

Inflammation

Inflammation is the means by which the body deals with insult and injury. Insult may be caused: mechanically (e.g., by pressure or foreign bodies), chemically (e.g., by toxins, acidity, alkalinity), physically (e.g., by temperature), by internal processes (e.g., uremia), and by microorganisms (e.g., bacteria, virus, parasites). Inflammation is a complicated and not fully understood communication between cellular and humoral elements.¹ Inflammation rids the body of foreign matter and disposes of damaged cells, and initiates wound healing. Inflammation is controlled by mast cells that are in close proximity to autonomic nerves. Mast cells are a constituents of connective tissues containing large granules that contain heparin,² serotonin, bradykinin,³ and histamine. These substances are released from the mast cell in response to injury and infection, and, by their degranulation, they control most of the processes of inflammation. Mast cells are responsive to other controls, for example, under the influence of progesterone they release serotonin, and under the influence of estrogen they release histamine. Another important pathway is known as the *arachidonic acid cascade* which is largely controlled by *eicosanoids*.⁴ Eicosanoids are local “hormones” made from 20-carbon essential fatty acids (AA, DGLA, EPA), they are short-lived and can affect many aspects of physiological function at the cellular level. Eicosanoids include all the prostaglandins, thromboxanes, and leukotrienes. Depending on genetic as well as other factors eicosanoids transform or control prostaglandins, thromboxanes, and leukotrienes all of which are inflammatory mediators. Eicosanoids can initiate, regulate, and terminate all local inflammatory responses.⁵ When inflammation affects a joint (such as in rheumatoid arthritis), the cartilage can be damaged by neutrophils⁶ and lysosomal enzymes⁷ that enter the area. This leads to a vicious cycle of repeated injury and persistent inflammation.

Inflammation may also lead to mental depression which is commonly seen in chronic pain patients. Indolamine 2,3 dioxygenase (IDO) is a rate-limiting enzyme in the degradation of tryptophan and is induced during inflammation by the cytokines interferon-gamma (IFN-gamma), interferon-alpha (ITN-alpha) and tumor necrosis factor-alpha (TNF-alpha) in a broad variety of cells. Elevated IDO can therefore enhance

1. Humoral response is one of the two forms of immune response to antigens such as bacteria and foreign tissue. It is mediated by B-cell lymphocytes marked by antibodies. Cellular immunity is dominated by T-cell lymphocytes. It is involved in resistance to infectious diseases, delayed hypersensitivity, resistance to cancer, autoimmune diseases, graft rejection, and allergies.
2. Heparin is an antithrombin factor that prevents intravascular clotting.
3. Bradykinin is a peptide of nonprotein origin containing nine amino acid residues and acts as a vasodilator.
4. Arachidonic acid is an essential fatty acid that is a component of lecithin (esterified phospholipid) and a basic material for the biosynthesis of some prostaglandins.

tryptophan degradation and subsequent serotonin depletion which may cause depression (Wichers and Maes 2004).

Anti-inflammatory drugs such as aspirin and other NSAIDs inhibit prostaglandin synthesis, which may affect inflammatory mediator production and cellular processes. Steroid hormones have been postulated to have a multitude of effects. Probably the most significant in this context is the stabilization of lysosomal membranes (Ryan and Majno 1983).⁸ Tripterygium Wilfordii (Lei Gong Teng) is a Chinese herb that has been shown to be quite effective in treating inflammation secondary to auto-immune disorders. It is a toxic herb that should be used with caution as it can cause internal bleeding, kidney damage, decrease in blood cell counts, decreased bone mineral density in females with lupus erythematosus (SLE), hair loss, immune system dysfunction, and even death.⁹ Symptoms of toxicity include: dizziness, palpitations, weakness, nausea, vomiting, stomach aches, diarrhea, pain in liver and kidney areas, bleeding of digestive tract, and respiratory and circulation exhaustion. Variations of Two-Marvel Powder (Er Miao San), Cinnamon Twig, Peony, and Anemarrhena Decoction (Gui Zhi Shao Yao Zhi Mu Tang), and White Tiger plus Cinnamon Twig Decoction (Bai Hu Jia Gui Zhi Tang) are often used to treat *active* inflammation.

Chronic Inflammation

Chronic inflammation can evolve from acute inflammation or occur without an acute phase. Histologically, chronic inflammation has two main features: The presence of granu-

5. Fatty acids are hydrocarbons of varying length with a carboxyl group (-COOH) at one end and a methyl group (-CH₃) at the other. Fatty acids are often classified by two types: 1) the saturation (saturated, monounsaturated, polyunsaturated, and trans fats), and by 2) the families of fats, based on physical structure (omega-3, omega-6, omega-9, etc.). Polyunsaturated fats are very susceptible to oxidative damage, and most saturated fats raise serum cholesterol levels. Omega-3 fatty acids make cell membranes more fluid and therefore more permeable. Of the two parent essential fatty acids, both are polyunsaturated. Linoleic acid (LA) is an omega-6 (n-6) oil, and linolenic acid (ALA) is an omega-3 (n-3) oil. Both LA and ALA are transformed by the body into longer and even more polyunsaturated fatty acids using the same cellular enzyme (delta 6 desaturase; which therefore can transform to both pro-inflammatory and anti-inflammatory depending on the amount of substrate from diet and genetic conditions). Many disorders as well as dietary influences can affect the enzyme delta 6 desaturase and thus change fatty acid balance. Three of the metabolites of the enzyme have 20 carbons and have important functions: dihomo gamma linolenic acid (DGLA), arachidonic acid (AA), and eicosapentaenoic acid (EPA).

Eicosanoids are made by the body via enzymic conversion: Prostaglandins are made by cyclooxygenase enzyme (COX), and leukotrienes and made by lipoxygenase enzymes. EPA can be further desaturate to produce docsaheptaenoic acid (DHA, 22:6 n-3; the longest of the fatty acids). DHA is a critical fatty acid that increases membrane fluidity and permeability which allows for proper cell receptor function as well as regulation of nutrients and waste product flow into and out of the cell. Omega 3 fatty acids (fish oils, containing EPA and DHA) are considered anti-inflammatory. However, the omega 6 fatty acid gamma linoletic acid (GLA) may be more appropriate for diabetic patients. The most common causes of fatty acid imbalance is a diet high in omega 6 (animal fat and shell fish), altered delta-6 desaturase activity, vitamin B-3, B-6, biotin, Ca, Zn, and Mg deficiency, and insulin dysregulation.

lation tissue¹⁰ and mononuclear predominance.¹¹ The combination of new blood vessels, fibroblasts, and extracellular matrix is termed “granulation tissue.” Mononuclear predominance can also be seen in the latter part of acute inflammation as mononuclear phagocytes¹² or macrophages.¹³ In comparison to ordinary loose connective tissue, granulation tissue is more cellular and contains neutrophils, inflammatory cells, and fibroblasts.¹⁴ Granulation tissue is more vascular and has “leaky” capillaries. The formation of granulation tissue is the response of connective tissue and vessels to irritation.

In some forms of chronic inflammation, other cell types appear. This suggests the development of immunologic reactions that may include lymphocytes,¹⁵ eosinophils, and plasma cells.¹⁶ In other forms, where no immune response is present, the mononuclear cells are almost entirely macrophages. When inflammation is chronic, the vascular component, vasodilation, and exudation is minimal, and, therefore, manifests clinically with little (possibly no) redness and heat (Ryan and Majno 1983).

Most chronic inflammation without bacterial invasion is pointless and may even prove to be harmful. For example, edema raises tissue tension and causes pain, impeding movements that are important for normal joint function and homeostasis. Pressure from edema to vascular tissues can result in poor drainage of toxins (*ibid*).

SELF-PERPETUATING INFLAMMATION. Self-perpetuating inflammation can result after trauma, especially with minor injuries to tendons and ligaments. Trauma leads to tissue destruction and the release of enzymes that then lead to →inflammation→growth of fibroblasts→formation of fibrils→rest→chaotically formed adherent scar→normal

6. Neutrophils are the circulating white blood cells essential for phagocytosis and proteolysis by which bacteria, cellular debris, and solid particles are removed and destroyed.
7. Enzymes with hydrolytic actions that function in intracellular digestive processes.
8. Cytoplasmic membrane-bound vesicle measuring 5-8 nm (primary lysosome) and containing a wide variety of glycoprotein hydrolytic enzymes.
9. Vitamin B-12 and B-6 as well as Glycine Pericarpium (Lu Dou Yi) can be added to minimize the risks.
10. Granulation tissue is any soft, pink, fleshy projection that forms during the healing process in a wound. It consists of capillaries surrounded by fibrous collagen.
11. Mononuclear cells are cells such as leukocytes, lymphocytes and monocytes, with round or oval nuclei.
12. A phagocyte is a cell that is able to surround, engulf, and digest microorganisms and cellular debris.
13. A macrophage is any phagocytic cell of the reticuloendothelial system including histocyte in loose connective tissue. Macrophages probably digest proteins and supply amino acids to the fibroblast.
14. A fibroblast is an undifferentiated cell in the connective tissue that gives rise to various precursor cells, such as the chondroblast, collagenblast, and osteoblast, that form the fibrous, binding, and supporting tissue of the body.

movement→re-injury/irritation→*self-perpetuating inflammation*. Treatment then may be needed to disinflate the scar, or to get rid of the chaotically formed scar, by deep cross-fiber massage or manipulative rupture (Ombregt et al *ibid*).¹⁷ Many conditions that have been labeled as inflammatory, such as chronic tennis-elbow, are not inflammatory.

NEUROGENIC INFLAMMATION. Recent research using immune-histochemical techniques suggests that when ligaments and other connective tissues in the spine (and other areas) that receive a supply of small-diameter fibers become irritated, an initiation of neurogenic inflammation occurs and commonly affects pain and sympathetic receptors. Neurogenic inflammation results from release of neuropeptides that interact with fibroblasts, mast cells, and immune cells in the surrounding connective tissues (Levine et al 1993). When irritated, some of the small-diameter sensory axons can secrete substance-P, which is a proinflammatory, vasodilatory neuropeptide, into the surrounding tissue. This release of an inflammatory agent from a peripheral nerve terminal is involved in initiating the processes of neurogenic inflammation and edema, and results in degranulation of mast cells. Neurogenic inflammation is thought to be a major factor in degenerative diseases and back pain chronicity (Willard *ibid*).

It must be remembered that inflammation anywhere in the body can result in musculoskeletal-like pain, and may be caused by bacteria, viruses, parasites, fungi, spirochetes, and cardiovascular or autoimmune diseases. Septic arthritis should be treated with complete rest and aggressive IV antibiotic therapy.

Wound Healing

Bioelectrical phenomena may initiate and regulate inflammatory process and repair (Oschman *ibid*). Becker (*ibid*) has shown the human body to be polarized. The central spinal axis is said to be positively charged and the periphery is said to be negatively charged. The normal voltage reading is said to be -10 μV; however, when a fracture occurs, the voltage decreases toward zero. Five days after the injury, the voltage is said to move toward normal, and by the fifteenth day, the voltage reading is within normal limits of -10 μV. It is possible that this polarity gradient is a electromotive force driving, in part, the current of injury and the inflammatory cascade that leads to healing. Nordenström has suggested that when an injury occurs, a positive charge builds up in the

15. A lymphocyte is a type of white blood cell that increases in number in response to infection. Lymphocyte increase permeability and help to activate the phagocytosis of damaged cells.
16. An eosinophil is a granulocytic, bilobed leukocyte (white blood cell) that increases in number in response to allergy and in some parasitic infections.
17. Since most degenerative tendinopathies are non-inflammatory and steroid injection does not result in lasting effects in relation to them, treatments that stimulate cell growth may be needed.

area of injury, which may then result in a potential gradient acting as a bioelectric battery. A change in the electrical insulating properties of capillary membranes is said to turn on the “biological battery.” As the membranes become less permeable to the flow of ions and more electrically insulated, the flow of intrinsic bioelectricity is forced to take the path of least resistance, which is through the bloodstream to the injured area.

When injury occurs, sensory information rapidly alerts the brain and begins the complex sequence of events to reinstate homeostasis. Cytokines¹⁸ are released within seconds after an injury. These substances, such as gamma-interferon, interleukins 1 and 6, and tumor necrosis factor, enter the blood stream in one to four minutes, and travel to the brain. The cytokines, therefore, are able to activate fibers that send messages to the brain and, concurrently, to breach the blood-brain barrier at specific sites and have an immediate affect on the hypothalamic cells. The cytokines, together with evaluative information from the brain, rapidly begin a sequence of activities aimed at the release and utilization of glucose for necessary actions, such as the removal of debris, the repair of tissues, and, sometimes, the raising of a fever to destroy bacteria and other foreign substances (Melzack *ibid*). Therefore, the sequences that result in wound healing and inflammation integrate both peripheral and brain functions.

Wound healing, regardless of the site of injury or degree of inflammation, occurs in three *overlapping phases* (Banks 1991). The first phase has three major affects: early wound / healing strength secondary to crosslinking, removal of damaged tissue, and recruitment of fibroblasts. The tissues regenerate largely due to inflammatory cells, vascular and lymphatic endothelial cells, and fibroblasts (Ombregt et al *ibid*).

• **First phase.** The first phase, *the inflammatory phase*, is characterized by ischemia, metabolic disturbance, and cell-membrane damage. It is time-dependent and is mediated by vascular, cellular, and chemical events, culminating in tissue repair and sometimes scar (adhesion) formation (Kannus 2000). The inflammatory phase can be divided into early and late stages.

— *Early Inflammatory Stage.* The first reaction is vasoconstriction of small local arterioles that last about five to ten minutes. It is followed by active vasodilatation and increased blood flow for one to three days, during which time, cellular debris and humoral factors attract the initial influx of granulocytes. The first to appear are platelets¹⁹ that secrete many chemical mediators of inflammation, resulting in the arachidonic acid cascade and the

release of growth factors such as platelet-derived growth factor (PDGF), platelet factor 4, insulin-like growth factor (IGF-1), and transforming growth factors.

- *Late (Second) Stage.* In the second stage, the monocytes and macrophages release polypeptide growth factors, which activate the fibroblasts. The second stage of the first inflammatory phase lasts about ten days.
- **Second Phase.** The second phase is *the granulation tissue formation* (proliferation) stage. It begins about two days after injury (overlapping with the first phase) and can last up to six to eight weeks. It is controlled by monocytes, which are pluripotential cells capable of essentially directing the complete sequence of events in this proliferative phase.²⁰
- Monocytes begin to form, mobilizing a soupy mixture of granulocytes and macrophages with infiltrating fibroblasts from granulation tissue. This is characteristic of a healing wound. Macrophages are capable of releasing numerous growth factors, chemotactants, and proteolytic enzymes. They can activate fibroblasts for tendon and ligament repair.
- **Third phase.** The third phase is *the matrix formation or remodeling maturation* aspect. It is characterized by a trend toward decreased cellularity, decreased synthetic activity, increased organization of extracellular matrix, and a more normal biochemical profile. Type 1 collagen starts to assume a normal orientation and replaces type 3 collagen. Increased chemical cross-linking results in increased strength.
- Fibroblasts remain to build a strong matrix of collagen. In tendon injury, there is intrinsic healing as a result of endotendon fibroblastic response.
- Matrix formation lasts about six months, at which point the tensile strength of the repaired tissue reaches about 50%.²¹ Full strength is only reached after one to three years. Collagen maturation and functional linear realignment are usually seen in about two months. Cellular response after tendon laceration can be extrinsic or intrinsic. The extrinsic response is a proliferation and bridging of the injury by epithelial cells. Intrinsic healing is the result of an endotendon fibroblastic response (Brown *ibid*). During maturation, the scar tissue is reshaped and strengthened by removing, reorganizing, and replacing cells and matrix (Ombregt et al *ibid*).

18. Cytokine is a generic term for nonantibody proteins released by one cell population (e.g., primed T lymphocytes) on contact with a specific antigen, which acts as intercellular mediators, as in the generation of an immune response.

19. Platelets are the smallest cells in the blood. They are essential for the coagulation of blood.

20. Some types of chronic inflammatory disorders such as tendinitis may occur due to the prolongation of this stage, which may be do to anti-inflammatory therapy.

21. For more information on acupuncture and dry needling, see Chapter 5.

Movement During the Healing Phase

Movement and activity are of primary importance in preserving homeostasis between collagen degradation and synthesis (Amiel and Woo 1981), and are advocated in TCM (and by Hippocrates) in the management of injuries. Movement encourages collagen to be laid down in the correct anatomical arrangement and helps increase the production of ground substance and intermolecular crosslinking, thereby increasing the strength of the tissue. This occurs by improved vascular remodeling (in a longitudinal orientation), and by causing the orientation of fibroblasts and collagen to be laid in parallel to the fibers (Gelberman et al 1989). Movement can also decrease the formation of abnormal scars and adhesions. The result is a more normal looking tissue rather than scar tissue, especially if it is due to treatment such as dry needling or (Dorman *ibid*) prolotherapy. Movement also prevents the randomness of collagen fibers found in regular scar tissue. Movement during the granulation phase (about the first ten days) should not be very stressful on the healing scar, as this can prevent normal healing. Another advantage of early mobilization is the positive affect on skeletal muscles with increased circulation, muscle strength and endurance, and maintenance of proprioceptive reflexes, which ensure the active stability of the joint (Ombregt, Bisschop and ter Veer 2002). Exercise increases production of insulin-like growth factor (IGF-1), which is known to stimulate collagen synthesis and cell replication (Brown *ibid*).

Factors That May Influence Healing

Continued joint inflammation can compromise the capacity of lymphatic drainage. When lymphatic drainage is inadequate, the continued edema and resulting pressure may affect healing. Edema can distort anatomical alignment and lead to joint instability, muscle dysfunctions, and ligamentous laxity. Prolonged inflammation and the resulting congestion (swelling) may result in bathing of tissues with serofibrous exudate with resulting adhesions and inflexibility. With poor circulation, congestion, hypoxia and continued re-injury from use, tissue regrowth takes the form of inferior quality granulation tissues, leading to the decreased organization of the extracellular matrix. Poorly healed tissues may be seen with chronic tendinitis, tendinosis, and inflammation of ligament. Therefore, it is important to pay attention to the progress of the healing and related activity of a recuperating patient Simkin (1990).

Healing can be influenced negatively by smoking, collagen diseases, nutritional deficiency, and some medications (Brown, Orme and Richardson 1986; Battié et al 1991, Lawson 1989, Brown *ibid*):

- Smoking can decrease fibrinolytic activity and nutritional supply to tissues including discs. This can lead to increased risk of poor healing and can cause disc pathologies and surgical and fracture nonunions.

- Medications, especially anti-inflammatories, may result in poor healing. High levels of corticosteroids can prevent the migration of macrophages.
- Collagen diseases such as Marfan's syndrome and Ehlers-Danlos syndrome result in enzymic deficiencies that influence healing.
- Nutritional deficiencies such as vitamin C, B1, zinc, sulfur, copper, manganese, boron, and proteins can inhibit healing.

Anti-Inflammatory Drugs

While Non-steroidal anti-inflammatory drugs (NSAIDs) often relieve symptoms, they are far from ideal therapeutic agents. NSAIDs work by inhibiting the production of prostaglandins and thus may interfere with normal tissue repair. They inhibit both helpful and non-helpful prostaglandins; hence they can result in unwanted side effects and *interfere* with healing. For example, a recent report presented at the American Orthopaedic Society for Sports Medicine stated that NSAIDs taken for two weeks inhibit tendon-to-bone healing in rotator cuff repair for eight weeks in rats (Medscape 2004). Indomethasin and Naproxen inhibit GAG synthesis and cell proliferation after tendon injury (*ibid*). Patients who use Piroxicam after knee injuries have increased anterior drawer signs compared to those that do not (Slyater et al *ibid*). At least five studies in both humans and animals have reported that NSAIDs may accelerate joint destruction (Newman and Ling 1985; Shield 1993; Brooks, Potter and Buchaman 1982; Ranningen and Langeland 1980; Brandt 1987). The newer COX-2 inhibitors have been shown to significantly inhibit experimentally-induced tibial fractures healing in mice by inhibiting the process of bone cell differentiation (O'Keefe 2002). Corticosteroids may also interfere with healing and the use of NSAIDs and corticosteroids may prolong inflammation in connective tissues (Viidik and Gottrup 1986). The long-term benefits of corticosteroid injections for lateral epicondylitis were shown *not* to be superior to physiotherapy and very comparable to no therapy at all (Smidt et al 2002). Corticosteroids have been associated with tendon ruptures and accelerated cartilage degeneration when used in weight bearing joint. They have been associated with aseptic necrosis and most patients using them develop some degree of osteoporosis.

NSAIDs can cause other serious side effects including peptic ulcer, and, less commonly, hepatic or renal failure. The use of NSAIDs causes about 2000-3000 *deaths* and cost \$200-760 million of treatment of side effects in the U.S., per year. Some estimates of deaths caused by NSAIDs in the U.S., are as high as 10,000-20,000 patients per year (Bjorkman *ibid*). It is estimated that 8% of the world adult population is prescribed an NSAID for a variety of conditions (Simon 1997, Bjorkman 1996). A study published in the Archives of Internal Medicine of NSAIDs taken by >80,000 female nurses over a two-year period has found that those who took NSAIDs for twenty-two days or more per month

had an 86% increased rate of developing hypertension. The researchers concluded that a substantial proportion of hypertension in the U.S., might be due to the regular use of analgesics. NSAIDs have also been associated with increased rates of non-Hodgkin's lymphoma.

Not all the effects of NSAIDs are harmful. A newly published study on the cyclooxygenase-2 (COX-2) inhibitor Celecoxib has shown it to "enhance the rate of synthesis of both hyaluronan and proteoglycans, and concomitantly reduce the net loss of these two glycosaminoglycans," which may, therefore, have protective effects on osteoarthritic cartilage (Manicourt et al 2003). NSAIDs may also protect against the development of glioblastoma multiforme (brain tumors; Niccole and Sivak-Sears 2004). Long-term use should probably be avoided although benefits such as prevention of fatal heart attacks, TIAs, and Alzheimer, and increased early detection of colon cancer have been suggested. Hence, the harm/benefit ratio between the use or nonuse of anti-inflammatory medications is difficult to judge. Inflammation is important for wound repair, but it can also lead to sensitization of nerves. Therefore, anti-inflammatory medication have both beneficial and harmful affects.²²

Three Phases of Degeneration

Kirkaldy-Willis and Burton (1992) described three phases to the degenerative process. These are: dysfunction, instability, and stabilization. Many of the treatment principles presented in this text are designed to address the consequences of these degenerative processes.

Dysfunction Phase

The dysfunction phase is seen in patients who usually have transient pain that responds well to manual therapies. Pathological tissue alterations are relatively minor, and, by and large, the patient presents with a joint or soft tissue pain that is difficult to document. These patients may have suffered a minor trauma or strain, often due to a lack of good physical condition.

SYMPTOMS AND SIGNS. The patient presents with acute, subacute, or chronic pain. The pain is usually unilateral but may refer in a myotomal or sclerotomal distribution. Often pain is relieved by rest. Patients usually have a postural component to their pain, that is, their pain is usually felt at end-range. The pain usually comes on only after prolonged loading at end-range, such as after sitting for while. Abnormal

motions at the affected joint are detectable but may be significant only during symptomatic periods.

If the muscle joint complex or posture is not corrected, soft tissue stress may result in pathological change, such as anoxia of muscle tissue with fibrotic deformations, joint restriction with consequent immobility and increased stress on the ligaments. This process then leads to the second phase: the instability phase.

Instability Phase

Here the patient presents with similar symptoms; however, chronicity is the rule. Patients respond only temporarily to manual therapies. The prolonged dysfunction, poor physiologic posture, immobility, lack of activity, and genetic and other individualized factors result in both mechanical and cellular stress on ligaments and other tissues. Ligaments lose their elastic character, and joint stability is lost. The discs begin to break down and may rupture. This results in an increasing rate of degeneration at the joint complex.

SYMPTOMS AND SIGNS. Signs of hypermobility and ligamentous pain are becoming more pronounced. Patients are often weak and often report a "giving way" or "catching" of the affected region. Discogenic symptoms are common.

Stabilization Phase

In this phase patients often report that a previous severe condition is becoming less painful and that they feel increasingly stiff. Aging causes the ligaments to shrink. Joints develop other ways to stabilize (often referred to as degenerative spondylolysis).

SYMPTOMS AND SIGNS. Patients often report feeling less incapacitated, unless degenerative deformations lead to compression phenomenon or sensitization develops.

TCM and the Degenerative Cascade

The following discussion integrates TCM and modern understanding of the degenerative cascade. The principles delineated here can be used to treat musculoskeletal disorders successfully. There is much overlap between the biomedical concept of the degenerative cascade and TCM's understanding of aging and tissue failure. TCM pattern diagnosis tends to change as the patient moves through the stages of their disease, and as the patient undergoes the aging process. The latter relates mainly to the Kidneys, Yin, Essence, and Blood. These diagnostic variations are reflected in the presentation of signs and symptoms representing Pathogenic Factors, the state of the Righteous-Qi (which indicates general health), and the condition of the Form (structure) of the being as a whole and its organs and tissues. In general, disease stages and the aging process undergo the following variations: stages (and processes) where the Righteous-Qi is strong and the Pathogenic Factors are weak; where the Righteous-Qi is strong but the Pathogenic Factors are even stron-

22. There are 2.2 million adverse drug reaction per year in the US and a minimum of 106,000 deaths per year from *appropriate* use of prescriptions drugs (Starfield 2000). Of the 198 drugs approved by the FDA from 1976-1985, 102 had to be withdrawn from the market or their label had to be changed due to side effects (FDA drug review 1990). Of all the drugs in the PDR only about 30% have a known mechanism of action.

ger (which means to some extent Righteous is weak if pathogens are strong); where the Righteous-Qi is deficient and the Pathogenic Factors are excessive; and where the Pathogenic Factors are eliminated and the Righteous-Qi is recovering. The degenerative cascade is therefore either related to the damage and breakdown of Form²³ by Pathogenic Factors (which damage the Kidneys, Liver, Spleen, and their related tissues as well as Essence and Blood) or to damage from depleted Essence and inherited or postnatal factors.²⁴

TCM disease mechanisms that reflect the progression of pathology in musculoskeletal disorders can be summarized as arising from Exterior, Interior, traumatic, or other miscellaneous origins. Early or abnormal degenerative conditions often involve weak (congenital) or depleted Essence.²⁵

Exterior Pathways

At first, external Pathogenic Factors penetrate the body through the skin, mouth, or nose. Depending on the patient's general condition, he or she develops a superficial syndrome, or, if the pathogens enter more deeply, they may or may not cause immediate symptoms. External Wind-Cold is said first to penetrate the Tai-Yang (UB) channels, and, unless treated, to continue inward (or manifest) via the six channels/stages. Wind-Heat and Dampness are more likely to penetrate through the mouth and nose and tend to progress quickly in the "four level pattern," from the Exterior-division (superficial) to Blood-division (deep) level, or to progress more slowly via the three Warmers, with Dampness often starting in the middle-warmer and causing digestive symptoms. These stages usually progress in an orderly manner from one to the next. However, in some cases the condition can progress in a non-orderly manner or even remain at the same stage for some time. The stronger the patient's Righteous-Qi, the more likely he/she is to develop a fever/inflammation and eliminate the pathogens. Weak patients often do not develop strong symptoms and are more likely to develop chronicity and retain hidden pathogens.²⁶

These models can be applied broadly; however, patients with musculoskeletal pain, especially when mild and non-traumatic, often do not, clinically, fit established TCM patterns. One can always "force" a pattern diagnosis by ignoring some signs and projecting others, but the clinical utility

of doing this is often not ideal. The interaction of the ideas that follow has occurred when the author has had to confront these issues.

In the *dysfunction/postural phase* of the degenerative cascade, insufficient *circulation* of Qi and Blood is often the cause of symptoms. External Pathogenic Factors may be one cause that interferes with normal Qi and Blood circulation (especially Dampness, as it is said that Dampness causes Qi-stagnation). These various factors cause stagnation/stasis (congestion) to develop and to advance the dysfunctional/postural phase. Symptoms come on when tissues are under stress and in need of extra nourishment. This stress then activates pain receptors (increase stagnation of Qi and Blood). The Pathogenic Factors are usually weak so that the patient feels symptoms only when the tissue is under prolonged loading and in need of extra nourishment. This nourishment is blocked by pathogens, or by *some other functional disturbance*.²⁷ Stagnation results in trapped Qi and Blood within an area (with signs such as local swelling or, possibly, an "inflated balloon-like pulse"); or the inability of Qi and Blood to enter an area, (with signs such as *flaccid localized tissues* or, possibly, decreased vessel tone and/or a "flat pulse" quality).²⁸ With time, lack of nourishment from poor circulation (or blocked circulation), or from pathogens damaging the Yin and Blood (because trapped pathogens often damage Yin/Blood/Essence as they easily transform into Heat or by obstructing flow), results in tissue failure and the patient develops *instability*. Eventually, Blood-stasis and pathogenic Dampness coalesce. This results in hard swellings and a proliferation of tissues with ossification/spurs, resulting in the *stabilization phase*. Hidden pathogens are said to lurk Interiorly and damage Yin and Essence, so that tissue nourishment may be affected, eventually leading to the degenerative cascade.²⁹

Interior Pathways

Emotions and/or lifestyle stresses result often in dysfunction of the Qi. This often means stagnation of the Qi. Because Qi moves the Blood, stagnant-Qi can result in poor Blood circulation. Many physical activities demand healthy circulation and tissue nourishment for normal joint and sinew renewal, cell division, and function. When these mechanisms are disturbed, tissue failure can follow. Another common complication of stagnant-Qi is that it can transform into Heat or Fire. This *pathogenic-Heat* can consume Yin/Essence and Blood, all of which then fail to nourish the sinews. The progression

23. Form is used here to describe structure, not the Taoist ideas of creation and the duality of "Form" and "No Form."

24. The most important acupuncture points that support Essence and Form are: CV-4, 6, 8 (and abdominal points in general), UB-24, 26, 38, 43, 60, GV-4, GB-39, Lu-9 and the rest of the 12 source points.

25. Not a classical statement however has been described to the author by a teacher which follows the Kidney school.

26. The priority of Exterior influences on musculoskeletal pain in TCM thinking is probably due to the strong influence of Zhang Zhong jing *Discussion on Cold Damage and Miscellaneous Disorders*. The severity of the disease may not be as obvious in Deficient and old patients.

27. Since often the patient does not have clear patterns associated with TCM ideas, except for channel disturbances, guiding ideas from Painful Obstruction (Bi) syndromes can only be theorized on. While herbs that deal with Pathogenic Factors are used in the next sections, their mechanism of action may be more due to their pharmacological effect on blood circulation than elimination of "Pathogens."

28. Lymphatic drainage (or swelling) increases the extent of tissue damage that follows tissue injury.

29. Not classical conclusions and discussions.

of TCM patterns usually reflects the stages of the condition as indexed by the three stages of degenerative cascade; often parallels the dysfunction/postural stage, the instability stage and the stabilization stage. These stages usually progress from one to the next. However, in some cases the condition can progress in a non-orderly manner or even remain at the same stage for some time, as mentioned above.

Another common Interior cause that can lead to the degenerative cascade is lack of inherited Essence or natural endowment (constitution), and decreasing normal bodily functions. Lowered normal functions leads to poor nourishment, and degeneration, or a lack of separation of the pure from the impure, leading to turbidity. This in turn can lead to an accumulation of Pathogenic Factors, mostly Dampness with obstructive-malnourishment, leading to the degenerative cascade.

Just like in Exterior pathways, with Interior pathways the *dysfunction/postural phase* is characterized by Qi and Blood stagnation resulting in symptoms when the tissues are under stress and in need of extra nourishment. Or the patient feels pain when staying still which aggravates the stagnation. Physical movements, which move Qi and Blood, reduce the patient's pain. With time, lack of nourishment from poor circulation or Heat damaging the Yin/Blood/Essence or Form, results in tissue failure and *instability develops*. The body's attempt at compensation will result in proliferated disorders (i.e., Yin producing Yang and vice versa). Hard obstructions (or tissues) develop, resulting in the *stabilization phase* (i.e., congealed/joined/mixed Phlegm/Dampness and Blood-stasis). The dysfunction/postural phase is also associated with *Deficient-detriment* (i.e., taxation, often with low back aching) and aching located at specific locations and which becomes worse on marked strain, in the morning on waking, and improves with light exercise.

Miscellaneous Factors

Many life stresses, dietary influences, iatrogenicity, infections, etc., can affect the body's immune systems/anti-pathogenic systems, or can cause direct insult. This can lead to musculoskeletal damage and pain, which appears, or not, as the *degenerative cascade*. Blood is said to be rejuvenated in the Liver during sleep (which may relate to the production of insulin-like growth hormones at night). Blood and Liver are in charge of nourishing and the strength of sinews. Lack of rest and sleep are increasingly part of modern life, both of which may contribute to the degenerative cascade. Yin, Blood, and Essence are necessary for the normal nourishment of the sinews and bones, all of which are dependent, in part, on healthy diet. Use of therapeutic and recreational drugs can damage the Organic/organic systems and bodily milieu needed for sinew and bone nourishment. Infections can lead to primary or secondary damage to the sinews and bones. High stress levels can result in disequilibrium of the adrenal system with high circulating cortisol levels. Cortisol disequilibrium has been related to the Kidneys in TCM.

Chronic high levels of cortisol and Kidney dysfunctions may result in muscle, connective tissue, and bone damage, mostly leading to degeneration (*ibid*). Chronic disorders often affect the normal function of the Kidneys which is needed for bone health as well as nourishment and activation of the Liver, which is then in charge of the sinews and movement of Qi and Blood. Finally, lack of physical activity is increasingly a cause of musculoskeletal pain syndromes. Balanced physical activity is also described in TCM has important for both physical conditioning as well as Organic health. Excessive physical exercise is thought to damage physical Form as well as the Spleen, Liver, and Kidney systems and their related tissues.

Trauma

Trauma can easily disturb local function and result in poor circulation and/or torn sinews and/or soft tissues. Often this means slight bleeding and hyperemia in the capillary beds, congestion of blood in the precapillary arterioles, edema, accumulation of fluid in the tissue spaces, and petechiae/hematoma/ecchymosis. The result is Blood-stasis and Fluid/fluid accumulation symptoms and signs. Blood-stasis irritates the free nerve endings (nociceptors/pain receptors) found in all connective tissues and leads to inflammation/pain, with or without heat. This process has local and generalized effects via the channel (or neural) systems. Channel (or segmental) effects can result in Organ/organ innervation dysfunction and symptoms. Muscle injury tends to affect the Spleen, sinew damage affects the Liver, and bone damage affects the Kidneys. Local inflammation, swelling, lymphatic congestion, and abnormal fibrosis then lead to the *degenerative cascade*. Facilitated segments are commonly seen (e.g., activation of the Shu-Mu circuits).

The Concept of the Degenerative Cascade in TCM practice³⁰

Many patients suffering from musculoskeletal pain, especially in the postural/dysfunction stage, do not present with clear symptoms and signs that correspond to TCM patterns (except channel diagnosis). Understanding the degenerative cascade, the pharmacological effects of herbs, and the physical effects of other traditional interventions can be used to successfully treat these patients. By and large, treatment during the *postural/dysfunction stage* involves: manual therapies to correct joint dysfunctions; channel therapies to open circulation and disperse Pathogenic Factors; and herbs that regulate Qi and Blood circulation, disperse and drain edema, and resolve Pathogenic Factors (depending on cause). Exercise instruction is mandatory if the patient is to arrest the progression of the degenerative cascade and for maintaining the effects of office intervention.

30. Not a classical discussion.

The following formulas can be used as *general* and *flexible guides*, and are often helpful when integrated with manual therapy, acupuncture, and exercise. The first guiding formula can be thought of as treating Pathogenic Factors (possibly) blocking circulation and as moving Qi, Blood, and Fluids. It may be used on patients lacking clear TCM symptoms and signs but whose symptoms are suspected (via the evaluation of risk factors) of being due to Pathogenic Factors. The acid surface herbs given in small dosages as well as Radix et Caulis (Ci Wu Jia) and Caulis Piperis (Hai Feng Teng) act as vasodilators and increase circulation to assist manual and needling therapies:³¹

Herba Schizonepetae (Jing Jie) 4g
 Fructus Fossythiae (Lian Qiao) 6g
 Fructus Arctii (Niu Bang Zi) 15g
 Herba Lophtheri (Dan Zhu Ye) 4g
 Rhizoma Ligustici Wallichii (Chuan Xiong) 6g
 Radix Paeoniae Alba (Bai Shao) 6g
 Ramulus Cinnamomi (Gui Zhi) 6g
 Radix Puerariae (Ge Gen) 20g
 Faeces Bombycis (Can Sha) 9g
 Flos Chrysanthemi (Ju Hua) 4g
 Rhizoma Anemarrhenae (Zhi Mu) 4g
 Radix et Caulis Acanthopanax (Ci Wu Jia) 15g
 Caulis Piperis Kadsurae (Hai Feng Teng) 15g

For suspected Phlegm (confusing symptoms that come and go) add: Rhizoma Acori Graminei (Shi Chang Pu) 6g, Rhizoma Gastrodiae Elatae (Tian Ma) 9g, Herba Eupatorii (Pei Lan) 6g.

For Qi and Blood stagnation (and/or beginning of Deficiency) from daily stress or physical exertion as commonly seen in sedentary patients or athletes that over train (often lacking clear TCM patterns of symptoms and signs) use:

Rhizoma Curcumae Longae (Jiang Huang) 9g
 Tuber Curcumae (Yu Jin) 6g
 Radix Paeoniae Alba (Bai Shao) 9g
 Fructus Arctii (Niu Bang Zi) 15g
 Poria (Fu Ling) 12g
 Fructus Hordei Vulgaris Geminatus (Mai Ya) 15g
 Radix Astragali (Huang Qi) 12g
 Flos Carthami (Hong Hua) 6g
 Radix Angelicae Sinensis (Dang Gui) 9g
 Semen Citri Reticulatae (Ju He) 6g
 Ramulus Mori (Sang Zhi) 12g
 Herba Eupatorii (Pei Lan) 6g
 Cortex Albizziae (He Huan Pi) 15g
 Caulis Polygoni Multiflorum (Ye Jiao Teng) 15g
 Radix et Caulis Acanthopanax (Ci Wu Jia) 15g
 Caulis Piperis Kadsurae (Hai Feng Teng) 15g

For patients with a *tendency* to develop Interior-Heat signs (often detected only via pulse and tongue) use:

Flos Chrysanthemi (Ju Hua) 6g
 Poria (Fu Ling) 12g
 Flos Puerariae (Ge Hua) 6g
 Rhizoma Anemarrhenae (Zhi Mu) 4g
 Rhizoma Ligustici Wallichii (Chuan Xiong) 3g
 Fructus Hordei Vulgaris Geminatus (Mai Ya) 12g
 Rhizoma Dioscoreae (Shan Yao) 9g
 Semen Cuscutae (Tu Si Zi) 9g

Semen Ziziphi Spinosae (Suan Zao Ren) 12g
 Radix Glycyrrhizae Uralensis (Gan Cao) 3g

For Qi-Blood-stagnation (fixed pain felt only at rest that improves temporarily with movement and exercise) add: Rhizoma Curcumae Longae (Jiang Huang) 9g, Tuber Curcumae (Yu Jin) 6g, Ramulus Mori (Sang Zhi) 12g.

For patients who suffer from Deficiency-detriment, mostly from an excessive use of physical resources or from a poor constitution, use modified Young Maiden Pill (Qing E Wan) and Seven-Treasure Special Pill for Beautiful Whiskers (Qi Bao Mei Ran Dan).³²

While by the time a patient enters the instability stage he/she is likely to present with a clearer TCM pattern diagnosis, some patients do not. In general, once the patient enters the *instability stage*, herbs and acupuncture therapy that increase nourishment to the sinews (mostly ligaments), joints, and bones are needed. More Blood-stasis-resolving and tonic herbs are added, and *strong periosteal* acupuncture is emphasized. The Liver is commonly treated. If needed, the patient is treated with prolotherapy. Strengthening exercises are very important but must be used with care and with an understanding of discogenic pain. Many “back” as well as Tai Chi and Qi Gong exercises can increase symptoms in patients with discogenic pain (especially those that emphasize flexion and pelvic tilts). A *guiding* (general) formula that can be integrated with the above therapies to strengthen the sinews and joints is:³³

Radix Notoginseng (San Qi) 20g
 Rhizoma Curcumae Longae (Jiang Huang) 9g
 Cortex Acanthopanax (Wu Jia Pi) 12g
 Radix Paeoniae Alba (Bai Shao) 15g
 Fructus Arctii (Niu Bang Zi) 30g
 Radix Astragali (Huang Qi) 20g
 Flos Carthami (Hong Hua) 12g
 Radix Angelicae Sinensis (Dang Gui) 12g
 Semen Citri Reticulatae (Ju He) 6g
 Caulis Spatholobi (Ji Xue Teng) 15g
 Herba Lycopodii (Shen Jin Cao) 9g
 Herba Cistanches (Rou Cang Rong) 12g
 Cortex Eucommiae (Du Zhong) 12g
 Radix Clematidis (Wei Ling Xian) 9g
 Radix Achyranthis Bidentatae (Huai Niu Xi) 12g
 Ramulus Mori (Sang Zhi) 12g
 Herba Eupatorii (Pei Lan) 6g
 Herba Epimedii (Yin Yang Huo) 9g
 Cortex Lycii Radicis (Di Gu Pi) 20g

31. It is important to understand that all the formulas in this section have been designed to assist manual and needling therapy. They are not intended to be used on their own. Their utility has been demonstrated often in the author’s clinic.

32. The ingredients of Young Maiden Pill (Qing E Wan) are: Ginger fried Eucommiae (Jiang Zhi Cao Du Zhong), Wine-fried Psoraleae (Jiu Chao Bu Go Zhi), Juglandis (Hu Tao Ren). Seven-Treasure Special Pill for Beautiful Whiskers (Qi Bao Mei Ran Dan) contains: Polygoni steamed in sesame seeds (He Shao Wu), Poria (Fu Ling), Achyranthis (Niu Xi), Angelica (Dang Gui), Lycii (Gou Qi Zi), Cuscutae (Tu Si Zi), Psoraleae fried with sesame seeds (Bu Gu Zhi).

33. While there are several herbs in this formula that are anti-inflammatory, it is the author’s clinical impression that the formula as a whole does not interfere with proper healing after induced ligamentous stimulation by prolotherapy or periosteal needling.

Modification of Young Maiden Pill (Qing E Wan) and Seven-Treasure Special Pill for Beautiful Whiskers (Qi Bao Mei Ran Dan) are used often as well.

The *stabilization phase* is by definition a chronic and enduring disease. In TCM, chronic disease is said to be mostly due to Deficiency, blockage, stasis, the network-vessels, and the Liver and Kidney Organs. It is this author's experience, however, that emphasis on resolving blockage/restrictions first may be more important than supplementation of the above Organs, especially when using acupuncture and manual techniques. This means that strong acupoint and dry needling stimulation is often needed, even in elderly or "Deficient" patients. Adhesions may be ruptured by strong manipulative techniques, though care and great skill must be used as the elderly can be easily injured.

Let me Emphasize that herbal treatment must be performed carefully and with the skillful application of TCM methods. Even in older patients, since they are often Deficient, the temptation to tonify too early or too forcefully can be strong. The practitioner must pay attention to blockages/restrictions (Excesses), as these often are the cause of pain, and Excesses can weaken the patient further. At the same time it would be a mistake to ignore a Deficient state; therefore, some support for the patient's Kidneys, Liver, Essence, Blood, Qi, Yin, and Yang are often important. A general *guiding* formula that addresses common pathologies at this stage is:

Radix Angelicae Sinesis (Dang Gui) 9g
Radix Paeoniae Alba (Bai Shao) 9g
Radix Rehmanniae (Shu Di) 9g
Caulis Spatholobi (Ji Xue Teng) 9g
Scorpio (Quan Xie) 3g
Semen Sinapis Albae (Bai Jie Zi) 5g
Agkistrodon Acutus (Bai Hua She) 9g
Nidus Vespaee (Feng Fang) 5g
Radix Salviae Miltiorrhizae (Dan Shen) 9g
Fructus Chaenomelis Lagenariae (Mu Gua) 9g
Radix Astragali (Huang Qi) 12-60g
Wine fried Rhizoma Rhei (Da Huang) 6g
Radix Angelicae Dahuricae (Bai Zhi) 5g
Herba Epimedii (Xian Ling Pi) 5g
Radix Dipsaci (Xu Duan) 9g
Cortex Lycii Radicis (Di Gu Pi) 30g
Herba Siegesbeckiae (Xi Xian Cao) 12g
Radix Aconiti Lateralis (Fu Zi) 6g
Spina Gleditsiae (Zao Jiao Xi) 12g
Rhizoma Pleionis (Shan Ci Gu) 6g

For more Yin-deficiency and Heat add: Radix Rehmanniae (Sheng Di) 12g, Radix Sophorae Flavescentis (Ku Shen) 9g, Rhizoma Anemarrhenae (Zhi Mu) 12g, Radix Pseudostellariae (Tai Zi Shen) 12g.

For stenosis and osteophytes add: Rhizoma Curcumae (E Zhu) 12g, Radix Aconiti Lateralis (Fu Zi) 3-30g, Thallus Algae (Kun Bu) 25g, Radix Scrophulariae (Xuan Shen) 20g, Colla Cornu Cervi (Lu Jiao Jiao) 12g, Herba Ephedra (Ma Huang) 3g.

To transform pathogenic accumulations in Deficient patients who cannot tolerate strong tonification, use:

Radix Notoginseng (San Qi) 12g
Rhizoma Atractylodis (Cang Zhu) 4g
Poriae Cocos (Fu Ling) 9g
Pericarpium Citri Reticulatae (Chen Pi) 3g
Rhizoma Cypri Rotundi (Xiang Fu) 6g
Rhizoma Zingiberis Officinalis (Sheng Jiang) 4g
Bulbus Fritillaria (Zhe Bai Mu) 15g
Radix Trichosanthis Kirilowii (Tian Hua Fen) 12g
Thallus Algae (Kun Bu) 25g
Fructus Schisandrae Chinensis (Wu Wei Zi) 6g
Scorpio (Quan Xie) 5g
Radix Angelicae Sinensis (Dang Gui) 9g
Caulis Spatholobi (Ji Xue Teng) 12g

In summary, while the above-discussed approach is not wholly "traditional," the author has used it successfully for many years and in numerous cases when TCM pattern diagnosis was difficult to apply.

