



The effect of transdermal T3 (3,3',5-triiodothyronine) on geloid masses found in patients with both fibromyalgia and myofascial pain : double-blinded, N of 1 clinical study.

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Certains patients présentant en même temps une fibromyalgie (FM) et un syndrome myofascial chronique (SMC) peuvent développer des masses géloïdes dans des sites anatomiques comprenant depuis longtemps des points gâchettes résistants [1]. Une étude récente montre que ces patients présentent également un taux très important d'acide hyaluronique dans le sang [2]. La triiodothyronine-3,3',5 (T3) peut moduler cette production. En partant de ce postulat, nous allons démontrer que l'administration transdermique de T3 peut modifier la consistance de ces masses. La majorité des patients ayant participé à cette étude ont rapporté une amélioration significative de leurs symptômes et/ou un traitement médicamenteux allégé. Sans être directement corrélée aux points gâchette, la masse géloïde est plutôt un phénomène discret rencontré plus particulièrement chez des patients présentant simultanément un syndrome myofascial chronique avec une fibromyalgie ou un autre syndrome douloureux chronique. L'approche thérapeutique par T3 facilite le traitement de ces zones douloureuses.

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Abstract

Purpose: To assess the effectiveness of topical 3,3',5-triiodothyronine (T3) on patients who have fibromyalgia syndrome (FMS), chronic myofascial pain (CMP) due to trigger points (TrPs) and geloid masses.

Subjects and Methods: Ten subjects with documented FMS tender points, CMP, and geloid masses were enrolled in a randomized, double-blinded N of 1 clinical trial. Initial questionnaires evaluated subjective patient perception of their pain and representative geloid mass areas were measured and rated with a tissue compliance meter. Transdermal creams, one a placebo, one with topical T3, were compounded and distributed in increments of 10 days. Participants filled out daily questionnaires and received a physical examination every 10 days.

Results: Topical T3 generally resulted in a softening of the geloid masses over time, allowing TrPs and taut bands to become more accessible and treatable. Some patients reported reduced pain, reduced medication use, increased function, and/or improved mood and cognitive skills.

Conclusions: T3 therapy did not affect the taut bands or TrPs directly, but by reducing the firmness of the geloid areas, made the TrPs more available for treatment. The presence of geloid masses may add to patient discomfort and loss of function, may contribute to loss of range of motion, and complicate treatment. It is important that clinicians be aware of and palpate specifically for these masses.

Key Words: fibromyalgia, myofascial pain, trigger point, geloid mass, triiodothyronine.

Some patients with both fibromyalgia syndrome (FMS) and chronic myofascial pain (CMP) may develop geloid masses in areas of long-standing resistant TrPs [1]. Recent research indicates that a subset of people with FMS has been shown to have excess hyaluronic acid (HA) in their blood [2]. 3,3',5-triiodothyronine (T3) has been shown to modulate the production of HA. We postulated that if HA,

naturally occurring in the ground substance between cells, was an important component of these geloid masses, that transdermal administration of T3 may alter their consistency.

Subjects and Methods

Between March of 2000 and May of 2000, 10 subjects with documented FMS tender points [3], chronic myofascial TrPs [4], and geloid masses were enrolled and 9 treated with topical T3 and a placebo in an N of 1 double-blind study. A "geloid mass" is defined as a geloid, rubbery or hard, clearly definable, discrete and measurable mass that is an extremely taut area of dense tissue with palpable margins. There is no presence of trophedema with matchstick sign or orange-peel skin [5] associated with the geloid mass, nor associated pitting edema. For the purpose of this study, only geloid masses \geq than 2.5 cm in diameter were evaluated; their texture could be in any stage of development, from easily pliable to hardened. Current thyroid supplementation or any history of abnormal thyroid function was considered exclusionary.

All patients were assessed prior to beginning the study; initial questionnaires documented subjective patient perception of their pain [6, p 478-485] and a minimum of 3 representative geloid mass areas per patient were rated using a tissue compliance meter [7]. The tissue compliance meter enables measurement of soft-tissue consistency in a consistent, objective and quantitative manner [7]. Pressure threshold and pain tolerance were measured at the medial deltoid and medial flare of the tibia directly on bone as a control. Pressure and pain tolerance measurements were taken at the outside and inside borders of specified geloid masses, and at the center of the mass exhibiting palpable differentiation in texture. These placements approximate the areas specified by Fischer for the documentation of myofascial TrPs [8]. Other measurements taken included the approximate size of each geloid mass, the approximate density/depth of the mass, and its texture. A numerical code was developed with descriptive characteristics to facilitate examination and description. Approximate range of motion on some involved muscle function groups was determined.

Transdermal T3 was formulated in a cream base at 7.5 mcgm/0.1 ml at a dosage of 0.2 ml/day, with matching placebo. Only the compounding pharmacist was unblinded to the content of each cream. Subject identification numbers were dictated by the order of the initial appointments. The first subject began with cream A, and the second with cream B, continuing alternately. Subjects were given 10 days' supply of T3 cream or placebo at each visit. To ensure consistency in application, subjects were instructed to always apply the cream to the area under the jaw line, first cleansing the area thoroughly, using soap and hot water, rinsing and drying, then applying 0.2 ml of the topical cream, rubbing it in gently but thoroughly. This was to be done at approximately the same time each day. Study participants were instructed to avoid washing or wetting that area (washing hair, swimming, etc.) for at least 4 hours after each application to ensure that all medication was absorbed. The creams were distributed in increments of 10 days, randomly beginning with either "A" or "B". Participants were instructed to fill out the brief pain inventory [6, p 61] daily, and rate their pain measurement on a visual analog scale (VAS) for pain level from 0 to 10 [6, p 87]. They were instructed to take normal pain relief medications if needed and to follow their normal physical therapy, stretching and exercise routines. They were requested not to add any additional medications or therapies until the study concluded.

Every 10 days over a period of 40 days the specific geloid masses were palpated and measured and subjects given a new 10-day supply of cream, switching from one formulation to the other, each patient serving as his/her own control. Subjects were called by telephone to check on their status between exams, and were supplied with phone numbers in case of questions or a change in symptoms. Subjects were given written instructions about possible symptoms of excess thyroid medication, including faster pulse rate, frequent bowel movements, hair loss, extra sweating to discomfort, shaking or tremor, unusual anxiety, acne, or leakage from the bladder.

A minimum of 3 geloid masses was assessed at each examination, although many of the test subjects had more. Palpating a single TrP can cause severe pain for days [4, p 117]. When both FMS and CMP are present, a physical examination can be exceedingly painful and have lasting repercussions for the

patient. These exams were done in a way so as to minimize discomfort, and with the understanding of the test participant.

General Observations General Observations

Some participants required help filling out initial forms. Cognitive deficits are commonly associated with FMS, as are the distraction and confusion that can accompany chronic pain states. Many participants also reported multiple head traumas. They generally had difficulty distinguishing between tenderness and pain. They often denied pain or pressure sensations during tissue compliance meter testing, and would abruptly reach a state of overwhelming pain intensity that threw them into an intense reaction. These reactions varied, including fight, flight, startle or freeze responses. These frequently took the form of denial, rapid talking to distract from pain, mentally disassociating from pain, hypersensitivity to further sensations, or muscle tensing against pressure or pain. The subjects usually appeared unaware that they were utilizing these mechanisms. Some patients had fibrotic or calcified areas, and/or contracted muscles due to TrPs, and this altered the tissue compliance meter readings.

Geloid masses, at the most obvious stage, felt swollen, or resembled the consistency of a (pre-implantation) silicon implant to the touch, with a palpable firm border specific and localized to the resistant TrP areas. No pitting was associated with these masses. On the initial exam, in many cases neither the underlying TrPs nor taut bands could be distinguished due to the texture of the overlying geloid mass. As the masses reduced in density, depth and/or size during cycles on T3, TrPs and/or taut bands were revealed. The TrPs became available and responsive to appropriate manual TrP treatment. The skin became less attached to the underlying layers. Geloid masses appeared to "melt" and became more malleable to palpation. While still having palpable margins and swelling, aggregations of smaller individual hardened areas became palpable within the softer mass, like BB shot in an inflated water balloon. In some cases, during a subject's second T3 cycle, there was dissolution of these nodule "beehives" into separate nodules and/or taut bands under the skin where the bulk of the geloid mass had been. During the intervening cycles on placebo, many of the patients experienced rehardening of the masses, with greater restriction of range of motion.

Geloid masses that were documented in the test subjects most typically occurred in the vicinity of multiple myofascial TrPs in the right quadriceps femoris muscle group [9] and bilateral pectoralis muscles [4]. Geloid masses associated with typical pectoralis TrP areas were often found proximal to the clavicle covering at least half the distance to the nipple. Some pectoral geloid masses extended to the axillary area from the sternalis, and/or into the serratus anterior. Most patients had bilateral geloid masses on the quadriceps femoris muscle group. The borders on the geloid masses were irregular, and were measured at the greatest dimension.

In some geloid masses, more frequently in the quadriceps muscle group, the change in density and texture indicated a slow melting into two separated masses within the original margins. In others, the original mass split into two separate masses. Each of these masses had discrete borders. These masses occurred in typical locations of myofascial TrPs [4, p 36]. In the case of dual masses, with one mass over another, there was a change in density, so that there were margins within margins. Some geloid masses actually became larger in size with T3 treatment, but were softer to palpation and more malleable, and with less depth. The melting appeared to occur first at the surface of the mass, progressing to deeper areas. As some of the geloid masses melted, it felt as if there were other geloid masses possibly associated with TrPs in different layers of the muscle tissue, and one mass had been engulfed by the other.

The center of each geloid mass occurred over typical TrP sites [4, 9], and the patients often exhibited typical symptoms associated with those sites. It was not possible to palpate the underlying TrPs in some subjects during the initial examination due to the pain touch produced. Some subjects were so sensitive to touch that they were unable to tolerate the 8.9 cm foam examining table. These subjects were provided a 17.8 cm thick air mattress over the table.

In these study participants, as in many patients with both FMS and CMP, on palpation the skin did not move easily over the underlying layers [10]. A broad flat thickening of subcutaneous tissue, sometimes

granular, with hypersensitive skin were often evident in the test subjects. This combination is referred to by Simons, Travell and Simons [4, p 115] as "panniculosis", and is associated with myofascial TrPs. In our subjects the panniculosis was a wholly separate phenomenon from the geloid masses.

Direct pressure on a geloid mass in some subjects caused sufficient pain to enhance FMS amplification of pain perception, which further aggravated TrP symptoms. After use of the tissue compliance meter, there was often an intense histamine reaction in the skin leaving red welts, even though some patients were on maximum dosage of antihistamine. This reaction has also been documented in skin covering muscles with TrPs [4, p 115].

Specific Case Highlights

This section includes some possibly significant commentary, findings and notation from the study records on a patient-by-patient basis. In general, by week 3 of the study, most of the participants suspected which cream was the T3, although there was often a lag time, due to the positive effect of the therapy.

Subject #1 male, age 55. On the first T3 cycle, patient remarked, "This is a hell of a placebo. I can walk down the stairs in the morning using my right foot every stair. I haven't been able to do that in 10 years." At the beginning of the study, all test areas tissues were taut, and the subject did not respond to pressure/pain at the maximum readings of the tissue compliance meter. The sizes of the geloid masses increased on the placebo, and decreased on the T3. There seemed to be a 3 to 5 day lag time from the beginning of each preparation until a change was noted. Only after the periods on the T3 was this patient able to feel pain on palpation. The geloid masses became softer and the "melting" phenomenon was evident after T3 therapy, and pain interfered less with mood. Patient one improved significantly on the T3 cream after the initial placebo cycle. The amount of pain medication also decreased substantially, and the activity level increased significantly.

Subject #2 female, age 52. This subject had difficulty filling out initial form. Cognitive difficulties were significant on the symptom list. There were two masses on the R. pectoralis at the beginning of the study (8.9 x 8.9 cm and 10.2 x 10.2 cm). By the end of the study they had combined into one mass (12.7 x 15.2 cm). Patient reported "unusual clearness of thinking" for the last few days on T3 therapy cycles. Her daughter asked her why she was "10 times happier". She reported that pain was no longer absorbing her. The switch to placebo provoked a relapse, and she reported that she was "edgy, and hurt more . . . I want to be happy again . . . Hoping I get the good meds soon." Relief remained for 5 days after switching to placebo, with a 5 to 6 day lag time before relief on T3.

Subject #3 female, age 44. Lyme Disease onset. History of incapacitating migraines. Undergoing heavy stress during study period. At the first two exams, tissue compliance meter control measurements indicated muscle myopathy, but this had begun to reverse by 3rd exam. During the T3 therapy, the patient reported that her bowel movements became dark green. She reported this had happened previously during estrogen therapy. She began to experience headaches, and was withdrawn from the study. This patient had completed one cycle of placebo and T3, and was withdrawn during the second placebo cycle.

Subject #4 female, age 59. Initial exam and exams after periods on placebo, tissue compliance meter control measurements were indicative of muscle myopathy [8]. After each cycle of T3 therapy, no myopathy was indicated. There was a lag time of about 4 days before noticing change on each cycle. Note of improved sleep and lessened pain on T3. Reported overall sense of well being, physically and emotionally, and a sense of mental clarity during the day. After the T3 therapy, she remarked, "I have no pain as I've had for past 18 months in left hip. I'm feeling an entire new sensation while walking! . . . There's a miracle going on here". By end of each placebo cycle she reported she was in severe pain all the time, and waking in pain again. At the first exam, the patient was measured with two geloid masses on the R. pectoral area and one on the R. quadriceps femoris . By the conclusion of the study, there was only one pectoralis mass, and the quadriceps mass had started to "melt", with one firmer and smaller geloid mass being palpable inside the larger quadratus mass. . During the last placebo cycle, the pain and other symptoms returned gradually, without an extended lag period .

Subject #5 female, age 67. High pain tolerance and then a startle response. At the end of the 2nd cycle of T3, the mass in the left pectoralis started separating with a slight fissure or divide in the middle. The patient was physically very active during the study period. By the 3rd day of T3 therapy, she noted feeling "fine" on waking. By the 5th day, she reported getting a lot done, and picking up the pace, "Noticed a quantum leap in ROM (range of motion)." During the first placebo cycle, some pain started to return by day 3. By day 4 of placebo, she reported fragmentation of thought and inability to finish tasks. She reported, "...brain fog back totally by day 5..." "Miss the clarity". On T3 therapy again, she noted, "something is lifting . . . my body felt increasingly lighter". As the generalized "old pain" (fibromyalgia) lifted, the "new pain" (myofascial trigger points) became more obvious. She reported a small amount of diarrhea, wild dreams, and some hair loss on T3. She noted that she dreaded the end of the trial because "am so much helped by T3, and so miserable without it . . . I can't get over how resilient I am if I get good sleep."

Subject #6 male, age 55. Extreme cognitive difficulty. No significant change on either placebo or T3.

Subject #7 female, age 48. Multiple severe stressors during study. Several times forgot to use the cream. Tissue compliance measurement controls showed evidence of myopathy [8]. The geloid masses were visible to untrained eye. Beginning at the sternal/clavicular junction, the entire clavicle was surrounded with a red, puffy, swollen mass. It was difficult to palpate due to severity of pain. By the conclusion of the study, the redness and swelling had subsided. The examiner could tell by palpation that the sternocleidomastoid (SCM) muscle was entirely fibrotic and the scalenes were calcified. This area was so sensitive the subject could barely be touched without pain. Attachment TrP taut bands were most prominent to palpation. The R quadriceps mass decreased from 25.4 x 38.1 cm to 15.2 x 27.0 cm by the end of the study. Subject reported that she was feeling somewhat better at the end of the study than when she began, but she was very tired and wished that she had more time to rest.

Subject #8 female, age 34. Immediately before the initial exam, subject reported she would be attempting to conceive during the test period and was withdrawn from the study.

Subject #9 female, age 50. On T3 therapy, subject reported that she felt a lot better, but then overextended herself, which resulted in increased pain and exacerbation of other symptoms. With a lag time of about 4 days, on T3 therapy there was an improvement in mood, ability to walk, and enjoyment of life, with less interference in general activity from pain. The geloid mass in the R quadriceps started out as a solid mass but began to melt by the end of the T3 therapy, with improvement in texture at both top and bottom of the mass.

Subject #10 male, 67. Patient reported there seemed to be less pain interference with life during the T3, with a 4-5 day lag time. During periodic phone call status checks; he reported that he felt much better during the T3 cycles.

Discussion

FMS and myofascial TrPs are two of the three most common sources of musculoskeletal pain, the other being articular dysfunction [4]. CMP and FMS are separate conditions, although they are often confused in the literature [11]. The majority of patients with FMS also have active myofascial TrPs [12; 13]. Both FMS and CMP may cause severe *muscle* pain, although current research supports FMS as a disturbance of the neuroendocrine axes [14]. The etiology is unknown. Although they often co-exist, FMS and CMP require different treatment approaches [4]. When they occur together, they may create more misery than simply the sum of the two conditions [10]. Many patients simply cannot endure studies that require them to cease their regular medication and other therapies for the duration of the study. Pain itself becomes a perpetuating factor, further sensitizing the central nervous system [10]. The authors began this study well aware of the added variables, but convinced that this was the most humane way to conduct this study.

Diagnosis of FMS for clinical research requires confirmed tenderness associated with 11 or more of 18 specified tender point sites, with widespread diffuse pain. FMS is described as a centrally mediated hypersensitivity to painful stimuli [3]. It is noninflammatory, with disruption of the hypothalamic-pituitary-adrenal axis and its reciprocal interactions with the hypothalamic-pituitary-gonadal axis, locus

ceruleus/norepinephrine sympathetic nervous system, hypothalamic-pituitary-thyroid axis, and hypothalamic-pituitary-growth hormone axis [15]. Allodynia (pain response from non painful stimuli) is also common [16], as well as lack of restorative sleep [17]. Research indicates the tendency to develop FMS is inherited [18, 19, 20, 21, 22]. The c-erbA beta1 gene may be involved in FMS [23], leading to partial thyroid resistance. One study found 12% of FMS patients have primary hypothyroidism, 44% have laboratory values consistent with central hypothyroidism, and 44% are euthyroid [24]. Euthyroid FMS may be associated with thyroid resistance that responds to treatment with T3 [25].

Myofascial pain due to TrPs has been identified [26] and confirmed [27] as a neuromuscular disease, rather than a syndrome. It is for this reason that the term "chronic myofascial pain (CMP)" is used in this paper, rather than the better known "myofascial pain syndrome (MPS)". This condition should not be confused with the generalized term "chronic pain syndrome", which is often dismissed as being psychological, nor used as a synonym for Temporomandibular Joint Dysfunction [28]. Trigger points can occur all over the body, and are specific areas of hyperirritability caused by excessive release of acetylcholine at dysfunctional motor end plates [4]. A myofascial TrP creates a localized region of great oxygen and energy demand with limited supply. A TrP contains multiple foci in constant energy crisis.

Referred pain from TrPs characteristically produces recognizable regional pain patterns. TrPs exhibit the following criteria: a palpable taut band, exquisite spot tenderness of a nodule in the taut band, patient recognition of pain complaint by pressure on the tender nodule, and a painful limit to full stretch range of motion. There is often apparent muscle weakness due to inhibition, and/or autonomic symptoms. Chronic myofascial pain is a primary cause of disability, and may develop secondary to trauma such as low back surgery, cervical whiplash, overuse, or repetitive strain. It often complicates other medical illnesses and injuries [4]. The presence of multiple TrPs with overlapping pain patterns can complicate identification of a single specific TrP pain pattern. This overlapping referral area is known as a "composite pain pattern" [4]. When primary TrPs develop satellite and secondary TrPs with composite pain patterns covering much of the body, they may produce the impression of generalized pain. It is often possible, by testing range of motion and becoming familiar with all of the individual pain patterns and associated signs and symptoms, to approximate where TrPs will be found. This will facilitate treatment.

Hyaluronic acid (HA), a constituent of ground substance found body-wide, can be synthesized by most cells [29]. HA is a common mediator in cell proliferation and wound healing, and it binds water molecules in its general vicinity, forming areas with unusual viscoelastic and biorheological properties. There are wide variations of HA in human saliva, [30], and this may be true of other tissue as well. T3 supplementation can reduce concentrations of HA [31].

Geloid masses are a totally discrete phenomenon from the tender points used as criteria for a diagnosis of FMS [3] as well as criteria presented for the diagnosis of TrPs [4]. The geloid masses evaluated in this study may have been described in previous research [32, 33, 34], although with different terminology. Serous exudate and glycosaminoglycan (GAG) accumulation in the region of a TrP nodule have been reported by Travell and Simons [35], but were not considered part of the TrP mechanism by these authors. Other researchers have described masses similar to the geloid mass in patients at that time diagnosed as having "myofibrositis" or "myogelosis" [32, 33, 34]. These articles were written before the establishment of criteria for FMS, and before the differences between FMS and myofascial TrPs were understood as they are today [11]. We believe that the biopsies in these studies may have been done on geloid masses. Awad [32] described this phenomenon in both early form (swollen and tender) or late form (firm and tough). Masses meeting both these descriptions were present in our study subjects. Brendstrup et al. described connective tissue hyperplasia, sero-fibrinous exudation and interstitial edema containing mucopolysaccharides (now called GAGs) and mast cells in patients with "fibrositis" [33]. The GAG hyaluronic acid (hyaluronan) is strongly water-binding, which may explain Brendstrup's finding of 8% higher fluid content in the "fibrositic" tissue than in the controls. The authors of both of those studies noted that although these were sites of clearly defined palpable changes, it took careful search and experienced palpation skills to be able to identify them. This may be a reason that the geloid mass has not been generally recognized.

Palpation is an art that improves with practice, and it has of late been grossly neglected in the medical arts. Palpation for geloid masses requires an experienced and very delicate touch. Poking or prodding the tissue is insufficient. To palpate the margins of the geloid mass, lay the flat hand gently on the skin,

with minimal pressure, and move slowly along the plane until you feel the margin. If the mass is still mobile, the center of the mass will often mold itself into your palm. Geloid masses should not be confused with myxedema. These masses are soft and have a rubbery texture in the early stages, with palpable margins and without color. Most masses the first two authors have seen do not develop unique coloration of the overlying skin. The change in color in the overlying skin in some masses that resolve with appropriate treatment suggests that future studies include before and after photographs. This could be done in such a way as to document changes in axial rotation and asymmetry during therapy.

Awad theorized trauma caused platelet release of serotonin, resulting in vasoconstriction and localized edema [32]. He observed degranulating mast cells that could result from the edema. Mast cells release histamine and heparin, resulting in histamine-aggravated edema. Researchers have found greater amounts of mast cells in dermal tissue of FMS patients [36]. The first two authors have observed that some patients with both FMS and myofascial TrPs bruise easily, and may develop histamine reactions to some forms of fascial bodywork. Release of histamine may lead to further edema, which could further aggravate the response. The presence of glycosaminoglycans (GAGs) was indicated in the masses Awad described. He found that corticosteroids caused a temporary reduction in the nodules, due to steroid inhibition of acid GAGs. This mechanism may be partly why some patients with FMS and CMP report short-term relief of the symptoms after steroid use, although steroids per se are not indicated for either condition.

It has been shown that fluid retention is common in FMS [37]. It has been documented that the amount of HA in areas of lymphedema is significantly greater than normal [38]. GAGs may modulate the ion pumps that regulate lymph accumulation [39]. The first author has noticed that many patients with FMS have insulin resistance, and this mechanism may be part of a feedback loop. Insulin resistance and/or reactive hypoglycemia may be perpetuating factors of both FMS and CMP, and may itself cause interstitial edema, also called lymphedema [10]. Myofascial TrPs may cause lymph and blood vessel (and nerve) entrapment [4]. The first author has observed that while many clinicians are familiar with peripheral edema, they often fail to recognize generalized or abdominal interstitial edema.

Excess HA has been found in other chronic conditions such as systemic sclerosis [40] and rheumatoid arthritis [41]. The Yaron study [42] in Israel reported serum HA levels in patients with FMS significantly higher than in either healthy patients or in patients with arthritis. High levels of HA in a subset of FMS patients may predispose patients to develop geloid masses in the area of myofascial TrPs. Another more recent study done in Denmark, using the same HA test as the Yaron study, found normal levels of HA in FMS patients [43]. It is not known what the significance of these differing results may be.

T3 is a major regulator of mitochondrial activity. Studies show that there may be a direct T3 mitochondrial pathway involved in the regulation of both fuel metabolism and cell differentiation [44]. Research indicates that patients with FMS have low levels of ATP at rest as well as during exercise [45].

Lowe found that approximately 50% of FMS patients might have euthyroid hypometabolism, and improve with T3 therapy but do not benefit from the use of synthetic T4, or desiccated thyroid [23]. His euthyroid FMS patients did not develop tissue thyrotoxicity from supraphysiologic dosages of T3. Lowe theorized that euthyroid FMS patients might have partial cellular resistance to thyroid hormone. Failed transcription regulation by thyroid hormone could explain serotonin deficiency and many other objective findings and symptoms of euthyroid FMS, including high hyaluronic acid levels, and cause tissue-specific hypothyroid-like symptoms despite normal circulating thyroid hormone levels. Lowe indicated that titration of dosage to the specific patient is necessary for optimal relief from symptoms without side effects, and we suggest that this be done in any future studies. His FMS patients with low thyroid or low normal thyroid responded well to a mixture of T3 and T4 [46]. This response has also been documented elsewhere [47]. The improvement of mood and cognitive dysfunction in FMS patients has been documented as effects of T3 therapy [46].

Recent research indicates that a myofascial TrP is always found in a taut band, which is structurally related to contraction knots caused by a *thousand-fold* increase in the release of acetylcholine in the motor endplate [4]. This releases excess calcium ions, causing a contracture in the area of the motor endplate. Myofascial TrPs are points of high conductance (low resistance) [4, p 117]. One study showed

that calcium could interact with GAGs to decrease cerebral electrical impedance, affecting neurotransmitter traffic [48]. That study also noted that GAGs not only produce higher viscosity and "hydration" ability, but they are involved with ion binding characteristics, ability to regulate diffusion, and macromolecular interaction.

In the observation of the first two authors, manual therapy of geloid masses in patients with both FMS and CMP requires extreme care, as the mass itself may often be too painful to touch directly. Care providers attempting direct compression methods will often cause severe pain, and can send the patient into flare or even shock responses. With a light flat hand, it is possible to work along the outer margins of the mass, pulling from the outside edge, stroking the fascia in different directions to release the constrictions. This became much easier to accomplish as the geloid masses melted with T3 therapy.

When a patient develops single or unilateral myofascial TrPs, documentation of TrPs often includes comparative testing on the contralateral, uninvolved side. In these subjects, there was no uninvolved side. Fisher indicates that myopathy is indicated by the tissue compliance meter if muscle tolerance (deltoid) is lower than bone tolerance (tibia) [8]. Many of these subjects showed indications of myopathy. Some of these reversed during T3 therapy.

Contractured muscles do not present in the relaxed state needed for typical tissue compliance measurement, and these patients had many muscles in chronic contracture. The numerical s allowed the examiner to note palpation findings, such as "mass firm to touch with skin elastic and palpable TrP and/or taut band", or "muscles fibrotic". When the muscles were fibrotic, the geloid mass dense and tight, and/or the contracture severe, the TrP and/or taut band were not always palpable, although the restricted range of motion and associated symptoms were often evident. TrPs with accompanying taut bands often became palpable and more easily treatable, and the geloid masses changed in both size and shape after T3 therapy. The TrPs and taut bands themselves were not obviously changed by the T3, but simply became more accessible to standard TrP therapy. These therapies include "barrier release method" and "spray and stretch", described in Travel and Simons' Myofascial Pain and Dysfunction: The Trigger Point Manual [4].

Some study participants had difficulty organizing themselves to give appropriate responses. Some indicated both pressure and pain responses to the inner and outer edges of a geloid mass, but when the meter was over the typical TrP area, the patients would deny pain or even sensation. The examiner might observe pain signals such as tensing, wincing, or altered breathing, yet they communicated no pain until it reached intolerable levels. When a certain threshold was reached, their reaction was abrupt and intense. Communication then took the form of yelling, screaming, or tears. Some had difficulty communicating feelings of pain or intensity of pain. Some patients may have learned to disassociate from pain as much as possible as a way of coping with it. Some subjects communicated a sensation of numbness on palpation or measurement in the area of the geloid mass that, upon further questioning, signified altered sensation. The response to pressure or pain would often change abruptly during the testing from "numb" to intense and intolerable pain with coexisting autonomic responses such as sweating, chills, or clammy skin.

It has been the observation of the first and second authors that some patients with both FMS and CMP report that areas with geloid masses cannot be included in bodywork without prompting a flare or other serious and lasting aggravation of a variety of FMS symptoms. *Clinicians can never underestimate the possible effects of FMS allodynia and hypersensitivity on CMP and TrP therapies.* Standard FMS and TrP therapies can be less effective and have more repercussions in a patient with both. For example, it has been documented that myofascial pain patients who have FMS have a greater incidence of post TrP injection soreness than patients with myofascial pain alone, and they get less relief for a shorter span of time [49]. The pain and associated symptoms of myofascial TrPs can be magnified by the central sensitization of FMS. At times, therapies that might prove beneficial in the long-term can cause difficulty for the patient in the short-term. Each of these conditions can aggravate and perpetuate the other [10]. Pain management strategies must be carefully coordinated and proceed slowly, allowing the patient to recover between therapy sessions. Care must be taken with each new therapy tried, with the understanding that the patient may need extra medication, mindwork and body-integration techniques such as craniosacral release, t'ai chi and gentle massage to help ease the body and mind through the

transitions. As the myofascia releases and the muscles find new and healthier positions, the patient may have difficulty balancing until the proprioceptors are retrained, for example. The first and second authors have observed that Attachment TrPs, formed in the areas of musculotendinous junction or osseous attachment [4, p 2], may often worsen with improvement of Central TrPs (in the belly of the muscle). This may be due to the extended range of motion of the muscle due to the release of the Central TrP. Geloid masses have been observed by the first two authors over areas of both Attachment TrPs and Central TrPs.

As pain and other symptoms eased and muscle function and range of motion improved, patients generally took less pain medication and increased activity level, remaining at a relatively stable pain level. They tended to overwork and overplay as their function improved. They reported that they felt so much better that they did what they could when they could, although they frequently noted that they were aware of overdoing. The first and second authors have observed that patients with FMS and chronic body-wide TrPs often habituate themselves to override overwhelming levels of pain in an attempt to remain functional. It is our opinion that the tissue compliance meter did not provide sufficient pressure to measure the high level of pain at which some of these patients exist, nor could it measure low enough to match their level of pressure sensitivity.

Conclusion

The geloid mass does not appear to be a part of the TrP phenomenon per se but may be a discrete phenomenon which may occur in patients who have CMP as well as FMS and/or other chronic pain conditions which interact to create the geloid mass. The mechanism is not yet known. This study indicates that the geloid mass may respond to transdermal T3. The repeated close association between the central portion of geloid masses and an underlying TrP suggests a meaningful relationship that is not yet clear. T3 therapy improved the geloid mass, but did not affect the taut bands or TrPs directly, merely rendered them more treatable. This differential is of importance to the fundamental theoretical mechanism-of-action. The presence of these geloid areas may add to patient discomfort and loss of function. They may contribute to loss of range of motion, and complicate treatment even more than usual when both CMP and FMS are present. It is important that therapists be aware of and palpate specifically for these masses, as they may be missed in the routine course of therapy, and may provide one reason why TrPs are responding poorly to usually effective therapy.

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References:

1. Starlanyl DJ, Jeffrey JL. Geloid masses in a patient with both fibromyalgia and chronic myofascial pain. *Phys Ther Case Rep* 2001; 4:22-31.
2. Yaron I, Buskila D, Shirazi I, Neumann I, Elkayam O, Parran P, et al. Elevated levels of hyaluronic acid in the sera of women with fibromyalgia. *J Rheumatol* 1997; 24:2221-4.
3. Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL, et al. The American College of Rheumatology Criteria for the Classification of Fibromyalgia. Report of the Multicenter Criteria Committee. *Arthritis Rheum* 1990;33:160-72.
4. Simons DG, Travell JG, Simons L S. Travell and Simons' myofascial pain and dysfunction: the trigger point manual, vol I. 2nd ed. Baltimore: Williams and Wilkins;1999.
5. Gunn CC. The Gunn approach to the treatment of chronic pain. New York: Churchill Livingstone;1996.
6. McCaffery M, Pasero C. Pain: clinical manual. St. Louis: Mosby Inc; 1999.
7. Fischer AA. New developments in diagnosis of myofascial pain and fibromyalgia. *Phys Med Rehabil Clin North Am* 1997;8:153-169.
8. Fischer AA. Documentation of myofascial trigger points. *Arch Phys Med Rehabil* 1988;69:286-291.
9. Travell JG, Simons DG. Myofascial pain and dysfunction: the trigger point manual, vol II. Baltimore: Williams and Wilkins;1992.
10. Starlanyl DJ, Copeland ME. Fibromyalgia and chronic myofascial pain syndrome: a survival manual. 2nd ed. Oakland: New Harbinger Publications; 2001.
11. Gerwin RD. Differential diagnosis of myofascial pain syndrome and fibromyalgia. *J Musculoskel Pain* 1999;7:209-215.
12. Gerwin RD. Study of 96 subjects examined both for fibromyalgia and myofascial pain. *J Musculoskel Pain* 1995; 3(suppl 1):121 [abstract].
13. Donaldson CCS, Stella GE, Mueller HH. Fibromyalgia: a retrospective study of 252 consecutive referrals. *Can J Clin Med* 1998 June;116-127.
14. Russell IJ. Fibromyalgia syndrome. In: Mense S, Simons DG, Russell IJ, editors. *Muscle pain: understanding its nature, diagnosis and treatment*. Baltimore: Lippincott, William and Wilkins; 2001. p. 289-337.

15. Weigent DA, Bradley LA, Blalock JE, Alarcon GS. Current concepts in the pathophysiology of abnormal pain perception in fibromyalgia. *Am J Med Sci* 1998;315:405-412.
16. Russell IJ. Advances in fibromyalgia: possible role for central neurochemicals. *Am J Med Sci* 1998;315:377-384.
17. Lentz MJ, Landis CA, Rothermel J, Shaver JL. Effects of selective slow wave sleep disruption on musculoskeletal pain and fatigue in middle aged women. *J Rheumatol* 1999;26:1586-92.
18. Buskila D, Neumann L. Fibromyalgia syndrome (FM) and nonarticular tenderness in relatives of patients with FM. *J Rheumatol* 1997;24:941-944.
19. Buskila D, Neumann L, Hazanov I, Carmi R. Familial aggregation in the fibromyalgia syndrome. *Semin Arthritis Rheum* 1996;26:605-611.
20. Pellegrino MJ, Waylonis GW, Sommer A. Familial occurrence of primary fibromyalgia. *Arch Phys Med Rehabil* 1989;70:61-63.
21. Waylonis GW, Heck W. Fibromyalgia syndrome: new associations. *Am J Phys Med Rehabil* 1992;71:343-8.
22. Yunus MB, Kahn MA, Rawlings KK, Green JR, Olson JM, Shah S. Genetic linkage analysis of multicase families with fibromyalgia syndrome. *J Rheumatol* 1999;26:408-12.
23. Lowe JC, Cullum ME, Graf LH Jr, Yellin J. Mutations in the *c-erbA* beta gene: do they underlie euthyroid fibromyalgia? *Med Hypo* 1997;48:125-135.
24. Lowe JC, Reichman A, Honeyman-Lowe GS, Yellin J. Thyroid status of fibromyalgia patients. *Clin Bull Myofasc Ther* 1998;3:69-70.
25. Lowe JC. Results of an open trial of T3 therapy with 77 euthyroid female fibromyalgia patients. *Clin Bull Myo Ther* 1997;2:7.
26. Simons DG. Diagnostic criteria of myofascial pain caused by trigger points. *J Musculoskel Pain*. 1999;7:111-120.
27. Hong CZ. Current research on myofascial trigger points-pathophysiological studies. *J Musculoskel Pain*. 1999;7:121-129.
28. Simons DG. Myofascial pain syndrome: one term but two concepts; a new understanding. *J Musculoskel Pain*. 1995;3:7-13.
29. Chen WYJ, Abatangelo G. Functions of hyaluronan in wound repair. *Wound Rep Reg* 1999;7:79-89.
30. Pogrel MA, Lowe MA, Stern R. Hyaluronan (hyaluronic acid) in human saliva. *Arch Oral Biol* 1996;41:667-71.
31. Duncan KG, Jumper MD, Ribeiro RC, Bailey KR, Yen PM, Sugawara A, et al. Human trabecular meshwork cells as a thyroid hormone target tissue; presence of functional thyroid hormone receptors. *Graefes Arch Clin Exp Ophthalmol* 1999; 237:231-40.
32. Awad E. Interstitial myofibrositis: hypothesis of the mechanism. *Arch Phys Med Rehabil*. 1973;54:440-453.
33. Brendstrup P, Jespersen K, Asboe-Hansen G. Morphological and chemical connective tissue changes in fibrositis muscles. *Ann Rheum Dis* 1957;16:438-440.
34. Reitingner A, Radner H, Tilscher H, Hanna M, Windisch A, Feigl W. Morphologic study of trigger points. *Manuelle Medizin* 1996;34:256-262.
35. Travell JG, Simons DG. *Myofascial pain and dysfunction: the trigger point manual, vol I. 1st ed.* Baltimore: Williams and Wilkins;1983. p 35.
36. Enestrom S, Bengtsson A, Frodin T. Dermal IgG deposits and increase of mast cells in patients with fibromyalgia—relevant findings or epiphenomena? *Scand J Rheumatol* 1997;26:308-313.
37. Deodhar AA, Fisher RA, Blacker CV, Woolf AD. Fluid retention syndrome and fibromyalgia. *Br J Rheumatol* 1994;33:576-582.
38. Liu NF, Zhang LR. Changes of tissue fluid hyaluronan (hyaluronic acid) in peripheral lymphedema. *Lymphology* 1983;31:173-9.
39. Mobashiri A. Correlation between [Na⁺], [glycosaminoglycan] and Na⁺/K⁺ pump density in the extracellular matrix of bovine articular cartilage. *Physiol Res* 1998;47:47-52.
40. Freitas JP, Filipe P, Emerit I, Meunier P, Manso CF, Guerra Rodrigo F. Hyaluronic acid in progressive systemic sclerosis. *Dermatology* 1996;192:46-9.
41. Yoshinoya S, Mizoguchi Y, Hashimoto Y, Yamada A, Uchida S, Taniguchi A, et al. Serum concentration of hyaluronic acid in healthy populations and patients with rheumatoid arthritis—relationship to clinical disease activity of RA. *Ryumachi* 1991;314:381-90.
42. Yaron I, Buskila D, Shirazi I, Neumann I, Elkayam O, Parran P, Yaron M. Elevated levels of hyaluronic acid in the sera of women with fibromyalgia. *J Rheumatol* 1997;24:2221-4.
43. Bliddal H, Moller HJ, Schaadt M, Danneskiold-Samsøe B. Patients with fibromyalgia have normal serum levels of hyaluronic acid. *J Rheumatol* 2000;27:2658-9.
44. Wrutniak-Cabello C, Casas F, Cabello G. Thyroid hormone action in mitochondria. *J Mol Endocrinol* 2001;26:67-77.
45. Park J, Phothiamat HP, Oates CT, Hernanz-Schulman M, Olsen NJ. Use of P-31 magnetic resonance spectroscopy to detect metabolic abnormalities in muscles of patients with fibromyalgia. *Arth Rheum* 1998;41:406-413.
46. Lowe J. *The metabolic treatment of fibromyalgia.* Boulder: McDowell Publishing Company; 2000. p. 1019.
47. Eisinger JB. Hypothyroidism treatment: one hormone or two? *Myalgias* 2000;2(Suppl 2):1-3.
48. Wang HH, Adey WR. Effects of cations and hyaluronidase on cerebral electrical impedance. *Exp Neurol* 1969;25:70-84.
49. Hong C-Z, Hsueh T-C. The difference in pain relief after trigger point injections in myofascial pain in patients with and without fibromyalgia. *Arch Phys Med Rehabil* 1996;77:1161-1166.