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Anatomy, Posture, Prevalence, Pain, Treatment and Interventions of Musculoskeletal Disorders

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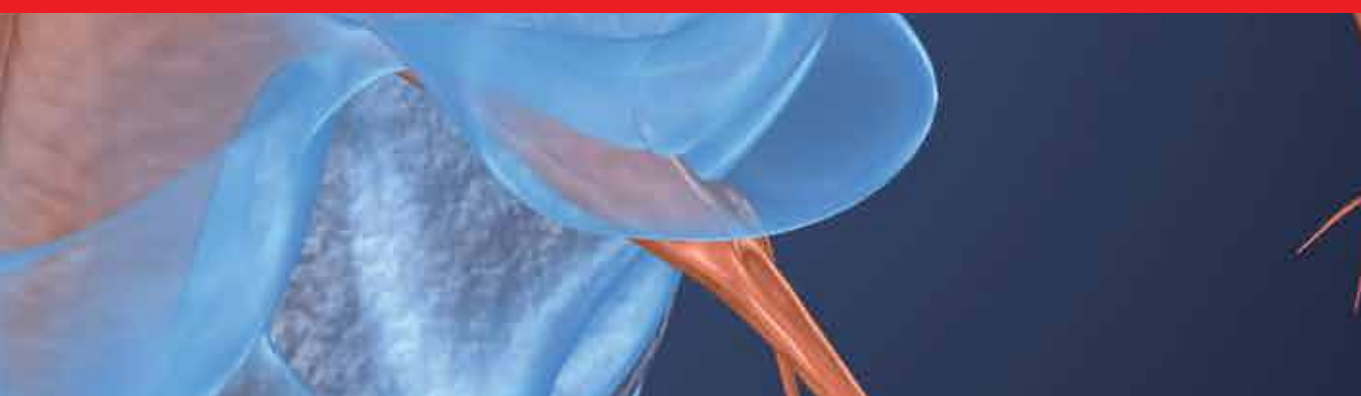

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Notice

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Meet the editor

Orhan Korhan graduated with a BS degree from Eastern Mediterranean University in 2000, an MS degree from the University of Louisville in 2002, and a PhD degree from Eastern Mediterranean University in Industrial Engineering in 2010. He has been working at Eastern Mediterranean University since 2009. He became an assistant professor in 2010 and associate professor in 2014. He is a board member of the Continuous Education Center and currently positioned as Academic Affairs Coordinator at the Rector's Office. He has been assigned to scientific committee of several international conferences and has published several books, book chapters, and papers in various countries. His current research interests include work-related musculoskeletal disorders, educational ergonomics, human computer interaction, and facility planning and design.

Contents

Preface

I have been working on musculoskeletal disorders (MSDs) for almost two decades. It was a long-term aim to work on such a book. InTech's invitation to edit this book has motivated me to reflect and share all the knowledge and experience I collected throughout the years.

This book covers topics on the anatomy, posture, prevalence, pain, treatment, and interventions for musculoskeletal disorders. Thus, it can be utilized as a guide to identify and analyze the risk factors, reveal the impact of prevention and intervention, and discuss treatment of these disorders.

In these chapters, you will find most of the significant aspects of MSDs. To this extent, a wide array of extensive and comprehensive discussions is provided on occupational, educational, and medical aspects of ergonomics.

The first step to cover was to select and disseminate the keywords, which helped us receive numerous abstracts. These abstracts were then carefully evaluated, and those that were believed to contribute significantly to the literature were invited to take their place in this book. It took several months to edit each and every word of the sent chapters. It was a very effective feedback process that we had with our authors.

In this book, you will read chapters from authors in Egypt, Finland, Germany, Italy, and the USA. They discussed the MSD-related topics from their perspectives and reflected and provided solution to the problems experienced from their own eyes. Thus, it makes the contents of this book interesting and very valuable.

I, hereby, would like to thank Ms. Martina Usljebrka who helped me with positive attitude at every single step of the publication process. Moreover, I would like to thank my dear wife, Bakiye Yalınç, for her support and encouragement.

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Risk Factors

Chapter 1

Muscle Pain and Muscle Spindles

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Additional information is available at the end of the chapter

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Abstract

Muscle pain is a common symptom associated with, for example, myofascial syndrome, fibromyalgia and polymyalgia rheumatica. Many diseases of the muscle tissue are, however, completely or nearly painless such as polymyositis and inclusion body myositis. Thus, a mere inflammation cannot be the cause of muscle pain. In needle electromyography (EMG), the insertion of a needle electrode causes pain but further advancement is usually painless. However, there are small spots of muscle tissue where sudden pain is elicited with the needle. In EMG, these 'active spots' are observed to produce spontaneous activity in the form of end plate noise and spikes (EPSs). End plate noise is elicited at the neuromuscular junction of α, β or γ motor neuron. EPSs are action potentials of γ or β motor units. Muscle spindles are the main nociceptors in muscle tissue, both in healthy muscle and in diseases with muscle pain by inflammation of the muscle spindles. Multiple possible mechanisms of muscle pain exist. Polymyalgia rheumatica may have interstitial pain and possibly pain associated with muscle spindle capsules. Delayed onset muscle soreness may reflect both interstitial muscle pain caused by minor injuries and pain generated in mildly inflamed muscle spindles.

Keywords: muscle pain, myalgia, myofascial syndrome, fibromyalgia, polymyalgia rheumatica, muscle spindle, nociception, fibrillation, fusimotor, electromyography, end plate activity, intrafusal, C-fibres, soreness, DOMS, trigger point, taut band, muscle afferents

1. Introduction

The generation of muscle pain is enigmatic. There may exist several mechanisms for pain production. Many diseases of the muscle tissue are completely or nearly painless, even if there are inflammatory histopathological findings. Thus, inflammation *per se* may not be reflected as muscle pain, although generally inflammation is considered to be associated with pain. In needle EMG, pain caused by the EMG needle seems to be localised in small spots. The EMG

activity in these 'active sites' consists of spontaneous electric activity (SEA), whereas in painless sites there is no spontaneous EMG activity. Trigger points, which are sensitive to manipulation and may be exquisitely painful, are a typical feature of muscle pain syndromes. Trigger points are situated in palpable taut bands of the muscle. The principal aim of this chapter is to discuss whether these localised pain spots may actually be inflamed muscle spindles with nociception.

2. Muscle pain produced by a needle during needle electromyography

Meadows [1] studied muscle pain during needle electromyography. He stated that there are sensory receptors associated with skeletal muscle that may give rise to the sensation of pain as observed after ischaemic exercise, or injection of 5–6% sodium chloride. Another form of muscle pain is encountered during the insertion of a concentric EMG needle electrode. When an EMG needle electrode is inserted into a muscle, transient pain is usually experienced, but once the needle has come to rest, the subject may be unaware of its presence. Meadows studied needle pain with concentric needle electrodes with external diameter of 0.46 and 0.30 mm, respectively, on his own vastus medialis muscles. 'When the needle is slowly advanced through the skin, pain is experienced on piercing the skin and again on piercing the muscle fascia, the latter case having a duller and less well-localized character. Further advancing of the needle is then usually quite painless. However, on infrequent occasions, a variably painful point may be reached during such a steady advance. If the needle is further advanced the pain usually subsides but in a few instances was found to be so intense, that further insertion was not attempted. Occasionally when the needle was critically positioned the slightest pressure on its butt caused intense pain which ceased as soon as the pressure was discontinued. It was sometimes apparent, that the site of such pain spots coincided with an increased resistance to the advancing needle, similar to that felt on encountering the muscle fascia when first entering the muscle. In the region of end plate zone advancing the needle sometimes caused a stab of pain which was associated with a twitch of a small fascicle or sometimes a greater part of the muscle'. He also studied pain produced by electrical stimulation through a concentric needle electrode, with the tip of the needle, positioned immediately adjacent to an extremely painful spot in the muscle. Single pulse of 0.05 ms and <5 V produced delayed discomfort and 10/s stimulation produced severe pain. No visible contraction could be seen. The same stimulation in other areas of the muscle was quite painless. Thus it was concluded that there are 'pain spots' in muscle tissue. However, the histological nature of the receptors was obscure. One point was of interest: when a pain spot was encountered, it was sometimes found that there was an increased resistance to the advancement of the needle at this point, suggesting that the receptors may be associated with intramuscular fascial planes.

3. Electromyography of pain spots, historical aspects

The first description of spontaneous EMG activity in pain spots was given by Jasper and Ballem [2]. They found local action potentials comparable to those described by Snodgrass and Sperry [3], and observed that these potentials were associated with particularly acute pain [2]. They

conjectured that the needle tip was penetrating a nerve and called these potentials 'nerve potentials'. Kugelberg and Petersén [4] described similar potentials in clinical EMG as 'protracted irregular activity'. 'Such discharge was mostly irregular, might be ordinary motor unit potential as in fasciculation or little amplitude and duration as in fibrillation'. Jones et al. [5] further studied the origin of 'nerve potentials' with electrically injected iron marks at sites of their appearance and found most of these iron dots close to peripheral intramuscular nerve twigs. Buchthal and Rosenfalck [6] observed that miniature end plate potentials (MEPPs), or end plate noise, were often associated with this activity, which they called 'spontaneous diphasic spikes'. Finally, Brown and Varkey [7] proved that 'nerve potentials' were postsynaptic, recorded from muscle fibres. Thereafter, the term 'nerve potentials' was rejected and at present these potentials are called 'end plate spikes' (EPSs). The general consensus was that EPSs were activated by the EMG needle, which causes action potentials, when it touches an intramuscular nerve twig or nerve terminal. Action potentials are recorded postsynaptically with the EMG needle. It was not considered, that an ectopic nerve potential spreads to both directions from the site of its origin [8] and thus a motor unit potential (MUP) or fasciculation potential should be recorded, not an EPS [9]. In addition, experimental studies do not support the hypothesis that irregular sustained action potentials like EPSs be activated by peripheral nerve injury or irritation [10–12]. To discuss the origin of EPSs, we have to look at the physiological properties of the muscle spindle.

4. Structure, vascular supply and innervation of the muscle spindle

Human muscle spindles are 7–10 mm long fusiform fluid-filled capsulated organs with equatorial (A) and polar (B) regions. The capsule of the muscle spindle is a lamellated structure, which prevents the diffusion of extrafusal substances into the intrafusal periaxial space [13]. The mean thickness of the capsule is 1.8 μm in the B region, 4.2 μm in the juxta B and A and 7.6 μm in the A region [14]. The periaxial space is between the outer and inner capsule of the spindle and it is full of highly viscous gel. There is a transcapsular potential of −15 mV, which is partly due to a relatively high [K^+] in the fluid. This may contribute to the excitability of the intrafusal endings. There are three types of intrafusal muscle fibres such as nuclear bag 1, nuclear bag 2 and nuclear chain fibres. One spindle has usually one bag 1 fibre, one bag 2 fibre and 4–7 nuclear chain fibres [13]. The muscle spindles are mainly distributed at the region of nerve entry into the muscle and around the subdivisions of the intramuscular nerves [13]. The distribution is thus different from that of the end plate zone, which usually is a relatively narrow band around muscle belly [15]. The main spindle artery is separated from those supplying extrafusal muscles, and in intrafusal capillaries, there is a blood nervous system barrier in both endoneurial and periaxial spaces [13]. The extrafusal capillaries are different and have efficient perfusion when compared to the intrafusal ones. Removal of substances which accumulate into the gel-filled periaxial space of the muscle spindle is a slow process. The sensory innervation of a muscle spindle consists of primary and secondary endings [13], and also III- and IV-afferents [16–19]. Also, autonomic innervation has been observed [19, 20].

The motor innervation consists of fusimotor (gamma) and skeletofusimotor (beta) nerve axons, both of which also have dynamic and static components. They adjust the responses of

the primary and secondary endings to the length and changes in the length of the muscle [21]. Dynamic gamma neurons innervate the bag 1 fibre by a p2 plate ending. Static gamma neurons innervate the bag 2 fibre and chain fibres by the trail endings. Dynamic skeletofusimotor beta neurons innervate the bag 1 fibre and extrafusal slow oxidative type 1 muscle fibres by p1 plate endings. Static beta neurons innervate the long chain fibres and extrafusal fast oxidative type 2 muscle fibres by p1 plate endings [13]. Each spindle receives about 7 motor axons, mean 3.2 beta and 3.8 gamma axons. The bag 1 fibre is almost always separately innervated by dynamic beta and gamma axons. Static beta branches supply exclusively the long chain poles. The bag 2 and chain fibres may receive a completely or variously segregated input in each pole [13].

5. Origin of end plate spikes

Where is the origin of EPSs if they are not nerve potentials or postsynaptic muscle fibre action potentials, activated by peripheral nerve injury? Partanen and Nousiainen [22] suggested that EPSs are action potentials of intrafusal muscle fibres such as small nuclear bag and nuclear chain muscle fibres inside the muscle spindles. EPSs can also be observed in active sites after manoeuvres for activating the gamma and beta motor activity such as passive stretch of the muscle, voluntary effort and repetitive nerve stimulation [9]. If multichannel EMG recordings are used, there are also different propagation patterns of EPSs such as local junction potentials as those observed in nuclear bag fibres [23], propagation for a very short distance as in nuclear chain fibres and propagation like MUPS but with the EPS firing pattern, as in beta (skeletofusimotor) motor units [9, 24, 25]. EPSs were also conjectured to be confined to the end plate zone of a muscle [26]. In fact EPSs can be found far from the end plate zone [9, 27]. It is a misconception that MEPPs are observed solely at the end plate zone, where the extrafusal neuromuscular junctions are situated [26]. Actually, MEPPs which are found far from the end plate zone, are mostly intrafusal representing synaptic activity of motor p2, p1 and trail endings. These MEPPs are often associated with EPSs, that is, gamma and/or beta motor unit potentials. At the end plate zone, MEPPs representing an alpha motor nerve terminal are not associated with EPSs [27, 28]. However, there are also muscle spindles at the end plate zone and thus, also MEPPs with EPSs may be found there.

Each pole of the muscle spindle receives 4–5 different motor axons and each gamma or beta axon innervates several spindles, but in a selective manner [13]. Thus junction and action potentials arise in several different spindles, when gamma and beta motor units are activated. This can also be seen in multichannel needle EMG recording. Synchronously firing EPSs may be found in remote active sites of a muscle, if these sites are innervated with the same gamma motor unit [27]. If EPSs in different remote active sites of a muscle are not innervated by the same gamma motor units, EPS firing is asynchronous. Intramuscular EPSs are not seen in the surface EMG, but MUPs of surface EMG are seen in the intramuscular sites with EPSs [27]. EPSs cannot be activated voluntarily, but voluntarily stopping of this activity is possible [27, 29]. Active spots with EPSs can also be stimulated with the concentric needle electrode, using electric impulses. With such stimulation, a reflex response resembling a myotatic reflex can be recorded [27]. Stimulation of an active spot with very small electric stimuli yields a response

on another active spot, and even late responses resembling F-waves. Thus, muscle spindles are electrically active structures in EMG, working in a network of gamma and beta motor units and having specific reflex responses [27].

6. End plate spikes are different from fibrillation potentials

In clinical EMG, EPSs may be confused with fibrillation potentials, which are spontaneous action potentials of muscle fibres, or pieces of muscle fibres, which have lost contact with their motor axons. The development of fibrillation potentials needs time and there may be both rhythmic and irregular fibrillation sequences [30]. However, fibrillation potentials are distinctly different from EPSs both by the wave form and by the firing properties [9]. There is also a rare type of fibrillation-like activity, 'myokymic' fibrillations, which are elicited by so-called 'giant miniature end plate potentials' [31, 32]. The essential difference between EPSs and fibrillation potentials is the fact that denervation causes prolongation of the refractory period of the muscle fibre and thus the fibrillation potential cannot recur as promptly as action potential in a normal muscle fibre [33]. This causes the relatively long minimum inter-potential interval of both rhythmic and irregular fibrillation potentials [31]. On the contrary, EPSs have numerous short intervals less than 30 ms [9].

7. Trigger points, taut bands and pain spots

Muscle pain with trigger points (TrPs) is observed in myofascial syndrome and fibromyalgia. In fibromyalgia, there are also other pain spots outside the muscle tissue [34]. Myofascial syndrome is common in medical practice, but also latent TrPs are common in young, asymptomatic persons [35]. The main symptoms of myofascial syndrome are the presence of palpable taut bands in muscles, spot tenderness with TrPs, referred pain, pain recognition and twitch response [36]. The prevailing hypothesis for TrPs and taut bands in myofascial syndrome is 'the integrated trigger point hypothesis' [36, 37]. In short, muscle overload may cause local ischaemia and hypoxia with energy crisis. This causes increased acidity and acetyl choline leakage from the nerve terminal. This is seen as increased spontaneous electrical activity (SEA) in EMG and it achieves local sarcomere contraction knots in muscle fibres. These are felt as taut bands in the muscle. Ischaemia, energy crisis and contraction metabolites increase the local concentration of inflammatory and pain metabolites leading to the development of painful trigger points. Shah et al. [38] found significantly increased concentrations of $[H^+]$, bradykinin, calcitonin gene-related peptide, substance P, tumour necrosis factor-α, interleukin-1β, serotonin and norepinephrine in active TrPs only. SEA in TrPs was stated to be different from spontaneous activity of normal neuromuscular junctions: the electrical discharges occur with frequencies that are 10–1000 times that of normal miniature end plate potentials [39].

However, in EMG studies, SEA is found in 5–10% of routine insertions of the needle into normal muscle [5, 40], without any evidence of dysfunctional end plates. The most common finding is EPSs with end plate noise in the background [25, 40]. For an electromyographer, it is very difficult to accept that MEPPs or end plate noise can achieve contraction knot in the

postsynaptic area of the muscle fibre. These wave forms in EMG are a very common finding in quite normal muscles, without any taut bands or trigger points. The situation may be different in experimental studies, where the function of acetylcholinesterase was blocked [41]. The findings of microdialysis of trigger points [38] can be explained by intrafusal microdialysis: a twitch elicited by insertion of the capillary needle may show a myotatic reflex by the activation of intrafusal 1a-afferents of the given muscle spindle. Taut bands may be the final result of sustained reflex activation of beta motor units by intrafusal II-, III- and IV-afferents [25, 27, 28]. Trigger points comprise inflamed and painful muscle spindles with overactive nociceptive afferents. There are somatic thin nerve axons inside the muscle spindle and in its capsule [19]. Thus, it is also conceivable that pain spots in routine EMG of healthy muscles [1] are in fact muscle spindles. Extrafusal muscle fibres in rigour in taut bands cannot produce action potentials, but they can show end plate noise at the neuromuscular junction. Thus, the finding of Simons et al. [42] in myofascial pain can be explained: they found end plate noise (EPN) without spikes (EPSs) in TrPs of all 11 muscles studied, but EPN was found only at four sites at the end plate zone outside of TrPs. The spikes were also observed, but they occurred unexpectedly: one at TrP site, 12 at end plate zone outside TrPs and two at taut band sites. The plausible explanation is that spikes (action potentials of gamma or beta motor units) were mostly blocked in motor units in rigour in TrPs and taut bands, but were readily found outside of these sites [27]. Another issue is the occurrence of end plate activity inside and outside TrPs. Some studies reported end plate activity in every TrP and total absence of such activity in the control points [43, 44]. However, it was showed, that the difference between TrPs and control points, as to the number of EPSs, may even be non-significant [45]. The exception is the upper trapezius muscle, where EPSs are significantly more numerous in TrPs than in control points [45]. The latter explanation is consistent with the fact that there are inflamed muscle spindles (with EPSs) in TrPs and normal muscle spindles (with EPSs) at the control points [27].

Ojala et al. [45] also found increased prevalence of complex repetitive discharges (CRDs) in 16% of patients with myofascial syndrome. CRDs may reflect ephaptic impulse transmission from II-afferents to gamma- or beta-motor efferents intrafusally. This may happen if the concentration of contraction metabolites, especially $[K^+]$ is increased in the periaxial space of muscle spindles after sustained fusimotor activation [46].

8. Interstitial muscle pain

Muscle pain is not always associated with trigger points and taut bands. Injection of hypertonic saline into the muscle causes pain [1, 47, 48], which evidently is interstitial activating mainly extrafusal pain C-fibres. C-fibres are known to be present in every tissue of the muscle with the exception of capillaries [18]. However, there is also evidence that hypertonic saline increases the sensitivity of muscle spindles to stretch [49], and thus also muscle spindles may be involved in the production of pain. The effect on pain caused by capsaicin injection does not differ from that of hypertonic saline injection [48]. In polymyalgia rheumatica, there is an abrupt onset of proximal pain and stiffness, especially in the neck and shoulder girdle. There are also signs of soft tissue oedema and inflammation. Tenosynovitis and bursitis are common. Polymyalgia rheumatica is also often associated with giant cell arteritis [50]. Trigger

points and taut bands are not typical for polymyalgia rheumatica, and muscle pain is evidently interstitial. EMG is usually normal, and this also is my experience as an electromyographist. Yet abnormalities consistent with either mild myopathic or neurogenic process have been reported in single patients [51]. There are numerous, but non-specific ultrastructural changes of muscle fibres in polymyalgia rheumatica. The endothelial cells of the capillaries showed no changes [52]. Any investigations on the histopathology of muscle spindles in polymyalgia rheumatica were not found. A tempting hypothesis is that there are inflammatory changes of the spindle capsule ('capsulitis'). The spindle capsule at about the equatorial region is made up of fibrous tissue lamellae which usually number 5–7, and are rather rich in endothelial-like nuclei. Among the lamellae lie several small blood vessels [53] as well as thin somatic nerve axons [18, 19]. The thick capsule on the equatorial area of the muscle spindle [14] may be felt as an increased resistance of the EMG needle resembling fascial planes [1, 27].

9. Delayed onset muscle soreness after exercise

Eccentric muscle contractions cause lesions of the muscle membrane and also ultrastuctural damage of muscle fibres. These kinds of lesions are not observed after concentric muscle efforts [54]. Up to six hypothesised theories have been proposed for the mechanism of delayed onset muscle soreness (DOMS) after exercise: lactic acid, muscle spasm, connective tissue damage, muscle damage, inflammation and the enzyme efflux theories. DOMS develops usually in 24 h after exercise in untrained persons [55]. It may be associated with fasciculations, visible spontaneous intermittent contractions of a portion of muscle. The origin of spontaneous fasciculation potentials is mainly distal [56].

10. Fasciculations as a sign of muscle injury after exercise

We studied the appearance of muscle fasciculations after exercise with stretch-shortening cycle (SSC), with partly eccentric contractions. Nine healthy men, aged 25–50 years, were recruited for the study. Spontaneous fasciculations of the soleus muscle were recorded immediately before and at 11 min after 100 jumps with the ball of the right foot with extended knee joint. Fasciculation potentials were recorded with two concentric needle electrodes (diameter 0.3 mm), interelectrode distance 10 mm. The recording was performed before exercise, and 1–2, 4–5, 6–7 and 10–11 min after exercise with Dantec Keypoint EMG machine and Sony DAT recorder. The needles were removed temporarily, and were not used during the exercise. There was a significant increase of the number of fasciculations, beginning at 4–5 min after the 100 jumps and increasing thereafter (**Table 1**). Statistical analyses were performed using IBM SPSS Statistics for Windows (Version 24.0, IBM Corp., Armonk, NY). The differences between the number of fasciculations before and after the 100 jumps (i.e. 1–2, 4–5, 6–7 and 10–11 min after the jumps) were normally distributed, as assessed by the Shapiro-Wilk test ($p > 0.05$). Therefore, a paired-samples t-test was used to determine whether there was a statistically significant difference in the mean number of fasciculations before and after the 100 jumps; the test was repeated for the four conditions corresponding to 1–2, 4–5, 6–7 and 10–11 min after the jumps. The level of significance was set at $\alpha = 0.05$.

N = 9	Mean	min	max	SD
Before	3.6	0	15	4.6
1–2 min after jumps	3.0	0	13	4.0
4–5 min after jumps	20.9*	1	55	18.3
6–7 min after jumps	34.1*	3	87	24.7
10–11 min after jumps	38.4*	4	88	24.4

*$p < 0.01$ (compared to the number of fasciculations before jumps, paired-samples t-test).

Table 1. Number of fasciculations before and after 100 jumps with the ball of foot.

There was no statistically significant difference in the mean number of fasciculations between the measurements before the jumps ($M = 3.56$, $SD = 4.58$) and 1–2 min after the 100 jumps ($M = 3.00$, $SD = 3.94$), $t(8) = -1.17$, $p = 0.28$, $r = 0.38$. However, the number of fasciculations was, on average, significantly greater for 4–5 min after the jumps ($M = 20.9$, $SD = 18.3$) in comparison to the number before the jumps, $t(8) = 3.58$, $p = 0.007$, $r = 0.78$. The increase in the number of fasciculations was further enhanced 6–7 min after the jumps ($M = 34.1$, $SD = 24.7$), $t(8) = 4.08$, $p = 0.004$, $r = 0.82$, and even more so for 10–11 min after the jumps ($M = 38.4$, $SD = 24.4$), $t(8) = 4.69$, $p = 0.002$, $r = 0.86$.

We conjectured that the eccentric phase of SSC contractions with minor injury [57] caused some biochemical substances, such as cytokines, creatine kinase and $[K^+]$, to be released. Increased extracellular concentration of these substances, especially $[K^+]$ [58], may elicit spontaneous ectopic potentials in intramuscular motor nerve twigs or nerve terminals, spreading to the corresponding motor units and recorded as fasciculation potentials in needle EMG (author's presentation in Single Fibre and Quantitative EMG Meeting, Nijmegen, The Netherlands, June 6–10, 2004). In this case, fasciculations reflect slight damage of muscle fibres caused by the exercise.

Both low-volume high-intensity interval exercise and continuous exercise cause DOMS. Pressure-pain threshold, pressure-pain tolerance and perceived pain intensity were changed in 24 h after exercise [59]. Tenderness to palpation is unevenly distributed in muscles with DOMS. There are regions that are tender to pressure and some regions that are not. Trigger points, referred pain or taut bands, are not observed (author's unpublished observations). Thus, DOMS may reflect both interstitial muscle pain and painful muscle spindles. A question remains: why is there a 24 h delay before the appearance of soreness? It may take time until the extracellular concentration of K^+, caused by the leakage through muscle membranes with minor injuries, is sufficient to increase the firing of interstitial C nerve axons. On the other hand, exercise is associated with overload of muscle and increased fusimotor activity, which increases the concentration of contraction metabolites in the periaxial space of muscle spindles. Accumulated contraction metabolites may induce increase of inflammation metabolites, cytocines and finally pain metabolites intrafusally. Intrafusal pain C-fibres are sensitised by increased periaxial concentration of $[K^+]$ [60]. Thus, there may be a slight inflammation of muscle spindles, and consequently increased pressure sensitivity and pain generated by the intrafusal C-fibres. The development of pain in this way apparently needs some time.

11. Final comments

The aim of this chapter is to emphasise the major role of muscle spindles in muscle pain. Inflammatory muscle diseases with major histopathological changes are usually not associated with muscle pain. On the other hand, another disease with minor histopathological changes, the myofascial syndrome, may have severe muscle pain and local tenderness to pressure in TrPs. This fact can be explained by inflammation and pain elicited in the muscle spindles. Painful spots in needle EMG may simply be muscle spindles with nociception. Polymyalgia rheumatica may be associated with interstitial muscle pain. It remains to be studied whether there is also pain caused by inflammation of the muscle spindle capsules. DOMS may express both interstitial pain and muscle spindle pain with mild intrafusal inflammation.

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Chapter 2

Analysis for Objective Evaluation the Stress of the Hand

Aydin Ünlü, Peter Gust and Frank Mersch

Additional information is available at the end of the chapter

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Abstract

The hand is constantly in contact with products and therefore stressed differently. Heavy stress is the cause of unpleasant sensation and can lead to common hand diseases in the worst case. The chapter starts with the description of hand diseases and with methods to determination of hand stress. Subsequently, the chapter is continued with a literature review of hand stress analysis refer to objectively methods. In the main part, two objective methods are developed and presented to analyze the hand stress. These methods allow the simulation and the measurement of hand stress. Compared to the classical approach, the results of the objective methods show a higher accuracy in faster review of hand stress. Finally, the chapter ends with a discussion of the results and gives opportunities to improve the hand model and the measurement system.

Keywords: pressure pain threshold (PPT), pressure discomfort threshold (PDT), digital hand model, handle design parameters, hand stress, hand tissue strain, wrist strain, hand posture, Job Strain Index (JSI), strain variables, sensor glove, JSI-system

1. Introduction

1.1. Hand diseases

People are constantly in contact with products and thereby stressed differently. In particular, high power transmissions, short rest periods as well as incorrect postures influence the health [1]. In this case, typical diseases may occur due to high stress. In the worst case, diseases in the wrist, for example, arthrosis can be caused by an incorrect estimation. An arthrosis on the wrist leads to a painful restriction of the mobility of the wrist. An anomaly of the compressive stress in the wrist is being held responsible for the high joint wear and the joint pain. An arthrosis at the thumb saddle is called as rhizarthrose [2].

Figure 1 shows a deformed joint site. The symptoms can only be alleviated by minimally invasive joint cleansing or by the severing of painful nerve fibers. In a last step, there remains in some cases only a partial stiffening of the carpal bones—or the supply of individual finger joints by arthroplasty or prosthetic. In the case of joint cleansing, a needle is inserted into the joint capsule. If the injection is deeply injected into the thumb saddle joint, the palmar-extending tendon of the flexor carpi radials can be injured [3].

A novel therapy involves a stabilization by kinesio-taping. In addition to the massage effects, that stimulate the flow of blood and lymph. The elastic adhesive tape supports joint functions. The influence of the tapes on the tensions corrects muscular imbalances so that a balance between the muscle groups can arise again. The stimulation of the proprioceptors in the joints ensures a better sense of movement. By stimulating the receptors, pain in the joint is relieved [4].

1.2. Determination of hand stress

In the application of hand-held products, the user is under different stress factors. These stress factors cause in human's strains, depending on individual characteristics and abilities. Stress means the physical characteristics of the work situation, for example, a force transmission on the hand. Strain, in contrast, refers to the reactions such as hand pain [5].

In most cases monitoring methods are used to determine the hand strain. These monitoring methods are based on the scoring of certain stressful situations. Thereby valid low scores lead to low strain. But in the most monitoring methods the level of detail of the hand is

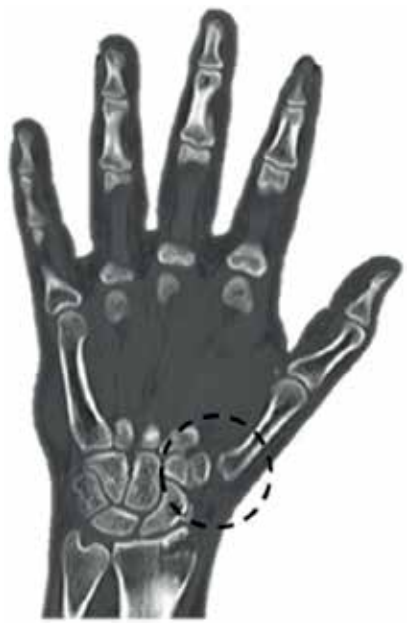

Figure 1. Computed-tomography of a rhizarthrosis.

limited to few positions. Therefore, Job Strain Index (JSI) by [6] is often determined for the evaluation of the hand strain. With regard to the development of a system to objectify hand strain, this chapter focuses on the JSI method.

The JSI method was published by [6] and deals with the evaluation of hand strain. Thereto, a manual work was observed for 3 min, and a so-called Job Strain Index (JSI) was calculated. The determination of the JSI is based on the estimate of six strain variables and on the multipliers determined by those. The strain variable, intensity of exertion (IE) refers to the maximum effort that can be exerted by a human being [10]. Hand-dependent maximum gripping forces by [7] can help to determine the effort. The strain variables, duration of exertion (DE) and efforts per minute (EM) result from the formulas for the maximum effort. For the estimation of hand/wrist posture (HWP), angle limits for the wrist extension (E), flexion (F) and ulnar deviation (D) are specified. The comparison of the JSI with the limits shows the risks of the hand health. **Table 1** shows a template for determining the multipliers.

Rating	Exertion intensity	Exertion duration	Exertion frequents	Hand posture	Work speed	Work duration
1	Light (1)	<10% (0.5)	<4 (0.5)	Very good (1)	Very slow (1)	<1 (0.25)
2	Somewhat hard (3)	10–29% (1)	4–8 (1)	Good (1)	Slow (1)	1–2 (0.5)
3	Hard (6)	30–49% (1.5)	9–14 (1.5)	Fair (1.5)	Fair (1)	2–4 (0.75)
4	Very hard (9)	50–79% (2)	15–19 (2)	Bad (2)	Fast (1.5)	4–8 (1)
5	Near maximal (13)	80–100% (3)	≥20 (3)	Very bad (3)	Very fast (2)	≥8 (1.5)
JSI = EI × ED × EF × HP × WS × WD						

Table 1. Template of JSI-determination.

2. Literature review

2.1. Simulation-models to determine the hand stress

To provide early ergonomic criteria for product design, digital hand models can be used for the simulation of hand stress. Digital hand models are generated by computer representations of the hand and can be simulated using either the multibody systems method (MBS) or the finite element method (FEM). It is also possible to couple the methods of FEM and MBS. In contrast to MBS models, FEM models are deformable and can calculate mechanical stresses such as pressure in certain parts of the body. MBS models consist of rigid non-deformable bodies connected to one another by kinematic joints. Using the MBS method, it is only possible to determine the kinematics of the body and the contact forces. These data are used, for example, as input data for FEM simulation [8]. Often the hand models are simulated as part models because of their complexity. This includes, for example, simulating finger models. For example, [9] developed a combined FEM and MBS finger

model of three finger segments with realistic bones, nails and soft tissue. In the dynamic simulation, the stiffness of the grip surface was varied and demonstrated in final results the decrease of the pressure distribution. The work [10] developed a FEM fingertip and simulated the pressure distribution on the fingertip when opening can a tab. The results revealed that over a large contact area pressure, distribution was reduced to the fingertip. With the thumb model the static pressure distribution for use of clip connections are simulated by [11]. These influences such as pressure level, material, geometry and position change of the clips are examined. This influence examination gives design proposals for clips [12]. Other digital hand models focus on realistic simulation. The work [13] presented a hand model for the simulation of non-linear contact deformations, in relation to realistic overlapping of the skin (**Figure 2**).

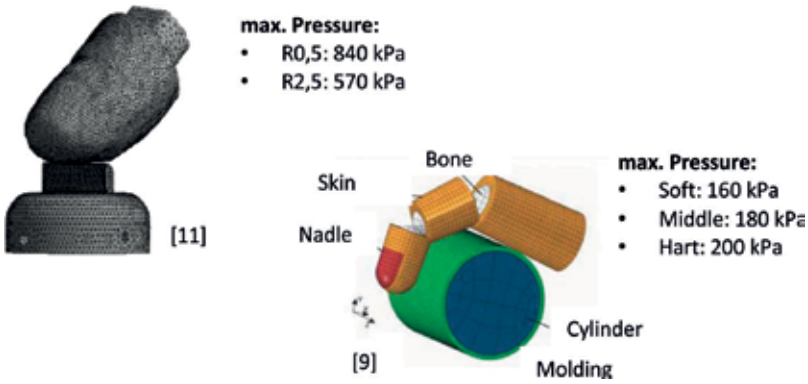

Figure 2. Example of hand models.

2.2. Support-systems to reduce the hand stress

In the context of the present work there exist sensor gloves to measure forces when gripping and using products. Some works are focused exclusively on the development of new sensor gloves. The research of [14] shows that the sensor gloves are exploring the relations between forces and other variables such as muscle tension [15], handling and feel [16] and the perceived gripping force [17].

Since 1991 are sensor gloves designed to measure forces in gripping and operation of handheld products. To measure the force distribution on the palm most sensor gloves have piezo (-resistive) sensors such as in Refs. [18, 19] or [20]. Due to the simple programming and low cost compared to capacitive sensors these are preferred. The force sensors are varying in the number and in the position on the hand and in their form. For the investigation of pressure distribution on the palm [21] develops a sensor system of six force sensors based on FSR sensors (FSR—Force Sensing Resistor). These resistive sensors are based on the measurement of the resistance change of semiconductor materials such as silicon. In applying three different shaped handles are pressed on the palm and then calculated from the force-measuring the pressure distribution.

To measure the hand posture there, exist optical methods and methods in which active sensors are attached to the hand [14]. This chapter deals with sensor gloves with active sensors, since optical methods require a complex experimental setup and capture only the movement and posture of the hand. Active sensors are placed in the design as a sensor glove directly to the hand and do not require complex experimental setup [22]. The sensor gloves are often equipped with fiber optic [23], strain gauges [24] or goniometers [25]. Through the further development of microelectronic sensors, circuits and batteries are designed with smaller size and weight. The data collection, processing and storage are done internally, or the data are transmitted to the computer externally via wireless protocols [26]. **Figure 3** shows new technologies with RFID to measure the time in relation of the motion.

Figure 3. Example of support-system by http://www.proglove.de (2017).

3. Simulation of hand stress

3.1. Comfortyping

The term "comforting" is an artistic word and has emerged from the composition of comfort and prototyping. Comfortyping is intended to function as a stand-alone simulation program, in which a digital hand model is included in the simulation environment. After importing a hand-held product as well as after selection of influencing variables, they should be calculated on the basis of their design proposals. A similar goal for assessing the ergonomics of the man-machine interface also exists as ergotyping of [27]. In contrast to this, the focus should be placed on the hand-arm system with Comfortyping. For example, it should be possible to deliver spline suggestions to the user, which can then be imported into the CAD system. For Comfortyping is a database with different influencing variables such as grip types, gripping forces as well as hand-type and handle-dependent material properties is required. The

program should offer a choice of three hand types with little, much as well as medium subcutaneous fat content. The work of [28] differ fleshy, tendinous and normal skin types. In addition, it should be possible to automatically scale the hand models by percentile and gender. A snap function should allow the hand model to take the product automatically.

A first approach for Comfortyping was developed with Recurdyn (see **Figure 1**). Here the grip of an iron bender was taken and defined the reduction of pressure peaks as well as a homogeneous pressure distribution as a target function. The MBS/FEM program Recurdyn has an Autodesign function and can iteratively optimize geometries. In the example, a shape change handle was constructed with six cylinders and pressed onto the palm of the hand with 200 N. In addition, the handle was gripped with 50 N gripping force. The geometry and material properties from the hand (skin type dependent) and the force and movement conditions from the iron bender (product-dependent) were selected from the database. For the target definition, the reduction and homogenization of the pressure distribution was selected manually (**Figure 4**).

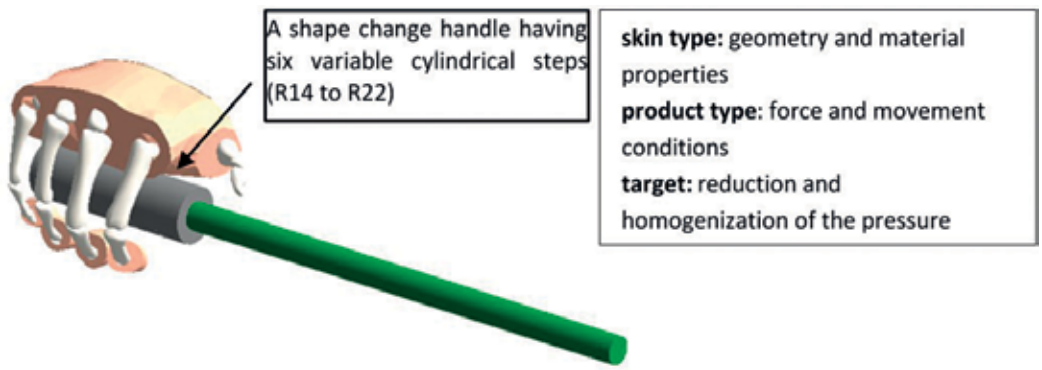

Figure 4. Comfortyping in RecurDyn.

3.2. Results

The results show before the optimization on the hand regions O and Q high pressure loads. The radius of all steps is R14. The pressure loads were redistributed to the hand center P with the optimization. For this purpose, the program changed the radius of the steps of the handle until a desired pressure distribution is obtained. To do this, the radius in the hand center changes to R22. This information is output as a spline into the CAD model of the handle. A pressure evaluation with different subjects confirmed the optimized grip shape as comfortable.

For comfort evaluation, the shape change handle was designed. The developed shape change handle consists of six spreader jaws, which can be moved by a threaded pin rotation. The threaded pins have right-hand and left-handed threads. The so-called entraining jaws spread the counter-jaw during an outward movement. To conceal the edges of the jaws, a rubber covering was applied. These six jaws have taken together the width of a male palm of the 50th percentile of about 95 cm. The whole mechanism was tested by FEM for strength and is made of ABS. Various tools can be connected to the shape change handle (**Figure 5**).

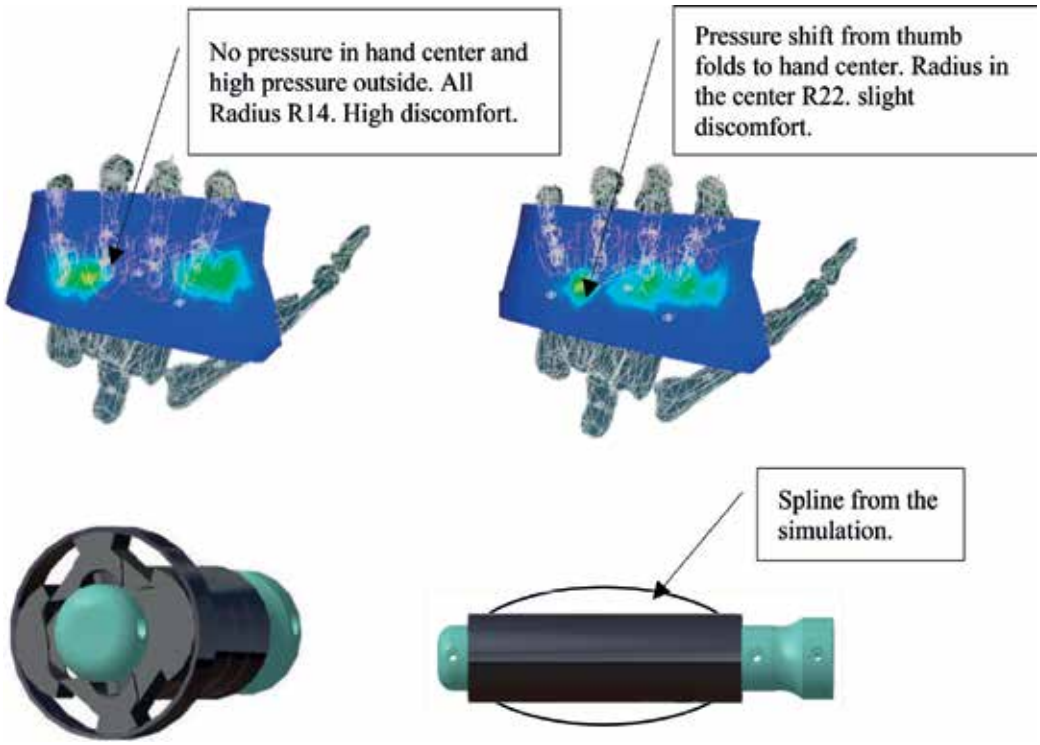

Figure 5. Results of Comfortyping.

4. Measurement of hand stress

4.1. JSI-system

The development of the JSI-System (Job-Strain-Index System) was made for a male person of the 50th percentile between 20 and 30 years (see **Figure 6**). As glove, a model (TouchGrip of UPIXX) in microfibre fabric was used. This remains firm in the fixed position of the sensors on the hand. For the sensors to measure the wrist angle ulnar and radial, a bending sensor (Interlink FSR 408) is mounted on the thumb side of the hand, at the level of the wrist. For the wrist angle, palmar and dorsal a potentiometer was used. To this on the back of the glove a sheet metal was sewn to attach the potentiometer. In the forearm a velcro strip was applied and on the velcro a sheet metal and a rod were attached. To measure the force distribution on the palm (thenar, hypothenar, palmar) and on the fingertips, were force sensors Interlink (FSR 402, FSR 400) adapted to the preparatory work of [21].

The wiring was led through a slot outwardly toward the back of the hand, so this could cause no hindrance on the palm. All signals of the sensors were lead to the microcontroller (Arduino MEGA 2560). The Arduino has been built with an LCD-Display in a plastic housing. Thus, it is possible to wear the evaluation system on a belt. For calibration, the raw data are transferred on the computer in Excel (PLX-DAQ: Parallax Data Acquisition Tool). Approximation

Figure 6. Prototype: JSI-system.

functions are derived from the raw data with the using of load cell and angle template. For the validation, several measurements by different forces and postures were accomplished. It was shown that the sensors measures are reproducible. For the evaluation of the JSI the measurements were compared with the limit values. The evaluation was performed in Excel according to the principle of the case distinction. Decisive for the strain variables are mainly maximum forces, angles and times [14].

4.2. Results

In the experiment, it shall be proven, if by using the prototype, the evaluation of the hand stress is faster and exacter than the classic JSI method. To show the applicability of the JSI-System, different strain cases are evaluated using the classic method and compared to the measured JSI. As an experiment angle bracket are assembled on Aluminum profiles in three different variations (see **Figure 7**).

Following work steps were performed:

1. Two slot nuts were placed in the slot.
2. One angle bracket was placed on the slot nuts.
3. Washers were placed on two bolts.
4. Both bolts were screwed into the slot nuts using an Allen wrench.
5. Both bolts were tightened with 20 Nm using a torque wrench

The experiment was performed in three variations to show the function of the JSI-System and the influence of force and angle on the result. In the first variant, the experiment is performed as described above. In the second variant during the tightening of the bolts using the torque wrench, a dorsal flexion of the wrist of about 45 degrees was provoked. Thereby the influence

Figure 7. Experiment.

of the hand posture on the strain magnitude should be examined. In the third variant, the handle of the torque wrench was grabbed in the middle to increase torque and also the force. Here should be examined the influence of an increased force on hand posture and the intensity of the exertion [14].

For the purpose of a subjects study the experiments were filmed. One variant took about 3 min. The first variant was performed ten times to analyze the results of the JSI-System for measuring a similar task several times. The subjects were tested independently from each other and were assigned to perform the JSI evaluation using the videos from the three experiments. Apart from the videos the examiners got following information:

1. The speed of work were felt as normal.
2. For the evaluation 8 h of work per day were assumed.
3. The torque was about 20 Nm.
4. The lever in the first and second variant was 29 cm.
5. The lever in the third variant was 15 cm.

The evaluation of the JSI in the subject's study took about 10–15 min for each variant. The measurement took as long as the activity, therefore 3 min. The comparison between the subject's study (average of individual JSI ratings) and the measurement shows that the estimation is varying a bit from the measurement. The largest deviation arises in the third test variant. The highest hand stress emerges from the extreme hand posture in the second variant. Examiner 5, for example, tends to give higher estimations than examiner 3. For the repetition

of the first variant a mean for the JSI of 1.055 with a standard deviation of 0.32 was measured. According to this, the spread lets us expect that the JSI measurements lay at 1.055 ± 0.32. The maximum spread is approximately ±0.5. These results indicate that during the experiments different influencing factors like the grip and strength of fingers, posture of hand and fingers etc. have influences on hand stress.

5. Conclusion

The literature review has shown that no digital hand models exist that are used for the simulation and analysis of influencing factors with respect to the pressure simulation. Either realistic skin deformation is simulated [13] or part models to study material investigation are used [9]. Here are no statements taken to the sensation of pressure. With the known hand models, a derating of the pressure distribution can be indeed proven; however, the inclusion of influences by [28] is ignored. With the help of the digital hand model, there is the ability to save subjects, expensive prototypes and pressure sensor mats in the development of hand-held products. The hand model can develop proposals for the design in a short time, and reduces the pressure load objectively. The comparison between the pressure simulation and pressure measurement showed that correct pressure loads are determined with the linear approach of the hand model. The literature review shows, in this context, such as the work of [10] that a linear material behavior on skin tissue can be assumed. However, the linear material behavior is permitted only for a certain range of forces and demands, for example, for the fingers typing e-modules. This effort can be eliminated in a non-linear material behavior. Since in most cases, skin damage due to shearing arises, for further development the expansion of the model for simulation of shear stress is recommended. Other criticisms of the model include the fixing of the metacarpals in the room. These ensure that the palm is immobile. In addition, the palm consists of a plurality of muscles which alter the mobility of the metacarpal bone. The application displays a new approach to produce an impact analysis. The results of the impact analysis can be implemented directly in the CAD model and give a product which produces low and evenly distributed pressure distributions on the hand tissues for the simulated factors. The impact analysis gives findings about which factors have an influence on the pressure distribution.

In summary, regarding the literature on the measurement of hand stress can be said, that there is no work, which uses a sensor glove to measure strain variables from the JSI method [14]. Very often sensor gloves with force sensors are used to obtain an indication of the power level, without taking the hand posture into account. In some works, such as [22], for example, only the movement or the hand posture for motion capture is measured with the sensor glove. Then the measurement data scored with RULA, without taking forces into account. None of the sensor gloves aims solely the ergonomic quality of a hand-held product. The developed JSI-System give an effective tool for assessing the hand stress based on JSI method. In addition, the examiners do not always have the same expertise and experience regarding the hand ergonomics and therefore evaluate differently. Regarding the standardization of JSI, with the JSI-System arises a potential for application in the industry. The JSI-System

allows the comparison of hand-held products and processes together. A misjudgement of hand stress can be ruled out. The measurement of hand stress takes much shorter than with the classic JSI-rating. The validation has shown that all sensors provide reproducible measurements for the short-term application. Also, the state of the art shows the use of the piezo (-resistive) sensors. However, for the industrial capability and long-term use, the sensors should be examined more closely to know limits as power level and duration of sensors. For further development, it is also advisable to integrate a simple replacement of the sensors, because the sensors can be damaged by their sensitivity during continuous use. Other criticisms of the prototypes include obstructing the movement of the hand as well as the outsiders of wired sensors. With the JSI-System is shown that strain variables from monitoring methods may be measured. This also means that other methods such as LMM or RULA can be performed with the measurement method. The high training costs for more accurate results, which are recommended by [29], can be reduced with systems such as the JSI-System. The fact that compressive forces on the hand and finger surface can be measured by the JSI-System opens the possibility of a pressure reduction for comfortable design of hand-held products. The JSI-System, combined with the work of [21] can be used to assess the pressure distribution and influence factors.

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Section 2

Prevention and Interventions

Chapter 3

Ergonomic Interventions for the Prevention of Musculoskeletal Disorders

Theresa Stack

Additional information is available at the end of the chapter

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Abstract

Nonfatal occupational injuries account for 95% of the total cases reported by private industry in 2015 with illness accounting for the remaining 5%. Employers recorded most illness cases as other illness which includes musculoskeletal disorders (MSD) and systemic disease. Musculoskeletal disorders (MSD) are a broad range of disorders involving damage to the muscles, tendons, ligaments, peripheral nerves, joints, cartilage, vertebral discs, bones, and supporting blood vessels. Work-related MSD is a subcategory of these disorders, which is caused or aggravated by working conditions. MSD occur slowly over time due to the repeated wear and tear or microtraumas to the body. Ergonomists seek to identify and rectify factors that negatively impact the physical health and efficiency of workers. Participatory ergonomic programs seek to maximize the involvement of the workers in this process based on the simple fact that the worker is the expert. The following interventions were possible through the practice of participatory ergonomics.

Keywords: work-related musculoskeletal disorders, ergonomic intervention, human performance, mission readiness

1. Watertight doors and accommodation ladders

An accommodation ladder is a portable flight of stairs that is attached to a ship. They are raised for protection while a ship is underway and then lowered when a ship reaches the port. Accommodation ladders have a high degree of articulation, each section is movable [1, 2].

The ladder has handrails on both sides for safety. Accommodation ladders are constructed in such a way that the steps are horizontal whatever the angle of inclination of the ladder because when a ship is in port, it raises and lowers with the tides. The lower end of the ladder is a platform on a roller to compensate for the motion of the ship in relation to the quay. Ladders are maintained by Navy personnel when used on Navy vessels.

One group of Southwest Maintenance Center personnel repairs and maintains the accommodation (ACCOM) ladders, also known as anchored ladders, and other watertight fixtures such as doors, scuttles, and hatches for ships home-ported in San Diego, CA. Ladders and fixtures are serviced when a ship returns to the port; the time between services varies based on the mission (**Figure 1**).

During an industrial hygienist inspection, a possible overexposure to physical work place risk factors was documented due to the repair position of the ACCOM ladder, length of time for maintenance, types of tasks being performed and complaints of fatigue. Personnel placed the ACCOM ladders on sawhorses to perform maintenance work and repair. They had to bend over, reach forward, and squat during repairs. SWRMC personnel identified this arrangement as unsuitable and unstable with the potential of the ladder falling over (**Figure 2**).

Figure 1. ACCOM ladder on work stands before intervention. The ladders are being disassembled for repair.

Figure 2. Assembling accommodation ladder requires long duration of highly repetitive motions while exerting force. Pneumatic tools are not allowed and therefore the exposure is combined with high and somewhat awkward hand forces.

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An initial ergonomics evaluation using the Navy's Safety Instruction evaluation tool (Physical Risk Factor Checklist [1]) found the task to rank a hazard. Navy guidance recommended immediate mitigation to reduce the risk of personnel injury. SWRMC shop personnel and the safety department practiced participatory ergonomics by working with the ergonomist and engineers to design and build a ladder turning fixture. The worker-based design was used as a foundation for the final holding device (**Figures 3** and **4**).

1.1. Pre-intervention

Pre-intervention: personnel were required to bend, stoop, twist, and kneel during the preventive maintenance (PM) process to access all sides of the ACCOM ladder. Short, infrequent exposure to awkward postures is typically tolerated by the workforce, while long exposures can cause injury. The fully assembled ladder was difficult to work on. It had to be manually

Figure 3. Assembling rails on an accommodation ladder.

Figure 4. A fully assembled accommodation ladder.

Figure 5. Watertight fitting.

turned to allow the personnel to work on its underside. Workers exerted unacceptably high forces while performing this heavy lifting task (**Figure 5**).

The combination of heavy lifting and sustained awkward postures placed those employees who were working on ACCOM ladders at an increased risk of developing work-related musculoskeletal disorders (WMSD) of the spine or shoulder. These disorders can be caused by exerting high forces which can contract muscles to their maximum capability; leading to fatigue and possible damage to the muscles and other soft tissues. Lifting outside of one's power zone (i.e., from knees to shoulders) increases stress on the spine. SWRMC personnel noted these postures when turning the heavy ACCOM ladders.

1.2. Post-intervention

Navy' management fully supported a project to mitigate the risk factors found with ACCOM repair by allowing SWRMC personnel time and the use of recourses to fabricate a prototype holding fixture. The original idea was integrated into the final design through repeated design review meetings with SWRMC personnel, the ergonomist, and an engineer. Although heavy lifting and somewhat awkward postures are still inherent to ACCOM ladder repair, the use of the ladder fixture has greatly reduced the severity and frequency of the exposure to ergonomic stressors. The design was then exported across multiple Navy maintenance activities.

The ladder fixture was provided to the shop along with additional tooling to assist personnel with the removal of seized parts on the ACCOM ladders and watertight fixtures. Designing the tooling was no small task due to the numerous positions and sizes of these parts which included a variety of bolts, bushings, and pins, many of which were one-of-a-kind.

Successful completion of this project has saved a considerable amount of time and effort during the preventative maintenance of ACCOM ladders and watertight fixtures (**Figures 6** and **7**).

In 5 years, seven injuries were reported; in the 2 years following the intervention, no injuries were reported. Using the average total cost per claim by nature of the injury data as published

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Figure 6. Welder demonstrates awkward postures which were quite common during welding tasks on the ACCOM ladder.

Figure 7. After the intervention, rotating ladder fixture allows one worker to safety turn the ladder and locks into place. The ladder system saves time and effort and reduces the risk of injury and equipment damage.

Nature of injury	Cost per claim	# of injuries	Direct cost
Sprain/strain	$19,507.00	5	$97,535
Cut/laceration	$17,239.00	1	$17,239
contusion/bruise	$17,870.00	1	$17,870
Total direct cost			$132,644

Table 1. Estimation of direct cost incurred due to injuries.

by the National Safety Councils Injury Facts 2010.[1] **Table 1** summarizes the assumed direct costs incurred due to injuries.

Indirect costs are calculated using the index from Liberty Mutual[2] that estimates businesses are faced with between $2 and $5 of indirect costs for each $1 of direct costs. An amount of $3 of indirect to every direct dollar was used for this project.

Direct cost	$132,644
Indirect cost	$397,932
Total injury costs	$530,576

Injury cost averaged over 6 years = $530,576/6 = $88,429 per year.

Return on investment calculation

Pre-intervention annual injury cost = $88,429.

Post-intervention annual injury cost = $0.

Annual cost difference (savings if injuries are avoided) = $88,429.

Expected tool service life = 10 years.

Improvement investment = $377,000.

Ten-year cost savings: $507,290.

10 (annual cost of pre-intervention) – [improvement cost + {10 (annual cost of post-intervention}] = 10 ($88,429.) – [$377,000. + {10 ($0.}] = $507,290.

The improvement breaks even in 4.3 years.

Improvement cost/annual cost savings = 377,000/88,429 = 4.26 years.

The calculations do not take into account the time savings and product quality improvement from using the solutions.

2. Laundry facility streamlines process

The US Naval Academy (USNA) laundry facility is a massive operation processing 1.6 M pounds of laundry per year. The laundry facility sorts and washes bulk laundry and dry cleans and irons uniforms at a rate of approximately 6500 pounds per day. Other operations include alternations for the 4500 cadets who attend the four-year undergraduate college. Graduates earn a Bachelor of Science and commissions as ensigns in the Navy or second lieutenants in the Marine Corps (**Figure 8**).

[1]National Safety Council Injury Facts 2010 Edition, p. 58.

[2]Liberty Mutual Work Place Injury Data, April 2002 (http://www.ergoweb.com/news/detail.cfm?id=569)

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Figure 8. Emptying 40-lb. laundry bags which were pulled down from the conveyor.

2.1. Pre-intervention

Originally, bags were received and manually lifted out of a box truck, onto a transport cart and then once again manually transferred to a conveyor system in the check-in area. The 40-pound laundry bags traveled down the conveyor system and were manually removed when pulled from shoulder height and emptied onto a sorting table. The bulk bag, one per cadet, contains a mesh net bag of smaller items and loose larger items. These items were sorted by color and tagged. The contents of the bags were then verified against the laundry ticket submitted. Mesh nets were sometimes unpinned to replace smaller items; all bags and nets were then secured with a white wire lock-tie and placed on the lower conveyor. This process required repeated heavy pushing and pulling in awkward postures, repetitive motions, repeated gripping and postural stress (**Figure 9**).

The ergonomic hazards associated with the laundry production were lifting over shoulder height, high hand forces from using the large pins to secure the net bags and postural stress from leaning forward during the sorting. Individuals in the sorting area worked 8 h shifts

Figure 9. Loading laundry conveyor by throwing 40-lb. bags.

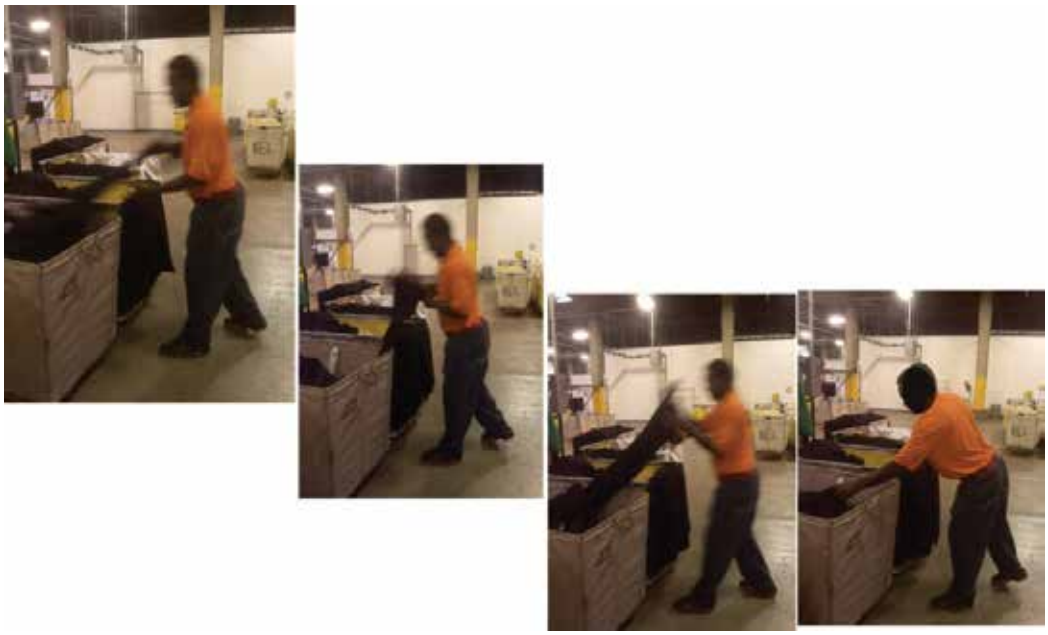

Figure 10. Highly repetitive dry cleaning laundry sorting.

pulling the 40-pound laundry bags from the top conveyor. Workers in the loading area worked the same duration but lifted the bags onto the transport system. The awkward posture and twisting while pulling or throwing the heavy bags exposed workers to a considerable physical stress (**Figure 10**).

2.2. Post-intervention

In 2013, the USNA facility redesign project began with the selection of equipment to reduce manual and repeated handling of the 40-lb. bags in the receiving and sorting area with an overhead monorail bag handling system. This $350,000 project improved working conditions for over 20 people and resulted in a tremendous drop-off in the number of injuries reported. The new system virtually eliminated manual moving of the bags and reduced complains of upper body fatigue. The monorail incoming bag system is a fast and efficient way to move material from the incoming truck to the sorting tables.

The overhead moving system was paired with dumping devices to eliminate pulling the cloths out of the bulk bags. Eliminating this step saved 3 min per bag. The cart dumpers provide exceptional emptying of laundry onto sorting tables eliminating the manual lift of the heavy bags from an over shoulder height position. With hands-free control, high-performance drive units and a 2000-pound capacity, the dumpers increase performance speeds over 30%. The adjustable height bag sorting table facilitates the initial break-up process and improves operator efficiency by reducing fatigue and excessive bending and twisting. In addition, the laundry bags were redesigned to include a loop/strap that allows each bag to be placed on a hook which conjoined to the overhead rail system (**Figure 11**).

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The monorail overhead bag system provides a fast, efficient automated mechanism to move laundry bags from truck to the sorting table. Each sorting table or check-in station has a call button that allows the check-in worker to call a bag to the work station, and then release the contents of the bag onto the station. The worker uses another call button to send the empty bag back. The systems' debagger capability automatically releases empty bags from the overhead rail without operator intervention. A workstation level conveyor allows workers to send

Figure 11. Cars full of laundry.

Figure 12. E-rail system.

checked-in and sorted items to the washroom department with minimal effort. These features help reduce the muscles loading and fatigue by eliminating the most stressful tasks (**Figure 12**).

3. Machine versus man power

Naval Air Weapons Station (NASW) China Lake is located in the California's Mojave Desert within the northwest section of San Bernardino County. NAWS China Lake is an airborne weapon testing and training range. Temperatures in China Lake rise over 100 degrees in the summer months.

NAWS China Lake is the Navy's largest single landholding, representing 34% of the Navy's total land worldwide. The 19,600 square miles of restricted airspace represents 12% of California's total airspace. NAWS China Lake provides an unprecedented venue for integrated testing and training for today's war fighters both on the ground and in the air. Because of the mission, like any research facility, NAWS China Lake generates hazardous waste (**Figure 13**).

3.1. Pre-intervention

NAWS environmental specialists retrieve, categorize, store, and dispose of various hazardous waste materials gathered from across the vast base. Different operations use different storage containers. NAWS follow strict hazardous waste protocols to prevent unauthorized waste from being disposed of illegally or accidentally (**Figure 14**).

When gathering the various waste streams, environmental protection specialists are exposed to a number of physical hazards, most notably heavy and awkward lifting, pulling/pushing, frequent standing, and temperature extremes. The physically demanding nature of the profession combined with the temperature extremes, placed the employees at an increased risk of developing additional or more severe WMSDs (**Figure 15**).

Figure 13. Before intervention, pulling super sacks (1 cu. yd.) of oil soaked rags onto lift gate.

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Figure 14. Before intervention, pushing plastic hopper onto rack truck.

Figure 15. Before intervention, off-loading truck at sorting area.

Environmental protection specialists repeatedly lifted, pulled, and pushed heavy items (e.g., batteries, oil rags, drums) as shown in the photos. The specialists lifted most items from ground level, and dragged or pushed them onto the lift gate. These items, such as solar and automotive batteries, drums, oil rags (over 2 million pounds a year), solvents, and cubic yard bulk bags (called super sacks), are handled multiple times throughout the disposal cycle.

The great expanse of the China Lake property means that items may be retrieved from various staging sites. Once back at the hazardous material processing/staging site, the items are removed from the truck. Some items are weighed while others are quickly categorized/staged for storage, and later moved again for disposal (**Figure 16**).

3.2. Post-intervention

Although the tasks of retrieving items from remote locations inherently requires the specialists to sit, climb, balance, stoop, kneel, crouch, crawl, lift 50 pounds and frequently walk and stand; the use of a crane installed on the back of the steak truck greatly reduced worker's exposure to

Figure 16. Totes of organized hazardous waste.

Figure 17. After intervention, truck mounted knuckle boom crane is sued in operations where other material handling equipment has not been capable of performing the waste removal.

physical work place risk factors. A crane now attached to the truck has eliminated much of the excessive materials handling and is capable of retrieving drums, super sacks or bulk bags (used for rags), and other heavy items from any storage surface (pavement or sand). The successful completion of this project has saved a considerable amount of time and effort during the movement of hazardous waste. The completed project replaces manual effort with machine power and improves the overall safety and health of the environmental specialists (**Figure 17**).

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through mishap prevention activities. The Navy Ergonomics program seeks initiatives to reduce exposure to injury risks and provides strategic direction to develop policies.

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Chapter 4

Ergonomics Education for Office Computer Workers: An Evidence-Based Strategy

Karthik Mani

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Abstract

Work-related musculoskeletal disorders (WMSDs) have become a growing concern in today's society due to their impact on insurance costs, productivity, and employee wellness. Computer workers are at risk of developing WMSDs due to the nature of their work and their work environment. To reduce the prevalence of WMSDs among computer workers, it is critical to promote awareness of various risk factors associated with WMSDs and educate them on healthy work behaviors. This chapter advocates ergonomics education as an evidence-based educational intervention to prevent WMSDs among office computer workers.

Keywords: computer ergonomics, educational intervention, musculoskeletal disorders, prevention, risk factors

1. Introduction

One of the contemporary health issues in today's society is work-related musculoskeletal disorders (WMSDs). Musculoskeletal disorders (MSDs) are injuries and illnesses that affect the muscles, nerves, tendons, ligaments, joints, or spinal discs. According to the United States (US) Bureau of Labor Statistics, MSDs include pinched nerve, herniated disc, meniscus tear, sprains, strains, tears, hernia (traumatic and nontraumatic), pain, swelling, numbness, carpal or tarsal tunnel syndrome, and Raynaud's syndrome; when the event or exposure leading to these injuries or illnesses is overexertion, bodily reaction, repetitive motion involving microtasks, and vibration [1]. Work-related disorders are prevalent among myriad occupational groups such as factory workers [2], truck drivers [3], hair dressers [4], allied health professionals [5], field workers [6], and computer workers [7, 8]. The regions that are prone to developing musculoskeletal injuries are the lower back, upper back, neck, and upper extremities [9].

WMSDs have enormous economic implications. The Institute of Medicine estimates that the total economic burden of WMSDs could be as high as $54 billion annually [10]. Ergonomic injuries related to computer work constitute a significant portion of WMSDs. The US Occupational Safety and Health Administration (OSHA) estimated that employers are "spending $20 billion a year on worker's compensation costs related to ergonomic injuries and illnesses" [11, p. 106].

Occupational injuries and illnesses have many direct and indirect cost implications. When calculating cost implications of WMSDs, one must give due consideration to all factors. Workers' compensation costs and charges involved in medical care and rehabilitation are considered direct costs, while lost productivity, lost time, training new staff, administrative costs, and temporary staffing are considered indirect costs. Web resources may assist employers to calculate cost implications of occupational injuries. For example, the OSHA Safety Pays website calculates the estimated total costs (direct and indirect) of common work-related injuries based on national worker's compensation data of the US [12].

In today's age, computer use has become an integral part of daily life. People use computers for various work-related and non–work-related tasks (social media, banking, shopping, etc.). Office computer workers (OCWs) use computers on an average of 6-12 hours a day [13]. The surge in computer use has also created a surge in computer work-related MSDs. Rehman et al. [8] stated that around 27% of computer users report backaches or discomfort. The chance of sustaining WMSDs is high when computer workers spend long hours on their computers. As the scope of this chapter is limited to the discussion of ergonomics related to the office computer worker population, the following sections review the risk factors related to office computer work, present ergonomics education as an effective intervention for OCWs, and highlight the role of employers and employees in preventing WMSDs among OCWs.

2. Risk factors

Factors that make a worker prone to developing WMSDs are called risk factors. **Table 1** lists various risk factors associated with WMSDs [**Table 1**. Risk factors for WMSDs]. Risk factors related to office computer work are classified into postural risk factors, environmental risk factors, individual risk factors, psychosocial risk factors, and risk factors associated with duration and intensity of office work.

2.1. Postural risk factors

Posture is the carriage of a body as a whole, the attitude of the body, or the position of the limbs [14]. The literature showed an established link between MSDs and improper posture at computer workstations [15, 16]. Sauter et al. [17] found that arm discomfort increased when keyboard height was above the elbow level. Chiu et al. [18] reported a significant association between head posture during computer work and neck pain. Eltayeb et al. [19] highlighted the significant associations between irregular "head and body posture" and "neck, shoulder and forearms/hands complaints."

Awkward and prolonged static postures contribute to musculoskeletal discomforts among OCWs. Twisting the torso to reach file cabinets, cradling the phone between the neck and

Awkward and prolonged static postures
Bending and twisting
Excessive work
Force
Glare
Job strain
Lifting
Monotonous activity
Pace of work
Repetition
Vibration

Table 1. Risk factors for WMSDs.

shoulder, curved sitting (bending the torso toward the monitor), slouched sitting with legs placed on an object under the work surface, and sitting on a high chair with dangling feet are some examples of awkward postures during office computer work. Postures with elevated or abducted shoulders are also considered awkward postures. These postures, when sustained, strain the lower back, shoulders, and neck muscle groups.

As computer workers often engage in tasks that demand high level of concentration, they get absorbed in their work and assume a given posture for long periods of time. During prolonged static sitting, the muscles that sustain body posture undergo a prolonged state of contraction, leading to decreased transportation of sugar and oxygen to dynamically contracting muscles. This causes an accumulation of waste products such as lactic acid and carbon dioxide in those muscles, leading to muscle spasms and fatigue. Prolonged sitting also contributes to myriad health issues such as low back pain [20], coronary artery disease, and kidney disease [21].

2.2. Environmental risk factors

Poor work environments augment the risk of WMSDs. Office work environments that are not conducive to their users can be referred to as "poor work environments." For instance, a workstation where the keyboard and mouse are placed at different levels, causing the user to elevate/abduct shoulders can be considered a poor workstation. A workstation without adjustable components (work surface, office chair, etc.) and necessary accessories (hands-free phone, document holder, etc.) can also be construed as a poor work environment. Further, environments with the heightened noise level, increased glare, and extreme temperatures are considered as poor work environments.

2.3. Individual risk factors

A computer worker may also become prone to developing WMSDs due to personal factors such as health history and poor work behaviors. Individual-related factors contribute to

WMSDs through their effect on body structure, function, and posture. Some of the individual-related risk factors are obesity, pregnancy, arthritis, trauma, and endocrinal disorders. Working without rest breaks, binge working, ignoring the body's warning signs such as pain and discomfort, ignoring flexibility/stretching exercises, failing to alternate work tasks, following poor working techniques, and failing to adjust workstation components as needed are the examples of some maladaptive work behaviors.

Gender has also been hypothesized as a risk factor. The literature reveals that women are at a relatively higher risk than men [22, 23]. This could be due to differences in anthropometrics and physiology in women. Also, women often assume responsibilities of non–work-related activities such as household tasks, which may add to muscle strain and make them more vulnerable to WMSDs.

2.4. Psychosocial risk factors

Psychological variables such as work pressure and job strain may also contribute to WMSDs. Hannan et al. [24] found a correlation between increased job strain and neck musculoskeletal symptoms. Perceived inadequate support from managers, low level of control, and information overload were also identified as psychosocial risk factors in the literature. With information overload, a worker spends an increasing amount of time using electronic gadgets and ignores proper work posture, thereby developing his/her risk for WMSDs. Mental stress can also augment the physical load during computer work because a computer worker with mental stress may exert more force on mouse or keyboard [25].

2.5. Risk factors associated with duration and intensity of work

Working on computers for long hours is a risk factor. The literature reveals a correlation between the duration of computer use and upper extremity (UE) pain, back pain, and eye strain [26]. Repetitive hand, wrist, and finger movements (e.g., typing for extended periods of time), speedy/jerky movements, and force applied while typing may also contribute to UE pain and musculoskeletal discomforts [25]. The demand for productivity and time pressure in today's work culture demand increased keying and extended hours of work from OCWs, thereby making them susceptible to WMSDs. Repetitive motions result in the vasoconstriction of arteries causing ischemic injury and edema due to anoxic damage [27].

3. Prevention of work-related musculoskeletal disorders

To prevent WMSDs, measures must be taken to avoid exposure to risk factors. These measures could be *technical* such as an elevated work surface for a tall worker, *organizational* such as conducting ergonomic workshops, and/or *personal* such as working with rest breaks [28]. Some of the WMSD prevention strategies in practice include workstation modification, task modification, and provision of necessary ergonomic accessories. However, "for these prevention measures to work, proper knowledge/awareness about how (a) the work-related factors contribute to WMSDs, (b) to carry out the work tasks safely, and (c) to effectively use the equipment, are essential" [13]. Robertson et al. [29] stated that the availability of adjustable office furniture

alone cannot reduce or prevent musculoskeletal injuries. For instance, a lot of computer workers sit on adjustable chairs without adjusting them due to lack of knowledge. Similarly, though many computer users know that bad posture is a risk factor, they continue to assume awkward and risky postures. Hence, to prevent WMSDs among OCWs and ensure their well-being, it is critical to educate them on "ergonomics" and "risk factors associated with WMSDs." An evidence-based strategy to impart this education is *Ergonomics Education* [13, 30].

4. Ergonomics education

Ergonomics means the science of fitting the job to the worker. In the context of office computer work, it refers to the computer user-workstation fit. Interventions that aim to enhance this fit are called ergonomic interventions. Ergonomic interventions differ from traditional therapeutic interventions because they target work posture, work habits, behaviors, and the environment [31]. They range from modifying workstations to long-term educational interventions with the aim of preventing and/or treating WMSDs.

Ergonomics is a recognized intervention strategy. Several occupational health and safety agencies across the world advocate for ergonomics. Many mid- and large-size technology companies offer ergonomic training to their employees as ergonomic interventions have been found to enhance productivity, improve worker well-being, and reduce WMSDs.

One of the well-documented ergonomic interventions is ergonomics education [30, 32, 33]. Ergonomics education is a strategy in which an ergonomic expert educates participants (workers) on ergonomic principles [see **Table 2**. Key ergonomic principles] and other necessary ergonomic information either on-site or virtually. The aim is to enhance participants' knowledge on WMSD risk factors, WMSD prevention strategies, and effective work behaviors. There are two primary objectives for any ergonomics education program. One is to help participants become aware of the risk factors and the other is to encourage participants to modify their work behavior.

Adequate clearance	Computer workers must have adequate thigh/knee clearance under their desk.
Adjustability	Computer workers must ensure that their workstation components, including the office chair, are adjustable.
Keep things within reach	Computer workers must keep frequently used items within forearm's distance and occasionally used items within arm's distance.
Minimize direct pressure	Computer workers must avoid resting their forearms/hands/thighs against sharp edges and hard surfaces.
Minimize fatigue	Computer workers must avoid prolonged work and sustained posture.
Work in good posture	Computer workers must be mindful of their posture and assume the ideal work posture at work.
Work at proper heights	Computer workers must adjust the workstation and chair as necessary to work at proper heights.

Table 2. Key ergonomic principles.

4.1. Types

Ergonomics education can be classified into traditional and participatory ergonomics education. In traditional ergonomics education, the information is presented via lectures, seminars, handouts, videos, etc., and participants assume a passive role. In participatory ergonomics education, participants interact with and learn from the expert using adult learning models [34, 35]. The difference between these two types of ergonomics education is the high level of interaction, which is present in the latter. Participatory ergonomics education was reported to achieve better outcomes than the traditional type [36].

4.2. Content

4.2.1. Anatomy and biomechanics

Ergonomics education programs for computer workers typically include content on biomechanics and anatomy of the back, neck, and upper extremities, as they are the body parts that are commonly affected during office computer work [9, 37]. When reviewing the anatomy and biomechanics of the back, ergonomic experts discuss the anatomy of the spinal curves and biomechanical alterations on the spine and intervertebral discs due to postural modifications. Experts also review the anatomy of two major muscles (trapezius and latissimus dorsi) that get used during office computer work and emphasize how these muscles get stretched or strained when a worker cradles the phone between the neck and shoulder, elevates the shoulders to reach high work surfaces, abducts the shoulders to reach the mouse and/or keyboard, hunches over computers, or reaches overhead to retrieve items.

When reviewing the anatomy of the upper extremities, ergonomic experts place a major emphasis on shoulder joints since awkward shoulder positions contribute significantly to WMSDs related to office computer work. They highlight three most common shoulder positions (elevated shoulders, rounded shoulders, and abducted shoulders) that contribute to UE/neck pain and discomfort. Ergonomic experts also review wrist and hand joints and underscore the importance of keeping wrists in a neutral position while working on computers, as incorrect position of these joints may lead to forearm and wrist pain, discomfort, or injury. Further, they review the impact of repetitive wrist and hand movements on forearm muscles and tendons. Information on conditions like muscle strain and carpal tunnel syndrome[1] (a condition that occurs due to increased pressure on the median nerve at wrist) is also presented during these sessions.

4.2.2. Mechanism of injury

Ergonomics education sessions highlight the mechanism of injury behind WMSDs. It has been a generally accepted notion that the theoretical mechanism behind WMSDs is repetitive microtraumas and their cumulative damage on musculoskeletal tissues. Ergonomic experts educate participants on various risk factors and how they affect musculoskeletal tissues and

[1]Though carpal tunnel syndrome (CTS) is a rare condition among office computer workers, certain conditions such as pregnancy, diabetes, and endocrinal disorders increase the likelihood of sustaining CTS.

contribute to WMSDs. They explain how sustained muscle activity leads to muscle spasms, how back rest angle of less than 95° adds pressure on ischial tuberosities, etc. In addition, they highlight the health issues associated with maladaptive work behaviors such as back pain, visual fatigue, visual dryness (due to constant watching of monitors), headaches, and weight gain.[2]

4.2.3. Ideal work posture and workstation

The content related to ideal work posture and workstation forms the core of ergonomics education programs for OCWs. The ideal work posture is the one where the back is straight or slightly reclined (95–110°), the shoulders are abducted less than 20°, the elbows are flexed at 90–100°, and the forearm is pronated with the wrist, hand, forearm in a straight line with the work item. Wrist extension or deviation of more than 15° must be avoided. For lower extremities, the legs need to be perpendicular to the floor, the thighs should be parallel to the floor, and the hip joint should be slightly higher than the knee joint. The feet should rest flat on the floor or a footrest.

According to the US OSHA, an ideal workstation has an adjustable work surface, a keyboard tray, a keyboard and input device (mouse) at the same level and frequently used items placed within easy reach. OSHA recommends a chair with adequate lumbar support, sufficient depth and width to accommodate the user, a seat front with a waterfall edge, and adequate thigh and knee clearance. In an ideal workstation, the top edge of the monitor lies at eye level[3] or slightly below and is placed at a distance from the user so that the user does not have to bend or extend the neck/head to see and read the monitor (approximately at an arm's length from the user). The monitors are placed perpendicular to the window to minimize glare. An ideal workstation also provides adequate space under the work surface so that the user can get close to the work surface and can cross his/her legs without bumping. It is recommended to leave the area under the desk free of storage. OSHA recommends that all workstation accessories and components be well maintained and serviced.

4.2.4. Work behaviors

Ergonomics education sessions also underscore the importance of work behaviors such as taking adequate rest breaks, engaging in exercise, being mindful of posture, and effectively arranging/adjusting the work surface. It is recommended that computer users take adequate rest breaks and vary their work tasks while working on computers [38]. OSHA recommends rest breaks for jobs that require prolonged posture and repetitive tasks. Henning et al. [39] highlighted the fact that frequent short rest breaks from computer-mediated work can benefit worker productivity and well-being. Galinsky [40] found that taking four supplemental 5-min rest breaks and two conventional rest breaks of 15 min

[2]Prolonged sitting at work causes biochemical alterations in lipase (an enzyme that metabolizes fat and glucose) activity. These biochemical changes in lipase activity disrupt fat metabolism, which leads to deposits of fats in adipose tissue rather than being metabolized by muscles and results in weight gain.
[3]The monitor can be positioned a little lower for individuals with bifocals or trifocals.

- Stretch the muscles slowly and avoid jerky movements [53].
- Stretch only to the point of comfortable stretch.
- Feel the stretch.
- Hold the stretch for 5-20 seconds.
- Repeat each stretching exercise 10 times or at least 3–4 times during each episode of exercise [43].
- Breathe slow, deep, and rhythmic while stretching.

Table 3. Stretching exercise guidelines.

throughout the work day can minimize discomfort without impairing productivity. Microbreaks at 20-min intervals were also reported to be effective [8]. During rest breaks, it is wise to step away from the workstation and walk around. Workers may visit a colleague's office, go to the print room, use the restroom or cafeteria, etc. To reduce eye discomfort and dryness, ergonomic experts recommend taking microbreaks to look 20 feet away from the monitor.

Ergonomic experts recommend that computer workers exercise at work [41], as the postural and proximal UE muscles undergo static loading during office computer work. They suggest that computer workers engage in stretching and flexibility exercises. Stretching exercises break cumulative musculoskeletal strain and relieve intervertebral disc pressure. Evidence supports the use of exercise to reduce musculoskeletal discomfort for computer workers [42]. By engaging in exercises, OCWs can reduce perceived discomfort [43], improve posture [44], and minimize fatigue [45]. Neck stretch, neck tilt, chin tuck, side stretch, and torso twist are some recommended exercises for the neck and upper body. Shoulder shrugs and rotations, wrist circles, and stretching the wrist flexors/extensors are some recommended exercises for the upper extremities. Hip marching, leg hug, leg extension, and ankle pumps are some of the exercises for the lower body.[4] Stretching exercises also have psychological benefits. Stretching increases mental alertness while decreasing anxiety and stress [46]. **Table 3** presents the stretching exercise guidelines [**Table 3**. Stretching exercise guidelines].

In office work environments, workers start the work day with good posture, but eventually recline or bend throughout the course of the day assuming risky postures and enhancing their risk for WMSDs [47]. Some workers habitually cradle the phone between the neck and shoulder so that their hands are free to type on the keyboard, thereby adding stress and strain to the lateral supporting muscles. Hence, ergonomic experts advise computer workers to be mindful of their posture when performing computer work. To help computer workers to be mindful of their posture, ergonomic experts suggest them to draw an

[4]It is critical to consult an ergonomics specialist, occupational therapist, physical therapist, physician, or other healthcare provider before engaging in any of the listed exercises or beginning an exercise regime. These exercises should not be considered complete or exhaustive and should not be used for self-treatment.

imaginary line that connects the ears, shoulders, and hip joints and advise to maintain the line. Ergonomic experts also show participants examples of good (ideal posture) and bad posture (slouching, keeping feet on chair frame, elevating shoulders, etc.) during ergonomics education sessions.

When delivering ergonomics education, experts emphasize that ergonomics is nothing but a fit between worker and work environment. They offer information on arranging the workstation and adjusting its components. They suggest that computer workers keep work items within reach. It is generally recommended to keep frequently used items within forearm reach and less frequently used items within arm's reach. During ergonomics education sessions, experts show participants how to adjust manual and pneumatic office chairs in addition to other workstation components. When teaching chair adjustment, the emphasis is on properly adjusting the backrest because backrests that are tilted too far forward or backward may contribute to back issues.

4.2.5. Ergonomic workstation issues

The problems associated with poor office chairs (fixed backrests/arm rests, too low or too high, too wide or too narrow, and sharp edges), poor workstations (sharp edges), and poor work environments (bad lighting, glare, hot/cold environments) are reviewed during ergonomics education sessions.

4.2.6. Ergonomic accessories

During ergonomics education sessions, ergonomic experts review various ergonomic accessories and their uses. Keyboard trays, footrests, glare protectors, document holders, large size mouse, hands-free telephones are some of the common accessories that are reviewed. According to ergonomic experts, there is no manufactured ergonomic device because what could be an ergonomically suitable device for a computer worker may not be suitable for another worker due to variations in anthropometric characteristics, nature of work tasks, and workstation arrangements.

4.3. Mode of delivery

Ergonomics education is delivered to computer workers through didactic lectures, PowerPoint presentations, discussions, demonstrations, video, workstation visits, one-to-one consultations, provision of resources, etc.

4.4. Materials

Ergonomic checklists, session handouts, brochures, and pictures of ideal work postures and workstations are some of the commonly provided materials at ergonomics education sessions. Product manuals are also used as ergonomics education tools. These manuals describe the product's features/specifications and how to use/operate the product.

5. Efficacy of ergonomics education

Ergonomics education has been found to be an effective strategy. The literature supports the use of ergonomics education to improve computer workers' awareness of risk factor [13], reduce musculoskeletal injuries [30, 48], improve workers' posture and workstation layout [48], increase perceived control over the physical environment, and improve workers' intrinsic motivation to alter posture and behaviors [29].

Ergonomics education enhances the knowledge about the risk factors associated with WMSDs. In a study conducted in a small nonprofit organization, the authors found that 89% of the participants were able to identify more risk factors and answer more questions correctly in a pre-/postknowledge test after a six-week on-site ergonomics education intervention [13]. Another large-scale field intervention study with more than 200 participants revealed that participants who received education and training to understand office ergonomic principles, perform self-evaluation of work places, and rearrange workstation demonstrated a significant increase in overall ergonomic knowledge [29].

Ergonomics education intervention was reported to be an effective intervention in reducing musculoskeletal pain and discomfort. Bohr [30] stated that those who received ergonomics education reported less pain or discomfort. Ketola et al. [36], through a randomized controlled trial, investigated the efficacy of ergonomics education on workstation changes and musculoskeletal disorders among computer users. Results identified that computer workers who underwent intensive ergonomics and ergonomics education interventions showed less musculoskeletal discomfort at the 2-month follow-up assessment post-intervention.

Several studies found that ergonomics education had a positive influence on the work posture of computer workers. Greene et al. [49] evaluated the effectiveness of an ergonomics training program in computer workers and found that the risk factor exposure of the intervention group participants was significantly reduced. The authors asserted that participative training in workstation ergonomics can improve work postures and work practices. Mahmud et al. [50] used a cluster randomized controlled trial design to investigate the effect of ergonomics education in reducing musculoskeletal disorders among computer users. When the outcomes were evaluated post-intervention, experimental group participants who received the ergonomics education demonstrated improved workstation habits and work posture. Through a cross-over trial that investigated the effectiveness of a 2-week workstation ergonomic intervention (consultation and provision of ergonomic accessories), the authors found that individualized ergonomic interventions may improve work-related posture and reduce low back pain [51]. Esmaeilzadeh et al. [48] examined the effect of ergonomic intervention on work-related UE MSDs among computer workers and found that the ergonomic training significantly improved participants' posture over 6 months.

Ergonomics education was reported to positively influence worker's behavior. Mani et al. [13] stated that after 6 weeks of intervention, study participants demonstrated healthy work behaviors such as adjusting their workstation, taking rest breaks, and engaging in stretching exercises. Robertson et al. [29] found that increased ergonomics knowledge resulted in behavioral translation. In their study, the experimental group participants demonstrated appropriate behavioral changes to their workstations when compared to the control group participants. The experimental group participants also adjusted their workstation and ergonomic accessories

post-intervention. Esmaeilzadeh et al. [48] also found a notable improvement in the workstation layouts of the experimental group participants 6 months post-intervention. Some studies reported less psychosocial stress [30] and an increased sense of control [29] as outcomes of ergonomics education.

6. Limitations of ergonomics education

One of the biggest limitations of any educational intervention is the retention of knowledge and ergonomics education intervention is not an exception. Studies that investigated the effectiveness of ergonomics education measured the outcome at different intervals that ranged from 1 week to as long as 30-month postintervention [13, 30, 36, 51]. Though the majority of the studies reported short-term improvements, evidence is scarce on long-term gains. One study reported improvements in work posture and reduction in pain during short- and long-term follow-ups [51]. However, another study that reported a short-term gain (2-month follow-up), failed to report a similar outcome at the 10-month follow-up. [36]. Ongoing ergonomics education sessions at specified intervals and provision of ergonomic resources to employees may overcome the problems with latency of knowledge. Showing pictures that highlight good versus bad postures during ergonomics education sessions and encouraging participants to identify what is wrong and why it is wrong may also help solidify their knowledge.

Another limitation of ergonomics education is the lack of application of the learning. Simply presenting the ergonomics information to employees does not solve the problem if they do not have the necessary ergonomic accessories. For instance, as a result of ergonomics education, an employee might become cognizant of the need to adjust his/her office chair to minimize the risk of WMSDs, but either does not have an office chair with adjustable components or has a chair with many adjustable features to the extent that he/she does not know how and what to adjust. Participatory ergonomics education, in which the participants are allowed to evaluate and modify their own workstation with the help of an ergonomic expert, may overcome this limitation to an extent.

Though ergonomics education reported to positively influence work behavior in a short term; in most instances, it fails to elicit the motivation required to induce permanent behavior change. Habits are powerful and difficult to overcome. Often, participants of ergonomics education were seen to resort to their old habits of work posture and behaviors. Ongoing participatory ergonomics education at specified intervals may overcome this limitation.

7. Role of employers

To prevent WMSDs, employers must work collaboratively with their employees and ergonomic experts. Employers must make every effort to offer ergonomic training programs to their employees, as WMSDs related to computer work are preventable and may save a significant amount of money for them. As stated elsewhere, the economic benefits of ergonomics education programs can be realized by reviewing direct and indirect cost implications on OSHA Safety Pays website. There are myriad ways an employer can offer ergonomics education. One

way to deliver ergonomics education is to make ergonomic resources easily accessible. For example, a company's intranet site may have a folder where employees can locate useful ergonomic information and resources. Recorded webinars can also be made available on the company's intranet site. Staff may be sent periodic e-blasts with ergonomic tips.

8. Role of employees

The prevalence of WMSDs can only be mitigated if employees act in concert with employers' efforts toward WMSD prevention. Employees should educate themselves on ergonomics, cultivate healthy work behaviors, undergo training programs offered by the employer, and learn to use ergonomic software applications. A variety of public and private web resources offer useful information related to computer ergonomics such as OSHA, Cornell University Ergonomics web, Canadian Center for Occupational Health and Safety, Office-ergo, and Velocity EHS. Software applications such as *Eyeleo, Workrave*, and *PC Work Break* remind computer users to take a rest break, stretch break, and/or eye break during the work day [52]. Some software applications also record the duration of computer usage. Employees may also download and use applications such as *ErgoMinder* and *ergoffice* on their personal digital assistants (smart phones/tablets) to cultivate effective work behaviors.

9. Conclusion

Multiple risk factors make computer workers susceptible to WMSDs. Research evidence favors the use of ergonomic interventions based on educational approaches due to their positive impact on participants' knowledge, behavior, and well-being. Ergonomics education, combined with organizational support and employee motivation to embrace adaptive work behaviors, appears to be a promising intervention to minimize the impact of WMSDs among the ever growing computer work population.

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Treatment

Chapter 5

Joint Instability as the Cause of Chronic Musculoskeletal Pain and Its Successful Treatment with Prolotherapy

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Additional information is available at the end of the chapter

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Abstract

This chapter is based on the premise that treatment with prolotherapy can greatly reduce chronic musculoskeletal pain, which affects more than 1 billion people worldwide. Although relatively unknown to mainstream medicine, prolotherapy has been used for decades to treat chronic musculoskeletal pain, doing so by correcting the underlying cause of that pain: joint instability due to ligament laxity. Discussions of joint instability, ligament physiology and biomechanics, compressive and shear forces, sites of instability, pain referral patterns, and ligament injury and healing demonstrate how they all interrelate to cause chronic pain. Treating chronic pain using nonsteroidal anti-inflammatory drugs, corticosteroids, and the rest, ice, compression, and elevation protocol actually inhibit the natural healing process of injured ligaments because they interrupt the inflammatory response, prevent joint swelling, and hinder cell proliferation, resulting in further ligament laxity and tissue regrowth that is inferior to native ligament tissue. Unlike conventional treatments, prolotherapy injects small volumes of an irritant solution into painful ligaments, tendons, joints, and surrounding joint spaces, initiating an inflammatory response which then attracts substances that promote normal cell and tissue growth. Their propagation stimulates the injured ligament to proliferate and grow at the injection sites, resulting in the regeneration of new tissue.

Keywords: chronic pain, joint instability, ligament laxity, prolotherapy, regenerative injection therapy

1. Introduction

"Keep people moving" is the mantra of the Global Alliance for Musculoskeletal Health—The Bone and Joint Decade (GAMH/BJD) 2010–2020, a global collaboration first launched in 2000 as the Bone and Joint Decade and dedicated to improving the health-related quality of life for

people with musculoskeletal disorders (MSKDs) throughout the world. A Bone and Joint Decade Global Minimum Standards of Care for Musculoskeletal Health was created to develop better treatment modalities according to evidence-based recommendations and will be focusing on two crucial areas—chronic pain and hip fractures [1]. The work of the Alliance has awakened the medical community to this urgency, resulting in a record number of research studies being published since 2002. Despite this, MSKDs remain a major cause of disability, ranking second worldwide and first in developed countries. Today, one in four people around the world suffer from long-standing loss of function and pain [2, 3]; Global Burden of Disease studies show that MSKDs cause 21.3% of all years lived with disability (YLDs) [4] and saw an increase of 61.6% in disability-adjusted life years (DALYs) from 1990 to 2016, with osteoarthritis showing the greatest increase [5]. DALY refers to the sum of YLDs and the years of life lost (YLLs) due to premature mortality. These data represent the enormous unmet need of finding effective ways to prevent and treat musculoskeletal conditions.

MSKDs are the most common cause of severe long-term pain [6]. Over 1.3 billion people worldwide are living with back pain, neck pain, osteoarthritis, or other painful musculoskeletal conditions [4]—a pandemic of epic proportions that modern medicine has been unable to rectify. That is because modern medicine has not identified or addressed the underlying cause of chronic musculoskeletal pain—namely, joint instability, which is the primary focus of this chapter, along with how to treat it successfully with prolotherapy.

2. Joint instability: the precursor to chronic pain

The human body has 360 joints, each of which contains at least two bones that are connected to one another by one or more ligaments. Joint instability occurs when there is excessive movement of these bones or increased speed of their motion relative to the other as tension is placed on the joint. This inability to maintain the relationship between adjacent bones under normal physiological forces puts extra pressure on intra-articular and surrounding joint structures, leading to joint degeneration, soft tissue damage or tears, and pain. Joints begin to degenerate or break down when the catabolic (destructive) processes exceed the anabolic (reparative) processes. Once the catabolic processes take over, the joint undergoes full cartilage loss, leaving it in a state of bone-on-bone without the cushioning effect of the cartilage tissue; thereafter, ligaments become overly stretched as they try to support the joint, leading to ligament laxity and excess motion in the joint. The end result is joint instability and disabling chronic musculoskeletal pain.

Each joint is designed to provide the precise amount of motion and stability needed for it to function as intended. Weight-bearing joints require more stability and, thus have less motion available. The hip is a major weight-bearing joint and, therefore, must be very stable to allow for ambulation. So too, is the lumbar spine, which must support the rest of the spinal column and the head. The facet joint capsule is the most richly innervated part of the spine in terms of nociception (pain perception) and proprioception (position sense) [7], and injury to the capsule ligaments there is the most common cause of spinal instability and spinal pain. In contrast, the

shoulder is the most dynamic joint in the body and must be very mobile, as it acts with the elbow to position the hand in space. The more intrinsically stable a joint is, the more it relies on bone and joint architecture for movement; the more intrinsically mobile a joint is, the more it relies on the ligaments for stability. While excess motion is a defining component of joint instability, the amount of force needed to produce any given range of motion in that joint becomes considerably less. That is why a second injury to the joint is much more likely to occur, even when the trauma seems relatively innocuous [8]. The integrity or lack thereof of the joint fluid, joint capsule, muscles, and tendons can also affect a joint's susceptibility to instability. Indeed, ligaments were never meant to stabilize the joints by themselves [9]. While ligaments are the primary passive joint stabilizers for most joints, muscles are the functional or dynamic joint stabilizers. The two are connected by the ligamento-muscular reflex. Therefore, when either structure becomes weakened, the other must take on more responsibility in maintaining the joint's stability.

Joint instability is caused by ligament laxity, which can occur after injury to one or more of the 900 ligaments that help support the joints of the body. Ligaments are dense bands of fibrous connective tissue that connect one bone to another and are the primary stabilizers of proper joint motion. When ligaments around a joint become weak, loose, or torn, they may not be able to hold the joint bones in place, causing one of the bones to partially dislocate or sublux. Subluxation occurs primarily because of laxity in a ligament and disrupts the connection of two adjacent bones in the joint. There are three primary ways that a ligament can become loose or torn: (1) trauma, a one-time substantial force, such as a whiplash injury; (2) overuse, a repetitive motion with a smaller intermittent force or creep, a steady load that puts a constant stretch on the ligament; (3) multidirectional instability, dislocation of a joint in different directions where the injury is severe enough to destroy the ligament. Tearing occurs when ligaments are stretched beyond their capacity to extend; once in this state, they are unable to return to their original length, even when the injurious force is removed [10].

2.1. Ligament physiology and biomechanics

Ligaments are taut bands of collagen that connect one bone to an adjacent bone to provide the primary stability in a joint. Collagen constitutes 70–80% of the dry weight of a ligament, the majority of which is type I collagen; the remaining constituents include elastin, glycoproteins, protein polysaccharides, glycolipids, fibrocytes, and water. Collagen has a relatively long turnover rate, with an average half-life of 300–500 days, which is slightly longer than that of bone. This means it can be several months before a ligament shows evidence of structural damage; this also affects its slow and often futile attempt to repair itself after injury [11]. One study demonstrated that ligaments were intact macroscopically at ultimate failure, but electron microscopy revealed widespread disruption of the collagen fibrils. However, once additional stress was applied, actual macroscopic disruption did occur, suggesting that microscopic failure of the collagen fibrils in grossly intact ligaments may be a significant cause of clinical instability [12].

Ligaments are viscoelastic tissues and thus, are pliant and flexible, allowing for natural movement of the attached bones they support; yet they are strong and inextensible when resistance to

applied forces is needed. Ligaments are able to do this because of a unique property known as crimping, whereby their collagen fibers are arranged in multiple directions so that they are aligned in an undulated or wavy pattern along their length when the ligament is relaxed, but become straighter when the ligament is stretched. Crimping allows ligaments to elongate and return to their original length without losing their strength or sustaining structural damage [13]. Although ligaments generally sustain tensile loads in one predominant direction, they are able to handle stresses in other directions, primarily because of their crimping behavior. When tension on a ligament increases, the collagen fibers progressively elongate (un-crimp) until all fibers are nearly linear, causing the ligament structure to become increasingly stiff. The stiffness of a material represents the material's ability to resist deformation and is found by dividing the change in load by the change in elongation. The signs and symptoms of joint instability reflect the loss of stiffness or strength in a ligament [14]. The crimping behavior of ligaments, as well as the interaction and cross-linking of collagen, elastin, and reticular fibers, is critical for normal joint mobility. These characteristics allow ligaments to have a limited range of strains over which they produce minimal resistance to movement. As a result, joints may easily be moved in certain directions and over certain ranges. Likewise, if a joint is displaced toward the outer limit of its normal range of motion, the strain of ligaments in that joint increases, causing recruitment of collagen fibers from their "crimp" state to a more straightened or stiff state. This allows the ligament to quickly increase its resistance to further elongation and stabilize the joint.

As viscoelastic tissues, ligaments also exhibit stress/strain behavior that is time-rate dependent and are stiffer and stronger at high-strain rather than low-strain rates. Therefore, ligaments are more likely to elongate under slower loading conditions, which would lower their risk of failure. Ligaments have a nonlinear, strain-stiffening structural response, which is thought to occur because of the crimp pattern of their collagen fibrils that elongate when small tensile loads are applied. As already mentioned, ligaments then become stiffer and stronger and, thus, larger forces are required to produce a given strain. Ligaments also possess a property known as creep, in which progressive elongation or a change in strain with constant load occurs overtime; this should not be confused with stress-relaxation, which occurs in a tissue that is stretched and held at a fixed length. In this latter state, the higher the strain or loading rate is, the larger the peak force/stress becomes and, thus, the greater the magnitude of the stress-relaxation. In contrast, creep is a constant state of stress with an increasing amount of strain and causes elongation over time when a constant force/stress is applied across the tissue [11]. Moreover, the extent of creep depends on the magnitude and duration of the applied stress, and the deformation or elongation may become so extensive that the tissue can no longer perform its function. In one study, the authors report that rat medial collateral ligaments were shown to exhibit consistent nonlinear behavior in which the rate of relaxation was dependent upon strain level and the rate of creep was dependent upon stress level [15].

While the primary function of ligaments is to prevent excessive joint motion, they have other important functions, including transmitting loads from bone to bone, mediating motions between opposing fibrocartilage and cartilage surfaces, acting as a joint-force sensor, and maintaining joint congruency [9]. Together, ligament function echoes one common theme: maintaining even stress across the joint surfaces. In doing so, ligaments also ensure that the stress placed across the joint surfaces is distributed over as large an area as possible, which

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allows the joint and its surfaces to handle the maximum amount of pressure, force, and stress when the loads are compressive. However, when a ligament is injured, the joint forces are suddenly concentrated in one area of the joint, which predisposes the joint surfaces to break-down and injury. The body instinctively reacts to distribute these forces more evenly by causing the joint to swell. This creates extra joint fluid that helps to distribute the forces within the joint more evenly and temporarily stabilizes the joint. Acute ligament injuries almost always result in joint swelling. These injuries also cause severe muscle spasms and tightness, especially when the spinal capsular ligaments in the lower back and neck are injured. Like joint swelling, muscle spasms are the body's response to stabilizing an unstable joint and dissipating pressures across the joint.

Ligaments can become injured when stretched as little as 5–10%, with failure occurring at 13–32% elongation [16, 17]. Thus, when too large a force is put on a ligament, it can elongate to a point where the tissue becomes permanently overstretched; if the force is not released, the ligament can completely fail or tear. For instance, anterior cruciate ligaments have been shown to fail at forces between 1730 and 2160 N [18, 19], and most studies report cervical ligament failure at around 100 N [20].

When ligament laxity occurs, there is a disconnect between the tissue's form and the function in that the additional length of the stretched-out ligament causes a permanent mechanical weakening in the tissue [21]. Simply put, the ligament has lost its stiffening capacity and can no longer support the joint or dissipate the forces placed on it. Ligament laxity in a joint is measured as the motions of translation and rotation at a given force or torque. There is a direct relationship between the amount of ligament lengthening and the amount of joint play or laxity [20, 22].

2.2. Compressive versus shear or rotational forces

The degree to which a ligament can become damaged depends on the magnitude, direction, and speed of the force put on the tissue. Ligaments, articular cartilage, and intervertebral disks can withstand compressive forces that are magnitudes greater than shear or rotational forces, which have a catabolic or break-down effect on these structures [23–25]. Thus, ligaments are less able to handle extension forces, especially when they are rotational or shear forces. "Sideways" sheer and rotational or torsional forces place greater demands on the joints and ligaments. As a result, these rotational-type forces are more likely to trigger an injury and generate pain. Once a ligament is injured, even a slight sheer force can cause tremendous pressure to develop within the joints. In some ways, the body can compensate for this. For instance, the oblique orientation of the interspinous ligaments in the lumbar spine is more conducive to axial rotation, enabling the tissues to resist posterior shear off the superior vertebrae and impose anterior shear forces during full flexion. These ligaments are similar to the collateral ligament in the knee in that they follow an arc throughout flexion to control the vertebral rotation. This helps the facet joints remain in contact and glide with the rotation [26]. Facet joints provide stability to the spine by restricting the range of motion of the superior vertebrae with respect to the inferior vertebrae and protecting the motion segments of the spine from high extension rotations and large shear displacements in the anterior direction [27, 28].

The most injurious movements for the intervertebral disks in the spine are flexion and axial rotation, the combination of which puts the greatest amount of stress on the ligaments and disks. It is this combined motion that causes most acute disk herniations. Flexion itself causes the upper vertebra to move anteriorly, which can compromise the integrity of the disk. During flexion, the nucleus becomes displaced posteriorly and begins to press on the posterior fibers of the annulus, increasing their tension, and the inferior articular processes of the upper vertebra glide upwards, freeing themselves from the superior articular processes of the lower vertebra. This causes the facet joint capsule, capsular ligaments, and other ligaments of the vertebral arch to become stretched. The tension imposed on these ligaments finally limits extension. Axial rotation, on the other hand, produces a strong shearing force that stretches the capsular ligaments and pulls the facet joints apart, while causing tension in the oblique central fibers of the annulus to build to a maximum. The nucleus then becomes compressed and the internal pressure there rises in proportion to the degree of rotation. The combined motions of flexion and axial rotation can be traumatic, as they produce increasing pressure inside the nucleus, tearing the annulus, and driving the nucleus posteriorly through cracks in the disk's structure. The result is a herniated disk.

Degenerative disk disease (DDD) begins with injury to the ligaments of the capsular or posterior ligamentous complex. Once the ligaments are stretched, an increase in the shear, rotational, and torsional forces on the intervertebral disks occurs, which causes the disks to deteriorate more quickly than normal. This stretching has a similar effect on the capsular and posterior ligament complex itself, as it causes increases in those same forces in that area of the spine. When the posterior ligamentous complex can no longer stabilize motion segments in the spine, the amount of motion with shear, bending, or torsion there can increase by as much as 270% [29].

Spondylolysis and spondylolisthesis are similar disorders of the spine that usually develop in adolescence and are caused by shearing forces or repetitive loading and hyperflexion/hyperextension of the spine. These types of motions, which are common in adolescents who participate in sports, put abnormal amounts of stress on the pars interarticularis, a small segment of bone within the neural arch that connects the superior and inferior articular facets [30]. Repetitive microtraumas to the pars often result in a stress reaction or fracture initially but can progress to spondylolysis and then to spondylolisthesis if not treated.

2.3. Locating the joint instability

The key to curing chronic pain is locating the joint instability, which can be difficult because it is only visible through rotational or shear forces. Stationary MRIs show density changes in tissue and do not show joint instability. Newer technologies, such as ultrasound and digital motion X-ray (DMX), are able to provide a clearer image of a ligament's structure and function. Kinematic or functional computerized tomography (fCT) and magnetic resonance imaging (fMRI) scans, as well as digital motion X-ray, are able to depict lumbar and cervical instability during motion. These types of radiographs are much more diagnostic, especially when patients have signs and symptoms of spinal instability, yet have normal MRIs in a fixed position. Studies have demonstrated the ability of kinematic radiographs to show excess vertebral motions and thereby document instability in degenerative disk disease, spondylolisthesis, and radiculopathy [31–35].

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Specific radiological changes that suggest spinal instability include disk narrowing with gas in the disk, traction spurs, and posterior joint and subluxation (abnormal rotatory alignment and abnormal separation of the spinous processes).

The source of chronic pain is not always the site of the instability and involves the kinetic chain (**Figure 1**). This term refers to the joints and joint structures in the spine and extremities that move or handle force with a certain motion or movement. More often than not, the instability is located in the joint closest to the site and the start of maximum pain perception, but it is not unusual for it to be in the second closest joint to the site and the start of maximum pain perception. This means that the instability is usually in the next joint up or down in the kinetic chain from the one where the pain is located. At times, the instability is in the second farthest joint away from the hub in the kinetic chain.

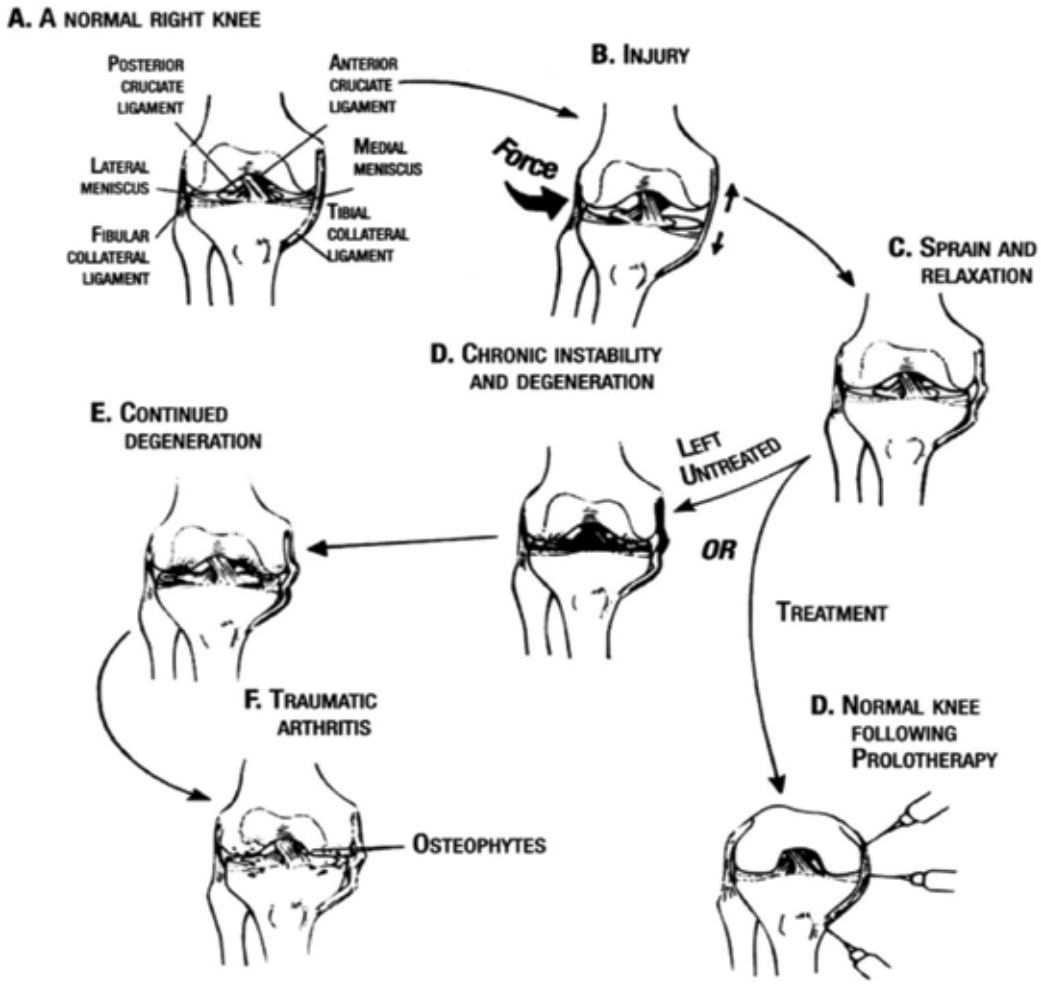

Figure 1. The kinetic chain-joint instability connection.

Ligaments contain an abundance of nerve receptors; thus, they are primary pain generators and act as the sensory organs of the joints by releasing pain signals to tell the brain what is occurring in and around the joint. Because of the high concentration of nerve endings in these tissues, even mild ligament injuries can cause severe pain (articulate cartilage is devoid of nerve endings, so joint pain never originates from this tissue). Generally, when ligaments are stretched too far or at too fast a rate, their nerve receptors fire and transmit pain signals to where the instability might be. However, the tissues have well-known pain referral patterns that often deviate from this. For instance, injury to a ligament in the hip may cause instability there, but the pain can be referred all the way down into the big toe, or it can be referred to the inner or outer thigh, or to the buttock region if the muscles that cross or move the hip joint tighten and spasm. When external rotation of the hip causes pain, there is likely to be instability in the anterior hip joint since the motion would have stretched the nerve endings of the iliofemoral ligament, which stabilizes that joint.

Hearing cracking sounds in a joint or feeling that bones are rubbing together when certain movements are executed is completely abnormal in the context of human movements. These sensations are called crepitation and are signs of joint instability, especially if the crepitation in that location is associated with pain. Left unattended, crepitation can cause long-term pain to develop. As with earlier examples, the site of instability is not always obvious. A person may complain of pain at the base of the neck but feel crepitation in the mid-thoracic region. The actual source of the instability is likely in the upper back where the crepitation is, not in the neck where the pain is felt. Another sign of segmental spinal instability is gapping, which can occur when the capsular ligaments become lax or weakened. Gapping refers to an increase in the space between the facet joints and can be seen on functional X-rays and MRI or CT scans [36].

Sometimes joint instability and pain occur after certain types of surgery. For instance, spinal instability is a common complication of foraminotomy/laminectomy surgery because bony stabilizing structures are removed from the lower back during the procedure [37]. Other studies have shown that there is a significant increase in annulus stresses and segmental mobility when the facet joints are removed [38, 39]. Some types of orthopedic surgery can worsen any existing joint instability if the procedure removes stabilizing structures, such as bone spurs (chondroplasty), menisci (meniscectomy), labrum (labral resection), and intervertebral disks (microdiscectomy). Doing so puts more stress on the surrounding ligaments and stabilizing structures and increases the risk of further instability. Fusion surgery is a case in point. While the procedure is intended to improve stability, it often leads to future instability because additional forces are put on the segments above and below the fused segment. For example, after an L4-S1 fusion, instability is likely to develop in either the L3-L4 segment of the spine or the sacroiliac joints because they are both adjacent to the fused segment that can no longer move. This condition is called adjacent segment disease. As a result, the spinal instability is not resolved but is perpetuated as the adjacent segment disease "travels" up and done the spine. Spinal fusion is why adjacent segment disease and subsequent degenerative disk disease have become so prevalent [40]. People who are contemplating fusion surgery need to realize that the procedure permanently fuses the affected segments, limiting motion in that part of the spine for the rest of a person's life.

The spine can move through six degrees-of-motion and the movements therein are either rotational or translational, meaning any excessive motion occurring between adjacent vertebrae can

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move in a clockwise or counterclockwise direction (rotational) or in a direction that is to the right or left or forwards or backwards (translational). The ligaments are the tissues that regulate these adjacent vertebral rotations and translations. Given this, spinal motion can be a complex combination of translations and rotations and any subsequent instability can be translational or rotational in nature or a combination of both. The intervertebral disks are primary restraints against the compressive forces of gravity, whereas the posterior ligamentous complex and facets joints are primary constraints against bending and twisting movements. This is why one simple ligament injury in the spine can cause both disk degeneration and spinal instability. Clinically, spinal stability enables the spine to maintain its alignment during loading and allows the neural structures it encloses to be protected without causing pain [41]. It is the collective job of the disks, ligaments, bones, and muscles to keep the spinal column in proper alignment, so the spinal cord and nerves remain protected. However, if the spine no longer has adequately functioning biomechanical properties, clinical stability is lost, giving rise to spinal instability and pain.

When surgeons use the term "spinal instability" as a diagnosis, especially in the case of spinal fusion, they are usually referring to macroinstability, such as dislocation of a joint or a large movement of an adjacent bone. This occurs when there is complete disruption of a ligament. However, ligaments, other soft tissues, and disks can become injured by much smaller movements. These small-scale motions are called microinstability. Most chronic pain is caused by subfailure ligament injury, which occurs when the ligament is stretched out or becomes partially torn, but not completely disrupted. Just one or two ligaments need be affected to cause ligament laxity and the subsequent extra movement of adjacent bones. For instance, the capsular ligaments holding the facet joints in place can became lax or stretched out by as little as 1–2 mm. What is taking place here is clearly a process of microinstability.

2.4. Ligament healing: an oxymoron of sorts

Ligaments are notoriously poor healers because they are hypovascular, meaning they have a low blood supply, appearing white when compared with the highly vascularized red-colored muscles that can heal relatively quickly on their own. Although ligaments heal poorly, they do go through a specialized sequence of overlapping but distinct cellular events. This healing cascade consists of three consecutive phases that occur over time: the acute inflammatory phase, the proliferative or regenerative/repair phase, and the tissue-remodeling phase. Depending on the severity of injury to the ligament, it can be weeks or months and, sometimes, years before the process of healing is complete.

However, slow this course of healing may be, it is compounded by the extreme physiological and structural changes that ligaments undergo after injury, as well as by the complex and dynamic cellular processes that take place during healing. These deleterious events cause alterations in the biology and biomechanics of the injured ligament, leading to inadequate healing and tissue formation that is inferior to native ligament tissue. There is ample evidence to support this, as the literature has described remodeled ligament tissue as "grossly, histologically, biochemically, and biomechanically similar to scar tissue" [42–44] and "grossly, microscopically, and functionally different from normal tissues" [45]. The incomplete healing of the ligament and lower integrity of the new tissue results in ligament laxity, predisposing the joint

to further injury. This cycle of ligament injury and ensuing laxity causes joint instability, which then leads to chronic pain and diminished function, often culminating in osteoarthritis of the affected joint [14]. Therefore, once ligaments are stretched beyond a certain point, they do not regain their normal power and length, both of which are needed for a joint to become stable again and function normally.

2.5. Standard treatments do not pass muster

The RICE (rest, ice, compression, and elevation) protocol, nonsteroidal anti-inflammatory drugs (NSAIDs), and corticosteroids normally prescribed by modern medicine all put too much strain on the ligaments during the healing process and have been shown to inhibit ligament healing and contribute to long-term pain from incomplete recovery of ligament strength. Despite the longtime acceptance of rest and immobilization as a standard therapy after ligament injury, evidence is revealing that the absence of joint motion can have a dramatic effect on healing ligaments. Studies have shown that immobilizing a joint with an injured ligament can cause a number of adverse side effects, such as formation of synovial adhesions [46], increased collagen degradation, decreased collagen synthesis [47], and more disorganized collagen fibrils [48, 49]. Immobilization also contributes to the injured ligament's more catabolic state in that it disrupts loading, which alters matrix turnover in the ligament, as well as the degree of orientation of the matrix collagen fibrils within the tissue [50]. Consequently, matrix degradation begins to exceed matrix formation; however, what newly synthesized matrix there appears less well organized, and the ligament tissue itself is less stiff and weaker [14]. Prolonged limb immobilization also decreases the content of water and glycosaminoglycans in the ligament, adding to the ligament's loss in mass and strength [50]. Decreased ligament loading also has a profound effect on the strength of the fibro-osseous junction because immobilization causes subperiosteal osteoclasts to resorb much of the bony inserts of the ligament, causing a substantial decline in the tensile strength at the bone ligament interface [51]. Not surprisingly, there is growing evidence of a shift in protocol, as a systematic review found no controlled studies on soft tissue injuries favoring immobilization in the treatment of ligament injuries [52].

For many years, NSAIDs have also been a mainstay treatment for ligament injuries, especially in the case of acute sports injuries, but research has shown that these anti-inflammatory drugs are only mildly effective in relieving the symptoms of most muscle, ligament, and tendon injuries and are potentially deleterious to soft tissue healing [53–55]. Additionally, NSAIDs have been shown to accelerate the deterioration of articular cartilage and increase joint space in osteoarthritis [56, 57]. Furthermore, patients who are prescribed NSAIDs may feel no discomfort because of their analgesic effects and ignore any symptoms of ligament injury, which could cause further damage to the ligament and delay the tissue's healing. Studies have also been conducted on the cyclooxygenase-2 (COX-2) inhibitor class of NSAIDs, and researchers have concluded that the use of these particular medications inhibits ligament healing, leading to impaired mechanical strength in the tissue [58–60]. As a class, NSAIDs are no longer recommended for chronic soft tissue injuries and their use is cautioned in athletes who have ligament injuries. In the case of acute ligament injuries, NSAIDs should only be used for the shortest period of time possible, if used at all [61, 62].

There is good reason to expect that taking NSAIDs might have an adverse effect on healing since they inhibit inflammation, such as prostaglandin-induced inflammation, which is an early sequel in the cascade of injury-induced events. The inflammatory response normally results in the recruitment of cells into the injured area where they remove necrotic debris and initiate the healing process [14]. However, NSAIDs have been shown to specifically block the cyclooxygenase enzymes that catalyze the conversion of arachidonic acid to prostaglandins, which are thought to play a role in ligament healing [63].

There is also mounting evidence that corticosteroid injections into injured ligaments have an adverse effect on healing [18, 64–69]. Like NSAIDs, corticosteroids cause deterioration of articular cartilage [70–72]. Furthermore, corticosteroid injections into ligaments and tendons have been shown to inhibit fibroblast function, adversely affecting collagen synthesis [73]. Given the inhibitory effects corticosteroid injections have on ligament healing, reviews have cautioned against their use for treating ligament injuries, especially in athletes [14, 22].

As said earlier, one of the primary functions of ligaments is to ensure that the stress placed across the joint surfaces goes across the joint evenly and is distributed over as large an area as possible. To more evenly distribute these forces while the ligament is healing, the body causes the joint to swell, creating extra joint fluid to help dissipate the forces within the joint and temporarily stabilize the joint. When the RICE protocol, NSAIDs and corticosteroids are used, they prematurely reduce the swelling. Without the protective effect of joint fluid from swelling, the forces across the soft tissues remain concentrated in one spot, which can cause them to fibrillate and eventually crack. When loose pieces of cartilage (i.e., loose bodies) fall into the joint, it has experienced too much pressure. Therefore, joint swelling has a purpose—to stabilize the joint and distribute the forces within the joint evenly. When RICE, NSAIDs, and corticosteroids stop the swelling in the joint, they inhibit ligament healing and leave the joint vulnerable to further injury because the joint instability has not been corrected. Without resolution of the instability, the arthritic process accelerates further. Joint instability can be diagnosed on physical examination in the hands of an experienced prolotherapist who has the palpatory skills to detect evidence of joint laxity or a loose-end feel to the ligament. End-feel is a subjective measure of the elasticity of tissue but can be quantified as the mechanical property of stiffness, which is calculated as the change in the applied force divided by the resulting change in position length.

3. Prolotherapy: the right treatment for resolving joint instability and chronic pain

Prolotherapy, also referred to as proliferation therapy or regenerative injection therapy (RIT), is a technique in which substances that promote growth of normal cells or tissues are propagated through the injection of small volumes of an irritant solution into painful ligaments, tendon insertions, joints, and in the surrounding joint spaces over several treatment sessions [74–76]. This stimulates the ligaments and tendons to proliferate and grow at the injection sites, naturally promoting the rejuvenation of new tissue. Dr. George S. Hackett, who was the pioneer of

prolotherapy and coined the term Prolotherapy, described the procedure as such: "The treatment consists of the injection of a solution within the relaxed ligament and tendon which will stimulate the production of new fibrous tissue and bone cells that will strengthen the 'weld' of fibrous tissue and bone to stabilize the articulation and permanently eliminate the disability" [78].

The injected substance (proliferant) used in prolotherapy is intended to mimic the body's natural healing process by initiating a local inflammatory response, which triggers a healing cascade characterized by the release of growth factors and collagen deposition, leading to proliferation, ligament tissue remodeling, and strengthening of new tissue (**Figure 2**) and resulting in a return of function and joint stability; with this course of treatment comes a reduction in pain [78, 79]. Prolotherapy treats the enthesis, which is where ligaments and tendons attach to bone; the fibro-osseous junction is the area where the injection is administered. Comprehensive prolotherapy refers to treatment of all of the significant stabilizing structures of the joint, as well as the ligaments and addresses what is at the core of chronic musculoskeletal pain: joint instability due to ligament injury and its subsequent weakness/laxity.

The most common proliferating solution used in prolotherapy is dextrose, a sugar found naturally in the body as D-glucose, which cells need to survive. Dextrose offers many benefits as a proliferant for musculoskeletal conditions and pain: it is a normal component of blood chemistry, it is water soluble and readily available, it has a high safety profile and is considered GRAS

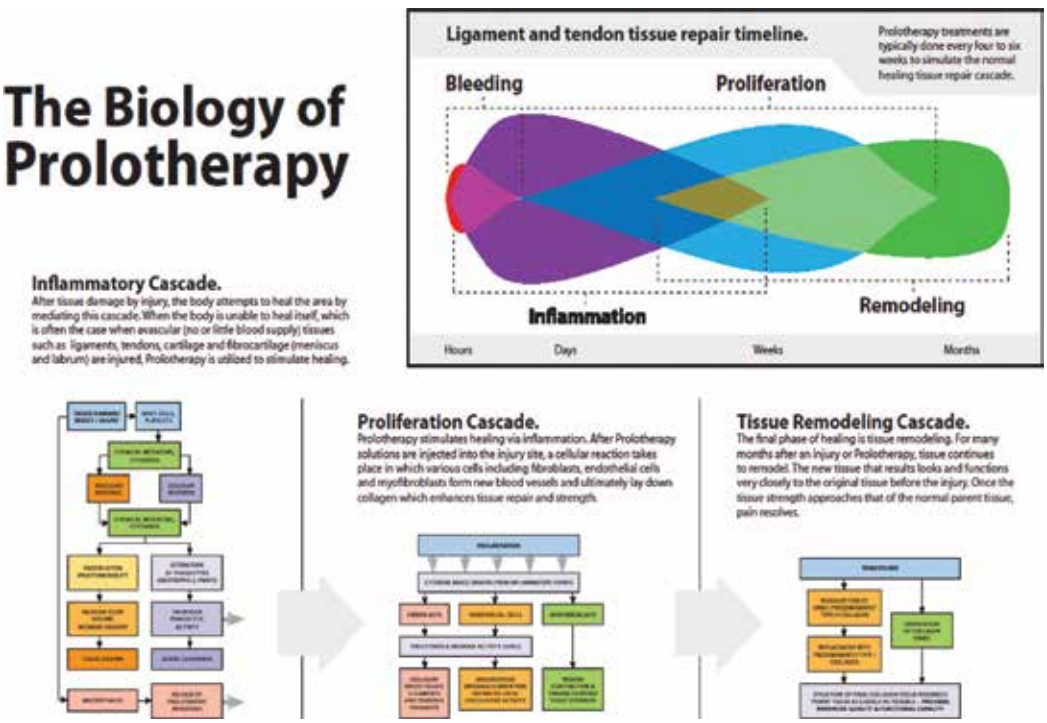

Figure 2. The biology of prolotherapy.

(generally recognized as safe) by the FDA. Other solutions that can be used in prolotherapy include pumice, P2G (phenol, glycerin, glucose), sodium morrhuate, polidocanol, sodium tetradecyl sulfate, manganese, zinc, and human growth hormone, as well as platelet-rich plasma, bone marrow, and lipoaspirate, which are forms of cellular prolotherapy and used for severe ligaments injuries.

The pioneering work of Dr. Hackett during the 1950s established a clear link between ligaments and joint pain by identifying ligaments as the main source of chronic musculoskeletal pain and then formalized prolotherapy as a viable therapeutic strategy to treat ligamentous laxity and related musculoskeletal conditions [77]. Today, prolotherapy is known to relieve pain by initiating healing and repair via an inflammatory healing cascade, wherein growth factors are released [80–87]. The release of these growth factors by prolotherapy induces ligament and tendon hypertrophy and strengthening [88–91], reduces neurogenic inflammation [92–94], and stabilizes unstable joints [89–91, 95, 96]. Prolotherapy is effective in reducing, and often eliminating, musculoskeletal pain in the joints of the body [77, 97–108].

Prolotherapy is a natural injection therapy that stimulates the body's response to injury and jumpstarts the repair process, resulting in the proliferation of cells that regenerate and strengthen ligaments, tendons, and other soft tissue structures associated with joint instability and chronic pain. The outcome of prolotherapy is the repair of tissues and strengthening of the joint-stabilizing structures, after which chronic pain subsides. There are several types of prolotherapy: comprehensive or Hackett-Hemwall prolotherapy, D-glucose or dextrose prolotherapy, and cellular prolotherapy, including bone marrow aspirates and platelet-rich plasma (PRP).

4. Conclusion

A review of the published literature indicates that prolotherapy is one of the safest and most effective treatment options for the billion or more people suffering from chronic musculoskeletal pain today. Unlike other pain therapies, prolotherapy strengthens and tightens ligaments that have become loose or lax and restores stability to unstable joints, relieving people of their pain and allowing them to return to an active lifestyle. The authors stand by their premise that prolotherapy is the best type of treatment for resolving the real cause of almost all chronic musculoskeletal pain: joint instability.

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Chapter 6

Skeletal Manifestations of Hyperparathyroidism

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Additional information is available at the end of the chapter

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Abstract

The presentation of hyperparathyroidism changed over the last decades which gave rise to more variable presentations than before. Hyperparathyroidism has a catabolic effect on the skeleton whether the disease is symptomatic or asymptomatic or normocalcemic. It is now understood that the effect of parathyroid hormone (PTH) on the bone is mediated by complex interaction between different bone cells and cells of the immune system especially T lymphocytes. Protecting the skeletal system against bone loss and pathological fractures is among the important treatment goals of hyperparathyroidism. To achieve this goal, more complex laboratory tests to monitor the bone turnover and imaging techniques and modalities as high-resolution peripheral quantitative computed tomography (HR-pQCT) and trabecular bone score (TBS) are employed. These imaging techniques showed the affection of microarchitecture of the cortical and the trabecular bone. For the time being, surgery and alendronate treatment are believed to reverse the catabolic effect of hyperparathyroidism on the bone. Vitamin D supplementation in case of vitamin D deficiency may also has a protective effect on the skeleton.

Keywords: osteitis fibrosa cystica (OFC), bisphosphonates, brown tumor, RANKL, parathyroid hormone, bone metabolism

1. Introduction

Over the last hundred years, the effect of parathyroid hormone (PTH) on bone metabolism was extensively discussed. PTH acts on the bone cells through several mediators, and its action involves a variety of cells. It is now understood that parathyroid hormone has both catabolic and anabolic effects on bone metabolism [1]. Mandl in Austria was the first to prove that the enlarged parathyroid was responsible for the skeletal manifestations of hyperparathyroidism after the first successful removal of parathyroid adenoma [2]. The clinical picture of the disease also changed dramatically over the years from a disease of "stones, bones,

abdominal groans, thrones and psychiatric overtone" to a disease which can be only detected by elevated calcium and the PTH level on laboratory tests or even the elevated PTH level with no hypercalcemia [2, 3]. This change in clinical presentation was accompanied by the introduction of newer lab tests to assess bone turnover and newer imaging techniques to assess the bone quality [2]. The treatment modalities also evolved, allowing more individualized approach for treating each patient [4].

2. Action of parathyroid hormone on the bone in hyperparathyroidism

The main function of PTH is to maintain calcium levels within the normal range thorough its action on the bone, kidneys, and intestine. It also decreases serum phosphorous through inhibiting renal reabsorption [5, 6]. PTH can produce catabolic or anabolic effect on bone metabolism depending on the level of the hormone, periodicity, and duration of exposure [6, 7]. Primary hyperparathyroidism (PHPT), continuous PTH infusion (cPTH), and intermittent PTH treatment (iPTH) increase bone turnover in trabecular and cortical bone and elevate the markers for bone resorption and formation [2, 8–10]. PHPT and cPTH enhance cortical bone loss by increasing osteoclastic activity but produce cancellous bone that is relatively preserved or modestly increased [2, 9, 11]. iPTH treatment stimulates trabecular bone formation by osteoblast stimulation and can cause small cortical bone loss [12, 13]. The pattern of bone loss in PHPT is different from the pattern of bone loss in osteoporosis. In osteoporosis, the trabecular bone loss predominates, while in PHPT the cortical bone loss predominates [14].

2.1. Action of parathyroid hormone on bone cells

Normally, bone structural integrity is maintained by the process or remodeling where the bone is removed by osteoclasts and new bone is synthesized by osteoblasts [15]. The osteoclasts and osteoblasts are arranged in a structure called the basic multicellular unit (BMU). A BMU consists of osteoclasts in front with osteoblasts, some blood vessels, and connective tissue behind [16, 17]. Osteoclasts are formed by fusion of mononuclear precursors, while osteoblasts originate from undifferentiated mesenchymal cells [16, 18]. Parathyroid hormone produces its effects by binding to its receptor PPR (also known as PTH-1R). While osteoblasts, osteocytes, and lymphocytes, mesenchymal stromal cells express PPR, osteoclasts respond indirectly to PTH through various mediators and cytokines produced by cells which carry PPR [6, 19–23]. It is now believed that osteocytes are the primary cellular target of PTH in the bone. Osteocytes are the main cells that express PPR in the musculoskeletal system [14]. Saini et al. designed a study where they generated mice with PPR deletion in osteocytes. These mice showed significant increase in bone mineral density (BMD), reduced osteoblast activity, and decreased skeletal response to anabolic or catabolic PTH regimen [24]. Other studies also supported the fact that osteocytes rather than osteoblasts are the main source of the receptor activator of nuclear factor kappa-B ligand (RANKL) in the process of osteoclastogenesis [25, 26]. Where mice lacking RANKL in osteocytes had less bone loss compared to control mice when they are exposed to dietary calcium deficiency for 30 days causing secondary hyperparathyroidism.

There was less RANKL expression and less osteoclast number in the group of mice lacking RANKL [25]. Another study was designed with a co-culture of osteoclast precursors and osteocytes. The study showed that RANKL is provided through dendritic processes of osteocytes to osteoclast precursor and that soluble RANKL had less contribution to osteoclastogenesis [27]. In humans, the RANKL/osteoprotegerin (OPG) ratio is higher in patients with PHPT than controls. This ratio is decreased with parathyroidectomy (PTx) or medical treatment by alendronate [28]. Another study on patients with PHPT showed that RANKL correlated with bone resorption markers in these patients and suggested that it can be used to determine patients of PHPT with greater risk of bone loss [13]. Another study was conducted on patients with PHPT where transiliac bone biopsy was done before PTx and 12 months after surgery and mRNA for RANKL and OPG were measured. The study showed that the mRNA ratio of RANKL/OPG decreased significantly after surgery [13].

PTH increases RANKL/OPG ratio with continuous exposure to high dose which produces catabolic effect as in hyperparathyroidism. This results in increased bone turnover, osteopenia, and bone loss in hyperparathyroidism. In addition, several extraskeletal manifestations of hyperparathyroidism are due to increased bone catabolism and hypercalcemia as nephrolithiasis, renal failure, peptic ulcer, and mental changes [2]. On the other hand, intermittent low-dose exposure to PTH has an anabolic effect through the SOST/sclerostin pathway [6].

The OPG-RANK-RANKL pathway is the mechanism by which hyperparathyroidism induces bone catabolism. PTH regulates the production of RANKL and its soluble decoy receptor OPG by osteoblasts and osteocytes [29–31]. RANKL binds to the receptor activator of nuclear factor kappa-B (RANK) on the osteoclast precursor stimulating their differentiation to osteoclasts and on the surface of the osteoclasts increasing their bone-resorbing activity. OPG inhibits the action of RANKL by binding to RANKL, thus preventing its access to the receptor RANK. In this way, the process of bone resorption is controlled by the balance between the concentration of RANKL and OPG [32–36]. In rats, continuous infusion of human PTH increased RANKL and RANKL mRNA expression and decreased OPG and OPG mRNA [37]. In vitro studies also showed that PTH activates of cAMP/PKA–CREB pathway increase the Tnfsf11 gene encoding RANKL, whereas a PTH inhibits the mRNA encoding for OPG expression through a PKA-CREB-AP-1 pathway [38–40].

2.2. Effect of parathyroid hormone on cells of the bone marrow and cells of the immune system

Cells of bone marrow also play a role in the effect of PTH on bone metabolism. Lymphocytes are believed to play a role on bone metabolism. T lymphocytes express PPR [23]. T cells express RANKL and CD40L on their surface that binds with RANK and CD40 in osteoclast precursors and osteoclasts to stimulate them [13, 41, 42]. Th17 cells form a subset of T lymphocytes that contribute to bone resorption. TH17 cells secrete IL-17, RANKL, TNF-α, IL-1, and IL-6, along with low levels of IFN-γ which contribute to osteoclastogenesis [43–46]. IL-17 stimulates the secretion of RANKL by osteoblasts and osteocytes and upregulates RANK [46, 47]. This is consistent with a human study that showed statistically significant elevation of IL-17 in postmenopausal women who had osteoporosis when compared with postmenopausal women who had osteopenia [47]. It is also noted that cPTH stimulates the production of TGF-β, IL-6, and TNF-α by bone cells and

stromal cells [7, 48, 49]. TGF-β and IL-6 direct the differentiation of naive CD4+ cells into TH17 cells [50–52]. TNF-α plays also an important role as a mediator of PTH catabolic action. PTH stimulates T cells to produce TNF-α. In mice lacking T-cell TNF-α, PTH failed to produce bone resorption but did not affect bone formation. Thus, in these mice there was no cortical bone loss, and there was increased trabecular bone formation [19]. TNF-α stimulates osteoclast formation and activity by multiple mechanisms. TNF-α increases the production of RANKL by osteoblasts and osteocytes. It also increases the expression of CD40 by stromal cells and osteoblasts increasing their responsiveness to CD40L expressed by T cells. Activation of CD40 on stromal cells and osteoblasts decreases the OPG secretion, thus increasing the RANKL/OPG ratio [7].

Bone marrow macrophages also play a role in the action of PTH on the bone. Macrophages express PPR. Depletion of the precursors of macrophages decreases the anabolic effect of iPTH [19]. The monocyte chemoattractant protein-1 (MCP-1) which is a chemotactic factor for monocyte and macrophages is a mediator for PHT-induced bone resorption [6]. MCP-1 was proven to attract pre-osteoclast in in vitro studies, thus increasing bone resorption [53]. It was found that the expression for MCP-1 increased by cPTH and iPTH in rat osteoblastic cells. With cPTH the MCP-1 expression was sustained, while with the anabolic protocol, the expression of MCP-1 was transient yet more pronounced. This suggests that the transient increase of bone resorption may be necessary before the anabolic effect of PTH on the bone [53, 54]. In human studies, MCP-1 levels correlate with PTH levels in patients with PHPT. After PTx, the levels of MCP-1 decreased significantly starting from 15 minutes following parathyroid adenoma removal [55].

3. Skeletal abnormalities in symptomatic hyperparathyroidism

3.1. Incidence

Hyperparathyroidism was first described in 1891 by von Recklinghausen. Despite of the fact that primary hyperparathyroidism was classically described as disease of "stones, bones, abdominal groans, thrones, and psychiatric overtone," the presentation of the disease changed dramatically over the past decades. Nowadays, the classical presentation with osteitis fibrosa cystica and pathological fractures is rarely seen in developed countries. Currently, larger numbers of patients are being identified with neuropsychiatric or cardiac manifestation and laboratory studies in the USA and Europe [2, 56]. In developing countries, the symptomatic form of PHPT was prevalent for a long time, but some countries as Brazil and China are having a shift toward the asymptomatic disease. However, other countries as India, Iran, Saudi Arabia, and Thailand still have high prevalence of the symptomatic form of the disease with pronounced skeletal manifestations [56–58].

3.2. Clinical manifestations

The signs and symptoms of severe bone disease include bone pain and pathologic fractures. Skeletal muscles are also affected by hyperparathyroidism where the patients have proximal muscle weakness and hyperreflexia [2, 59].

One of the features of skeletal involvement in hyperparathyroidism is hungry bone syndrome. It is characterized by hypocalcemia and hypophosphatemia following PTx. It is thought to be

due to withdrawal of osteoclast stimulation by high levels of PTH. This condition is treated by high doses of calcium and vitamin D [60, 61].

3.3. Investigations

3.3.1. Imaging

3.3.1.1. Radiography

Plain X-rays can show the classical findings of osteitis fibrosa cystica. This is characterized by marked thinning of the cortex (demineralization). Salt and pepper appearance for skull X-rays is also seen. Bone resorption of distal third of the clavicle is also seen. Hand X-rays show subperiosteal bone erosions in the distal phalanges and the lateral aspects of middle phalanges. Lytic lesions can also be seen in the pelvis and long bones with pathological fractures. Lytic lesions are referred to as brown tumors; these are a mixture of hemosiderin (hence, the brown color on pathological examination), woven bone, fibrous tissue, and osteoclasts. However, the lesions are nonneoplastic [2].

3.3.1.2. Bone mineral density

Bone mineral density can be measured by dual energy X-ray absorptiometry (DEXA) scan in all patients where measurements should be taken for lumbar spine, hip regions (total hip and femoral neck), and distal 1/3 of the radius. It is important to measure the bone mineral density in distal radius as it is a cortical site, and hyperparathyroidism is known to have catabolic effect on cortical bone [2, 56].

3.3.1.3. High-resolution peripheral quantitative computed tomography (HR-pQCT)

This is a noninvasive technique that allows assessment of the cortical and trabecular bone quality in PHPT [56]. HR-pQCT measures volumetric bone density, bone geometry, skeletal microarchitecture, and bone strength in the cortical and trabecular compartments. HR-pQCT showed that microarchitectural deterioration in both cortical and cancellous sites has decreased volumetric densities, more widely spaced, and heterogeneously distributed trabeculae and thinner cortices [62–64].

3.3.1.4. Trabecular bone score (TBS)

TBS is obtained from DEXA scan by applying special software. It is a textural analysis that provides an indirect index of trabecular microarchitecture. It can differentiate between DEXA scans showing similar bone densities. A high TBS is associated with a dense trabecular network and greater bone strength, and a low TBS indicates poor microarchitecture and poor strength [65–67].

3.3.2. Histomorphometry

Histomorphometry of transiliac biopsy will show reduced width of the cortex with increased porosity, while the trabecular bone is preserved [14].

3.3.3. Laboratory tests

In severe PHPT, serum calcium and parathormone are elevated. There are special markers for bone elevation as osteocalcin, type I procollagen peptide, and alkaline phosphatase. Alkaline phosphatase is much above the normal in all cases of hyperparathyroidism with increased bone turnover. Markers of bone resorption are also typically elevated PHPT. These include deoxypyridinoline, N-telopeptide, and C-telopeptide. These markers are products of breakdown of type 1 collagen [2]. Renal functions and urinary calcium should be evaluated. 25OH vitamin D levels should be as lower as the levels of 25OH vitamin D correlate with higher bone turnover and lower BMD, and both improve with repletion of 25OH vitamin D [68, 69].

4. Skeletal abnormalities in asymptomatic primary hyperparathyroidism

4.1. Manifestations

In 1970s, the wide availability of measurement of serum calcium changed the clinical presentation of hyperparathyroidism giving rise to the entity of asymptomatic primary hyperparathyroidism [14]. These are patients with hypercalcemia and elevated PTH but who are discovered accidentally while doing laboratory studies [58]. These patients have no X-ray finding of symptomatic hyperparathyroidism previously described [58]. These patients show decreased bone mass in cortical sites when measured by DEXA scan. Thus, DEXA scan shows reduction of bone mineral density at distal 1/3 of forearm (which is composed primarily of cortical bone), while bone density of lumbar spine (which is formed mainly of trabecular bone) is preserved. However, bone scan may remain stable for years in patients with asymptomatic hyperparathyroidism. Rubin et al. noted that the BMD of the lumbar spine remained stable for 15 years while it started to fall in cortical sites before 10 years [70, 71]. Micro-CT and histomorphometric studies show reduction of cortical bone with preservation of cancellous bone in PHPT [70, 71]. However, clinical studies showed that patients with hyperparathyroidism have higher risk of fractures both at cortical and cancellous sites [72, 73]. HR-pQCT helped to resolve this controversy. HR-pQCT showed that microarchitectural deterioration in both cortical and cancellous sites has decreased volumetric densities, more widely spaced, and heterogeneously distributed trabeculae and thinner cortices [62–64]. These studies also highlighted that weight bearing is a factor that can prevent the microarchitectural deterioration where they showed that the radius is more negatively affected than the tibias [63, 64]. Stein et al. performed individual trabecula segmentation that gave an insight into the trabecular microstructure. They found that the number of plate-like trabeculae is reduced relative to the rod-like trabeculae (decrease P-R ratio); there is reduced connectivity and less axially aligned trabecular network [64]. Another imaging modality which can show skeletal affection in asymptomatic cases is the trabecular bone score (TBS). Romagnoli et al. showed that TBS was significantly lower in patients with PHPT compared to controls. Among patients with PHPT, TBS was significantly lower in patients with vertebral fractures when compared to patients without vertebral fractures [74]. Eller-Vainicher et al. showed that TBS was associated with vertebral fractures regardless of age, gender, BMD, and BMI [75].

4.2. Natural history of bone disease in asymptomatic hyperparathyroidism

Age and female genders are associated with higher fracture risk in PHPT [73]. Currently, it is still unclear whether fracture risk assessment tools as FRAX can help to predict risk of fractures in patients with PHPT or not [14]. Concerning changes in BMD over time, Rao et al. monitored 80 patients with asymptomatic PHPT for a mean of 46 month. They did not observe deterioration of biochemical markers nor BMD measurements [74]. Silverberg et al. followed up 121 patients with PHPT of whom 101 were asymptomatic for up to 10 years. Twenty-five percent of patients showed disease progression. They also noted that patients younger than 50 years old had more likelihood of disease progression [71]. Rao et al. conducted randomized controlled trial on patients with PHPT and concluded that BMD at the hip and spine improves after PTx [76]. Rubin et al. studied 116 patients with PHPT of whom 99 were asymptomatic, PTX improved the biochemical markers and BMD, and without surgery PHPT progressed in one third of the cases [76]. Eller-Vainicher et al. studied 92 patients with PHPT and 98 controls for 24 months. DEXA scan and TBS in patients treated surgically and conservatively. In the surgical group, BMD and TBS increased significantly although it remained lower than controls. In the conservative group, BMD showed a decrease which was not statistically significant, and TBS showed a decrease which was not statistically significant; except in three patients who had vertebral fractures, the TBS showed a statistically significant decrease [75]. Hansen et al. measured BMD and HR-pQCT in women with PHPT before and 1 year after PTx. BMD improved after PTx, and HR-pQCT showed improvement of the cortical and trabecular parameters of the radius and tibia [77].

5. Skeletal abnormalities in normocalcemic primary hyperparathyroidism

5.1. Manifestations

This is a cohort of patients which includes patients with normal total and ionized calcium but elevated PTH in the absence of causes of secondary hyperparathyroidism. This may be due to target organ resistance of the bone and kidney, or these patients are in early stages of the disease [78, 79]. Lowe et al. described a cohort of patients in whom 57% had osteoporosis, 11% had fragility fractures, and 14% had renal stones [80]. Amaral et al. compared normocalcemic to hypercalcemic PHPT patients. They found that 15% of normocalcemic patients had previous fractures compared to 10.8% of normocalcemic patients and the incidence of renal stones was 18.2 in normocalcemic vs. 18.9% of hypercalcemic patients [80]. Charopoulos et al. used peripheral quantitative CT to compare the effect of normocalcemic PHPT to the effect of hypercalcemic PHPT on volumetric BMD and bone geometry. They noted the catabolic effect on both groups although it is more severe in the hypercalcemic group. In the normocalcemic group, cortical properties were adversely affected, while the trabecular properties were preserved [80].

5.2. Natural history of bone disease in asymptomatic hyperparathyroidism

The natural history of bone loss in normocalcemic hyperparathyroidism is not fully defined. Lowe et al. showed decrease in BMD by at least 5% in 43% of the patients [80]. Koumakis

et al. measured BMD before and 12 months after PTx for patients with normocalcemic and hypercalcemic PHPT. Both groups showed statistically significant improvement of BMD at the postoperative measurement [14].

6. Treatment

6.1. Effect of surgery on the skeletal manifestations of hyperparathyroidism

Skeletal affection is among the indications of surgery in hyperparathyroidism. Even in asymptomatic cases, surgery is suggested for perimenopausal or postmenopausal women and men 50 years or older who have a T-score of −2.5 or less for any skeletal site. In premenopausal women and men under 50 years old, T-score of less than −2.5 is the cutoff for surgery. The presence of fragility fractures is also among the surgical indication [2, 4, 81].

Surgery improves the bone turnover marker and PTH level. Within the first year following surgery, the BMD improves [70, 71, 82, 83]. This is due to uncoupling of bone resorption where the osteoclast stimulation by PTH stops, while bone formation continues [84]. Rubin et al. showed that the gain in BMD was sustainable up to 15 years following surgery at cortical and cancellous sites despite of expected age-related losses in BMD. The increases in BMD were recorded in the study at years 1, 5, and 10 and showed that the lumbar spine increased to 9, 6, and 12%; the femoral neck 1, 7, and 10%; and the distal radius 4, 8, and 7% [70]. Christiansen et al. studied the BMD and bone turnover markers for the first 6 months after surgery. They reported that the bone turnover markers were normalized and increased bone density in regions rich in cancellous bone but not cortical bone [82]. Similarly, Silverberg et al. noted improvement of BMD in lumbar spine and femoral neck but not the radius [71]. This may be explained by the fact that remodeling in cortical sites is slower than in trabecular bone. Thus, it takes a longer time for changes to be more pronounced [70]. Surgery also decreases the risk of fractures in hyperparathyroidism [72, 85, 86]. Vestergaard et al. demonstrated that the risk of fractures started to increase 10 years prior to surgery and reached its maximum 5–6 years following surgery. This risk falls back to normal after surgery [72]. Rudser et al. compared patients on dialysis who receive PTx to patients on dialysis without PTx. Fracture risks were lower among hemodialysis patients who underwent PTx compared to the dialysis patients who did not undergo PTx [84].

6.2. Effect of pharmacological treatment on skeletal manifestations of hyperparathyroidism

6.2.1. Bisphosphonates

Bisphosphonates (BP) are used in treatment of hyperparathyroidism as they act by inhibiting osteoclastic activity which is the cause of hypercalcemia and bone loss [2]. Several studies assessed the use of alendronate in hyperparathyroidism. Studies reported a reduction in the level of bone turnover markers and an increase in BMD. The increase in BMD was more for the trabecular than the cortical sites [87–92]. Although alendronate can lower the serum calcium initially, serum calcium tends to rise over 6 months, and the level of PTH may increase more than the pretreatment level [2, 90–93]. Pamidronate in several studies showed lowering of the serum calcium. However, due to limited time frame, no changes in BMD nor complications

were reported [94–100]. Clodronate use was associated with lowering of the serum calcium [101–103]. Several studies using clodronate reported lowering of urinary hydroxyproline and hence decreased bone turnover [101–103]. The use of risedronate in treatment of hyperparathyroidism was assessed in few studies [104, 105]. Tournis et al. reported that surgery is superior to risedronate as it improved the BMD and trabecular mineralization. Risedronate treatment in their study did not result in significant change in volumetric BMD or peripheral quantitative computed tomography [104]. A small number of studies reported the use of several BPs. Lee et al. reported the can prevent hungry bone syndrome among a very small number of patients [104]. Two other studies reported increase in BMD in the lumbar spine and hip [85, 106].

In conclusion, alendronate is the most studied BP in hyperparathyroidism. It decreases bone turnover and increased BMD. The effect of alendronate on serum calcium appears to be short lived.

6.2.2. Cinacalcet

This is a calcimimetic agent which increases the sensitivity of calcium-sensing receptors of the parathyroid gland to calcium, thus decreasing PTH secretion [107]. The effect of cinacalcet on bone turnover markers and BMD appears to be controversial. Several studies measured bone turnover markers with either decrease in the markers [108], no change [109, 110], or increase in the level of the markers [111, 112]. Similarly, the reported effects on BMD were an increase in BMD [113], a decrease [114], and no change [108, 111, 112]. Faggiano et al. compared cinacalcet monotherapy with cinacalcet with alendronate. The patients who received the combined therapy had better improvement of BMD in lumbar spine and hip compared to the monotherapy group. There was no significant difference between biochemical changes in both groups [108]. Moe et al. studied the effect of cinacalcet in reducing the fracture risk in patients receiving hemodialysis. There was no significant effect of cinacalcet on fracture reduction in the intention-to-treat analysis. However, a lag-sensoring analysis which took into consideration the crossover effect showed significant reduction of fracture risk in patients who received cinacalcet [84].

6.2.3. Vitamin D and calcium

Dietary calcium deficiency can induce elevation of PTH levels. Low vitamin D levels are associated with increased bone turnover, deteriorated hip geometry, and lower BMD [68, 84, 115]. Patients with low calcium intake and PHPT who received calcium supplementation had lower levels of PTH and improved BMD of femoral neck [116]. For patients with vitamin D deficiency, vitamin D repletion may decrease PTH levels and improved bone mineral density [116–118]. However, vitamin D supplementation may slightly increase serum calcium levels and urinary calcium excretion; thus, monitoring of calcium levels is valuable [81, 119, 120].

6.2.4. Other treatments of hyperparathyroidism which affect bone metabolism

Estrogen was found to improve BMD in women with hyperparathyroidism. The BMD of the lumbar spine and femoral neck increases, and bone turnover markers decrease with estrogen administration which has no or minimal effect on serum calcium [121, 122]. Raloxifene was also associated with improved BMD in PHPT [123, 124]. However, there is no data on the effect of estrogen or raloxifene on reducing the risk of fracture [120].

Denosumab is a monoclonal antibody against RANKL that inhibits the binding of RANKL to RANK [125]. A study was conducted on patients with secondary hyperparathyroidism on dialysis in whom denosumab was administered. The BMD improved in the femoral neck and lumbar spine. However, a transient increase in PTH levels occurred in the patients.

7. Conclusion

Despite of the fact that many patients with hyperparathyroidism do not show symptoms of skeletal affection, clinicians always need to keep an eye on the catabolic effect of hyperparathyroidism on the skeletal system. Better understanding of the mechanism of action of PTH of bone showed that many cells and mediators can influence the RANK/RANKL/OPG system, namely, T lymphocytes. Newer imaging modalities as TBS and HR-pQCT can be useful for detecting subtle bony changes. While parathyroidectomy is proven to reverse the skeletal effects of hyperparathyroidism, many patients may not be indicated for surgery, yet they should receive medical treatment that will protect them from the catabolic effect on the bone. Alendronate was extensively studied and showed to decrease bone turnover and increase BMD. Vitamin D supplementation for patients with vitamin D deficiency has a protective effect on the bone. Denosumab also has a protective effect, but clinical data about its use for patients with hyperparathyroidism is still limited.

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Conflict of interest

The author has no conflict of interests to declare.

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Chapter 7

SAPHO Syndrome

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Additional information is available at the end of the chapter

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Abstract

SAPHO syndrome is an entity that associates musculoskeletal disorders with dermatological alterations. The most characteristic clinical manifestation of the SAPHO syndrome is pain in the anterior chest wall, due to the involvement of the sternoclavicular and costochondral joints. The etiology of SAPHO syndrome is unclear. The treatment is not protocolized. Nonsteroidal anti-inflammatory drugs (NSAIDs), sulfasalazine, systemic corticosteroids, colchicine, methotrexate, and antibiotics such as tetracyclines have been used with varying results. The use of bisphosphonates has been described as effective. Biological therapy also seems to be effective. More trials with these drugs are needed to evaluate their effectiveness against this disease and to establish the number of doses, the amount, and the interval between them. In this chapter we describe the case of a patient with SAPHO syndrome who had a good response to oral alendronate.

Keywords: SAPHO syndrome, palmoplantar pustulosis, hyperostosis, acne

1. Introduction

SAPHO syndrome is an entity that associates musculoskeletal disorders with dermatological alterations, which may appear simultaneously or successively throughout a patient's life. The term is an acronym for the most common manifestations such as synovitis, acne, palmoplantar pustulosis, hyperostosis, and osteitis (**Table 1**). Bone lesions may present without relation to the appearance of cutaneous lesions.

– Synovitis
– Acne
– Palmoplantar pustulosis
– Hyperostosis
– Osteitis

Table 1. Types of SAPHO syndrome.

2. Etiology

The etiology of SAPHO syndrome is unclear. It is thought that it may have a multifactorial origin where genetic, environmental, immunological [1], and infectious causes intervene. Some bacteria, such as the *Bacillus Propionibacterium acnes*, could act as a triggering factor [2]. However, the possible pathogenic role of this or other germs in a genetically predisposed patient has not been proven.

3. Epidemiology

Its prevalence is unknown, and it can be described in different ways (**Table 2**). A few cases have been reported in Spain to date. It usually occurs in childhood and adolescence and usually affects to the female gender.

A patient with SAPHO syndrome who had a good response to oral alendronate has been described, although this is not the first choice recommended for treatment (there are a few reports in the medical literature).

– Pseudoseptic acute arthritis and palmoplantar pustulosis
– Arthro-osteitis with palmoplantar pustulosis
– Manubrium-sternal arthritis and pustular psoriasis
– Symmetric multifocal chronic osteomyelitis
– Bilateral clavicular osteomyelitis with palmar and plantar pustulosis
– Chronic sclerosing osteitis
– Chronic multifocal osteomyelitis of unknown etiology
– Skeletal muscle syndromes associated with acne
– Pustular palmoplantar arthritis
– Hyperostosis of the sternal manubrium
– Recurrent hyperostosis of the mandible
– Bone lesions in palmoplantar pustulosis
– Sternocostoclavicular hyperostosis
– Sternocostoclavicular arthro-osteitis

Table 2. Synonyms of the SAPHO syndrome.

4. Literature review

The SAPHO syndrome is a rare entity that was first described in the 1980s [3]; since then many cases have been diagnosed in different regions, and it seems to maintain a certain geographic distribution, in which an increase in prevalence in Central European countries [4]. The syndrome can appear at any age, but it usually occurs in childhood and adolescence and usually affects the female gender [5]. Many authors have questioned the SAPHO syndrome as an independent entity since its discovery [6], although nowadays it seems that it is widely accepted, given its clinical and radiological characteristics that differentiate it from other diseases. Its physiopathology remains to be clarified. In the literature there are few cases described which hinder the development of controlled clinical trials to find an adequate treatment. Current treatments and their benefits are based on personal experiences [7]. In most cases NSAIDs manage to control the pain and inflammation of the affected joints, but cases in which this medication is not effective pose a difficulty for medical staff. Intravenous bisphosphonates, such as pamidronate and zoledronate, seem to be the most effective drugs due to the experiences described to date [8]. However, a suitable dosage has not yet been found. It is also being tested with another type of medication such as TNF-α antagonists [9, 10], which may be effective, but more studies and a larger number of patients are needed in order to obtain significant results.

5. Clinical case

The case of a 45-year-old woman who came for consultation due to costal pain and in the right renal fossa is presented. The pain was continuous, did not give in to rest, and did not increase with exercise; it was not related to any trigger, and she had it for 3–4 months. Any micturition syndrome or fever was not reported. She had not had any weight loss. The patient was a smoker [11] and had a history of hypercholesterolemia, renal lithiasis, osteoporosis in treatment with calcium/vitamin D, and palmoplantar psoriasis on treatment with acitretin.

On the physical examination, pustule-erythematous, confluent lesions were found in the palms of both hands and on both soles of the feet. In addition, although she described it as costal, she presented localized pain in the sternoclavicular and chondrosternal region that increased to acupressure. She also had pain in the right renal fossa with a positive percussion fist.

Before these findings, various tests such as hemogram, biochemistry, coagulation, systematic urine, and chest X-ray were requested, with normal results. SVS, autoimmunity, and HLA-B27 were negative. Chest and abdomen CT were requested with the following report: probable areas of atelectasis/fibrous tracts in both lung bases; small bilateral renal cortical cysts; nonobstructive right renal lithiasis; arteriosclerosis of the aortoiliac axis; apparent increase of density of the subcutaneous at the level of the interlabial cleft, to be assessed in the clinical context of the patient; and degenerative alterations in the axial skeleton.

A bone densitometry was performed, showing a T-score of −2.6 in the lumbar spine (L1–L4), compatible with osteoporosis. There was also a study in her neck, trochanter and total femur compatible with osteopenia.

Before the clinical suspicion, a bone scan [12] was requested. It showed a pathological focus on the right sternoclavicular joint, compatible with SAPHO syndrome, with hyperostosis of the joint (**Figure 1**).

Treatment was established with colchicine 0.5 mg 1/24 h. Methotrexate 15 mg IM/week (the Mantoux-Booster test was previously requested and serologies for HBV, HCV, and HIV that were negative): folic acid one tablet 1 day after the administration of methotrexate and alendronate one tablet/week. Treatment with oral bisphosphonates was decided [13] despite the scarce records in the literature (agreed with the patient who did not want intravenous treatment and opted for oral treatment). This dose and frequency of administration were decided since it is the one used in the treatment of postmenopausal osteoporosis.

At 6 weeks, the patient was reevaluated and presented an almost total decrease in sternoclavicular pain and a marked improvement in the palmoplantar lesions.

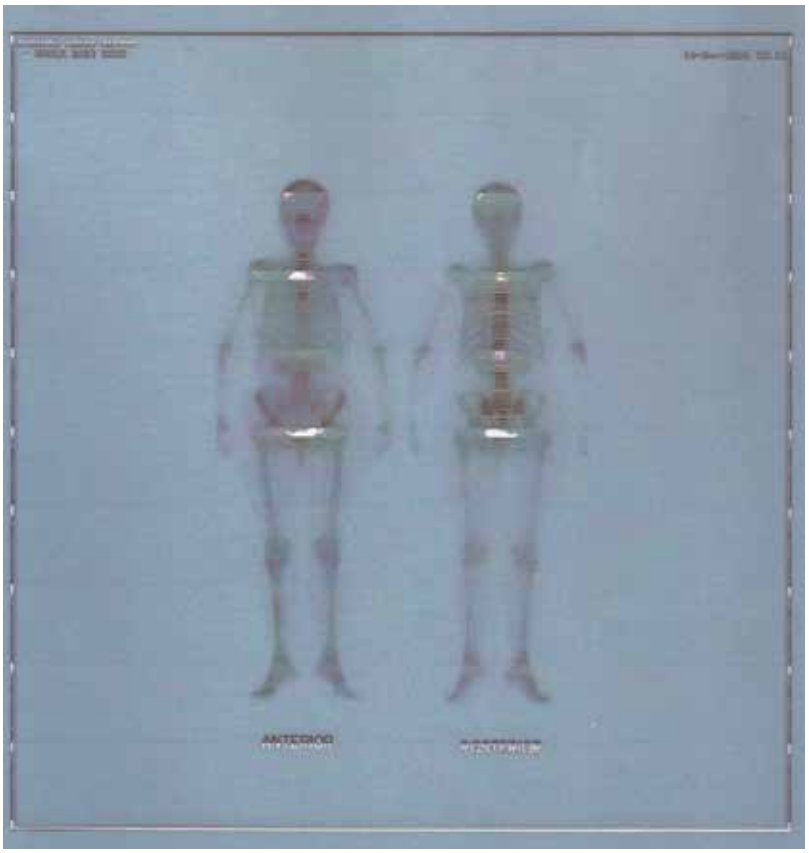

Figure 1. Hyperostosis on the right sternoclavicular joint, compatible with SAPHO syndrome, can be seen.

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6. Clinic

SAPHO syndrome is an entity that associates musculoskeletal disorders with dermatological alterations (**Table 3**).

The most characteristic clinical manifestation of the SAPHO syndrome is pain in the anterior chest wall, due to the involvement of the sternoclavicular and costochondral joints. Less commonly, the sacroiliac, intervertebral, or peripheral joints are affected. It could also affect the jaw. It is usually presented symmetrically, bilaterally, and in outbreaks. In adults, disease predominates in the sternocostoclavicular region (65–90% of patients). All the components of the anterior chest wall might be affected. The second affected region is the spine (33% of cases), mostly at the dorsal level. Nonspecific spondylitis, osteosclerosis of one or more vertebral bodies, and paravertebral ossifications could be observed. Ninety-two percent of patients have arthritis with involvement their knees, hips, ankles, feet, and hands.

1. Chronic multifocal relapsing osteomyelitis
Generally sterile
With/without coccyx affection
With/without skin affection
2. Acute/subacute/chronic arthritis in addition to:
Palmoplantar pustulosis
Pustular psoriasis
Severe acne
3. Sterile osteitis in any localization in addition to
Palmoplantar pustulosis
Pustular psoriasis
Vulgar psoriasis
Severe acne

Table 3. Diagnostic criteria: one of the three presentations is enough for diagnosis.

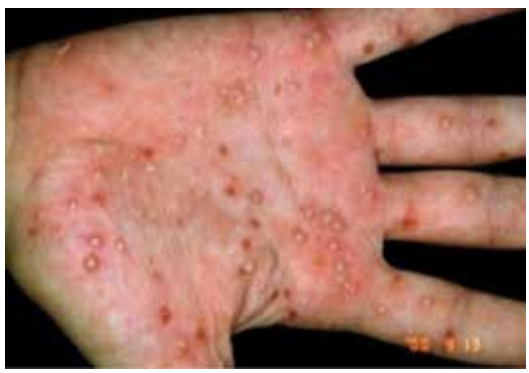

Figure 2. Inflammatory pustules with erythema that affect palms of hands.

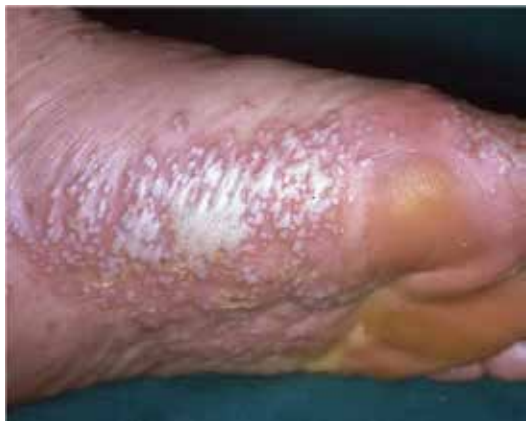

Figure 3. Pustular lesions, symmetric, with desquamation that affects the soles of the feet.

– Acne-associated syndrome
– PAPA syndrome
– PASH syndrome
– Arthritis associated with hidradenitis suppurativa
– Follicular occlusion triad
– Behçet disease
– Minocycline-induced autoimmune syndromes
– Isotretinoin side effect
– Pustular psoriasis
– Sneddon-Wilkinson disease
– Pustulotic arthro-osteitis
– Acquired hyperostosis syndrome
– Chronic recurrent multifocal osteomyelitis
– Diffuse sclerosing osteomyelitis of the mandible
– Majeed syndrome
– Nonbacterial osteitis
– Tuberculous spondylitis
– Secondary syphilis
– Primary bone tumors
– Metastatic tumors

Table 4. Differential diagnosis of SAPHO syndrome.

In children it usually affects to the long bones such as the tibia and femur, clavicle, and lumbar spine.

Skin involvement is more variable and includes palmoplantar pustulosis, acne conglobata or fulminating, suppurative hidradenitis, dissecting cellulitis, or pustular psoriasis. The most predominant is palmoplantar pustulosis, which is characterized by inflammatory pustules,

symmetric, and sterile, with erythema and desquamation, which affect palms of the hands (**Figure 2**) and soles of the feet (**Figure 3**). The pathogenesis of the disease remains unknown, and there is still a debate about whether palmoplantar pustulosis is a variant of psoriasis or a distinct condition.

The SAPHO syndrome could present several clinical manifestations and therefore originate different differential diagnoses (**Table 4**). This is very important in neoplastic disease context, since it is necessary to avoid errors in the diagnosis that lead to aggressive treatment in a disease that it usually develops benign.

7. Diagnosis

The diagnosis is basically clinical and is complemented by imaging tests. Due to its low prevalence, it is necessary to have a high index of suspicion. The analytical data are usually nonspecific but have value in excluding other pathologies. Mild leukocytosis, anemia, or an increase in inflammatory markers might occur. A simple radiography, bone scan with technetium 99 m, and CT are useful. Simple X-ray is of little use since it is usually normal. Bone scintigraphy provides much information, and the pattern of symmetrical sternoclavicular hypercaptation in "bull's head" (where the sternal manubrium represents the skull and the sternoclavicular joints and the clavicles correspond to the horns) is very typical. CT provides us with a lot of information as it is the technique that best visualizes the joints of the anterior thoracic wall, showing a hyperostosis of this zone.

Biopsy and cultures of the affected joints are reserved for doubtful cases and to rule out other diagnostic possibilities. Imaging allows differential diagnosis with other processes (osteomyelitis, Paget's disease, bone metastases, Tietze syndrome, other spondyloarthropathies).

In some patients, cutaneous manifestations might appear after years of nonspecific joint symptoms, making diagnosis even more difficult.

8. Evolution

SAPHO syndrome is a chronic disease that develops in form of outbreaks and remissions but in which radiological progression is slow [14]. Prognosis is usually good, but there are cases in which the pain that is produced is very intense and difficult to control it. Sometimes the onset of the disease could be acute and crippling. It has been observed that those factors such as female gender, anterior chest wall involvement, peripheral arthritis, skin lesions and elevation of acute phase reactants at onset of disease are related to the chronicity of the disease.

In a minority of patients, disease heals spontaneously or follows a chronically indolent course.

Complications are rare. Peripheral arthritis could become erosive in a minority of cases. Venous thrombosis could be observed due to an important disseminated inflammation from bones or joints to the adjacent tissue (especially as a result of clavicular hypertrophy), inflammatory masses in the anterior mediastinum, thoracic gorge syndrome that the swelling is

confused with a tumor (signs mainly observed at clavicular level), etc. Recurrent chronic multifocal osteomyelitis could cause permanent bone deformities, irregularities in limb length, and growth problems.

9. Treatment

With a little-known entity with few studies, this treatment is not protocolized [15] (**Table 5**). Nonsteroidal anti-inflammatory drugs (NSAIDs), sulfasalazine, systemic corticosteroids, colchicine, methotrexate, and antibiotics such as tetracyclines have been used with varying results.

NSAIDs and analgesics are used as a symptomatic treatment of disease. There is no NSAID that has shown to be more effective than other. Almost all patients receive NSAIDs, obtaining a good result, but due to recurrence, loss of efficacy, or progression of disease, it is necessary to establish other treatments.

As we have said before, it is believed that this disease might have an infectious origin, mainly *Propionibacterium acnes*, so several antibiotics have been used, although they have not been proved to be really effective. Tetracyclines have been shown to be effective in controlling severe forms of acne [16].

Immunosuppressants, such as sulfasalazine or methotrexate, have been used in cases resistant to NSAIDs [17] and antibiotics, and although they have shown improvement in some patients, results have not been conclusive, and there are studies in this regard.

The use of bisphosphonates has been described as effective, although the majority of cases in which it has been used have been endovenous. Bisphosphonates are synthetic analogs of pyrophosphate; their function is to inhibit bone resorption by altering the function and metabolism of osteoclasts. Due to these properties, they have been used in treatment of primary and secondary osteoporosis, Paget's disease, bone metastasis, and disorders of bone metabolism [18].

Pamidronate and zoledronic acid have been used. Pamidronate has been used at a dose of 60 mg/day IV in a single dose, during a very short cycle of days in a row or repeating the dose several months later [19]. In most cases an improvement in pain and in the evolution of

Symptomatic	Modifier of disease
– Analgesics	– Antibiotics
– NSAIDs	– Sulfasalazine
– Glucocorticoids	– Methotrexate
– Calcitonin	– Leflunomide
	– Bisphosphonates
	– TNF antagonists

Table 5. SAPHO syndrome treatment.

the disease was found. This is due to an action on bone remodeling that interferes with the production of proinflammatory cytokines.

Zoledronic acid is the most potent bisphosphonate and is usually used in hypercalcemias of tumoral origin. It has been used at a dose of 4 mg IV in a single dose with repetition at 6 months if there was no improvement [20], obtaining good results (decrease in pain and regression of disease).

In the treatment with biological therapy, anti-tumor necrosis factor (TNF) drugs have been used with promising results.

Although NSAIDs usually control pain and inflammation, it is often necessary to use disease-modifying drugs to improve symptoms. In this regard, it seems that IV bisphosphonates have been the most effective, but the dose and interval have not been unified.

Biological therapy also seems to show effectiveness [21]. More trials with these drugs would be needed to test their effectiveness against this disease and protocol the number of doses, the amount, and the interval between them.

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Musculoskeletal disorders are defined as disorders that affect a part of the body's musculoskeletal system, which includes bones, nerves, tendons, ligaments, joints, cartilage, blood vessels, and spinal disks. These are the injuries that result from repeated motions, vibrations, and forces placed on human bodies while performing various job actions. They are extremely common and costly problems for people and companies. Thus, this book is designed to include a wide array of extensive and comprehensive discussions provided on occupational, educational, and medical aspects of ergonomics. Thus, it can be utilized as a guide to identify and analyze the risk factors, reveal the impact of prevention and intervention, and discuss treatment of musculoskeletal disorders.

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