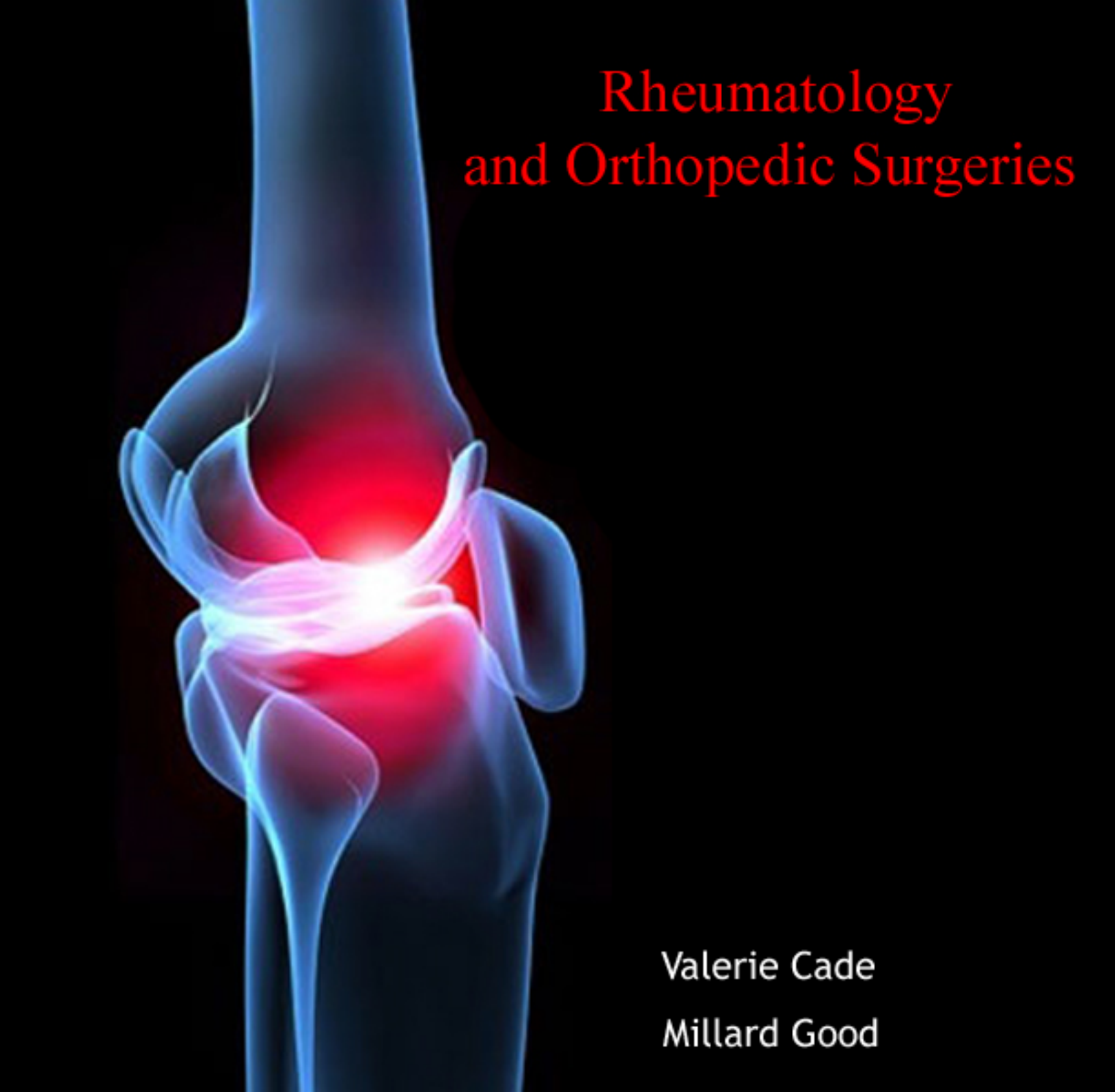


Rheumatology and Orthopedic Surgeries

Valerie Cade

Millard Good

First Edition, 2012

ISBN 978-81-323-1432-5

Published by:
College Publishing House
4735/22 Prakashdeep Bldg,
Ansari Road, Darya Ganj,
Delhi - 110002
Email: info@wtbooks.com

Table of Contents

Chapter 1

Rheumatology

Rheumatology is a sub-specialty in internal medicine and pediatrics, devoted to the diagnosis and therapy of conditions and diseases affecting the joints, muscles, and bones. Clinicians who specialize in rheumatology are called **rheumatologists**. Rheumatologists deal mainly with clinical problems involving joints, soft tissues, certain autoimmune diseases, and the allied conditions of connective tissues. Essentially, they medically treat diseases, disorders, etc., that affect the musculoskeletal system. This includes many autoimmune diseases, as these conditions often cause rheumatic issues.

The term *rheumatology* originates from the Greek word *rheuma*, meaning "that which flows as a river or stream," and the suffix *-ology*, meaning "the study of."

Rheumatology is a rapidly evolving medical specialty, with advancements owing largely to new scientific discoveries about the immunology of these disorders. Because the characteristics of some rheumatological disorders are often best explained by immunology, the pathogenesis of many major rheumatological disorders are now described in terms of the autoimmune system, viz., as an autoimmune disease. Correspondingly, most new treatment modalities are also based on clinical research in immunology and the resulting improved understanding of the genetic bases of rheumatological disorders. Future treatment may include gene therapy, as well. Evidence-based medical treatment of rheumatological disorders has helped patients with rheumatism lead a near normal life.

Rheumatism

Rheumatism is a non-specific term used to describe any painful disorder affecting the loco-motor system including joints, muscles, connective tissues, soft tissues around the joints and bones. The term rheumatism is also used to describe rheumatic fever affecting heart valves. However, the medical profession uses specific terms to describe rheumatological disorders such as rheumatoid arthritis, ankylosing spondylitis, gout and systemic lupus erythematosus and so on in the medical literature.

Rheumatology is now emerging as an important clinical specialty recognized all over the world. This speciality is rapidly improving and well established along with properly organized post graduate training programs. The term describing clinicians dealing with rheumatism as "rheumatologists" is now a well established term commonly used by the

medical community, even though it is not adequately described in dictionaries established for languages. Rheumatologists all over the world are now capable of treating most of the chronic rheumatological disorders with a much better outcome for the patients. This is due to the discovery of new disease modifying agents called biologics which is now a well established form of treatment for the patients suffering with chronic and disabling joint disorders.

Rheumatologist

A **rheumatologist** is a physician specialized in the field of medical sub-specialty called rheumatology, and holds either a a board certification after specialized training afterDoctor of Medicine Degree (M.D.) through fellowship programs in the United States or specialist registrars positions in the Unitied Kingdoms or DM in India or equivalent programs elsewhere in the world. In the United States, training in this field requires four years undergraduate school, four years of medical school, and then three years of residency, followed by two or three years additional Fellowship training. The number of years allocated for specialized training in rheumatology for postgraduate trainees in different countries could vary according to the requirements of different countries. Rheumatologists are internists or pediatricians who are qualified by additional postgraduate training and experience in the diagnosis and treatment of arthritis and other diseases of the joints, muscles and bones. Many rheumatologists also conduct research to determine the cause and better treatments for these disabling and sometimes fatal diseases. Treatment modalities are based on scientific research, currently, practice of rheumatology is largely evidence based. Clinicians who specialize on this specialty are called Rheumatologists.

Rheumatologists treat arthritis, certain autoimmune diseases, musculoskeletal pain disorders and osteoporosis. There are more than 200 types of these diseases, including rheumatoid arthritis, osteoarthritis, gout, lupus, back pain, osteoporosis, and tendinitis. Some of these are very serious diseases that can be difficult to diagnose and treat. They treat soft tissue problems related to musculoskeletal system sports related soft tissue disorders and the specialty is also interrelated with physiotherapy, physical medicine and rehabilitation of disabled patients. Patient education programs and occupational therapy also go hand in hand with this specialty.

There are many international organizations representing rheumatologists all over the world. The American College of Rheumatology (ACR), the Association of Rheumatology Health Professionals (ARHP), the European League Against Rheumatism (EULAR), Asia Pacific League of Associations for Rheumatology (APLAR), International League of Associations for Rheumatology (ILAR) are the main international organizations established and organizing many activities related to this specialty, these organizations strive to propagate and consolidate Rheumatology endeavors internationally, furthermore, there are associations and colleges of Rheumatology representing Rheumatologists from each and every nation scattered throughout the world which represent the above mentioned organizations from each nation. Rheumatologists are physicians specialized in rheumatic diseases.

For example, there are approximately 480 consultant rheumatologists in the UK. Rheumatologists are increasing in numbers in all countries, as there is an increasing demand for specialists on this field with an increasing population of aging patients who need specialized treatment.

Diseases

Diseases diagnosed or managed by the rheumatologist include:

- Rheumatoid arthritis
- Lupus
- Sjögren's syndrome
- scleroderma (systemic sclerosis)
- dermatomyositis
- polychondritis
- polymyositis
- polymyalgia rheumatica
- osteoarthritis
- septic arthritis
- sarcoidosis
- gout, pseudogout
- spondyloarthropathies
    - ankylosing spondylitis
    - reactive arthritis (aka **reactive arthropathy)
    - psoriatic arthropathy
    - enteropathic spondylitis
- vasculitis
    - polyarteritis nodosa
    - Henoch-Schönlein purpura
    - serum sickness
    - Wegener's granulomatosis
    - giant cell arteritis
    - temporal arteritis
    - Takayasu's arteritis
    - Behçet's syndrome
    - Kawasaki's disease (mucocutaneous lymph node syndrome)
    - Buerger's disease (thromboangiitis obliterans)

Juvenile Idiopathic Arthritis(JIA);

(JIA inccudes a wide range Joint Disoders affecting Children)

Rheumatic arthritis;

Soft Tissue Rheumatism; (Localizes diseases and lesions affecting the joints and structures around the joints including tendons, ligaments capsules, bursae, Stress

Fractures, muscles, nerve entrapment, vascular lesions, ganglion, connective tissue abnormalities and localised Soft tissues disorders etc.)

Diseases affecting bones;

Osteoporosis, osteomalacia, renal osteodystrophy, Fluorosis, Rickets Etc.

Congenital and familial Disorders affecting Joints;

Hyperextensible joints;

Ehlers-Danlos Syndrome,Achondroplasisa, Marfan's Syndrome etc.

Diagnosis

Apart from an extensive medical history, there are useful methods of diagnosis both performed easy enough in a physical examination and, on the other hand, more complicated ones, often requiring a rheumatologist or other specialised physicians.

Physical examination

Following are examples of methods of diagnosis able to be performed in a normal physical examination.

- Schober's test tests the flexion of the lower back.
- Multiple joint inspection
- Musculoskeletal Examination
    - Screening Musculoskeletal Exam (SMSE) - a rapid assessment of structure and function
    - General Musculoskeletal Exam (GMSE) - a comprehensive assessment of joint inflammation
    - Regional Musculoskeletal Exam (RMSE)- focused assessments of structure, function and inflammation combined with special testing

Specialised

- Laboratory tests (e.g. Erythrocyte Sedimentation Rate, Rheumatoid Factor, Anti-CCP (Anti-Cyclic Citrullinated Peptide antibody), ANA (Anti-Nuclear Antibody))
- X-rays of affected joints and other imaging methods
- Cytopathology and chemical pathology of fluid aspirated from affected joints (e.g. to differentiate between septic arthritis and gout)

Treatment

Most rheumatic diseases are treated with analgesics, NSAIDs (Non-Steroid Anti-Inflammatory Drugs), steroids (in serious cases), DMARDs (Disease-Modifying Anti-Rheumatic Drugs), monoclonal antibodies, such as infliximab and adalimumab, and the soluble TNF receptor etanercept and Methotrexate for moderate to severe Rheumatoid arthritis. Biologic agent Rituximab (Anti-B-Cell Therapy) is now licensed for use in refractory Rheumatoid Arthritis. Physiotherapy is vital in the treatment of many rheumatological disorders. Occupational therapy can help patients finding alternative ways for common movements which would otherwise be restricted by their disease. Patients with rheumatoid arthritis often need a long term, coordinated and a multidisciplinary team approach towards management of individual patients, treatment is often tailored according the individual needs of the individual patient which is also dependent on the response and the tolerability of medications.

Scientific research

Recently, a large body of scientific research deals with the background of autoimmune disease, the cause of many rheumatic disorders. Also, the field of osteoimmunology has emerged to further examine the interactions between the immune system, joints and bones. Epidemiological studies and medication trials are also being conducted. Scientific research on biologics and clinical trials on monoclonal antibody therapies have added a new dimension to the medical treatment of arthritic disorders.

Chapter 2

Rheumatism and Rheumatoid Arthritis

Rheumatism

Rheumatism	
ICD-10	M79.0
ICD-9	729.0
MeSH	D012216

Rheumatism or **rheumatic disorder** is a non-specific term for medical problems affecting the joints and connective tissue. The study of, and therapeutic interventions in, such disorders is called rheumatology.

Terminology

The term "rheumatism" is still used in colloquial speech and historical contexts, but is no longer frequently used in medical or technical literature; there is no longer any recognized disorder simply called "rheumatism". Some countries use the word rheumatism to describe fibromyalgia syndrome. The traditional term covers such a range of different problems that to ascribe symptoms to "rheumatism" is not to say very much. Nevertheless, sources dealing with rheumatism tend to focus on arthritis. However, "non-articular rheumatism", also known as "regional pain syndrome" or "soft tissue rheumatism" can cause significant discomfort and difficulty. Furthermore, arthritis and rheumatism between them cover at least 200 different conditions.

The term "Rheumatic Diseases" is used in MeSH to refer to connective tissue disorders.

Palindromic rheumatism has been theorized to be a form of rheumatoid arthritis.

Types

The major rheumatic disorders currently recognized include:

- Ankylosing spondylitis
- Back pain
- Bursitis/Tendinitis, Shoulder pain, wrist, biceps, leg, knee (patellar), ankle, hip, and Achilles
- Capsulitis
- Neck pain
- Osteoarthritis
- Psoriatic arthritis
- Rheumatic fever
- Rheumatic heart disease (a long-term complication of Rheumatic fever)
- Rheumatoid arthritis
- Systemic lupus erythematosus
- Temporal arteritis and Polymyalgia rheumatica
- Tenosynovitis
- Myositis.

Although these disorders probably have little in common in terms of their epidemiology, they do share two characteristics: they cause chronic (though often intermittent) pain, and they are difficult to treat. They are also, collectively, very common.

Treatment

A vast number of traditional herbal remedies were recommended for "rheumatism". Modern medicine, both conventional and complementary, recognises that the different rheumatic disorders have different causes (and several of them have multiple causes) and require different kinds of treatment.

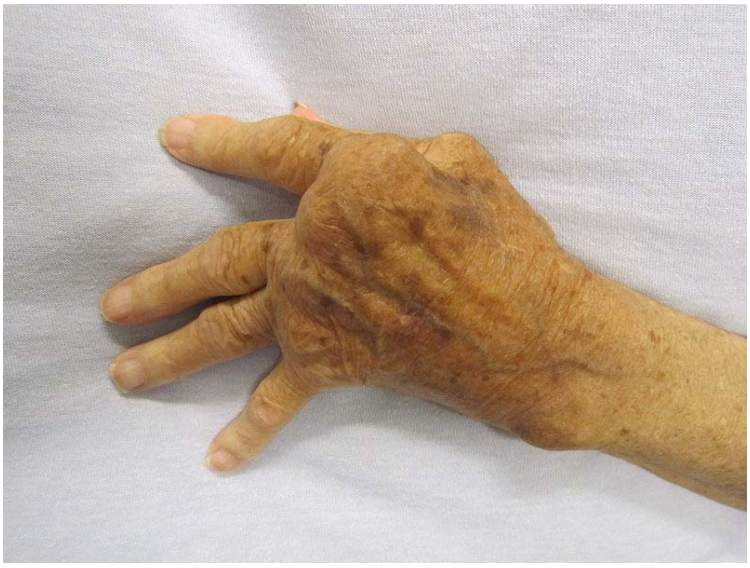
Nevertheless, initial therapy of the major rheumatological diseases is with analgesics, such as paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs), members of which are ibuprofen and diclofenac. Often, stronger analgesics are required.

"Rheumatism" and weather

There has long been said to be a link between "rheumatic" pain and the weather. There appears to be no firm evidence in favour or against; a 1995 questionnaire given to 557 people by A. Naser and others at the Brigham and Women's Hospital's Pain Management Center concludes that "changes in barometric pressure are the main link between weather and pain. Low pressure is generally associated with cold, wet weather and an increase in pain. Clear, dry conditions signal high pressure and a decrease in pain".

Rheumatoid Arthritis

Rheumatoid arthritis



A hand affected by rheumatoid arthritis

ICD-10	M05.-M06.
ICD-9	714
OMIM	180300
DiseasesDB	11506
MedlinePlus	000431
eMedicine	article/331715 article/1266195 article/305417 article/401271 article/335186 article/808419
MeSH	D001172

Rheumatoid arthritis (**RA**) is a chronic, systemic inflammatory disorder that may affect many tissues and organs, but principally attacks synovial joints. The process produces an inflammatory response of the synovium (synovitis) secondary to hyperplasia of synovial cells, excess synovial fluid, and the development of pannus in the synovium. The pathology of the disease process often leads to the destruction of articular cartilage and ankylosis of the joints. Rheumatoid arthritis can also produce diffuse inflammation in the lungs, pericardium, pleura, and sclera, and also nodular lesions, most common in subcutaneous tissue. Although the cause of rheumatoid arthritis is unknown,

autoimmunity plays a pivotal role in both its chronicity and progression, and RA is considered a systemic autoimmune disease.

About 1% of the world's population is afflicted by rheumatoid arthritis, women three times more often than men. Onset is most frequent between the ages of 40 and 50, but people of any age can be affected. It can be a disabling and painful condition, which can lead to substantial loss of functioning and mobility if not adequately treated. It is a clinical diagnosis made on the basis of symptoms, physical exam, radiographs (X-rays) and labs, although the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) publish diagnostic guidelines. Diagnosis and long-term management are typically performed by a rheumatologist, an expert in auto-immune diseases.

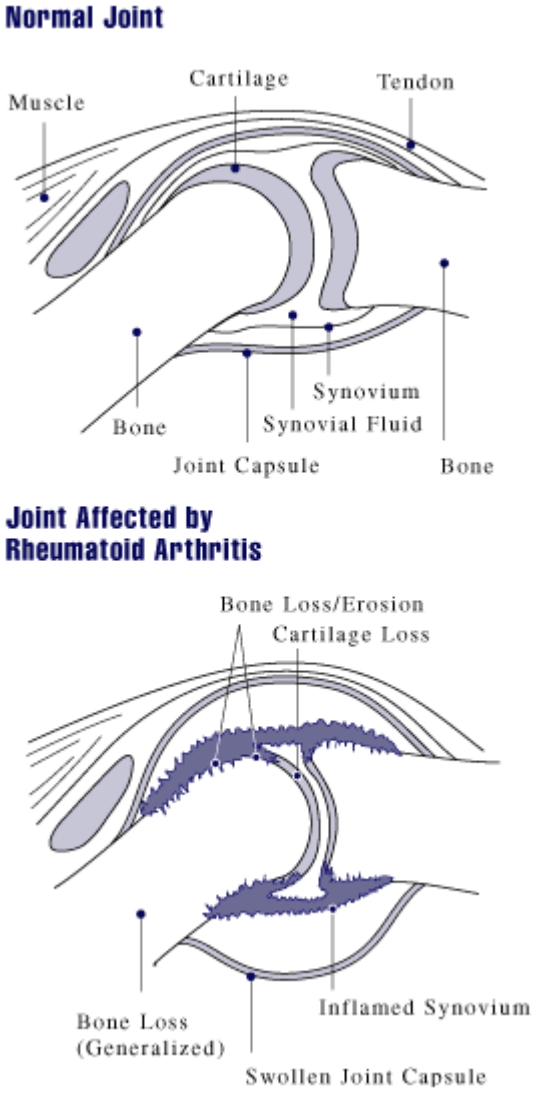
Various treatments are available. Non-pharmacological treatment includes physical therapy, orthoses, occupational therapy and nutritional therapy but do not stop progression of joint destruction. Analgesia (painkillers) and anti-inflammatory drugs, including steroids, are used to suppress the symptoms, while disease-modifying antirheumatic drugs (DMARDs) are required to inhibit or halt the underlying immune process and prevent long-term damage. In recent times, the newer group of biologics has increased treatment options.

The name is based on the term "rheumatic fever", an illness which includes joint pain and is derived from the Greek word *ῥεύμα-rheuma (nom.), ῥεύματος-rheumatos (gen.)* ("flow, current"). The suffix *-oid* ("resembling") gives the translation as *joint inflammation that resembles rheumatic fever*. The first recognized description of rheumatoid arthritis was made in 1800 by Dr Augustin Jacob Landré-Beauvais (1772–1840) of Paris.

Signs and symptoms

While rheumatoid arthritis primarily affects joints, problems involving other organs of the body are known to occur. Extra-articular ("outside the joints") manifestations other than anemia (which is very common) are clinically evident in about 15–25% of individuals with rheumatoid arthritis. It can be difficult to determine whether disease manifestations are directly caused by the rheumatoid process itself, or from side effects of the medications commonly used to treat it – for example, lung fibrosis from methotrexate or osteoporosis from corticosteroids.

Joints



A diagram showing how rheumatoid arthritis affects a joint

The arthritis of joints known as synovitis is inflammation of the synovial membrane that lines joints and tendon sheaths. Joints become swollen, tender and warm, and stiffness limits their movement. With time RA nearly always affects multiple joints (it is a polyarthritis), most commonly small joints of the hands, feet and cervical spine, but larger joints like the shoulder and knee can also be involved. Synovitis can lead to tethering of tissue with loss of movement and erosion of the joint surface causing deformity and loss of function.

Rheumatoid arthritis typically manifests with signs of inflammation, with the affected joints being swollen, warm, painful and stiff, particularly early in the morning on waking or following prolonged inactivity. Increased stiffness early in the morning is often a prominent feature of the disease and typically lasts for more than an hour. Gentle

movements may relieve symptoms in early stages of the disease. These signs help distinguish rheumatoid from non-inflammatory problems of the joints, often referred to as osteoarthritis or "wear-and-tear" arthritis. In arthritis of non-inflammatory causes, signs of inflammation and early morning stiffness are less prominent with stiffness typically less than 1 hour, and movements induce pain caused by mechanical arthritis. In RA, the joints are often affected in a fairly symmetrical fashion, although this is not specific, and the initial presentation may be asymmetrical.

As the pathology progresses the inflammatory activity leads to tendon tethering and erosion and destruction of the joint surface, which impairs range of movement and leads to deformity. The fingers may suffer from almost any deformity depending on which joints are most involved. Medical students are taught to learn names for specific deformities, such as ulnar deviation, boutonniere deformity, swan neck deformity and "Z-thumb," but these are of no more significance to diagnosis or disability than other variants, since they occur in osteoarthritis as well. "Z-thumb" or "Z-deformity" consists of hyperextension of the interphalangeal joint, fixed flexion and subluxation of the metacarpophalangeal joint and gives a "Z" appearance to the thumb.

Skin

The *rheumatoid nodule*, which is often subcutaneous, is the cutaneous feature most characteristic of rheumatoid arthritis. The initial pathologic process in nodule formation is unknown but may be essentially the same as the synovitis, since similar structural features occur in both. The nodule has a central area of fibrinoid necrosis that may be fissured and which corresponds to the fibrin-rich necrotic material found in and around an affected synovial space. Surrounding the necrosis is a layer of palisading macrophages and fibroblasts, corresponding to the intimal layer in synovium and a cuff of connective tissue containing clusters of lymphocytes and plasma cells, corresponding to the subintimal zone in synovitis. The typical rheumatoid nodule may be a few millimetres to a few centimetres in diameter and is usually found over bony prominences, such as the olecranon, the calcaneal tuberosity, the metacarpophalangeal joint, or other areas that sustain repeated mechanical stress. Nodules are associated with a positive RF (rheumatoid factor) titer and severe erosive arthritis. Rarely, these can occur in internal organs or at diverse sites on the body.

Several forms of *vasculitis* occur in rheumatoid arthritis. A benign form occurs as microinfarcts around the nailfolds. More severe forms include livedo reticularis, which is a network (reticulum) of erythematous to purplish discoloration of the skin caused by the presence of an obliterative cutaneous capillaropathy.

Other, rather rare, skin associated symptoms include:

- pyoderma gangrenosum, a necrotizing, ulcerative, noninfectious neutrophilic dermatosis.
- Sweet's syndrome, a neutrophilic dermatosis usually associated with myeloproliferative disorders

- drug reactions
- erythema nodosum
- lobular panniculitis
- atrophy of digital skin
- palmar erythema
- diffuse thinning (rice paper skin), and skin fragility (often worsened by corticosteroid use).

Lungs

Fibrosis of the lungs is a recognized response to rheumatoid disease. It is also a rare but well recognized consequence of therapy (for example with methotrexate and leflunomide). Caplan's syndrome describes lung nodules in individuals with rheumatoid arthritis and additional exposure to coal dust. Pleural effusions are also associated with rheumatoid arthritis. Another complication of RA is Rheumatoid Lung Disease. It is estimated that about one quarter of Americans with RA develop Rheumatoid Lung Disease.

Kidneys

Renal amyloidosis can occur as a consequence of chronic inflammation. Rheumatoid arthritis may affect the kidney glomerulus directly through a vasculopathy or a mesangial infiltrate but this is less well documented. Treatment with Penicillamine and gold salts are recognized causes of membranous nephropathy.

Heart and blood vessels

People with rheumatoid arthritis are more prone to atherosclerosis, and risk of myocardial infarction (heart attack) and stroke is markedly increased. Other possible complications that may arise include: pericarditis, endocarditis, left ventricular failure, valvulitis and fibrosis. Many people with rheumatoid arthritis do not experience the same chest pain that others feel when they have angina or myocardial infarction. To reduce cardiovascular risk, it is crucial to maintain optimal control of the inflammation caused by rheumatoid arthritis (which may be involved in causing the cardiovascular risk), and to use exercise and medications appropriately to reduce other cardiovascular risk factors such as blood lipids and blood pressure. Doctors who treat rheumatoid arthritis patients should be sensitive to cardiovascular risk when prescribing anti-inflammatory medications, and may want to consider prescribing routine use of low doses of aspirin if the gastrointestinal effects are tolerable.

Other

Ocular

The eye is directly affected in the form of episcleritis which when severe can very rarely progress to perforating scleromalacia. Rather more common is the indirect effect of keratoconjunctivitis sicca, which is a dryness of eyes and mouth caused by lymphocyte infiltration of lacrimal and salivary glands. When severe, dryness

of the cornea can lead to keratitis and loss of vision. Preventive treatment of severe dryness with measures such as nasolacrimal duct occlusion is important.

Hepatic

Cytokine production in joints and/or hepatic Kupffer cells leads to increased activity of hepatocytes with increased production of acute-phase proteins, such as C-reactive protein, and increased release of enzymes such as alkaline phosphatase into the blood. In Felty's syndrome, Kuppfer cell activation is so marked that the resulting increase in hepatocyte activity is associated with nodular hyperplasia of the liver, which may be palpably enlarged. Although Kupffer cells are within the hepatic parenchyma, they are separate from hepatocytes. As a result there is little or no microscopic evidence of hepatitis (immune-mediated destruction of hepatocytes). Hepatic involvement in RA is essentially asymptomatic.

Hematological

Anemia is by far the most common abnormality of the blood cells. Rheumatoid arthritis may cause a warm autoimmune hemolytic anemia. The red cells are of normal size and colour (normocytic and normochromic). A low white blood cell count (neutropenia) usually only occurs in patients with Felty's syndrome with an enlarged liver and spleen. The mechanism of neutropenia is complex. An increased platelet count (thrombocytosis) occurs when inflammation is uncontrolled, as does the anemia.

Neurological

Peripheral neuropathy and mononeuritis multiplex may occur. The most common problem is carpal tunnel syndrome caused by compression of the median nerve by swelling around the wrist. Atlanto-axial subluxation can occur, owing to erosion of the odontoid process and or/transverse ligaments in the cervical spine's connection to the skull. Such an erosion (>3mm) can give rise to vertebrae slipping over one another and compressing the spinal cord. Clumsiness is initially experienced, but without due care this can progress to quadriplegia.

Constitutional symptoms

Constitutional symptoms including fatigue, low grade fever, malaise, morning stiffness, loss of appetite and loss of weight are common systemic manifestations seen in patients with active rheumatoid arthritis.

Osteoporosis

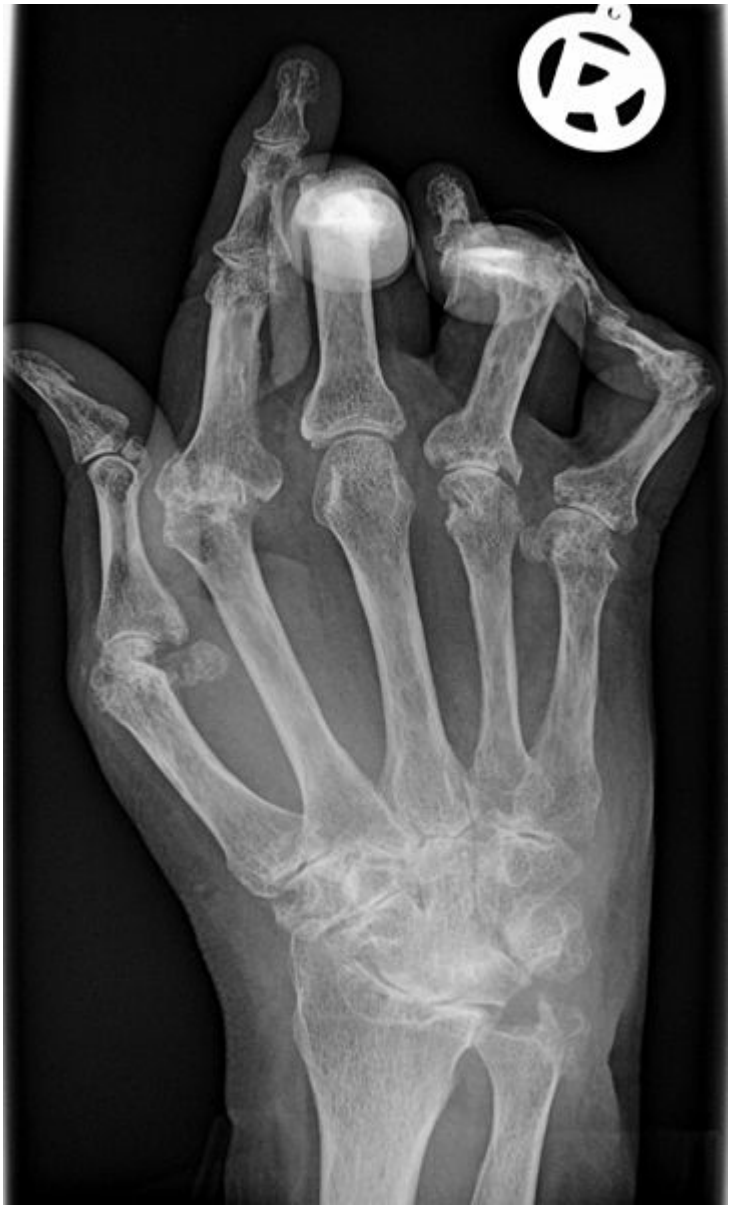
Local osteoporosis occurs in RA around inflamed joints. It is postulated to be partially caused by inflammatory cytokines. More general osteoporosis is probably contributed to by immobility, systemic cytokine effects, local cytokine release in bone marrow and corticosteroid therapy.

Lymphoma

The incidence of lymphoma is increased in RA, although it is still uncommon.

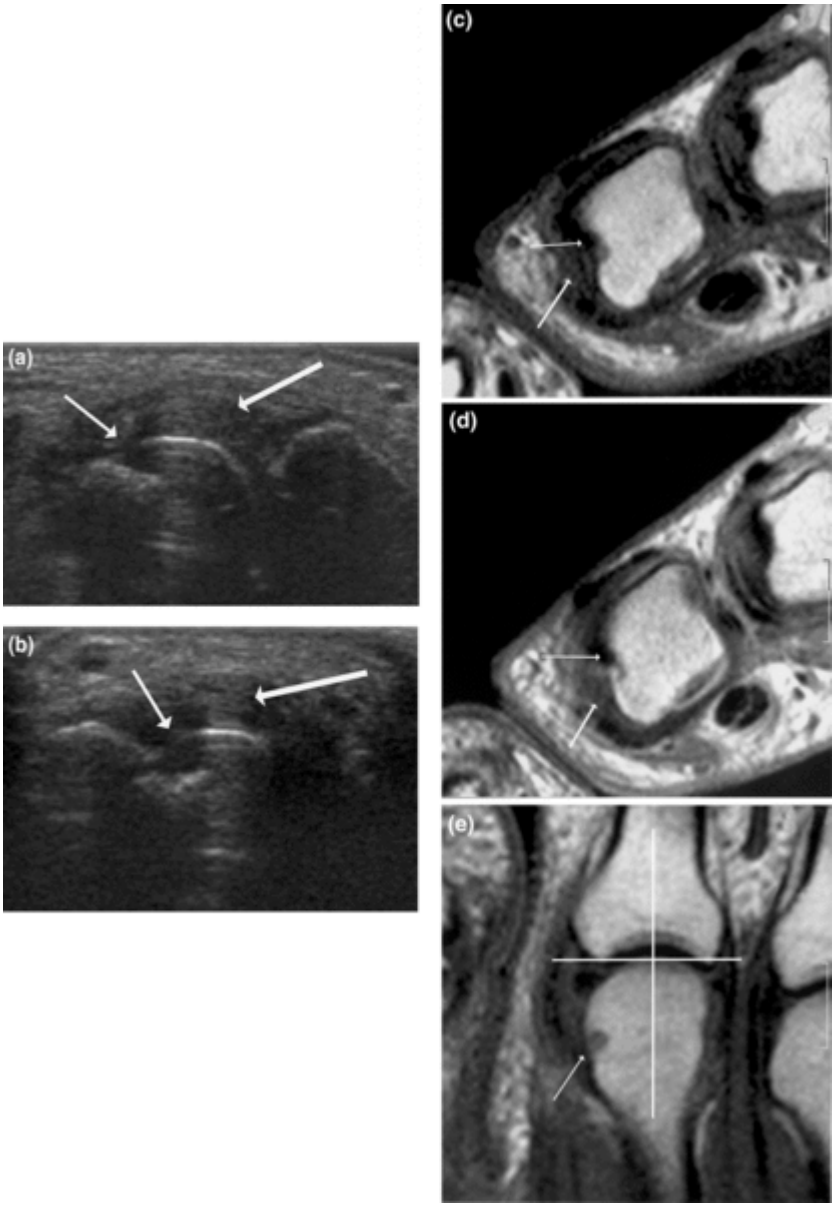
Diagnosis

Imaging



X-ray of the hand in rheumatoid arthritis

Appearance of synovial fluid from a joint with inflammatory arthritis



Signs of destruction and inflammation on ultrasonography and magnetic resonance imaging in the second metacarpophalangeal joint in established rheumatoid arthritis. Thin arrows indicate an erosive change; thick arrows indicate synovitis. Ultrasonography (left side of image) in the (a) longitudinal and (b) the transverse planes shows both signs of destruction and inflammation. Axial T1-weighted magnetic resonance images were obtained (c) before and (d) after contrast administration, also demonstrating synovitis. Additionally, a coronal T1-weighted magnetic resonance image (e) before contrast administration visualizes the same bone erosion as shown in panels c and d.

X-rays of the hands and feet are generally performed in people with a polyarthritis. In rheumatoid arthritis, there may be no changes in the early stages of the disease, or the x-ray may demonstrate juxta-articular osteopenia, soft tissue swelling and loss of joint

space. As the disease advances, there may be bony erosions and subluxation. X-rays of other joints may be taken if symptoms of pain or swelling occur in those joints.

Other medical imaging techniques such as magnetic resonance imaging (MRI) and ultrasound are also used in rheumatoid arthritis.

There have been technical advances in ultrasonography. High-frequency transducers (10 MHz or higher) have improved the spatial resolution of ultrasound images; these images can depict 20% more erosions than conventional radiography. Also, color Doppler and power Doppler ultrasound, which show vascular signals of active synovitis depending on the degree of inflammation, are useful in assessing synovial inflammation. This is important, since in the early stages of rheumatoid arthritis, the synovium is primarily affected, and synovitis seems to be the best predictive marker of future joint damage.

Blood tests

When RA is clinically suspected, immunological studies are required, such as testing for the presence of rheumatoid factor (RF, a non-specific antibody). A negative RF does not rule out RA; rather, the arthritis is called *seronegative*. This is the case in about 15% of patients. During the first year of illness, rheumatoid factor is more likely to be negative with some individuals converting to seropositive status over time. RF is also seen in other illnesses, for example Sjögren's syndrome, Hepatitis C, chronic infections and in approximately 10% of the healthy population, therefore the test is not very specific.

Because of this low specificity, new serological tests have been developed, which test for the presence of the anti-citrullinated protein antibodies (ACPAs) or anti-CCP. Like RF, these tests are positive in only a proportion (67%) of all RA cases, but are rarely positive if RA is not present, giving it a specificity of around 95%. As with RF, there is evidence for ACPAs being present in many cases even before onset of clinical disease.

The most common tests for ACPAs are the anti-CCP (cyclic citrullinated peptide) test and the Anti-MCV assay (antibodies against mutated citrullinated Vimentin). Recently a serological point-of-care test (POCT) for the early detection of RA has been developed. This assay combines the detection of rheumatoid factor and anti-MCV for diagnosis of rheumatoid arthritis and shows a sensitivity of 72% and specificity of 99.7%.

Also, several other blood tests are usually done to allow for other causes of arthritis, such as lupus erythematosus. The erythrocyte sedimentation rate (ESR), C-reactive protein, full blood count, renal function, liver enzymes and other immunological tests (e.g., antinuclear antibody/ANA) are all performed at this stage. Elevated ferritin levels can reveal hemochromatosis, a mimic RA, or be a sign of Still's disease, a seronegative, usually juvenile, variant of rheumatoid.

Criteria

In 2010 the *2010 ACR / EULAR Rheumatoid Arthritis Classification Criteria* were introduced. These new classification criteria overruled the "old" ACR criteria of 1987 and are adapted for early RA diagnosis. The "new" classification criteria, jointly published by the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) establish a point value between 0 and 10. Every patient with a point total of 6 or higher is unequivocally classified as an RA patient, provided he has synovitis in at least one joint and given that there is no other diagnosis better explaining the synovitis. Four areas are covered in the diagnosis:

- joint involvement – depending on the type and number of joints: up to 5 points
- serological parameters – including the rheumatoid factors as well as ACPA – "ACPA" stands for "anti-citrullinated protein antibody": up to 3 points depending on titre level
- acute phase reactants: 1 point for elevated erythrocyte sedimentation rate, ESR, or elevated CRP value (c-reactive protein)
- duration of arthritis: 1 point for symptoms lasting six weeks or longer

The new criteria accommodate to the growing understanding of rheumatoid arthritis and the improvements in diagnosing RA and disease treatment. In the "new" criteria serology and autoimmune diagnostics carries major weight, as ACPA detection is appropriate to diagnose the disease in an early state, before joints destructions occur. Destruction of the joints viewed in radiological images was a significant point of the ACR criteria from 1987. This criterion no longer is regarded to be relevant, as this is just the type of damage that treatment is meant to avoid.

The criteria are not intended for the diagnosis for routine clinical care; they were primarily intended to categorize research (*classification* criteria). In clinical practice, the following criteria apply:

- two or more swollen joints
- morning stiffness lasting more than one hour for at least six weeks
- the detection of rheumatoid factors or autoantibodies against ACPA such as autoantibodies to mutated citrullinated vimentin can confirm the suspicion of rheumatoid arthritis. A negative autoantibody result does not exclude a diagnosis of RA.

Differential diagnoses

Several other medical conditions can resemble RA, and usually need to be distinguished from it at the time of diagnosis:

- Crystal induced arthritis (gout, and pseudogout) – usually involves particular joints and can be distinguished with aspiration of joint fluid if in doubt
- Osteoarthritis – distinguished with X-rays of the affected joints and blood tests

- Systemic lupus erythematosus (SLE) – distinguished by specific clinical symptoms and blood tests (antibodies against double-stranded DNA)
- One of the several types of psoriatic arthritis resembles RA – nail changes and skin symptoms distinguish between them
- Lyme disease causes erosive arthritis and may closely resemble RA – it may be distinguished by blood test in endemic areas
- Reactive arthritis (previously Reiter's disease) – asymmetrically involves heel, sacroiliac joints, and large joints of the leg. It is usually associated with urethritis, conjunctivitis, iritis, painless buccal ulcers, and keratoderma blennorrhagica.
- Ankylosing spondylitis – this involves the spine and is usually diagnosed in males, although a RA-like symmetrical small-joint polyarthritis may occur in the context of this condition.
- Hepatitis C – RA-like symmetrical small-joint polyarthritis may occur in the context of this condition. Hepatitis C may also induce Rheumatoid Factor auto-antibodies

Rarer causes that usually behave differently but may cause joint pains:

- Sarcoidosis, amyloidosis, and Whipple's disease can also resemble RA.
- Hemochromatosis may cause hand joint arthritis.
- Acute rheumatic fever can be differentiated from RA by a migratory pattern of joint involvement and evidence of antecedent streptococcal infection. Bacterial arthritis (such as streptococcus) is usually asymmetric, while RA usually involves both sides of the body symmetrically.
- Gonococcal arthritis (another bacterial arthritis) is also initially migratory and can involve tendons around the wrists and ankles.

Pathophysiology and causes

Rheumatoid arthritis is a form of autoimmunity, the causes of which are still incompletely known. It is a systemic (whole body) disorder principally affecting synovial tissues.

The key pieces of evidence relating to pathogenesis are:

1. A genetic link with HLA-DR4 and related allotypes of MHC Class II and the T cell-associated protein PTPN22.

2. A link with cigarette smoking that appears to be causal.

3. A remarkable deceleration of disease progression in many cases by blockade of the cytokine TNF (alpha).

4. A similar dramatic response in many cases to depletion of B lymphocytes, but no comparable response to depletion of T lymphocytes.

5. A more or less random pattern of whether and when predisposed individuals are affected.

6. The presence of autoantibodies to IgGFc, known as rheumatoid factors (RF), and antibodies to citrullinated peptides (ACPA).

These data suggest that the disease involves abnormal B cell–T cell interaction, with presentation of antigens by B cells to T cells via HLA-DR eliciting T cell help and consequent production of RF and ACPA. Inflammation is then driven either by B cell or T cell products stimulating release of TNF and other cytokines. The process may be facilitated by an effect of smoking on citrullination but the stochastic (random) epidemiology suggests that the rate limiting step in genesis of disease in predisposed individuals may be an inherent stochastic process within the immune response such as immunoglobulin or T cell receptor gene recombination and mutation.

If TNF release is stimulated by B cell products in the form of RF or ACPA -containing immune complexes, through activation of immunoglobulin Fc receptors, then RA can be seen as a form of Type III hypersensitivity. If TNF release is stimulated by T cell products such as interleukin-17 it might be considered closer to type IV hypersensitivity although this terminology may be getting somewhat dated and unhelpful. The debate on the relative roles of immune complexes and T cell products in inflammation in RA has continued for 30 years. There is little doubt that both B and T cells are essential to the disease. However, there is good evidence for neither cell being necessary at the site of inflammation. This tends to favour immune complexes (based on antibody synthesised elsewhere) as the initiators, even if not the sole perpetuators of inflammation. Moreover, work by Thurlings and others in Paul-Peter Tak's group and also by Arthur Kavanagh's group suggest that if any immune cells are relevant locally they are the plasma cells, which derive from B cells and produce in bulk the antibodies selected at the B cell stage.

Although TNF appears to be the dominant, other cytokines (chemical mediators) are likely to be involved in inflammation in RA. Blockade of TNF does not benefit all patients or all tissues (lung disease and nodules may get worse). Blockade of IL-1, IL-15 and IL-6 also have beneficial effects and IL-17 may be important. Constitutional symptoms such as fever, malaise, loss of appetite and weight loss are also caused by cytokines released in to the blood stream.

As with most autoimmune diseases, it is important to distinguish between the cause(s) that trigger the process, and those that may permit it to persist and progress.

Possible infectious triggers

It has long been suspected that certain infections could be triggers for this disease. The "mistaken identity" theory suggests that an infection triggers an immune response, leaving behind antibodies that should be specific to that organism. The antibodies are not sufficiently specific, though, and set off an immune attack against part of the host. Because the normal host molecule "looks like" a molecule on the offending organism that

triggered the initial immune reaction—this phenomenon is called molecular mimicry. Some infectious organisms suspected of triggering rheumatoid arthritis include *Mycoplasma*, *Erysipelothrix*, parvovirus B19 and rubella, *but these associations have never been supported in epidemiological studies*. Nor has convincing evidence been presented for other types of triggers such as food allergies.

Epidemiological studies have confirmed a potential association between RA and two herpesvirus infections: Epstein-Barr virus (EBV) and Human Herpes Virus 6 (HHV-6). Individuals with RA are more likely to exhibit an abnormal immune response to the Epstein-Barr virus. The allele HLA-DRB1*0404 is associated with low frequencies of T cells specific for the EBV glycoprotein 110 and predisposes one to develop RA.

Psychological factors

There is no evidence that physical and emotional effects or stress could be a trigger for the disease. The many negative findings suggest that either the trigger varies, or that it might in fact be a chance event inherent with the immune response, as suggested by Edwards et al.

Continued abnormal immune response

The factors that allow an abnormal immune response, once initiated, to become permanent and chronic, are becoming more clearly understood. The genetic association with HLA-DR4, as well as the newly discovered associations with the gene PTPN22 and with two additional genes, all implicate altered thresholds in regulation of the adaptive immune response. It has also become clear from recent studies that these genetic factors may interact with the most clearly defined environmental risk factor for rheumatoid arthritis, namely cigarette smoking Other environmental factors also appear to modulate the risk of acquiring RA, and hormonal factors in the individual may explain some features of the disease, such as the higher occurrence in women, the not-infrequent onset after child-birth, and the (slight) modulation of disease risk by hormonal medications. Exactly how altered regulatory thresholds allow the triggering of a specific autoimmune response remains uncertain. However, one possibility is that negative feedback mechanisms that normally maintain tolerance of self are overtaken by aberrant positive feedback mechanisms for certain antigens such as IgG Fc (bound by RF) and citrullinated fibrinogen (bound by ACPA).

Once the abnormal immune response has become established (which may take several years before any symptoms occur), plasma cells derived from B lymphocytes produce rheumatoid factors and ACPA of the IgG and IgM classes in large quantities. These are not deposited in the way that they are in systemic lupus. Rather, they appear to activate macrophages through Fc receptor and perhaps complement binding. This can contribute to inflammation of the synovium, in terms of edema, vasodilation and infiltration by activated T-cells (mainly CD4 in nodular aggregates and CD8 in diffuse infiltrates). Synovial macrophages and dendritic cells further function as antigen presenting cells by expressing MHC class II molecules, leading to an established local immune reaction in

the tissue. The disease progresses in concert with formation of granulation tissue at the edges of the synovial lining (pannus) with extensive angiogenesis and production of enzymes that cause tissue damage. Modern pharmacological treatments of RA target these mediators. Once the inflammatory reaction is established, the synovium thickens, the cartilage and the underlying bone begins to disintegrate and evidence of joint destruction accrues.

Treatment

There is no known cure for rheumatoid arthritis, but many different types of treatment can alleviate symptoms and/or modify the disease process. Recommendations of the American College of Rheumatology (ACR), published in 2008, followed a trend in supporting earlier, more aggressive treatment of RA, and reflected heightened expectations of treatment effectiveness, including remission or substantial alleviation of symptoms for a rising percentage of patients.

The goal of treatment is twofold: alleviating the current symptoms, and preventing the future destruction of the joints with the resulting handicap if the disease is left unchecked. These two goals may not always coincide: while pain relievers may achieve the first goal, they do not have any impact on the long-term consequences. For these reasons, the ACR recommends that RA should generally be treated with at least one specific anti-rheumatic medication, also named DMARD (see below), to which other medications may be added depending on how long a person has had RA, how active the disease is, and prognostic factors (such as X-ray evidence of bone erosion; elevation of blood factors such as Rheumatoid factor, anti-cyclic citrullinated peptide, C-reactive protein, and erythrocyte sedimentation rate; age and gender; physical functioning; and smoking, for example).

Cortisone therapy has offered relief in the past, but its long-term effects have been deemed undesirable. However, cortisone injections can be valuable adjuncts to a long-term treatment plan, and using low dosages of daily cortisone (e.g., prednisone or prednisolone, 5–7.5 mg daily) can also have an important benefit if added to a proper specific anti-rheumatic treatment.

Pharmacological treatment of RA can be divided into disease-modifying antirheumatic drugs (DMARDs), anti-inflammatory agents and analgesics. Treatment also includes rest and physical activity.

Disease modifying anti-rheumatic drugs (DMARDs)

The term Disease modifying anti-rheumatic drug (DMARD) originally meant a drug that affects biological measures such as ESR and haemoglobin and autoantibody levels, but is now usually used to mean a drug that reduces the rate of damage to bone and cartilage. DMARDs have been found both to produce durable symptomatic remissions and to delay or halt progression. This is important as such damage is usually irreversible. Anti-inflammatories and analgesics improve pain and stiffness but do not prevent joint damage or slow the disease progression.

There is an increasing recognition among rheumatologists that permanent damage to the joints occurs at a very early stage in the disease. In the past it was common to start with just an anti-inflammatory drug, and assess progression clinically and using X-rays. If there was evidence that joint damage was starting to occur then a more potent DMARD would be prescribed. Ultrasound and MRI are more sensitive methods of imaging the joints and have demonstrated that joint damage occurs much earlier and in more sufferers than was previously thought. People with normal X-rays will often have erosions detectable by ultrasound that X ray could not demonstrate. The aim now is to treat before damage occurs.

There may be other reasons why starting DMARDs early is beneficial as well as prevention of structural joint damage. From the earliest stages of the disease, the joints are infiltrated by cells of the immune system that signal to one another in ways that may involve a variety of positive feedback loops (it has long been observed that a single corticosteroid injection may abort synovitis in a particular joint for long periods). Interrupting this process as early as possible with an effective DMARD (such as methotrexate) appears to improve the outcome from the RA for years afterwards. Delaying therapy for as little as a few months after the onset of symptoms can result in worse outcomes in the long term. There is therefore considerable interest in establishing the most effective therapy with early arthritis, when they are most responsive to therapy and have the most to gain.

Disease modifying anti-rheumatic drugs have been used in the treatment of rheumatic arthritis for a long time now. Over 90% of rheumatologists now use combination therapy of multiple disease modifying drugs for rheumatoid arthritis as it has become apparent that using combination of these drugs does not increase their relative toxicity profiles. Common combinations of DMARDs include methotrexate – hydroxychloroquine, methotrexate – sulfasalazine, sulfasalazine – hydroxychloroquine, and methotrexate – hydroxychloroquine – sulfasalazine.

In order to be effective, disease modifying anti-rheumatic drugs must be administered before the deformities appear or the erosive disease occurs. Usually, Rheumatologists do not wait for the fulfillment of the criteria for classification of RA as published by the American College of Rheumatology (ACR) and start treatment with this type of drugs if the pain and synovitis persist and the function is compromised.

Traditional small molecular mass drugs

Chemically synthesised DMARDs:

- azathioprine
- ciclosporin (cyclosporine A)
- D-penicillamine
- gold salts
- hydroxychloroquine
- leflunomide

- methotrexate (MTX)
- minocycline
- sulfasalazine (SSZ)

Cytotoxic drugs:

- Cyclophosphamide

The most important and most common adverse events relate to liver and bone marrow toxicity (MTX, SSZ, leflunomide, azathioprine, gold compounds, D-penicillamine), renal toxicity (cyclosporine A, parenteral gold salts, D-penicillamine), pneumonitis (MTX), allergic skin reactions (gold compounds, SSZ), autoimmunity (D-penicillamine, SSZ, minocycline) and infections (azathioprine, cyclosporine A).

Hydroxychloroquine may cause ocular toxicity, although this is rare, and because hydroxychloroquine does not affect the bone marrow or liver it is often considered to be the DMARD with the least toxicity. Unfortunately hydroxychloroquine is not very potent, and is usually insufficient to control symptoms on its own.

Methotrexate is considered by many rheumatologists to be the most important and useful DMARD, largely because of lower drop-out rates for reasons of toxicity. Nevertheless, methotrexate is often considered as a very 'toxic' drug. This reputation is not entirely justified, and at times can result in people being denied the most effective treatment for their arthritis. Although methotrexate does have the potential to suppress bone marrow or cause hepatitis, these effects can be monitored using regular blood tests, and the drug withdrawn at an early stage if the tests are abnormal before any serious harm is done (typically the blood tests return to normal after stopping the drug). In clinical trials, where one of a range of different DMARDs were used, people who were prescribed methotrexate stayed on their medication the longest (the others stopped because of either side-effects or failure of the drug to control the arthritis). Methotrexate is often preferred by rheumatologists because if it does not control arthritis on its own then it works well in combination with many other drugs, especially the biological agents. Other DMARDs may not be as effective or as safe in combination with biological agents.

Sulphasalazine : Although it appears to be a highly efficient drug in the treatment of rheumatoid arthritis, sulphasalazine may cause side effects that can range in severity from mild to serious. Mild side effects that may arise from treatment with sulphasalazine include nausea and skin rash. Generally, nausea that appears as a result of treatment with this DMARD occurs in the first days of treatment and then it tends to diminish to disappearance. To avoid nausea, specialists recommend starting with low doses and then gradually increasing them until the usual dosage is achieved. Skin rash has been reported in nearly 5% of the patients and it may present pruritus. Rare side effects include Stevens–Johnson syndrome and reduced fertility due to reversible oligospermia. Severe side effects that can appear from therapy with sulphasalazine, though rare, are aplastic anemia and neutropenia which may result in the death of the patient. The latter is estimated to have occurred in approximately 2% of the patients but death and further

complications were avoided by removing the drug from the patient's therapy. Also, according to WHO, there have been approximately 700 of patients in whom this medicine caused blood dyscrasis. Leukopenia has also been reported in therapies with sulphasalazine, but in very rare cases.

Anti-malarials such as chloroquine and hydroxychloroquine have been used to treat rheumatoid arthritis. It has been pointed out, through clinical studies, that chloroquine has a higher toxicity compared to hydroxychloroquine. Although hydroxyxhloroquine appears to be more efficient in treating rheumatoid arthritis than placebo, it is also inferior to sulphasalazine, especially in what concerns preventing the joint damage that is caused by the disease. As most drugs, anti-malarials may also produce side effects. Mild side effects from hydroxychloroquine include nausea and skin rash. More serious, bone marrow suppression may occur, though rare. Also, aplastic anemia and agranulocytosis can develop as a result of anti-malarial therapy and may potentially cause the death of the patient. A much more worrisome side effect from treatment with anti-malarials is the damage that these drugs seem to be causing to the cornea and retina. Recent studies have however shown that if the dosage of hydroxychloroquine given to the patients does not exceed 6.5 mg/kg, the risks of developing ocular complications are minimal.

Gold compounds are also options in treating this type of disease. Specialists agree that injectable gold is much more effective in the treatment of rheumatoid arthritis than auranofin. Yet, this type of drug has been shown to be more efficient than placebo and even though its level of toxicity is quite low, auranofin seems to be causing more side effects than any other type of DMARD. Auranofin is therefore not considered efficient in the treatment of rheumatoid arthritis because of its poor results and because it is intolerable for most patients. Sodium aurothiomalate (Myocrisin) on the other hand is another type of gold compound that is injected and which appears to be as efficient as sulphasalazine, d-penicillamine and methotrexate. Given that there is not enough proof that gold compounds are indeed efficient in preventing the progression of erosions and the high toxicity of these drugs, they are usually not included in the treatment plan for rheumatoid arthritis.

A Cochrane systematic review has determined that Abatacept was an effective treatment for rheumatoid arthritis. Against placebo, it was found to increase mobility and make patients twice as likely to achieve a 50% improvement in symptoms. However Cochrane has called for more studies to be conducted, given the lack of evidence to distinguish between the biologics available for rheumatoid arthritis.

Biological agents

Biological agents (biologics) include:

- tumor necrosis factor alpha (TNFα) blockers – etanercept (Enbrel), infliximab (Remicade), adalimumab (Humira), certolizumab pegol (Cimzia), golimumab (Simponi)
- Interleukin 1 (IL-1) blockers – anakinra (Kineret)

- monoclonal antibodies against B cells – rituximab (Rituxan)
- T cell costimulation blocker – abatacept (Orencia)
- Interleukin 6 (IL-6) blockers – tocilizumab (an anti-IL-6 receptor antibody) (RoActemra, Actemra)

Anti-inflammatory agents and analgesics

Anti-inflammatory agents include:

- glucocorticoids
- Non-steroidal anti-inflammatory drug (NSAIDs, most also act as analgesics)

Analgesics include:

- paracetamol (acetaminophen in US and Canada)
- opiates
- diproqualone
- lidocaine topical

Historic treatments for RA have also included: rest, ice, compression and elevation, acupuncture, apple diet, nutmeg, some light exercise every now and then, nettles, bee venom, copper bracelets, rhubarb diet, extractions of teeth, fasting, honey, vitamins, insulin, magnets, and electroconvulsive therapy (ECT). Most of these have either had no effect at all, or their effects have been modest and transient, while not being generalizable.

NSAIDs used in the treatment of RA include ibuprofen, naproxen, meloxicam, etodolac, nabumetone, sulindac, tolementin, choline magnesium salicylate, diclofenac, diflusinal, indomethicin, Ketoprofen, Oxaprozin, and piroxicam.

Cortisone therapy became a controversial medical solution because even though it can provide great relief, there are some questions as to the usefulness of the procedure over a long period of time.

Other therapies

Other therapies are weight loss, orthoses, occupational therapy, podiatry, physiotherapy, immunoadsorption therapy, joint injections, and special tools to improve hand movements (e.g. special tin-openers). Regular exercise is important for maintaining joint mobility and making the joint muscles stronger. A Cochrane Review of studies determined that exercise programs designed to improve strength and stamina were safe and led to moderate benefits for RA sufferers.

Ayurveda, mostly in southern India, is another source of treatment, and while it is popular in India there are no studies to show that it benefits patients with RA.

A survey in the United Kingdom between 1998 and 2002 found that arthritis, in its various forms, was among the five most common reasons for the medicinal use of cannabis.

The Prosorba column blood filtering device (removing IgG) was approved by the FDA in 1999 for treatment of RA However it was discontinued at the end of 2006.

The effectiveness of treating RA with acupuncture is inconclusive, and "more rigorous research seems to be warranted" according to one study.

One study of 873 patients with RA found that those who drank some alcohol (none drank more than 10 units of alcohol a week) had reduced severity of symptoms compared to those who drank no alcohol. However a spokeswoman for the Arthritis Research UK (who co-funded the study) warned that some RA treatments, like methotrexate, could damage the liver when taken with large amounts of alcohol.

Severely affected joints may require joint replacement surgery, such as knee replacement.

Prognosis

The course of the disease varies greatly. Some people have mild short-term symptoms, but in most the disease is progressive for life. Around 20%-30% will have subcutaneous nodules (known as rheumatoid nodules); this is associated with a poor prognosis.

Disability

- Daily living activities are impaired in most individuals.
- After 5 years of disease, approximately 33% of sufferers will not be working.
- After 10 years, approximately half will have substantial functional disability.

Prognostic factors

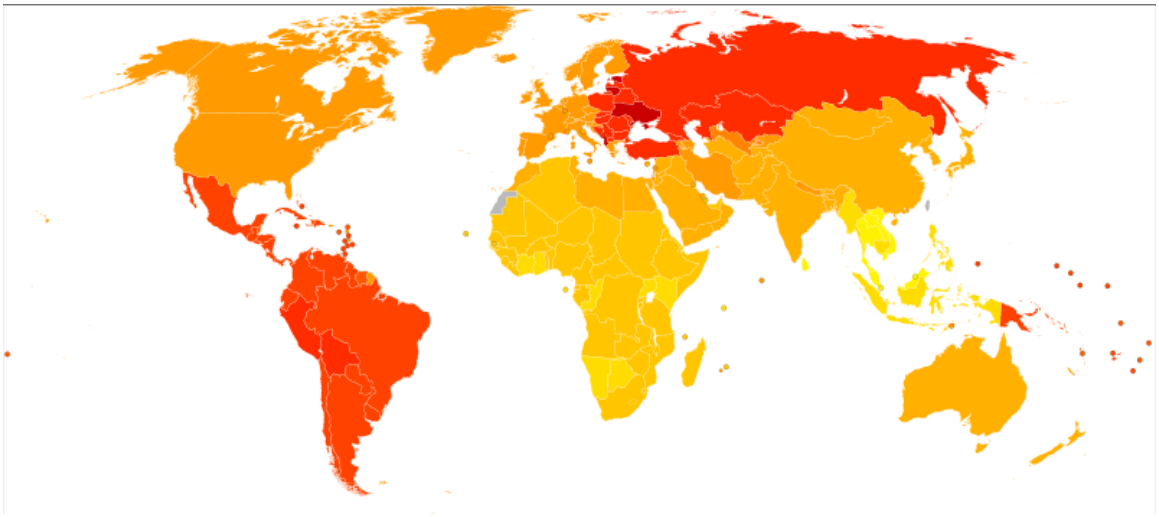
Poor prognostic factors include persistent synovitis, early erosive disease,extra-articular findings (including subcutaneous rheumatoid nodules), positive serum RF findings, positive serum anti-CCP autoantibodies, carriership of HLA-DR4 "Shared Epitope" alleles, family history of RA, poor functional status, socioeconomic factors, elevated acute phase response (erythrocyte sedimentation rate [ESR], C-reactive protein [CRP]), and increased clinical severity.

Mortality

Estimates of the life-shortening effect of RA vary; most sources cite a lifespan reduction of 5 to 10 years. According to the UK's National Rheumatoid Arthritis Society, "Young age at onset, long disease duration, the concurrent presence of other health problems (called co-morbidity), and characteristics of severe RA—such as poor functional ability or overall health status, a lot of joint damage on x-rays, the need for hospitalisation or

involvement of organs other than the joints—have been shown to associate with higher mortality". Positive responses to treatment may indicate a better prognosis. A 2005 study by the Mayo Clinic noted that RA sufferers suffer a doubled risk of heart disease, independent of other risk factors such as diabetes, alcohol abuse, and elevated cholesterol, blood pressure and body mass index. The mechanism by which RA causes this increased risk remains unknown; the presence of chronic inflammation has been proposed as a contributing factor.

Epidemiology



Disability-adjusted life year for rheumatoid arthritis per 100,000 inhabitants in 2004.
- no data
- less than 40
- 40-50
- 50-60
- 60-70
- 70-80
- 80-90
- 90-100
- 100-110
- 110-120
- 120-130
- 130-140
- more than 140

The incidence of RA is in the region of 3 cases per 10,000 population per annum. Onset is uncommon under the age of 15 and from then on the incidence rises with age until the age of 80. The prevalence rate is 1%, with women affected three to five times as often as men. It is 4 times more common in smokers than non-smokers. A study in 2010 found that those who drank modest amounts of alcohol regularly were four times less likely to get rheumatoid arthritis than those who never drank. Some Native American groups have higher prevalence rates (5-6%) and people from the Caribbean region have lower

prevalence rates. First-degree relatives prevalence rate is 2-3% and disease genetic concordance in monozygotic twins is approximately 15-20%.

It is strongly associated with the inherited tissue type Major histocompatibility complex (MHC) antigen HLA-DR4 (most specifically DR0401 and 0404)—hence family history is an important risk factor.

Rheumatoid arthritis affects women three times more often than men, and it can first develop at any age. The risk of first developing the disease (the disease incidence) appears to be greatest for women between 40 and 50 years of age, and for men somewhat later. RA is a chronic disease, and although rarely, a spontaneous remission may occur, the natural course is almost invariably one of persistent symptoms, waxing and waning in intensity, and a progressive deterioration of joint structures leading to deformations and disability.

History

The first known traces of arthritis date back at least as far as 4500 BC. A text dated 123 AD first describes symptoms very similar to rheumatoid arthritis. It was noted in skeletal remains of Native Americans found in Tennessee. In the Old World the disease is vanishingly rare before the 1600s. and on this basis investigators believe it spread across the Atlantic during the Age of Exploration. In 1859 the disease acquired its current name.

An anomaly has been noticed from investigation of Precolumbian bones. The bones from the Tennessee site show no signs of tuberculosis even though it was prevalent at the time throughout the Americas. Jim Mobley, at Pfizer, has discovered a historical pattern of epidemics of tuberculosis followed by a surge in the number of rheumatoid arthritis cases a few generations later. Mobley attributes the spikes in arthritis to selective pressure caused by tuberculosis. A hypervigilant immune system is protective against tuberculosis at the cost of an increased risk of autoimmune disease.

The art of Peter Paul Rubens may possibly depict the effects of rheumatoid arthritis. In his later paintings, his rendered hands show, in the opinion of some physicians, increasing deformity consistent with the symptoms of the disease. Rheumatoid arthritis appears to some to have been depicted in 16th century paintings. However, it is generally recognised in art historical circles that the painting of hands in the sixteenth and seventeenth century followed certain stylised conventions, most clearly seen in the Mannerist movement. It was conventional, for instance to show the upheld right hand of Christ in what now appears a deformed posture. These conventions are easily misinterpreted as portrayals of disease. They are much too widespread for this to be plausible.

The first recognized description of rheumatoid arthritis was in 1800 by the French physician Dr Augustin Jacob Landré-Beauvais (1772–1840) who was based in the famed Salpêtrière Hospital in Paris. The name "rheumatoid arthritis" itself was coined in 1859 by British rheumatologist Dr Alfred Baring Garrod.

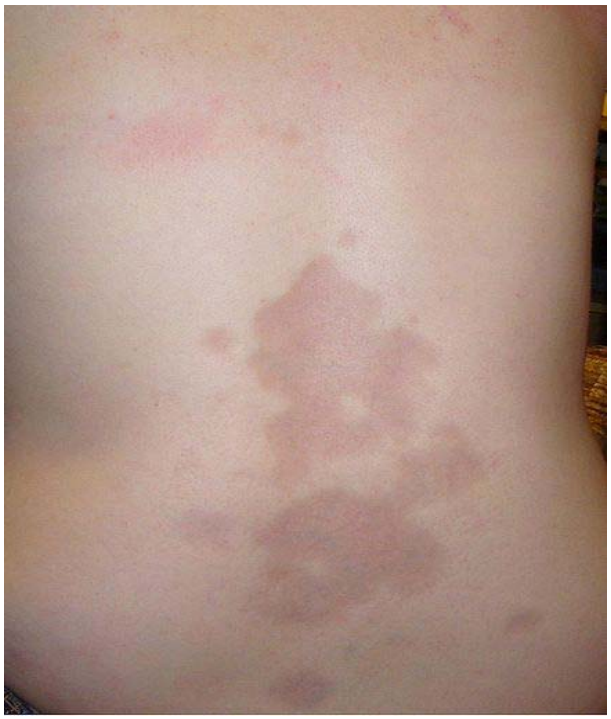
Notable cases

- Dorothy Hodgkin, Nobel prize winning scientist, developed severe deforming rheumatoid arthritis at age 28. In spite of this she continued her career and developed X-ray crystallography, which underpins much of the information known about rheumatoid arthritis. She also discovered the structure of insulin and enabled the discovery of the genetic code.
- Auguste Renoir, impressionist painter, whose later 'softer' style might have reflected in some way his severe disability.
- Christiaan Barnard, the first surgeon to perform a human-to-human heart transplant had to retire owing to the condition. He also wrote a book on living with arthritis.
- James Coburn claimed to have healed the condition using pills containing a sulfur-containing compound on his return to acting.
- Erik Lindbergh, aviator and member of the X-Prize administration. Erik has been a spokesman for the arthritis drug Enbrel, as a result of his success with the treatment.
- Bob Mortimer British comedian and actor.
- Kathleen Turner and Aida Turturro have worked to raise public awareness of the condition
- Billy Bowden, international cricket umpire who had to retire from active play because of rheumatoid arhtirits.
- Melvin Franklin, bass singer of the Temptations. He treated RA with cortisone shots so he could perform.
- Jamie Farr, American actor, famous for his role as Max Klinger on the 1970s television series M*A*S*H.
- Sandy Koufax, An American Hall-of-Fame baseball pitcher who played from 1955 to 1966 for the Los Angeles Dodgers.
- Raoul Dufy, French artist (1877-1953), continued to paint despite RA and was one of the first patients ever treated with cortisone, in a Boston hospital.

Chapter 3

Scleroderma

Scleroderma



ICD-10 L94.0-L94.1, M34.

ICD-9 701.0 710.1

Scleroderma is a chronic systemic autoimmune disease characterized by fibrosis (or hardening), vascular alterations, and autoantibodies. There are two major forms:

Limited systemic sclerosis/scleroderma involves cutaneous manifestations that mainly affect the hands, arms and face. Previously called CREST syndrome in reference to the following complications: **C**alcinosis, **R**aynaud's phenomenon, **E**sophageal dysfunction, **S**clerodactyly, and **T**elangiectasias. Additionally, pulmonary arterial hypertension may occur in up to one third of patients and is the most serious complication for this form of scleroderma.

Diffuse systemic sclerosis/scleroderma is rapidly progressing and affects a large area of the skin and one or more internal organs, frequently the kidneys, esophagus, heart and lungs. This form of scleroderma can be quite disabling. There are no treatments for scleroderma itself, but individual organ system complications are treated. Other forms of scleroderma include Systemic sine scleroderma, which lacks skin changes, but has systemic manifestations, and two localized forms which affect the skin, but not the internal organs: morphea, and linear scleroderma.

Prognosis is generally good for limited cutaneous scleroderma patients who escape pulmonary complications. Prognosis is worse for diffuse cutaneous disease, particularly in older age, and for males. Death occurs most often from pulmonary, heart and kidney complications. In diffuse cutaneous disease, 5-year survival is 70%, 10-year survival 55%.

The cause is unknown. Scleroderma runs in families, but the genes have not been identified. It affects the small blood vessels known as arterioles, in all organs. First, the endothelial cells of the arteriole die off, along with smooth muscle cells, by a process of apoptosis. They are replaced by collagen and other fibrous material. Inflammatory cells, particularly CD4+ helper T cells, infiltrate the arteriole, and cause further damage. Many of the inflammatory and destructive protein signals have been identified, and they are potential targets for drugs that could interrupt the process.

Classification

Scleroderma is characterized by the appearance of circumscribed or diffuse, hard, smooth, ivory-colored areas that are immobile, and which give the appearance of hidebound skin, a disease occurring in both localized and systemic forms:

- Localized scleroderma
    - Localized morphea
    - Morphea-lichen sclerosus et atrophicus overlap
    - Generalized morphea
    - Atrophoderma of Pasini and Pierini
    - Pansclerotic morphea
    - Morphea profunda
    - Linear scleroderma
- Systemic scleroderma
    - CREST syndrome
    - Progressive systemic sclerosis

Diagnosis

Typical scleroderma is classically defined as symmetrical skin thickening, with about 90% of cases also presenting with Raynaud's phenomenon, nail-fold capillary changes, and anti-nuclear antibodies. Patients may or may not experience systemic organ involvement. Atypical scleroderma may show any variation of these changes without skin

changes or with finger swelling only. Additional symptoms of scleroderma typically present themselves within two years of Raynaud's phenomenon.

Laboratory testing can show anti-topoisomerase antibodies (causing a diffuse systemic form), or anti-centromere antibodies (causing a limited systemic form, and the CREST syndrome). Other autoantibodies can be seen, such as anti-U3 or anti-RNA polymerase.

Severe complications from scleroderma include:

- Heart: Untreated high blood pressure strains the heart; irregular heart rhythm and enlargement of the heart lead to heart failure.
- Kidney: scleroderma renal crisis in which malignant hypertension develops and causes acute renal failure. This was once a common cause of death, but now is easy to treat with ACE inhibitors.
- Lung: Two-thirds of all patients suffer from respiratory problems such as shortness of breath, coughing, difficulty breathing, alveolitis (inflammation of lung air sacs), pneumonia, and cancer.
- Digestive: Esophagus damage can make it difficult to swallow food, and acid reflux is common. The stomach can develop watermelon stomach (gastric antral vascular ectasia, GAVE) which occasionally may bleed profusely. A sluggish intestine may cause pain & bloating; undigested food can result in diarrhea, weight loss and anemia.
- Skin and joints: Carpal tunnel syndrome is common, as are muscle weakness, joint pain, and stiffness.

Treatment

There is no direct cure for scleroderma. Because the exact cause is unknown, any treatment is patient-specific and aimed at ameliorating symptoms of the disease. For example, patients who experience Raynaud's phenomenon may be treated with agents to increase blood flow to the fingers, including nifedipine, amlodipine, diltiazem, felodipine, or nicardipine.

Fibrosis of the skin has been treated with varying degrees of success with agents such as d-penicillamine, colchicine, PUVA, Relaxin, and cyclosporine.

Because scleroderma is an autoimmune disease, one of the major pillars of treatment involves the use of immunosuppressive agents. These drugs include methotrexate, cyclophosphamide, azathioprine, and mycophenolate.

In Traditional Chinese Medicine, scleroderma may be treated as an issue of blood stasis, kidney deficiency, and/or spleen deficiency. Chinese herbology treatments include blood vitalizers, yang tonics, spleen qi tonics, and warming agents.

Prognosis

Individuals with morphea or limited scleroderma have a relatively positive outlook. They will usually die from another disease, not the scleroderma. Those with very widespread skin and organ involvement (systemic) have a negative prognosis. More women have scleroderma, but the disease kills more men. Following diagnosis, two-thirds of patients live at least 11 years. The higher the patient's age at diagnosis, the more likely they are to die from the disease.

People with scleroderma have very different life expectancies. Some—for example, those with limited or mild diffuse disease—can expect to live 20 to 50 years after diagnosis, just like anyone else. Others with severe, rapidly progressive disease—a group which makes up less than 10% of the total number of patients with diffuse scleroderma—might have a 50% chance of a five-year survival.

Epidemiology

This disease is found among all races worldwide, but women are four times more likely to develop scleroderma than men. In the United States, approximately one person in 1,000 is affected. Children rarely suffer the systemic type, but localized scleroderma is common. Most adults are diagnosed after their 30th birthday and before age 50. The disease has high rates among the native American Choctaw tribe and African-American females.

History

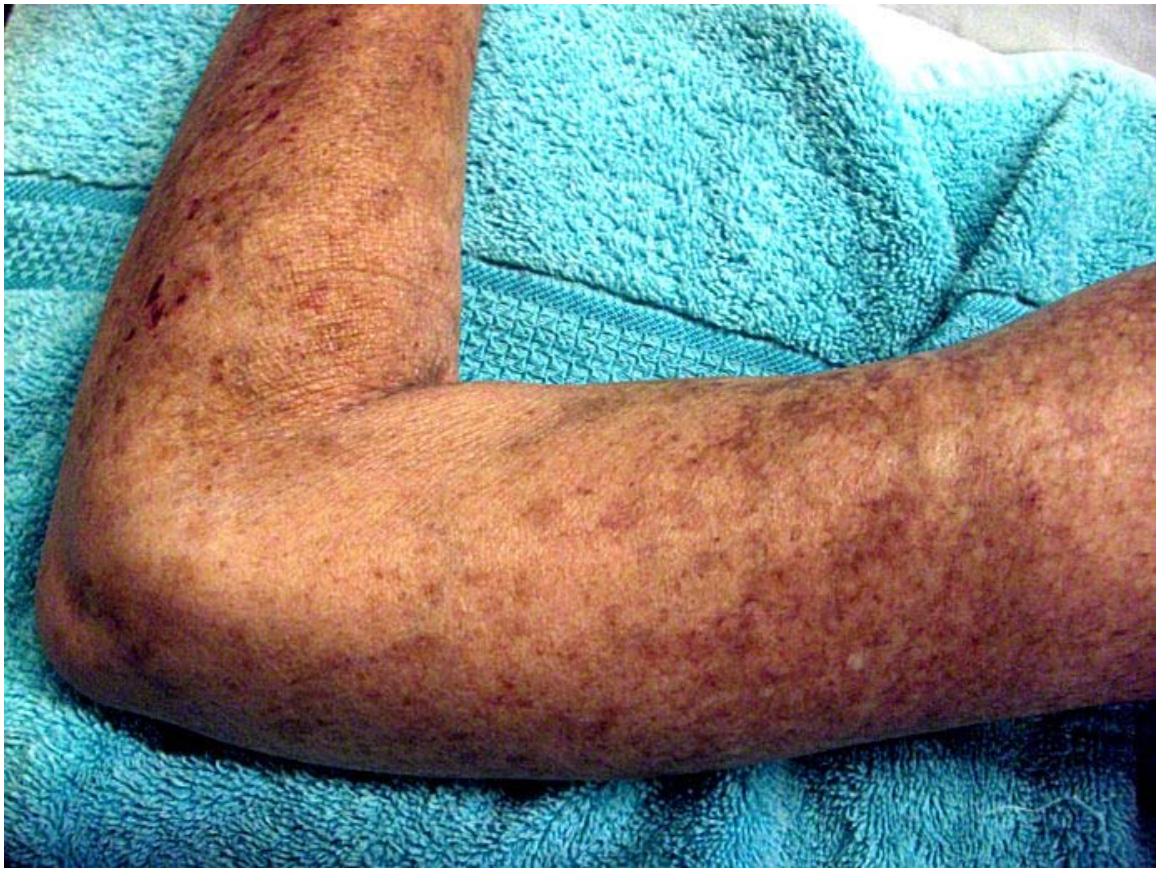
Cases of skin disease similar to scleroderma may be found in the writings of Hippocrates as far back as 460–370 B.C. Oribasius (325–403 A.D.) and Paulus Agineta (625–690 A.D.), also wrote on the subject. It is difficult for us to know if these were truly examples of scleroderma because the descriptions were inexact.

The first definite description of the disease was by Carlo Curzio in a monograph published in Naples in 1753. This account produced considerable interest in French and English medical circles.

The account concerns a young woman of 17 named Patrizia Galiera, who was admitted to the hospital and assigned to Dr. Curzio. Her symptoms as described by the doctor involved hardness of the skin (differing in degree from place to place), tightness around the mouth, and hardness around the neck. He noted loss of warmth in the skin but no other problem in pulse, respiration, or digestion.

Much of the report contains details of the treatment, which included warm milk and vapor baths, bleeding from the foot, and small doses of quicksilver. After 11 months, the skin became soft and flexible, and all natural functions were restored.

Curzio's observations were published in French in 1755 and aroused considerable interest. The early dermatological texts of R. William in London (1808) and his student, J. L. Alibert, in Paris (1818) referred to Curzio's observation.

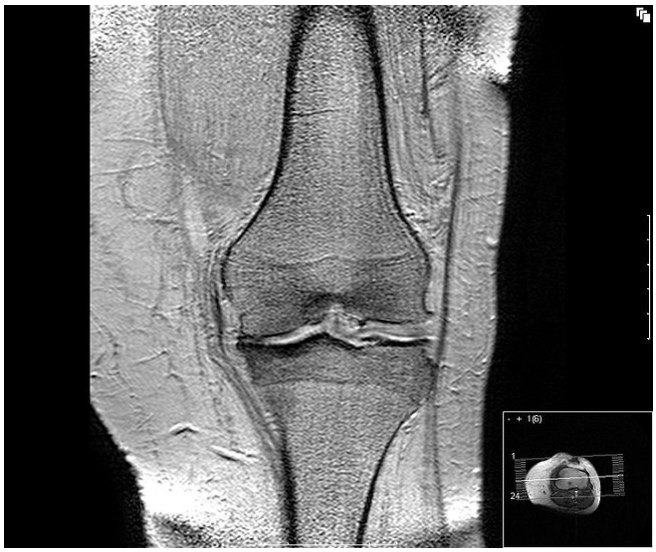


Left arm of Scleroderma patient, showing skin lesions

Chapter 4

Osteoarthritis

Osteoarthritis



ICD-10	M15.-M19., M47.
ICD-9	715
OMIM	165720
DiseasesDB	9313
MedlinePlus	000423
eMedicine	med/1682 orthoped/427 pmr/93 radio/492
MeSH	D010003

Osteoarthritis (OA) also known as **degenerative arthritis** or **degenerative joint disease**, is a group of mechanical abnormalities involving degradation of joints, including articular cartilage and subchondral bone. Symptoms may include joint pain, tenderness, stiffness, locking, and sometimes an effusion. A variety of causes—hereditary, developmental, metabolic, and mechanical—may initiate processes leading to loss of

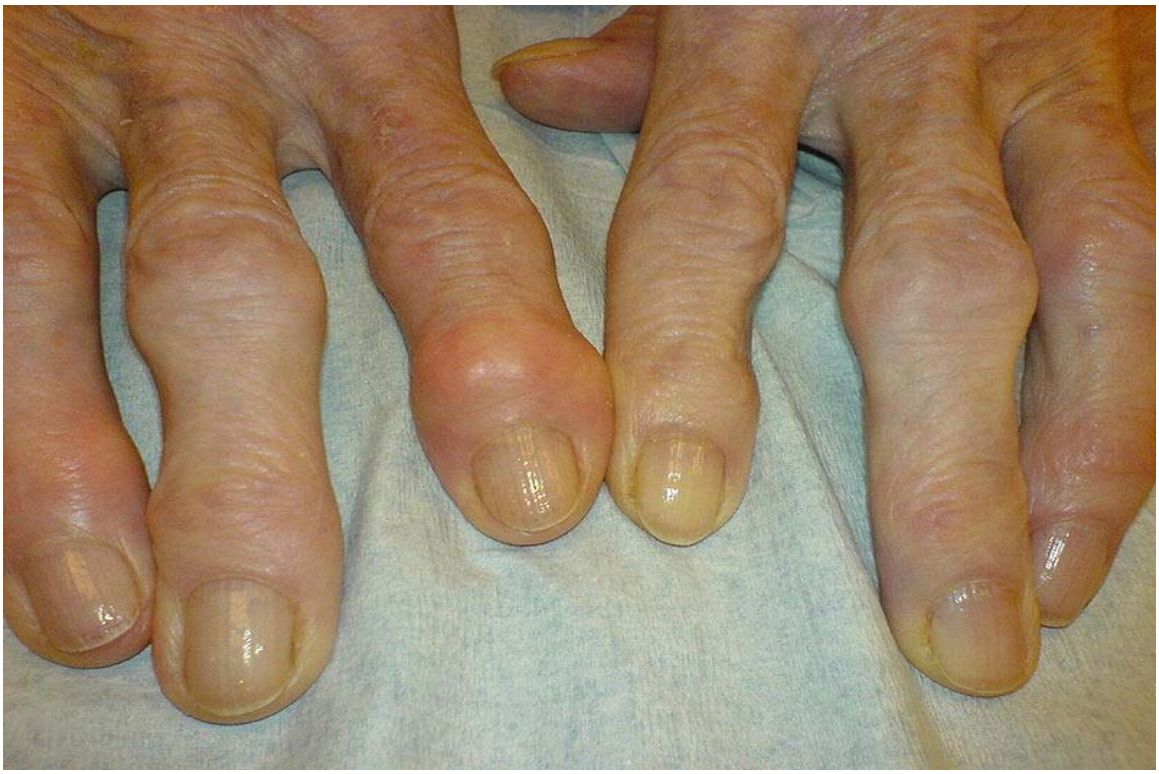
cartilage. When bone surfaces become less well protected by cartilage, bone may be exposed and damaged. As a result of decreased movement secondary to pain, regional muscles may atrophy, and ligaments may become more lax.

Treatment generally involves a combination of exercise, lifestyle modification and analgesics. If pain becomes debilitating joint replacement surgery may be used to improve the quality of life. OA is the most common form of arthritis, and the leading cause of chronic disability in the United States. It affects about 8 million people in the United Kingdom and nearly 27 million people in the United States.

Classification

Osteoarthritis can be classified into either primary or secondary depending on if there is or is not an identifiable underlying cause.

Signs and symptoms



Bouchard's nodes and Heberden's nodes may form in osteoarthritis

The main symptom is pain, causing loss of ability and often stiffness. "Pain" is generally described as a sharp ache, or a burning sensation in the associate muscles and tendons. OA can cause a crackling noise (called "crepitus") when the affected joint is moved or touched, and patients may experience muscle spasm and contractions in the tendons. Occasionally, the joints may also be filled with fluid. Humid and cold weather increases the pain in many patients.

OA commonly affects the hands, feet, spine, and the large weight bearing joints, such as the hips and knees, although in theory, any joint in the body can be affected. As OA progresses, the affected joints appear larger, are stiff and painful, and usually feel *worse*, the more they are used throughout the day, thus distinguishing it from rheumatoid arthritis.

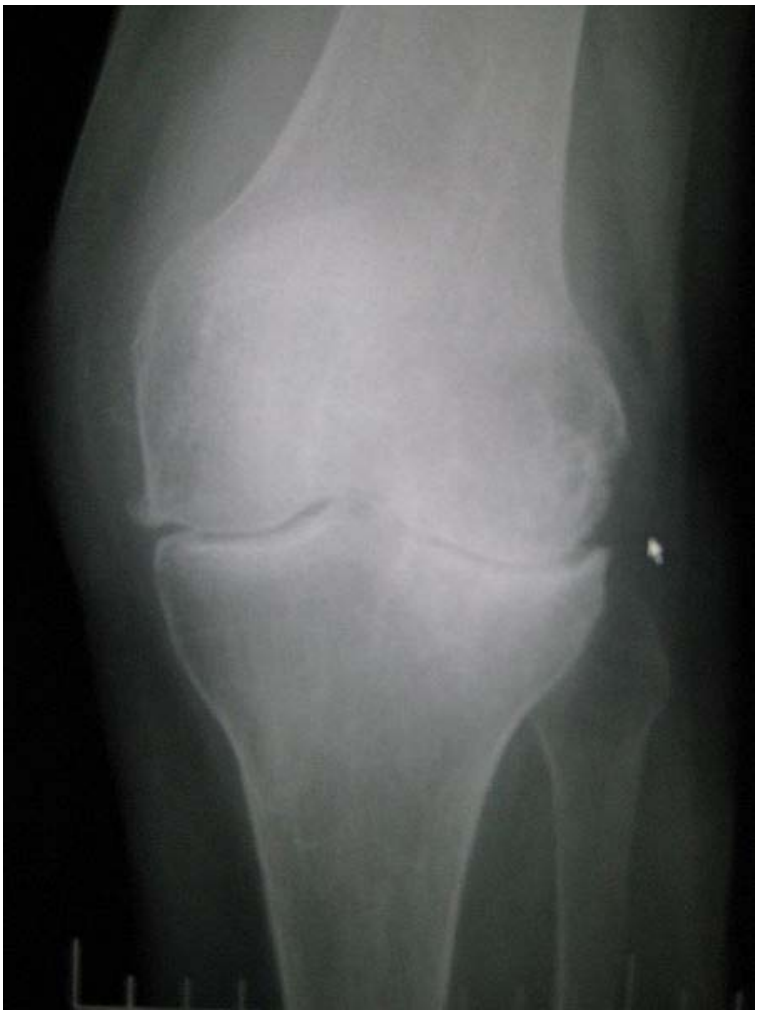
In smaller joints, such as at the fingers, hard bony enlargements, called Heberden's nodes (on the distal interphalangeal joints) and/or Bouchard's nodes (on the proximal interphalangeal joints), may form, and though they are not necessarily painful, they do limit the movement of the fingers significantly. OA at the toes leads to the formation of bunions, rendering them red or swollen. Some people notice these physical changes before they experience any pain.

OA is the most common cause of joint effusion, sometimes called *water on the knee* in lay terms, an accumulation of excess fluid in or around the knee joint.

Causes

Exercise, including running in the absence of injury, has not been found to increase one's risk of developing osteoarthritis. Some investigators believe that mechanical stress on joints underlies all osteoarthritis, with many and varied sources of mechanical stress, including misalignments of bones caused by congenital or pathogenic causes; mechanical injury; overweight; loss of strength in muscles supporting joints; and impairment of peripheral nerves, leading to sudden or uncoordinated movements that overstress joints.

Primary



Primary osteoarthritis of the left knee. Note the osteophytes, narrowing of the joint space (arrow), and increased subchondral bone density (arrow).

This type of OA is a chronic degenerative disorder related to but not caused by aging, as there are people well into their nineties who have no clinical or functional signs of the disease. As a person ages, the water content of the cartilage decreases as a result of a reduced proteoglycan content, thus causing the cartilage to be less resilient. Without the protective effects of the proteoglycans, the collagen fibers of the cartilage can become susceptible to degradation and thus exacerbate the degeneration. Inflammation of the surrounding joint capsule can also occur, though often mild (compared to that which occurs in rheumatoid arthritis). This can happen as breakdown products from the cartilage are released into the synovial space, and the cells lining the joint attempt to remove them. New bone outgrowths, called "spurs" or osteophytes, can form on the margins of the joints, possibly in an attempt to improve the congruence of the articular cartilage surfaces. These bone changes, together with the inflammation, can be both painful and debilitating.

A number of studies have shown that there is a greater prevalence of the disease between siblings and especially identical twins, indicating a hereditary basis. Up to 60% of OA cases are thought to result from genetic factors.

Both primary generalized nodal OA and erosive OA (EOA. also called inflammatory OA) are sub-sets of primary OA. EOA is a much less common, and more aggressive inflammatory form of OA which often affects the DIPs and has characteristic changes on X-Ray.

Secondary

This type of OA is caused by other factors but the resulting pathology is the same as for primary OA:

- Congenital disorders of joints
- Diabetes.
- Inflammatory diseases (such as Perthes' disease), (Lyme disease), and all chronic forms of arthritis (e.g. costochondritis, gout, and rheumatoid arthritis). In gout, uric acid crystals cause the cartilage to degenerate at a faster pace.
- Injury to joints, as a result of an accident or orthodontic operations.
- Septic arthritis (infection of a joint)
- Ligamentous deterioration or instability may be a factor.
- Marfan syndrome
- Obesity
- Alkaptonuria
- Hemochromatosis and Wilson's disease

Diagnosis

Diagnosis is made with reasonable certainty based on history and clinical examination. X-rays may confirm the diagnosis. The typical changes seen on X-ray include: joint space narrowing, subchondral sclerosis (increased bony formation around the joint), subchondral cyst formation, and osteophytes. Plain films may not correlate with the findings on physical examination or with the degree of pain. Usually other imaging techniques are not necessary to clinically diagnose osteoarthritis.

In 1990, the American College of Rheumatology, using data from a multi-center study, developed a set of criteria for the diagnosis of hand osteoarthritis based on hard tissue enlargement and swelling of certain joints. These criteria were found to be 92% sensitive and 98% specific for hand osteoarthritis versus other entities such as rheumatoid arthritis and spondyloarthropathies.

Related pathologies whose names may be confused with osteoarthritis include pseudo-arthrosis. This is derived from the Greek words pseudo, meaning "false", and arthrosis, meaning "joint." Radiographic diagnosis results in diagnosis of a fracture within a joint,

which is not to be confused with osteoarthritis which is a degenerative pathology affecting a high incidence of distal phalangeal joints of female patients.

Treatment

Lifestyle modification (such as weight loss and exercise) and analgesics are the mainstay of treatment. Acetaminophen / paracetamol is used first line and NSAIDS are only recommended as add on therapy if pain relief is not sufficient. This is due to the relative greater safety of acetaminophen.

Physical therapy

Physical therapy has been shown to significantly improve function, decrease pain, and delay need for surgical intervention in advanced cases. Exercise prescribed by a physical therapist has been shown to be more effective than medications in treating osteoarthritis of the knee. Functional, gait, and balance training has been recommended to address impairments of proprioception, balance, and strength in individuals with lower extremity arthritis as these can contribute to higher falls in older individuals. Splinting of the thumb for OA of the base of the thumb leads to improvements after one year.

Lifestyle modification

Exercise

For most people with OA, graded exercise should be the mainstay of their self-management. Moderate exercise leads to improved functioning and decreased pain in people with osteoarthritis of the knee.

Education

For overweight people, weight loss may be an important factor. Patient education has been shown to be helpful in the self-management of arthritis. It decreases pain, improving function, reducing stiffness and fatigue, and reducing medical usage. A meta-analysis has shown patient education can provide on average 20% more pain relief when compared to NSAIDs alone in patients with hip OA.

Medication

Analgesics

Acetaminophen is the first line treatment for OA. For mild to moderate symptoms effectiveness is similar to NSAIDs, though for more severe symptoms NSAIDs may be more effective. Non-steroidal anti-inflammatory drugs (NSAID) such as ibuprofen while more effective in severe cases are associated with greater side effects such as gastrointestinal bleeding. Another class of NSAIDs, COX-2 selective inhibitors (such as celecoxib) are equally effective to NSAIDs but no safer in terms of side effects. They are however much more expensive. There are several NSAIDs available for topical use

including diclofenac. They have less systemic side-effects and at least some therapeutic effect. While opioid analgesic such as morphine and fentanyl improve pain this benefit is outweighed by frequent adverse events and thus they should not routinely be used.

Other

Oral steroids are not recommended in the treatment of OA because of their modest benefit and high rate of adverse effects. Injection of glucocorticoids (such as hydrocortisone) leads to short term pain relief that may last between a few weeks and a few months. Topical capsaicin and joint injections of hyaluronic acid have not been found to lead to significant improvement.

Tanezumab, a monoclonal antibody that binds and inhibits nerve growth factor, appears to relieve joint pain enough to improve function in people with osteoarthritis of the knee, according to research published online Sept. 29 in the New England Journal of Medicine. The FDA is reviewing the safety of tanezumab that could still emerge as an effective treatment for the pain of osteoarthritis.

While electrostimulation techniques (NEST) have been used for twenty years to treat osteoarthritis in the knee, a Cochrane Review of studies determined that there is no evidence to show that it reduces pain or disability.

Surgery

If the above management is ineffective, joint replacement surgery or resurfacing may be required in advanced cases. Arthroscopic surgical intervention for osteoarthritis of the knee however has been found to be no better than placebo at relieving symptoms.

Alternative medicine

Many alternative medicines are purporting to decrease pain associated with arthritis, however there is no evidence supporting benefits for most alternative treatments including: vitamin A, C, and E, ginger, turmeric, omega-3 fatty acids, and chondroitin sulfate, glucosamine and these are thus not recommended. Glucosamine was once believed to be effective however a recent analysis has found that it is no better than placebo.S-Adenosyl methionine may relieve pain similar to nonsteroidal anti-inflammatory drugs.

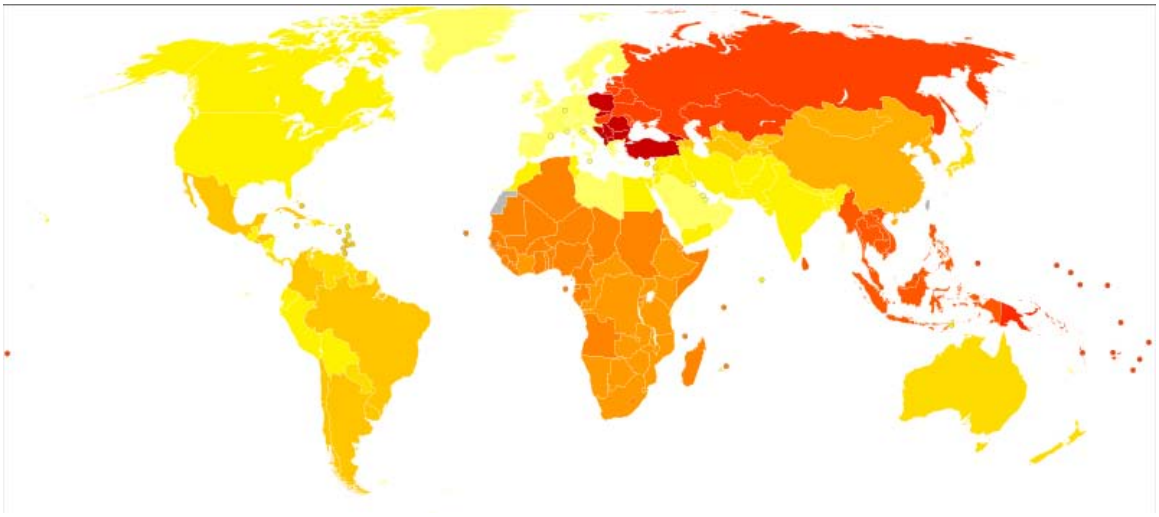
Acupuncture

A Cochrane review found that while acupuncture leads to a statistically significant improvement in pain this improvement is small and of questionable clinical significance. Acupuncture does not seem to produce long-term benefits.

Glucosamine

Controversy surrounds glucosamine. A 2010 meta-analysis has found that it is no better than placebo. Some older reviews conclude that glucosamine sulfate was an effective treatment while some others have found it ineffective. A difference has been found between trials involving glucosamine sulfate and glucosamine hydrochloride, with glucosamine sulfate showing a benefit and glucosamine hydrochloride not. The OARSI recommends that glucosamine be discontinued if no effect is observed after six months.

Epidemiology



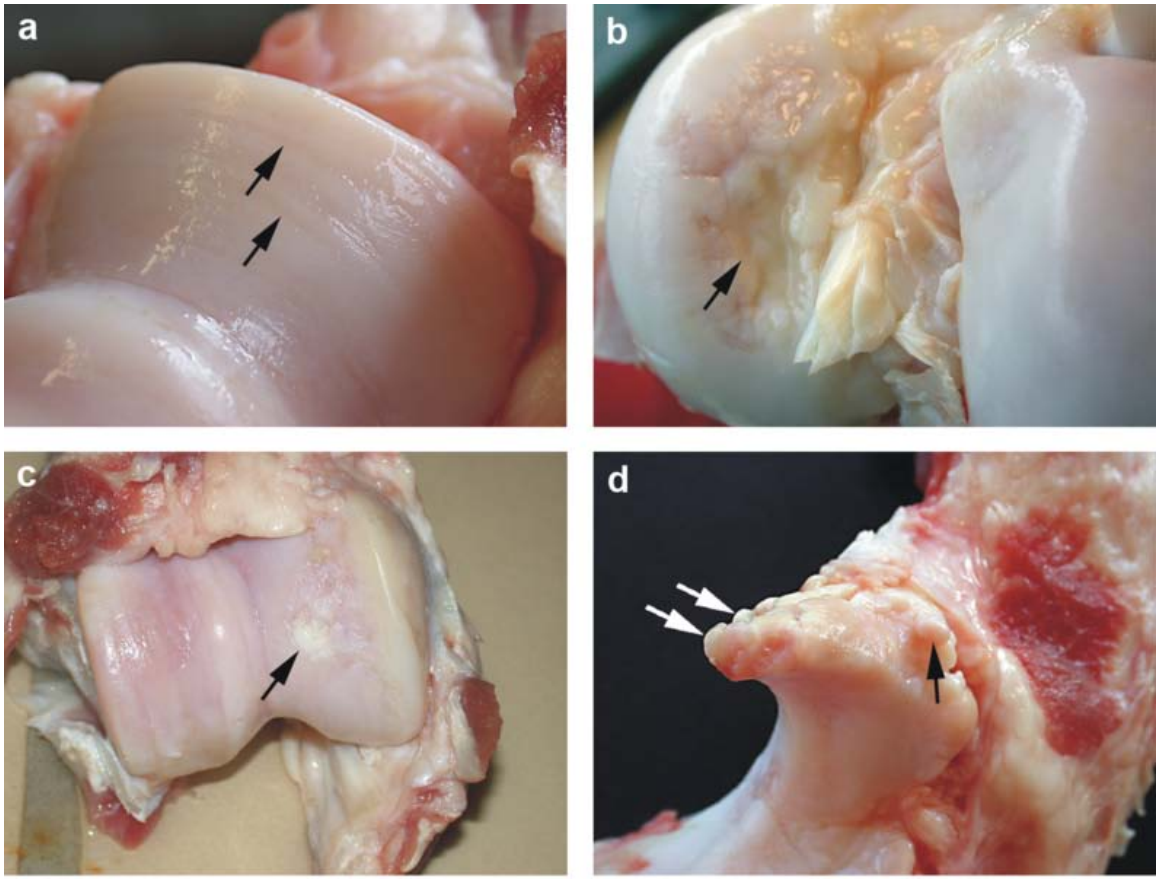
Disability-adjusted life year for osteoarthritis per 100,000 inhabitants in 2004.
- no data
- ≤ 200
- 200-220
- 220-240
- 240-260
- 260-280
- 280-300
- 300-320
- 320-340
- 340-360
- 360-380
- 380-400
- ≥ 400

Osteoarthritis affects nearly 27 million people in the United States, accounting for 25% of visits to primary care physicians, and half of all NSAID prescriptions. It is estimated that 80% of the population have radiographic evidence of OA by age 65, although only 60% of those will have symptoms. In the United States, hospitalizations for osteoarthritis increased from 322,000 in 1993 to 735,000 in 2006.

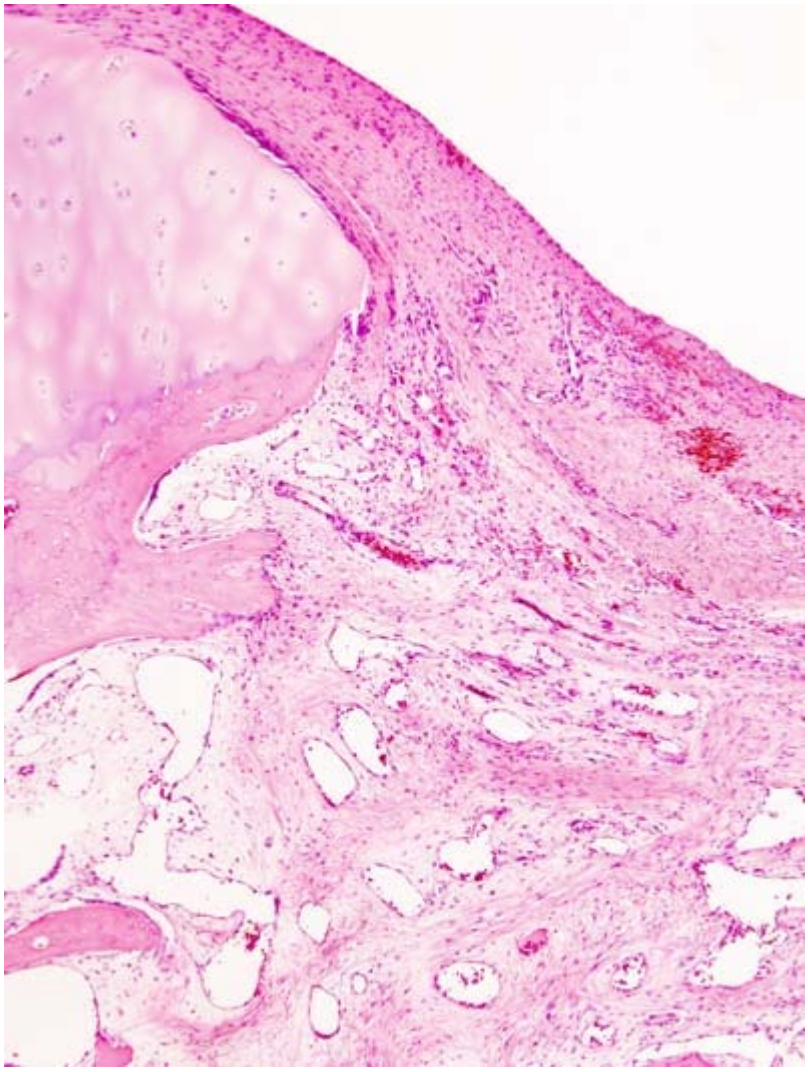
Etymology

Osteoarthritis is derived from the Greek word "*osteo*", meaning "of the bone", "*arthro*", meaning "joint", and "*itis*", meaning inflammation, although the "itis" of osteo arthritis is somewhat of a misnomer—inflammation is not a conspicuous feature.

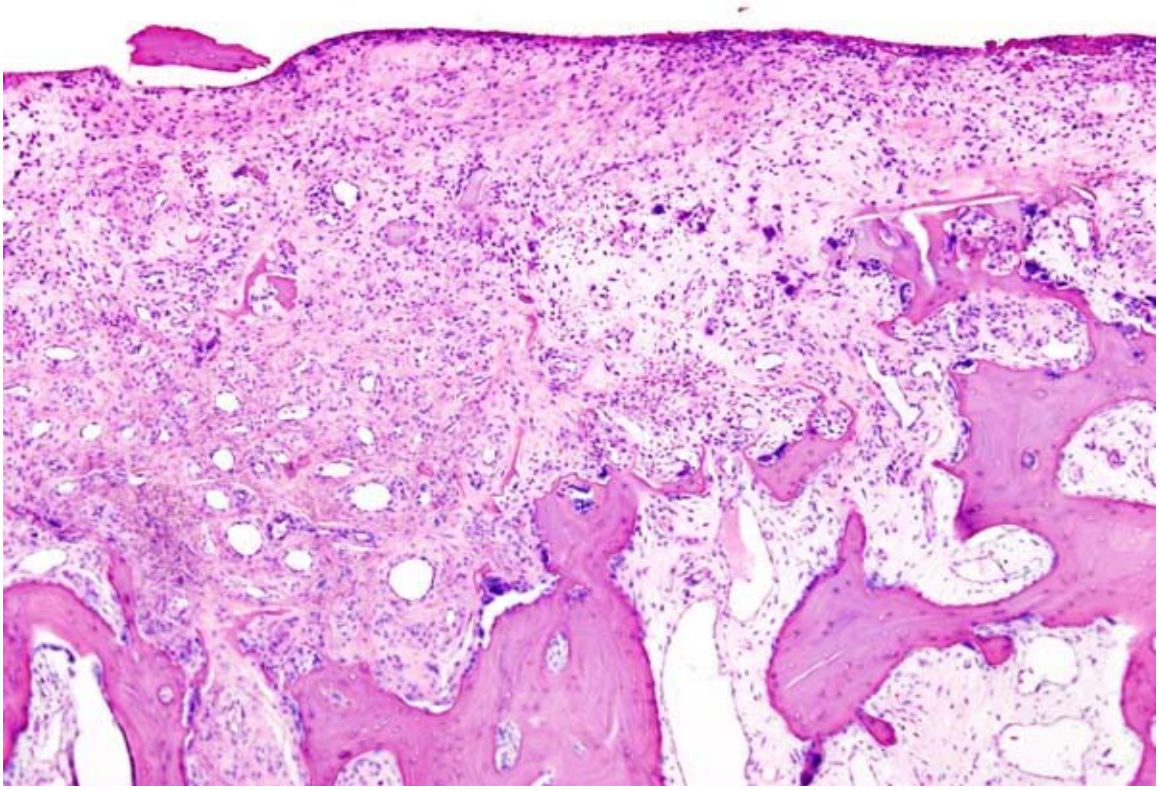
Additional Images

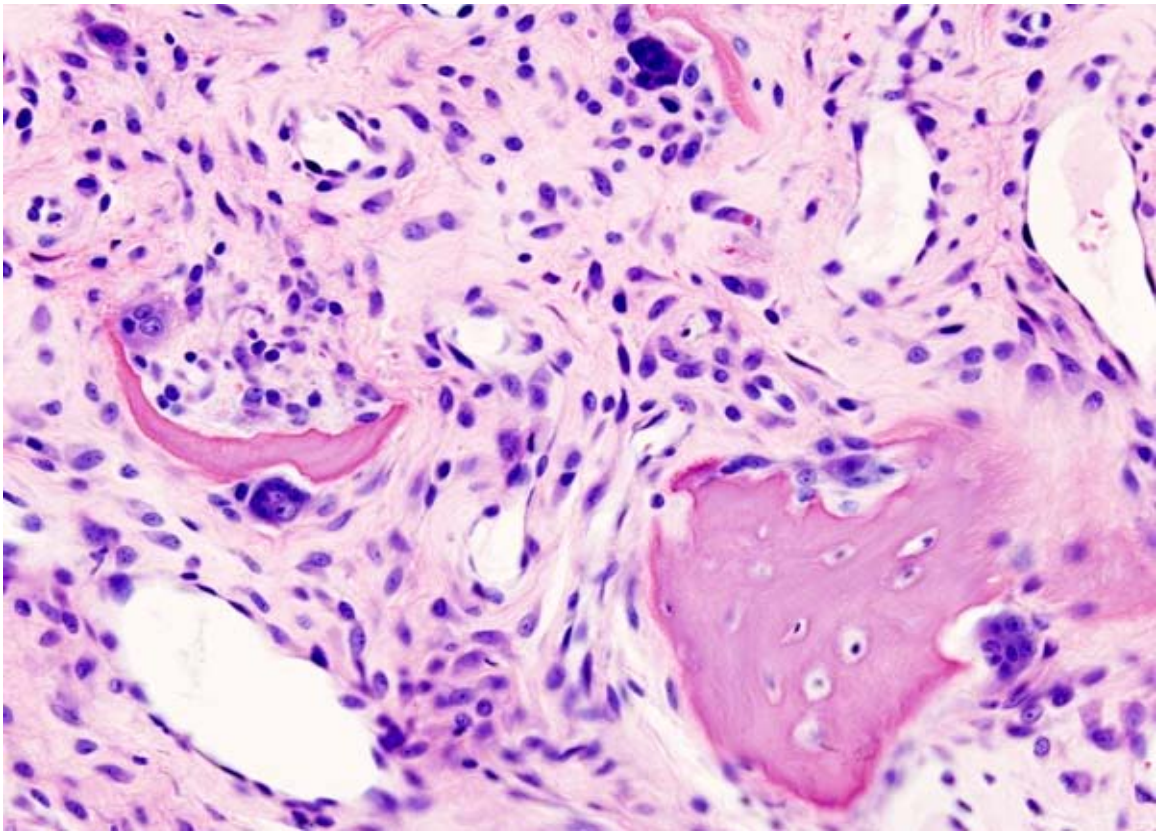


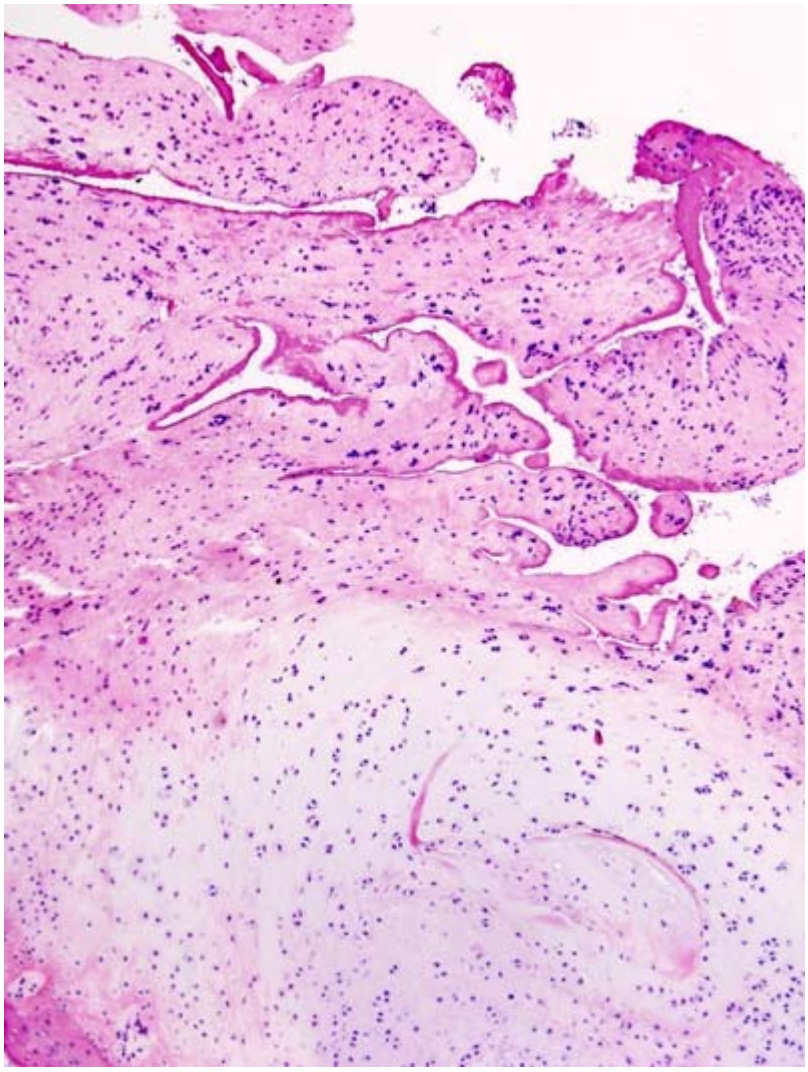
Damaged cartilage in gross pathological specimen from sows. (a) cartilage erosion (b)cartilage ulceration (c)cartilage repair (d)osteophyte (bone spur) formation.

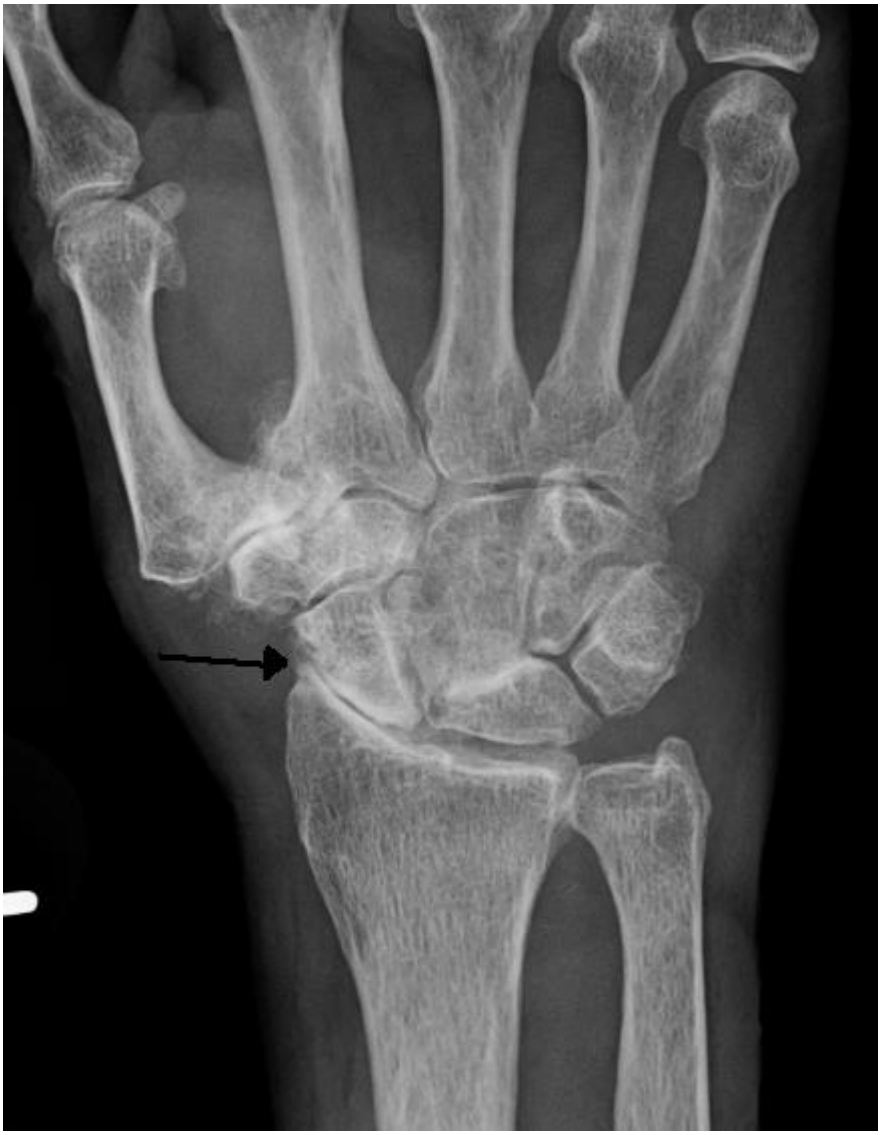


Histopathology of osteoarthrosis of a knee joint in an elderly female patient





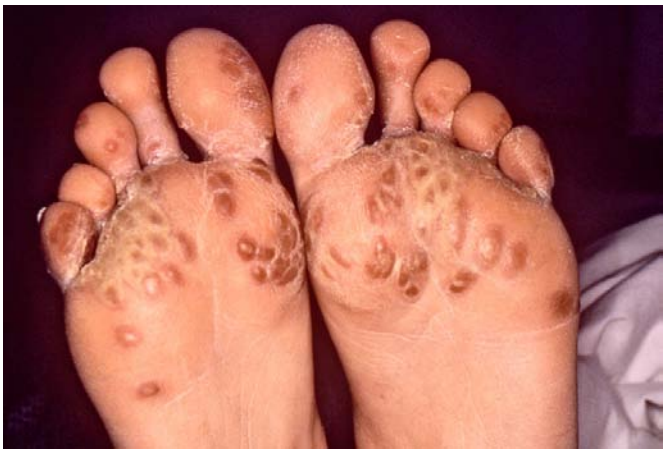




Severe osteoarthritis and osteopenia of the carpel joint and 1st carpometacarpel joint

Chapter 5

Reactive Arthritis

Reiters's Syndrome

Diagnosis revealed that the rash on the bottom of this individual's feet, known as *keratoderma blennorrhagica*, was due to Reiter's syndrome.
ICD-10 M02.
ICD-9 099.3
DiseasesDB 29524
eMedicine med/1998
MeSH *C01.539.100.500*

Reactive arthritis (**Reiter's Syndrome** or Reiter's arthritis), is classified as an autoimmune condition that develops in response to an infection in another part of the body. Coming into contact with bacteria and developing an infection can trigger the disease. It has symptoms similar to various other conditions collectively known as "arthritis". By the time the patient presents with symptoms, often time the "trigger" infection has been cured or is in remission in chronic cases, thus making determination of the initial cause difficult.

Reactive arthritis has also been known as **Reiter's Syndrome**, **arthritis urethritica**, **venereal arthritis** and **polyarteritis enterica**. It is a type of seronegative spondyloarthropathy. The original name "Reiter's syndrome", named after the German physician Hans Conrad Julius Reiter for his contributions to identification and description of the disease, has become unpopular in the past decade as Reiter's history of Nazi party membership, allegations of experimentation in the Buchenwald concentration camp, and prosecution in Nuremburg as a war criminal, have come to light.

The manifestations of Reactive arthritis include the following triad of symptoms: an inflammatory arthritis of large joints including commonly the knee and the back (due to involvement of the sacroiliac joint), inflammation of the eyes in the form of (conjunctivitis or uveitis), and urethritis in men or cervicitis in women. Patients can also present with mucocutaneous lesions, as well as psoriasis-like skin lesions such as circinate balanitis, and keratoderma blennorrhagica. Enthesitis can involve the Achilles tendon resulting in heel pain. Not all affected persons have all the manifestations, and the formal definition of the disease is the occurrence of otherwise unexplained non-infectious inflammatory arthritis combined with urethritis in men, or cervicitis in women.

Reactive arthritis is an RF-seronegative, HLA-B27-linked spondyloarthropathy (autoimmune damage to the cartilages of joints) often precipitated by genitourinary or gastrointestinal infections. The most common triggers are sexually transmitted *Chlamydial* infections and perhaps, less commonly, *Neisseria gonorrhea*; and *Salmonella*, *Shigella*, or *Campylobacter* intestinal infections.

Reactive arthritis most commonly strikes individuals aged 20–40 year of age, and is more common in men than in women, and more common in whites than in blacks. This is owing to the high frequency the of HLA-B27 gene in the white population. Patients with HIV have an increased risk of developing reactive arthritis as well.

Signs and symptoms

Symptoms generally appear within 1–3 weeks but can range from 4 to 35 days from the onset of the inciting episode of the disease.

The classical presentation is that the first symptom experienced is a urinary symptom such as burning pain on urination (dysuria) or an increased frequency of urination. Other urogenital problems may arise such as prostatitis in men and cervicitis, salpingitis and/or vulvovaginitis in women. The arthritis that follows usually affects the large joints such as the knees causing pain and swelling with relative sparing of small joints such as the wrist and hand.

Eye involvement occurs in about 50% of men with urogenital reactive arthritis and about 75% of men with enteric reactive arthritis. Conjunctivitis and uveitis can include redness of the eyes, eye pain and irritation, or blurred vision. Eye involvement typically occurs early in the course of reactive arthritis, and symptoms may come and go.

Roughly 20 to 40 percent of the men with the disease develop penile lesions called balanitis circinata (circinate balanitis). A small percentage of men and women develop small hard nodules called keratoderma blennorrhagica on the soles of the feet and, less commonly, on the palms of the hands or elsewhere. In addition, some individuals with reactive arthritis develop mouth ulcers that come and go. In some cases, these ulcers are painless and go unnoticed. Some patients suffer serious gastrointestinal problems similar to those of the Crohn's disease.

About 10 percent of the people with reactive arthritis, especially those with a prolonged course of the disease, will develop cardiac manifestations, including aortic regurgitation and pericarditis. Reiter's Syndrome has been described as a pre-cursor to other spondylarthropies, including ankylosing spondylitis.

Causes

It is set off by a preceding infection, the most common of which would be a genital infection with *Chlamydia trachomatis* in the US. Other bacteria known to cause reactive arthritis which are more common worldwide are *Ureaplasma urealyticum*, *Salmonella* spp., *Shigella* spp., *Yersinia* spp., and *Campylobacter* spp. A bout of food poisoning or a gastrointestinal infection may also precede the disease (those last four genera of bacteria mentioned are enteric bacteria). There is some circumstantial evidence for other organisms causing the disease, but the details are unclear. Reactive arthritis usually manifests about 1–3 weeks after a known infection. The mechanism of interaction between the infecting organism and the host is unknown. Synovial fluid cultures are negative, suggesting that reactive arthritis is caused either by an over-stimulated autoimmune response or by bacterial antigens which have somehow become deposited in the joints.

Diagnosis

There are few clinical symptoms, but the clinical picture is dominated by polyarthritis. There is pain, swelling, redness, and heat in the joints affected. MRI is effective in diagnosis.

The urethra, cervix and the throat may be swabbed in an attempt to culture the causative organisms. Cultures may be carried out on urine and stool samples. Arthrocentesis can be done in order to study the synovial fluid from an affected joint for further cell count, and for culture.

Also, an blood test for the genetic marker HLA-B27 may be given to determine if the patient has the gene. About 75 percent of all the patients with Reiter's arthritis have the gene. C-Reactive Protein (CRP), and Erythrocyte Sedimentation Rate (ESR) are non-specific tests that can be done to corroborate the diagnosis of the syndrome.

Diagnostic Criteria

Although there are no definitive criteria to diagnose the existence of Reiter's arthritis, the American College of Rheumatology has published sensitivity and specificity guidelines.

Percent Sensitivity and Specificity of Various Criteria for Typical Reiter's Syndrome		
Method of diagnosis	*Sensitivity*	*Specificity*
1. Episode of arthritis of more than 1 month with urethritis and/or cervicitis	84.3%	98.2%
2. Episode of arthritis of more than 1 month and either urethritis or cervicitis, or bilateral conjunctivitis	85.5%	96.4%
3. Episode of arthritis, conjunctivitis, and urethritis	50.6%	98.8%
4. Episode of arthritis of more than 1 month, conjunctivitis, and urethritis	48.2%	98.8%

Treatment

The main goal of treatment is to identify and eradicate the underlying infectious source with the appropriate antibiotics if still present. Otherwise, treatment is symptomatic for each problem. Analgesics particularly NSAIDs, steroids and immunosuppressants may be needed for patients with severe reactive symptoms that do not respond to any other treatment.

Prognosis

Reactive arthritis may be self-limiting, frequently recurring, chronic or progressive. Most patients have severe symptoms lasting a few weeks to six months. Fifteen to 50 percent of cases have recurrent bouts of arthritis. Chronic arthritis or sacroiliitis occurs in 15-30 percent of cases. Repeated attacks over many years are common, and patients sometimes end up with chronic and disabling arthritis, heart disease, amyloid deposits, Ankylosing Spondylitus, immunoglobulin A nephropathy, cardiac conduction abnormalities, or aortitis with aortic regurgitation. However, most people with reactive arthritis can expect to live normal life spans and maintain a near-normal lifestyle with modest adaptations to protect the involved organs.

Epidemiology

Because women may be underdiagnosed, the exact incidence of reactive arthritis is difficult to estimate. A few studies have been completed, though. In Norway between 1988 and 1990, incidence was 4.6 cases per 100,000 for Chlamydia-induced reactive

arthritis and 5 cases per 100,000 for that induced by enteric bacteria. In 1978 in Finland, the annual incidence was found to be 43.6 per 100,000.

History

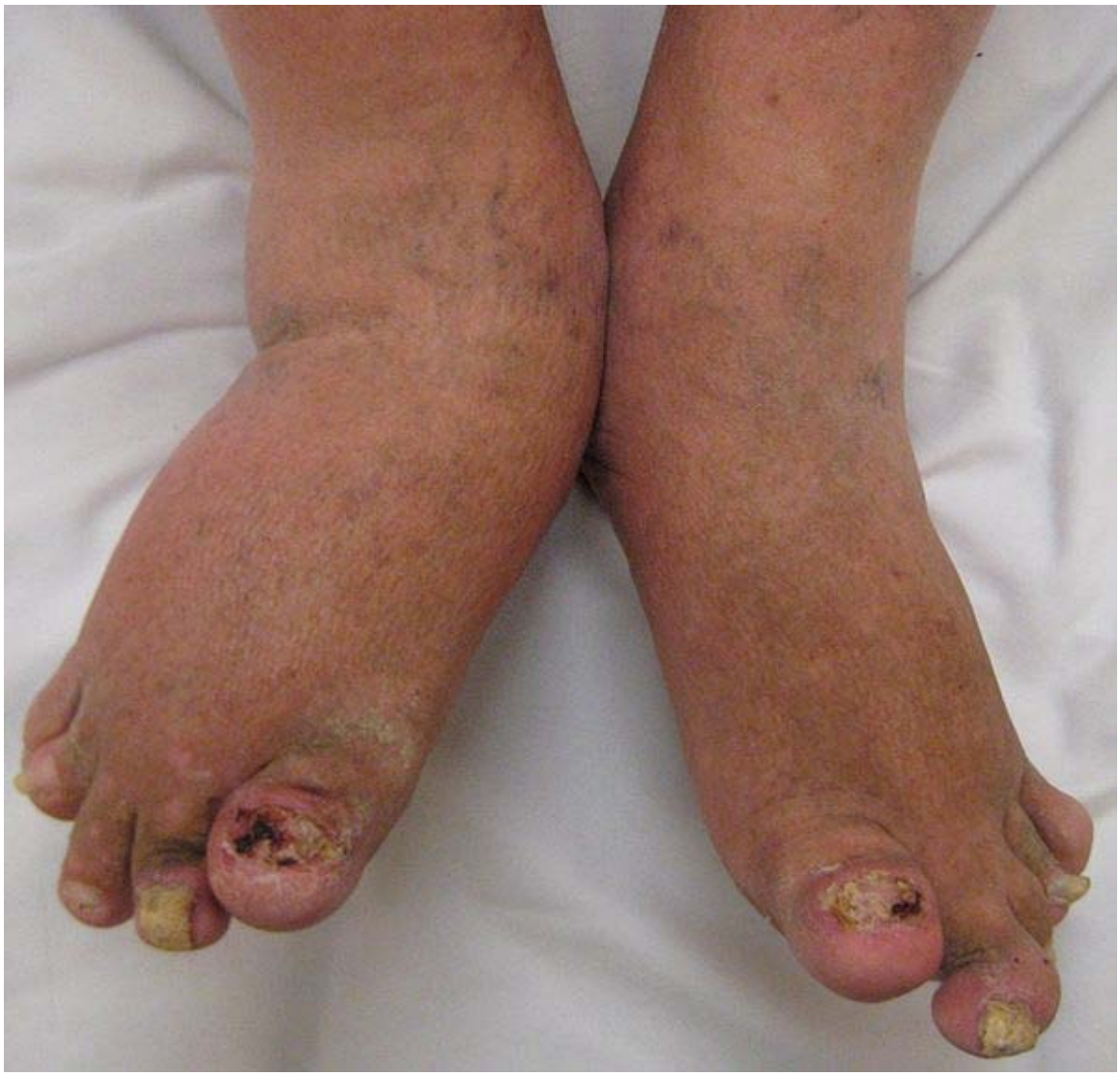
Reiter's arthritis was first described by Dr. Hans Conrad Julius Reiter, a German military physician who in 1916 described the disease in a World War I soldier who had recovered from a bout of diarrhea. There is movement that the term *Reiter's syndrome* should be phased out, partly owing to a move in the field of medicine to give descriptive names rather than personal names to conditions, and partly owing to allegations of Dr. Reiter's experiments in Nazi concentration camps. However, the term remains one of the more recognized references to the disease.

Famous individuals

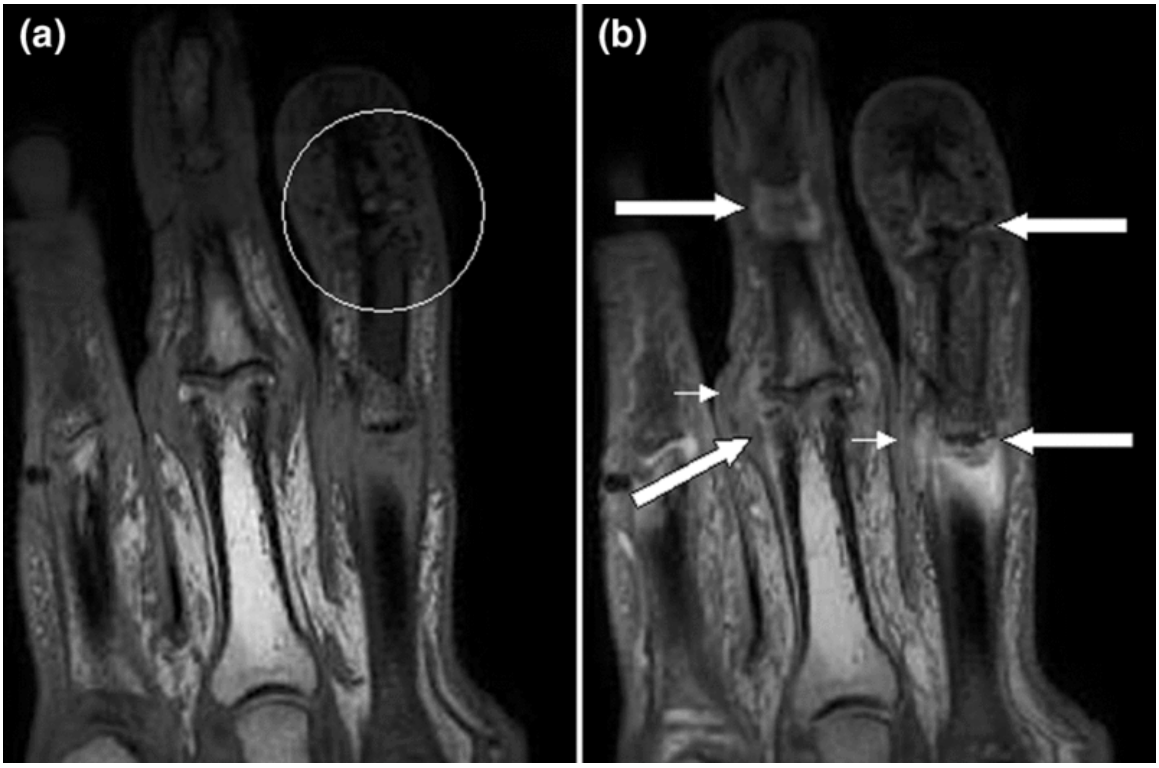
Scottish association football player Ian Murray has suffered from Reiter's arthritis. Former Kiss guitarist Mark St. John suffered from Reiter's arthritis. He was promptly replaced.

Chapter 6

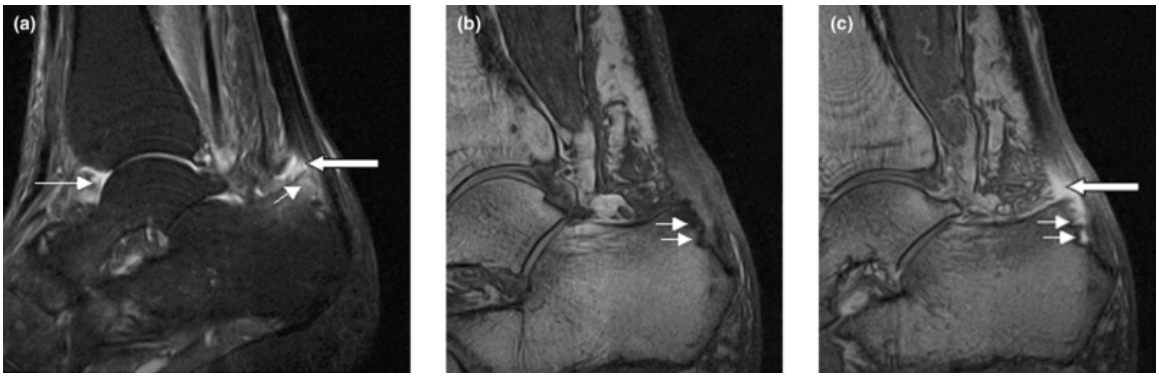
Psoriatic Arthritis



Severe psoriatic arthritis of both feet and ankles. Note the changes to the nails.



Magnetic resonance images of the fingers in psoriatic arthritis. Shown are T1-weighted (a) pre-contrast and (b) post-contrast coronal images. Enhancement of the synovial membrane at the third and fourth proximal interphalangeal (PIP) and distal interphalangeal (DIP) joints is seen, indicating active synovitis (inflammation of the synovial membrane; large arrows). There is joint space narrowing with bone proliferation at the third PIP joint and erosions are present at the fourth DIP joint (white circle). Extracapsular enhancement (small arrows) is seen medial to the third and fourth PIP joints, indicating probable enthesitis (inflammation of a tendon insertion).



Sagittal magnetic resonance images of the ankle region in psoriatic arthritis. (a) Short tau inversion recovery (STIR) image, showing high signal intensity at the Achilles tendon insertion (enthesitis, thick arrow) and in the synovium of the ankle joint (synovitis, long thin arrow). Bone marrow oedema is seen at the tendon insertion (short thin arrow). (b,c) T1 weighted images of a different section of the same patient, before (panel b) and after

(panel c) intravenous contrast injection, confirm inflammation (large arrow) at the enthesis and reveal bone erosion at tendon insertion (short thin arrows).

Psoriatic arthritis (also **arthritis psoriatica**, **arthropathic psoriasis** or **psoriatic arthropathy**) is a type of inflammatory arthritis[:427-436:194] that, according to the National Psoriasis Foundation, affects around 10-30% of people suffering from the chronic skin condition psoriasis. Psoriatic arthritis is said to be a seronegative spondyloarthropathy and therefore occurs more commonly in patients with tissue type HLA-B27. Treatment of psoriatic arthritis is similar to that of rheumatoid arthritis. More than 80% of patients with psoriatic arthritis will have psoriatic nail lesions characterised by pitting of the nails, or more extremely, loss of the nail itself (onycholysis).

Psoriatic arthritis can develop at any age, however on average it tends to appear about 10 years after the first signs of psoriasis. For the majority of people this is between the ages of 30 and 50, but it can also affect children. Men and women are equally affected by this condition. In about one in seven cases the arthritis symptoms may occur before any skin involvement.

Presentation

As well as causing joint inflammation, psoriatic arthritis can cause tendinitis and a sausage-like swelling of the digits known as dactylitis. Radiology will give the appearance of "fluffy, new" bone.

Causes

The exact causes are not yet known, but several genetic associations have been identified.

Types of psoriatic arthritis

There are five main types of psoriatic arthritis:

- **Symmetric**: This type accounts for around 50% of cases, and affects joints on both sides of the body simultaneously. This type is most similar to rheumatoid arthritis and is disabling in around 50% of all cases.

- **Asymmetric**: This type affects around 35% of patients and is generally mild. This type does not occur in the same joints on both sides of the body and usually only involves fewer than 3 joints.

- **Arthritis mutilans** (M07.1): Affects less than 5% of patients and is a severe, deforming and destructive arthritis. This condition can progress over months or years causing severe joint damage. Arthritis mutilans has also be called chronic absorptive arthritis, and may be seen in rheumatoid arthritis as well.

- **Spondylitis** (M07.2): This type is characterised by stiffness of the spine or neck, but can also affect the hands and feet, in a similar fashion to symmetric arthritis.

- **Distal interphalangeal predominant** (M07.0): This type of psoriatic arthritis is found in about 5% of patients, and is characterised by inflammation and stiffness in the joints nearest to the ends of the fingers and toes. Nail changes are often marked.

Treatments

The underlying process in psoriatic arthritis is inflammation, therefore treatments are directed at reducing and controlling inflammation. First line medications are NSAIDs such as ibuprofen and naproxen followed by more potent NSAIDs like diclofenac, indomethacin, and etodolac.

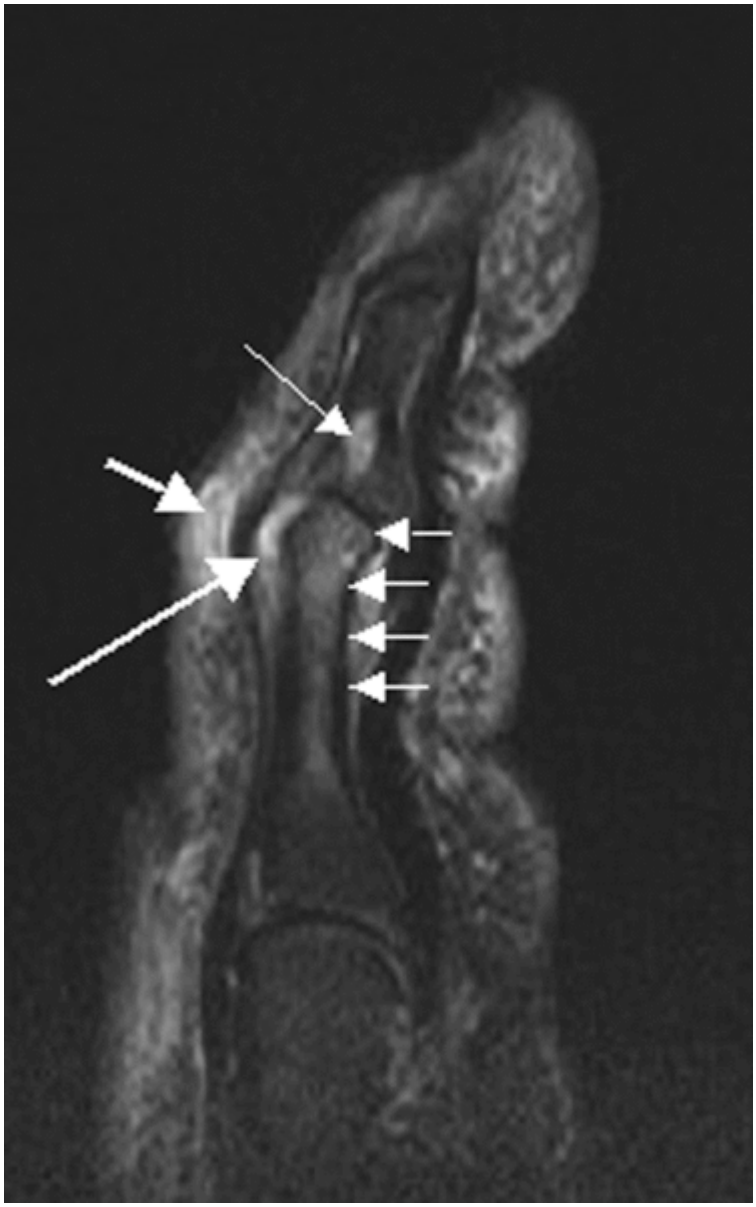
Other treatment options for this disease include joint injections with corticosteroids - this is only practical if a few joints are affected.

If acceptable control is not achieved using NSAIDs or joint injections then second line treatments with immunosuppressants such as methotrexate or leflunomide are added to the treatment regimen. An advantage of immunosuppressive treatment is that it also treats the psoriasis in addition to the arthropathy.

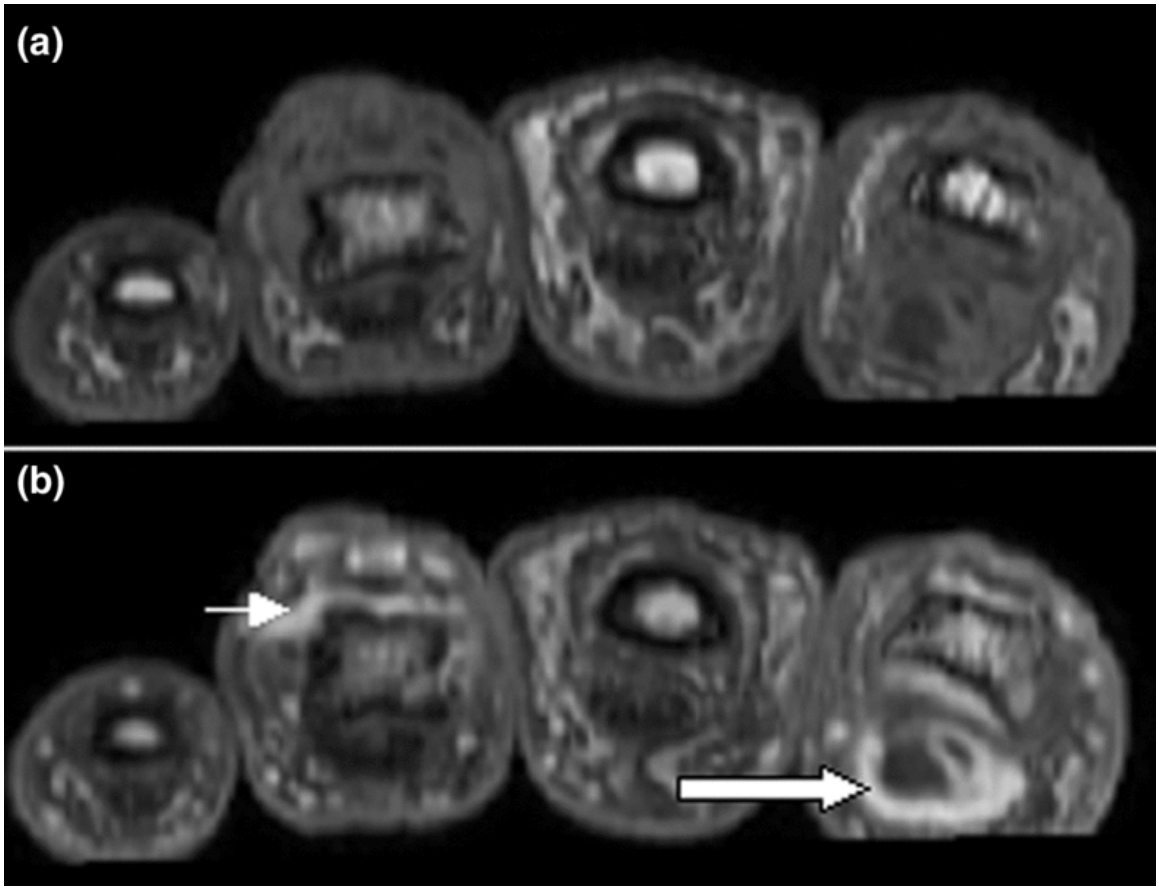
Recently, a new class of therapeutics developed using recombinant DNA technology called TNF-α inhibitors have become available, for example, infliximab, etanercept, golimumab, certolizumab pegol and adalimumab. These are becoming increasingly commonly used but are usually reserved for the most severe cases. As more is learned regarding the long-term safety of these biologic agents there is a trend toward earlier use to prevent irreversible joint destruction.

In psoriatic arthritis patients with severe joint damage orthopedic surgery may be implemented to correct joint destruction, usually with use of a joint replacement. Surgery is effective for pain alleviation, correcting joint disfigurement, and reinforcing joint usefulness and strength.

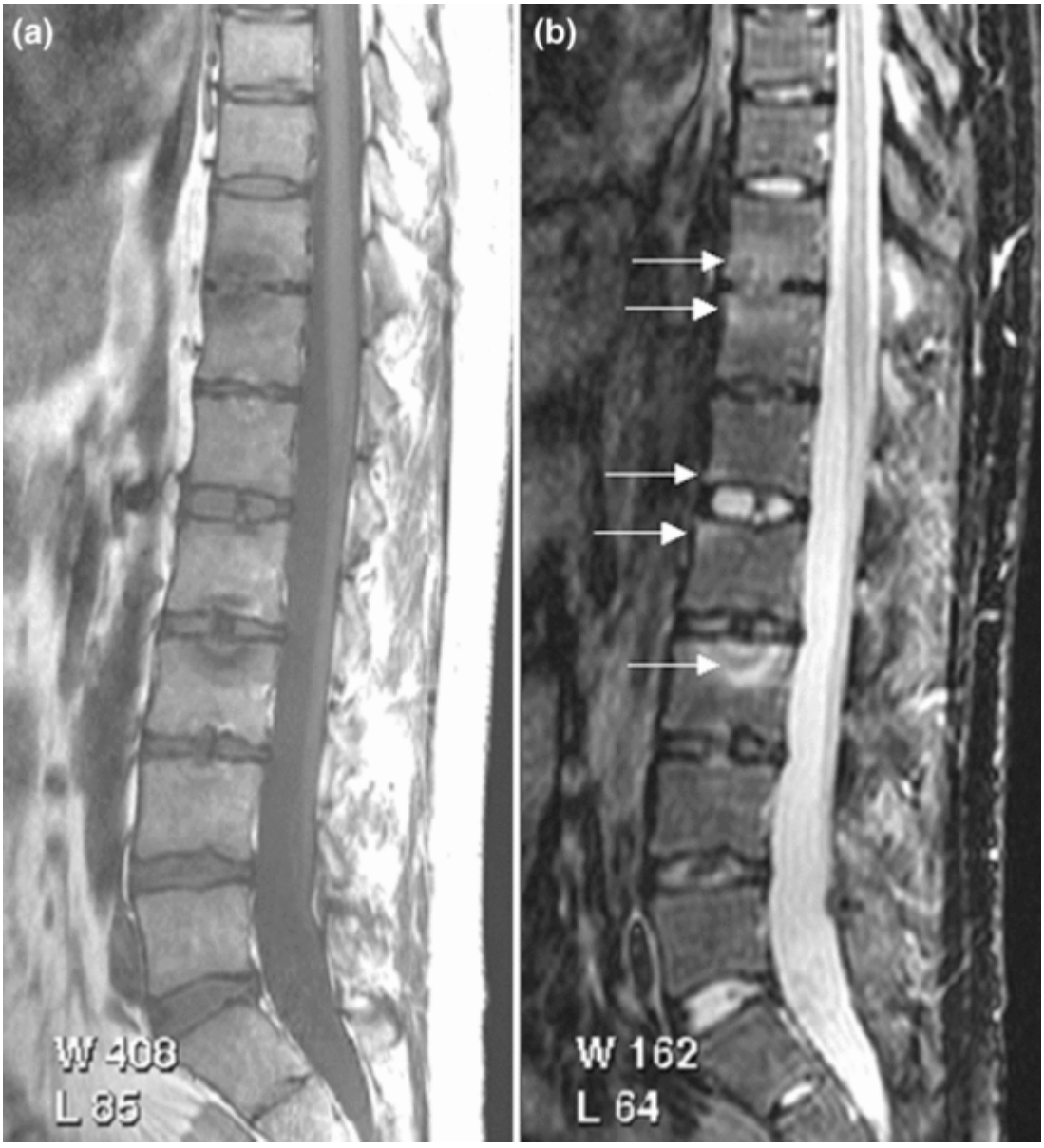
Additional images



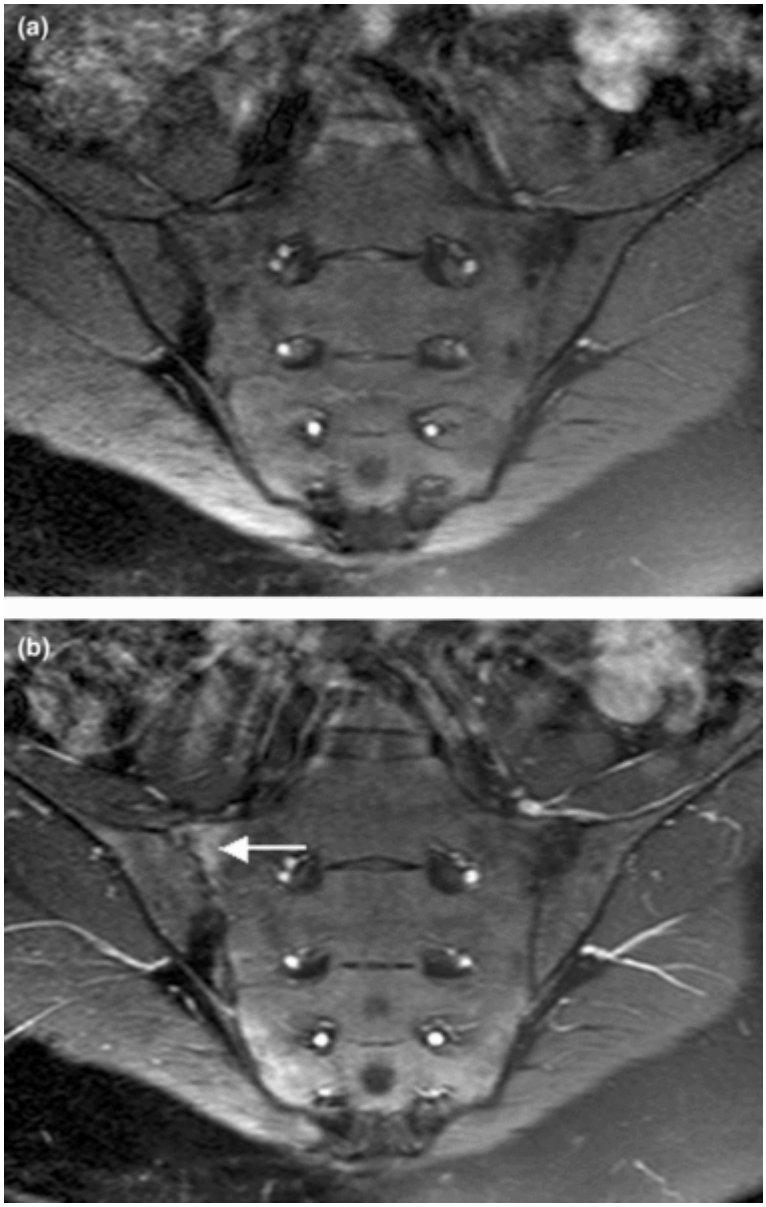
Magnetic resonance image of the index finger in psoriatic arthritis (mutilans form). Shown is a T2 weighted fat suppressed sagittal image. Focal increased signal (probable erosion) is seen at the base of the middle phalanx (long thin arrow). There is synovitis at the proximal interphalangeal joint (long thick arrow) plus increased signal in the overlying soft tissues indicating oedema (short thick arrow). There is also diffuse bone oedema (short thin arrows) involving the head of the proximal phalanx and extending distally down the shaft.



Magnetic resonance images of the fingers in psoriatic arthritis. Shown are T1 weighted axial (a) pre-contrast and (b) post-contrast images exhibiting dactylitis due to flexor tenosynovitis at the second finger with enhancement and thickening of the tendon sheath (large arrow). Synovitis is seen in the fourth proximal interphalangeal joint (small arrow).



(a) T1-weighted and (b) short tau inversion recovery (STIR) magnetic resonance images of lumbar and lower thoracic spine in psoriatic arthritis. Signs of active inflammation are seen at several levels (arrows). In particular, anterior spondylitis is seen at level L1/L2 and an inflammatory Andersson lesion at the upper vertebral endplate of L3.

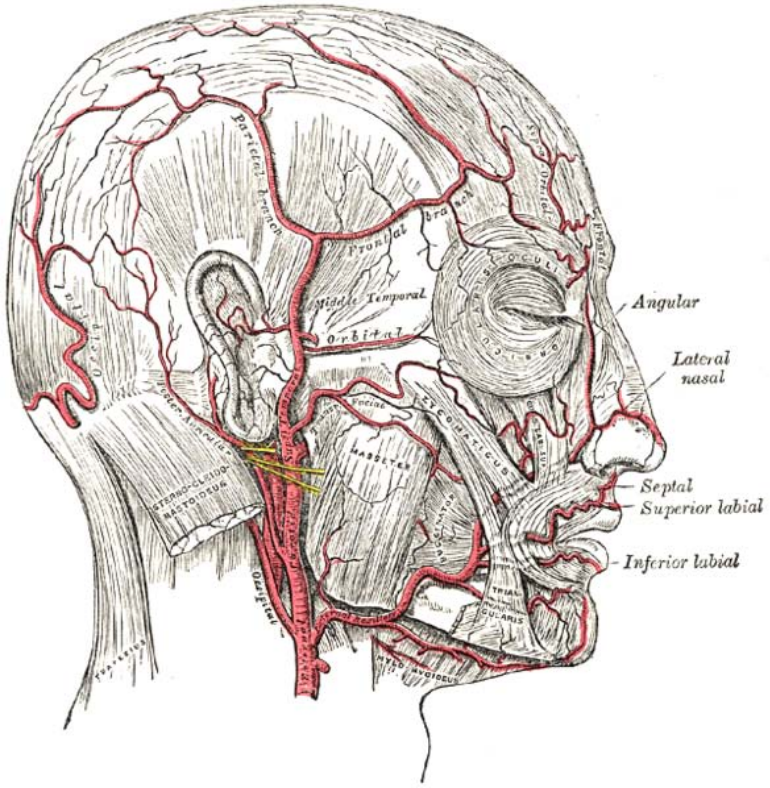


Magnetic resonance images of sacroiliac joints. Shown are T1-weighted semi-coronal magnetic resonance images through the sacroiliac joints (a) before and (b) after intravenous contrast injection. Enhancement is seen at the right sacroiliac joint (arrow, left side of image), indicating active sacroiliitis.

Chapter 7

Giant Cell Arteritis

Giant cell arteritis



The arteries of the face and scalp.

ICD-10	M31.5-M31.6
ICD-9	446.5
OMIM	187360
DiseasesDB	12938
eMedicine	neuro/592
MeSH	D013700

Giant cell arteritis (**GCA** or **temporal arteritis**) is an inflammatory disease of blood vessels (most commonly large and medium arteries of the head). It is a form of vasculitis.

The name (giant cell arteritis) reflects the type of inflammatory cell that is involved (as seen on biopsy).

The terms "giant cell arteritis" and "temporal arteritis" are sometimes used interchangeably, because of the frequent involvement of the temporal artery. However, it can involve other large vessels (such as the aorta in "giant cell aortitis". Giant cell arteritis of the temporal artery is referred to as "temporal arteritis," and is also known as "Cranial arteritis" and "Horton's disease."

Associated conditions

The disorder may coexist (in one quarter of cases) with polymyalgia rheumatica (PMR), which is characterized by sudden onset of pain and stiffness in muscles (pelvis, shoulder) of the body and is seen in the elderly. GCA and PMR are so closely linked that they are often considered to be different manifestations of the same disease process. Other diseases related with temporal arteritis are systemic lupus erythematosus, rheumatoid arthritis and severe infections.

Symptoms

It is more common in females than males by a ratio of 3:1. The mean age of onset is about 70 years, and it is rare in those less than 50 years of age.

Patients present with:

- bruits
- fever
- headache
- tenderness and sensitivity on the scalp
- jaw claudication (pain in jaw when chewing)
- tongue claudication (pain in tongue when chewing) and necrosis
- reduced visual acuity (blurred vision)
- acute visual loss (sudden blindness)
- diplopia (double vision)
- acute tinnitus (ringing in the ears)

The inflammation may affect blood supply to the eye and blurred vision or sudden blindness may occur. In 76% of cases involving the eye, the ophthalmic artery is involved causing anterior ischemic optic neuropathy. Loss of vision in both eyes may occur very abruptly and this disease is therefore a medical emergency.

Diagnosis

Physical exam

- Palpation of the head reveals prominent temporal arteries with or without pulsation.
- The temporal area may be tender.
- Decreased pulses may be found throughout the body.
- Evidence of ischemia may be noted on fundal exam.

Laboratory tests

- LFTs, liver function tests, are abnormal particularly raised ALP- alkaline phosphatase
- Erythrocyte sedimentation rate, an inflammatory marker, >60 mm/hour (normal 10–40 mm/hour), but may be normal in approximately 20% of cases.
- C-reactive protein, another inflammatory marker, is also commonly elevated.
- Platelets may also be elevated.

Biopsy

The gold standard for diagnosing temporal arteritis is biopsy, which involves removing a small part of the vessel and examining it microscopically for giant cells infiltrating the tissue. Since the blood vessels are involved in a patchy pattern, there may be unaffected areas on the vessel and the biopsy might have been taken from these parts. Unilateral biopsy of a 1.5–3 cm length is 85-90% sensitive. So, a negative result does not definitely rule out the diagnosis.

Imaging studies

Radiological examination of the temporal artery with ultrasound yields a halo sign. Contrast enhanced brain MRI and CT is generally negative in this disorder. Recent studies have shown that 3T MRI using super high resolution imaging and contrast injection can non-invasively diagnose this disorder with high specificity and sensitivity.

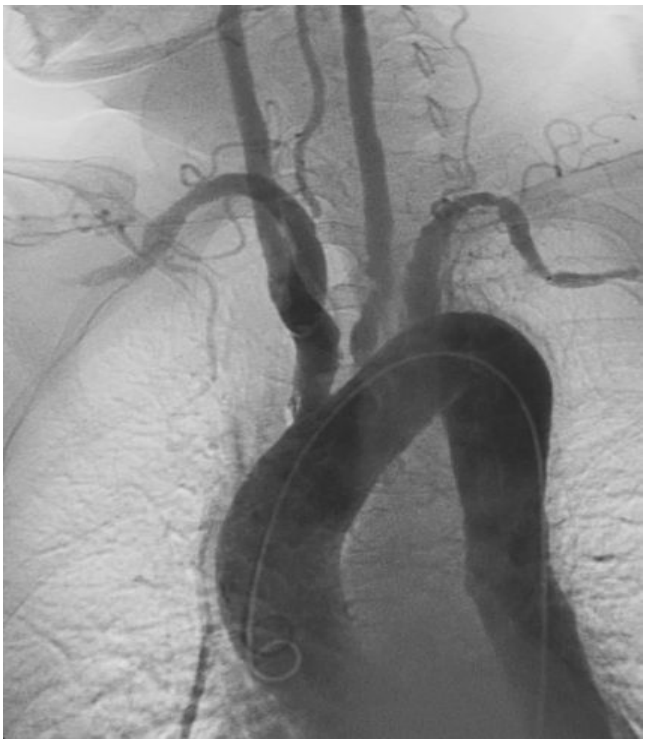
Treatment

Corticosteroids, typically high-dose prednisone (40–60 mg bd), must be started as soon as the diagnosis is suspected (even before the diagnosis is confirmed by biopsy) to prevent irreversible blindness secondary to ophthalmic artery occlusion. Steroids do not prevent the diagnosis from later being confirmed by biopsy, although certain changes in the histology may be observed towards the end of the first week of treatment and are more difficult to identify after a couple of months. The dose of prednisone is lowered after 2–4 weeks, and slowly tapered over 9–12 months. Oral steroids are at least as effective as intravenous steroids, except in the treatment of acute visual loss where intravenous steroids appear to offer significant benefit over oral steroids

Chapter 8

Takayasu's Arteritis

Takayasu's arteritis



ICD-10	M31.4
ICD-9	446.7
OMIM	207600
DiseasesDB	12879
MedlinePlus	001250
eMedicine	med/2232 ped/1956 neuro/361 radio/51
MeSH	D013625

Takayasu's arteritis (also known as "aortic arch syndrome", "nonspecific aortoarteritis" and the "pulseless disease"[:841]) is a form of large vessel granulomatous vasculitis with massive intimal fibrosis and vascular narrowing affecting often young or middle-aged women of Asian decent. It mainly affects the aorta (the main blood vessel leaving the heart) and its branches, as well as the pulmonary arteries. Females are about 8-9 times more likely to be affected than males. Patients often notice the disease symptoms between 15 and 30 years of age. In the Western world, atherosclerosis is a more frequent cause of obstruction of the aortic arch vessels than Takayasu's arteritis. Takayasu's arteritis is similar to other forms of vasculitis, including giant cell arteritis. Due to obstruction of the main branches of the aorta, including the left common carotid artery, the brachiocephalic artery, and the left subclavian artery, Takayasu's arteritis can present as pulseless upper extremities (arms, hands, and wrists with weak or absent pulses on the physical examination) which may be why it is also commonly referred to as the "pulseless disease."

Pathophysiology

Although its etiology is unknown, the condition is characterized by segmental and patchy granulomatous inflammation of the aorta and its major derivative branches. This inflammation leads to arterial stenosis, thrombosis, and aneurysms. There is also irregular fibrosis of the blood vessels due to chronic vasculitis leading to sometimes massive intimal fibrosis (fibrosis of the inner section of the blood vessels). Prominent narrowing due to inflammtion, granuloma, and fibrosis is often seen in arterial studies such as Magnetic resonance angiography (MRA), computed tomography angiography (CTA), or arterial angiography (DSA).

Symptoms

Some patients develop an initial "inflammatory phase" characterized by systemic illness with symptoms of malaise, fever, night sweats, weight loss, arthralgia, and fatigue. There is also often anemia and marked elevation of the ESR or C-reactive protein (nonspecific markers of inflammation). The intial "inflammatory phase" is often followed by a secondary "pulseless phase." The "pulseless phase" is characterized by vascular insufficiency from intimal narrowing of the vessels manifesting as arm or leg claudication, renal artery stenosis causing hypertension, and neurological manifestations due to decreased blood flow to the brain. Of note is the function of renal artery stenosis in causation of high blood pressure: Normally perfused kidneys produce proportionate amount of a substance called renin. Stenosis of the renal arteries, causes hypoperfusion (decresaed blood flow) of the juxtaglomerular apparatus, resulting in exaggerated secretion of renin, and high blood levels of aldosterone, eventually leading to water and salt retention and high blood pressure. The neurological symptoms of the disease vary depending on the degree, and the nature of the blood vessel obstruction and can range from lightheadedness, to seizures in severe cases. One rare but important feature of the Takayasu's arteritis is ocular involvement in form of visual field defects, vision loss, or retinal hemorrhage Some patients with Takayasu's arteritis may present with only late vascular changes, without an antecedent systemic illness. In the late stage, weakness of

the arterial walls may give rise to localized aneurysms. As with all aneurysms, possibility of rupture and vascular bleeding is existent and requires monitoring. Raynaud's phenomenon is commonly found in this disease, mainly due to decreased circulation of the blood to the arms.

Treatments

The great majority of patients with Takayasu's arteritis respond to steroids such as prednisone. The usual starting dose is approximately 1 milligram per kilogram of the body weight per day (for most people, this is approximately 60 milligrams a day). Because of the significant side effects of long-term high–dose prednisone use, the starting dose is tapered over several weeks to a dose that the physician feels is tolerable for the patient.

Surgical options may need to be explored for patients who do not respond to steroids. Re-perfusion of tissue can be achieved by large vessel reconstructive surgery such as bypass grafting. Grafting autologous tissue has the highest rates of success. Percutaneous transluminal coronary angioplasty (PTCA) is not as effective in the long term but has fewer risks.

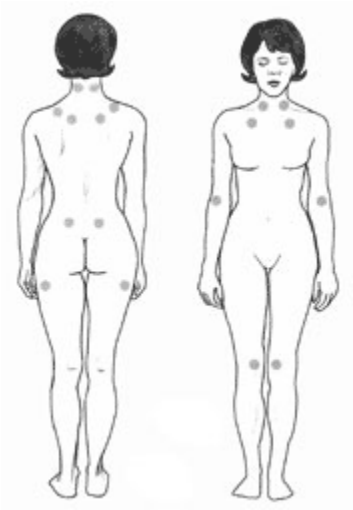
History

The first case of Takayasu's arteritis was described in 1908 by a Japanese opthalmologist, Mikito Takayasu at the Annual Meeting of the Japan Ophthalmology Society. Takayasu described a peculiar "wreathlike" appearance of the blood vessels in the back of the eye (retina). Two Japanese physicians at the same meeting (Drs. Onishi and Kagoshima) also reported similar eye findings in patients whose wrist pulses were absent. It is now known that the blood vessel malformations that occur in the retina are an angiogenic response to the arterial narrowings in the neck, and that the absence of pulses noted in some patients occurs because of narrowings of the blood vessels to the arms. The eye findings described by Takayasu are rarely seen in patients from North America and British Columbia.

Chapter 9

Fibromyalgia

Fibromyalgia



The location of the nine paired tender points that comprise the 1990 American College of Rheumatology criteria for fibromyalgia.

ICD-10	M79.7
ICD-9	729.1
MedlinePlus	000427
eMedicine	med/790 med/2934 ped/777 pmr/47
MeSH	D005356

Fibromyalgia (new Latin, *fibro*-, fibrous tissues, Gk. *myo*-, muscle, Gk. *algos*-, pain, meaning muscle and connective tissue pain; also referred to as **FM** or **FMS**) is a medical disorder characterized by chronic widespread pain and allodynia, a heightened and painful response to pressure. Fibromyalgia symptoms are not restricted to pain, leading to the use of the alternative term **fibromyalgia syndrome** for the condition. Other symptoms include debilitating fatigue, sleep disturbance, and joint stiffness. Some

patients may also report difficulty with swallowing, bowel and bladder abnormalities, numbness and tingling, and cognitive dysfunction. Fibromyalgia is frequently comorbid with psychiatric conditions such as depression and anxiety and stress-related disorders such as posttraumatic stress disorder. Not all people with fibromyalgia experience all associated symptoms. Fibromyalgia is estimated to affect 2–4% of the population, with a female to male incidence ratio of approximately 9:1.

Evidence from research conducted in the last three decades has revealed abnormalities within the central nervous system affecting brain regions that may be linked both to clinical symptoms and research phenomena. These studies show a correlation, but not causation. Some research suggests that alterations in the central nervous system might be the result of childhood stress, or prolonged or severe stress.

Historically, fibromyalgia has been considered either a musculoskeletal disease or neuropsychiatric condition. Although there is as yet no cure for fibromyalgia, some treatments have been demonstrated by controlled clinical trials to be effective in reducing symptoms, including medications, behavioral interventions, patient education, and exercise. The most recent approach of a diagnosis of fibromyalgia involves pain index and a measure of key symptoms and severity.

Fibromyalgia is considered a controversial diagnosis, due to lacking scientific consensus to its cause. Not all members of the medical community consider fibromyalgia a disease because of a lack of abnormalities on physical examination and the absence of objective diagnostic tests.

Signs and symptoms

The defining symptoms of fibromyalgia are chronic, widespread pain, fatigue, and heightened pain in response to tactile pressure (allodynia). Other symptoms may include tingling of the skin, prolonged muscle spasms, weakness in the limbs, nerve pain, muscle twitching, palpitations, functional bowel disturbances, and chronic sleep disturbances.

Many patients experience cognitive dysfunction (known as "brain fog" or "fibrofog"), which may be characterized by impaired concentration, problems with short and long-term memory, short-term memory consolidation, impaired speed of performance, inability to multi-task, cognitive overload, and diminished attention span. Fibromyalgia is often associated with anxiety, and depressive symptoms.

Other symptoms often attributed to fibromyalgia that may possibly be due to a comorbid disorder include myofascial pain syndrome, also referred to as chronic myofascial pain, diffuse non-dermatomal paresthesias, functional bowel disturbances and irritable bowel syndrome (possibly linked to lower levels of ghrelin), genitourinary symptoms and interstitial cystitis, dermatological disorders, headaches, myoclonic twitches, and symptomatic hypoglycemia. Although fibromyalgia is classified based on the presence of chronic widespread pain, pain may also be localized in areas such as the shoulders, neck, low back, hips, or other areas. Many sufferers also experience varying degrees of facial

pain and have high rates of comorbid temporomandibular joint disorder. 20–30% of patients with rheumatoid arthritis and systemic lupus erythematosus may also have fibromyalgia.

Causation hypotheses

The cause of fibromyalgia is currently unknown. However, several hypotheses have been developed including "central sensitization". This theory proposes that fibromyalgia patients have a lower threshold for pain because of increased sensitivity in the brain to pain signals.

Genetic predisposition

There is evidence that genetic factors may play a role in the development of fibromyalgia. For example, there is a high aggregation of fibromyalgia in families. The mode of inheritance is currently unknown, but it is most probably polygenic. Research has also demonstrated that fibromyalgia is potentially associated with polymorphisms of genes in the serotoninergic, dopaminergic and catecholaminergic systems. However, these polymorphisms are not specific for fibromyalgia and are associated with a variety of allied disorders (e.g. chronic fatigue syndrome, irritable bowel syndrome) and with depression.

Stress

Stress may be an important precipitating factor in the development of fibromyalgia. Fibromyalgia is frequently comorbid with stress-related disorders such as chronic fatigue, posttraumatic stress disorder, irritable bowel syndrome and depression. Two studies that employed single-voxel magnetic resonance spectroscopy (1H-MRS) reported metabolic abnormalities within the hippocampal complex in patients with fibromyalgia. As the hippocampus plays crucial roles in maintenance of cognitive functions, sleep regulation, and pain perception, it was suggested that metabolic dysfunction of the hippocampus may be implicated in the appearance of these symptoms.

Other authors have proposed that, because exposure to stressful conditions can alter the function of the hypothalamic-pituitary-adrenal (HPA) axis, the development of fibromyalgia may stem from stress-induced disruption of the HPA axis.

Dopamine dysfunction (hypodopaminergia)

The "dopamine hypothesis of fibromyalgia" proposes that the central abnormality responsible for symptoms associated with fibromyalgia is a disruption of normal dopamine-related neurotransmission. Insufficient dopamine in a part of the body is termed hypodopaminergia. Dopamine is a catecholamine neurotransmitter with roles in pain perception and natural analgesia. There is also strong evidence for a role of dopamine in restless leg syndrome, which is a condition found frequently in patients with fibromyalgia. Some fibromyalgia patients responded in controlled trials to pramipexole, a

dopamine agonist that selectively stimulates dopamine D2/D3 receptors and is used to treat both Parkinson's disease and restless leg syndrome.

Abnormal serotonin metabolism

In 1975, researchers hypothesized that serotonin, a neurotransmitter that regulates sleep patterns, mood, concentration and pain, could be involved in the pathophysiology of fibromyalgia-associated symptoms. In 1992, decreased serotonin metabolites in patient blood samples and cerebrospinal fluid were reported. However, selective serotonin reuptake inhibitors (SSRIs) have met with limited success in alleviating the symptoms of the disorder, while drugs with activity as mixed serotonin-norepinephrine reuptake inhibitors (SNRIs) have been more successful. In controlled trials funded by Eli Lily, Duloxetine (Cymbalta), an SNRI originally used to treat depression and painful diabetic neuropathy, was demonstrated to relieve fibromyalgia symptoms in some women, however male subjects failed to improve significantly. The Food and Drug Administration regulators approved the drug for the treatment of fibromyalgia in June 2008. However, the relevance of dysregulated serotonin metabolism to pathophysiology is a matter of debate. Complicating the analysis, one of the more effective types of medication for the treatment of the disorder (i.e. serotonin 5-HT3 antagonists) actually blocks some of the effects of serotonin.

Deficient growth hormone (GH) secretion

Levels of hormones under the direct or indirect control of growth hormone (GH), including IGF-1, cortisol, leptin and neuropeptide Y may be abnormal in people with fibromyalgia, but supplementing growth hormone in patients does not have large effects, and a 2007 literature review reported a need for "further study before any solid recommendations can be made". There is disagreement about the role of HGH in fibromyalgia.

Psychological factors

Controversial theories propose that fibromyalgia is a psychosomatic illness. There is strong evidence that major depression is associated with fibromyalgia, although the nature of the association is debated. A comprehensive review into the relationship between fibromyalgia and major depressive disorder (MDD) found substantial similarities in neuroendocrine abnormalities, psychological characteristics, physical symptoms and treatments between fibromyalgia and MDD, but currently available findings do not support the assumption that MDD and fibromyalgia refer to the same underlying construct or can be seen as subsidiaries of one disease concept. Indeed, the sensation of pain has at least two dimensions: a sensory dimension which processes the magnitude and location of the pain, and an affective-motivational dimension which processes the unpleasantness. Accordingly, a study that employed functional magnetic resonance imaging to evaluate brain responses to experimental pain among fibromyalgia patients found that depressive symptoms were associated with the magnitude of clinically-induced pain response specifically in areas of the brain that participate in

affective pain processing, but not in areas involved in sensory processing which indicates that the amplification of the sensory dimension of pain in fibromyalgia occurs independently of mood or emotional processes.

Physical trauma

Neck trauma seems to increase the risk of developing fibromyalgia.

Other hypotheses

Other hypotheses have been proposed. One of these is an aberrant immune response to intestinal bacteria.

Pathophysiology

Sleep disturbances

In 1975, Moldofsky and colleagues reported the presence of anomalous alpha wave activity (typically associated with arousal states) measured by electroencephalogram (EEG) during non-rapid eye movement sleep of "fibrositis syndrome" patients. By disrupting stage IV sleep consistently in young, healthy subjects, the researchers reproduced a significant increase in muscle tenderness similar to that experienced in "neurasthenic musculoskeletal pain syndrome" but which resolved when the subjects were able to resume their normal sleep patterns.

Poly-modal sensitivity

Results from studies examining responses to experimental stimulation suggest that fibromyalgia patients may have heightened sensitivity of the nociceptive system, which senses pressure, heat, cold, electrical and chemical stimulation. Experiments examining pain regulatory systems have shown that fibromyalgia patients display an exaggerated wind-up in response to repetitive stimulation and an absence of exercise-induced analgesic response.

Neuroendocrine disruption

Patients with fibromyalgia may have alterations of normal neuroendocrine function, characterized by mild hypocortisolemia, hyperreactivity of pituitary adrenocorticotropin hormone release in response to challenge, and glucocorticoid feedback resistance. Low insulin-like growth factor 1 (IGF-1) levels in some fibromyalgia patients have led to the theory that these patients may actually have a different, treatable syndrome, adult growth hormone deficiency. Other abnormalities include reduced responsivity of thyrotropin and thyroid hormones to thyroid-releasing hormone, a mild elevation of prolactin levels with disinhibition of prolactin release in response to challenge and hyposecretion of adrenal androgens.

These changes might result from chronic stress, which, after being perceived and processed by the central nervous system, activates hypothalamic corticotrophin-releasing hormone neurons. Chronic overactivity of these neurons could disrupt normal function of the pituitary-adrenal axis and cause an increased stimulation of hypothalamic somatostatin secretion, which, in turn, could inhibit the secretion of other hormones.

Sympathetic hyperactivity

Functional analysis of the autonomic system in patients with fibromyalgia has demonstrated disturbed activity characterized by hyperactivity of the sympathetic nervous system at baseline with reduced sympathoadrenal reactivity in response to a variety of stressors including physical exertion and mental stress. Fibromyalgia patients demonstrate lower heart rate variability, an index of sympathetic/parasympathetic balance, indicating sustained sympathetic hyperactivity, especially at night. In addition, plasma levels of neuropeptide Y, which is co-localized with norepinephrine in the sympathetic nervous system, have been reported as low in patients with fibromyalgia, while circulating levels of epinephrine and norepinephrine have been variously reported as low, normal and high. Administration of interleukin-6, a cytokine capable of stimulating the release of hypothalamic corticotropin-releasing hormone which in turn stimulates activity within the sympathetic nervous system, results in a dramatic increase in circulating norepinephrine levels and a significantly greater increase in heart rate over baseline in fibromyalgia patients as compared to healthy controls.

Cerebrospinal fluid abnormalities

One of the most reproduced laboratory finding in patients with fibromyalgia is an elevation in cerebrospinal fluid levels of substance P, a putative nociceptive neurotransmitter. Metabolites for the monoamine neurotransmitters serotonin, norepinephrine, and dopamine—all of which play a role in natural analgesia—have been shown to be lower, while concentrations of endogenous opioids (i.e., endorphins and enkephalins) appear to be higher. The mean concentration of nerve growth factor, a substance known to participate in structural and functional plasticity of nociceptive pathways within the dorsal root ganglia and spinal cord, is elevated. There is also evidence for increased excitatory amino acid release within cerebrospinal fluid, with a correlation demonstrated between levels for metabolites of glutamate and nitric oxide and clinical indices of pain.

Brain imaging studies

Evidence of abnormal brain involvement in fibromyalgia has been provided via functional neuroimaging. The first findings reported were decreased blood flow within the thalamus and elements of the basal ganglia and mid-brain (i.e., pontine nucleus). Differential activation in response to painful stimulation has also been demonstrated. Brain centers showing hyperactivation in response to noxious stimulation include such pain-related brain centers as the primary and secondary somatosensory cortices, anterior cingulate cortex, and insular cortex. Patients also exhibit neural activation in brain

regions associated with pain perception in response to nonpainful stimuli in such areas as the prefrontal, supplemental motor, insular, and cingulate cortices. Evidence of hippocampal disruption indicated by reduced brain metabolite ratios has been demonstrated by studies using single-voxel magnetic resonance spectroscopy (1H-MRS). A significant negative correlation was demonstrated between abnormal metabolite ratios and a validated index of the clinical severity (i.e. the Fibromyalgia Impact Questionnaire). Correlations between clinical pain severity and concentrations of the excitatory amino acid neurotransmitter glutamate within the insular cortex have also been demonstrated using 1H-MRS. An acceleration of normal age-related brain atrophy has been demonstrated using voxel-based morphometry (VBM) with areas of reduced gray matter located in the cingulate cortex, insula and parahippocampal gyrus. Grey matter loss appears to increase 9.5 times the normal rate with each year. Studies utilizing positron emission tomography have demonstrated reduced dopamine synthesis in the brainstem and elements of the limbic cortex. A significant negative correlation between pain severity and dopamine synthesis was demonstrated within the insular cortex. A subsequent study demonstrated gross disruption of dopaminergic reactivity in response to a tonic pain stimulus within the basal ganglia with a significant positive correlation between the defining feature of the disorder (i.e. tender point index) and dopamine D2 receptor binding potential specifically in the right putamen. Finally, reduced availability of mu-opioid receptors in the ventral striatum/nucleus accumbens and cingulate cortex has been demonstrated, with a significant negative correlation between affective pain levels and receptor availability in the nucleus accumbens.

Diagnosis

There is no one test that fully shows if someone has fibromyalgia. There is still debate over what should be considered essential diagnostic criteria and whether objective diagnosis is possible. The difficulty with diagnosing fibromyalgia is that, in most cases, laboratory testing appears normal and that many of the symptoms mimic those of other rheumatic conditions such as arthritis or osteoporosis. In general, most doctors diagnose patients with a process called differential diagnosis, which means that doctors consider all of the possible things that might be wrong with the patient based on the patient's symptoms, gender, age, geographic location, medical history and other factors. They then narrow down the diagnosis to the most likely one. The most widely accepted set of classification criteria for research purposes was elaborated in 1990 by the Multicenter Criteria Committee of the American College of Rheumatology. These criteria, which are known informally as "the ACR 1990", define fibromyalgia according to the presence of the following criteria:

- A history of widespread pain lasting more than three months—affecting all four quadrants of the body, i.e., both sides, and above and below the waist.
- Tender points—there are 18 designated possible tender points (although a person with the disorder may feel pain in other areas as well). During diagnosis, four kilograms-force (39 newtons) of force is exerted at each of the 18 points; the patient must feel pain at 11 or more of these points for fibromyalgia to be

considered. Four kilograms of force is about the amount of pressure required to blanch the thumbnail when applying pressure.

The ACR criteria for classification of patients were originally established as inclusion criteria for research purposes and were not intended for clinical diagnosis but have now become the *de facto* diagnostic criteria in the clinical setting. It should be noted that the number of tender points that may be active at any one time may vary with time and circumstance. A controversial study done by a legal team looking to prove their client's disability based primarily on tender points and their widespread presence in non-litigious communities prompted the lead author of the ACR criteria to now question the useful validity of tender points in diagnosis. Since the ACR criteria were originally published, research with mechanical devices that exert defined pressure indicate that diagnosis of fibromyalgia cannot be done objectively by machine and require a physician's subjective estimate of how much pressure should be exerted.

Treatment

As with many other medically unexplained syndromes, there is no known cure or universally accepted treatment for fibromyalgia, and treatment is typically aimed at symptom management. Developments in the understanding of the pathophysiology of the disorder have led to improvements in treatment, which include prescription medication, behavioral intervention, exercise, and alternative and complementary medicine. Indeed, integrated treatment plans that incorporate medication, patient education, aerobic exercise and cognitive-behavioral therapy have been shown to be effective in alleviating pain and other fibromyalgia-related symptoms. In 2005, the American Pain Society produced comprehensive guidelines for patient evaluation and management. More recently, the European League Against Rheumatism (EULAR) issued updated treatment guidelines.

Psychological/behavioural therapies

Cognitive behavioural therapy (CBT) and related psychological/behavioral therapies are evidence-based treatments which have shown to be moderately effective in randomized controlled trials. The greatest benefit occurs when CBT is used along with exercise.

Pharmaceutical

There are three medications that have been approved by the FDA for treatment of Fibromyalgia. Lyrica was approved in June, 2007, Cymbalta was approved in June, 2008, and Milnacipran was approved in January, 2009. Cymbalta and Lyrica were shown to reduce pain in a substantial number of patients with fibromyalgia, but there were others who didn't benefit. In a review in the 2009 Journal of Rheumatology, fibromyalgia researcher H.A. Smythe writes, “patients receive some benefit, but when side effects make the patient dull, lethargic, or fat, neither their goals nor those of society are satisfactorily met”.

Antidepressants

A 2009 meta-analysis in the Journal of the American Medical Association reported that some antidepressants were effective, but with small effect sizes, against pain, fatigue, sleep disturbance, and depression in fibromyalgia. The analysis found "strong evidence against a favorable effect of antidepressants on fatigue". The authors conclude that the goal of antidepressants in fibromyalgia should be, at most, a "possible symptom reduction", and the results must be balanced against side effects. Tricyclic antidepressants were the most effective against pain, fatigue, and sleep problems, but have many side effects due to interaction with adrenergic, cholinergic or histaminergic receptors, and sodium channels. Selective serotonin reuptake inhibitors (SSRIs) and Serotonin-norepinephrine reuptake inhibitors (SNRIs) had lower effects.

Anti-seizure medication

The anti-seizure drugs gabapentin (Neurontin) and pregabalin (Lyrica) have been tested. Gabapentin is approved for use in treatment of neuropathic pain but not fibromyalgia. Pregabalin, originally labeled for the treatment of nerve pain suffered by diabetics, has been cleared by the US Food and Drug Administration for treatment of fibromyalgia. A randomized controlled trial of pregabalin 450 mg/day found that 6 patients is the number needed to treat for one patient to have a 50% reduction in pain. A Cochrane Database analysis of pregabalin use in chronic pain concluded that "A minority of patients will have substantial benefit with pregabalin, and more will have moderate benefit. Many will have no or trivial benefit, or will discontinue because of adverse events."

Dopamine agonists

Dopamine agonists (e.g. pramipexole (Mirapex) and ropinirole (ReQuip) resulted in some improvement in a minority of patients, but numerous side effects, including the onset of impulse control disorders like compulsive gambling and shopping, have led to concern about this approach. A trial of transdermal rotigotine is currently ongoing.

Muscle relaxants

Cyclobenzaprine is a muscle relaxant medication used to relieve skeletal muscle spasms and associated pain in acute musculoskeletal conditions. It is the most well-studied drug for this application, and it also has been used off-label for fibromyalgia treatment.

Tizanidine (brandnames **Zanaflex**, **Sirdalud**) is a muscle relaxant centrally acting α-2 adrenergic agonist. It is used to treat the spasms, cramping, and tightness of muscles caused by medical problems such as multiple sclerosis, spastic diplegia, back pain, or certain other injuries to the spine or central nervous system. It is also prescribed off-label for some symptoms of fibromyalgia.

Opioids

According to a 2004 review of fibromyalgia treatment studies, there is moderate evidence to support the effectiveness of Tramadol by itself or combined with acetaminophen, although the long-term effectiveness and tolerability are unknown. The review also stated that opioids other than Tramadol have not had random controlled trials, and "should be considered only after all other medicinal and nonmedicinal therapies have been exhausted". Other opioids are widely used by fibromyalgia patients despite a lack of clinical trials and the potential for addiction and abuse. An analysis of insurance claims by 52,000 fibromyalgia patients showed that 40% had received opioids in any given year, predominantly short-acting agents.

Investigational medications

Investigational medications include cannabinoids and the 5-HT3 receptor antagonist tropisetron. A controlled study of guaifenesin failed to demonstrate any benefits from this treatment.

Physical treatments

Exercise improves fitness and sleep and may reduce pain and fatigue in some people with fibromyalgia. In particular, there is strong evidence that cardiovascular exercise is effective for some patients. Chiropractic care of fibromyalgia lacks scientific evidence and treatment is not currently supported.

Costs of fibromyalgia

Patients with fibromyalgia have higher health care costs and utilization. A study of almost 20,000 Humana members enrolled in Medicare Advantage and commercial plans compared costs and medical utilizations and found that persons with fibromyalgia used twice as much pain-related medication as those without fibromyalgia. Furthermore, the use of medications and medical necessities increased markedly across many measures once diagnosis was made.

Prognosis

Although in itself neither degenerative nor fatal, the chronic pain of fibromyalgia is pervasive and persistent. Most fibromyalgia patients report that their symptoms do not improve over time. An evaluation of 332 consecutive new fibromyalgia patients found that disease-related factors such as pain and psychological factors such as work status, helplessness, education, and coping ability had an independent and significant relationship to FM symptom severity and function.

Epidemiology

Fibromyalgia is seen in about 2% of the general population and affects more females than males, with a ratio of 9:1 by ACR criteria. It is most commonly diagnosed in individuals between the ages of 20 and 50, though onset can occur in childhood.

History

Many names, including “muscular rheumatism”, “fibrositis”, “psychogenic rheumatism”, and “neurasthenia” were applied historically to symptoms resembling those of fibromyalgia. The term *fibromyalgia* was coined by researcher Mohammed Yunus as a synonym for fibrositis and was first used in a scientific publication in 1981. Fibromyalgia is from the Latin *fibra* (fiber) and the Greek words *myo* (muscle) and *algos* (pain).

Historical perspectives on the development of the fibromyalgia concept note the “central importance” of a 1977 paper by Smythe and Moldofsky on fibrositis. The first clinical, controlled study of the characteristics of fibromyalgia syndrome was published in 1981, providing support for symptom associations. In 1984, an interconnection between fibromyalgia syndrome and other similar conditions was proposed, and in 1986, trials of the first proposed medications for fibromyalgia were published.

A 1987 article in the Journal of the American Medical Association used the term "fibromyalgia syndrome" while saying it was a "controversial condition". The American College of Rheumatology (ACR) published its first classification criteria for fibromyalgia in 1990, although these are not strictly diagnostic criteria.

Controversies

Fibromyalgia continues to be a disputed diagnosis. Many members of the medical community do not consider fibromyalgia a disease because of a lack of abnormalities on physical examination, and the absence of objective diagnostic tests.

Several controversial issues exist with regard to fibromyalgia that range from questions regarding the validity of the disorder as a clinical entity, to issues regarding primary pathophysiology and the potential existence of fibromyalgia subtypes.

According to Frederick Wolfe, highly cited fibromyalgia researcher and lead author of the 1990 paper that first defined the ACR fibromyalgia classification criteria, "the large majority of physicians, sociologists, and medical historians" are skeptical about the validity of fibromyalgia as a clinical entity. Some call fibromyalgia a “non-disease” and “an over-inclusive and ultimately meaningless label.” Wolfe now questions the validity of fibromyalgia as a disease. He considers fibromyalgia a physical response to stress, depression, and economic and social anxiety, and believes the associated symptoms are a normal part of everyday life. In 2009, he wrote, "the tendency to respond with distress to physical and mental stressors is part of the human condition." Wolfe and other opponents

of the fibromyalgia concept say that labeling fibromyalgia as a "disease" simply legitimizes patients' sickness behavior, slowing their recovery and harming them..

Patients, their advocacy groups, and specialists in the field argue that sufferers have been too readily dismissed and often treated unfairly due to assumptions that somatization, hypochondriasis, or depression best explains what cannot readily be attributed a cause. Further understanding, symptom management, and treatment was not possible under these circumstances. These claims have been supported by the professional legitimization of the condition, which has led to an substantial increase of research and resulted in significant new findings.

In a study of 100 individuals identified as having fibromyalgia, physical functioning decreased slightly over time, and individuals who had been diagnosed earlier had larger numbers of reported symptoms and greater severity. However, there was also a statistically significant improvement in satisfaction with health following classification. The authors of the study concluded that the 'fibromyalgia label' does not have a meaningful adverse effect on clinical outcome over the long term.

The validity of fibromyalgia as a unique clinical entity is also a matter of contention because "no discrete boundary separates syndromes such as FMS, chronic fatigue syndrome, irritable bowel syndrome, or chronic muscular headaches." Because of this considerable symptomatic overlap, some researchers have proposed that fibromyalgia and other syndromes with overlapping symptoms be classified as functional somatic syndromes for some purposes.

Some researchers believe that differences in psychological and autonomic nervous system profiles among affected individuals may indicate the existence of fibromyalgia subtypes. A 2007 review divides individuals with fibromyalgia into four groups as well as "mixed types":

1. "extreme sensitivity to pain but no associated psychiatric conditions" (may respond to medications that block the 5-HT3 receptor)
2. "fibromyalgia and comorbid, pain-related depression" (may respond to antidepressants)
3. "depression with concomitant fibromyalgia syndrome" (may respond to antidepressants)
4. "fibromyalgia due to somatization" (may respond to psychotherapy).

Other researchers have suggested that depression may be a result of coping with the disabling impacts of a, thus far, incurable disease.

Chapter 10

GALS Screen

A **GALS screen** is an examination used by doctors and other healthcare professionals to detect locomotor abnormalities and functional disability relating to gait, arms, legs and the spine.

Questions

- Do you have any stiffness or pain in your back, or any muscles or joints?
- Can you dress yourself without any problem?
- Can you walk up and down stairs without problem?

Examination

Gait

Ask the patient to walk a short distance, turn and then walk back.

Observation: looking for symmetry, smoothness of movement, normal stride length, pelvic tilt, arm swing, normal heel strike, stance, toe-off, swing through and ability to turn with ease. Note any antalgic, trendelenburg, hemiplegic or parkinsonian gait features.

Arms, legs and spine

From behind

Inspect for: a straight spine (note any scoliosis), normal paraspinal muscle bulk, symmetrical shoulder and gluteal muscle bulk, symmetry of iliac crests, absence of popliteal swellings, absence of foot or hindfoot swellings.

Palpate: over mid supraspinatus and roll the skin over the trapezius to test for signs of hyperalgesia or fibromyalgia.

From the side

Inspect for: normal cervical and lumbar lordosis and normal thoracic kyphosis. Whilst standing beside the patient place your index finger on one of the lumbar vertebral spinous processes, and your middle finger on the next one down and ask the patient to bend over and touch their toes, keeping their legs straight. Normally, as the patient bends, the spinous processes will move apart, so your fingers will move apart also. Note whether this is the case.

From the front

Inspect for: normal and symmetrical shoulder and quadriceps muscle bulk, no knee swellings, no deformity of mid or hind feet.

Now ask the patient to do the following noting any painful, restricted or asymmetrical movements:

Test rotation of the thoracic and lumbar spine. Gently hold the patient's hips still and ask them to: "Turn your shoulders round as far as you can to the left, then do the same to the right."

Test lateral flexion of the thoracic and lumbar spine: "Stand up straight and then slide the palm of your right hand down your thigh towards your knee, bending your shoulder down to the side." "Now do the same with your left hand down your left leg."

"Bend your left ear down towards your left shoulder and then your right ear down towards your right shoulder" to test for pain free cervical spine lateral flexion.

Now test for stiffness or pain flexing or extending the cervical spine: "bend your neck forwards to try to touch your chin against your chest." "bend your neck back to lift your chin."

"open your jaw and move it from side to side" to test for pain free normal tempero-mandibular joint movement.

"put your hands behind your head with your elbows as far back as they can go. Now try to touch the small of your back" to test for normal sterno-clavicular, gleno-humeral and acromio-clavicular joint movement.

"put your hands by your sides with your elbows straight" looking for full elbow extension.

"put your hands out in front of you with your palms down and fingers out straight" looking for ability to extend fingers, and inspecting for any swelling or deformity of the fingers or wrists.

"now turn your hands over" making sure that supination is normal (watch for external rotation of the shoulder to compensate for poor supination). Inspect the palms for any signs or swellings.

"now make a fist with both hands around my fingers and squeeze tightly" test the grip for normal and symmetrical power.

"place the tip of each finger onto the thumb" to test for fine precision pinch. You may also do a metacapral squeeze at this point to test for metacarpal phalangeal tenderness.

Now lay the patient down.

For both legs compare true (ASIS to medial malleolus) and apparent (umbilicus to medial malleolus) leg length.

Ask the patient to:

"put your heel onto your bottom" to test knee flexion. Place your hand over the knee and then the hip joints feeling for crepitus as the patient moves these joints.

Now test internal rotation of the hip with the knee joint flexed to 90 degrees (moving the foot laterally with the knee flexed causes internal rotation of the hip joint - early OA causes pain and limitation of this movement).

Test for the balloon sign on the knees.

Inspect the soles of the feet for any calluses, or skin changes.

Squeeze the metatarsal joints to test for any tenderness.

pGALS

The paediatric assessment of the musculoskeletal system includes all the components of the adult version with several minor additions:

Gait

Ask the child to walk on their tip toes and also upon their heels

From the front

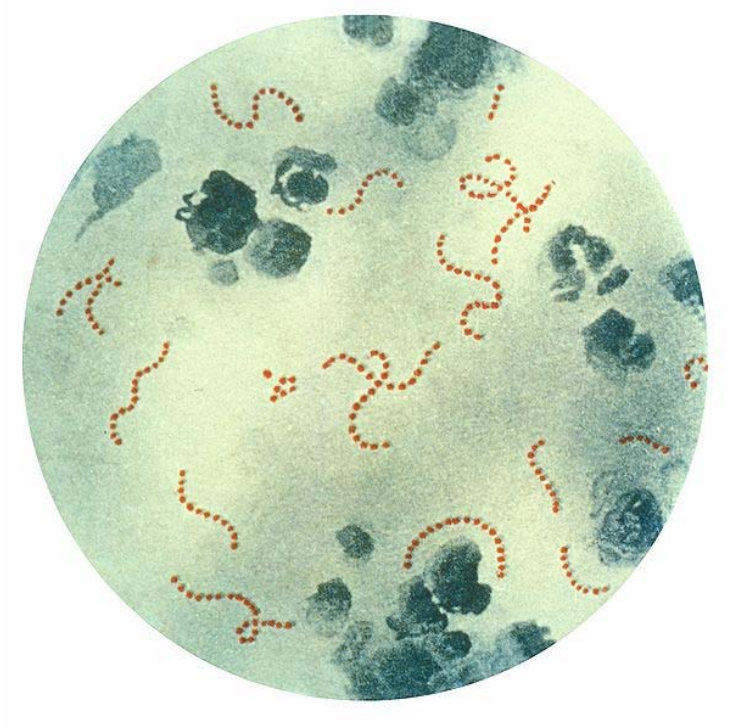
Ask the child to put their hands together (as if praying) and also put their hands back to back. Also have them reach up their arms towards the sky.

Additionally, when assessing the spine ask the child to open their mouth and insert three of their own fingers into their mouth.

Chapter 11

Rheumatic Fever

Rheumatic fever

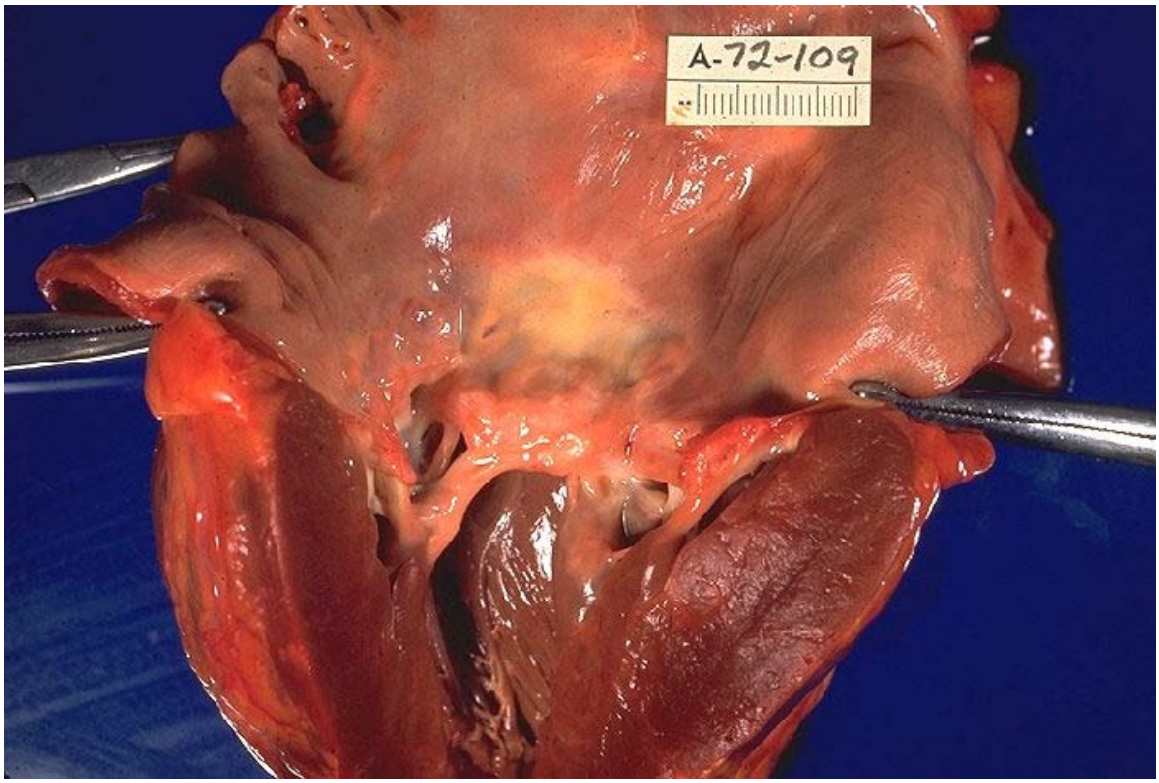


Streptococcus pyogenes bacteria, Pappenheim's stain

ICD-10	I00.-I02.
ICD-9	390–392
DiseasesDB	11487
MedlinePlus	003940
eMedicine	med/3435 med/2922 emerg/509 ped/2006
MeSH	D012213

Rheumatic fever is an inflammatory disease that occurs following a Group A streptococcal infection, (such as strep throat or scarlet fever). Believed to be caused by antibody cross-reactivity that can involve the heart, joints, skin, and brain, the illness typically develops two to three weeks after a streptococcal infection. Acute rheumatic fever commonly appears in children between the ages of 5 and 17, with only 20% of first-time attacks occurring in adults. The illness is so named because of its similarity in presentation to rheumatism.

Diagnosis



Rheumatic heart disease at autopsy with characteristic findings (thickened mitral valve, thickened chordae tendineae, hypertrophied left ventricular myocardium).

Modified Jones criteria were first published in 1944 by T. Duckett Jones, MD. They have been periodically revised by the American Heart Association in collaboration with other groups. According to revised Jones criteria, the diagnosis of rheumatic fever can be made when two of the major criteria, or one major criterion plus two minor criteria, are present along with evidence of streptococcal infection. Exceptions are chorea and indolent carditis, each of which by itself can indicate rheumatic fever.

Major criteria

- Migratory polyarthritis: a temporary migrating inflammation of the large joints, usually starting in the legs and migrating upwards.

- Carditis: inflammation of the heart muscle which can manifest as congestive heart failure with shortness of breath, pericarditis with a rub, or a new heart murmur.
- Subcutaneous nodules: painless, firm collections of collagen fibers over bones or tendons. They commonly appear on the back of the wrist, the outside elbow, and the front of the knees.
- Erythema marginatum: a long lasting rash that begins on the trunk or arms as macules and spreads outward to form a snake like ring while clearing in the middle. This rash never starts on the face and it is made worse with heat.
- Sydenham's chorea (St. Vitus' dance): a characteristic series of rapid movements without purpose of the face and arms. This can occur very late in the disease.

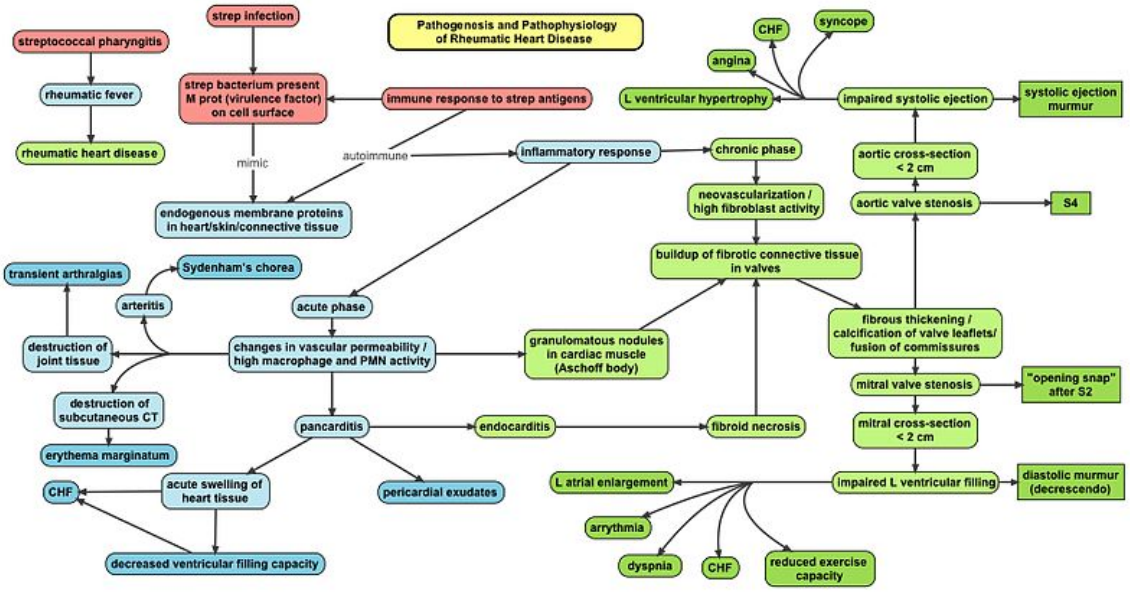
Minor criteria

- Fever
- Arthralgia: Joint pain without swelling (Cannot be included if Polyarthritis is present as a major symptom)
- Raised erythrocyte sedimentation rate or C reactive protein
- Leukocytosis
- ECG showing features of heart block, such as a prolonged PR interval (Cannot be included if Cariditis is present as a major symptom)
- Supporting evidence of streptococcal infection: elevated or rising antistreptolysin O titre or DNAase.
- Previous episode of rheumatic fever or inactive heart disease

Other signs and symptoms

- Abdominal pain
- Nose bleeds

Pathophysiology



Pathophysiology of rheumatic heart disease

Rheumatic fever is a systemic disease affecting the peri-arteriolar connective tissue and can occur after an untreated Group A Beta hemolytic streptococcal pharyngeal infection. It is believed to be caused by antibody cross-reactivity. This cross-reactivity is a Type II hypersensitivity reaction and is termed *molecular mimicry*. Usually, self reactive B cells remain anergic in the periphery without T cell co-stimulation. During a Streptococcus infection, mature antigen presenting cells such as B cells present the bacterial antigen to CD4-T cells which differentiate into helper T_2 cells. Helper T_2 cells subsequently activate the B cells to become plasma cells and induce the production of antibodies against the cell wall of Streptococcus. However the antibodies may also react against the myocardium and joints, producing the symptoms of rheumatic fever.

Group A *streptococcus pyogenes* has a cell wall composed of branched polymers which sometimes contain M protein that are highly antigenic. The antibodies which the immune system generates against the M protein may cross react with cardiac myofiber protein myosin,heart muscle glycogen and smooth muscle cells of arteries, inducing cytokine release and tissue destruction. However, the only proven cross reaction is with perivascular connective tissue. This inflammation occurs through direct attachment of complement and Fc receptor-mediated recruitment of neutrophils and macrophages. Characteristic Aschoff bodies, composed of swollen eosinophilic collagen surrounded by lymphocytes and macrophages can be seen on light microscopy. The larger macrophages may become Aschoff giant cells. Acute rheumatic valvular lesions may also involve a cell-mediated immunity reaction as these lesions predominantly contain T-helper cells and macrophages.

In acute rheumatic fever, these lesions can be found in any layer of the heart and is hence called pancarditis. The inflammation may cause a serofibrinous pericardial exudates described as "bread-and-butter" pericarditis, which usually resolves without sequelae. Involvement of the endocardium typically results in fibrinoid necrosis and verrucae formation along the lines of closure of the left-sided heart valves. Warty projections arise from the deposition, while subendothelial lesions may induce irregular thickenings called MacCallum plaques.

Chronic rheumatic heart disease is characterized by repeated inflammation with fibrinous resolution. The cardinal anatomic changes of the valve include leaflet thickening, commissural fusion and shortening and thickening of the tendinous cords.

Prevention

Prevention of recurrence is achieved by eradicating the acute infection and prophylaxis with antibiotics. The American Heart Association recommends daily or monthly prophylaxis continue long-term, perhaps for life.

Treatment

The management of acute rheumatic fever is geared toward the reduction of inflammation with anti-inflammatory medications such as aspirin or corticosteroids. Individuals with positive cultures for strep throat should also be treated with antibiotics. Aspirin is the drug of choice and should be given at high doses of 100 mg/kg/day. One should watch for side effects like gastritis and salicylate poisoning. In children and teenagers, the use of aspirin and aspirin-containing products can be associated with Reye's syndrome, a serious and potentially deadly condition. The risks, benefits and alternative treatments must always be considered when administering aspirin and aspirin-containing products in children and teenagers. Ibuprofen for pain and discomfort and corticosteroids for moderate to severe inflammatory reactions manifested by rheumatic fever should be considered in children and teenagers. Steroids are reserved for cases where there is evidence of involvement of heart. The use of steroids may prevent further scarring of tissue and may prevent development of sequelae such as mitral stenosis. Monthly injections of longacting penicillin must be given for a period of five years in patients having one attack of rheumatic fever. If there is evidence of carditis, the length of Penidure therapy may be up to 40 years. Another important cornerstone in treating rheumatic fever includes the continual use of low-dose antibiotics (such as penicillin, sulfadiazine, or erythromycin) to prevent recurrence.

Infection

Patients with positive cultures for *Streptococcus pyogenes* should be treated with penicillin as long as allergy is not present. This treatment will not alter the course of the acute disease.

The most appropriate treatment stated in the Oxford Handbook of Clinical Medicine for rheumatic fever is benzylpenicillin.

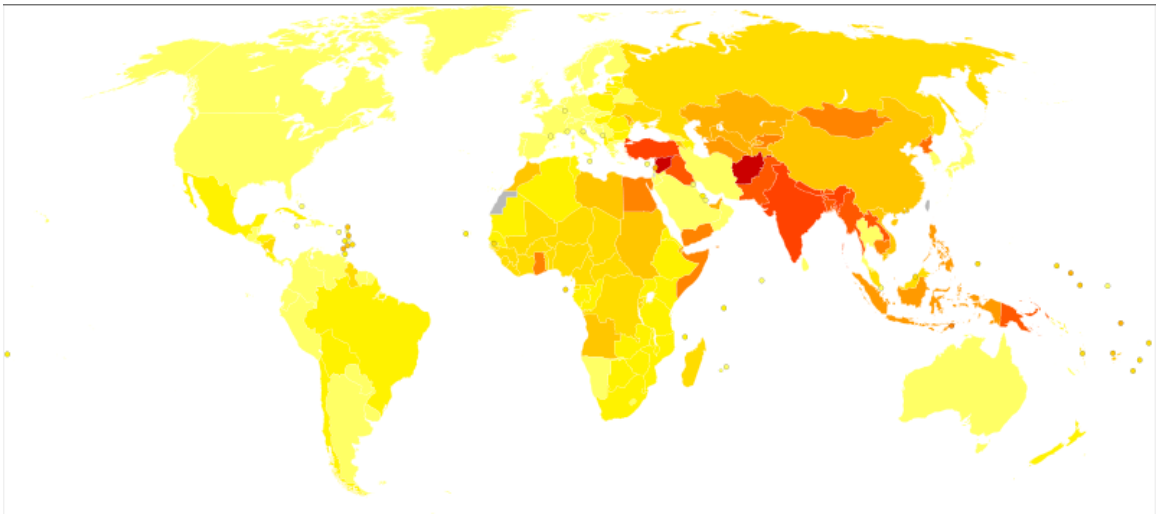
Inflammation

Patients with significant symptoms may require corticosteroids. Salicylates are useful for pain.

Heart failure

Some patients develop significant carditis which manifests as congestive heart failure. This requires the usual treatment for heart failure: diuretics and digoxin. Unlike normal heart failure, rheumatic heart failure responds well to corticosteroids.

Epidemiology



Disability-adjusted life year for rheumatic heart disease per 100,000 inhabitants in 2004.

- no data
- less than 20
- 20-40
- 40-60
- 60-80
- 80-100
- 100-120
- 120-140
- 140-160
- 160-180
- 180-200
- 200-330
- more than 330

Rheumatic fever is common worldwide and responsible for many cases of damaged heart valves. In Western countries, it became fairly rare since the 1960s, probably due to widespread use of antibiotics to treat streptococcus infections. While it is far less common in the United States since the beginning of the 20th century, there have been a few outbreaks since the 1980s. Although the disease seldom occurs, it is serious and has a mortality of 2–5%.

Rheumatic fever primarily affects children between ages 5 and 17 years and occurs approximately 20 days after strep throat. In up to a third of cases, the underlying strep infection may not have caused any symptoms.

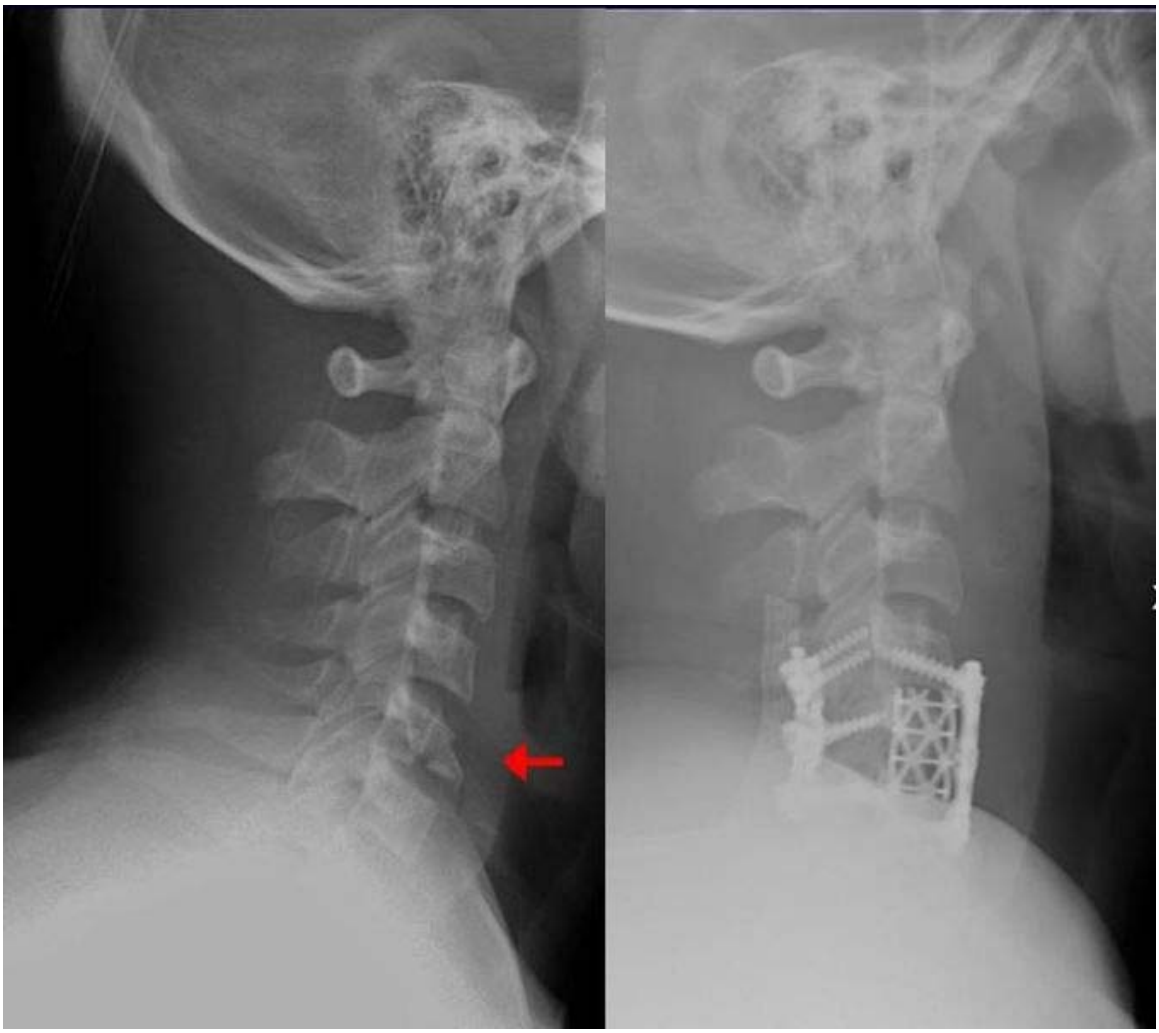
The rate of development of rheumatic fever in individuals with untreated strep infection is estimated to be 3%. The incidence of recurrence with a subsequent untreated infection is substantially greater (about 50%). The rate of development is far lower in individuals who have received antibiotic treatment. Persons who have suffered a case of rheumatic fever have a tendency to develop flare-ups with repeated strep infections.

The recurrence of rheumatic fever is relatively common in the absence of maintenance of low dose antibiotics, especially during the first three to five years after the first episode. Heart complications may be long-term and severe, particularly if valves are involved.

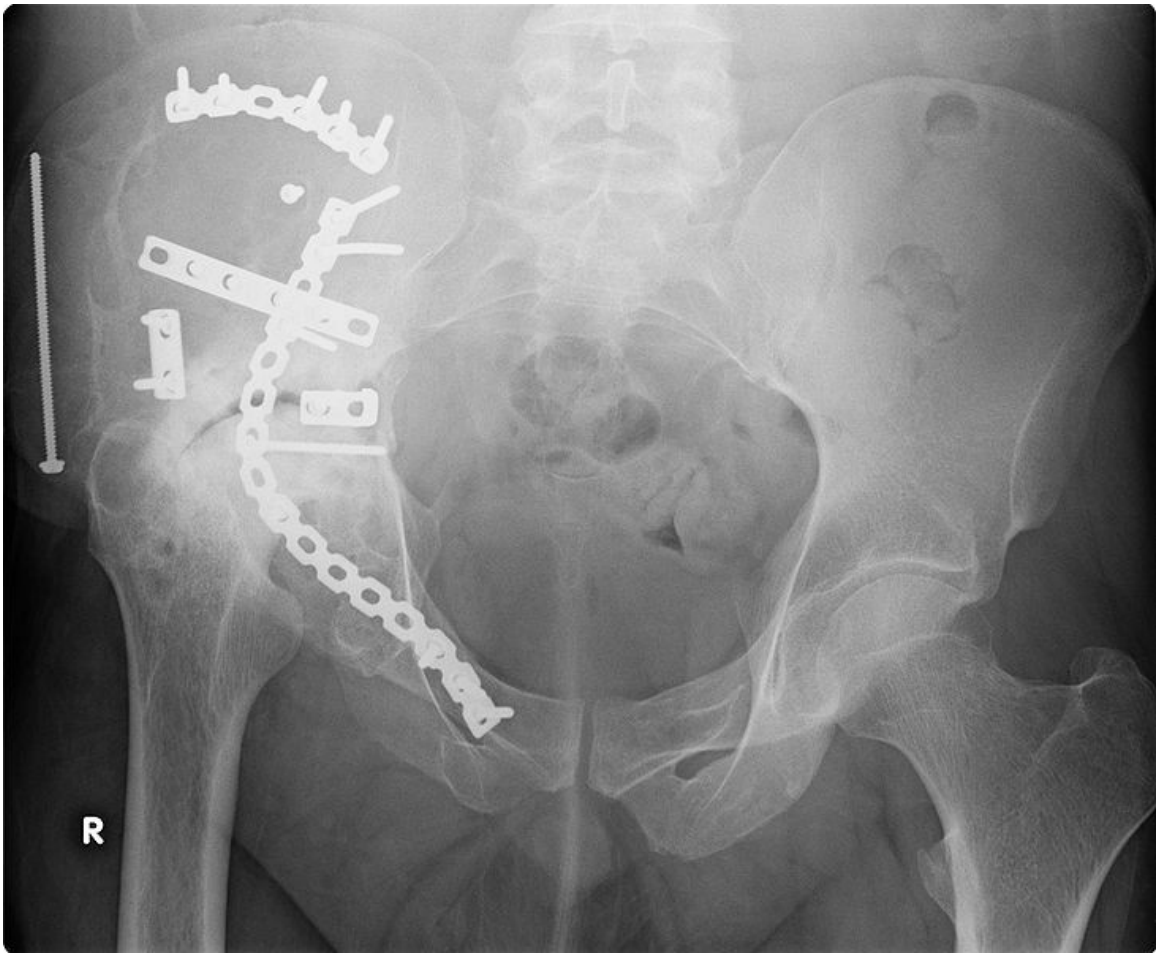
Survivors of Rheumatic fever often have to take penicillin to prevent streptococcal infection which could possibly lead to another case of Rheumatic fever that could prove fatal.

Chapter 12

Orthopedic Surgery



This fracture of the lower cervical vertebrae, known as a "teardrop fracture", is one of the conditions treated by orthopedic surgeons and neurosurgeons.



This image, taken in September 2006, shows extensive repair work to the right acetabulum 6 years after it was carried out (2000). Further damage to the joint is visible due to the onset of arthritis.

Orthopedic surgery or **orthopedics** (also spelled **orthopaedic surgery** and **orthopaedics**) is the branch of surgery concerned with conditions involving the musculoskeletal system. Orthopedic surgeons use both surgical and nonsurgical means to treat musculoskeletal trauma, sports injuries, degenerative diseases, infections, tumors, and congenital disorders.

Nicholas Andry coined the word "orthopaedics", derived from Greek words for *orthos* ("correct", "straight") and *paideion* ("child"), when he published *Orthopaedia: or the Art of Correcting and Preventing Deformities in Children* in 1741. Correction of spinal and bony deformities became the cornerstone of orthopaedic practice. Today, over 6 months of training is dedicated to the treatment of the pediatric population.

In the United States *orthopedics* is standard, although the majority of university and residency programs, and even the American Academy of Orthopaedic Surgeons, still use Andry's spelling. Elsewhere, usage is not uniform; in Canada, both spellings are

acceptable; *orthopaedics* usually prevails in the rest of the Commonwealth, especially in Britain.

Training

In the United States, orthopedic surgeons have typically completed four years of undergraduate education and four years of medical school. Subsequently, these medical school graduates undergo residency training in orthopedic surgery. The five-year residency consists of one year of general surgery training followed by four years of training in orthopedic surgery.

Selection for residency training in orthopedic surgery is extremely competitive. Approximately 700 physicians complete orthopedic residency training per year in the United States. About 10 percent of current orthopedic surgery residents are women; about 20 percent are members of minority groups. There are approximately 20,400 actively practicing orthopedic surgeons and residents in the United States. According to the latest Occupational Outlook Handbook (2009–2010) published by the United States Department of Labor, between 3–4% of all practicing physicians are orthopedic surgeons.

Many orthopedic surgeons elect to do further training, or fellowships, after completing their residency training. Fellowship training in an orthopedic subspeciality is typically one year in duration (sometimes two) and sometimes has a research component involved with the clinical and operative training. Examples of orthopedic subspecialty training in the United States are:

- Hand surgery
- Shoulder and elbow surgery
- Total joint reconstruction (arthroplasty)
- Pediatric orthopedics
- Foot and ankle surgery
- Spine surgery
- Musculoskeletal oncology
- Surgical sports medicine
- Orthopedic trauma

These specialty areas of medicine are not exclusive to orthopedic surgery. For example, hand surgery is practiced by some plastic surgeons and spine surgery is practiced by most neurosurgeons. Additionally, foot and ankle surgery is practiced by board-certified Doctors of Podiatric Medicine (D.P.M.) in the United States. Some family practice physicians practice sports medicine; however, their scope of practice is non-operative.

After completion of specialty residency/registrar training, an orthopedic surgeon is then eligible for board certification. Certification by the American Board of Orthopaedic Surgery means that the orthopedic surgeon has met the specified educational, evaluation, and examination requirements of the Board. The process requires successful completion of a standardized written exam followed by an oral exam focused on the surgeon's

clinical and surgical performance over a 6-month period. In Canada, the certifying organization is the Royal College of Physicians and Surgeons of Canada; in Australia and New Zealand it is the Royal Australasian College of Surgeons.

In the United States, specialists in hand surgery and sports medicine may obtain a Certificate of Added Qualifications (CAQ) in addition to their board certification by successfully completing a separate standardized examination. There is no additional certification process for the other subspecialties.

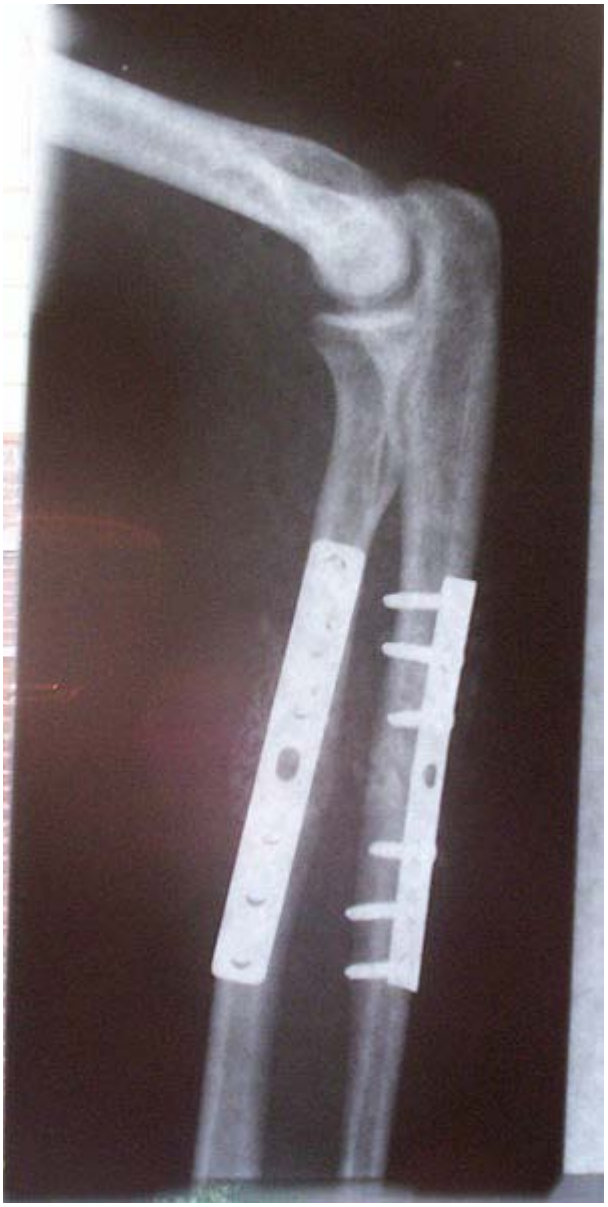
Practice

According to applications for board certification from 1999 to 2003, the top 25 most common procedures (in order) performed by orthopedic surgeons are as follows:

1. Knee arthroscopy and meniscectomy
2. Shoulder arthroscopy and decompression
3. Carpal tunnel release
4. Knee arthroscopy and chondroplasty
5. Removal of support implant
6. Knee arthroscopy and anterior cruciate ligament reconstruction
7. Knee replacement
8. Repair of femoral neck fracture
9. Repair of trochanteric fracture
10. Debridement of skin/muscle/bone/fracture
11. Knee arthroscopy repair of both menisci
12. Hip replacement
13. Shoulder arthroscopy/distal clavicle excision
14. Repair of rotator cuff tendon
15. Repair fracture of radius (bone)/ulna
16. Laminectomy
17. Repair of ankle fracture (bimalleolar type)
18. Shoulder arthroscopy and debridement
19. Lumbar spinal fusion
20. Repair fracture of the distal part of radius
21. Low back intervertebral disc surgery
22. Incise finger tendon sheath
23. Repair of ankle fracture (fibula)
24. Repair of femoral shaft fracture
25. Repair of trochanteric fracture

A typical schedule for a practicing orthopedic surgeon involves 50–55 hours of work per week divided among clinic, surgery, various administrative duties and possibly teaching and/or research if in an academic setting. In 2009, the median salary for an orthopedic surgeon in the United States was $406,847.

History



Orthopedic implants to repair fractures to the radius and ulna. Note the visible break in the ulna. (right forearm)

Jean-Andre Venel established the first orthopedic institute in 1780, which was the first hospital dedicated to the treatment of children's skeletal deformities. He is considered by some to be the father of orthopedics or the first true orthopedist in consideration of the establishment of his hospital and for his published methods.

Antonius Mathysen, a Dutch military surgeon, invented the plaster of Paris cast in 1851. Many developments in orthopedic surgery resulted from experiences during wartime. On the battlefields of the Middle Ages the injured were treated with bandages soaked in

horses' blood which dried to form a stiff, but unsanitary, splint. Traction and splinting developed during World War I. The use of intramedullary rods to treat fractures of the femur and tibia was pioneered by Gerhard Küntscher of Germany. This made a noticeable difference to the speed of recovery of injured German soldiers during World War II and led to more widespread adoption of intramedullary fixation of fractures in the rest of the world. However, traction was the standard method of treating thigh bone fractures until the late 1970s when the Harborview Medical Center in Seattle group popularized intramedullary fixation without opening up the fracture. External fixation of fractures was refined by American surgeons during the Vietnam War but a major contribution was made by Gavril Abramovich Ilizarov in the USSR. He was sent, without much orthopedic training, to look after injured Russian soldiers in Siberia in the 1950s. With no equipment he was confronted with crippling conditions of unhealed, infected, and malaligned fractures. With the help of the local bicycle shop he devised ring external fixators tensioned like the spokes of a bicycle. With this equipment he achieved healing, realignment and lengthening to a degree unheard of elsewhere. His Ilizarov apparatus is still used today as one of the distraction osteogenesis methods.

Ruth Jackson became the first female Board-certified Orthopaedic Surgeon in the U.S in 1937. Orthopaedics continues to be a male-dominated field. In 2006, 12.4% of orthopaedics residents were women.

David L. MacIntosh pioneered the first successful surgery for the management of the torn anterior cruciate ligament (ACL) of the knee. This common and serious injury in skiers, field athletes, and dancers invariably brought an end to their athletics due to permanent joint instability. Working with injured football players, Dr MacIntosh devised a way to re-route viable ligament from adjacent structures to preserve the strong and complex mechanics of the knee joint and restore stability. The subsequent development of ACL reconstruction surgery has allowed numerous athletes to return to the demands of sports at all levels.

Modern orthopedic surgery and musculoskeletal research has sought to make surgery less invasive and to make implanted components better and more durable.

Arthroscopy

The use of arthroscopic techniques has been particularly important for injured patients. Arthroscopy was pioneered in the early 1950s by Dr. Masaki Watanabe of Japan to perform minimally invasive cartilage surgery and reconstructions of torn ligaments. Arthroscopy helped patients recover from the surgery in a matter of days, rather than the weeks to months required by conventional, 'open' surgery. Knee arthroscopy is one of the most common operations performed by orthopedic surgeons today and is often combined with meniscectomy or chondroplasty. The majority of orthopedic procedures are now performed arthroscopically.

Arthroplasty

The modern total hip replacement was pioneered by Sir John Charnley in England in the 1960s. He found that joint surfaces could be replaced by metal or high density polyethylene implants cemented to the bone with methyl methacrylate bone cement. Since Charnley, there have been continuous improvements in the design and technique of joint replacement (arthroplasty) with many contributors, including W. H. Harris, the son of R. I. Harris, whose team at Harvard pioneered uncemented arthroplasty techniques with the bone bonding directly to the implant.

Knee replacements using similar technology were started by McIntosh in rheumatoid arthritis patients and later by Gunston and Marmor for osteoarthritis in the 1970s developed by Dr John Insall in New York utilizing a fixed bearing system, and by Dr Frederick Buechel and Dr Michael Pappas utilizing a mobile bearing system.

Uni-compartmental knee replacement, in which only one weight-bearing surface of an arthritic knee is replaced, is an alternative to a total knee replacement in a select patient population.

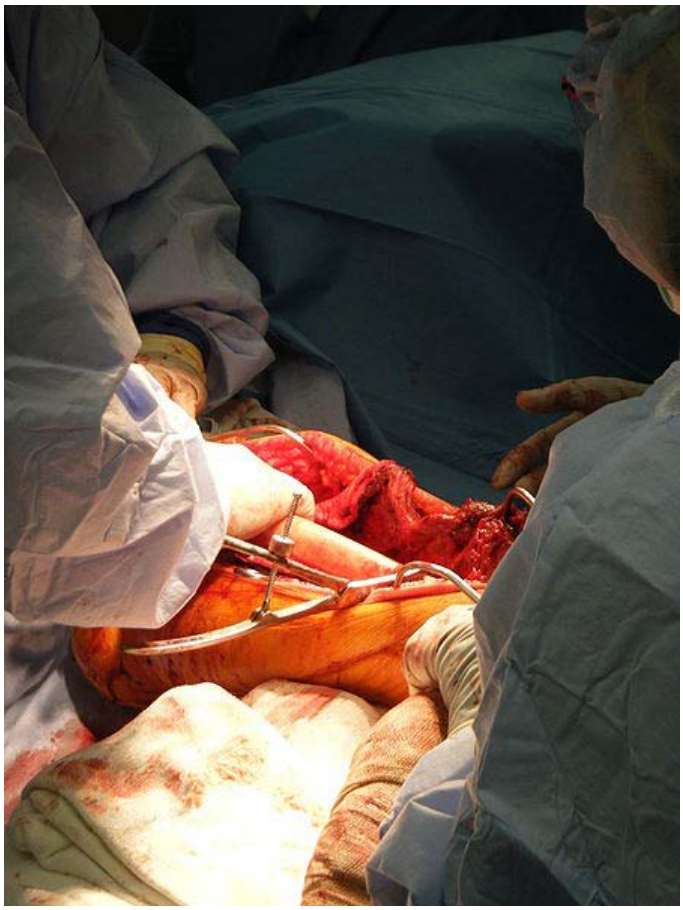
Joint replacements are available for other joints on a limited basis, most notably shoulder, elbow, wrist, ankle, spine, and fingers.

In recent years, surface replacement of joints, in particular the hip joint, have become more popular amongst younger and more active patients. This type of operation delays the need for the more traditional and less bone-conserving total hip replacement, but carries significant risks of early failure from fracture and bone death.

One of the main problems with joint replacements is wear of the bearing surfaces of components. This can lead to damage to surrounding bone and contribute to eventual failure of the implant. Use of alternative bearing surfaces has increased in recent years, particularly in younger patients, in an attempt to improve the wear characteristics of joint replacement components. These include ceramics and all-metal implants (as opposed to the original metal-on-plastic). The plastic (actually ultra high-molecular-weight polyethylene) can also be altered in ways that may improve wear characteristics.

Chapter 13

Bone Grafting



A surgeon places a bone graft into position during a limb salvage

Bone grafting is a surgical procedure that replaces missing bone in order to repair bone fractures that are extremely complex, pose a significant health risk to the patient, or fail to heal properly.

Bone generally has the ability to regenerate completely but requires a very small fracture space or some sort of scaffold to do so. Bone grafts may be autologous (bone harvested from the patient's own body, often from the iliac crest), allograft (cadaveric bone usually obtained from a bone bank), or synthetic (often made of hydroxyapatite or other

naturally-occurring and biocompatible substances) with similar mechanical properties to bone. Most bone grafts are expected to be reabsorbed and replaced as the natural bone heals over a few months' time.

The principles involved in successful bone grafts include osteoconduction (guiding the reparative growth of the natural bone), osteoinduction (encouraging undifferentiated cells to become active osteoblasts), and osteogenesis (living bone cells in the graft material contribute to bone remodeling). Osteogenesis only occurs with autografts.

Biological mechanism

Properties of various types of bone graft sources.

	Osteoconductive	Osteoinductive	Osteogenic
Alloplast	+	–	–
Xenograft	+	–	–
Allograft	+	+/–	–
Autograft	+	+	+

Bone grafting is possible because bone tissue, unlike most other tissues, has the ability to regenerate completely if provided the space into which to grow. As native bone grows, it will generally replace the graft material completely, resulting in a fully integrated region of new bone. The biologic mechanisms that provide a rationale for bone grafting are osteoconduction, osteoinduction and osteogenesis.

Osteoconduction

Osteoconduction occurs when the bone graft material serves as a scaffold for new bone growth that is perpetuated by the native bone. Osteoblasts from the margin of the defect that is being grafted utilize the bone graft material as a framework upon which to spread and generate new bone. In the very least, a bone graft material should be osteoconductive.

Osteoinduction

Osteoinduction involves the stimulation of osteoprogenitor cells to differentiate into osteoblasts that then begin new bone formation. The most widely studied type of osteoinductive cell mediators are **bone morphogenetic proteins** (BMPs). A bone graft material that is osteoconductive and osteoinductive will not only serve as a scaffold for currently existing osteoblasts but will also trigger the formation of new osteoblasts, theoretically promoting faster integration of the graft.

Osteopromotion

Osteopromotion involves the enhancement of osteoinduction without the possession of osteoinductive properties. For example, enamel matrix derivative has been shown to

enhance the osteoinductive effect of demineralized freeze dried bone allograft (DFDBA), but will not stimulate *de novo* bone growth alone.

Osteogenesis

Osteogenesis occurs when vital osteoblasts originating from the bone graft material contribute to new bone growth along with bone growth generated via the other two mechanisms.

Types and Tissue Sources

Autograft

Autologous (or autogenous) bone grafting involves utilizing bone obtained from the same individual receiving the graft. Bone can be harvested from non-essential bones, such as from the iliac crest, or more commonly in oral and maxillofacial surgery, from the mandibular symphysis (chin area) or anterior mandibular ramus (the coronoid process); this is particularly true for *block grafts*, in which a small block of bone is placed whole in the area being grafted. When a block graft will be performed, autogenous bone is the most preferred because there is less risk of the graft rejection because the graft originated from the patient's own body. As indicated in the chart above, such a graft would be osteoinductive and osteogenic, as well as osteoconductive. A negative aspect of autologous grafts is that an additional surgical site is required, in effect adding another potential location for post-operative pain and complications.

Autologous bone is typically harvested from intra-oral sources as the chin or extra-oral sources as the iliac crest, the fibula, the ribs, the mandible and even parts of the skull.

All bone requires a blood supply in the transplanted site. Depending on where the transplant site is and the size of the graft, an additional blood supply may be required. For these types of grafts, extraction of the part of the periosteum and accompanying blood vesels along with donor bone is required. This kind of graft is known as a vital bone graft.

An autograft may also be performed without a solid bony structure, for example using bone reamed from the anterior superior iliac spine. In this case there is an osteoinductive and osteogenic action, however there is no osteoconductive action, as there is no solid bony structure.

A bone allograft

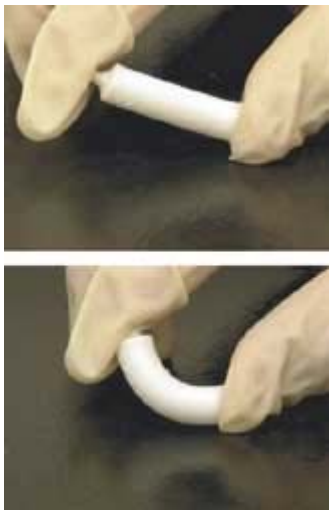
Allografts

Allograft bone, like autogenous bone, is derived from humans; the difference is that allograft is harvested from an individual other than the one receiving the graft. Allograft bone is taken from cadavers that have donated their bone so that it can be used for living people who are in need of it; it is typically sourced from a bone bank.

There are three types of bone allograft available:

1. Fresh or fresh-frozen bone
2. Freeze-dried bone allograft (FDBA)
3. Demineralized freeze-dried bone allograft (DFDBA)

Synthetic variants



Flexible hydrogel-HA composite, which has a mineral-to-organic matrix ratio approximating that of human bone.

Artificial bone can be created from ceramics such as calcium phosphates (e.g. hydroxyapatite and tricalcium phosphate), Bioglass and calcium sulphate; all of which are biologically active to different degrees depending on solubility in the physiological environment. These materials can be doped with growth factors, ions such as strontium or mixed with bone marrow aspirate to increase biological activity. Some authors believe this method is inferior to autogenous bone grafting however infection and rejection of the graft is much less of a risk, the mechanical properties such as Young's modulus are comparable to bone. The presence of elements such as strontium can result in higher bone mineral density and enhanced osteoblast proliferation in vivo.

Xenografts

Xenograft bone substitute has its origin from a species other than human, such as bovine. Xenografts are usually only distributed as a calcified matrix. In January 2010 Italian scientists announced a breakthrough in the use of wood as a bone substitute, though this technique is not expected to be used for humans until at the earliest 2015.

Alloplastic grafts

Alloplastic grafts may be made from hydroxylapatite, a naturally occurring mineral that is also the main mineral component of bone. They may be made from bioactive glass. Hydroxylapetite is a Synthetic Bone Graft, which is the most used now among other synthetic due to its osteoconduction, hardness and acceptability by bone. Some synthetic bone grafts are made of calcium carbonate, which start to decrease in usage because it is completely resorbable in short time which make the bone easy to break again. Finally used is the tricalcium phosphate which now used in combination with hydroxylapatite thus give both effect osteoconduction and resorbability.

Growth Factors

Growth Factor enhanced grafts are produced using recombinant DNA technology. They consist of either Human Growth Factors or Morphogens (Bone Morphogenic Proteins in conjunction with a carrier medium, such as collagen).

Uses

The most common use of bone grafting is in the application of dental implants, in order to restore the edentulous area of a missing tooth. Dental implants require bones underneath them for support and to have the implant integrate properly into the mouth. People who have been edentulous (without teeth) for a prolonged period may not have enough bone left in the necessary locations. In this case, bone can be taken from the chin or from the pilot holes for the implants or even from the iliac crest of the pelvis and inserted into the mouth underneath the new implant.

In general, bone grafts are either used en block (such as from the chin or the ascending ramus area of the lower jaw) or particulated, in order to be able to adapt it better to a defect.

Another common bone graft, which is more substantial than those used for dental implants, is of the fibular shaft. After the segment of the fibular shaft has been removed normal activities such as running and jumping are permitted on the leg with the bone deficit. The grafted, vascularized fibulas have been used to restore skeletal integrity to long bones of limbs in which congenital bone defects exist and to replace segments of bone after trauma or malignant tumor invasion. The periosteum and nutrient artery are generally removed with the piece of bone so that the graft will remain alive and grow when transplanted into the new host site. Once the transplanted bone is secured into its new location it generally restores blood supply to the bone in which it has been attached.

Besides the main use of bone grafting – dental implants – this procedure is used to fuse joints to prevent movement, repair broken bones that have bone loss, and repair broken bone that has not yet healed.

Bone grafts are used in hopes that the defective bone will be healed or will regrow with little to no graft rejection.

Procedure

Depending on where the bone graft is needed, a different doctor may be requested to do the surgery. Doctors that do bone graft procedures are commonly orthopedic surgeons, otolaryngology head and neck surgeons, neurosurgeons, craniofacial surgeons, oral and maxillofacial surgeons,Podiatric Surgeons and periodontists.

Risks

As with any procedure, there are risks involved; among these include reactions to medicine and problems breathing, bleeding, and infection. Infection is reported to occur in less than 1% of cases and is curable with antibiotics. Overall, patients with a preexisting illness are at a higher risk of getting an infection as opposed to those who are overall healthy.

Risks for grafts from the iliac crest

Some of the potential risks and complications of bone grafts employing the iliac crest as a donor site include:

- *acquired* bowel herniation (this becomes a risk for larger donor sites (>4 cm)). About 20 cases have been reported in the literature from 1945 till 1989 and only a few hundred cases have been reported worldwide
- meralgia paresthetica (injury to the lateral femoral cutaneous nerve also called Bernhardt-Roth's syndrome)
- pelvic instability
- fracture (extremely rare and usually with other factors)
- injury to the clunial nerves (this will cause posterior pelvic pain which is worsened by sitting)
- injury to the ilioinguinal nerve
- infection
- minor hematoma (a common occurrence)
- deep hematoma requiring surgical intervention
- seroma
- ureteral injury
- pseudoaneurysm of iliac artery (rare)
- tumor transplantation
- cosmetic defects (chiefly caused by not preserving the superior pelvic brim)
- chronic pain

Bone grafts harvested from the posterior iliac crest in general have less morbidity, but depending on the type of surgery, may require a flip while the patient is under general anesthesia.

Recovery and Aftercare

The amount of time it takes for an individual to recovery depends on the severity of the injury being treated and lasts anywhere from 2 weeks to 2 months with a possibility of vigorous exercise being barred for up to 6 months.

Costs

Bone graft procedures consist of more than just the surgery. The average cost of bone graft procedures ranges from approximately $33,860 to $37,227. Besides the cost of the bone graft itself (ranging from $250 to $900) other expenses for the procedure include: surgeon's fees (these vary), anesthesiologist fees (approximately $350 to $400 per hour), hospital charges (these vary; averaging about $1,500 to $1,800 a day), medication charges ($200 to $400), and additional fees for services such as medical supplies, diagnostic procedures, equipment use fees, etc.

Chapter 14

Osteotomy

An **osteotomy** is a surgical operation whereby a bone is cut to shorten, lengthen, or change its alignment. It is sometimes performed to correct a hallux valgus, or to straighten a bone that has healed crookedly following a fracture. It is also used to correct a coxa vara, genu valgum, and genu varum. The operation is done under a general anaesthetic.

Osteotomy is one method to relieve pain in arthritis, especially of the hip and knee. It is being replaced by joint replacement in the older patient.

Due to the serious nature of this procedure, recovery may be extensive. Careful consultation with a physician is important in order to ensure proper planning during a recovery phase. Tools exist to assist recovering patients who may have non weight bearing requirements and include bedpans, dressing sticks, long-handled shoe-horns, grabbers/reachers and specialized walkers and wheelchairs.

Osteotomies of the hip

Two main types of osteotomies are used in the correction of hip dysplasias and deformities to improve alignment/interaction of acetabulum - (socket) - and femoral head (femur head) - (ball), **innominate osteotomies** and **femoral osteotomies**. The bones are cut, reshaped or partially removed to realign the load bearing surfaces of the joint.

Adjustments are made to part of the hip-bone. Many operating methods and variations have been developed. They are defined by the type of cut and adjustment made Some acetabular procedures are named after the surgeons who first described them as Salter (R. Salter), Dega (W. Dega), Sutherland (D.H. Sutherland), Chiari (K. Chiari): other names one may encounter are Ludlov, P. Pemberton, and James B. Steele. Some are named after the shape of cut (e.g. Chevron, Wedge) or the way the bones are aligned (Dial=old style rotary dial phone).

Femoral osteotomies, as the name indicates, involves adjustments made to the femur head and/or the femur.

Osteotomy of the knee

Knee osteotomy is commonly used to realign arthritic damage on one side of the knee. The goal is to shift the patient's body weight off the damaged area to the other side of the knee, where the cartilage is still healthy. Surgeons remove a wedge of the tibia from underneath the unhealthy side of the knee, which allows the tibia and femur to bend away from the damaged cartilage.

A model for this is the hinges on a door. When the door is shut, the hinges are flush against the wall. As the door swings open, one side of the door remains pressed against the wall as space opens up on the other side. Removing just a small wedge of bone can "swing" the knee open, pressing the healthy tissue together as space opens up between the femur and tibia on the damaged side so that the arthritic surfaces do not rub against each other.

Osteotomy is also used as an alternative treatment to total knee replacement in younger and active patients. Because prosthetic knees may wear out over time, an osteotomy procedure can enable younger, active osteoarthritis patients to continue using the healthy portion of their knee. The procedure can delay the need for a total knee replacement for up to ten years.

Surgery

The location of the removed wedge of bone depends on where osteoarthritis has damaged the knee cartilage. The most common type of osteotomy performed on arthritic knees is a high tibial osteotomy, which addresses cartilage damage on the inside (medial) portion of the knee. The procedure usually takes 60 to 90 minutes to perform.

During a high tibial osteotomy, surgeons remove a wedge of bone from the outside of the knee, which causes the leg to bend slightly inward. This resembles the realigning of a bowlegged knee to a knock-kneed position. The patient's weight is transferred to the outside (lateral) portion of the knee, where the cartilage is still healthy.

After regional or general anesthesia is administered, the surgical team sterilizes the leg with antibacterial solution. Surgeons map out the exact size of the bone wedge they will remove, using an X-ray, CT scan, or 3D computer modeling. A four- to five-inch incision is made down the front and outside of the knee, starting below the kneecap and extending below the top of the shinbone.

Guide wires are drilled into the top of the shinbone (tibia plateau) from the outside (lateral side) of the knee. The wires usually outline a triangle form in the shinbone.

A standard oscillating saw is run along the guide wires, removing most of the bone wedge from underneath the outside of the knee, below the healthy cartilage. The cartilage surface on the top of the outside (lateral side) of the shinbone is left intact. The top of the shinbone is then lowered on the outside and attached with surgical staples or screws,

depending on the size of the wedge that was removed. The layers of tissue in the knee are stitched together, usually with absorbable sutures.

Rehabilitation and Prevention

A fall or torque to the leg during the first two months after surgery may jeopardize healing. Patients must exercise extreme caution during all activities, including walking, until healing is complete.

After rehabilitation, preventing osteoarthritis involves slowing the progression and spread of the disease. Maintaining aerobic cardiovascular fitness has been an effective method for preventing the progression of osteoarthritis. Light, daily exercise is much better for an arthritic knee than occasional, heavy exercise.

It is especially important to avoid any serious knee injuries, such as torn ligaments or fractured bones, because arthritis can complicate knee injury treatment. High-impact or repetitive stress sports, like football and distance running, should be avoided.

Because osteoarthritis has multiple causes and may be related to genetic factors, no universal prevention tactic exists.

General recommendations include:

- Keeping a slight bend in the knees will take the pressure off during standing.
- Avoid activities that causes pain which lasts over an hour.
- Perform controlled range of motion activities that do not overload the joint.
- Avoid heavy impact on the knees during everyday and athletic activities.
- Gently strengthen thigh and lower leg muscles to help protect the bones and cartilage in the knee.
- Non-contact activities keep joints and bones healthy and maintain fitness over time. Exercise also helps promote weight loss, which can take stress off knees.

Osteotomy of the jaw

Mandibular and Maxillary

This is performed to realign the mandible (lower jaw) or maxilla (upper jaw) with the rest of the skull and/or teeth. This is usually performed to correct skeletal malocclusions, that is discrepancies in tooth position that cannot be corrected by simple orthodontic movement, and realignment of the temporomandibular joints, or to correct facial deformities such as mandibular retrognathia. There is little scarring, and all of the surgery takes places inside of the mouth. Orthodontic braces may have to be worn pre- and post-operation to realign the teeth to match the newly realigned jaw.

Osteotomy of the Chin

Chin Osteotomy is most often done to correct a vertically short chin. As opposed to putting an implant on top of the chin bone to bring it forward, an alternative approach is to cut the chin bone itself and bring it forward or other directions as well. It can also be used to lengthen the chin (which is more difficult with an implant) or to shorten or narrow a chin. (which is impossible with an implant).

Chin osteotomies (cutting the bone and moving it) are done through an incision inside the mouth. It is technically more difficult than an implant and has more swelling and recovery than a simple chin implant. Also, there is usually temporary loss of feeling of the lip and chin after that takes several weeks to months for full return of sensation.

Veterinary Osteotomy Procedures

In veterinary medicine, osteotomies are frequently performed to address rupture of the canine cranial cruciate ligament, which is analogous to the anterior cruciate ligament. The tibial plateau leveling osteotomy and tibial tuberosity advancement are two of the most common ostetomy procedures performed in the United States. Recovery is often 6–8 weeks and the osteotomy can be filled with autologous bone grafts, scaffolds (hydroxyapatite, TR Matrix, etc.) or ceramics.

Chapter 15

Ilizarov Apparatus

An Ilizarov apparatus treating a fractured tibia and fibula

The **Ilizarov apparatus** is named after the orthopedic surgeon, Gavril Abramovich Ilizarov, from the Soviet Union who pioneered the technique. It is used in surgical procedures to lengthen or reshape limb bones; treat complex and/or open bone fractures; and in cases of infected non-unions of bones that are not amenable with other techniques.

History

Professor Gavril Abramovich Ilizarov invented this procedure in the 1950s after having to treat orthopedic conditions in the Kurgan region of Siberia, then in the Soviet Union. The procedure, and the first apparatus he designed for it, was inspired by a shaft bow harness on a horse carriage. Originally bicycle parts were used for the frame.

This novel technique was introduced to the West in the 1980s, predominantly via Italian surgeons. It gained popularity in the 1990s, and has been used successfully by many surgeons throughout the world. In most developing countries it is a highly specialised technique used mainly for deformity correction by experienced surgeons due to its complexity. Further development of the ring construct led to the Taylor Spatial Frame which is more versatile and far easier to use, but very costly. Though nowadays intramedullary limb lengthening devices are also available, they are not suitable for deformity correction of bones.

Mechanics and physics

The device is a specialized form of external fixator, a circular fixator, modular in construction. Stainless steel (or titanium) rings are fixed to the bone via stainless heavy-gauge wire (called "pins" or Kirschner wires). The rings are connected to each other with threaded rods attached through adjustable nuts. The circular construction and tensioned wires of the Ilizarov apparatus provide far more structural support than the traditional monolateral fixator system. This allows early weightbearing.

The top rings of the Ilizarov (fixed to the healthy bone by the tensioned wire) allow force to be transferred through the external frame (the vertical metal rods), bypassing the fracture site. Force is then transferred back to the healthy bone through the bottom ring and the tensioned wires. This allows the Ilizarov apparatus to act as a sort of bridge, both immobilizing the fracture site and relieving it of stress, while allowing for the movement of the entire limb and partial weight-bearing. Middle rings (and tensioned wires) act to hold the bone fragments in place and to give greater structural support to the apparatus and limb. However, the critical load bearing rings are the top and bottom rings which transfer the force from the healthy bone down to the healthy bone, bypassing the fracture site.

Bone lengthening/reshaping

In addition to being used to support a fractured limb, the Ilizarov frame is also commonly used to correct deformity through distraction osteogenesis.

The procedure consists of an initial surgery, during which the bone is surgically fractured and the ring apparatus is attached. As the patient recovers, the fractured bone begins to grow together. While the bone is growing, the frame is adjusted by means of turning the nuts, thus increasing the space between two rings. As the rings are connected to opposite sides of the fracture, this adjustment, done four times a day, moves the now-healing fracture apart by approximately one millimeter per day. The incremental daily increases

result in a considerable lengthening of the limb over time. Once the lengthening phase is complete, the apparatus stays on the limb for a consolidation period. The patient is able to fully weight bear on the Ilizarov frame, using crutches initially and pain is lessened. Once healing is complete, a second surgery is necessary to remove the ring apparatus. The result is a limb that is significantly longer. Additional surgery may be necessary, in the case of leg lengthening, to lengthen the Achilles tendon to accommodate the longer bone length. The major advantage of this procedure is that because the apparatus provides complete support while the bone is recovering the patient can remain active aiding recovery.

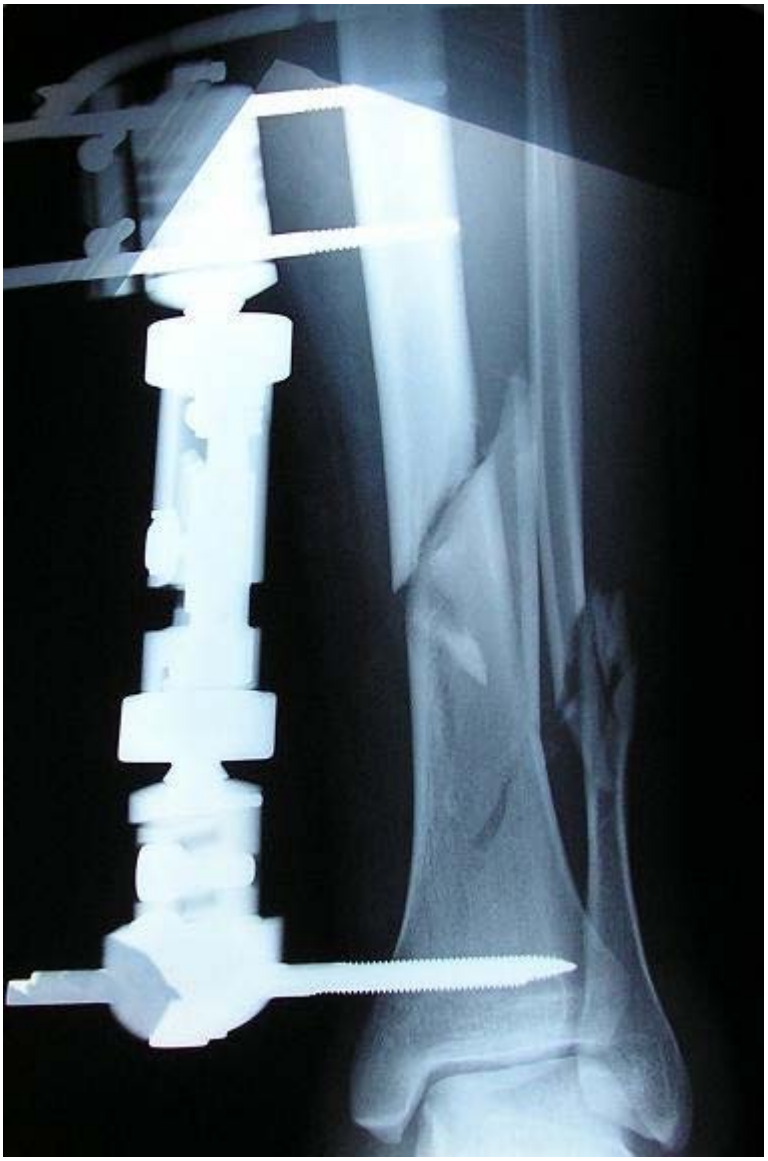
A further use is of bone transport, whereby a defect in a long bone can be treated by transporting a segment of bone, whilst simultaneously lengthening regenerate to reduce the defect and finally dock with the other segment, producing a single bony unit.

While the Ilizarov apparatus is minimally invasive (no large incisions are made,) it is not free of complications. Pain is common and can be severe, but is treatable with analgesics. Careful attention to cleaning and hygiene is necessary to prevent pin site infection. Other complications include swelling, muscle transfixion, and joint contractures. Physical therapy is often indicated.

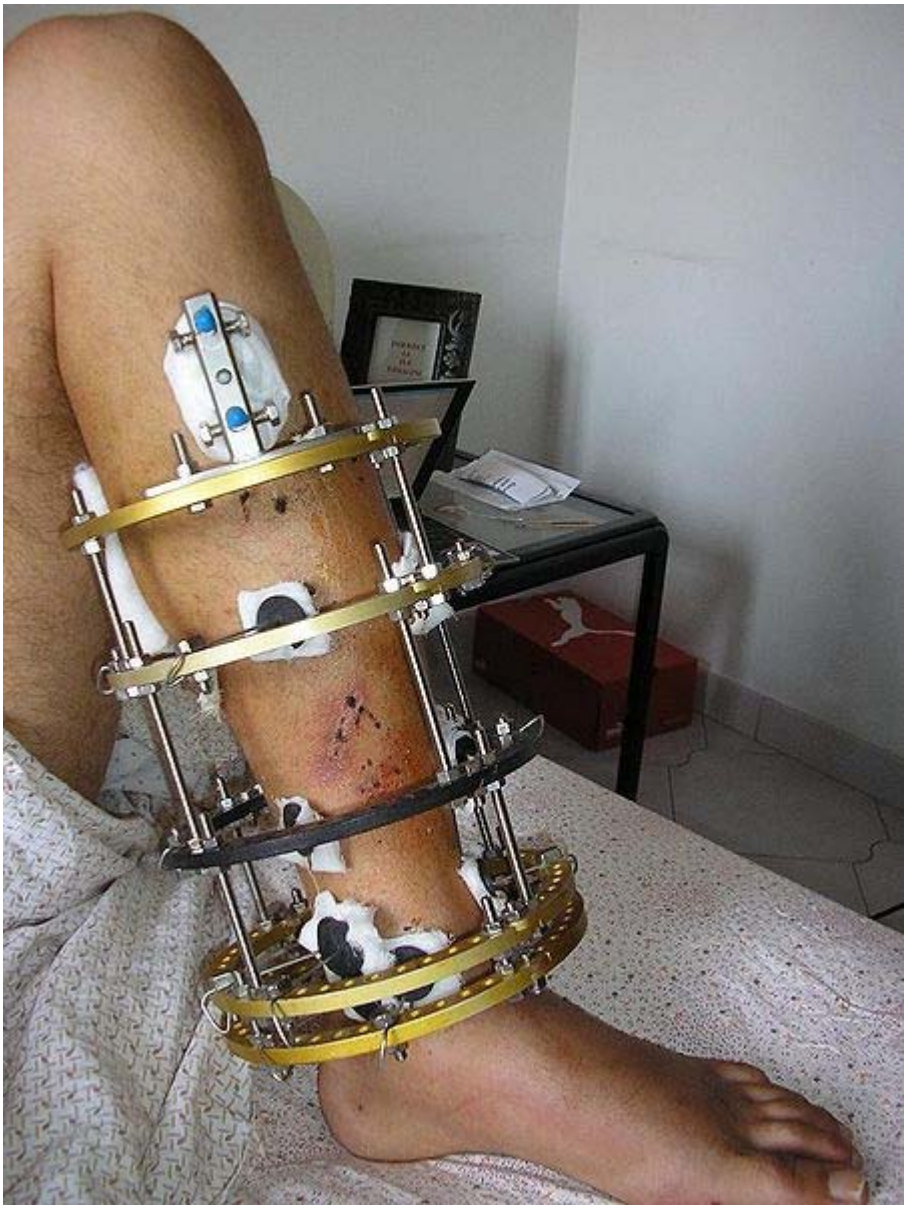
Bone fracture treatment

The Ilizarov method is widely used to treat complex and/or open bone fractures. This method is preferred over conventional treatment options (such as internal fixator or cast) where there is a high risk of infection or the fracture is of such severity that internal fixators are unworkable.

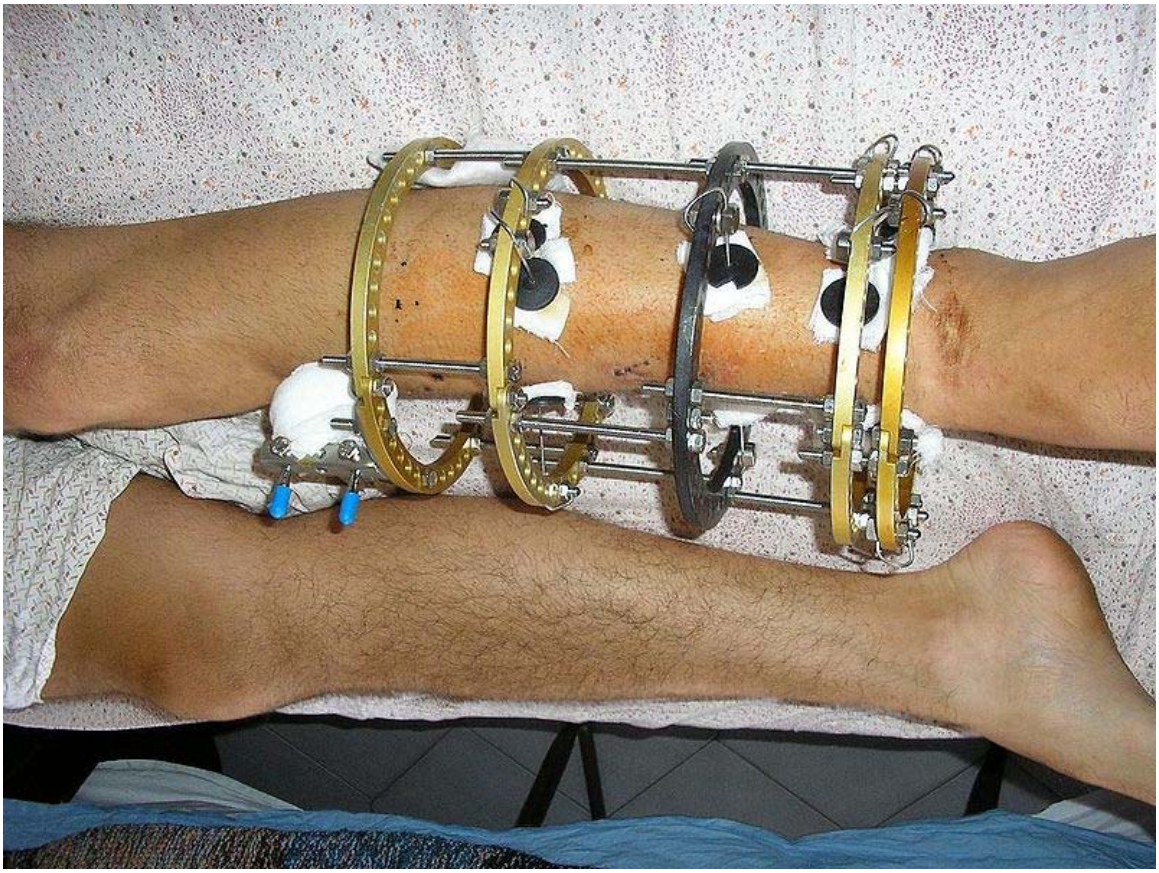
The following case study illustrates the Ilizarov apparatus treatment procedure for a fractured limb. The photographs are of the same patient during the course of treatment.



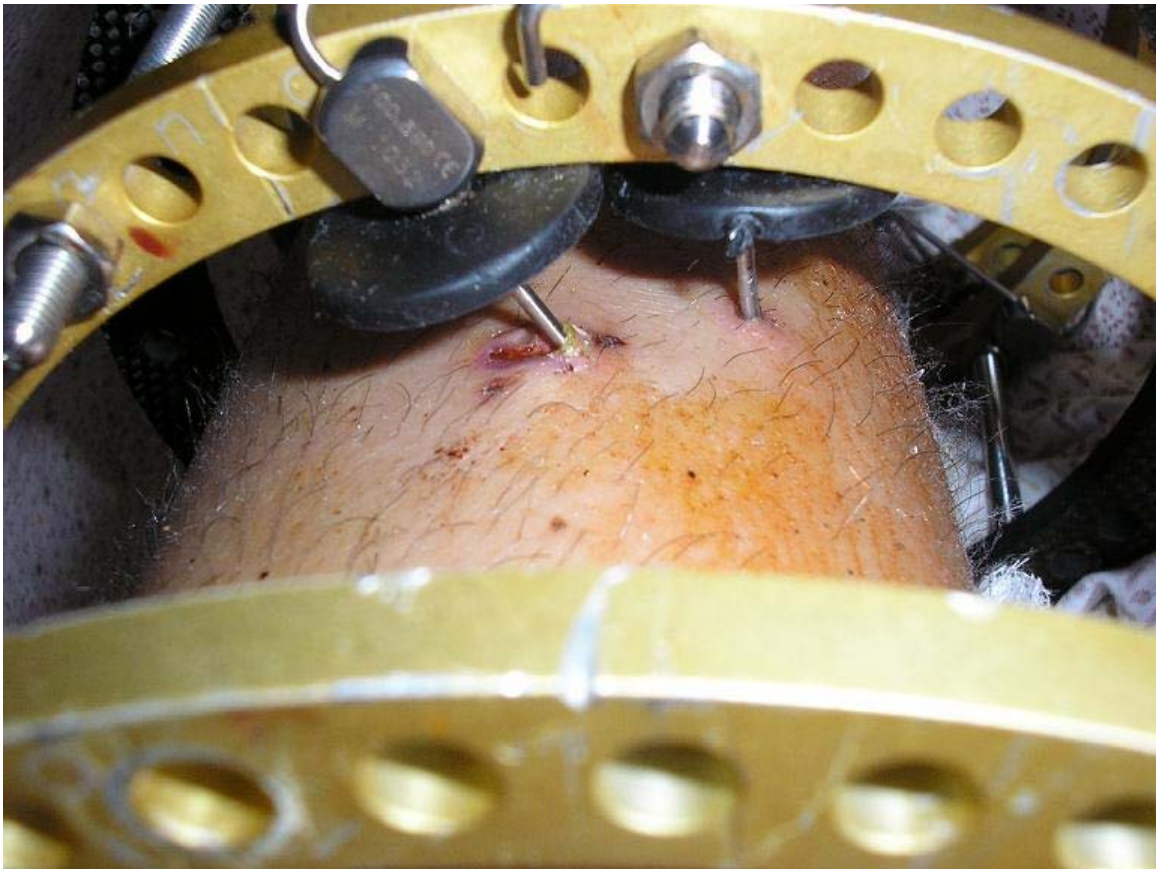
X-Ray of fracture and initial external fixator applied within 24 hours of patient's admission to hospital



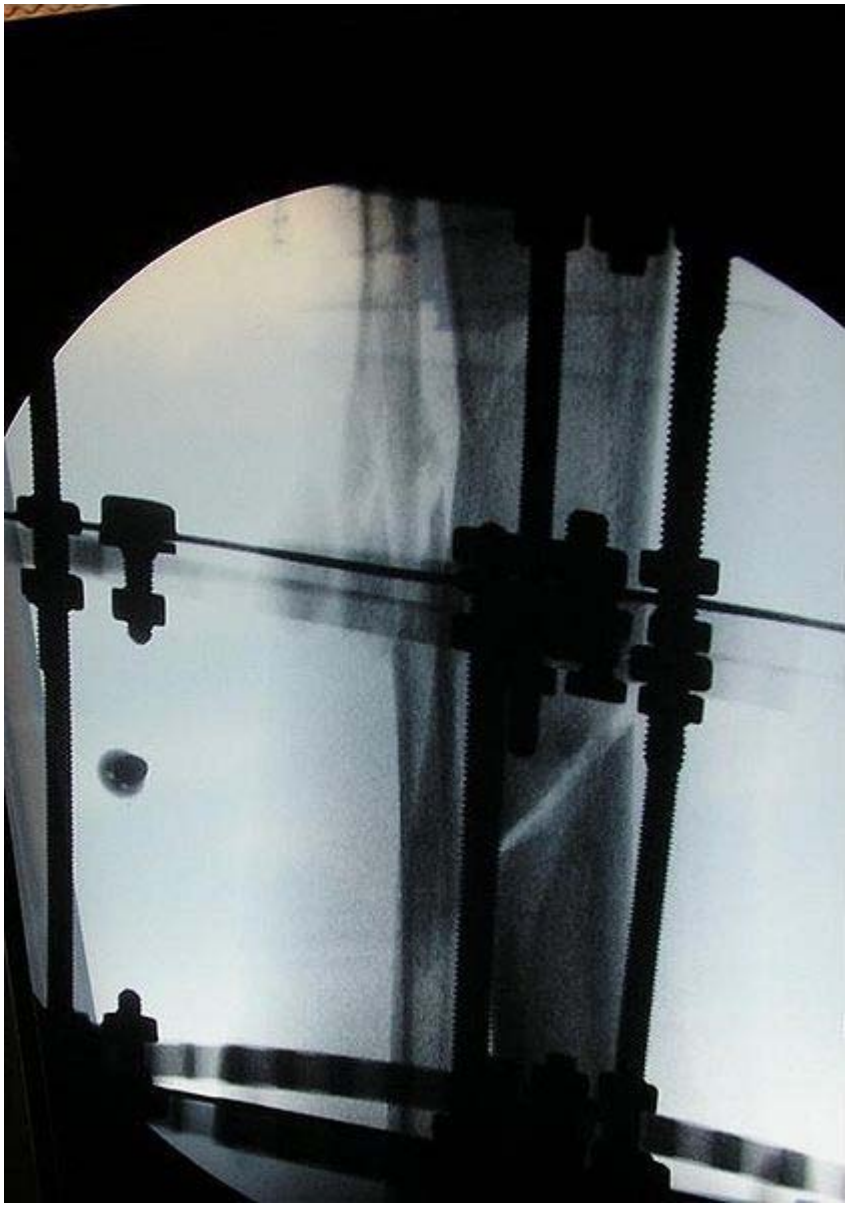
Front-left view of the Ilizarov apparatus treating a fractured tibia and fibula. The patient suffered an open fracture. It is located slightly above black metal ring. Photographs 1 through 4 are taken four weeks following the fracture and two weeks following the installation of the Ilizarov apparatus.



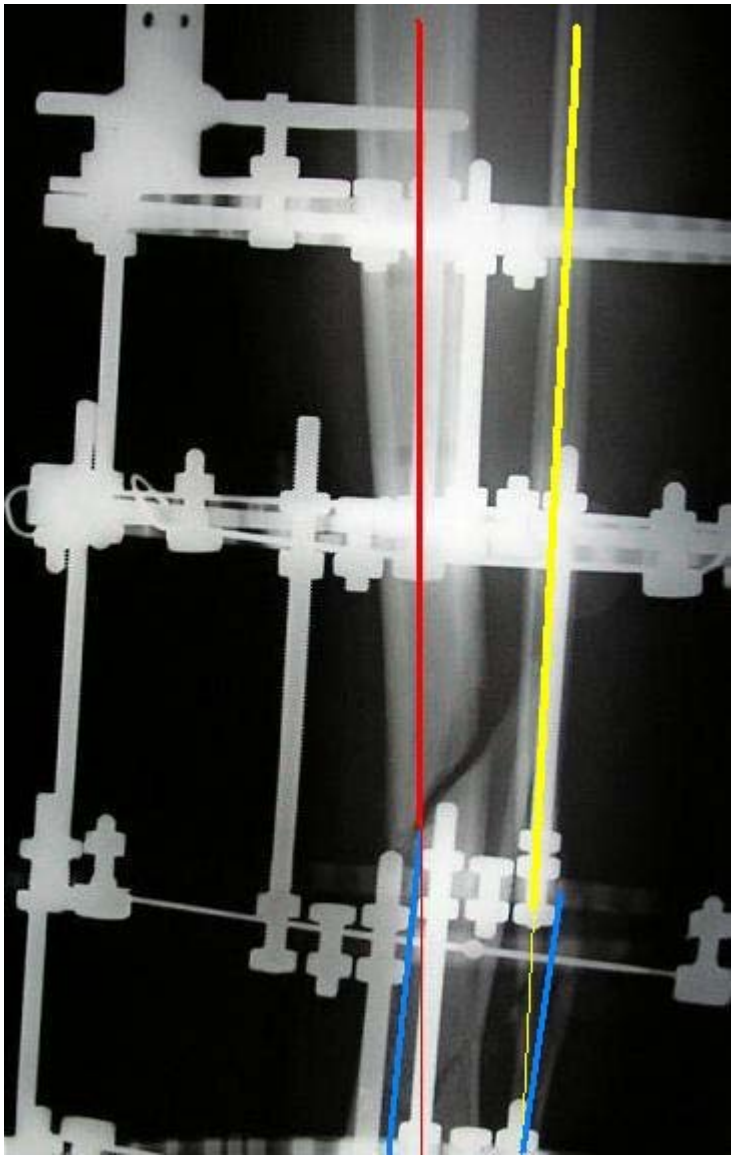
Front (top) view with a view of the healthy leg. The patient is lying on his stomach.



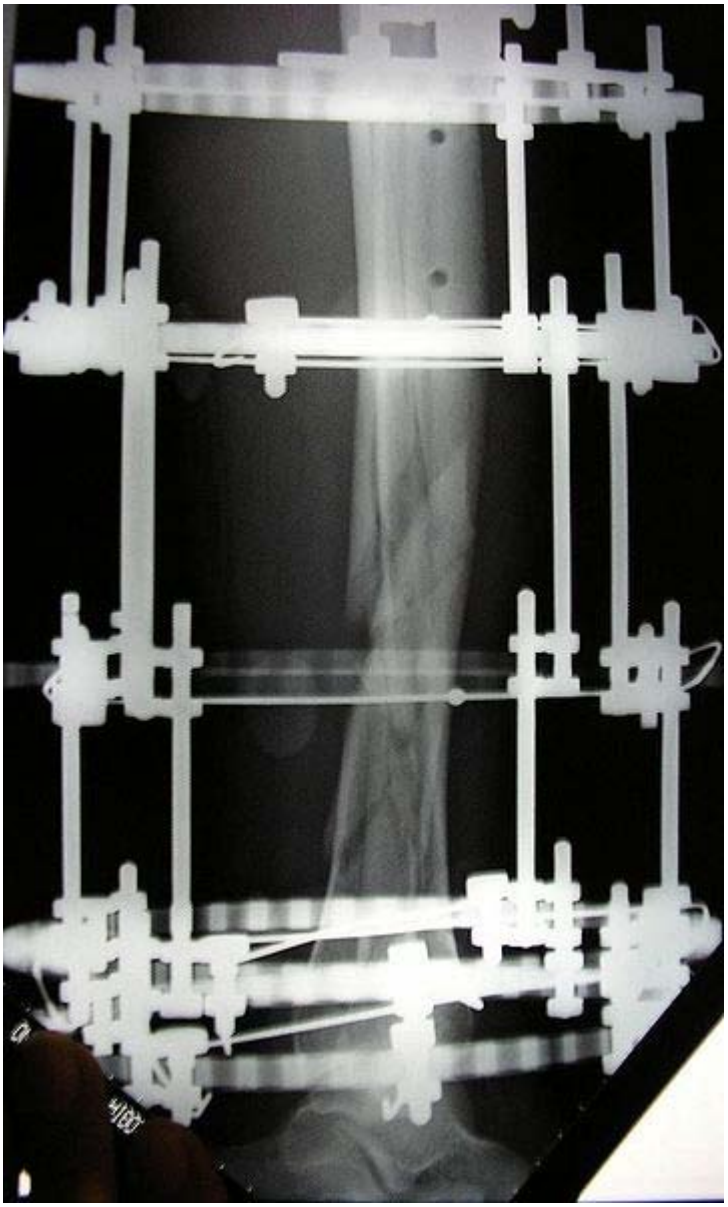
View of several pin sites (two weeks following surgery)



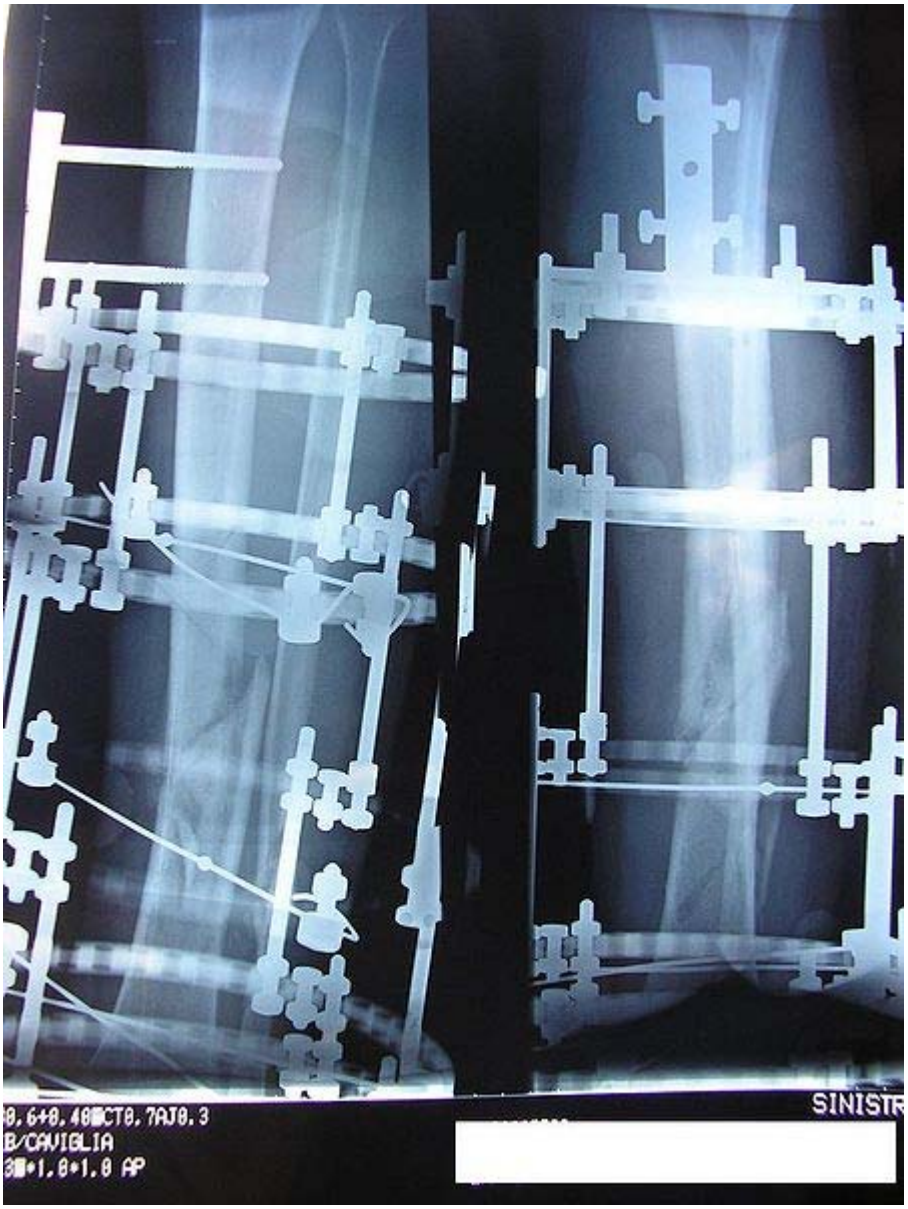
X-Ray of the fracture site immediately following the application of the Ilizarov method



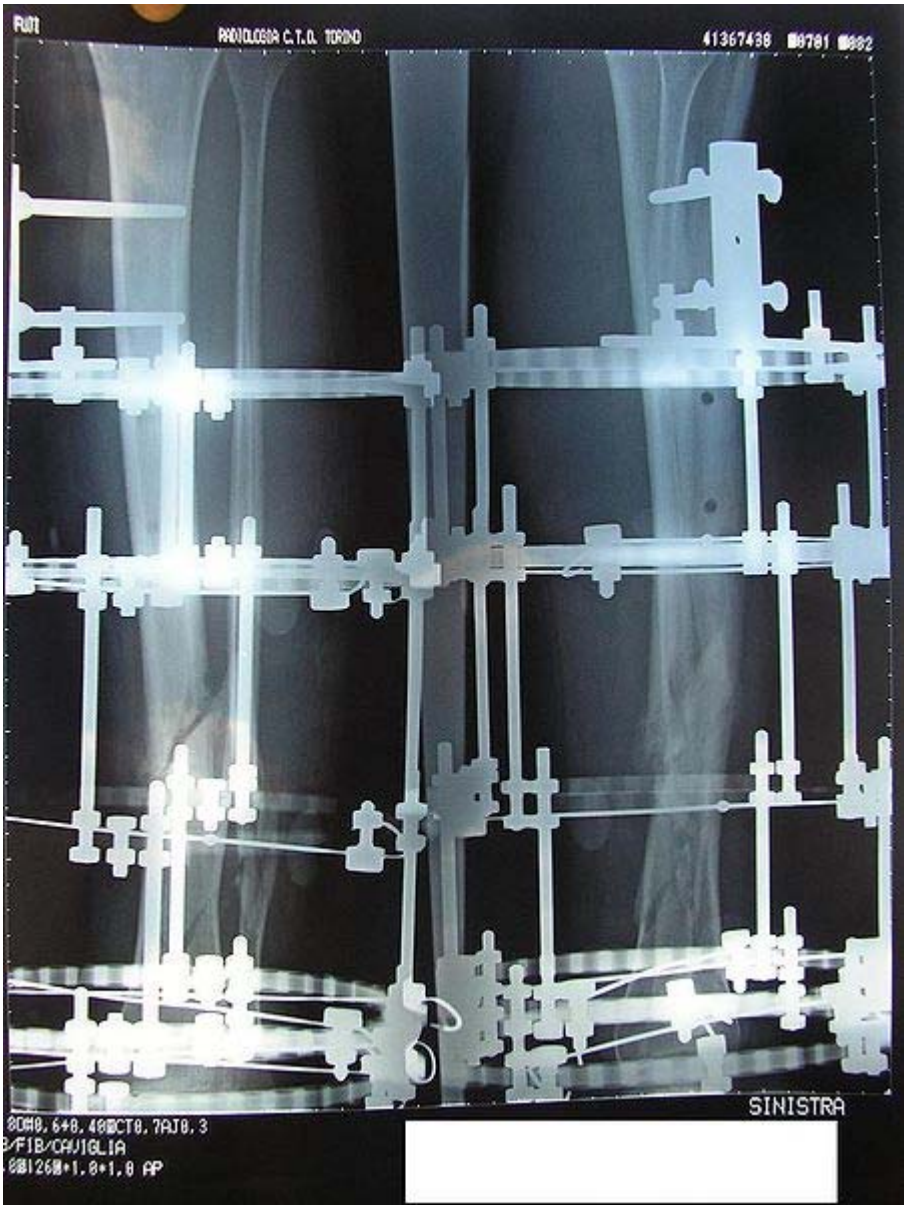
X-Ray of the fracture site, part 1 (two months following fracture)



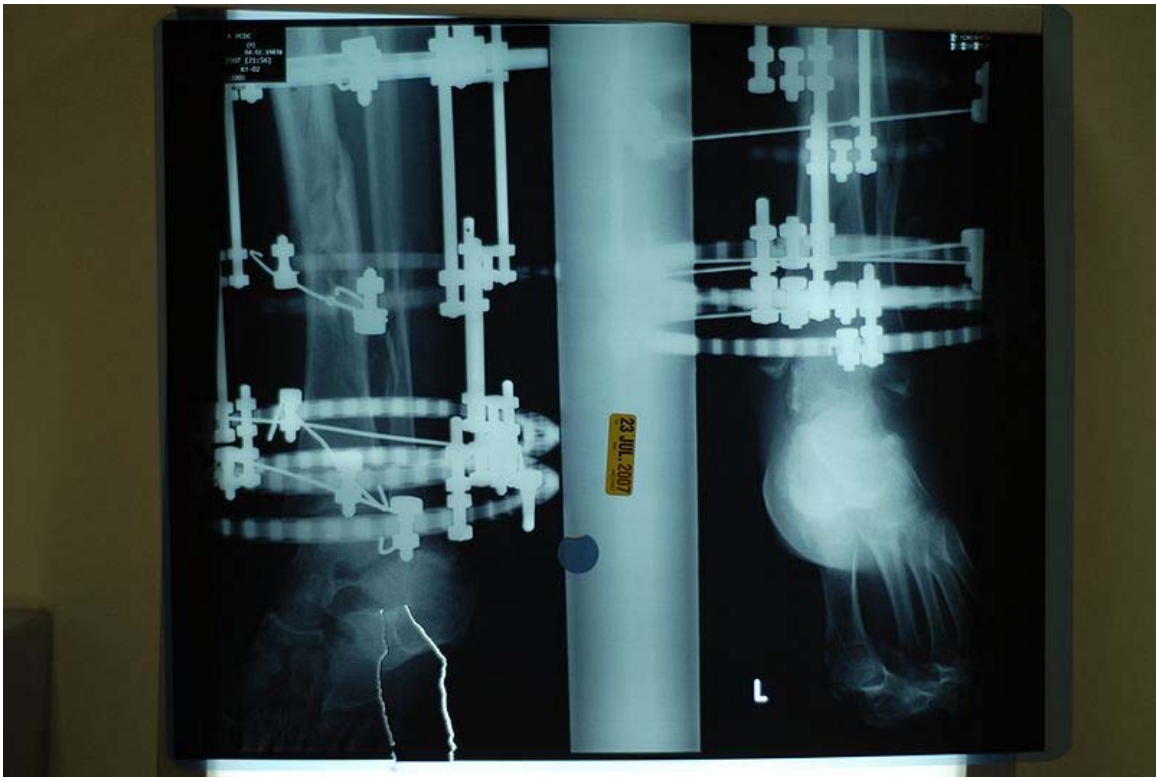
X-Ray of the fracture site, part 2 (two months following fracture)



X-Ray of the fracture site (three months following fracture)



X-Ray of the fracture site, part 2 (three months following fracture)



X-Ray of the fracture site, part 2 (four months following fracture)

Chapter 16

Distraction Osteogenesis

Distraction osteogenesis, also called **callus distraction**, **callotasis** and **osteodistraction** is a surgical process used to reconstruct skeletal deformities and lengthen the long bones of the body. A corticotomy is used to fracture the bone into two segments, and the two bone ends of the bone are gradually moved apart during the distraction phase, allowing new bone to form in the gap. When the desired or possible length is reached, a *consolidation phase* follows in which the bone is allowed to keep healing. Distraction osteogenesis has the benefit of simultaneously increasing bone length and the volume of surrounding soft tissues.

Although distraction technology has been used mainly in the field of orthopedics, early results in rats and humans indicated that the process can be applied to correct deformities of the jaw. These techniques are now utilised extensively by maxillofacial surgeons for the correction of micrognathia, midface, and fronto-orbital hypoplasia in patients with craniofacial deformities.

History

In 1905, Alessandro Codivilla introduced surgical practices for lengthening of the lower limbs. Early techniques had a high number of complications, particularly during healing, and often resulted in a failure to achieve the goal of the surgery.

In 1934 the New York Hospital For Joint Disease worked on an early method developed by Ilizarov. The major item that the US team of surgeons developed was the metal frame the leg was placed in to hold it perfectly in place till the cut made in the bone was healed over.

The breakthrough came with a technique introduced by Russian orthopedic surgeon Gavril Ilizarov. Ilizarov developed a procedure based on the biology of the bone and on the ability of the surrounding soft-tissues to regenerate under tension; the technique involved an external fixator, the Ilizarov apparatus, structured as a modular ring. Although the types of complications remained the same (infection, the most common complication occurring particularly along the pin tracks, pain, nerve and soft tissue irritation) the Ilizarov technique reduced the frequency and severity of the complications. The Ilizarov technique made the surgery safer, and allowed the goal of lengthening the limb to be achieved.

Difficulties arising during distraction osteogenesis

Difficulties that may arise during distraction osteogenesis are commonly classified in medical scientific literature according to the standard introduced by professor Dror Paley in a 1990 article. Paley distinguished among problems (defined as "*a difficulty that arises during the distraction or fixation period that is fully resolved by the end of the treatment period by non operative means*"), obstacles, and complications.

Techniques

Using exclusively an external fixator

The most common is the Ilizarov surgery with the Ilizarov external fixator. Other external fixators are Wagner, Orthofix and Judet. Dr. Helong Bai (8th Hospital in Chongqing, China) developed the technique "Micro-wound" with a different apparatus.

Ilizarov surgery

Ilizarov surgery, developed by Gavriel Ilizarov, a Russian orthopedic surgeon, in 1951, is the oldest and most common method of distraction osteogenesis. It often brings complications, while some new methods have a much lower rate of complications.

The process involves the following:

- Shattered bones and devascularised ones are removed from the patient, leaving a gap;
- The healthy part of the upper bone is broken into two segments with an external saw;
- The leg is then fitted with the Ilizarov frame that pierces through the skin, muscles, and bone;
- Screws attached to the middle bone are turned 1 millimetre (mm) per day, so that new bone tissues that are formed in the growth zone are gradually pulled apart to increase the gap (One millimetre has been found to be the optimal bone distraction rate. Lengthening too fast overstretches the soft tissues, resulting not

only in pain, but also in the inability of the bone to fill up the gap; too slow, and the bone hardens before the full lengthening process is complete.);
- After the gap is closed, the patient continues to wear the frame until the new bone solidifies; the waiting period is usually 120 days before the leg can be used.

Ilizarov surgery is extremely painful, uncomfortable, infection-prone, and often causes unsightly scars. Frames used to be made of stainless steel rings weighing up to 7 kilogram (kg), but newer models are made of Carbon fiber reinforced plastic, which though lighter, are equally cumbersome.

Derivative devices provide physicians better control over the bone axis and angle during elongation, such as the Taylor Spacial Frame (TSF) which is computer assisted. The downside of these developments are their relative complexity and resulting longer learning curve.

For decades, the Ilizarov procedure was the best chance for shattered bones to be restored, and crooked ones straightened. Breakthroughs in distraction osteogenesis in the 1990s, however, have resulted in less painful (albeit more expensive) alternatives, such as unilateral rails.

Using exclusively an intramedullary nail

The techniques that use an intramedullary nail without an external fixator are: Albizzia, Bliskunov, Fitbone and ISKD.

Intramedullary skeletal kinetic distractor

In 2001, the "Intramedullary skeletal kinetic distractor" (ISKD) was introduced, allowing lengthening to take place internally, thereby drastically reducing the risk of infections and scarring. The ISKD device was designed by Dr. J. Dean Cole, MD of Orlando, Florida.

With ISKD, a telescopic rod that can be gradually extended by knee or ankle rotations is implanted into the bone. Lengthening is monitored by a hand-held external magnetic sensor that tracks the rotation of an internal magnet on a daily basis.

ISKD requires a physical leg movement to "click" the device into lengthening. In this method, there is no risk of accidentally over-stretching the bone due to the lengthener being preset to the desired fully extended length. However, there is a risk of growing the bone too quickly. Bone growth is monitored by measuring changes in the magnetic field of an embedded magnet in the system. The poles of the magnet change as the device grows. However, if the motion of the leg makes the device grow too quickly, and the magnet switches poles twice between measurements, then that growth is not recorded. This leads to overly rapid growth which can cause a number of issues such as nerve damage or causing breaks in the bone.

While there is some pain associated with the immediate post-op lengthening, the initial lengthening procedure is not to begin until one week after surgery. Furthermore, there is no noticeable "click" to the patient as there is less than nine degrees of rotation of the two bone segments in relation to one another.

Regularly used at a handful of medical centers mostly in the United States, only several dozens of ISKD devices are implanted each year. An improved version is currently being developed by its manufacturer (Orthofix).

Fitbone surgery

A form of surgery involving an intramedullar, fully implantable, electronically-motorised limb-lengthening implant, called "Fitbone", is a technologically advanced, though relatively complex, device.

Developed in Germany by Augustin Betz and Rainer Baumgart, the first successful operations were performed in 1996 and the technique was patented in 1997. Thus far, most of the surgeries using this method have been performed in Munich, Germany by Baumgart and Peter Thaller. The first successful surgeries in Asia have been performed since 2001 by Dr Sarbjit Singh in Tan Tock Seng Hospital, Singapore, and Dr Sittiporn, Bumrungrad Hospital, Bangkok. In December 2005 Fitbone surgery was done in Malaysia at the Mahkota Orthopaedic Reconstruction and Limb Lengthening Center, Melaka by Thirukumaran Subramaniam and Jeyaratnam T Satkunasingam. Dr. Bruce Foster of Adelaide, Australia, chairman of the "Bone Growth Foundation" — a charity established with the aim of helping children with crippling bone growth problems — is currently the only surgeon that uses the "Fitbone" device in the southern hemisphere.

Fitbone comprises a telescopic nail implant that can extend, powered by an electric motor and controlled by a receiver with an antenna that is buried under the skin; the receiver in turn is controlled by a hand-held radio-frequency transmitter. The procedure for lengthening the lower leg is as follows:

- A two-centimetre incision is made at the patient's knee, and a reamer is used to create enough space in the bone for a stainless steel nail.
- The bone is cut about 14 cm below the knee from the inside with an internal saw.
- The stainless steel nail is held in place by two screws. The top of the nail is attached to a tiny, plastic-encased receiver that is placed under the skin.
- The patient controls the lengthening process. By pushing a button on the transmitter when it is placed against the antenna, the built-in motor extends the nail one millimetre per day. When the leg has grown to the desired length, lengthening stops, and the bone is allowed to solidify.
- The device can be removed about two years after the initial surgery.

This procedure, however, comes at a price. While the Ilizarov external fixator costs approximately USD$4,000, and the ISKD implant about USD$8,000, the *Fitbone* device carries a price tag of roughly USD$15,000 (all prices exclusive of surgery costs).

The Bliskunov and Albizzia devices are currently not available.

Future technology

Due to shortcomings of current external and internal devices and the evident market potential of cosmetic limb elongation, a growing number of companies are researching potential intramedullary technologies. These include:

- Concepts based on electromagnetic actuation
- Concepts based on smart material integration
- Concepts based on manual actuation
- Concepts based on electronic actuation

Biotechnological advances, such as in stem cell research, may become the next generation standard of care for limb elongation once it matures, possibly within a decade or two.

Post-surgical care

Following the initial surgery, patients must undergo a demanding physiotherapy regime comprising stretching exercises and at times, they may be required to be hooked up to a "continuous passive motion" device. The purpose is to avoid stiffness and to stimulate the muscles, nerves and blood vessels to grow alongside the bone. Patients are often prescribed painkillers and are unable to work while undergoing rehabilitation.

Aspects in limb lengthening

Maxillofacial Distraction Osteogenesis

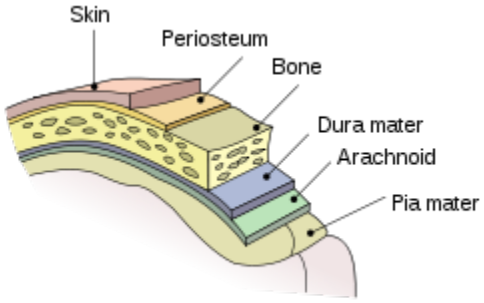
Correcting the majority of congenital craniofacial defects, as well as some facial injuries resulting from trauma, requires making bones longer. Distraction osteogenesis is an effective way to grow new bone, but it is much more difficult to accomplish in the face than in other areas of the body. Bones must often be moved in three dimensions, as opposed to just one, as in a limb, and scarring must be kept to a minimum. Researchers are attempting to improve the distraction devices used in the face. Until recently, the mechanisms were external and only operated along straight lines. Now, maxillofacial surgeons can use curvilinear devices capable of moving bone in three dimensions.

These new devices still need to be improved. They depend on patient caretakers reliably turning a screw. The next goal is to create devices that will move bone continuously, not in daily increments of 1 mm. These continuously moving devices would cause less pain, wouldn't require daily patient compliance, and might promote faster bone growth. At the moment, researchers are testing a continuously moving device in animal models, and they have found that the device's components are durable, that its user interface works, and that it is tolerated by the body. When the position sensor in the device is perfected, the device will be ready to use in people.

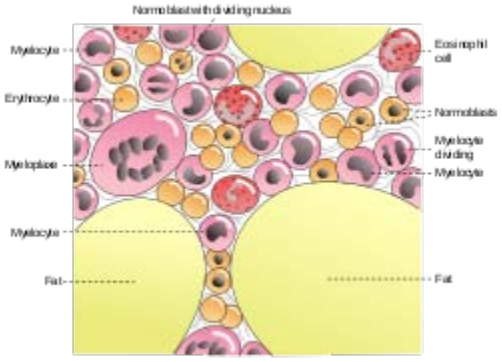
In distraction osteogenesis procedures involving the face, it is critical that bone movements be carefully planned before a device is implanted. No existing device is capable of changing its trajectory mid-course, and small skeletal changes lead to large changes in the structure of the face. Recently researchers have developed state-of-the-art software capable of simulating the entire process of distraction osteogenesis. The 3-D planning tool uses data from CT scans to create a segmented model of the patient's skull, and it then calculates the vector of movement required to achieve desirable bone positioning. Outcome CT scans can be overlaid on the original model to assess the effectiveness of the procedure. In the future, researchers hope that the distraction devices used in maxillofacial procedures will continue to improve, along with the corresponding software.

General solid bone regeneration

Distraction osteogenesis



The periosteum appears just below the skin.



bone marrow

The most important aspects for the success of bone distraction are an intact medullary blood supply, preservation of soft-tissue envelope, primarily the periosteum (which helps preserve the blood supply) and secondarly bone marrow and the stability of the fixator.

Distraction rate

The distraction rate must be gradual, as a rapid rate of distraction will result in a fibrous union in which the bone pieces are joined by fibrous, rather than osseous tissue.

Too slow of a distraction rate would result in early bone consolidation. A common distraction rate for lower limbs is 1 millimeter per day.

Complications

In a 2004 study lengthening with an exclusively intramedullary nail (Albizzia) had a "significant lower rate" of complications respect to exclusively external methods (Judet, Orthofix, Ilizarov and Wagner fixators).

Possible uses of distraction osteogenesis

Although distraction osteogenesis is most often used in the treatment of post-traumatic injuries, it is increasingly used to correct limb discrepancies caused by congenital conditions and old injuries. A list of the possible uses of distraction osteogenesis are as follows:

- Congenital deformities (birth defects):
  - Congenital short femur;
  - Fibular hemimelia (absence of the fibula, which is one of the two bones between the knee and the ankle);
  - Hemiatrophy (atrophy of half of the body); and
  - Ollier's disease.
- Developmental deformities
  - Neurofibromatosis (a rare condition which causes overgrowth in one leg); and
  - Bow legs, resulting from rickets or secondary arthritis.
- Post-traumatic injuries
  - Growth plates fractures;
  - Malunion or non-union (when bones do not completely join, or join in a faulty position after a fracture);
  - Shortening and deformity; and
  - Bone defects.
- Infections and diseases
  - Osteomyelitis (a bone infection, usually caused by bacteria);
  - Septic arthritis (infections or bacterial arthritis); and
  - Poliomyelitis (a viral disease which may result in the atrophy of muscles, causing permanent deformity).
- After tumors
- Short stature
  - Achondroplasia (a form of dwarfism where arms and legs are very short, but torso is more normal in size); and
  - Constitutional short stature.

Cosmetic lengthening of limbs

Generally, doctors tend to discourage cosmetic lengthening for people who want to add a couple of inches to their frames because such people are:

- breaking perfectly functional limbs;
- confining themselves unnecessarily to crutches or a wheelchair for over a year;
- voluntarily subjecting themselves to pain and discomfort;
- exposing themselves to unnecessary risk of infections, of damaged nerves and blood vessels, and fat embolism that can result in death; and
- incurring unnecessary expenses as the procedure is relatively expensive.

People insistent on doing the procedure, however, are required by some doctors to undergo a thorough body image assessment by a psychologist to help determine how far the person's quality of life has been affected by his perceived lack of height, and if doing the surgery will make a marked difference. The entire evaluation, which includes in-depth doctor-patient discussions, usually takes months during which time, the doctors hope that their patients will change their minds.

Chapter 17

Articular Cartilage Repair

The aim of an **articular cartilage repair treatment** is to restore the surface of an articular joint's hyaline cartilage. Over the last decades, surgeons and researchers have been working hard to elaborate surgical cartilage repair interventions. Though these solutions do not perfectly *restore* articular cartilage, some of the latest technologies start to bring very promising results in *repairing* cartilage from traumatic injuries or chondropathies. These treatments are especially targeted by patients who suffer from articular cartilage damage. They provide pain relief while at the same time slowing down the progression of damage or considerably delaying joint replacement (knee replacement) surgery. Most importantly, articular cartilage repair treatments help patients to return to their original lifestyle; regaining mobility, going back to work and even practicing sports again.

Different articular cartilage repair procedures

Though the different articular cartilage procedures differ in the used technologies and surgical techniques, they all share the aim to repair articular cartilage whilst keeping options open for alternative treatments in the future. Broadly taken, there are five major types of articular cartilage repair:

Arthroscopic Lavage / Debridement

Arthroscopic lavage is a "cleaning up" procedure of the knee joint. This short term solution is not considered an articular cartilage repair procedure but rather a *palliative treatment* to reduce pain, mechanical restriction and inflammation. Lavage focusses on removing degenerative articular cartilage flaps and fibrous tissue. The main target group are patients with very small defects of the articular cartilage.

Marrow Stimulation Techniques (Microfracture Surgery and others)

Marrow stimulating techniques attempt to solve articular cartilage damage through an arthroscopic procedure. Firstly, damaged cartilage is drilled or punched until the underlying bone is exposed. By doing this, the subchondral bone is perforated to generate a blood clot within the defect. Studies, however, have shown that marrow stimulation techniques often have insufficiently filled the chondral defect and the repair material is often fibrocartilage (which is not as good mechanically as hyaline cartilage). The blood

clot takes about 8 weeks to become fibrous tissue and it takes 4 months to become fibrocartilage. This has implications for the rehabilitation.

Further on, chances are high that after only 1 or 2 years of the surgery symptoms start to return as the fibrocartilage wears away, forcing the patient to reengage in articular cartilage repair. This is not always the case and microfracture surgery is therefore considered to be an *intermediate* step.

An evolvement of the microfracture technique is the implantation of a collagen membrane onto the site of the microfracture to protect and stabilize the blood clot and to enhances the chondrogenic differentiation of the MSCs. This technique is known as AMIC (Autologous Matrix-Induced Chondrogenesis) and was first published in 2003.

Osteochondral Autografts and Allografts

This technique/repair requires transplant sections of bone and cartilage. First, the damaged section of bone and cartilage is removed from the joint. Then a new healthy dowel of bone with its cartilage covering is punched out of the same joint and replanted into the hole left from removing the old damaged bone and cartilage. The healthy bone and cartilage are taken from areas of low stress in the joint so as to prevent weakening the joint. Depending on the severity and overall size of the damage multiple plugs or dowels may be required to adequately repair the joint, which becomes difficult for Osteochondral Autografts. For Osteochondral Allografts the plugs are taken from deceased donors. This has the advantage that more osteochondral tissue is available and larger damages can be repaired. There are, however, ethical considerations and worries on the histocompatibility.

Cell Based Repairs

Aiming to obtain the best possible results, scientists have strived to replace damaged articular cartilage with healthy articular cartilage. Previous repair procedures, however, always generated fibrocartilage or, at best, a combination of hyaline and fibrocartilage repair tissue. Autologous chondrocyte implantation (ACI) procedures are cell-based repairs that aim to achieve a repair consisting of healthy articular cartilage.

ACI articular cartilage repair procedures take place in three stages. First, cartilage cells are extracted arthroscopically from the patient's healthy articular cartilage that is located in a non load-bearing area of either the intercondylar notch or the superior ridge of the femoral condyles. Then these extracted cells are transferred to an *in vitro* environment in specialised laboratories where they grow and replicate, for approximately four to six weeks, until their population has increased to a sufficient amount. Finally, the patient undergoes a second surgery where the *in vitro* chondrocytes are applied to the damaged area. In this procedure, chondrocytes are injected and applied to the damaged area in combination with either a membrane or a matrix structure. These transplanted cells thrive in their new environment, forming new articular cartilage.

Autologous Mesenchymal Stem Cell Transplant

For years, the concept of harvesting stem cells and re-implanting them into one's own body to regenerate organs and tissues has been embraced and researched in animal models. In particular, mesenchymal stem cells have been shown in animal models to regenerate cartilage. Recently, there has been a published case report of decrease in knee pain in a single individual using autologous mesenchymal stem cells.An advantage to this approach is that a person's own stem cells are used, avoiding transmission of genetic diseases. It is also minimally invasive, minimally painful and has a very short recovery period. This alternative to the current available treatments was shown not to cause cancer in half the patients who were followed for 3 years after the procedure.

The importance of rehabilitation in articular cartilage repair

Rehabilitation following any articular cartilage repair procedure is paramount for the success of any articular cartilage resurfacing technique. The rehabilitation is often long and demanding. The main reason is that it takes a long time for the cartilage cells to adapt and mature into repair tissue. Cartilage is a slow adapting substance. Where a muscle takes approximately 35 weeks to fully adapt itself, cartilage only undergoes 75% adaptation in 2 years. If the rehabilitation period is too short, the cartilage repair might be put under too much stress, causing the repair to fail.

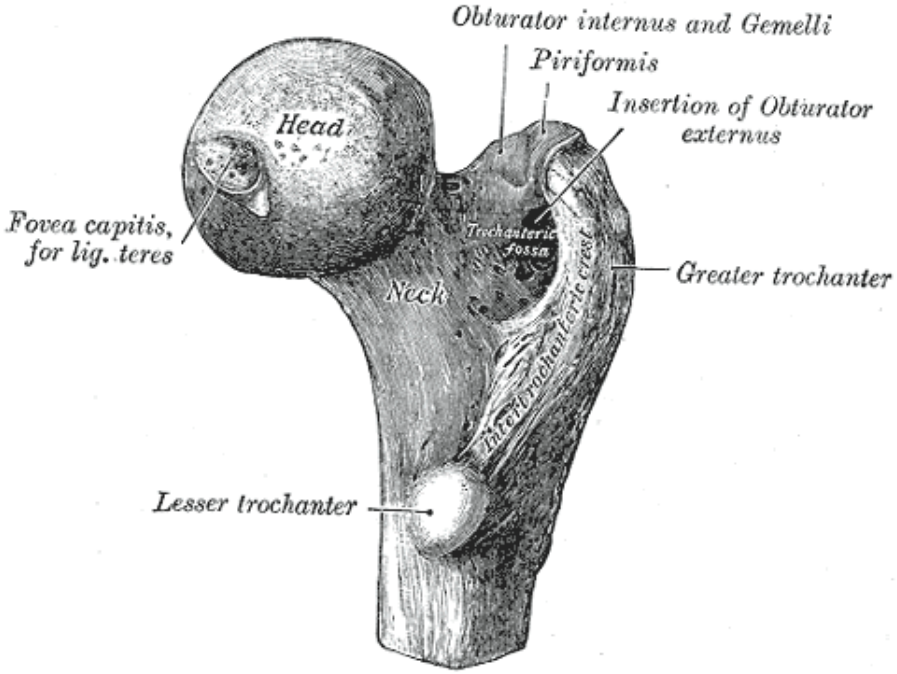
Concerns

New research by Dr. Robert Litchfield, September 2008, of the University of Western Ontario concluded that routinely practised knee surgery is ineffective at reducing joint pain or improving joint function in people with osteoarthritis. The researchers did however find that arthroscopic surgery did help a minority of patients with milder symptoms, large tears or other damage to the meniscus) — cartilage pads that improve the congruence between femur and tibia bones.

Chapter 18

Femoral Head Ostectomy and Astragalectomy

Femoral head ostectomy



The Femoral Head and Neck

Femoral Head Ostectomy (FHO) is a surgical procedure that removes the femoral head and neck from the femur. FHO surgery is performed to alleviate pain. It is a salvage procedure, reserved for condition where pain can not be alleviated in any other way. It is common in veterinary surgery. Other names are *Excision Arthroplasty of the femoral head and neck*, *Girdlestone's Operation* and *Femoral Head and Neck Ostectomy*.

History

FHO was first described by Gathorne Robert Girdlestone(1881–1950) in 1945. He originally designed the procedure for treating tuberculosis and other disorders of the hips. This has led to the procedure also being known as a "Girdlestone operation". Other surgeons added various modifications to the procedure to improve recovery and outcomes. FHO was first described in veterinary science in 1961 by J.S.A. Spreull. It can be suggested however that the technique was developed concurrently at other locations.

Indications in veterinary science

Small breeds of dog, cats and small horses, donkeys and ponies have all had the procedure performed successfully. Hip dysplasia, an extremely painful congenital condition found in many dog breeds and some cats, is an example of such a condition where this procedure may be used. It is also performed in cases of trauma where the head of the femur is badly broken or severed, or in response to other diseases of the hip bone, such As Legg-Calve-Perthes' disease. It is sometimes the procedure of last resort when other methods have failed and or sepsis of the joint has occurred, but it can be indicated when the hip joint is severely affected or if arthritis In the joint is serious enough. It can also be indicated in small animals with pelvic fractures, particularly fractures of the acetabulum (socket of the pelvis).

Procedure

The procedure exposes the head section of the femur bone (the ball of the ball and socket joint), and then the head is removed using a small saw or a bone hammer and chisel. Rarely both sides are done in one operation, most times one side is done and allowed to heal before the other side is done.

Unlike most other hip surgeries, the head of the femur is not replaced, but is allowed to heal and develop its own fibrous scar tissue so that the joint is no longer bone−to-bone, a pseudoarthrosis (also called a "false joint"). The neck of the femur is usually removed at the same time as the head. This prevents the post operative complication of bone rubbing on bone and continued pain. This has led to the procedure often also called "Femoral head and neck ostectomy".

Animals who have had FHO surgery are required to maintain a lower weight throughout their lives to compensate for the loss of skeletal integrity, and generally have less mobility than normal.

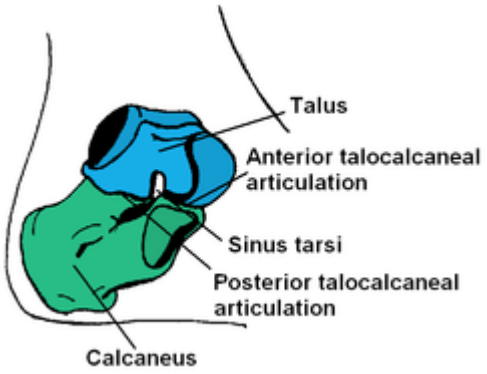
Other species

Small horses and ponies can have an ostectomy without an osteotomy of the greater trochanter. As a salvage procedure, this is usually performed in those animals which have the specific injury of a fracture of the capital physis. These patients would not return to

function as a riding horse and the procedure may be performed for those animals involved in breeding, milking, and being kept as companion animals.

Astragalectomy

Bone: Talus bone



Subtalar Joint

Latin	*Astragalus*
Gray's	*subject #63 266*
MeSH	*Talus*

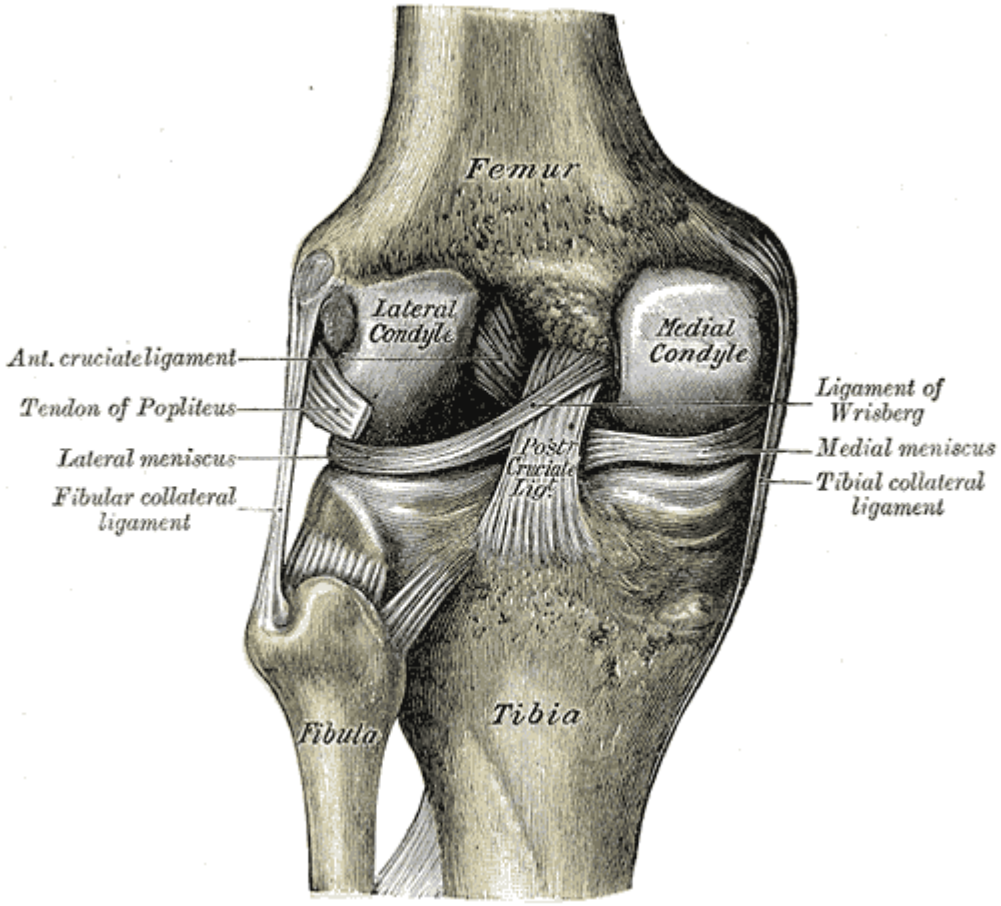
Astragalectomy, sometimes called a **talectomy** is a surgical operation for removal of the talus bone (astragalus) for stabilization of the ankle.

Historically, an astragalectomy was used in cases of severe ankle trauma and congenial talipes equinovarus (clubfoot). Presently, it is not a common operation, however it still used in cases of a deformed calcaneus, foot paralysis following poliomyelitis, and also rigid clubfoot deformities that are secondary to spina bifida or arthrogryposis (AMC). The surgery is also performed in severe cases of pulverized or infected open fractures.

Generally, the surgical procedure involves making an anterolateral incision, stripping the ligaments from both malleoli and the calcaneus so that the foot can be displaced posteriorly. The talus is then resected, and the foot is placed so that the lateral malleolus rests opposite the calcaneocuboid joint, and the medial malleolus lies just above and behind the navicular bone. The foot is held in place with a surgical pin or with Kirschner wire. After the operation, the patient wears an above-knee cast for six weeks, followed by a below-knee cast for eighteen weeks.

Chapter 19

Microfracture Surgery



Left knee-joint from behind, showing interior ligaments. (Lateral meniscus and medial meniscus are cartilage.)

Microfracture surgery is one of the articular cartilage repair surgical techniques that works by creating tiny fractures in the underlying bone. This causes new cartilage to develop from a so-called super-clot. Microfracture surgery has gained a profile in the sports world in recent years; numerous professional athletes including members of the NBA (most notably Anfernee Hardaway, Jason Kidd, Greg Oden, Allan Houston, Kenyon Martin, Tracy McGrady, Chris Webber, and Amar'e Stoudemire), MLB, NFL and NHL have undergone the procedure.

The surgery is quick (taking as short as 30 minutes but sometimes lasting as long as 90 minutes), is minimally invasive, and can have a significantly shorter recovery time than an arthroplasty (knee replacement). Combined with a high rate of success, these factors have caused orthopedic surgeons to use the procedure with increasing frequency.

Background

Chronic articular cartilage defects do not heal spontaneously. However, acute traumatic osteochondral lesions or surgically created lesions extending into subchondral bone, e.g. by Pridie drilling, spongialization abrasion or microfracture causing the release of pluripotent mesenchymal stem cells from the bone marrow, may heal with repair tissue consisting of fibrous tissue, fibrocartilage or hyaline-like cartilage. The quality of the repair tissue after these "bone marrow stimulating techniques" depends on various factors including the species and age of the individual, the size and localization of the articular cartilage defect, the surgical technique, e.g., how the subchondral bone plate is treated, and the postoperative rehabilitation protocol.

Development

The surgery was developed in the late 1980s and early 1990s by Dr. Richard Steadman of the Steadman-Hawkins clinic in Vail, Colorado. Steadman slowly refined the procedure through research (including tests on horses). After Steadman experienced success with the surgery, professional athletes started taking notice. The surgery was soon called "controversial" by many sportswriters, due to a lack of studies on the long-term effects and the fact that an unsuccessful surgery could end an athlete's career. However, Steadman and other researchers have proven that compared to other treatments, the procedure is safe and effective, even in the long term. Dr. Steadman has also adapted the surgery into a treatment to help reattach torn ligaments (a technique he calls the "healing response") that he successfully used on alpine skiier Bode Miller. Possible applications in the hip and ankle joints have also been speculated on.

Procedure

The surgery is performed by arthroscopy, after the joint is cleaned of calcified cartilage. Through use of an awl, the surgeon creates tiny fractures in the subchondral bone plate. Blood and bone marrow (which contains stem cells) seep out of the fractures, creating a blood clot that releases cartilage-building cells. The microfractures are treated as an injury by the body, which is why the surgery results in new, replacement cartilage. The procedure is less effective in treating older patients, overweight patients, or a cartilage lesion larger than 2.5 cm. Further on, chances are high that after only 1 or 2 years of the surgery symptoms start to return as the fibrocartilage wears away, forcing the patient to reengage in articular cartilage repair. This is not always the case and microfracture surgery is therefore considered to be an intermediate step.

The effectiveness of cartilage growth after microfracture surgery is thought to be dependent on the patient's bone marrow stem cell population and some think increasing

the number of stem cells increases the chances of success. A couple of physicians are promoting an alternative treatment implanting autologous mesenchymal stem cells directly into the cartilage defect, without having to penetrate the subchondral bone.

Microfracture Reports

Studies have shown that microfracture techniques do not fill in the chondral defect fully, forming fibrocartilage rather than hyaline cartilage. Fibrocartilage is not as mechanically sound as hyaline cartilage; it is much denser and unable to withstand the demands of everyday activities as well as the original cartilage and is thus at higher risk of breaking down. The blood clot is very delicate after surgery and needs to be protected. In terms of time, the clot takes about 8 weeks to 15 weeks convert to fibrous tissue and is usually fibrocartilage by about four months post surgery, holding implications for the rehabilitation.

Chondrocyte Implantation procedures (CCI), a cell based articular cartilage repair procedure that aims to provide complete hyaline repair tissues for articular cartilage repair, have been posed by some as an alternative to microfracture surgery. In February 2008, Saris *et. al* published a large-scale study claiming that CCI results in better structural repair for symptomatic cartilage defects of the knee than microfracture surgery. According to the study, one year after treatment, the tissue regenerate associated with CCI is of better quality than that of microfracture surgery.

Use in professional sports

There have been many notable professional athletes who have undergone the procedure. Partially because of the high level of stress placed on the knees by these athletes, the surgery is not a panacea and results have been mixed. Many players' careers effectively end despite the surgery. However, some players such as Jason Kidd, Steve Yzerman, John Stockton, Kenyon Martin and Zach Randolph have been able to return at or near their pre-surgery form while players Ron Harper, Brian Grant, Chris Webber, Allan Houston, Penny Hardaway, and the late Derek Smith never regained their old form. Others such as Jamal Mashburn and Terrell Brandon never recovered and retired. Portland Trail Blazers rookie Greg Oden underwent the procedure on his left knee in early September 2007 and missed the entire 2007-2008 NBA season. At only 19 at the time of the surgery, doctors were confident that he would return to at or near full strength by the 2008-2009 season; he had a second microfracture surgery, this time on his right knee, in November 2010. The Detroit Pistons player, Tracy McGrady also under went microfracture surgery, doctors were confident that the 2 time scoring champion will return to full strength. As of 2010 he has not had the same speed and jumping ability as he formerly did.

In October 2005, young star Amar'e Stoudemire of the NBA's Phoenix Suns underwent one of the highest-profile microfracture surgeries to date. He returned to the court in March 2006 and initially appeared to have made a full recovery, but subsequently started feeling stiffness in both knees (his right knee had been overcompensating for the injured

left knee). He and the team doctor decided he needed more time to rehab and he did not return until the 2006-2007 NBA season. During the 2006-2007 season, Stoudemire returned to form, averaging 20.4 points and 9.6 rebounds per game while playing in all 82 regular-season games and the 2007 NBA All-Star Game. His recent success has brought positive publicity to the procedure, further distancing it from a previous reputation as a possible "career death sentence" in the sports world, though he was one of the youngest of the aforementioned players to undergo the surgery.

Recovery

Current studies have shown a success rate of 75 to 80 percent among patients 45 years of age or younger, even among professional athletes. With the help of physical therapy, patients can often return to sports (or other intense activities) in about four months. However, this is a best-case scenario and depends on the severity of the cartilage damage (and any other conditions existing in the knee). Normal patients and professional athletes who play at the highest level however are quite different, as Chris Webber, who underwent the surgery, has stated that a full recovery in four months is nearly impossible. Webber returned to the NBA eight months after his surgery but was never the same.

Microfracture surgery itself is relatively minor. It is an outpatient procedure and causes only small discomfort. The harder part is the restrictions that are placed on the patient during the post-operative recovery period. This can be a major challenge for many patients. For optimal re-growth of joint surface, the patients need to be very patient and also extremely cooperative. They usually need to be on crutches for four to six weeks (sometimes longer). Sometimes a brace is needed. This all depends on the size and/or location of the joint surface defect that is being repaired or regenerated. The patients are encouraged to spend approximately 6–8 hours a day on a CPM (Continuous Passive Motion) machine that helps with optimal re-growth of joint surface. Patients usually feel pretty good and think they can avoid these critically important steps, and even start running and jumping (or playing sports) before the internal aspects of the knee, and the joint surface, are ready.

Steadman cites the significance of a patient's natural joint alignment in addition to disciplined rehabilitation in recovery from the procedure.

Chapter 20

Knee Cartilage Replacement Therapy

Articular cartilage, most notably that which is found in the knee joint, is generally characterized by very low friction, high wear resistance, and poor regenerative qualities. It is responsible for much of the compressive resistance and load bearing qualities of the knee joint and, without it, walking is painful to impossible. Osteoarthritis is a common condition of cartilage failure that can lead to limited range of motion, bone damage and invariably, pain. Due to a combination of acute stress and chronic fatigue, osteoarthritis directly manifests itself in a wearing away of the articulating surface and, in extreme cases, bone can be exposed in the joint. Some additional examples of cartilage failure mechanisms include cellular matrix linkage rupture, chondrocyte protein synthesis inhibition, and chondrocyte apoptosis. There are several different repair options available for cartilage damage or failure.

Non-surgical treatments

Osteoarthritis is the second leading cause of disability in the elderly population in the United States. It is a degenerative disorder that generally starts off relatively mild and escalates with time and wear. For those patients experiencing mild to moderate symptoms, the disorder can be dealt with by several non-surgical treatments. The use of braces and drug therapies, such as anti-inflammatories (ex. diclofenac, ibuprofen, and naproxen), COX-2 selective inhibitors, hydrocortisone,have been shown to alleviate the pain caused by cartilage deficiency and some claim they may slow the degenerative process.

Non-biological treatments

This type of repair, short of total joint replacement, can be divided into three groups.

Chondrectomy and debridement

Treatments that remove the diseased and undermined cartilage with an aim to stop inflammation and pain include shaving (chondrectomy) and debridement.

It is interesting to note that debridement, introduced by Magnuson in 1941, does not have any scientific basis for existence; in fact, it is deleterious in terms of knee biomechanics. It is used palliatively as it temporarily relieves pain associated with arthritic

inflammation. Many insurance companies (ex. Aetna) consider the procedure experimental because there is no evidence proving its effectiveness.

Abrasion and microfracture surgery

Another group of treatments consists of a range of abrasive procedures aimed at triggering cartilage production, such as drilling, microfracture surgery, chondroplasty, and spongialization.

Abrasion, drilling, and microfracture originated 20 years ago. They rely on the phenomenon of spontaneous repair of the cartilage tissue following vascular injury to the subchondral bone.

Laser-assisted treatments

Laser assisted treatments, currently experimental, compose a third category; they combine the removal of diseased cartilage with cartilage reshaping and also induce cartilage proliferation.

Laser abrasion provides gentle cutting of the cartilage. It uses heat to induce alterations in the physical matrix, which results in shape change and stress reduction. Improving this therapy to make it more spatially selective would avoid excessive tissue damage such as air bubble formation, tissue necrosis, reactive synovitis, chondrolysis, and an acceleration of articular cartilage degeneration.

Autologous matrix-induced chondrogenesis

Autologous matrix-induced chondrogenesis, which is also known as **AMIC**, is a biological treatment option for articular cartilage damage bone marrow stimulating technique in combination with a collagen membrane. It is based on the microfracture surgery with the application of a bi-layer collagen I/III membrane.

The AMIC technique was developed to improve some of the shortfalls of microfracture surgery such as variable repair cartilage volume and functional deterioration over time. The collagen membrane protects and stabilizes the MSCs released through microfracture and enhances their chondrogenic differentiation.

Autologous chondrocyte implantation

Despite advances in materials science and innovations in knee repair, no current therapy can mimic the extraordinary biomechanical properties of cartilage. This notion drives initiatives in cell-based replacement technologies, such as autologous chondrocyte implantation (ACI).

A systematic review was published in 2010 evaluating the evidence for autologous chondrocyte implantation. The conclusions are that it is an effective treatment for full

thickness chondral defects. The evidence does not suggest ACI is superior to other treatments.

In the United States, Genzyme Corporation provides the only FDA approved ACI treatment, Carticel. The Carticel treatment is designated for young, healthy patients with medium to large sized damage to cartilage. The procedure is not applicable to osteoarthritis patients.

During an initial procedure, the patient's own chondrocytes are removed arthroscopically from a non load-bearing area from either the intercondylar notch or the superior ridge of the medial or lateral femoral condyles. The 10,000 cells that are originally harvested are grown *in vitro* at Genzyme biosurgery for approximately six weeks until the population reaches 10-12 million cells. After this cell proliferation period, the patient undergoes a second surgery in which the millions of chondrocytes are surgically injected into the patient. These cells are held in place by a periosteal flap, a small piece of soft tissue from the tibia, which is sutured over the damaged area to serve as a watertight lid. The implanted chondrocytes can then divide and integrate with surrounding tissue under the flap and potentially generate hyaline-like cartilage.

Though Carticel has not been studied as an effective procedure through a wide range of patient backgrounds, results suggest that some patients can return to pre-injury function. Over 10,000 procedures have been performed since Carticel was introduced in 1995, and approximately 1,500-3,000 are performed per year. The cost of the treatment ranges from $20,000-$35,000. CARTICEL II is the second generation of the CARTICEL procedure. It is uses a "Fleece matrix" into which the grown harvested chondrocyte cells are planted. This fleece is then re-introduced back into the body usually via arthroscopy to begin the healing process. This CARTICEL II procedure is about to undergo clinical trials under the supervision of the FDA in the United States. This newer technique is known as matrix autologous chondrocyte implantation or (MACI). It is also available in Germany, UK, and Australia.

BioTissue Technologies GmbH (Freiburg, Germany) has since moved the CARTICEL technology forward. A patient's hyaline biopsy is taken, sent to their lab and grown into a 3D matrix of resorbable tissue. This matrix is then supplied back to the surgeon who then implants it back into the patient either via an open or arthroscopic procedure. It appears to be a lot simpler technique and resolves some of the issues of using Carticel under a periosteal patch. Other companies offering similar products include FAB (Fidia Advanced Biopolymers), Geistlich Biomaterials and Arthro Kinetics.

Another German company, co.don AG has recently launched a treatment called CHONDROSPHERE, which represents an evolutionary third generation compared to Genzyme's first generation liquid product or BioTissue Technologies' second generation 3D matrix. CHONDROSPHERE technology is 100% autologous as no synthetic/animal/human donor material is used in its production. The cells are building spheroids with an average diameter of 1mm by producing their own matrix which is then implanted through a syringe.

Autologous mesenchymal stem cell transplantation

For years, the concept of harvesting stem cells and re-implanting them into one's own body to regenerate organs and tissues has been embraced and researched in animal models. In particular, mesenchymal stem cells have been shown in animal models to regenerate cartilage. Recently, there has been a published case report of successful cartilage growth in human knees using autologous mesenchymal stem cells. An advantage to this approach is that a person's own stem cells are used, avoiding transmission of genetic diseases. It is also minimally invasive, minimally painful and has a very short recovery period. This procedure has been performed in over 400 patients, and costs over $7,000. There are some unresolved issues between the FDA and the Colorado clinic performing the above mentioned procedures.

Osteochondral autograft

Osteochondral autograft (OATS) is a technique that requires that the surgeon transplant sections of bone and cartilage. First, the damaged section of bone and cartilage is removed from the joint. Then a new healthy dowel of bone with its cartilage covering is removed from the same joint and transplanted or grafted into the hole left from removing the old damaged bone and cartilage. The healthy bone and cartilage are taken from areas of low stress in the joint so as to prevent weakening the joint. Depending on the severity and overall size of the damage multiple *plugs* or dowels may be required to adequately repair the joint. A similar treatment is known as mosaicplasty, and is talked about in the next paragraph.

Grafting

There are three methods of grafting cartilage defects, including periosteal grafting, osteochondral grafting (mosaicplasty), and articular cartilage paste grafting. Periosteal grafts are harvested from the perichondrial tissue and grafted to the articular cartilage defect. Given low long-term success rates, perichondrial grafting alone has not been clinically accepted as a particularly excellent therapy. Mosaicplasty, a form of chondral grafting, is a therapy designed to replace cartilage on the surface of the knee joint that has been damaged by trauma or arthritis by implanting osteochondral plugs. The implants can be autogenic (autologous) or allogenic. Paste grafting involves replacing damaged cartilage with autologous cartilage and cancellous bone from the intercondylar notch in the center of the knee that is first morselized into a paste (typically with hydroxyapatite) to better fill the defect and more successfully promote chondrocyte activity and cartilage formation. These procedures are often performed arthroscopically.

Joint replacement

Total joint replacement is reserved for the most severe and recalcitrant forms of osteoarthritis. When other forms of treatment fail or when patients are unlikely to succeed with lesser therapies, the last option to treat defective cartilage is to replace all or part of the joint. In knee joint replacement, the worn out surfaces of the knee are resurfaced with

metal and plastic, replacing the poorly functioning natural joint with new surfaces that slide together smoothly. The dysfunctional joint is removed and pain is relieved. Total knee replacement is considered a relatively routine surgery with a 95% success rate at 20 years. There are more than 300,000 total knee replacements in the United States each year. The average patient age is between 65 and 75. Of these surgeries, approximately 80% are unilateral (only one knee replaced) and 20% are bilateral. Interestingly, women undergo the procedure more often than men, making up 60% of the patient population.

Chapter 21

Arthrodesis and Joint Replacement

Arthrodesis

Arthrodesis, also known as *artificial ankylosis* or *syndesis*, is the artificial induction of joint ossification between two bones via surgery. This is done to relieve intractable pain in a joint which cannot be managed by pain medication, splints, or other normally-indicated treatments. The typical causes of such pain are fractures which disrupt the joint, and arthritis. It is most commonly performed on joints in the spine, hand, ankle, and foot. Historically, knee and hip arthrodeses were also performed as pain relieving procedures, however with the great successes achieved in hip and knee arthroplasty, arthrodesis of these large joints has fallen out of favour as a primary procedure, and now are only used as procedures of last-resort in some failed arthroplasties.

It can be done in several ways:

- A bone graft can be created between the two bones using a bone from elsewhere in the person's body (autograft) or using donor bone (allograft) from a *bone bank*.
    - Bone autograft is generally preferred by surgeons because, as well as eliminating the risks associated with allografts, bone autograft contains native bone-forming cells (osteoblasts), so the graft actually forms new bone itself (osteoinductive), as well as acting as a matrix or scaffold to new bone growing from the bones being bridged (osteoconductive). The main drawback of bone autograft is the limited supply available for harvest.
    - Bone allograft has the advantage of being available in far larger quantities than autograft; however, the treatment process the bone goes through following harvest, which usually involves deep-freezing and may also involve demineralization, irradiation and/or freeze-drying, kills living bone or bone marrow cells. This significantly reduces the immunogenicity (risk of graft rejection) such that no anti rejection drugs are needed and, combined with appropriate donor screening practices, these processing and preservation practices can significantly reduce the risk of disease transmission. In spite of all of this processing, cancellous allograft bone retains its osteoconductive properties. Furthermore, certain processing practices have been shown to also retain the acid-stable osteoinductive

proteins in cortical bone grafts, so that many bone allografts can be considered both osteoconductive and osteoinductive.

- A variety of *synthetic bone substitutes* are commercially available. These are usually hydroxyapatite or tricalcium phosphate based granules formed into a coralline or trabecular structure to mimic the structure of cancellous bone. They act solely as an osteoconductive matrix. Some manufacturers have recently begun supplying these products with soluble bone-forming factors such as bone morphogenetic protein to attempt to create a synthetic product with osteoinductive properties.
- Metal implants can be attached to the two bones to hold them together in a position which favors bone growth.
- A combination of the above methods is also commonly employed to facilitate bony fusion.

At the completion of surgery and healing, which takes place over a period of several weeks to over a year, the two adjoining bones are fused and no motion takes place between them. This can have the effect of actually strengthening the bones, as in anterior cervical fusion.

Joint replacement

A **joint replacement** is needed when "an arthritic or damaged joint is removed and replaced with an artificial joint, called a prosthesis". **Arthroplasty** [from Greek *arthron*, joint, limb, articulate, + -plassein, to form, mould, forge, feign, make an image of], or joint replacement surgery, is a procedure of orthopedic surgery, in which the arthritic or dysfunctional joint surface is replaced with an orthopaedic prosthesis. When joint replacement surgery occurs, the artificial surfaces of the joint replacement are shaped in such a way as to allow joint movement similar to that of a healthy and natural joint. A person who has injured or damaged their joint may experience extremely severe pain at the site of the joint. In certain instances when the pain is extremely severe, one may "avoid using the joint, weakening the muscles around the joint and making it even more difficult to move the joint". In such a severe case, one may consider a Joint Replacement as a possible solution. Examinations and tests will be performed to assess the severity of the joint damage. If less invasive alternatives don't alleviate pain and damage, Total Joint Replacement will be considered.

Background

Two previously popular forms of arthroplasty were: (1) **interpositional arthroplasty**, with interposition of some other tissue like skin, muscle or tendon to keep inflammatory surfaces apart and (2) **excisional arthroplasty** in which the joint surface and bone were removed leaving scar tissue to fill in the gap. Other forms of arthroplasty include

resection(al) arthroplasty, **resurfacing arthroplasty**, **mold arthroplasty**, **cup arthroplasty**, **silicone replacement arthroplasty**, etc. Osteotomy to restore or modify joint congruity is also an arthroplasty.

For the last 45 years the most successful and common form of arthroplasty is the surgical replacement of an arthritic, destructive, or necrotic joint or joint surface with a prosthesis. For example a hip joint that is affected by osteoarthritis may be replaced entirely (total hip arthroplasty) with a prosthetic hip. This would involve replacing both the acetabulum (hip socket) and the head and neck of the femur. The purpose of this procedure is to relieve pain, to restore range of motion and to improve walking ability, thus leading to the improvement of muscle strength.

Joint replacement surgery is becoming a more common practice. The knee joint and hip joint are replaced most often. "About 773,000 Americans have a hip or knee replaced each year". Many of the orthopaedic surgeons performing arthorplasty "have been replacing joints for several decades"; this wealth of experiences makes for a much more positive and desirable patient outcome.

Indications

- Osteoarthritis (OA)
- Rheumatoid arthritis (RA)
- Avascular necrosis (AVN) or osteonecrosis (ON)
- Congenital dislocation of the hip joint (CDH)
- Hip dysplasia (human)
- Acetabular dysplasia (shallow hip socket)
- Frozen shoulder & Loose shoulder
- Traumatized and malaligned joint
- Joint stiffness

Timeline

Because of the major surgery a complete pre-anaesthetic work-up is required. In elderly patients this usually would include ECG, urine tests, hematology and blood tests. Cross match of blood is routine also as a high percentage of patients receive a blood transfusion. Pre-operative planning requires accurate Xrays of the affected joint. The implant design is selected and the size matched to the xray images (a process known as templating).

A few days hospitalization followed by several weeks of protected function, healing and rehabilitation. This may then be followed by several months of slow improvement in strength and endurance.

Early mobilisation of the patient is thought to be the key to reducing the chances of complications such as venous thromboembolism and Pneumonia. Modern practice is to mobilize patients as soon as possible and ambulate with walking aids when tolerated.

Depending on the joint involved and the pre-op status of the patient the time of hospitalization varies from 1 day to 2 weeks with the average being 4–7 days in most regions.

Physiotherapy is used extensively to help patients recover function after joint replacement surgery. A graded exercise programme is needed. Initially the patients' muscles have not healed after the surgery; exercises for range of motion of the joints and ambulation should not be strenuous. Later when the muscle is healed the aim of exercise expands to include strengthening and recovery of function.

Risks and complications

Medical risks

The Stress of the operation may result in medical problems of varying incidence and severity.

- Heart Attack
- Stroke
- Venous Thromboembolism
- Pneumonia
- Increased confusion
- Urinary Tract Infection (UTI)

Intra-operative risks

- Mal-position of the components
  - Shortening
  - Instability/dislocation
  - Loss of range of motion
- Fracture of the adjacent bone
- Nerve damage
- Damage to blood vessels

Immediate risks

- Infection
  - Superficial
  - Deep
- Dislocation

Medium-term risks

- Dislocation
- Persistent pain
- Loss of range of motion

- Weakness
- Indolent infection

Long-term risks

- Loosening of the components: the bond between the bone and the components or the cement may break down or fatigue. As a result the component moves inside the bone causing pain. Fragments of wear debris may cause an inflammatory reaction with bone absorption which can cause loosening. This phenomenon is known as osteolysis.

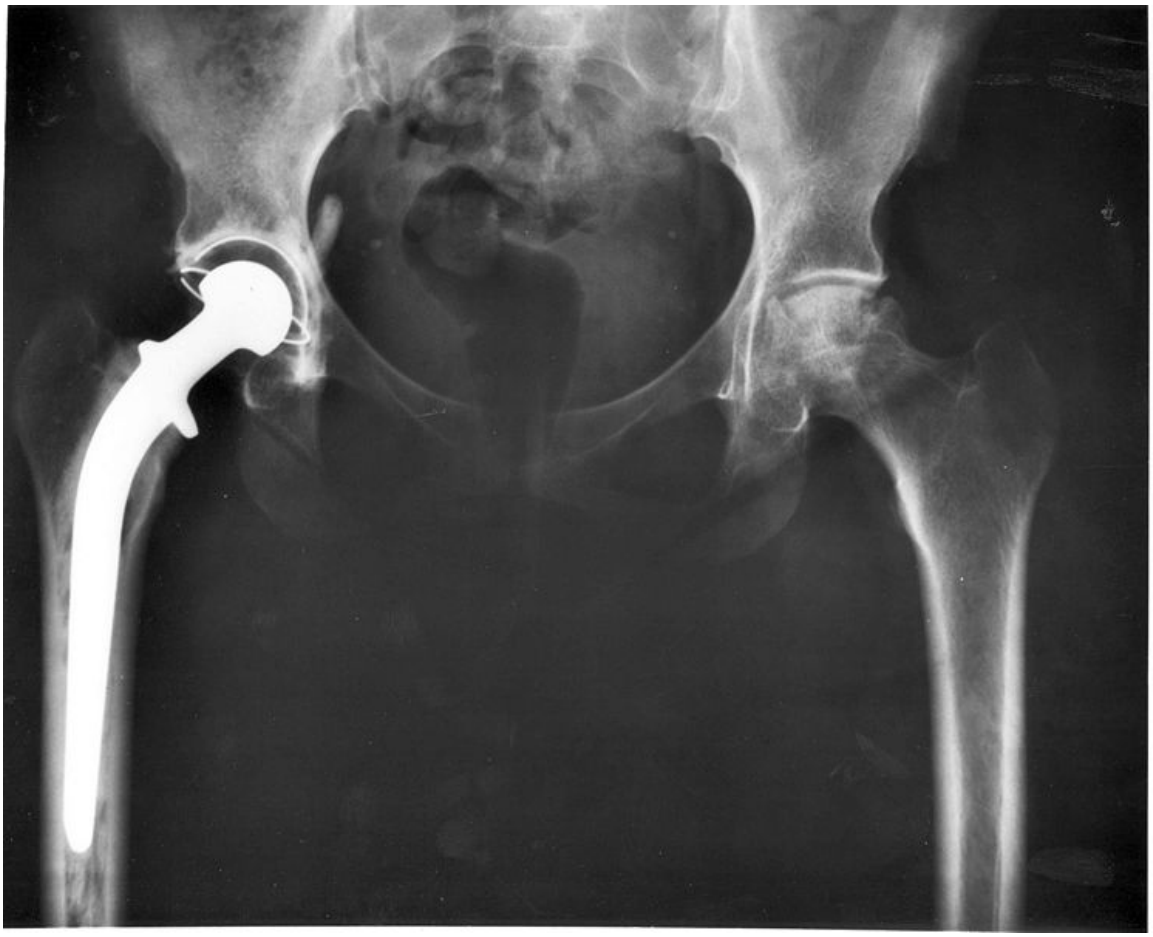
- Polyethylene synovitis - Wear of the weight-bearing surfaces: polyethylene is thought to wear in weight-bearing joints such as the hip at a rate of 0.3mm per year. This may be a problem in itself since the bearing surfaces are often less than 10 mm thick and may deform as they get thinner. The wear debris may also cause problems.

There are many controversies. Much of the research effort of the orthopedic-community is directed to studying and improving joint replacement. The main controversies are

- The best or most appropriate bearing surface - metal/polyethylene, metal-metal, ceramic-ceramic
- Cemented vs uncemented fixation of the components
- Minimally invasive surgery

Chapter 22

Hip Replacement



In this X-ray, the patient's right hip (left of image) has been replaced, with the ball of this ball-and-socket joint replaced by a metal head that is set in the thighbone or femur and the socket replaced by a white plastic cup (clear in this X-ray). Pelvic anatomy consistent with that of a female (large infrapubic angle, large pelvic opening).

Hip replacement is a surgical procedure in which the hip joint is replaced by a prosthetic implant. Hip replacement surgery can be performed as a total replacement or a hemi (half) replacement. Such joint replacement orthopaedic surgery generally is conducted to relieve arthritis pain or fix severe physical joint damage as part of hip fracture treatment.

A total hip replacement (total hip arthroplasty) consists of replacing both the acetabulum and the femoral head while hemiarthroplasty generally only replaces the femoral head. Hip replacement is currently the most successful and reliable orthopaedic operation with 97% of patients reporting improved outcome.

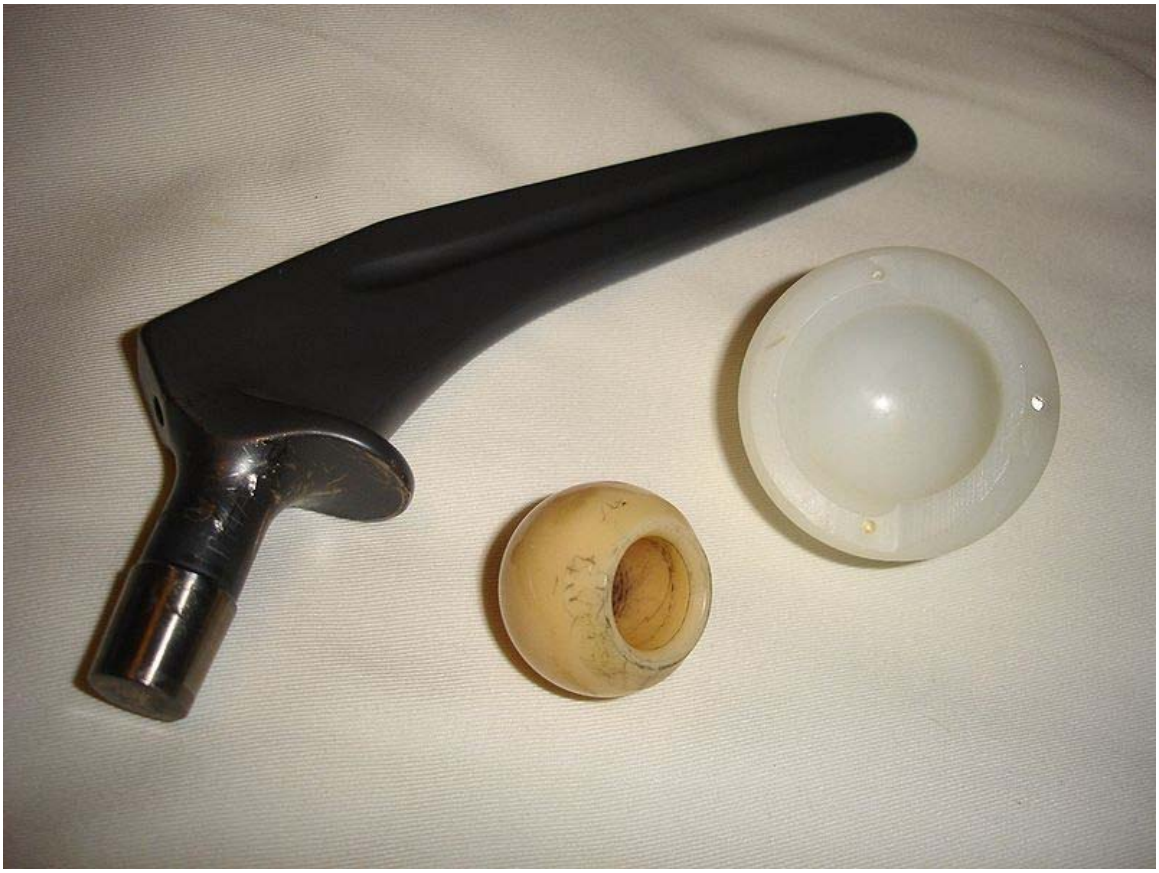
History

The earliest recorded attempts at hip replacement (Gluck T, 1891), which were carried out in Germany, used ivory to replace the femoral head (the ball on the femur).

In 1940 at Johns Hopkins hospital, Dr. Austin T. Moore (1899–1963), an American surgeon, reported and performed the first metallic hip replacement surgery. The original prosthesis he designed was a proximal femoral replacement, with a large fixed head, made of the Cobalt-Chrome alloy Vitallium. It was about a foot in length and it bolted to the resected end of the femoral shaft (hemiarthroplasty). This was unlike later (and current) hip replacement prostheses which are inserted within the medullary canal of the femur. A later version of Dr. Moore's prosthesis, the so-called Austin Moore, introduced in 1952 is still in use today.

In 1960 a Burmese orthopaedic surgeon, Dr. San Baw (29 June 1922 – 7 December 1984), pioneered the use of ivory hip prostheses to replace ununited fractures of the neck of femur when he first used an ivory prosthesis to replace the fractured hip bone of an 83 year old Burmese Buddhist nun, Daw Punya. This was done while Dr. San Baw was the chief of orthopaedic surgery at Mandalay General Hospital in Mandalay, Burma. Dr. San Baw used over 300 ivory hip replacements from the 1960s to 1980s. He presented a paper entitled "Ivory hip replacements for ununited fractures of the neck of femur" at the conference of the British Orthopaedic Association held in London in September 1969. An 88% success rate was discerned in that Dr. San Baw's patients ranging from the ages of 24 to 87 were able to walk, squat, ride a bicycle and play football a few weeks after their fractured hip bones were replaced with ivory prostheses. Ivory may have been used because it was cheaper than metal at that time in Burma and also was thought to have good biomechanical properties including biological bonding of ivory with the human tissues nearby. An extract from Dr San Baw's paper, which he presented at the British Orthopaedic Association's Conference in 1969, is published in Journal of Bone and Joint Surgery (British edition), February 1970. With modern hip replacement surgery, one can expect to walk immediately post-op.

Modern process



A titanium hip prosthesis, with a ceramic head and polyethylene acetabular cup

The modern artificial joint owes much to the work of Dr. Sir John Charnley at Wrightington Hospital; his work in the field of tribology resulted in a design that almost completely replaced the other designs by the 1970s. Charnley's design consisted of three parts—

1. stainless steel one piece femoral stem and head
2. polyethylene (originally teflon), acetabular component, both of which were fixed to the bone using
3. PMMA (acrylic) bone cement

The replacement joint, which was known as the Low Friction Arthroplasty, was lubricated with synovial fluid. The small femoral head (7/8" (22.2 mm)) was chosen for Dr. Charnley's belief that it would have lower friction against the acetabular component and thus wear out the acetabulum more slowly. Unfortunately, the smaller head dislocated more easily. Alternative designs with larger heads such as the Mueller prosthesis were proposed. Stability was improved, but acetabular wear and subsequent failure rates were increased with these designs. The Teflon acetabular components of Dr. Charnley's early designs failed within a year or two of implantation. This prompted a search for a more suitable material. A German salesman showed a polyethylene gear

sample to Dr. Charnley's machinist sparking the idea to use this material for the acetabular component. The Ultra High Molecular Weight Polyethylene or UHMWPE acetabular component was introduced in 1962. Dr. Charnley's other major contribution was to use polymethylmethacrylate (PMMA) bone cement to attach the two components to the bone. For over two decades, the Charnley Low Friction Arthroplasty, and derivative designs were the most used systems in the world.

The Exeter hip stem was also developed in the United Kingdom during the same time as the Charnley device. This is also a cemented device, but with a slightly different stem geometry. Both deigns have shown excellent long term durability when properly placed.

Early implant designs loosened from their attachment to the bones becoming painful typically ten to twelve years after placement. In additional to the devices loosening, erosion of the bone around the implant was seen on x-rays. Initially surgeons believed this was caused by an abnormal reaction in response to the cement holding the implant in place. That belief prompted a search for an alternative method to attach the implants. The Austin Moore device had a small hole in the stem into which bone graft was placed before implanting the stem. It was hoped bone would then grow through the window over time and hold the stem in position. Success was unpredictable and the fixation not very robust. In the early 1980s surgeons in the United States applied a coating of small beads to the Austin Moore device and implanted it without cement. The beads were constructed so that the gaps between beads matched the size or the pores in native bone. Over time bone cells from the patient would grow into these spaces and fix the stem in position. The stem was modified slightly to fit more tightly into the femoral canal resulting in the Anatomic Medullary Locking (AML) stem design. With time other forms of stem surface treatment and stem geometry have been developed and improved.

Initial hip designs were made up of a one piece femoral component and one piece acetabular component. Current designs have a femoral stem and separate head piece. Using an independent head allows the surgeon to adjust leg length (some heads seat more or less onto the stem) and to select from various materials from which the head is formed. A modern acetabulum component is also made up of two parts: a metal shell with a coating for bone attachment and a separate liner. First the shell is placed first. It's position can be adjusted unlike the original cemented cup design. Once proper positioning is obtained, the surgeon may select a liner made from various materials.

To combat the loosening caused by polyethylene wear debris, hip manufacturers developed improved and novel materials for the acetabular liners. Ceramic heads mated with regular polyethylene liners or a ceramic liner were the first significant alternative. Metal liners to mate with a metal head were also developed. At the same time these designs were being developed, the problems that caused polyethylene wear were determined and manufacturing of this material improved. Highly-crosslinked UHMWPE was introduced in the late 1990s. The most recent data comparing the various bearing surfaces has shown no clinically significant differences in their performance. Potential early problems with each material is discussed below. Performance data after 20 or 30 years may be needed to demonstrate significant differences in the devices. All of the

newer materials allow use of larger diameter femoral heads. Use of larger heads significantly decreases the chance of the hip dislocating which remains the greatest complication of the surgery.

To date, when currently available implants are used, there is no demonstrable difference in performance of cemented versus uncemented stems, and no significant difference in the clinical performance of the various methods of surface treatment of uncemented devices. Uncemented stems are selected for patients with good quality bone that can resist the forces needed to drive the stem in tightly. Cemented devices are typically selected for patients with poor quality bone who are at risk of fracture during stem insertion. Cemented stems are less expensive due to lower manufacturing cost, but require good surgical technique to place them correctly. Uncemented stems can cause pain with activity in up to 20% of patients during the first year after placement as the bone adapts to the device. This is rarely seen with cemented stems.

Once an uncommon operation reserved for frail patients with a limited life expectancy, hip replacement is now common, even among active athletes including racecar drivers Bobby Labonte and Dale Jarrett, and British Open runner-up, golfer Tom Watson.

Indications

Total hip replacement is most commonly used to treat joint failure caused by osteoarthritis. Other indications include rheumatoid arthritis, avascular necrosis, traumatic arthritis, protrusio acetabuli, certain hip fractures, benign and malignant bone tumors, arthritis associated with Paget's disease, ankylosing spondylitis and juvenile rheumatoid arthritis. The aims of the procedure are pain relief and improvement in hip function. Hip replacement is usually considered only once other therapies, such as physical therapy and pain medications, have failed.

Techniques

There are several different incisions, defined by their relation to the gluteus medius. The approaches are posterior (Moore), lateral (Hardinge or Liverpool), antero-lateral (Watson-Jones), anterior (Smith-Petersen) and greater trochanter osteotomy. There is no compelling evidence in the literature for any particular approach, but consensus of professional opinion favours either modified anterio-lateral (Hardinge) or posterior approach.

Posterior approach

The *posterior (Moore or Southern) approach* accesses the joint and capsule through the back, taking piriformis muscle and the short external rotators off the femur. This approach gives excellent access to the acetabulum and femur and preserves the hip abductors and thus minimises the risk of abductor dysfunction post operatively. It has the advantage of becoming a more extensile approach if needed. Critics cite a higher

dislocation rate, although repair of the capsule, piriformis and the short external rotators along with use of modern large diameter head balls negates this risk.

Lateral approach

The *lateral approach* is also commonly used for hip replacement. The approach requires elevation of the hip abductors (gluteus medius and gluteus minimus) in order to access the joint. The abductors may be lifted up by osteotomy of the greater trochanter and reapplying it afterwards using wires (as per Charnley), or may be divided at their tendinous portion, or through the functional tendon (as per Hardinge) and repaired using sutures.

Antero-lateral approach

The *anterolateral approach* develops the interval between the tensor fasciae latae and the gluteus medius.

Anterior approach

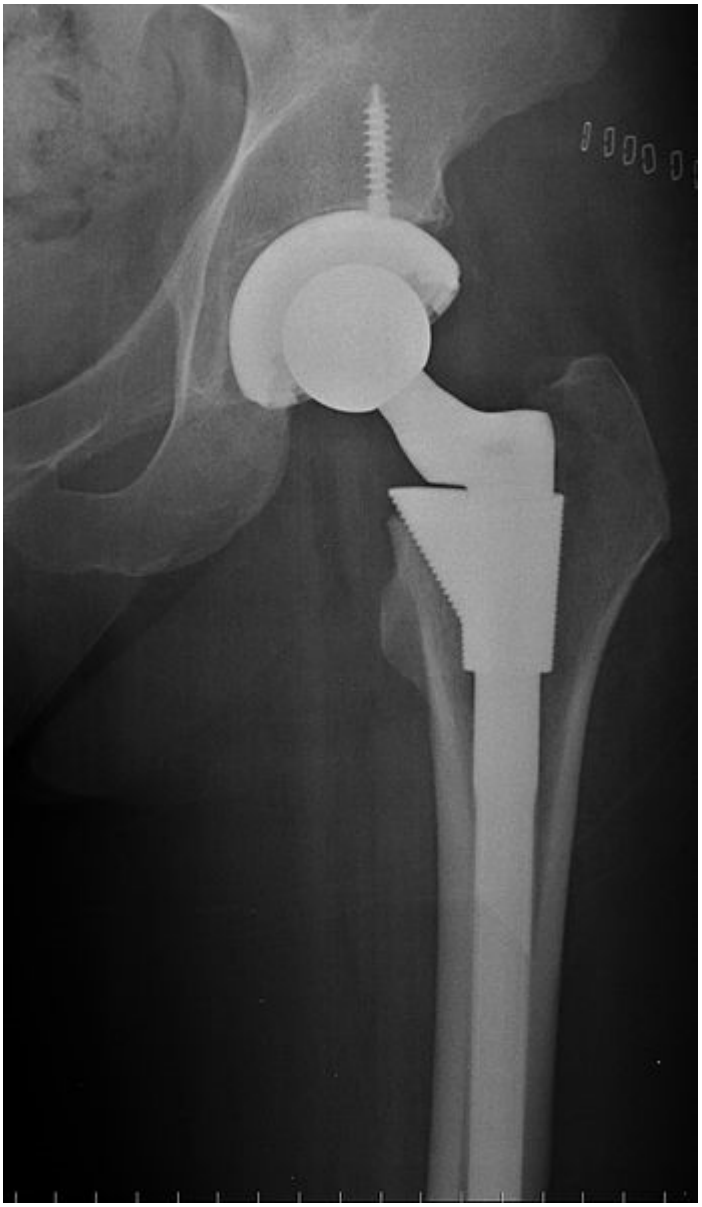
The *anterior approach* utilises an interval between the sartorius muscle and tensor fascia latae. Dr. Joel Matta has adapted this approach commonly used for pelvic fracture repair surgery in conjunction with a traction table for use when performing hip replacement. When used with older hip implant systems that had a small diameter head, dislocation rates were reduced compared to surgery performed through a posterior approach. With modern implant designs, dislocation rates are similar regardless of the approach and probably more a function of surgeon experience. There is a 10% rate of numbness in the thigh following this approach due to injury to the lateral femoral cutaneous nerve.

Minimally invasive approach

The double incision surgery and minimally invasive surgery seeks to reduce soft tissue damage through reducing the size of the incision. However, component positioning accuracy and visualization of the bone structures is significantly impaired. This can result in unintended fractures and soft tissue injury. Surgeons using these approaches are advised to use intraoperative x-ray fluoroscopy or computer guidance systems.

Computer Assisted Surgery techniques are also available to guide the surgeon to provide enhanced accuracy. Several commercial CAS systems are available for use worldwide. HipNav was the first system developed specifically for total hip replacement, and included navigation and preoperative planning based on a preoperative CT scan of the patient. Improved patient outcomes and reduced complications have not been demonstrated when these systems are used when compared to standard techniques.

Implants



Cement free implant 16 days after surgery. Femoral component is cobalt chromium combined with titanium which induces bone growth into the implant. Ceramic head. Acetabular cup coated with bone growth inducing material and held temporarily in place with a single screw.

The prosthetic implant used in hip replacement consist of different parts, the acetabular cup, the femoral component and the articular interface. Options exist for different patients and indications. Correct selection of the prosthesis is important.

Acetabular Cup

The Acetabular cup is the component which is placed into the acetabulum (hip socket). Cartilage and bone are removed from the acetabulum and the acetabular cup is attached using friction or cement. Some acetabular cups are one piece, others are modular. One piece (monobloc) shells are either polyethylene or metal, they have their articular surface machined on the inside surface of the cup and do not rely on a locking mechanism to hold a liner inplace. A monobloc polyethylene cup is cemented in place while a metal cup is held in place by a metal coating on the outside of the cup. Modular cups consist of two pieces, a shell and liner. The shell is made of metal, the outside has a porous coating while the inside contains a locking mechanism designed to accept a liner. Two types of porous coating used to form a friction fit are sintered beads or a foam metal design to mimic the trabeculi of cancellous bone. Additional fixation is achieved as bone grows onto or into the porous coating. Screws can be used to lag the shell to the bone providing even more fixation. Polyethylene liners are placed into the shell and connected by a rim locking mechanism, ceramic and metal liners are attached with a Morse taper.

Femoral Component

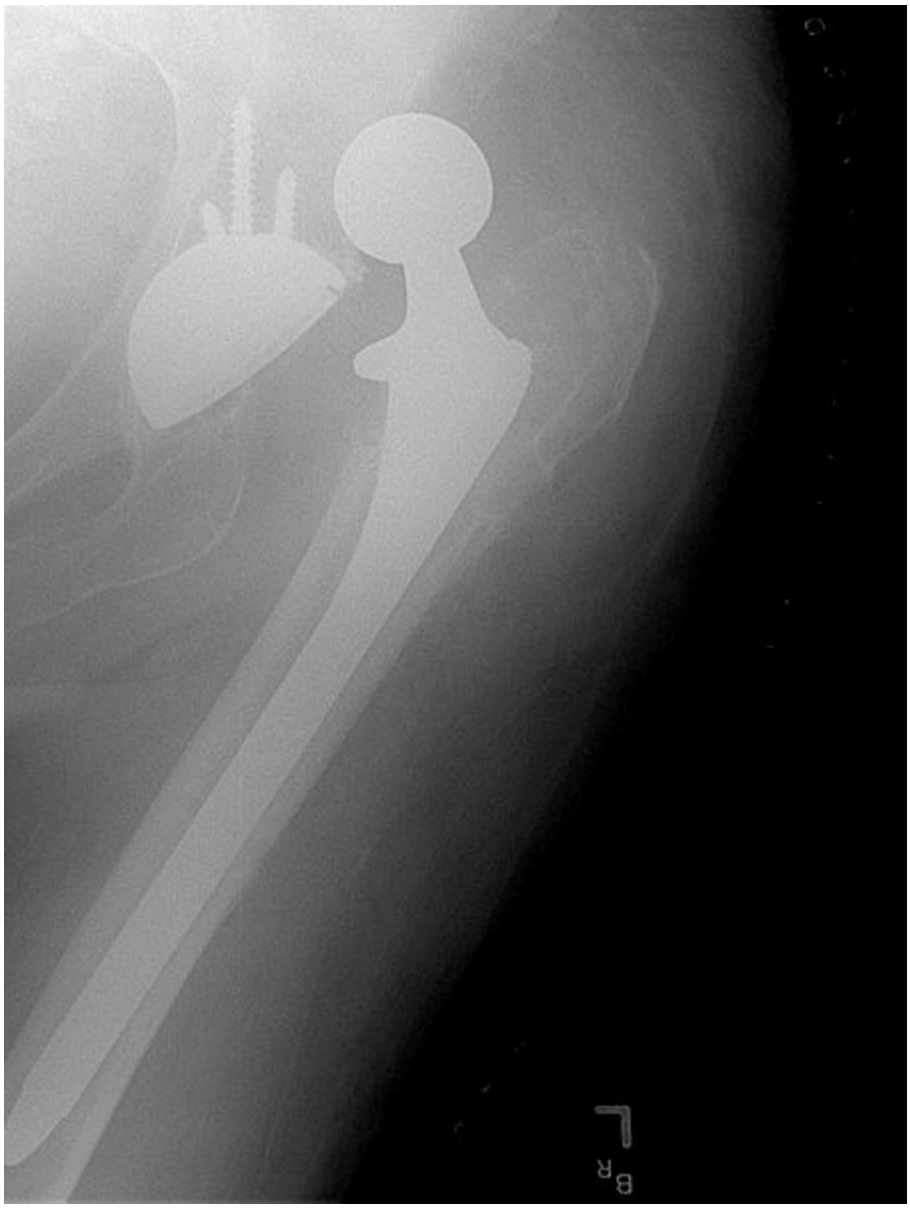
The femoral component is the component that fits in the femur (thigh bone). Bone is removed and the femur is shaped to accept the femoral stem with attached prosthetic femoral head (ball). There are two types of fixation, cemented and uncemented. Cemented stems use acrylic bone cement to form a mantle between the stem and to the bone. Uncemented stems use friction, shape and surface coatings to stimulate bone to remodel and bond to the implant. Stems are made of multiple materials, titanium, cobalt chromium and stainless steel and they can be monolithic or modular. Modular components consist of different head dimension and/or modular neck orientations, these attach via a Morse taper. These options allow for variability in leg length, offset and version. Femoral heads are made of metal or ceramic. Metal heads, made of cobalt chromium for hardness, are machined to size and then polished to reduce their coefficient of friction and minimize the wear they generate. Ceramics heads have a lower coefficient of friction than cobalt chrome however they are more brittle.

Articular Interface

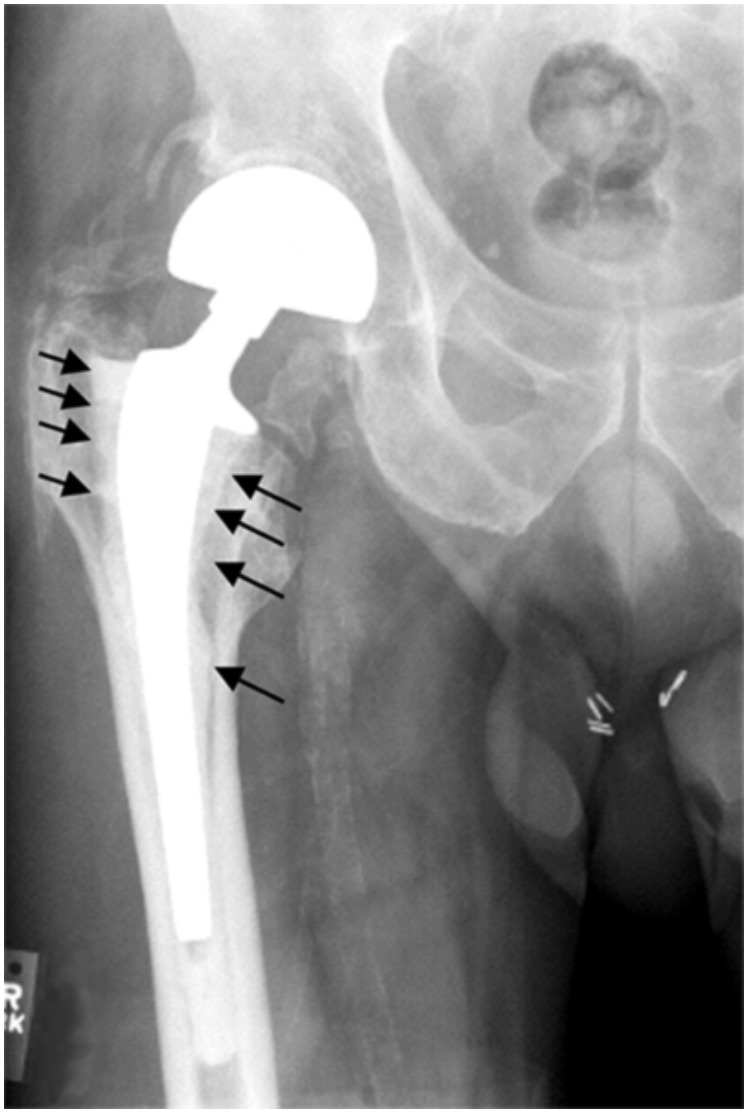
The articular interface is not actually part of the either implant, rather it is the area between the acetabular cup and femoral component. The articular interface of the hip is a simple ball and socket joint. Size, material properties and machining tolerances at the articular interface can be selected based on patient demand to optimise implant function and longevity while mitigating associated risks. The interface size is measured by the outside diameter the head or the inside diameter of the socket. Common sizes of femoral heads are 28 mm, 32 mm and 36 mm, while a 22.25 mm was common in the first modern prostheses, now even larger sizes are available 38–54+. Larger diameter heads lead to increased stability and range of motion while lowering the risk of dislocation. At the same time they also are subject to higher stresses such as friction and inertia. Different combinations of material have different physical properties which can be coupled reduce

the amount of wear debris generated by friction. Typical pairing of materials include metal on polyethylene (MOP), metal on crosslinked polyethylene (MOXP), ceramic on ceramic (COC), ceramic on crosslinked polyethylene (COXP) and metal on metal (MOM). Each combination has different advantages and disadvantages.

Risks and complications



Dislocated artificial hip



Hip prosthesis displaying aseptic loosening (arrows)

Risks and complications in hip replacement are similar to those associated with all joint replacements. They can include dislocation, loosening, impingement, infection, osteolysis, metal sensitivity, nerve palsy, pain and death.

Dislocation

Dislocation is the most common complication of hip replacement surgery. At surgery the femoral head is taken out of the socket, hip implants are placed and the hip put back into proper position. It takes eight to twelve weeks for the soft tissues injured or cut during surgery to heal. During this period, the hip ball can come out of the socket. The chance of this is diminished if less tissue is cut, if the tissue cut is repaired and if large diameter head balls are used. Surgeons who perform more of the operations each year tend to have fewer patients dislocate. Doing the surgery from an anterior aproach seems to lower

dislocation rates when small diameter heads are used, but the benefit has not been shown when compared to modern posterior incisions with the use of larger diameter heads. Patient can decrease the risk further by keeping the leg out of certain positions during the first few months after surgery. Use of alcohol by patients during this early period is also associated with an increased rate of dislocation.

Osteolysis

In the long term, many problems relate to osteolysis from polyethylene wear debris, fine bits of plastic that come off the cup liner over time. An inflammatory process causes bone resorption that may lead to subsequent loosening of the hip implants and even fractures in the bone around the implants. In an attempt to eliminate the generation of wear particles, ceramic bearing surfaces are being used in the hope that they will have less wear and less osteolysis with better long term results. Metal cup liners joined with metal heads (metal-on-metal hip arthroplasty) were also developed for similar reasons. In the lab these show excellent wear characteristics and benefit from a different mode of lubrication. At the same time these two bearing surfaces were being developed, highly cross linked polyethylene plastic liners were also developed. The greater cross linking significantly reduces the amount of plastic wear debris given off over time. These new prostheses do not always have the long term track record of established metal on poly bearings. Ceramic pieces can break leading to catastrophic failure. This occurs in about 2% of the time. They may also cause an audible, high pitched squeaking noise with activity. Metal-on-metal arthroplasty releases metal particulate debris into the body raising concerns about the potential dangers of these accumulating in the body over time. Highly cross linked polyethylene is not as strong as regular polyethylene. These plastic liners can crack or break free of the metal shell that holds them.

Metal sensitivity

Concerns are being raised about the metal sensitivity and potential dangers of metal particulate debris. There are new publications that have demonstrated development of *pseudotumors*, soft tissue masses containing necrotic tissue, around the hip joint. It appears these masses are more common in women and these patients show a higher level of iron in the blood. The cause is unknown and is probably multifactorial. There may be a toxic reaction to an excess of particulate metal wear debris or a hypersensitivity reaction to a normal amount of metal debris.

Metal hypersensitivity is a well-established phenomenon and is common, affecting about 10–15% of the population. Contact with metals can cause immune reactions such as skin hives, eczema, redness and itching. Although little is known about the short and long term pharmacodynamics and bioavailability of circulating metal degradation products in vivo, there have been many reports of immunologic type responses temporally associated with implantation of metal components. Individual case reports link hypersensitivity immune reactions with adverse performance of metallic clinical cardiovascular, orthopedic and plastic surgical and dental implants.

By 2010 reports in the orthopaedic literature have increasingly cited the problem of early failure of metal on metal prostheses in a small percentage of patients. Failures may relate to release of minute metallic particles or metal ions from wear of the implants, causing pain and disability severe enough to require revision surgery in 1–3% of patients. Design deficits of some prothesis models, especially with heat-treated alloys and a lack of special surgical experience accounts for most of the failures. Surgeons at leading medical centers such as the Mayo Clinic have reported reducing by 80 percent their use of metal-on-metal implants over the last year in favor of those made from other materials, like combinations of metal and plastic. The cause of these failures remain controversial, and may include both design factors, technique factors, and factors related to patient immune responses (allergy type reactions). In the United Kingdom the Medicines and Healthcare products Regulatory Agency commenced an annual monitoring regime for metal-on-metal hip replacement patients from May 2010. Data which is shown in The Australian Orthopaedic Association's 2008 National Joint Replacement Registry, a record of nearly every hip implanted in that country over the previous 10 years, tracked 6,773 BHR (Birmingham Hip Resurfacing) Hips and found that less than one-third of one percent may have been revised due to the patient's reaction to the metal component. Other similar metal-on-metal designs have not fared as well, where some reports show 76% to 100% of the people with these metal-on-metal implants and have aseptic implant failures requiring revision also have evidence of histological inflammation accompanied by extensive lymphocyte infiltrates, characteristic of delayed type hypersensitivity responses. It is not clear to what extent this phenomenon negatively affect orthopedic patients. However for patients presenting with signs of an allergic reactions, evaluation for sensitivity should be conducted. Removal of the device that is not needed should be considered, since removal may alleviate the symptoms. Patients who have allergic reactions to cheap jewelry are more likely to have a reactions to orthopedic implants. It is important to note that there is increasing awareness of the phenomenon of metal sensitivity and many surgeons now take this into account when planning which implant is optimal for each patient.

Nerve palsy

Post operative sciatic nerve palsy is another possible complication. The incidence of this complication is low. Femoral nerve palsy is another but much more rare complication. Both of these will typically resolve over time, but the healing process is slow. Patients with pre-existing nerve injury are at greater risk of experiencing this complication and are also slower to recover.

Chronic pain

A few patients who have had a hip replacement suffer chronic pain after the surgery. Groin pain can develop if the tendon that raises the hip (iliopsoas) rubs against the edge of the acetabular cup. Bursitis can develop at the trochanter where a surgical scar crosses the bone, or if the femoral component used pushes the leg out to the side too far. Also some patients can experience pain in cold or damp weather. Incision made in the front of the hip (anterior approach) can cut a nerve running down the thigh leading to numbness

in the thigh and occasionally chronic pain at the point where the nerve was cut (a neuroma).

Death

Rates of death for elective hip replacements are much less than 1%.

Metal toxicity

Most hip replacements consist of cobalt and chromium alloys. They release these ions into the blood. There have been reports of cobalt toxicity with hip replacement patients.

Leg Length Inequality

The leg can be lengthened or shortened during surgery. Unequal legs are the most common complaint by patients after surgery with over lengthening the most common problem. Sometimes the leg seems long immediately after surgery when in fact both are equal length. An arthritic hip can develop contractures that make the leg behave like it is short. When these are relieved with replacement surgery and normal motion and function are restored, the body feels that the limb is now longer then it was. If the legs are truly equal, the sense of this resolves within a month or two of surgery. If the leg is unequal, it will not. A shoe lift for the short leg, or in extreme cases, a corrective operation may be needed.

True leg length inequality is caused by improper implant selection. The femoral component may be too large and stick out of the femur further then needed. The head ball selected may sit too proud on the stem. Stiffness in the lower back from arthritis or previous fusion surgery seems to magnify the perception of leg length inequality.

Alternatives and variations of hip replacement

Conservative management

The first line approach as an alternative to hip replacement is conservative management which involves a multimodal approach of medication, activity modification and physical therapy. Conservative management can prevent or delay the need for hip replacement.

Hemiarthroplasty

Hemiarthroplasty is a surgical procedure which replaces one half of the joint with an artificial surface and leaves the other part in its natural (pre-operative) state. This class of procedure is most commonly performed on the hip after a subcapital (just below the head) fracture the neck of the femur (a hip fracture). The procedure is performed by removing the head of the femur and replacing it with a metal or composite prosthesis. The most commonly used prosthesis designs are the Austin Moore prosthesis and the Thompson Prosthesis. More recently a composite of metal and HDPE which forms two

interphases (bipolar prosthesis) has also been used. The bipolar prosthesis has not been shown to have any advantage over monopolar designs. The procedure is recommended only for elderly and frail patients, due to their lower life expectancy and activity level. This is because with the passage of time the prosthesis tends to loosen or to erode the acetabulum.

Hip resurfacing

Hip Resurfacing is an alternative to hip replacement surgery. It is a bone conserving procedure that places a metal cap on the femoral head instead of amputating it. There is no long stem placed down the femur so it is more like a natural hip and may allow patients a return to many activities, including marathons and triathlons, some patients have even completed Ironman and Ultraman competitions following hip resurfacing surgery although patients must have good bone quality to qualify for it. It has been used in Europe for over 17 years and become a common procedure. The first device, the BHR or Birmingham Hip Resurfacing device was approved by the FDA on May 9, 2006. The Australian Registry hip resurfacing data for 2009, 70 percent of which comes from BHR Hip procedures, indicates that for men under age 65, hip resurfacing performs at the same or a better rate than total hip replacement.

Viscosupplementation

Current alternatives also include viscosupplementation, or the injection of artificial lubricants into the joint.

Some believe the future of osteoarthritis treatment is bioengineering, targeting the growth and/or repair of the damaged, arthritic joint. Centeno et al. have reported on the partial regeneration of an arthritic human hip joint using mesenchymal stem cells in one patient. It is yet to be shown that this result will apply to a larger group of patients and result in significant benefits. The FDA has stated that this procedure is being practiced without conforming to regulations, but Centeno claims it is exempt from FDA regulation. It has not been shown in controlled clinical trials to be effective, and costs over $7,000.