Editorial

The Frozen Shoulder syndrome plus other evidence and the Utah Paradigm suggest the syndrome's pathogenesis and new targets for collagenous tissue research

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Abstract

Sometimes naturally occurring disorders combined with other evidence can provide a "virtual laboratory" exercise that answers old questions and reveals new problems and questions that need appropriately "targeted" research. This article provides an example that involves the frozen shoulder syndrome, for which varied evidence and insights of the still-evolving Utah paradigm of skeletal physiology suggest a plausible pathogenesis. It involves organ- and tissue-level vital-biomechanical features of collagenous tissues that need systematic study. The features include diametric modeling, irreversible creep, a creep compensation mechanism, the regional acceleratory phenomenon, and the signals and thresholds that can help to determine how and where those things act in anatomical space. Such features participate in many extraskeletal as well as skeletal disorders, so the frozen shoulder syndrome can provide an instructive model of them. As an aside, in over 120 consecutive cases managed by me since 1956 this syndrome resolved completely in six or less months without treatment. That shows this untreated syndrome is usually if not always self limited. While I respect the doubts of colleagues who do not agree yet, that experience shows the conclusion is correct.

I. Introduction

Insights of the Utah paradigm of skeletal physiology[2,17,21, 25,26,29,34,45,48], plus other evidence and a 54 year personal experience with the frozen shoulder syndrome, suggest its pathogenesis and special targets for collagenous tissue research that have considerable clinical relevance. Part II of this article reviews that syndrome. Part III summarizes my experience with it. Part IV discusses its pathogenesis and some of its implications for collagenous tissue disorders in hard and soft tissue organs. Part V offers closing comments. Table 1 lists some clinical problems that depend wholly or in part on collagenous tissue, and some medical specialties that deal with them.

II. The frozen shoulder syndrome (generally accepted features)

1) *Clinical features*[3,8,36-41]. Also called pericapsulitis, adhesive capsulitis and periarthritis, this uncommon syn-

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drome usually affects men and women over 40 years of age; it seldom if ever affects children[32]. Most cases do not follow an injury, but some do. A poorly localized ache in the affected shoulder begins at rest and at night. Pain occurs when the shoulder is moved to the limits of its ranges of motion. Mild but diffuse tenderness of the shoulder can occur. Glenohumeral motion slowly decreases until patients substitute scapulothoracic motion for it. The first and greatest decreases in motion affect abduction and external rotation. The deltoid and supra- and infraspinatus muscles atrophy. I have not seen or heard of a recurrence of this syndrome in the same shoulder, but within a decade about one patient in ten can develop it in the other one[22]. A similar uncommon phenomenon called "trismus" by dental people can affect the temporomandibular joint.

2) *Laboratory and other findings*. No consistent abnormalities have appeared in routine blood and urine tests, or in cultures from the affected shoulder, or in hepatic, renal, thyroid and collagen-disease profiles, or in the sedimentation rate, serum protein electrophoretic pattern, synovial fluid or synovium. After a month or so scintograms can show a mild increase of the bone-seeking isotope in the humeral head of the affected shoulder, which can also show an osteopenia on ordinary X-rays. The subdeltoid bursa and glenohumeral joint may demonstrate reduced fluid capacity during arthrograms.

SOME CLINICAL-PATHOLOGIC CONDITIONS THAT INVOLVE COLLAGENOUS TISSUE VITAL BIOMECHANICS (wholly or in part)	
Pericardial stenosis	Frozen shoulder syndrome
Esophageal stricture	Rheumatoid arthritis
Dupuytren's disease	Ureteral strictures
Peyronie's disease	Varices
Post-polio joint contractures	Intestinal adhesions
Contractures of incisions	Patella baja
Patella alta	Fracture healing
Soft tissue healing	Algodystrophy
Burns	Hernias
Myopia	Hyperopia

SOME MEDICAL SPECIALTIES INVOLVED IN SUCH CONDITIONS	
Plastic surgery	Orthopaedic surgery
Cardiovascular disease	Physical medicine
Sports medicine	General surgery
Rheumatology	Rehabilitation
Ophthalmology	Dermatology
Urology	Gastroenterology
Cerebral palsy	Pediatrics

Table 1

3) *On the anatomical pathology.* Early authorities thought intraarticular adhesions cause this syndrome[3,8]. Not so. Contracted collagenous components of the shoulder capsule and ligaments (and of the scapulohumeral muscles?) cause it. They can rupture audibly during manipulations under anesthesia, and they can reduce the fluid capacity of the subdeltoid bursa and shoulder joint during arthrograms. On opening or arthroscoping these shoulders many surgeons noted various abnormalities[3,23,24,38], but they differed from patient to patient and surgeon to surgeon. Previous treatments could have caused many such findings, since one would seldom operate on these shoulders unless symptoms persisted or increased during other therapy.

4) *Conventional treatment[9,38-41].* No consensus exists about the best treatment of this syndrome. Current treatments include A), daily stretching of the shoulder's ranges of motion (nearly invariably prescribed). They also include varied combinations of B), other kinds of physical therapy, C) injections into the subdeltoid bursa or shoulder joint, D) oral medications and analgesics, E) shoulder manipulation under anesthesia[6], F) and surgical release of the joint's capsule and ligaments[40,41]. G) Most authors found this syndrome took from one to over three years to resolve, and some patients had permanently impaired shoulder function.

III. The author's experience

When I outlined some of the above treatments to Yale orthopaedic residents in 1956, one of them (Dr. Leland Lugar, now deceased) said a senior physician told him such patients only needed analgesics to let them sleep, because if untreated the syndrome would resolve by itself. Accordingly a new patient with this syndrome took Tylenol with codeine for her night pain but had no other treatment. To my surprise, in the next four months her syndrome did resolve.

1) *Post-1956 management.* After that 1956 experience I managed over 120 more such cases similarly (about three per year). Specifically, A) an analgesic was prescribed for the night pain, usually for less than three months, B) patients were told to avoid shoulder stretching exercises and activities that caused pain as long as they did, C) and they had no other therapy at all.

Within four to six months the syndrome resolved in all those patients too. That experience revealed two things: The untreated syndrome is self-limited without lasting ill effects, and it has two overlapping phases[22]. A) In the initial *night pain phase* vaguely localized pain begins in one shoulder, usually without known cause and mainly at rest and at night. This rest pain peaks in about two months and then disappears in the next two months. B) At first shoulder motion is normal, but when the night pain becomes severe limited external glenohumeral rotation and abduction have usually begun. In about two more months little glenohumeral motion remains. In that full *frozen shoulder phase* only forcing motion to the glenohumeral limits causes pain. At rest little or no pain occurs. After about two more months normal glenohumeral motion returns and all shoulder pain ceases. Or:

|......rest/night pain phase.......| (≈ 4 months)
          |.......frozen shoulder phase....... | (≈ 4 months)

Hence this syndrome's true "natural" course of about six months.

2) *Comments:* Few orthopaedists presently accept that experience (some do[36]). But those who reported longer and more troubled courses for this syndrome analyzed patients treated with intensive stretching[23,38,40,41], which I found increased the pain, prolonged recovery, required more and stronger analgesics, and sometimes led to permanently impaired shoulder function. Curiously, shoulder manipulation under anesthesia (by other surgeons) when the night pain and frozen shoulder phases overlapped usually ended the night pain phase (exception: a patient with a later-discovered Pancoast tumor in the ipsilateral lung). In the night pain phase unusual tenderness often occurs deep in the soft tissues of the neck behind the clavicular origin of the ipsilateral sternocleidomastoid muscle. Its significance is unknown.

3) *On the need (?) for early shoulder motion.* Orthopaedists usually prescribe stretching exercises for this syndrome to "prevent permanent stiffness". Yet in 53 years of ortho-

paedic work the only permanently stiff shoulders I saw came from severe intrinsic joint disease (post-traumatic or otherwise), after a stroke, or after aggressive treatment of this syndrome. While some other joints can develop permanently limited motion after severe sprains, dislocations, local fractures or burns, permanent shoulder stiffening from such causes is rare. Of course early motion of this joint has other benefits.

IV. On the syndrome's pathology and pathogenesis

1) *On the disturbed tissue.* Since this syndrome stems mainly from problems in collagenous tissues in the joint capsule and ligaments (and in the intrinsic shoulder muscles?), we need to understand the physiology of the collagen in the affected tissues, and its organization from the ultrastructural to the macroscopic levels. We also need to distinguish *strengthened* collagenous tissue structures from contracted or *shortened* ones, since different mechanisms usually cause each[16].

2) *On strengthening.* By 1972 I had suggested special strain threshold ranges could make modeling thicken and strengthen bones, ligaments and tendons until subsequent strains fell to or below those thresholds[13]. Subsequent research did find that bone has a modeling threshold centered in the 1000-2000 microstrain region in young adults [12,45,48], when bone's ultimate strength as a strain is a range centered near 25,000 microstrain[28,35].

For ligament and tendon that and other evidence led to this "stretch hypertrophy" rule in 1972: " Intermittent stretch causes collagenous tissues to hypertrophy until the resulting increase in strength reduces elongation in tension to some minimum level"[13]. Varied evidence[37,43,47] suggests the strain threshold for that "diametric modeling" in young adults may lie in the 40,000 microstrain region (a 4% stretch). When expressed as a strain the ultimate strength of young-adult ligament and tendon is a range centered near 70,000 microstrain (a 7% stretch)[35,53]. This modeling threshold would make the strength of every ligament and tendon in the body exactly fit the needs of its typical peak tension loads. However shortened instead of strengthened collagenous tissues seems to be this syndrome's chief problem.

3) *On shortening.* Some cellular mechanism(s) that may depend on actin can shorten collagenous tissues[10,51]. Besides the frozen shoulder syndrome, other orthopaedic examples include: A) Slow contractures of the palmar and plantar fascia in Dupuytren's disease[1]; B) contractures of joint capsules and ligaments (and muscles?) in limbs casted for long times, in some cases of osteoarthritis, after some paralyses and pareses from anterior poliomyelitis and cerebral palsy, and after severe sprains or dislocations of some joints[11,32]; C) the tendency for such contractures to recur after wedging casts or constant traction correct them; D) and the post-injury patella baja syndrome in which the infrapatellar tendon (some call it the patellar ligament)

shortens[31].

Excessive shortening can affect extraskeletal collagen too. Some examples: E) The tendency for longitudinal incisions across the flexor surfaces of normally moving - not immobilized[22] - fingers, elbows and knees to shorten and require corrective Z-plasties[49]; F) acquired (not congenital) pericardial stenosis in which the pericardium shrinks and loses its extensibility, which limits filling of the ventricles[4]; G) slow contractures of intestinal adhesions that can cause a bowel obstruction months or years after the laparotomy that caused them; H) many ureteral, urethral and esophageal strictures[4]; I) and contractures of the penile cavernosae in Peyronie's disease[1].

I called that a creep compensation mechanism[13], since it could prevent a slow, irreversible stretching of tension-loaded fascia, ligaments and tendons. Engineers call that phenomenon "creep" (see the Glossary). In the frozen shoulder syndrome that mechanism would shorten the joint's capsule and ligaments (and the collagen in the intrinsic shoulder muscles?). Since the untreated syndrome resolves spontaneously but the kinds of contractures in "A-I" above do not, one wonders why. Section #1,B in Part V below mentions a possible answer.

If excessive creep compensation causes one group of problems, too little of it might cause unusual laxity of affected structures. This occurs too. A few examples include: J) Laxity of ligaments and the dermis in Ehler-Danlos syndrome[5]; K) esophageal and lower-limb varices in which the collagenous adventitia around veins expands or "balloons"[4]; L) ligament laxity in many cases of rheumatoid arthritis, especially of metacarpal-phalangeal joint collateral ligaments[48]; M) patella alta, in which stretching of the infrapatellar tendon lets the patella lie too far proximally on the femoral condyles[30]; N) slow dislocation of the hip in some infants, or in some older children with spastic cerebral palsy (it cannot occur unless the hip capsule stretches irreversibly)[11,15,32]; O) and joint laxity in other situations[44].

Since the things in "A-O" above affect limited anatomical regions instead of all the body's collagenous structures, that begs the question of why. Possible answers follow.

4) *Thoughts on control of creep compensation.* If a stimulus above some threshold strength can turn creep compensation on, increasing the stimulus strength should do it. But so could lowering the threshold, so smaller stimuli than before could turn it on. That might help to explain things like "A-I" above. Yet if that occurs in the frozen shoulder syndrome it must be temporary, since the untreated syndrome resolves spontaneously while the "A-I" examples do not. On the other hand, raising such a threshold could keep creep compensation off when it should turn on. That might help to explain things like "J-O" above.

Two strain levels help to control bone's responses to mechanical stimuli. Where dynamic strains stay in the lower level only lamellar bone is formed, but where larger strains occur (usually above 3000 microstrain) woven bone usually forms instead[17,35]. Might creep compensation in collagenous

tissues have a similar "dual" property? Could normal low-level demands make the mechanism function in a very slow mode, but could higher-level demands make a more vigorous mode shorten collagenous tissues more quickly and help to explain "A-I" above? If so that could help to explain why tension-loaded joint capsules, tendons and ligaments do not normally shorten throughout life, but why some local stimuli can make them do it only in that region.

5) *The regional acceleratory phenomenon (RAP).* General features. Normally infection, trauma and some tumors accelerate all ongoing regional tissue processes [17,33,34,52]. That defines the RAP. In hard and soft tissues it normally hastens perfusion and healing, and it increases resistance to infection. It can last for many months in a bone or joint, depending on the severity of the original injury or other stimulus. a) A RAP helps to cause increased regional soft and hard tissue turnover after fractures and other injuries, during infections, and after surgical procedures[6]. b) The increased remodeling space that accompanies increased bone turnover during a RAP can cause an osteopenia[35]. c) A RAP can hasten the development of joint contractures after major regional surgery, trauma or burns. d) A RAP increases bone formation by increasing bone remodeling. e) Excessive and unduly prolonged RAPs cause algodystrophy, also known as migratory osteoporosis[7]. RAPs also help to cause Sudek's atrophy[48]. f) Things that increase musculo-skeletal pain usually increase and prolong a RAP[22].

First described long ago[14], the RAP became well known to people doing live-animal bone research[26-28,35].

In the frozen shoulder syndrome. A) A RAP is part of this syndrome[22] and it may hasten the untreated syndrome's evolution. B) By increasing regional bone remodeling and formation that RAP would cause the mildly "hot" shoulders that can occur in scintograms during this syndrome[38] (two such shoulders the author biopsied in the 1960s did show increased bone turnover in the humeral head). C) The increased remodeling space that accompanies a RAP, plus mechanical disuse due to pain, should cause or help to cause this syndrome's regional osteopenia[17,19]. D) Osteopenias weaken bones, which could help to explain why manipulations of these shoulders under anesthesia sometimes fracture the humerus[38]. E) Aggressive stretching and surgical procedures should accentuate and prolong that RAP, which may help to explain the prolonged course most physicians note who prescribe or do such things. F) The clinical behavior of normal, impaired and excessive RAPs suggests threshold signal strength(s) help to turn them on and off[22].

V. Comments and Conclusion

1) *On the Utah paradigm.* A) Collagen's involvement in many clinical disorders stimulated intensive cell- and molecular-biologic research on its physiology[5], but that research assumed chiefly fibroblasts cause such disorders[20]. Or: Agent → fibroblasts → health/disease. To that idea the Utah paradigm added later-discovered "nephron-equivalent" mechanisms and functions (see the Glossary), and Table 2 lists some examples. B) That paradigm suggests that if an extraneous influence disturbed a collagenous tissue

Diametric modeling	determines thickness, strength and stiffness of tendon, ligament, fascia and joint capsules in response to repeated dynamic tension strains above a modeling threshold range; analogous to formation drifts in bone modeling[28].
Micromodeling	determines the light microscopic and ultrastructural organization of the tissue; it helps to make scar different from tendon, tendon different from fascia, woven bone different from lamellar bone, and fibrocartilage different from hyaline cartilage.**
Creep	here a slow, irreversible - not viscoelastic - stretching under tension loading.
Creep compensation	prevents and/or corrects irreversible creep, possibly in two modes, a slow and a fast one.
Collagenous tissue BMU (Basic Multicellular Unit)	An analog of the remodeling BMU in bone[17,48].**
Microdamage (fatigue damage)	its strain threshold, occurrence, detection, repair.**
End-growth in length at muscle and bone, and interstitial growth in length.	
Disuse responses	they reduce thickness, strength, stiffness, and collagen and proteoglycan content.**
The tissue's mechanostat	a complex mechanism that orchestrates the above activities in ways that make collagenous structures strong enough to keep typical peak voluntary tension loads from rupturing them or causing a fatigue failure.**
The tissue's Regional Acceleratory Phenomenon (RAP).	
The "loading history", the "strain history", transients, and steady states.	
*: Modified from[17] **: Discussed in[17] but not here	

Table 2. Vital-Biomechanical features of collagenous tissues and organs ("nephron equivalents" and their functions that need systematic study)*.

organ's mechanical functions but did not change the thresholds of the mechanisms that control or help to control those functions, then if the extraneous influence subsided normal function would tend to return. That does occur after most injuries and infections of fascia, joint capsules, ligaments and tendons, as well as in untreated frozen shoulder syndromes. One wonders what "extraneous" influences could incite that syndrome mainly in the shoulder and temporomandibular joints[22].

2) *Summation:* This "virtual laboratory" exercise does suggest answers for some old questions, and it does reveal new targets for organ-, tissue-, cell- and molecular-level research on collagenous tissues and organs made from them. Those targets include the entries in Table 2 as well as the roles in such things of normal and abnormal proteoglycans and collagen types, and many nonmechanical factors. And of course the roles of "X", what we do not know yet but should.

Do the above paragraphs outline the "whole story" for the frozen shoulder syndrome and collagenous tissues and organs? History responds thus: whatever we know now, more always remains. Thus future studies could add more surprises to any some readers might think they already found in this article.

Glossary

creep: here, a slow irreversible and non-viscoelastic stretching (also called "plastic flow") of a collagenous structure due to the tension loads on it. During general growth of the body the collagenous capsules of organs like the liver, heart, lung, kidney, gut and pancreas, and the deep fascia throughout the body, slowly and irreversibly stretch to accommodate the increasing volumes of the organs they encapsulate. While physiologists call that a kind of growth, as defined here it is also creep. This creep also helps to explain the elongation of ligaments during growth of the body[16,50], and the stretching of such structures in joints with contractures by constant traction or wedging casts. Such things are only some of the proof that this creep occurs in these tissues. Nota bene: Many biomechanicians use creep to designate an elastic and reversible slow deformation in viscoelastic materials. This text does not use the word in that sense.

diametric modeling: see "modeling" below.

effector cells: in collagenous tissues these are the fibroblasts that make the collagen and associated proteoglycans, but not the precursor or other "supporting" cells needed to create and help to control the fibroblasts.

fibroblast: here, a cell involved in making new collagenous tissue. Distinguished from their precursor cells and from fibrocytes, the apparently "resting" cells in mature collagenous tissue.

microstrain: see "strain" below.

modeling: the biologic processes that produce functionally purposeful sizes, shapes and organization in skeletal organs. In *diametric modeling* of collagenous tissue structures,

fibroblasts would make new collagen when strains reach or exceed a putative modeling threshold[16]. That would increase the affected structure's diameter, thickness, stiffness and strength, but not its length. When that reduced further strains to or below that threshold this modeling would turn off. Clinical-pathologic evidence reviewed elsewhere[17] shows this modeling threshold exists, so the valid issues lie in its magnitude, how to express it, and what things help to control it. In bones resorption and formation drifts provide modeling[28,35].

nephron equivalents: to understand renal function requires understanding the kidney's many kinds of cells and the structure and functions of nephrons made with those cells. Nephrons provide functions no single kind of cell can provide but which are essential for the organ's functions and an individual's health. Bone, cartilage, collagenous tissue, dentin and cementum (the skeleton's chief structural tissues) have "nephron equivalents" that have the same relationship as nephrons to their individual cells and to the tissue's and organ's functions and health[42]. Small cohorts of workers (including Prof. WSS Jee and me) began to recognize the skeleton's nephron equivalents after 1963. Previously none were known as such.

nonmechanical factors: here, things like age, sex, hormones, vitamins, minerals, nutrition, race, genetic endowment and expression, cytokines, ligands, drugs, pH, oxygen tension, apoptosis, etc.

remodeling space: increased BMU-based remodeling increases the number of holes in a bone or excavations on its surfaces. This can temporarily remove over 30% of a bone, but when remodeling decreases to normal the existing holes fill up with new bone, which restores the "missing" bone. Before that refill temporary osteopenia exists relative to the original bone "mass".

strain: the deformation or change in dimensions and/or shape caused by a load on any structure or structural material. It includes stretching, shortening, twisting and/or bending. Special gages can measure it in the laboratory and *in vivo*. Loads always cause strains, even if very small ones. Biomechanicians often express strain in microstrain units. A tension strain of 1000 microstrain would stretch a tendon elastically by 0.1% of its original length; 10,000 microstrain would stretch it by 1.0% of that length; and 100,000 microstrain would stretch it by 10% (and rupture it). We can measure strain directly but must infer or calculate stress from other data.

vital biomechanics: a subfield of general biomechanics that concerns how a skeleton's biologic mechanisms adapt it to its voluntary mechanical usage and loads to let it endure them for life without breaking spontaneously. It concerns bones, joints, tendons, ligaments and fascia, the structural tissues used to construct them, and the thresholds that help to control the rates and end points of the biologic activities in those tissues. Some object to the "vital", since "bio-" already implies it. Good point; suggestions for a better term would be welcome.

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