

ILLNESS CONSTRUCTS IN MUSCULOSKELETAL MEDICINE

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INTRODUCTION

In spite of advances in diagnosis and therapeutics, as well as a better understanding of the pathophysiology of many diseases, much illness remains poorly understood. Given the human mind's tendency to see patterns and rationalize observations to fit preconceptions, it is not surprising that even the most puzzling illnesses are often described in terms that seem to imply a level of knowledge and understanding that we can only wish for at present. Many of the labels and concepts used to describe nonspecific, puzzling illnesses have become accepted as verifiable diseases even though there is no identifiable pathophysiology and there is no experiment that can be done to verify or falsify the hypothesis that disease is present. Many of these illnesses are, at present, no more than social constructs.

Webster's dictionary defines a social construct as "a social mechanism, phenomenon, or category created and developed by society; a perception of an individual, group, or idea that is 'constructed' through cultural or social practice"¹. In other words, social constructs are things that exist because we, as a society, agree to behave as if they exist. An example is the social construction of beauty across cultures. In western society, thinness is a widely accepted prerequisite for beauty² whereas other cultures celebrate female obesity³. Society helps construct the perception of what foods are palatable. For instance, in Sardinia, Casu Marzu--a cheese infested with live maggots--is considered a delicacy. The social construct of bereavement can be illustrated by contrasting the somber mood familiar to many of us with the Day of the Dead in Mexico and traditional New Orleans funerals, which are joyous, musical celebrations of the *life* and memories that were shared with the deceased.

Social constructs are common in medicine, where they are often referred to as illness constructs. For example, we had the illness construct of consumption that gave way to tuberculosis after Koch introduced his scientific postulates and solid scientific data proving that the illness was the result of infection with *Mycobacterium tuberculosis* and firmly established the germ theory of disease. Many of the illness concepts developed in attempt to better address puzzling illnesses represents illness constructs. The problem is that we talk about these illness constructs as if they were as well understood as tuberculosis, when they really are more comparable to consumption, at least at present.

Illness constructs are prevalent throughout modern medicine. In particular, many disabling musculoskeletal pain conditions are diagnosed and treated as various illness constructs. One typical feature of these illness constructs is disproportionate pain and disability associated with little or no objective pathophysiology or impairment. It can be argued that these illness constructs do more harm than good. There are certainly many important and inarguable examples of this throughout history (think bloodletting). Expert opinion and consensus, often based on theoretical disease mechanisms and on anecdotal accounts, have had a profound influence on shaping ideas about certain diseases. Strong advocates, whether be it physicians, drug companies or social dynamics, have also had their share in molding certain illness concepts.

This review explores illness constructs in modern medicine (and musculoskeletal medicine in particular) and emphasizes important differences between illness constructs and verifiable pathology that affect optimal patient care.

DEFINITIONS

Disease: The word disease typically refers to a verifiable objective pathophysiological process.

Illness: In contrast, illness refers to an unhealthy state independent of the presence or absence of objective, verifiable pathophysiology. One can have a disease and feel well and one can feel ill in the absence of any anatomical or physiological abnormalities.

Science: Science is the branch of knowledge that produces theoretical explanations of natural phenomena based on experiments and observations. The key element is experimentation, where hypotheses are challenged and revised according to ability to verify or falsify them with reproducible objective observations. Science is what humans use to overcome the tendency

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to confirm our own biases. We need science to avoid fooling ourselves and to avoid being fooled by others.

Syndrome: A syndrome is a set of signs and symptoms that appear together and characterize a disease or medical condition. In medicine, illnesses are often referred to as syndromes at a stage when the pathophysiology is not well understood and the diagnostic methods are still debated or inadequate. It can be argued, that when pathophysiology and reproducible objective diagnosis are well-established, the “syndrome” is less useful and applicable. For instance, it is often the case that patients with a particular syndrome may in fact have one of several different diseases. Said differently, scientific hypothesis testing in the form of reproducible objective verification is more reliable and valid than what can be gleaned from an interview and physical examination alone.

Illness construct: An illness construct is an illness that exists because we, as a society, agree to behave as if it exists, independent of disease or pathophysiology. While disease relates to pathophysiology, the experience of illness is socially constructed. A person’s experiences and conceptions of sickness cannot be separated from macrosocial phenomena⁴. Illness behavior reflects historical context and specific intellectual, economic and other shared interests. Cultural, ethnic, family background, religious denomination, social class, personality, personal experience and psychosocial circumstances all determine how a person responds to disease or injury⁵.

Functional: The word functional traditionally denotes a disorder with no objective verifiable pathophysiology that explains the syndrome. The term “functional” and its contrary “organic” (indicating verifiable pathophysiology) are now largely discouraged, in part because they perpetuate the myth of a mind-body duality or dichotomy when it is becoming clear that all illness is biopsychosocial. The term “functional” is being replaced by the terms “medically unexplained”, “nonspecific”, or “idiopathic”.

ILLNESS CONSTRUCTS IN MEDICINE

At a time when we often stand in awe of the advancements and powers of modern medicine, the substantial prevalence of illness constructs is notable. Common features include: 1) The lack of an objective definition or diagnostic test that allows for experiments which verify or falsify the hypothesis that disease (pathophysiology) is present; 2) The pathophysiology, etiology and treatment of these illnesses are incompletely understood, based primarily on rationale and analogy, and open to debate; 3) Symptoms tend to be vague, diffuse, and disproportionate. These illness constructs are typically a so-called “diagnosis of exclusion” and seem to represent an alternative to acknowledging puzzlement, uncertainty, and the limits of modern medicine. The following are examples of illness constructs:

GASTROINTESTINAL SYSTEM

Irritable bowel syndrome (IBS) is a bowel disorder characterized by abdominal pain or discomfort and altered bowel habits in the absence of detectable pathophysiology.

Functional Dyspepsia: a bowel disorder characterized by persistent epigastric pain or discomfort in the absence of

detectable pathophysiology. This disorder is often categorized into 4 clinical groups⁶: 1) Reflux-like (symptoms of regurgitation and reflux). This group is especially controversial due to its overlap with Negative Esophageal Reflux Disease (this is defined as the presence of typical symptoms of gastroesophageal reflux disease caused by intra-esophageal acid, in the absence of visible esophageal mucosal injury at endoscopy)⁷; 2) Ulcer-like (symptoms of epigastric pain); 3) dysmotility-like (symptoms of nausea, bloating, fullness); and 4) nonspecific.

Functional Constipation: A group of idiopathic disorders which present as persistent, difficult, infrequent, or seemingly incomplete evacuation in the absence of pathophysiology⁸.

GENITOURINARY SYSTEM

Interstitial cystitis is characterized by pain with bladder filling that is relieved by emptying and is often associated with urgency and frequency⁹. This is a so-called “diagnosis of exclusion” typically applied when patients with these symptoms have a negative urine culture and cytology.

Chronic Pelvic Pain is an entity defined by disabling menstrual or nonmenstrual pain below the umbilicus of at least 6 months’ duration in the absence of pathophysiology⁹.

Noninflammatory chronic nonbacterial prostatitis (NIH consensus classification class IIIb prostatitis): The National Institute of Health consensus classification of prostatitis syndromes categorizes class III prostatitis and the chronic pelvic pain syndrome together. This entity is characterized by a symptom complex including irritative voiding symptoms and perineal, suprapubic, and genital pain. Whereas Chronic Inflammatory Prostatitis, Class IIIa must have leucocytes in prostatic secretions, postprostate massage urine or semen, Class IIIb by definition, must have the absence of a bacterial etiology and no evidence of inflammation, such as leucocytosis¹⁰.

CARDIOLOGY

Atypical chest pain: (also described as non-specific chest pain and syndrome X). The coronary artery anatomy is normal and there is no clear physical cause to explain the chest pain. A 2005 Cochrane review concluded that cognitive behavioral therapy is of some benefit for atypical chest pain¹¹.

DENTISTRY

Masticatory Muscle Myofascial Pain: Nonspecific and idiopathic pain in the muscles of mastication¹².

OTOLARYNGOLOGY

Globus hystericus: The sensation of a lump in the throat without a demonstrable anatomical anomaly of the esophago-pharynx or manifest pathophysiology of deglutition¹³.

ALLERGY

Multiple Chemical Sensitivities (idiopathic environmental intolerance): A disorder characterized by a wide spectrum of somatic and cognitive symptoms attributed to exposure to low levels of chemicals with no detectable pathophysiology¹⁴.

Sick Building Syndrome (also referred to as nonspecific building illness¹⁵): A diverse constellation of symptoms (including mucous membrane irritation, headache, cognitive complaints) associated with the occupancy of particular offices, homes, buildings for which no definite etiologic agent can be

identified. SBS is often differentiated from building related illness, in which symptoms can be explained by specific medical diagnoses such as allergy and infection¹⁶.

OTHER

Gulf War Syndrome: A variety of medically unexplained symptoms including cognitive disturbances, fatigue, headaches, and pains that emerged in veterans of the 1991 Gulf War¹⁴.

COMMON PSYCHOLOGICAL FEATURES

According to Kroenke and Colleagues¹⁷, between one third and one half of all physical complaints are not associated with identifiable pathophysiology. Amongst these patients, a depressive disorder can be diagnosed at least 50% of the time and an anxiety disorder diagnosed at least 40% of the time. Various studies have highlighted the strong relationship between the number of medically unexplained symptoms (called functional complaints in the past) and anxiety and depression^{18, 19, 20}. Furthermore, Wessely et al²¹ have made several observations that support a common ground for these nonspecific illness constructs, including:

1. The existence of an overlap in the case definitions of specific functional syndromes.
2. Patients with one functional syndrome frequently meet the diagnostic criteria for other functional syndromes.
3. Patients with different functional syndromes share common non-symptom characteristics. That is, almost all functional syndromes are more common in women, a strong association between the range of functional disorders and psychological distress exists, and a similar pathophysiology related to the central nervous system has been used to explain several disorders including chronic fatigue syndrome (CFS), irritable bowel syndrome (IBS) and functional dyspepsia. A history of childhood maltreatment and abuse may exist. In addition difficult relations between the physician and patient are commonplace among these disorders.
4. Many, but not all, somatic syndromes respond to similar therapies such as anti-depressants and psychological therapies, in particular CBT^{11,53}.

ILLNESS CONSTRUCTS IN MUSCULOSKELETAL MEDICINE

In order to better understand how illness constructs have emerged, we will look at historical examples of how puzzling illnesses, expert opinion and consensus (based on theoretical disease mechanisms and on anecdotal accounts) and social and economic forces have contributed to illness constructs with a focus on illnesses constructs in musculoskeletal medicine.

FIBROMYALGIA (FM)

Sir William Richard Gowers, a British neurologist during the late 19th century and early 20th century, was a transcendent figure in neurology^{22, 23}. Gowers developed landmark descrip-

tions of muscular and neurological diseases such as epilepsy, migraine and neurosyphilis²⁴. Indeed, the terms “Gowers’ sign” (a physical finding observed in Duchene’s Muscular Dystrophy) and Gowers’ tract (a synonym for the anterior spinocerebellar tract) have been named in his honor. In 1904, in an attempt to rationalize the cause of his own back pain, Gowers laid the foundations of what we now know as fibromyalgia²⁵. Gowers explained that contraction of the back muscles caused tension in related fibrous structures which ultimately caused his back pain. He named this entity “fibrositis”²⁵. Over the next several decades, various theories about the pathophysiology of fibrositis emerged and declined. This included inflammation of fibrous tissue²⁶ and fat lobule herniations²⁷. In the 1980’s the drug company Merck Sharp and Dohme, pushed for expanding the indications for the use of its muscle relaxant Flexoril to include Fibrositis^{28, 29}. Merck underwrote a symposium on the topic and created a new committee of the American College of Rheumatologists and in 1986, the term “Fibromyalgia” was published in the American Journal of Medicine²⁸. In 1990, further legitimacy was granted to fibromyalgia when the American College of Rheumatology established the criteria for the classification of Fibromyalgia³⁰: widespread pain and tenderness in 11 out of 18 tender point sites.

A new pathophysiologic mechanism based on the concept of neurotransmitters and central sensitivity syndromes has recently been proposed and exploited by the drug industry. In 2007, Lyrica became the first Food and Drug Administration (FDA) approved medication for treating fibromyalgia³¹, granting yet more legitimacy to this illness construct. In August 2007, the National Fibromyalgia Association (NFA), sponsored by Pfizer launched a “national educational campaign aimed at increasing understanding of fibromyalgia among patients, healthcare providers and the public”³². In their television advertisement they stress that fibromyalgia is “very real chronic widespread pain and tenderness that affects millions”, which reflects the separation of mental and physical aspects of illness and the stigmatization of the mental aspects as if they were not “real”. However, no objective diagnostic test can verify the presence or absence of fibromyalgia, and Dr. Wolfe, the first author of the original 1990 classification criteria now considers this condition to be a physical reaction to stress, depression, social and economic anxiety³³—in essence a somatoform disorder.

WHIPLASH

Today, the term “whiplash” is commonly used to imply cervical spine damage caused by a rapid and sudden extension followed by flexion of the neck following a motor vehicle or other accident. However, in 1928 when Harold Crowe first coined the term “whiplash”, he was referring to the mechanism of injury sustained during traffic accidents³⁴. In 1945, Davis³⁵ and other physicians introduced the term into medical literature and legal action for compensation soon followed. The term whiplash was misunderstood and became an accepted “disease” by physicians, patients and attorneys. This misunderstanding of whiplash consequently led to its misapplication by many physicians and others³⁴.

Whiplash remains a clinical diagnosis, made by considering the mechanism of injury and the patient's symptoms^{36, 37}. There are no specific blood tests, neuropsychological studies, or electrophysiological tests that can diagnose whiplash³⁶.

The Quebec Task force established classification grades for whiplash³⁸. Grades I & II are based only on the subjective assessment of the patient, while grades III & IV require clear objective criteria (diminished deep tendon reflexes, objective motor power deficits, imaging showing a vertebral fracture, etc). Most whiplash claimants fall into the Grade I & II categories, where no objective measure can reliably detect any pathology, either in the acute or chronic settings³⁹.

Litigation can be largely credited with shaping the whiplash illness construct. There have been reports highlighting the stark difference between the incidence of whiplash across different countries. In countries where whiplash is perceived as a serious health concern, persistent whiplash symptoms are commonly seen⁴⁰. In other countries, for instance Lithuania, it was reported that chronic whiplash was either rare or did not exist⁴¹.

CHRONIC FATIGUE SYNDROME (CFS)

Chronic Fatigue Syndrome (also known as Myalgic Encephalopathy [ME] in the United Kingdom) is a syndrome characterized by unexplained fatigue, self reported cognitive impairment, headaches, unrefreshing sleep, muscle pain and multijoint pain without joint swelling or warmth⁴².

CFS came into being in 1987 when Buchwald and Colleagues used the term "chronic fatigue syndrome" to describe patients suffering from a disease "consistent with chronic active EBV infection"⁴³. In 1988 "CFS" became globally accepted when the CDC defined its diagnostic criteria⁴⁴. CFS/ME has not been associated with any pathophysiology and the diagnosis cannot be verified or falsified using objective diagnostic testing^{45, 46}—it is a syndrome and an illness construct.

CFS seems to be the modern manifestation of "neurasthenia", introduced by George Beard⁴⁷ in the late 1800's. Neurasthenia was a popular diagnosis characterized by symptoms of physical and mental fatigue mainly in the privileged social class^{48, 49}. However, by the early 1930's medical skepticism, advances in psychiatric nosology and demographic changes caused a rapid decline in the diagnosis of neurasthenia^{50, 51, 52}. Several other illness constructs have been applied to this syndrome including the vapors, effort syndrome, chronic brucellosis, epidemic neuromyasthenia, hypoglycemia, multiple chemical sensitivity syndrome, chronic candidiasis, and chronic mononucleosis⁴². A recent Cochrane review found cognitive behavioral therapy to be more effective than the treatment typically provided for CFS⁵³.

PIRIFORMIS SYNDROME

The Piriformis Syndrome manifests as pain in the buttock and the hamstring that simulates radiculopathy and is based on the rationale of sciatic nerve dysfunction due to compression by the piriformis muscle⁵⁴. In 1928, Yeoman described the involvement of the piriformis muscle as a potential cause of sciatica⁵⁵; however, in 1934, when Mixter and Barr⁵⁶ described the pathophysiology of a herniated nucleus pulposus caus-

ing spinal nerve root compression and sciatic pain, piriformis muscle theories declined⁵⁷. Today, piriformis syndrome is back to where it began: an illness construct used to try to make sense of puzzling cases of very low back pain. Although the FAIR (hip flexion-adduction-internal-rotation) electrophysiologic technique has been proposed for making the diagnosis, it has not been validated⁵⁴.

RADIAL TUNNEL SYNDROME (RTS)

RTS is pain in the lateral aspect of the elbow and forearm without motor or sensory deficits, based on the rationale that such pain can be caused by compression of the radial nerve, at any of various sites along its course, as it passes through the elbow and the proximal forearm. While carpal tunnel syndrome and cubital tunnel syndrome have verifiable pathophysiology (abnormal electromyography and nerve conduction), RTS is characterized by normal electrophysiology and subjective interpretations of operative findings. Radial Tunnel Syndrome was first described in 1972 when Roles and Maudsley proposed it as a pathophysiologic rationale for tennis elbow that did not respond to treatment⁵⁸. The historical context was the "age of compressive neuropathy" following George Phalen's popularization of both the diagnosis and treatment of "carpal tunnel syndrome"^{59, 60, 61} and Feindel and Stratford's description of cubital tunnel syndrome in 1958⁶². As the newly understood pathophysiologic processes of peripheral nerve compression were applied more generally, the result was the more debatable illness constructs of tarsal tunnel syndrome in 1962^{63, 64}, radial tunnel syndrome and pronator syndrome⁶⁵.

PRONATOR SYNDROME

Henrik Seyffarth proposed pronator syndrome (compression of the median nerve in the proximal forearm where it passes between the two heads of the pronator teres muscle) in analogy with another debatable nerve compression syndrome (the scalenus syndrome) in an attempt to explain nonspecific lower arm pain⁶⁵. As with other illness constructs, the diagnosis is based on symptoms and signs⁶⁶ (the syndrome), and it is accepted that electrophysiological testing is almost always normal (no verifiable pathophysiology).

REPETITIVE STRAIN INJURY (RSI)

In 1971, David Ferguson, of the University of Sydney introduced the term Repetitive Strain Injury (RSI) to Australia in an attempt to understand ill defined activity related arm pains at work⁶⁷. The rationale is that repetitive or sustained submaximal exertion of soft tissue can cause damage or injury⁶⁸. This illness construct was widely adopted in the absence of objective evidence of any pathophysiology or "injury". About a decade later Australia faced an unprecedented RSI epidemic that involved public sector workers, teachers, nurses, assembly line employees and even school children^{69, 70}. A number of factors popularized the spread of RSI including the belief that foreign companies had dumped outdated keyboards on the local market, and the emphasis on the need for early recognition and treatment by trade unions and physicians^{71, 72}. However, compensation has been suggested as the single most important factor for fueling the epidemic⁷³. By the mid 1980's,

it was established that social factors rather than physical injury had been the cause of RSI and the epidemic came to an abrupt end. The factors that contributed to this demise included the reduction in compensation by the Australian government and ironically, the media⁶⁹.

FOCAL DYSTONIA

Focal dystonia (including previous manifestations as writer's, musician's, pianist's, golfer's and computer operator's cramp⁷⁴) is characterized by a painless, motor control disorder localized to the groups of muscles that control fine movements. Patients experience task related hand dysfunction, without motor weakness. The proposed pathophysiology is abnormalities in the basal ganglia and dysfunction of the cortico-striatothalamo-cortical circuits⁷⁵, but the diagnosis is clinical and no objective diagnostic tool can be used to verify or falsify this condition.

In the 1830's, the first writer's cramp epidemic was reported. It emerged in British clerks experiencing social change: the reason was attributed to a new steel penpoint⁷⁶. In the early 1900's, "telegraphist cramp" emerged in British telegraphers sending morse code⁷⁶. It has been suggested that the RSI epidemic in Australia in the 1980's is a more modern manifestation of the same phenomenon, with a different name⁷⁷.

COMPLEX REGIONAL PAIN SYNDROME (CRPS)

Previously known as Causalgia and Reflex Sympathetic Dystrophy Syndrome (RSDS), Complex Regional Pain Syndrome is the latest term for this entity. CRPS has been classified into 2 types⁷⁸: Type 1 is independent of and Type 2 is associated with nerve injury.

The roots of CRPS date back to 1864 when Mitchell described symptoms of RSDS in soldiers of the civil war, and in 1872 coined the term "causalgia"⁷⁹. In 1916 LeRiche linked the ischemic limb to causalgia and described how the stripping of the peri-arterial sympathetic nerve plexus improved the pain in one of his patients⁸⁰. This empirical account set the scene for the incorporation of the sympathetic nervous system (SNS) into the pathophysiology and treatment of causalgia for the next several decades⁸¹. 1946: Evans used the term "reflex sympathetic dystrophy"⁸². Due to the presumed involvement of the SNS in this condition, sympathetic blocks and sympathectomies were widely used to treat this condition, largely with unsuccessful results^{83, 84}. In actual fact, a Cochrane review by Mailis-Gagnon and Furlan concluded that the complications of surgical and chemical sympathectomies may be significant in worsening the pain, contributing to new pain syndromes and causing abnormal forms of sweating⁸⁴. In 1994, in an attempt to reduce the frequency of sympathetic blocks and underscore the absence of specificity⁸⁵, the International Association for the Study of Pain introduced the term "complex regional pain syndrome" (CRPS) to describe RSDS (CRPS I), causalgia (CRPS II) and related syndromes⁷⁸. It can be argued that this introduced greater confusion in the diagnosis and treatment of RSDS/CRPS^{81, 85}.

CRPS remains a syndrome and illness construct with no objectively verifiable pathophysiology. Techniques such as

sweat measurement, sympathetic skin responses, thermography, skin, nerve, muscle, synovial biopsies and others have been utilized for investigating the CRPS patient, but remain experimental^{81, 85}.

CHRONIC LYME DISEASE (CLD)

Lyme disease (a term introduced in 1976⁸⁶) is transmitted to humans when *Borrelia Burgdorferi*, a spirochete bacteria, enters the blood stream via the bite of an Ixodes tick. The disease includes dermatologic, musculoskeletal, cardiac and neurologic manifestations.

Patients diagnosed with Chronic Lyme Disease experience a syndrome comparable to Chronic Fatigue Syndrome. According to this illness construct, the diagnosis is made in the presence or absence of clinical or serologic evidence of previous Lyme disease infection⁸⁷ and even when patients have not been to Lyme endemic areas^{88, 89}. While Lyme disease can usually be cured with a course of oral or intravenous antibiotics⁹⁰, CLD seems to have no cure and is conceived of as requiring consistent intravenous antibiotic treatment, which can harm patients and contribute to antibiotic resistance and other problems⁹¹.

To increase physician awareness of *Borrelia Burgdorferi* infection, Lyme disease's mimicry of other diseases was emphasized⁹²--Indeed, it was referred to as the "great imitator"⁹³. By the early 1990's however, it was noted that the diagnosis of Lyme disease was being used inappropriately and overdiagnosed^{94, 95}. It is notable that other illness constructs such as fibromyalgia and chronic fatigue syndrome were seen as the correct alternative diagnoses^{90, 94, 95, 96}, reflecting a general distaste for and reluctance to consider somatoform disorders or at a minimum—the biopsychosocial nature of the human experience of illness.

The prevalence of this illness construct has been ascribed to a combination of the limitations of the diagnostic techniques⁹⁰, Lyme fervor on part of the treating physicians^{94, 97}, and the media, which made this relatively uncommon disease, seem endemic⁹². Lyme disease is boasted as the most common tick borne disease in the US, but this translates to an estimated 20,000 new cases every year⁹⁸ (out of a population of 307 million). News stories describing patients with Lyme disease being abandoned by their physicians are often seen^{99, 100}. The internet has an overabundance of websites and reports discussing Lyme disease and can be regarded as a double edged sword. One blog spot, where people can post entries about their personal experiences with "Lyme disease" claims to have over 5 million readers¹⁰¹. In addition, when patients read medical literature without some assistance from a physician, they may perceive subjective and incorrect conclusions. Furthermore, chronic lyme disease support groups, societies and charitable foundations⁸⁷ have become a formidable social force in both propagating and defending this illness construct. For instance, an antitrust investigation against the Infectious Disease Society of America by Connecticut's attorney general was settled in 2008, requiring the IDSA to review treatment guidelines it established in 2006 - which did not support long term antibiotic treatment for chronic Lyme disease¹⁰².

THE DRAWBACKS OF ILLNESS CONSTRUCTS

To summarize, a notable number of medical diagnoses are taken at face value as having an objective, verifiable pathophysiological disease process when they are in fact, more appropriately considered as illness constructs. Just as consumption proved to be tuberculosis, it is possible that many of these illness constructs will one day be better understood—they will transform from syndromes into verifiable diseases. But for now we must be honest with ourselves and our patients that these illnesses are idiopathic and may prove to be as useless and potentially harmful as the illness constructs upon which bloodletting and many hysterectomies were based.

The distinction between verifiable disease and illness construct is important because the name and conception of a particular condition affects not only a patient's coping but also the treatment the patient expects and, at times, the treatment that the patient is provided. For example, when pain with typing is diagnosed as a repetitive strain injury it is implied that repetitive activities can cause not just pain but damage. Such an idea is disabling through the worry or guilt that becomes associated with activity. The illness and illness behaviors are thus reinforced. Alternatively, if the same problem is understood as normal physiological pains with activity, quality of life can be maintained. The negative impact of the term repetitive strain injury is well documented in Australia, where the introduction of the term led to an epidemic of "repetitive strain injury" and subsequent medicalization and demonization of occupational hand use, and increased disability. These were all reduced greatly when the social situation changed and the diagnosis became noncompensable¹⁰³.

AN APPROACH TO PUZZLING ILLNESSES

Puzzling illnesses are common. Patients often present with symptoms that are vague, diffuse, do not fit within a pattern of symptoms specific for a discrete condition, and symptoms that are out of proportion to what is expected based on medical findings, making diagnosis elusive. In such situations, taking a step back, rather than jumping into diagnosis or treatment is important, yet difficult.

It helps to be mindful that most disease and illness occurs on a continuous spectrum. This is often difficult to grasp as the human mind tends towards black and white, all or none thinking (dichotomizing). In addition, the human mind seeks cause-effect relationships, perhaps because the identification of preventive measures provided an evolutionary advantage. It is therefore no surprise that both providers and patients intuitively conceive of illness in mechanical, fixable terms. Unfortunately, this intelligent and rationale approach may raise unrealistic expectations and misconceptions. This goes hand in hand with the tendency toward magical thinking, where the mind entertains anything imaginable as possible. In addition, once a perception about a condition has been formed, the mind will automatically retain evidence that supports the perception and disregard evidence against it¹⁰⁴. While these aspects of the normal functioning of the human mind have a notable influence

on illness behavior, consideration and discussion of the psychosocial and behavioral facets of illness is largely dichotomized in our society, in that most people consider the mental aspect of illness as separated and distinct from the physical aspect of illness. In addition, most people consider psychological illness as all or none (e.g., depressed or not depressed), when in reality they occur on a continuum. Finally, the mental aspects of illness are stigmatized and even demonized. The consequence of the dichotomization and stigmatization of the psychosocial aspects of illness is that patients are easily offended by discussion of the cognitive, emotional, social and behavioral aspects of illness (e.g. "Are you saying it's all in my head").

Being mindful about the workings of the mind and the biases of our culture is extremely important in providing patient care that is as accurate and as free from bias as possible. Best evidence regarding how to handle diagnostic uncertainty, interpretation of diagnostic tests, descriptions and conceptions of illness, the psychosocial aspects of illness, and what constitutes effective treatment, may be counter intuitive and contrary to the patient's and even the health provider's bias.

Diagnostic uncertainty is common, particularly with respect to pain. Uncertainty and lack of control can be distressing for both the patient and the health provider. Both patient and provider tend to operate with excessive confidence that a diagnostic test will show the root of the problem when in reality no test is perfect, and the utility of diagnostic testing is affected by the likelihood of verifiable disease being present. In a setting of diagnostic uncertainty and puzzlement, the prevalence of a specific disease in the population of patients being tested will be very low. When likelihood of a disease is low, the impact of false positive tests will be greater. This is captured in statistical diagnostic performance characteristics such as prevalence adjusted positive and negative predictive values, and likelihood ratios. A good example is "suspected scaphoid fracture". Even when using a diagnostic test that is 90% sensitive and specific, the fact that only 1 in 10 or 20 patients with a suspected scaphoid fracture has a true fracture means that a "positive" test will correspond with a true fracture less than half the time¹⁰⁵. In sum, there is substantial risk of overdiagnosis and overtreatment in the setting of diagnostic uncertainty.

Another issue is the incomplete correlation between findings on diagnostic tests and symptoms. For example, radiographic signs of arthrosis have limited correlation with pain complaints. As another example, 50% of normal asymptomatic wrists have a ganglion cyst detected on magnetic resonance imaging¹⁰⁶. Overdiagnosis in the setting of diagnosis uncertainty, combined with the limited correlation between diagnostic test results and illness, clearly show that diagnostic tests must be used with great care.

In addition to avoidance of unnecessary diagnostic tests, health care providers should also be mindful of using medical treatments, as positive responses to such treatments may be due to the placebo or meaning effect, regression to the mean, or the normal course of the condition. For example, if a patient reports relief from a corticosteroid injection for lateral epicon-

dylosis, he or she may be experiencing the placebo/meaning effect (in which an inactive or inert intervention results in symptom relief largely on the basis of an investment of hope and belief on the part of the patient), regression to the mean (the fact that all illnesses wax and wane in symptom severity and the patient may have received an injection at a symptom peak and by regression alone gone to a better symptom level, unrelated to any influence of the intervention itself), and the normal self-limiting course of the disease (the illness would have improved with or without the injection).

When faced with a puzzling condition the best approach is a comprehensive one, which takes into account all opportunities for health and wellness, reinforces positive messages, and emphasizes quality of life over cure. Such a comprehensive approach is biopsychosocial, combining cognitive, behavioral, affective, sociocultural, biological and coping style factors. A large body of research supports comprehensive approaches. With regard to cognitive processes, research shows that patients' attitudes, beliefs, self-efficacy, expectations and coping resources are important determinants of disability^{107, 108}. Distorted interpretations known as "cognitive errors" affect perception of illness, affective distress, and disability^{109, 110}. A cognitive error is a negatively distorted belief about oneself or one's situation. The most common cognitive errors in pain patients are catastrophizing (rumination, magnification and helplessness), overgeneralization (assumption that the impact of an event (negative) will apply to outcomes of future or similar events), personalization (interpreting negative events as reflecting personal meaning or responsibility), and selective abstractions (selectively attending to negative aspects of an experience).

In addition active, rather than passive coping strategies, such as efforts to function in spite of illness or to distract oneself from illness, are associated with adaptive functioning, while passive coping strategies, such as depending on others for help, letting illness dictate and restrict activity level, are related to greater symptoms and depression^{111, 112}. Avoidance of activity leads to anticipatory anxiety about symptoms (e.g., muscle tension and other symptoms associated with fight or flight or sympathetic activation). Over time, more activities are perceived as dangerous or aversive and are avoided. This may lead to both deconditioning and less effective coping strategies.

Depression is the strongest predictor of health status across diseases and cultures¹¹³. Health anxiety is also an important risk factor for chronic pain and disability^{114, 115}. An additional correlate is anger, which may affect symptoms via biological (increased arousal) mechanisms and may interfere with acceptance and adherence to treatment. Anger can take the form of frustrations related to the persistence of symptoms, lack of etiology or other aspects of uncertainty, treatment failures, worker's compensation or other disability disputes, and problems with finances and family relations.

Intuitive responses to illness are influenced by prior experiences and social/cultural norms. There are ethnic and gender differences in beliefs about pain and responses to pain. Social

factors influence how families respond to illness and interact with patients. For example, children acquire attitudes about health and health care, perceptions and interpretations of symptoms, and cognitive and behavioral responses to injury not only from their parents, but from cultural stereotypes and the social environment as well.

The label or illness construct we employ when dealing with puzzling illness without verifiable pathology impacts the treatment we chose, as well as our patient's coping and disability. Most illness constructs are the product of the biomedical approach typical of modern medicine which attempts to reduce all illness to objective pathophysiological processes (e.g., disease), even when these are only rationale or hypothesis with no objective verification. While a biomedical diagnosis provides a type of reassurance and grounding to both patient and provider, reliance on the biomedical framework alone can be disappointing and counterproductive. The patient is happy that a cause for his symptoms has been identified, and this gives initial hope for becoming symptom free. The physician is also hopeful that there are medical treatments that can fix the condition, since the cause has been identified. Biomedical illness constructs tend to medicalize symptoms, increase resource utilization (multiple doctor visits, diagnostic tests, and treatments), and expose patients to iatrogenic problems. Furthermore, illness constructs tend to make patients more passive, and risk decreasing development of self-efficacy, adaptation, and resiliency, as all of the patient's hopes are placed on external factors, while the patient is not told what he or she can do to help their situation. In addition to becoming dependent on medical treatment, patients also start avoiding activities, become less involved in life and more focused on their condition, which, over time, leads to increased disability and decreased quality of life. This has been identified as part of the pathway that leads to chronic illness¹¹⁶.

In the biomedical model, psychological treatments are reserved as a last resort when medical and surgical treatments are not successful. Diagnoses of hypochondriasis, somatoform pain disorder with psychological features, and depression are frequently employed in such situation. Although this approach can lead to referrals and appropriate treatments (Cognitive Behavioral), referrals are given perhaps too late, when resources are depleted and patients are in the habit of being ill. These labels are also stigmatizing and potentially offensive to patients, who believe that medical doctors have lost faith in them, are casting them aside or believe that they are making things up.

Under a biopsychosocial framework, the biological and psychosocial are considered simultaneously in collaborative care provided by experts in all aspects of the patient's illness. Patients benefit from an understanding of how increased health concern (which may represent in of itself a biological predisposition, and which often runs in families), depression, and misconceptions about symptoms, can lead to an amplification of normal aches and pains or bodily processes and increased disability. This occurs in a context where the optimal diagnostic and therapeutic strategies are used to address the pathophysiology.

With regard to illness constructs, or an absence of verifiable pathophysiology, it seems preferable to use a nomenclature that recognize our current biomedical shortcomings while emphasizing that symptoms are common and consistent with good health. Excellent examples of this include the terms backache and headache. The mind-body connection is implicit in these terms, since we are used to working with these illnesses and see them as consistent with an active and fulfilling life. Instead of using the illness constructs of radial tunnel syndrome or repeti-

tive strain injury to manage arm pain, it would seem preferable to start with a baseline diagnosis of arm ache (nonspecific arm pain, idiopathic arm pain) in order to frame the illness in the most positive, optimistic, enabling, and practical construction that is consistent with current evidence. In any case, let's not overlook the substantial opportunities afforded by the identification of a high prevalence of treatable psychosocial stressors in patients with unexplained symptoms (including most illness constructs).

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