dose is 100 IU subcutaneously daily or every other day. Both forms should be taken concurrently with calcium and vitamin D supplementation. (Merck, 2005)
- *Sodium fluoride*, with a dosage of 50 mg per day, concurrent with 1g or more of calcium appears to increase bone mass, but because it decreases bone density and makes bones more fragile, it is not a drug of choice. (Merck, 2005)
- *Androgen*. Short term therapy, of less than 3 months, is sometimes considered when the patient is plagued with uncontrollable fractures. Because androgenic anabolic steroids (stanozolol and nandrolone) have the risk of hepatotoxicity and can lower the concentrations of lipoproteins, their use is limited despite the fact that they do increase bone density in women. Men also take androgens for replacement treatment when there is an androgen deficiency. (Merck, 2005)

GOUT

ETIOLOGY AND PREVALENCE

The cause of gout is unknown but a number of things appear to lead to the under secretion and the over production of uric acid, those things that lead to and characterize this form of arthritis.

Some of these factors include:

- genetics (fructose intolerance, increased activity of hypoxanthine guanine phosphoribosyl transferase and the hyperactivity of phosphoribosyl pyrophosphate);
- environment (diuretics, ethanol abuse, a diet high in purines, and extreme muscular exertion);
- some diseases (sickle cell anemia, diabetes mellitus, hypertension, polycythemia, renal disease and leukemia) and;
- the absence of the enzyme uricase.

The more developed nations of the world have a greater incidence of gout than undeveloped nations and men are affected with gout more than women. It is rare in women prior to menopause and its appearance in women after menopause appears to be associated with the use of diuretics. More severe symptoms are found among those that have had a bout of gout before the age of 30. (Langford & Thompson, 2000; Merck & Co., 2005)

PATHOPHYSIOLOGY

An overproduction of uric acid and an undersecretion of uric acid lead to gout. Crystals of monosodium urate form when uric acid builds up in the system. When these crystals are deposited into tissues surrounding peripheral joints, such as tendons, cartilage and ligaments and in other tissue, such as the ear, the person is affected by gout. These crystals are then periodically released from time to time, for some unknown reason, during an acute attack of inflammation. Over time, the monosodium urate crystals can also be deposited in organs, such as the kidney, and in larger joints. (Langford & Thompson, 2000; Merck & Co., 2005)

SIGNS AND SYMPTOMS

An acute attack of gout can occur at any time without any warning but it sometimes follows a stressor (physical or emotional), surgery, an overabundance of foods high in purines, alcohol, an infection and fatigue.

The first sign is usually nocturnal pain in one or more peripheral joints. The great toe is affected most often, however, it can also affect the knee, ankle, instep, wrist, and elbow.

Other signs and symptoms include:

- acute pain which can be very severe,
- redness,
- swelling,
- tenderness,
- warm, shiny, tense purple or red skin color over the affected joint(s),
- tachycardia,
- malaise,

- chills,
- fever,
- leukocytosis, and
- limited joint movement. (Langford & Thompson, 2000; Merck & Co., 2005)

THE COMPLICATIONS OF GOUT

Acute attacks of gout can occur several times a year unless prophylactic treatment is given. Eventually, without treatment, chronic arthritis, chronic joint pain, erosive, permanent joint deformity, and limitations of joint mobility and function can occur.

The joints that are most often affected are those of the feet and hands, however, the shoulder, cervical spine, sacroiliac, hip and sternoclavicular joints can also be affected with gout. Cyclosporine induced gout typically begins in the larger central joints, like the sacroiliac, hands and hip. It can also damage the renal tubules.

Urolithiasis (uric acid or calcium oxalate stones) occurs in approximately 20% of people with gout. Obstruction, infection, renal dysfunction can follow. (Langford & Thompson, 2000; Merck & Co., 2005)

DIAGNOSIS

The diagnosis of gout is based on the following data:

- physical exam
- elevated serum uric acid (although about 30% of patients have normal levels)
- the presence of urate crystals in the synovial fluid
- the presence of crystals on compensated polarized light microscopy
- a response to colchicines in 24 hours or less during an acute attack
- visible tophi on an x-ray (tophi less than 5 mm in diameter are not visible on an x-ray)
- the presence of subcutaneous tophi (Langford & Thompson, 2000; Merck & Co., 2005)

PREVENTION

Daily prophylactic doses of colchicine and allopurinol are used to prevent recurring attacks of gout when the patient is affected with chronic gout. (Langford & Thompson, 2000; Merck & Co., 2005)

TREATMENT

The goals of treatment include:

- the prevention of acute attacks,
- ending an acute attack when it does occur,
- the prevention of further crystal deposits and
- eliminating existing tophi.

Coexisting conditions, such as hyperlipidemia, diabetes, obesity and hypertension must be controlled and managed.

Surgery

At times, large crystal deposits, referred to as tophi, are surgically removed. (Merck & Co., 2005)

Medications

- *Colchicine* is a uricosuric medication used for both acute attacks of gouty arthritis and chronic gout that is accompanied by recurrent and frequent acute attacks. Its mechanisms of action lower serum uric acid levels by inhibiting the reabsorption of uric acid.

When used for the treatment of acute gout attacks, the response to colchicine is typically quite dramatic in terms of its effect. Joint pain usually subsides after only 12 hours of treatment and the joint pain may disappear completely in 48 hours or less. Although colchicine does not retard the progressive joint damage of gout that is produced by tophi, it can prevent it by lowering

and maintaining the serum urate concentration at or near its normal level.

Colchicine is contraindicated with a hypersensitivity to it. It is also contraindicated with high dose aspirin therapy and among patients that have severe gastrointestinal, hepatic or renal impairment. It should be used with caution when a patient has a blood dyscrasia, is pregnant or lactating and among the elderly and pediatric populations. The elderly may be adversely affected with electrolyte imbalances if they experience vomiting as a result of the colchicine therapy.

Some of the side effects and adverse drug reactions associated with colchicines are:

- oliguria,
- renal impairment,
- hematuria,
- nausea,
- vomiting,
- anorexia,
- peripheral neuritis,
- peptic ulcer,
- myopathy, and
- hematological changes (thrombocytopenia, aplastic anemia, agranulocytosis and pancytopenia).

The usual adult dosage of colchicine is 0.5 mg to 1.2 mg (usually 1 mg) by mouth every 2 hours for acute attacks of gout until the therapeutic response is obtained or diarrhea or vomiting occur. The maximum dosage is 7 mg over 48 hours. The prophylactic dosage is 0.5 to 1.8 mg every day for long term therapy.

This medication should be taken on an empty stomach to enhance absorption. Intravenous colchicine can be given when the patient's gastrointestinal tract is not tolerating po colchicine. (Merck & Co., 2005; Skidmore-Roth, Linda, 2004)

- *Probenecid* (Benemid) another uric acid lowering medication, is used for the prevention of hyperuricemia and gouty arthritis. Specifically, it lowers the reabsorption of uric acid, therefore and reduces serum uric acid levels by promoting its excretion.

This medication is contraindicated with renal and hepatic disease, hypersensitivity and among patients who have uric acid calculi. It must be used cautiously during pregnancy.

Some of the side effects and adverse effects of probenecid are:

- nausea, vomiting and anorexia,
- bradycardia,
- gastric irritation,
- drowsiness,
- headache,
- dermatitis, pruritus, and rash,
- glycosuria, frequency and thirst,
- hypokalemia,
- acidosis,
- hyperchloremia, and
- hyperglycemia.

More serious side effects and adverse reactions include hepatic necrosis, nephrotic syndrome and apnea.

The usual adult dosage of probenecid for hyperuricemia is 250 mg two times a day for one week which can be increased by 250 mg to 500 mg a day or bid until the uric acid level normalizes. The maximum daily dosage is 2 g. The maintenance dose is 500 mg per day.

Patients taking probenecid should be instructed to drink plenty of fluids (2 to 3 liters per day) to decrease their risk of uric acid stones. They should also be advised to take the medication with food or milk and to take an antacid to decrease the risk of gastrointestinal side effects.

When a patient is taking probenecid, the following have to be monitored and assessed.

- uric acid levels,
- urinary pH, glucose and output,
- electrolytes,
- respiratory status,

- mobility and joint pain,
- central nervous system status.

An overdose can be signaled with confusion, hyperreflexia, twitching and headache. (Skidmore-Roth, Linda, 2004)

- *Allopurinol* is another uricosuric agent used for the treatment of chronic gout, calcium oxalate calculi, and Chagas' disease. Its mechanism of action decreases the amount of uric acid that is synthesized. It is used to prevent an attack of gout and to treat hyperuricemia.

It is contraindicated in patients who have had a prior severe allergic reaction to it. It should be used cautiously with pregnancy, lactation and among children. Cautious use is also advised when the patient has had a prior mild allergic reaction to it and for those with renal insufficiency or hepatic disease. Baseline and ongoing liver function studies should be done because this medication is hepatotoxic.

Some of the adverse reactions associated with allopurinol are GI irritation, neuritis, fever, drowsiness, pruritic rash, leukocytosis, thrombocytopenia, eosinophilia, leukocytosis, bone marrow suppression, hepatitis, cataracts and renal impairment. The adult dosage of allopurinol for gout may range from 200 to 600 mg/day in divided doses to inhibit uric acid synthesis and to control serum urate concentration. The maximum daily dosage is 800 mg a day. (Skidmore-Roth, Linda, 2004)

- *Sulfinpyrazone*, another medication used for gout, increases the excretion of uric acid by inhibiting the reabsorption of urates in the tubules. The recommended adult dosage for gout is 100 to 200 mg bid for a week and then 200 mg to 400 mg twice a day but not to exceed 800 mg per day

Sulfinpyrazone is contraindicated for patients with GI inflammation, active peptic ulcers, blood dyscrasias, hypersensitivity and a creatinine clearance of <50 mL/min. It must be used with caution during pregnancy.

Some of the side effects of sulfinpyrazone are rash, flushing, headache, dizziness, tinnitus, polyuria, anemia, increased bleeding time, renal calculi and leukopenia. More serious adverse

reactions include apnea, hepatic necrosis, GI bleeding, agranulocytosis and coma. (Skidmore-Roth, Linda, 2004)

- *Salicylates and nonsteroidal anti-inflammatory medications (NSAIDs)*. These medications were detailed above.
- *Analgesics*. In addition to the NSAIDs, other analgesics, such as codeine 30 mg to 60 mg may be used to manage the pain. (Merck & Co., 2005)
- *Sodium Bicarbonate* is used to alkalize urine for patients that have calculi formation. The usual adult dosage is 325 mg to 2 g four times a day or 48 mEq (4g) followed by 12 to 24 mEq q4h. (Skidmore-Roth, Linda, 2004)

Diet

People that have gout should:

- avoid alcohol,
- eat a nutritious diet without purine rich foods, and
- increase their fluid intake to decrease urate crystal precipitation and to decrease the risk of dehydration. (Merck & Co., 2005; Skidmore-Roth, Linda, 2004)

Other Interventions

The patient should lose weight, as indicated, to avoid additional stress on the joints. At times, splinting the inflamed joint may be beneficial in reducing the pain and decreasing the risk of deformity. (Merck & Co., 2005)

Joint Aspiration

Some gout attacks are treated with the aspiration of affected joints after which corticosteroid esters are instilled. Depending on the size of

the joint, prednisolone tebutate from 10 mg to 50 mg is used. (Merck & Co., 2005)

Exercise and Rest

During the acute phase of a gout attack, the joint should be rested. After that, normal exercise and rest is recommended. (Merck & Co., 2005)

SUMMARY

The implications of arthritis involve the entire health care team. The treatment of arthritis often involves multiple interventions such as medications, pain relief, physical and/or occupational therapy, applications of heat or cold and patient/family education. A team approach involving a number of professional disciplines and a thorough knowledge of arthritis are the keys to success in the management of this widespread and often chronic disease.

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