INTRODUCTION

It is estimated that the majority of the population throughout the countries of the Western type of civilisation over age of fifty will experience some signs of arthritis. It is considered the number one crippler in the nations of the so called developed countries. Osteoarthritis is the most common degenerative joint disease. The cartilage in the joints that covers the end of the bones starts to wear away. This involves the tendons, ligaments, and muscles, too. On the other hand Rheumatoid arthritis (RA) is a chronic (systemic autoimmune) inflammatory disorder which attacks the cartilage, connective tissue and small blood vessels throughout the body. Rheumatoid arthritis is causing stiffness, deformity, and pain in the joints and muscles, ending up in severe deformities. It can affect the lungs, blood vessels, the spleen, skin and kidneys, as well. Early signs are fatigue, muscular aches and pains, stiffness in the small joints and swelling.

Arthritis also includes bursitis and gout. Symptoms are pain and inflammation in the joints. Arthritic changes could appear on the neck, back, shoulders, knees, wrists, elbows, fingers, toes, and hips. Stiffness an pain on arising in the mornings is common

Fossils show that even the dinosaurs had arthritis, but unfortunately the disease outlived them! Many varieties of joint-related disorders have been described, all of which result in destruction of the hyaline – glassy cartilage that lines the ends of the bones. The remaining cartilage cells try to heal the defect by proliferating and making more cartilage. They are almost never equal to the task, and scar tissue fills the rest of the hole. The result is pain, for scar tissue is too spongy to bear much weight or keep the bones from grinding against each other.

STRUCTURE AND FUNCTION OF JOINTS

The site where two or more bones are attached is called a joint (articulation). The primary function of joints is to provide stability and mobility to the skeleton. Whether a joint provides stability or mobility depends on its location and its structure. Generally, joints that stabilize the skeleton have a simpler structure than those that enable the skeleton to move. Most joints provide both stability and mobility to some degree.

The classification of joints is based both on the degree of movement they permit and on the connecting tissues that hold them together.

- Based on movement, a joint is classified as a synarthrosis (immovable joint), an amphiarthrosis (slightly movable joint), or a diarthrosis (freely movable joint).
- On the basis of connective structures, joints are classified broadly as fibrous, cartilaginous, and synovial.

Each of these three structural classifications can be subdivided according to the shape and...
contour of the articulating surfaces (ends) of the bones and the type of motion the joint permits.

**Fibrous Joints**

A joint in which bone is united directly to bone by fibrous connective tissue is called a **fibrous joint**. Generally, fibrous joints are **synarthroses** (immovable), but many fibrous joints allow some movement. The degree of movement depends on the distance between the bones and the flexibility of the fibrous connective tissue.

Fibrous joints are further subdivided into three types: **sutures**, **syndesmoses**, and **gomphoses**. A **suture** has a thin layer of dense fibrous tissue that binds together interlocking flat bones in the skulls of young children. Sutures form an extremely tight union that permits no motion. By adulthood the fibrous tissue has been replaced by bone. A **syndesmosis** is a joint in which the two bony surfaces are united by a ligament or membrane. The fibres of ligaments are flexible and stretch, permitting a limited amount of movements. The paired bones of the lower arm (**radius and ulna**) and the lower leg (**tibia and fibula**) and their ligaments are syndesmotic joints. A **gomphosis** is a special type of fibrous joint in which a conical projection fits into a complementary socket and is held there by a ligament. The teeth held in the maxilla or mandible are gomphosis joints.

**Cartilaginous Joints**

The two types of cartilaginous joints are: **symphyses** and **synchondroses**. A **symphysis** is a cartilaginous joint in which bones are united by a **pad** or **disk of fibrous cartilage**. The articulating surfaces of the two bones are usually covered by a thin layer of **hyaline (glassy) cartilage**, and the thick pad of fibro cartilage acts as a **shock absorber** and **stabilizer**. Examples of symphyses are the **symphysis pubis**, which joins the two pubic bones, and the **intervertebral disks**, which join the bodies of the vertebrae. A **synchondrosis** is a joint in which hyaline cartilage, rather than fibro cartilage, connects the two bones. The joints between the ribs and the sternum are synchondroses. The hyaline cartilage of these joints is called **costal cartilage**. Slight movement at the synchondroses between the ribs and the sternum allows the chest to move outward and upward during breathing.

**Synovial Joints**

**Synovial joints** (diarthroses) are the most movable and the most complex joints in the body. A synovial joint consists of the following parts:

1. A fibrous joint capsule (articular capsule)
2. A synovial membrane that lines the inner surface of the joint capsule
3. A joint cavity (synovial cavity), a space formed by the capsule
4. Synovial fluid, which fills the joint cavity and lubricates the joint surface, and
5. Articular cartilage, which covers and pads the articulating bony surfaces

**Joint capsule**

The fibrous joint capsule (articular capsule) is a connective tissue that covers the ends of the bones where they meet in the joint. Sharpe fibres firmly attach the proximal and distal capsule to the periosteum, ligaments and tendons, which also reinforce the capsule. The joint capsule is made up of parallel, interlacing bundles of dense, white fibrous tissue. It is richly supplied with nerves, blood vessels, and lymphatic vessels. The nerves within and around the joint capsule are sensitive ones. They respond to the rate and direction of motion, compression, tension, vibration, and pain.

**Synovial membrane**

The **synovial membrane** (synovium) is the smooth, delicate inner lining of the joint capsule. It lines the non-articular portion of the synovial joint and any ligaments or tendons that traverse the joint cavity. The synovial membrane is made up of two layers – a vascular layer called the **sub-intima** and a thin cellular layer called the **intima**. The vascular sub-intima merges with the fibrous joint capsule and is composed of loose fibrous connective tissue, elastin fibres, fat cells, fibroblasts, macrophages, and mast cells. The intima consists of rows of synovial cells embedded in a fibre-free intercellular matrix. The intima contains two types of synovial cells: type-A cells and type-B cells. The **type-A cells** ingest and remove bacteria and particles of debris by phagocytosis in the joint cavity. The **type-B cells** secrete **hyaluronic acid** (HA) (a **glycosaminoglycan, GAG**), which is a binding agent that gives synovial fluid its viscous quality, able to lubricate. The syno-
vial membrane is richly supplied with blood and lymphatic vessels; therefore it is capable of rapid repair and regeneration.

**Joint cavity**

The joint (synovial) cavity is an enclosed, fluid-filled space between the articulating surfaces of the two bones, facing each other. This small cavity, often called the joint space, enables the two bones to move “against” one another, without any mechanical friction. The synovial cavity is surrounded by the synovial membrane and filled with a clear, viscous, slick fluid called the synovial fluid.

**Synovial fluid**

Synovial fluid is in essence super filtrated plasma from blood vessels in the synovial membrane, enriched with specific glycoproteins, secreted by the local cells. Synovial fluid lubricates the joint surfaces, nourishes the pad of the articular cartilage that covers the ends of the bones, and contains free-floating synovial cells and various leukocytes which phagocyte joint debris and micro organisms. Loss of synovial fluid leads to rapid deterioration of articular cartilage.

**Articular cartilage**

Articular cartilage is a layer of hyaline (glassy) cartilage that covers the end of each bone. It may be thick or thin, depending on the size of the joint, – which face each other on the two bone ends –, and the amount of weight and shearing force the joint normally withstands. The function of articular cartilage is to reduce friction in the joint and to distribute the forces of weight bearing. Articular cartilage is composed of chondrocytes (cartilage cells, making up about 2% of the tissue) and an intercellular matrix (a ground substance) made up of collagen (making up about 10% to 30% of weight), and water. The water content ranges from 60% to almost 80% of the net weight of the cartilage. Individual molecules rapidly enter or exit at the articular cartilage to contribute to the resiliency of the tissue.

**COMPOSITION AND FUNCTION OF CONNECTIVE TISSUE**

The term connective tissues usually refer to those structures that are responsible for the form and shape of the body. Connective tissue varies considerably in structure and function but is most common as the framework on which epithelial cells cluster to form organs. Other functions of connective tissue include binding tissues and organs together, supporting them in their locations, and serving as storage sites for excess nutrients. In case of homeostatic and/or metabolic imbalance, the connective tissue serves also as a depot for metabolic intermediary products, waste and of toxic substances.

In contrast to epithelial tissue, connective tissue is characterised by an abundant extra cellular matrix which surrounds few cells. The extra cellular matrix is composed of ground substance and fibres.

Ground substance is a homogenous mass that varies in consistency from fluid to semi-solid gel.

Fibres produced by connective tissue cells (fibroblasts) are found within the ground substance. The three types of fibres are: Collageneous (white), elastic (yellow), and reticular (meshwork-like).

Collagene fibres are formed of bundles of smaller fibres (fibrils) appearing as wavy- (meandering) -bands under the microscope. These fibres are composed of the protein collagen and are strong and elastic.

Elastic fibres are long, branching fibres composed of a protein called elastin that enables the fibres to return to their original length after stretching. Elastin occurs not only as a fibre but also as a compound of membranes, particularly the membranes of blood vessels, especially arterial ones.

Reticular fibres are thin, short, branching fibres that form an inelastic network made of collagen-like protein called reticulum. Reticular fibres form the internal framework (stroma) to which the epithelial cells and glands are attached. They are found in loose connective tissue (Hungarian – lazrostos kötőszövet, Serbian – rastresito vezivno tkivo), generally in bone marrow and in the parenchyma (i.e., the essential substance of an organ rather than its framework) of the liver, spleen, and lymph nodes.

Connective tissues are classified according to the consistency (e.g., loose, dense) of the ground
substance and the type and organization of the fibres within it.

As mentioned previously, the term connective tissue is most often applied to tissues such as bone, cartilage, tendons, fascia, and the capsules of the joints. However, connective tissues also contribute to the major structure of large blood vessel walls. All organs, however, have some connective tissue components which are responsible not only for form but also for mechanical, biochemical and biophysical properties of the tissues. This type of connective tissue is called ground-substance and it plays an extremely important role in the process termed basic-regulation. Connective tissues are composed not only of the specialised cells responsible for their formation, but also of an extra cellular matrix whose composition determines the properties of that specific tissue. The extra cellular matrix, in turn, usually contains a fibrillar protein or proteins, or globular proteins, some of which are glycoprotein; variable proportions of proteoglycans (PGs), and in the case of a specialised connective tissue such as bone, a mineral phase as well. Some connective tissues, such as cartilage, are relatively avascular and turn over (metabolise) very slowly, whereas bone, even in adults, has a high metabolic rate and is continually being remodelled. Considerable information is now available concerning the composition, biosynthesis, and degradation of connective tissues and how disease states may alter their composition by affecting biosynthesis and degradation.

Connective tissues as organs are composed of vascular elements, specialised cells, and extra cellular material (EC matrix, ground-substance). Some connective tissues are exceedingly vascular, of which a good example is bone. Bones possess a unique arrangement of blood vessels: The arterial supply is represented by a principal nutrient artery and a network of periostal arteries which end into the cortical venous channels and the central venous sinuses of the medulla of bone. The veins of bones drain the haematopoietic elements of the bone marrow, whereas cortical venous channels serve the non-marrow-containing portions of compact bone. Bone cells (osteocytes) are connected to each other through micro canaliculi and depend upon continuous vascular supply for their nutrition.

In contrast, cartilage is avascular, and cartilage cells must derive their nutrition from neighbouring tissues. For example, the cells in articular cartilage obtain their nutrition by repeated compression and release of compression (like a pumping action). By this means metabolic substrates can be delivered and metabolic products removed from the environment of the cells. Thus, chondrocytes have low oxygen consumption and a high rate of glycolysis compared with bone cells, which depend upon an abundant arterial supply. With the possible exception of cartilage, the vasculature is usually intimately related to the function of most connective tissues. Indeed, blood vessel walls are themselves a form of connective tissue, and their cellular elements are capable of synthesizing matrix components. Furthermore, the blood circulation may actually be the source of connective tissue cells. For example, circulating monocytes can, under some circumstances, differentiate into tissue osteoclasts/osteoblasts (specialised bone macrophages). In bone, the specialized vascular areas that make up the sinuses in the marrow also contribute to skeletal function. Haematopoietic elements are thought to be responsible for precursor cells destined to become osteoclasts, whereas stromal elements of the marrow may be the source of precursor cells that differentiate into osteoblasts. According to their function, both osteoclasts, and osteoblasts are in essence specific macrophages.

The cells of each connective tissue are responsible for the synthesis and organization of the extra cellular matrix that characterizes that specific tissue. Thus, osteoblasts and chondrocytes synthesize and secrete the characteristic matrix of bone, and cartilage, respectively. In other connective tissues the predominant cells that are responsible for the formation of connective tissue matrix (ground-substance) are usually called fibroblasts.

However, all fibroblasts do not necessarily produce the same kind of matrix. Fibroblasts in tendons, for example, may produce the large, densely packed collagen fibres that are highly organized along their long axis with respect to each other, whereas fibroblasts may also synthesize the loosely woven stroma of parenchymal organs or other types of fibrous networks in tissues such as dermis (the subcutaneous layer of the skin). With respect to collagen, different cells
– for example, osteoblasts and dermal fibroblasts – may produce the same protein with the same primary structure, yet other functions of each of these cells determine post-translational modification of the primary structure of these proteins. The specialised cells of each connective tissue also produce other components of the extra cellular matrix that determine the function of that tissue. In cartilage, for example, the chondrocyte secretes not only the specific type II collagen, but also the proteoglycan(s). In bone, the osteoblast is also involved in the formation of the mineral phase, which must be deposited in an ordered fashion with respect to the matrix. A single fibroblast can stain with antibodies to both type I, and type III collagen, implying that the same cell can synthesize and secrete two different macromolecules. Primitive mesenchymal cells may differentiate into cells that assume phenotypic characteristics of mature connective tissue cells. Such differentiation is under many different controls, including factors derived from immune competent cells, hormones, and neuronal influences. Connective tissues also underlie epithelial structures. These epithelial cells may synthesize specialized matrices such as basement membranes, which also contain specific (type IV) collagens.

The extra cellular matrices of connective tissues contain not only substances formed by the cells of that connective tissue but also electrolytes and low molecular weight materials derived from the vascular system. The unique properties of each matrix in turn may determine the distribution of such substances. For example, the proteoglycans (PGs) of articular cartilage with their large “domain” and high electro negative charge are responsible for the presence of large amounts of the bound water. This water is responsible for the ability of cartilage to comply under strain (mechanical stress) and regain the original shape (elasticity). On the other hand, when bone, cartilage, and dentin are calcified, water is lost as it is replaced by the inorganic mineral phase. Thus, some extra cellular tissues such as mineralised bone have a fluid volume considerably lower than that of other tissues. Some connective tissues also contain high molecular weight (HMW) materials derived from plasma. From the biochemical point of view, the function of most of these components is largely unknown. In the case of bone, there is evidence that specific glycoproteins derived from plasma are incorporated into the matrix. However, lately the extremely important biophysical character of the connective tissue – especially its ground substance or extra cellular matrix – is recognised as the pathway of transmission within the complex and interwoven net of inter-cellular communication.

The intercellular matrix is produced by the chondrocytes, which synthesize and extrude collagen, which, like the collagen produced by bone cells, is distributed throughout the cartilage in a highly organized system of fibres. Collagen fibres in cartilage are made up of many fine fibrils that, like bone fibrils, are assembled in an orderly fashion that makes them resistant to physical, metabolic, or chemical breakdown. The main differences between bone collagen and cartilage collagen are the amino acid content of the alpha chains and the composition of the fibrils. Bone collagen fibrils are made up of two types: type I chains and type II chains. Approximately 90% of the cartilage collagen fibrils are made up of three identical type II chains, with the remaining 10% made up of types V, VI, IX, X, and XI chains. At the surface of articular cartilage, the collagen fibres run parallel to the joint surface and are closely compacted into a dense, protective mat. The proteoglycans (PGs) act as a pump, permitting enough fluid film is always present on the surface of the cartilage, even after hours of weight bearing. The pumping action of proteoglycans also draws synovial fluid back into the cartilage after a weight-bearing load is released. Mobility and weight bearing are necessary for the pumping action of proteoglycans to occur. Non-use of a joint quickly reduces the pumping action, which changes the composition of the matrix and interferes with the nutrition of the chondrocytes.

LOSS OF THE CARTILAGE

Cartilage cells synthesize both collagen and proteoglycans. Injury or inflammation reduces the amounts of proteoglycans situated outside the cells. The trabecular structure of the bone beneath the cartilage allows the division of press- ing force, which also prevents the wearing out of cartilage. In articular complaints of different origin the structural components may get modified,
cell functions may be damaged. The enzymatic degradation of proteoglycans and the collagen causes the deterioration of cartilage and bones. The regeneration of collagen is limited both in dimension and direction, therefore the damage becomes irreversible relatively quickly, pain and limitation of motion, articular instability as well as deformity present themselves.

Articular cartilage has no blood vessels, lymph vessels, or nerves. Therefore it is insensitive to pain and regenerates slowly and minimally after injury. Regeneration occurs primarily at sites where the articular cartilage meets the synovial membrane, where blood vessels and nutrients are available.

**MOVEMENT**

Synovial joints are described as uniaxial, bi-axial, or multiaxial according to the shapes of the bone ends and the type of movement occurring at the joint. Usually one of the bones is stable and serves as an axis for the motion of the other bone. The body movements made possible by various synovial joints are either circular or angular.

**FIBROUS PROTEINS
COLLAGENS AND THEIR STRUCTURE**

In most connective tissues, the major component of the organic portion is a fibrous protein such as collagen or elastin. Collagen is the major fibrillar protein of most connective tissues and indeed may be the predominant protein of such connective tissues as bone, where it represents approximately 95 per cent of the total organic matter. The term collagen refers to a class of protein that is characterized by its amino acid composition and structural organization of the polypeptide chains. Most collagens have regions containing the specific collagen triple helix determined by the primary structure (that is, a glycine residue in every third position). This structure is stabilized by post-translational modifications, particularly hydroxylation of specific prolyl residues. The non-collagenous regions of the molecule may be integral parts of the collagen structure or may be present only during intermediate stages of biosynthesis and removed prior to deposition of the finished product. For the purposes of this discussion, the term procollagen will be used to refer to the completed precursor molecule stripped from the polyribosomes and is assembled intra cellularly. The term collagen molecule refers to a structure of a higher order that is formed by a specific alignment of the collagen molecules and that must also have some relationship with non-collagenous components in tissues. Most tissues contain different kinds of collagens, each of which is a protein with a different primary structure determined by a different gene. Moreover, some of these collagens with the same primary structure may have unique post-translational modifications that are characteristic of that organ or tissue.

**EXTRACELLULAR MATRIX
BASIC REGULATION OF THE GROUND-SUBSTANCE (EXTRACELLULAR MATRIX)**

In multicellular organisms, Homo included, the cells modify the content of certain compartments of their immediate environment (primarily the interstitial fluid and the blood plasma) by discharging therein a large amount of secretory proteins, glycoproteins, and proteoglycans. In the interstitium, these secretory products and the structures they form, together with associated small solutes, ions, and water, constitute the extracellular matrix.

The proteins of the blood plasma synthesised and secreted primarily by the hepatocytes and plasma cells, function, among the others, in osmotic regulation, metabolic transport, control of blood coagulation, and immune responses. Normally, blood vessels retain the large molecular weight proteins, allowing only water, and small molecular weight compounds to diffuse freely into the interstitial space. In other words interstitial fluid and lymph are free of plasmatic proteins, but due to the special composition of the extracellular matrix of the ground substance, the Starling’s extra capillary flow enables the exchange processes between the filtrating force of arterioles and the vacuum-like-action of venules.

**Structure and chemistry**

A wide variety of cell types (mesenchymal as well as epithelial cells) secrete a variety of procollagen molecules into the interstitium (extra
cellular space) of the tissues. In this case, post-translational modifications continue after secretory discharge: partial proteolysis by procollagen proteases (produced apparently by the same cells that secrete procollagens) remove amino acid sequences from both the amino- (N-) terminal, and carboxy- (C-) terminal (end) of the discharged molecules, thereby converting them to collagens. These proteolytic steps make possible the staggered lateral aggregation of collagens into banding patterns building long fibres of variable diameter and characteristic. Only certain collagens, i.e., collagen types I, II and III, form fibres as described above. Protocollagen type IV is not proteolytically processed upon discharge; therefore as a result, it does not form fibrils. Instead, it generates, by interaction with the other glycoproteins, such as – collagen V, fibronectin, laminin, entactin and proteoglycans (PG), a laminated meshwork known as basement membrane or basal laminae. Basement membranes unsheath cells that are long-term non migrating residents of the interstitia, e.g., smooth and striated muscle cells, Schwann cells, etc. They also form a continuous substrate under all endothelia and epithelia. In basement membranes, collagen type IV is the molecular constituent that imparts tensile strength to the structure – for example, the glomerular capillaries, alveoli, and capillary network in general. Laminin, a heavy molecular weight (HMW) glycoprotein, facilitates the attachment of epithelial cells to different substrates, basement membranes included. Fibronectin, a ~ 450 Kilo Dalton (KD) glycoprotein, acts as a diversified linker: the molecule has distinct specific domains that recognise collagens, proteoglycans, and receptors on the plasmalemma of adjacent (epithelial and mesenchymal) cells. Integral membrane proteins interact with fibronectin outside the cell and with peripheral membrane proteins (or cytoskeletal proteins) inside the cell to create a mechanically continuous system.

Proteoglycans (PGs) are large molecules with a large number of covalently linked glycosaminoglycan chains. The chains are sulphated (to a variable degree!) in the case of chondroitin-, heparan-, dermatan-, and keratan-sulphate, and non-sulphated in the case of hyaluronate and heparin. The proteoglycans associated with basement membranes provide them with fixed negative charges that affect their permeability; in addition, they form clusters that seem to function as attachment sites for endothelial or epithelial cells.

Proteoglycans (PGs) are present as soluble residential components in the interstitial fluid and as integral or adsorbed proteins on cellular membranes. In the interstitial space, they control the degree of hydration of the extra cellular matrix and the diffusion of large and small solutes, acting in the last case, much like ion exchange columns.

**Biosynthesis**

All the molecules of the extra cellular matrix are glycoproteins produced by both epithelial and mesenchymal cells, in steps common to all secretory proteins. Elastin and elastic fibres are produced as far as is known, only by mesenchymal cells, primarily by fibroblasts and smooth muscle cells. Among the proteins of the extra cellular matrix, collagens represent a special case. They are the products of a relatively large family of genes. They are long (~ 320 nm) polypeptide chains that are extensively modified by hydroxylation of their numerous proline residues. This modification makes possible the association of three polypeptide chains into a triple helical structure that is responsible for the characteristically high tensile strength of collagen fibrils. Again, some of their lysine residues are hydroxilated to be used later for intermolecular crosslinkage. In the biosynthesis of collagens, the intracellular stage produces triple helices and the extra cellular stage generates fibrils.

**Function**

By its fibrillar components, the extra cellular matrix creates a solid framework that is maintained under tension by the high degree of hydration of its proteoglycans and in which collagen fibrils are deposited along lines of propagation of the physical forces exerted on the system. Linkers, such fibronectin and laminin, attach the cells to the framework, thereby creating a mechanically continuous system that can resist pressure, stress, and tension by distributing their impact throughout the entire system. The extra cellular matrix is produced by cells that can alter its chemical composition in specific ways, depending on the local population. But once produced, extra cellular matrix affects the cells that have created it. Extra cellular matrix controls the at-
tachment, mobility, shape and – in subtle ways – the metabolism of cells. Cells and intracellular matrix become extensively interdependent as structurally and functionally integrated parts at a higher level of biologic organisation characteristic for tissues and organs in multicellular organism.

DEGENERATIVE PROCESSES OF JOINTS AND THE CONNECTIVE TISSUE FROM THE POINT OF VIEW OF THE ACADEMIC MEDICINE

It appears that as some people age, they lose the ability to produce sufficient levels of glucosamine. The result is that their cartilage loses its ability to act as a shock absorber. The weight-bearing joints, like the knees, hips, and joints of the hands are the most often affected with osteoarthritis. In affected joints, there is much cartilage destruction followed by the hardening and the formation of large bone spurs (exostoses) in the joint margins. Generally there are no characteristic signs of inflammation. Special symptoms may vary depending on the affected joint. Pain, deformity, and limitation of motion in the joints results.

The onset of osteoarthritis (OA) can be very subtle – morning joint stiffness is often the first symptom. As the disease progresses, there is pain on motion of the involved joint that is worsened by prolonged activity and relieved by rest. Generally there are no characteristic signs of inflammation. Special symptoms may vary depending on the affected joint. Pain, deformity, and limitation of motion in the joints results.

DEGENERATIVE PROCESSES OF JOINTS AND THE CONNECTIVE TISSUE ACCORDING TO THE TEACHINGS OF NATUROPATHIC MEDICINE

Naturopathy has a different view upon the factors triggering the problem. As in case of other civilization diseases, deterioration of connective tissues and locomotor organs are considered to be triggered mainly by improper diet, sedentary lifestyle, continuous, chronic stressful way of life, and more importantly, by pessimistic, anxious, or depressive state of mind. Connective tissues are a huge storehouse of non-eliminated, metabolic waste products, which are – on the long run – harmful substances. Connective tissue can for a while compensate for the non-equilibrium of homeostasis and metabolic disturbances, but finally it gets wearied out and ill itself. This is the point where “unexpectedly” locomotor disorders and deformations come into the picture. This can be the explanation why the development of osteoarthritis (OA) often happens unnoticed. In the majority of cases, the first symptom is stiffness of joints in the morning. As the disease advances, the moving of the joint in question becomes painful, which worsens when moved continuously, and alleviates in rest.

Contributing factors accelerating the development of clogging of the ground substance of the connective tissue with non-eliminated metabolic waste products include: constipation, stagnation of blood and lymphatic fluid (lymphostasis), and lack of blood supply to the muscles, tendons and joints, as well. Unhealthy (poor diet) high in meat, white flour and sugar products as well as stress can be a predisposing factor for the development of arthrosis (rheuma). Arthritis, in general, also could be caused by infection, autoimmune disorders (psoriasis for example), and venereal diseases. Allergies and intolerance to certain food can potentate the symptoms of arthritis especially vegetables from the nightshade family. These are potatoes, green peppers (paprika), tomatoes, eggplant and also, tobacco. They all interfere with collagen repair.

Arthritis is also characterised with calcium deposition in the joints. The same aetiology is responsible for the loss of calcium from the matrix of the bones. Because of the excess of calcium, the synovial fluid turns unstable and calcium settles in the joints. Another theory also tries to explain the role of emotions as contributing factors in the development of arthritis. Deep seated repressed emotions, including inflexibility in our lives, resentments, fear, anger, hatred and negative thoughts of all kind can influence very unfavourable general and local metabolic processes creating a predisposing sequence of events leading to arthritic changes.

Stress causes the destruction of protein which is necessary for cartilage repair.
The Stress & Collagen, Elastin Connection

- Collagen and elastin are the major structural proteins of the skin, muscles and blood vessels. Elevated levels of cortisol catabolise these proteins faster than the body can replace them. The skin, muscles and the blood vessels lose their tone and elasticity.
- Stress ages the organism prematurely (appearance of wrinkles, stretch marks - stria, blue spider naevus venules, and purple patches – purpura in the skin). Weakened blood vessel walls are prone to leaking water and plasma proteins into the tissues, causing fluid retention (interstitial oedema formation).
- Vitamins -C, -A, and -B6, as well as minerals zinc, manganese and silica are the principal nutrients needed for collagen and elastin synthesis. They always should be supplemented during times of stress, but they can be fully effective only together with a complete multivitamin-mineral formula.
- The chronic distress (prolonged stress) results in elevated levels of cortisol within the plasma and white blood cells. The cortisol suppresses their normal function and predisposes the body to infections, and on the long run, also to allergies. Normal, resting levels of cortisol do not have this effect.

Stress also prevents allergy to cure!

Collagen, inflammation, wound healing

Collagen is the most abundant protein in the body and is the material of tissue repair. It is present in skin, bones, teeth, blood vessels, tendons, cartilage and connective tissue.

Collagen is produced in fibroblasts as a polypeptide of repeating sequences of the amino acids: glycine, proline, hydroxyproline, lysine, and hydroxylysine.

Proline and lysine are enzymatically hydroxylated after the polypeptide chain is synthesized, and their hydroxylation is absolutely necessary for collagen polymerization and function. Co-factors that are necessary for hydroxylation include: iron, ascorbic acid (vitamin C), alpha-ketoglutarate (from the Krebs cycle), and molecular oxygen (O₂). Absence of these cofactors results in incomplete wound healing.

Immature collagen, termed procollagen, is secreted by the fibroblasts as a complex of three polypeptide chains cross linked by intermolecular bonds. Procollagen must be activated further by the removal of a small polypeptide sequence catalysed by a specific protease. As the scar tissue matures, collagen molecules are cross linked by intra molecular bonds to form collagen fibrils. Cross linking involves the formation of covalent bonds between lysine residues. At this point the secreted collagen molecules are still of a gel – like consistency in the wound. With further cross linking the fibrils form fibres. This process takes several months. The collagen is initially deposited randomly, but during remodelling of the scar tissue formed, the fibres are dissolved by enzyme collagenase and re-formed (remodelled). During this period, the fibres re-orient along the lines of mechanical stress and further cross-linking adds strength.

Wound contraction is the final process of the reconstructive phase of healing. It is necessary for closure of all wounds, but especially those that heal by secondary intention (Serbian -sekundarno granulaciono tkivo). Contraction is noticeable 6 to 12 days after injury. In normal healing, contraction may account to inward movement of the wound edge by approximately 0.5 mm/day.

Atherosclerosis

Atherosclerosis and its complications have reached epidemic proportions throughout the Western world. Heart disease alone accounts for 36 per cent of all deaths and strokes, another complication of atherosclerosis is responsible for at least 43 per cent of all deaths in the Western countries. Because atherosclerosis is largely a disease of diet and lifestyle, many of these deaths could be significantly delayed through a healthier diet and lifestyle.

Arterial Structure

An artery is divided into three major layers:

- Intima – represents the endothelium (internal lining of the artery) and consists of a layer of endothelial cells. Glycosaminoglycans (GAGs) are naturally present on the vessel surface, where they protect the endothelial cells from damage and pro-
mote their repair. Beneath the surface of cells lays the internal elastic membrane composed of a layer of GAGs and other ground substance compounds. It provides support to the endothelial cells and separates the endothelium from the smooth muscle layer.

- **Media** – consist primarily of smooth muscle cells. Interposed among the cells are GAGs and other ground substance structures that provide support and elasticity to the artery.
- **Adventitia** – external elastic membrane consists primarily of connective tissue, and provides structural support and elasticity to the artery.

### Development of Atherosclerosis

No single theory of the development of atherosclerosis that has been formulated so far satisfies all investigators. However, the most widely accepted explanation theorises, that the lesions of atherosclerosis are initiated in response to injury of the endothelial cells, lining the inner surface of the artery, the arterial endothelium. More detailed progression of the atherosclerotic process is as follows:

1. The initial step in the development of atherosclerosis is damage to the endothelium by free radicals. Immune, physical, mechanical, viral, chemical and drug induced changes all can cause damage that can lead to plaque development.
2. Once the endothelium has been damaged, sites of injury become more permeable to plasma constituents, especially lipoproteins (fat-carrying proteins). The binding of lipoproteins to glycosaminoglycans leads to a breakdown in the integrity of the ground substance matrix and causes an increased affinity for cholesterol. Injury to endothelium induces it to secrete growth factor(s), or cause platelets to adhere. Monocytes (large mononuclear macro phagocytic white blood cells) and platelets adhere to the damaged area, where they release growth factors that stimulate smooth muscle cells to migrate from media into the intima and replicate.
3. The local concentration of lipoproteins, monocytes, and platelets leads to the migration of smooth muscle cells from the media into the intima, where they undergo proliferation. The smooth muscle cells dump cellular debris into the intima, leading to further development of plaque (atheroma).
4. The formation of a fibrous cap (consisting of collagen, elastin, and glycosaminoglycans) over the intimal surface occurs. Neutral fat and cholesterol deposits accumulate.
5. The plaque continues to grow until eventually it blocks the artery. Blockage is usually around 90 per cent before symptoms of atherosclerosis – i.e., local ischemia and consequent hypoxia – are apparent.
6. Alternatively, the endothelium may remain intact, but growth factors secreted by smooth muscle and endothelial cells continue to enlarge the plaque.

### Arterial Disorders

Aortic and arterial glycosaminoglycans (GAGs) are essential for maintaining arterial health. In addition, arterial GAGs have many important effects that interfere with the progression of atherosclerosis, including preventing damage to the surface of the artery, formation of damaging blood clots, migration of smooth muscle cells into the intima, and formation of fat and cholesterol deposits. They also lower total cholesterol levels while raising HDL cholesterol.

Symptoms of cerebral vascular insufficiency can induce short-term memory loss, vertigo, headache, ringing in the ears, and depression. These symptoms are often referred to as “symptoms of ageing” and represent almost entirely a reduced supply of blood and oxygen to the brain because of atherosclerosis. Symptoms of peripheral vascular disease can include coldness of hands or feet, pain, muscle cramps, and impotence (in males).

### Venous Disorders

Veins are fairly frail structures. Defects in the wall of veins lead to venous-dilation and damage to the valves. When the valves become incompetent and damaged the increased pressure results in bulging veins known as varicose veins. Varicose veins affect nearly 50 per cent of middle-aged adults. The veins just under the skin of the legs are the veins most commonly affected because of the tremendous strain standing have on these veins. When an individual stands for prolonged
periods of time, the pressure exerted against the vein can increase up to ten times. Hence, individuals with occupations that require long periods of standing are at greatest risk for developing varicose veins.

Women are affected about four times as frequently as men; obese individuals have a much greater risk; and the risk increases with age because of loss of tissue tone, loss of muscle mass, and weakening of the venous walls. Pregnancy may also lead to the development of varicose veins because pregnancy increases venous pressure in the legs.

Several theories exist to explain the cause of varicose veins:

- Genetic weakness of the veins or venous valves
- Excessive venous pressure because of a low-fibre-induced increase in abdominal pressure during defecation
- Long periods of standing and/or heavy lifting
- Damage to the vascular walls because of either abnormalities in the proteoglycans of the connective tissue or excessive release of cellular enzymes that break down the ground substance, resulting in increased capillary permeability and loss of integrity of the venous structure

Cellulite is the so-called “gellosis” of the subcutaneous connective tissue. The skin covering the affected area - especially when it is squeezed with fingers acting “pincer-like” - looks like the outer surface of an orange. It shows as lumps, bumps or dimple deposits on the hips, thighs and buttocks. Cellulite is predominantly found in women, who produce extra oestrogen. When the liver cannot excrete the oestrogen properly, it encourages water and fat build-up within the subcutaneous connective tissue, which starts behaving “jelly-like”.

The causes of cellulite are multifactorial. Simply stated, cellulite is a sign of the unhealthy life-style, due to stressful activities day by day, lack of exercise and poor circulation, too much starches and sweets, and the wrong kind of fats. In the majority of cases there is also an underactive bowel created by poor nutrition (“junk food”) and elimination which is incomplete removal of waste products from the colon. Poor lymphatic drainage can be a problem and exercise will help. Fat trapped between the cells where they are held by hardened connective tissue and where they collect toxins and pockets of water, give the skin the orange appearance.

A lasting approach to eliminating cellulite consists of a matter of changing life style, keeping the colon functioning properly and eating lots of raw fruits and vegetables. Cellulite is very hard to eliminate, but with desire and determination, it can be done. JointProteX can be an additional help in solving this really unpleasant problem.

What can we do then for ourselves, if the disease has already developed, or if we would like to prevent it?

The JointProteX, the new product of Cali-Vita offers effective help in preserving and/or regaining the health of connective tissues. It contains substances which are normally not included in our diet, or only in insufficient amounts.

Components of JointProteX

<table>
<thead>
<tr>
<th>Component</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucosamine HCl (shellfish)</td>
<td>250 mg</td>
</tr>
<tr>
<td>Chondroitin sulphate</td>
<td>200 mg</td>
</tr>
<tr>
<td>Methyl-sulphonyl-methane (MSM)</td>
<td>150 mg</td>
</tr>
<tr>
<td>Glycosaminoglycan</td>
<td>150 mg</td>
</tr>
<tr>
<td>Hyaluronic acid (complex)</td>
<td>50 mg</td>
</tr>
<tr>
<td>Cetyl myristoleate (CMT)</td>
<td>50 mg</td>
</tr>
<tr>
<td>Boswellia serrata extract (25%)</td>
<td>50 mg</td>
</tr>
<tr>
<td>Filipendula ulmaria (meadowsweet)</td>
<td>40 mg</td>
</tr>
<tr>
<td>Turmeric extract (95%)</td>
<td>10 mg</td>
</tr>
<tr>
<td>Zinc (gluconate)</td>
<td>5 mg</td>
</tr>
<tr>
<td>Manganese (gluconate)</td>
<td>1 mg</td>
</tr>
</tbody>
</table>

Directions: Take 3×1 tablet daily with meals or as directed.

JointProteX contains significant amounts of glucosamine, chondroitin sulphate, methyl-sulphonylmethan (MSM), glycosaminoglycan, hyaluronic acid complex, cetyl myristoleate (CMT), boswellic-acid extract from boswellia serrata, meadowsweet (Filipendula ulmaria), as well as 95% of turmeric extract, zinc and manganese.
GLUCOSAMINE

The body manufactures glucosamine, a simple compound composed of one glucose and an amine molecule (amine = NH₂, a nitrogen and two hydrogen atoms). Its physiological function on joints is to stimulate the synthesis of glycosaminoglycans (GAGs), which are key structural components of cartilage. Glucosamine also promotes the incorporation of sulphur into cartilage. Because of this effect, glucosamine sulphate may be the best source of glucosamine. There are no food sources of glucosamine. Commercially available sources of glucosamine are derived from chitin, the specially processed exoskeleton of shrimp, shellfish lobsters, and crabs.

The inability to produce glucosamine may be the major factor leading to osteoarthritis (OA), the most common form of arthritis (also known as degenerative joint disease or rheumatic disorder). This link led researchers in Europe to ask an important question: What would happen if individuals with osteoarthritis took glucosamine? The results were astonishing.

Available forms

Glucosamine is available as glucosamine sulphate, glucosamine hydrochloride, and N-acetyl-glucosamine (NAG). Detailed human studies on the absorption, distribution, and elimination of orally administered glucosamine sulphate show an absorption rate as high as 98 per cent. Once absorbed, it then travels primarily to joint tissues, where it is incorporated into the connective tissue matrix of cartilage, ligaments, and tendons. In addition, there are impressive clinical studies on thousands of patients.

Studies on laboratory animals offer further evidence of the superiority of glucosamine sulphate over NAG (N-acetyl-glucosamine). Over years, numerous researchers have repeatedly demonstrated that glucosamine is superior to NAG in terms of absorption, and utilisation by at least a factor of two to one. These researchers have concluded that „glucosamine is a more efficient precursor of macromolecular hexosamine (glycosaminoglycans), than N-acetyl-glucosamine. It is possible that N-acetyl-glucosamine does not penetrate the cell membranes and, as a result, it is not available for incorporation into glycoproteins and mucopolysaccharides”. This preference is exhibited by the fact that the absorption of glucosamine sulphate is an active process. In other words, there are mechanisms in the body that are designed specifically for the absorption and utilisation of glucosamine sulphate.

Principal uses

The primary use of glucosamine is the treatment of osteoarthritis (OA) (other terms: degenerative osteoarthritis, „chronic rheumatism”). Osteoarthritis, or degenerative joint disease, is the most common form of arthritis. It is seen primarily, but not exclusively, in the elderly. Surveys indicate that over 40 million Americans have osteoarthritis, including 80 per cent of persons over 50. Under 45, osteoarthritis is much more common in men; after 45, it is ten times more common in women than men.

The weight-bearing joints, like the knees, hips, and joints of the hands are the most often affected with osteoarthritis. In affected joints, there is much cartilage destruction followed by the hardening and the formation of large bone spurs (exostoses) in the joint margins. Pain, deformity, and limitation of motion in the joints results. Inflammation is usually minimal.

The onset of osteoarthritis can be very subtle – morning joint stiffness is often the first symptom. As the disease progresses, there is pain on motion of the involved joint that is worsened by prolonged activity and relieved by rest. There are usually no signs of inflammation.

Glucosamine is a safe and effective natural alternative to aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs). Clinical and experimental research indicates that current drugs used in osteoarthritis treatment may be producing short-term benefit but on the long-run are actually accelerating the progression of joint destruction. The first drug generally used in the treatment of osteoarthritis is aspirin. It is often quite effective in relieving both the pain and inflammation and is relatively inexpensive. However, since the therapeutic dose required is relatively high (2 to 4 grams per day), toxicity often occurs. Tinnitus (ringing in the ears), and gastric irritation are early manifestations of toxicity.

Other non-steroidal anti-inflammatory drugs (NSAIDs) are often used, especially when aspirin is ineffective or intolerable. Representative of this
class of drugs are ibuprofen (Motrin), fenoprofen (Nalfon), indomethacin (Indocin), naproxen (Naprosyn), tolmetin (Tolectin), and sulindac (Clinoril). These drugs are also associated with side effects that include gastrointestinal upset, headaches, and dizziness, and are therefore recommended only for short periods of time.

One side effect of aspirin and other NSAIDs often not mentioned is their inhibition of cartilage repair and acceleration of cartilage destruction. Since osteoarthritis is caused by a degeneration of cartilage, NSAIDs possibly worsen the condition by inhibiting cartilage formation and accelerating cartilage destruction even though they are fairly effective in suppressing the symptoms. This has been upheld in clinical studies that show NSAIDs use is associated with acceleration of osteoarthritis and increased joint destruction.

Simply stated, aspirin and other NSAIDs appear to suppress the symptoms but accelerate the progression of osteoarthritis. Their use should be avoided.

Clinical trials with Glucosamine sulphate and other forms of glucosamine

Numerous double – blind studies have shown glucosamine sulphate produces much better results than NSAIDs and placebo in relieving the pain and inflammation of osteoarthritis despite the fact that it exhibits very little direct anti-inflammatory effect and no direct analgesic or pain-relieving (pain-killer) effects. While NSAIDs offer purely symptomatic relief and may actually promote the disease process, glucosamine sulphate appears to address the cause of osteoarthritis. By getting at the root of the problem, glucosamine sulphate not only improves the symptoms – including pain- but also helps the body repair its own damaged joints. This effect is outstanding, especially in light of glucosamine’s safety and lack of any side effect.

The beneficial results with glucosamine are more obvious the longer it is used. Because it is not an anti-inflammatory or pain-relieving drug per se, it takes a while longer than NSAIDs to produce results. But once it starts working, it produces much better results. For example, in one study that compared glucosamine sulphate to ibuprofen, pain scores decreased faster in the first 2 weeks in the ibuprofen group; however, by week 4 the group receiving the glucosamine sulphate was doing significantly better than the ibuprofen group. Physicians rating the overall response as good or fair rated 44 per cent of the glucosamine sulphate-treated patients as good compared to only 15 per cent of the ibuprofen group.

In addition to showing benefit in double-blind studies, oral glucosamine sulphate offered significant benefit in an open trial involving 252 doctors and 1,506 patients in Portugal. This large study provides valuable clinical information on the appropriate use of glucosamine sulphate. The patients received 500 miligrams of glucosamine sulphate three times daily over a period of 50 days. The results were analysed and showed that the symptoms of pain at rest, on standing, on exercise, and on limited active and passive movements improved steadily throughout the treatment period. Objective therapeutic efficacy was rated as „good” in 59 per cent of the patients and „sufficient” in a further 36 per cent. Therefore, a total of 95 per cent of the patients achieved benefit from glucosamine sulphate. The results with glucosamine sulphate were rated by both doctors and patients as being significantly better than those obtained with previous treatment, including NSAIDs, vitamin therapy, and cartilage extracts. Glucosamine sulphate produced good benefit in a significant portion of patients who had not responded to any other medical treatment.

In the study, obesity was associated with a significant shift from good to fair. This finding may indicate that higher dosages may be required for obese individuals or that oral glucosamine is not enough to counteract the stress of obesity on the joints. Patients with peptic ulcers and individuals taking diuretics were also associated with a shift from good to sufficient in efficacy and tolerance. Individuals taking diuretics may need to increase the dosage to compensate for the reduced effectiveness.

The improvement with glucosamine lasted for a period of 6 to 12 weeks after the end of treatment. This result indicates that glucosamine may have to be taken for long periods of time or in repeated short-term courses. Given the safety and excellent tolerability of glucosamine, it is suitable for long-term, continuous use.

Interestingly, the amino sugar glucosamine, prescribed in combination with chondroitin and
now being used by so many arthritis sufferers, specifically binds wheat germ lectin.

Researchers observed that wheat germ agglutinin (WGA) dramatically enhanced the activity of membrane-bound maltase— an enzyme that helps to break down complex sugars into simple sugars in the small intestine. Under the same conditions, aminopeptidase – an enzyme that breaks down polypeptides into amino acids – was inhibited by wheat germ lectin.

Lectins activate autoantibodies in inflammatory and autoimmune diseases. Almost everyone has antibodies to dietary lectins in their bloodstream. Some of these have been linked to immune damage to the kidneys in patients with nephropathy (a kidney disease). It has been suggested that the antibody produced in rheumatoid arthritis may in fact require activation by wheat germ lectin.

Dr Peter D’Adamo the author of the book titled: “Live Right For (4) Your Type” (blood type) believes that many cases of fibromyalgia, a common, painful inflammatory disorder of the muscle tissue, may in fact stem from intolerance to wheat. Fibromyalgia sufferers might try avoiding wheat products for a period of time, to discover whether or not it has any positive effects on their condition. Interestingly, the amino sugar glucosamine, prescribed in combination with chondroitin and now being used by so many arthritis sufferers specifically binds wheat germ lectin.

Safety issues
Glucosamine has an excellent safety record in animal and human studies. Based on these studies, many experts recommend that glucosamine sulphate „be considered as a drug of choice for prolonged oral treatment of rheumatic disorders.”

Side effects, when they do appear, are generally limited to light or moderate gastrointestinal symptoms, including stomach upset, heartburn, diarrhoea, nausea, and indigestion. If these symptoms occur, try taking the glucosamine sulphate during a meal. The sulphate form of sulphur is present in relatively high concentrations in human blood. In short, glucosamine sulphate is extremely well tolerated, and no allergic reactions have been reported.

Interactions
Individuals taking diuretics may need to take higher dosages (20 milligrams per kilogram body weight daily).

Beneficial effects
Glucosamine sulphate’s beneficial effects are straightforward – it stimulates the manufacture of substances necessary for proper joint function and is responsible for stimulating joint repair.

CHONDROITIN

Chondroitin, which is found in high concentration in the gristle around the joints of animals, draws fluid to the cells in the joint; that fluid provides lubrication and helps bone glide smoothly with each movement. In addition, chondroitin works with glucosamine (sulphate) to replenish collagen and other components that provide the building blocks for cartilage. Several clinical studies, clearly showed that when arthritic patients were given chondroitin sulphates they not only experienced significant relief in pain and an increase in mobility but felt positive effects long after they discontinued taking the chondroitin. This is good evidence that the treatment did not simply mask the pain but actually helped to restore lost cartilage.

Possible benefits:
• reduces arthritic pain.
• regrows cartilage.

GLYCOSAMINOGLYCANs

Glycosaminoglycans provide the skeletal framework of the vein and are therefore essential in maintaining the structure and integrity of veins. Without proper structural support, veins lose their shape and become bulging and unsightly. Individuals with poor venous function of the legs typically experience such symptoms as a sense of heaviness in the legs, tingling sensations, fluid retention, itching, and painful cramps. These symptoms are improved with GAGs because of its ability to improve the structure and function of the vein, thereby allowing improved blood flow.

On a final note, two double-blind studies compared aortic GAGs (72 milligrams per day) to fla-
vonoid extracts, hydroxyl-ethyl-rutosides (1,000 milligrams per day), and bilberry extract (320 milligrams per day), in the treatment of haemorrhoids and varicose veins. The GAGs produced far better results. In fact, in the study examining haemorrhoids the authors suggested that it should be used as the “drug of first choice” in the non-surgical treatment of acute haemorrhoidal pain and disease.

**Principal Uses**

Glycosaminoglycans (GAGs) may be useful in enhancing the function, structure, and integrity of arteries and veins. GAGs have many important effects that interfere with the progression of atherosclerosis, including prevention of damage to the inner surface (coating) of the artery, formation of damaging blood clots, migration of smooth muscle cells into the intima, and formation of fat and cholesterol deposits. They also lower total cholesterol levels while raising HDL-cholesterol.

Glycosaminoglycans (GAGs), dermatan sulphate, heparin sulphate, hyaluronic acid, chondroitin sulphate, and related hexosaminoglycans act simultaneously and in a synergistic fashion. Beneficial effects in the treatment of atherosclerosis have been noted when using composite formulas containing the above listed compounds.

**CETYL MYRISTOLEATE (CM)**

*Cetyl myristoleate (CM)* is a relatively new compound used in natural treatment for arthritis. It is getting good reviews by users, although there are only a few clinical studies of it. Cetyl myristoleate (CM) was discovered in the 1970s by Harry W. Diehl, a researcher at the National Institute of Arthritis, Metabolic and Digestive Diseases, who was reportedly seeking an effective treatment for a friend who suffered from a particularly debilitating case of arthritis. Diehl noticed that one breed of mouse used in the laboratory – the Swiss albino mouse – did not get arthritis even when it was exposed to a particular micro organism that normally causes arthritis in animals. Diehl suspected that the Swiss albino mice had some kind of inborn protection – an arthritic protective factor – which prevented them from developing arthritis. He hoped that if he identified a mysterious anti arthritic substance it would also work on humans.

Diehl eventually isolated Cetyl myristoleate (CM), a fatty acid that occurs in small amounts in foods such as nuts, vegetables, and butter and in many different species of animals. Swiss albino mice have unusually high levels of this fatty acid. In a fascinating experiment, Diehl tested CM on laboratory rats that he injected with Freud’s adjuvant, an arthritis-causing agent. Two groups of rats were injected with the arthritis-causing agent, but one group was also given CM. Predictably, the group that did not receive the CM developed arthritis, but amazingly, the group that was given CM remained arthritis free.

Since Cetyl myristoleate (CM) is non-toxic, Diehl gave it to family members and friends with arthritis who found that it worked well in controlling their arthritic symptoms. In 1991, Diehl developed a commercial brand of CM for osteoarthritis, sold primarily through mail order. Other brands of CM are now being brought to the market. As of this writing, there are no double blind clinical studies of CM, and most of the positive reports of it are purely anecdotal. Even its most ardent proponents admit that it does not work for everyone, but, then again, neither does any arthritic treatment. Typically, arthritis sufferers have to try several different treatments until they find one that works for them. The *JointProtex formula* also contains Cetyl myristoleate (CM), in order to fortify (in synergical fashion) the beneficial joint protecting and regenerating actions of other components included in the formula.

**BOSWELLIA SERRATA – INDIAN FRANKINCENSE**

Boswellia serrata, also known as Sallai Gugal, is closely related to Frankincense (Boswellia glabra) one of the gifts brought by the Wise Men to celebrate the birth of Jesus. *Boswellia serrata*, which is endemic in Western India, has attracted a lot of attention lately in the medical community world wide because it possesses a strong anti-inflammatory action that is just as efficacious as most non steroidal anti inflammatory drugs (NSAIDs) used in the treatment of osteoarthritic disorders, but without their unpleasant side effects.
Active Compounds: The gum oleoresin consists of essential oils, gum and terpenoids. The terpenoid portion contains the **boswellic acids (BAs)** that have been shown to be the active constituents in boswellia or guggal. Today, extracts are typically standardized to contain at least 37.5 to 65% of boswellic acids.

Research conducted in India found that an extract of Boswellia was more beneficial, less toxic, and more potent than the standard drug of choice for rheumatic disorders, Ketoprofen (**benzoyl hydrotropic acid**). Ketoprofen is preferred over other anti-inflammatory drugs such as indomethacin, phenylbutazone or acetylsalicylic acid. **Boswellic acids (BAs)** are believed to suppress tissue proliferator found in the inflamed areas and, also prevents the breakdown of connective tissue. Boswellia inhibits leukotriene synthesis in vitro by inhibiting 5-lipoxygenase activity both in rat neutrophils and human platelets.

The mechanism is similar to the action of non-steroidal groups of anti-arthritis drugs with no side effects, such as, gastric irritation and ulcerogenic activity. A purified compound of the Boswellia is marketed in India with the brand name “Sallaki”. Many studies conducted since the original study has confirmed that Boswellia serrata has potent anti-inflammatory and anti-arthritis activity. Boswellia was found to improve blood supply to the joints and restore integrity of vessels weakened by spasm. Boswellia Serrata may also be useful for the treatment of rheumatoid arthritis with no side effects as those seen with traditional drugs. Boswellia is used extensively in Ayurveda to reduce the symptoms of arthritis.

**Boswellia is used for:**
- Bursitis
- Osteoarthritis
- Rheumatoid arthritis

Boswellia was found to improve blood supply to the joints and restore integrity of vessels weakened by spasm.

Boswellia serrata may also be useful for the treatment of rheumatoid arthritis with no side effects from the traditional drugs of choice.

A single-blinded, randomized, placebo-controlled study demonstrated improvement in pain and disability in OA using a formula that contained boswellia, withania, curcuma, and a zinc complex. Two randomized, controlled trials have assessed the effect on OA using multiple plant-based formulations, including boswellia as a single agent. One study revealed significant improvement in symptomatic OA and one did not. No prospective, clinical studies using boswellia as a single agent have been performed in patients with OA. Interestingly, boswellia has been commonly used as an anti-inflammatory agent for arthritis, asthma, and ulcerative colitis in Ayurvedic medicine. According to studies conducted in India, boswellia can lower high blood levels of cholesterol and triglyceride, two risk factors for heart disease and stroke.

Due to its beneficial actions, Boswellia serrata is also included in Joint ProteX formula.

**MEADOWSWEET (LAT. FILIPENDULA ULMARIA; SPIREA ULMARIA)**

**Meadowsweet** is used in colds, flu, chronic gastritis, rheumatoid arthritis and inflammation of the nerves, muscles and skin. Part of the anti-inflammatory activity appears to be due to its ability to inhibit complement activation and T-cell proliferation and interfere with reactive oxygen species (ROS) or ROS production by polymorphonuclear (PMN )granulocytes confirmed by in vitro studies. Due to the small amounts of salicylates in the herb, it is unknown if they contribute to the anti-inflammatory activity. It contains flavonoids like **spiraeoside and other quercetin and kaempferol** derivatives, essential oils composed of salicylaldehyde, methyl salicylate, anisaldehyde, benzyl alcohol and phenylethyl alcohol. It also contains significant amounts of **silicic acid** whose silicon contents are indispensable in the development of a healthy connective tissue.

**Contraindications:** Meadowsweet may cause allergic hypersensitivity in persons sensitive to salicylates.

**METHYLSULPHONYLMETHANE (MSM)**

About 2000 years ago, **Hippocrates**, known as the father of modern medicine, used sulphur fumes from garlic to treat many different dis-
eases, including cancer. Sulphur, a non-metallic mineral, is found in virtually every cell of the body and is essential for nearly every bodily function. Only recently have we begun to rediscover the power of sulphur, particularly one form of organic sulphur: Methylsulphonylmethane (MSM), which is easily absorbed by the body.

*Methylsulphonylmethane (MSM)* is a sulphur-containing organic compound which plays an important role in the synthesis of the proteins in connective tissue, as it *donates sulphur* (acts as a sulphur-donor) for the protein synthesis of the connective tissues. In lack of MSM some amino acids are unable to integrate into the complex protein molecule of connective tissue, and the resulting substance of connective tissue will be unstable, and inadequately structured.

MSM is found in plants, meat, eggs, poultry, and dairy foods. It is used by the body to make important enzymes, antibodies, glutathione (the body’s main antioxidant), and connective tissue, such as cartilage, collagen, hair, nails, and skin. MSM is critical for the production of amino acids, the building blocks that form protein. Without MSM and other sulphur compounds, protein cannot hold its molecular structure. It is difficult to get enough MSM through food, however, since it is often destroyed during processing. On the basis of numerous studies conducted on the role of MSM in the body, it has been implicated that even a mild MSM deficiency can contribute to many medical problems, either directly or indirectly.

MSM is an effective treatment for arthritis, which is caused by the wearing away cartilage, the substance that cushions bones. The effectiveness of MSM is enhanced by one other sulphur containing compound, *glucosamine*, which has recently been touted as the “arthritis cure”; the two “sulphur sisters” work especially well together. People report that the supplements can significantly reduce the pain, stiffness, and tenderness typical of arthritis.

MSM is also important for wound healing: It promotes the formation of collagen, which helps produce new skin. People who take MSM also report that it can strengthen their hair and nails and is especially good for brittle, peeling nails. It makes hair thicker and shinier.

Several studies have documented the potential of MSM as a treatment for a wide variety of ailments. MSM is particularly effective in relieving severe allergic symptoms and asthma. MSM is recommended along with vitamin C and other bioflavonoids to several allergy sufferers, and the results have been nothing short of amazing. Within two weeks, the annoying symptoms, such as runny nose and watery eyes, simply disappeared, even at the height of hay fever season.

**Possible benefits:**
- relieves pain and inflammation from arthritis.
- promotes wound healing.
- reduce allergic symptoms.

**TURMERIC (CURCUMIN) (LAT. CURCUMA LONGA)**

*Curcuma longa* is a perennial plant whose rhizome has long been used for medicinal purposes and as a colouring agent for foods. The powder called *turmeric*, contains *curcumin* — a polyphenol composed of two *ferulic acid* molecules linked together, chemically termed *diferuloylmethane*. Turmeric contains two curcumin derivatives. The therapeutic uses of curcumin, are very similar to those of many flavonoids, *cyanidin* included. In an experimental study (published in the Journal of the American College of Nutrition) administration of curcumin prevented cancer development in the 68% of the treated animals. Curcumin is a potent anticancer compound which can retard cancer at both the initiation and promotion phases — just like cyanidin and many other bioflavonoids. Moreover curcumin shares many of the same mechanisms of action, namely the antioxidative effects, stimulation of drug-metabolising enzymes like the glutathione-S-transferases, and it also contributes to the increased levels of glutathione in the liver and other tissues.

Curcumin has well documented anti-inflammatory effects in a variety of animal models. Two main mechanisms of action are inhibition of lipoxygenase activity (the generation of leucotrienes) and a strong antioxidative effect. Not surprisingly, cyanidin and many other bioflavonoids exhibit, also powerful anti-inflammatory activity with identical mechanisms of action. Two double-blind, clinical trials of curcumin supplements (in arthritis and postoperative inflammation) docu-
mented its therapeutic usefulness. The doses used were 120 and 1,200 mg/day/person.

The list of medical applications common to curcumin and flavonoids is a long one, and includes: protection against chemically induced liver damage, improvement in the lipid profile of blood, reduction in the extent of platelet aggregation, antimicrobial effects, and immune stimulation.

Turmeric, known as the “spice of life” is also widely used in Indian cooking. One of its active principles curcumin is a potent antioxidant. Therefore today, curcumin is included in many herbal formulas designed to relieve rheumatoid arthritis. In double-blind studies with arthritis patients, curcumin produced significant improvement comparable with phenylbutazone, a prescription nonsteroidal anti-inflammatory drug (NSAID), but without the known side effects of the latter one. Turmeric, a long-time folk remedy for liver disorders, can reduce inflammation in the liver and strengthen liver function, and has also been used as an effective treatment for gallbladder disease.

Curcumin does lower the levels of intestinal toxins. Curcumin is a chemoprotective, especially for non-secretors (blood sub-type). Curcumin is also a potent inhibitor of polyamine synthesis. It is usable by all blood types. Turmeric has many beneficial properties. It contains powerful antioxidant, anti-carcinogenic, and anti-inflammatory compounds, decreases ornithine decarboxylase (ODC) activity, promotes gastric integrity, increases mucin production, offers gastro-protective effects, promotes secretion of digestive enzymes, and improves liver function.

Because of its multifaceted actions turmeric has also been included into JointProteX formula.

MANGANESE

Manganese is an essential micro mineral in every species studied. The “Estimated Safe And Adequate Daily Dietary Intake” of manganese has been set at 2-5 mg per day for adults. Whole grains and cereal products are the richest dietary sources of manganese. Fruits and vegetables contain moderate amounts, whereas dairy products, meat, fish, and poultry are poor sources of this mineral. Green tea is exceptionally rich in manganese.

Manganese deficiency symptoms in animals include: poor reproductive performance, growth retardation, congenital malformations in the offspring, abnormal formation of bone and cartilage, and impaired glucose tolerance. Manganese deficiency has not been observed in humans, save for a single case report.

Biological Effects

Human body needs manganese for proper formation of bone and cartilage, for normal glucose metabolism, and as a part of the endogenous antioxidant superoxide dismutase (SOD). Manganese is an essential component of two mitochondrial enzymes: super oxide dismutase (SOD) and pyruvate carboxylase (PC). The former is used to detoxify oxygen radicals, while the latter is a key enzyme in gluconeogenesis (the resynthesis of glucose in the body). In addition, several enzymes are non-specifically activated by manganese. Minute quantities of manganese are needed for protein and fat metabolism, healthy nerves, healthy immune system and blood sugar regulation. It aids in the utilisation of glucose in the peripheral tissues. Therefore, it is necessary for energy production. Manganese is essential for iron-deficient anaemics and is also needed for the utilisation of thiamine (vitamin B1) and tocopherol (vitamin E). Manganese works well with the B-complex vitamins to give an overall feeling of well-being. It is found in many enzymes in the body. Manganese is a key element in the production of enzymes needed to oxidise fats and metabolise purines. This is a trace mineral essential for the proper function of the pituitary gland as well as the healthy function of all the body’s glands. It also helps in reproduction and in normal functioning of the central nervous system.

Clinical Applications

Supplemental manganese has not been well studied with respect to clinical applications. Some evidence exists suggesting that manganese deficiency impairs glucose homeostasis by decreasing gluconeogenesis. Moreover, recent findings indicate that manganese deficiency reduces the number of insulin receptors in adipose (fat) cells, and hence impairs glucose transport and metabolism in peripheral tissues. Finally, several stud-
ies in animals have reported that supplemental manganese enhanced certain aspects of cellular and humoral immunity. The amount needed by humans is uncertain. The RDA (Recommended Daily Allowance) handbook recommends a provisional daily intake of 2.5-5.0 milligrams (mg).

Because of their greater bone and soft tissue turnover and their higher metabolism of glucose, athletes (and individuals physically active on a regular basis) may need more manganese than sedentary people but there are no controlled studies of effects of exercise on manganese levels. As there are no norms for humans, one cannot measure the manganese status of the body. The famous Colgan Institute supplements athletes with 2.0-5.0 mg/day of manganese.

**Safety (Toxicity)**

Manganese is considered one of the least toxic of the trace elements if taken by the mouth. Dietary manganese supplements have never been reported to evoke toxic side-effects, even in dosages of up to 10 mg/day. Manganese toxicity is extremely rare in humans, and has only been observed in workers exposed to high concentrations of manganese dust or fumes in air. Manganese toxicity has been recorded in steel and chemical industry workers under the term: locura man
ganica (permanent insanity), and therefore some medical people unfamiliar with dietary supplements exceptionally wary against minerals, in general, so manganese, as well.

**Summary Of Clinical Applications:**
- Glucose homeostasis
- Enhancement of immune responses
- Maintenance of joint and bone health

**ZINC**

Our body contains approximately 2-3 grams of zinc, which is distributed throughout the body. Zinc is an essential component of several dozen enzymes associated with many different metabolic processes. The highest concentrations of zinc are found in the eyes, liver, bone, prostate, semen, and hair. However, there are no true storage depots for this mineral. We are dependent upon a continual external supply, as the relatively small body pool of biologically available zinc appears to be used up rather rapidly. Perhaps the most critical role zinc plays is in the synthesis of the nucleic acids RNA and DNA, which are essential for cell division, cell repair, and cell growth. This would help explain its involvement in growth, development and, in aiding reproductive function. There is evidence that the importance of zinc for growth begins as early as in the womb. Several studies link low zinc levels with complications during pregnancy, miscarriage, and birth defects. Studies have also found large percentages of apparently healthy children to be deficient in zinc. They showed symptoms of suboptimal growth, in addition to a loss of taste acuity and poor appetite.

Zinc may play a multifaceted role in protecting us from harmful substances. It protects the liver from damage due to poisoning from the common cleaning solvent carbon tetrachloride. Zinc is known to prevent the absorption of lead and cadmium and so may alleviate the toxic effects of these heavy metals, which are regularly present in polluted air, and may be present in drinking water. Lead exposure can occur due to water flowing through lead plumbing, air pollution, car and bus exhaust fumes, and industrial waste. Cadmium, which can be leached from galvanized or black polyethylene pipes, is also present in exhaust fumes, cigarette smoke, and industrial waste, and has been shown to raise blood pressure. Zinc may also be protective against the harmful effects of free radicals through its influence on cell membrane stability. The highest concentration of zinc in the human body is in the eye, especially iris and, retina. Although the exact mechanism of its functions are largely unknown, zinc seems to be involved with the activation of vitamin A in the eye and thus is a factor in night vision. There is a growing body of evidence to indicate that zinc is also related to other eye conditions such as impaired color discrimination, cataract formation, and optic neuritis.

**ADJUNCT NUTRITIONAL THERAPY**

**Water** supply is extremely important for all – healthy and ill people alike – but especially when there is a need for continual detoxication of the body. For this purpose 1.5 to 2 litre daily of the already synthesizable alkaline (pH 9, 0) water is the most suitable. In lack of alkaline water, distilled water can serve as an alternative. We really need healthy, clear water, but water can be found
in plants, and what is more, in organic bond, as a biologically active water, which is an adequate form for our body to take up. Those consuming lots of fresh raw vegetables and fruits can drink less. The best drink is the juice of vegetables and fruits from chemical-free cultivation, herbal teas made with distilled water, for lack of better, clear spring water and mineral water, and in fasting periods alkaline and distilled water.

When there are joint problems, there are usually also gastrointestinal disorders present. It is, therefore, important to take care of digestion and the “cleanness” of colon. Sodium and potassium rich herbs and food help in neutralisation (organic) acids and their elimination from the body, respectively. In individuals affected with arthritis there is usually a deficiency of certain minerals – iron, sulphur, silicon and zinc included.

Many people have had success on a vegetarian diet. Use brown rice, millet, buckwheat, fruit, vegetables, seeds, nuts, sprouts, green drinks, and fresh vegetable juices. Avoid citrus juices as they may contribute to swollen joints. Eliminate sugar, refined flour products, table salt, alcohol, tea and coffee.

**Beneficial herbs**

Herbs that will help in arthritis are: alfalfa (Medicago sativa), aloe (Aloe vera), burdock (Arctium lappa), cat’s claw (Uncaria tomentosa), purple and pale cone flower (Echinacea purpurea et pallida), horsetail (Equisetum arvense), kelp (Laminaria digitata) and bladderwrack (Fucus vesiculosus), Pau D’arco (Tabebuia impetiginosa), saffron (Crocus sativus), slippery elm (Ulmus fulva) and yucca (Yucca shidigirea).

**Other beneficial supplements**

Besides of JointProteX, the following products of CaliVita also offer active ingredients helpful for the maintenance, continuous renewal and restoration of connective tissues: Fish Oil concentrate containing omega-3 fatty acids, Super Soya Lecithin and Triple Potency Lecithin, every formula containing vitamin C and bioflavonoids, and amino acid formulas, especially those that contain lysine, prolyne and threonin. Green Care (alfalfa), Yucca, White Willow (salicin content!), Immunaid and Virago containing cat’s claw and zinc – the latter includes other important active agents as well – completely support, boost and complement the beneficial effects of JointProteX. The precondition of the detoxification of the body is a healthy and clean alimentary canal. For this purpose Digestive enzymes, ParaProteX and OxyMax offer effective help.

**Vitamins, minerals and supplements**

Vitamin A and E help prevent free radical damage. Vitamin C helps to rebuild cartilage, necessary for the formation of collagen found in the bones, cartilage and connective tissues. Vitamin B-complex and iron are necessary for nerves, digestion and rich blood.

Minerals are essential for joint, muscle and bone repair, especially silicon, calcium, magnesium, selenium, and zinc.

Chlorophyll and blue-green algae are rich in nutrients and help in the assimilation of essential vitamins and minerals.

Lecithin eliminates cholesterol and toxins and helps in repairing the nerves. Salmon oil and flaxseed oil are necessary for joint repair.

**Selenium.**

Selenium is an essential micromineral (a “trace” element). It acts as a helper to other nutrients, especially vitamin E. Namely, selenium functions as an antioxidant via its role in the enzyme glutathione peroxidase (GP) – an enzyme which prevents oxidative damage by detoxifying hydrogen peroxide as well as lipid peroxides. *Glutathione* – an antioxidant containing a sulphhydril – group is also essential for the glutathione peroxidase activity. Thereby selenium functions as an antioxidant in the body, working in concert with glutathione, vitamins E, C and other antioxidants. Selenium helps the body utilize oxygen and assists in the normal regenerative and growth function. It may help prevent chromosome breakage that causes birth defects. Selenium also protects against the toxic effects of heavy metals (i.e., mercury, lead and cadmium). In experimental and clinical studies has been shown, that selenium possesses a beneficial effect in cases with arthritis.

**Bio Resonance Therapy (BRT)**

Several experiments in the 1950s suggested that a voltage differential governed restitution of cartilage was possible in some animals – rats and
rabbits. Human capacities for repair of certain tissues are greater than most people realize, and there are already promising ways of enhancing some of them.

Every living cell in the human body generates an electromagnetic field, and this energy field is one way that the cells communicate with each other to initiate and regulate various physiological processes. BioHarmonex is an electronic device that emits an extremely low intensity pulsed electromagnetic field (ELF). The external electromagnetic field provided by the BioHarmonex, is intended to influence and stimulate the natural electromagnetic field generated by specific tissues in the body, thereby enhancing the metabolism’s natural function and healing power.

**BioHarmonex** – its programs developed for: Bones/spine (and joints), Immune, Forever Young, Hormone, Pain, Weightloss, Detox, Circulation, Digestion – all can be helpful in the alleviation of unpleasant signs and symptoms of arthrosis/arthritis.

**REFERENCES**


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