

The Intersection of the Origin of Chronic Disease
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Osteoarthritis, rheumatoid arthritis, osteoporosis, periodontal disease, coronary heart disease, metabolic syndrome and type 2 diabetes- they sound like very different diseases that are treated by a variety of medical specialists. The question of our age, however, is whether as a group their etiologies have anything in common, and whether there is a connection of this shared etiology to the philosophy and practice of chiropractic medicine? I propose to demonstrate these connections in this article.

In August of 2007 a collaborative group of medical scientists from Columbia University, Cambridge University, Hershey Medical College, Northwestern School of Medicine and the Laboratory for Endocrinology Research in Lyon , France authored a research paper that had the medical world rapt with attention. This was the report that the skeleton was an endocrine organ and had an effect on insulin signaling and adipocyte (fat cell) expression of adiponectin (*Cell* 2007; 130:456-69). This extraordinary research discovery links obesity, insulin resistance/metabolic syndrome, diabetes and heart disease to bone physiology and the release from bone of hormonal messenger substances such as osteocalcin that regulate energy metabolism and the insulin/glucose axis. In essence it defines skeletal function and health as playing a principle role in the risk to diseases of metabolism and bioenergetics. The fact that the bone hormone osteocalcin “speaks” to the adipocyte and insulin secreting beta-cell of the endocrine pancreas, thereby influencing both the insulin sensitizing and anti-inflammatory protein adiponectin and insulin action, demonstrates that skeletal health is related to the prevention of diabetes and heart disease associated with cardiometabolic/insulin resistance syndrome. The walls among medical specialties are coming down, and what is emerging is the recognition that diseases are not independent processes, but rather share common causes.

It is known that skeletal health is dependent upon lifestyle, genetic, structural and nutritional factors. The lack of weight bearing activities reduces the activity of the bone rebuilding osteoblast that in turn reduces the release from bone of osteocalcin. The reduction in the release of osteocalcin in turn adversely influences insulin signaling and increases the risk to many chronic diseases. Structural integrity, weight-bearing exercise, the absence of chronic inflammation, and good nutrition all play important roles in maintaining the functional health of the bone remodeling cells, the osteoblast and osteoclast.

These interconnections among different cell types help to explain the recent recognition of the connection between osteoarthritis and rheumatoid arthritis. It has been discovered that osteoarthritis is not a simple result of “wear and tear” on the joint, but rather is an inflammatory process that engages the synovium, connective tissue and joint lubricant substances as well as the bone. Inflammatory processes are found in the joint space with increased osteoclastogenesis and angiogenesis which are the hallmarks of progressive osteoarthritis (*Rheumatology* 2005; 44:7-16). These are characteristics that in part are shared with the etiology of rheumatoid arthritis suggesting that common therapeutic

approaches to both the prevention and management of both conditions might be called for.

Musculoskeletal integrity is critically important in reducing the risk to inflammation. It might not be the “wear and tear” that is the problem in osteoarthritis, but how the musculoskeletal system responds to stress factors that result in the potential release of inflammatory mediators such as interleukin-1, interleukin-6 or tumor necrosis factor alpha. Many factors can increase the inflammatory response including chronic infection, xenobiotic or heavy metal toxicity, or intestinal dysbiosis and food allergy. All of these factors are modifiable in the patient if the practitioner asks the correct questions of the patient related to their family history, personal health history, diet, environment, lifestyle, and exercise patterns. Even periodontal disease which is a chronic inflammatory condition of the gums and periodontal connective tissue has recently been identified to be associated with osteoporosis, heart disease and diabetes.

The inflammatory signaling process that connects the etiology of diseases as different as type 2 diabetes to arthritis is to a great extent regulated by the activity of a family of enzymes produced in every cell termed “kinases”. Specific kinases regulate the translation of events that occur outside the cell to the genes of the cell where different cellular events are triggered. The activation of the inflammatory family of kinases results in a variety of clinical effects including arthritis, type 2 diabetes, heart disease, neurodegenerative diseases, metabolic syndrome and even certain forms of cancer (*Biochem Journal* 2003; 371: 199-204). Certain phytonutrients and other natural products have been found to modulate kinase function and serve as “brakes” that help to prevent the inflammatory process from running out of control (*Current Medicinal Chemistry* 2006; 13: 935-958). These phytonutrients have been defined as selective kinase response modulators, or SKRMs. Well publicized examples of this anti-inflammatory effect of phytonutrient kinase modulators include hops-derived reduced iso-alpha acids, specific catechins from acacia nilotica and O-methylated catechins from tea leaves (*J Immunology* 2004; 172: 4486-4492). These substances can be used in supplementary form to “reset” inflammatory kinase signaling, and therefore have influence on all the cell types that have enhanced inflammatory functions. This is why it has been shown that specific phytonutrient concentrates are useful for the prevention and management of many different diseases in that they regulate the signaling that induces the primary cause of the disease rather than just treating its effect (*Ann N.Y. Acad Sci* 2007; 1114: 372-380). In essence this new class of nutritional products treats the intersection of the cause of a family of chronic diseases that share a common mechanism of origin.

A patient with a history of chronic inflammatory disorders would therefore be a candidate for a personalized intervention program that incorporates regular musculoskeletal therapy, diet and nutrient intervention with such things as a low allergy-potential diet along with supplementary intake of anti-inflammatory nutrients such as fish oils containing omega-3 EPA/DHA and botanicals such as hops-derived phytochemicals, curcumin, boswellia serata, and ginger. Additionally a supplementary program of probiotics such as specific strains of lactobacillus acidophilus and bifidobacteria might be administered to improve gastrointestinal immune function and lower inflammation.

It has been found that altered mechanical signaling through the connective tissue and fascia also increases the production of inflammatory mediators that may contribute to the potentiating of the underlying cause of diseases as far ranging as arthritis, type 2 diabetes and bone loss of osteoporosis (*FASEB J* 2001;15: 2275-2282). This discovery suggests a mechanistic role for physical medicine, structural medicine and acupuncture in the treatment of these conditions (*Anatomical Record* 2002;269:257-265). It is very interesting that in September 2007 the first international conference on fascia was held under the sponsorship of the National Institutes of Health (*Science* 2007; 318: 1234-1235). This conference brought together body work practitioners with basic scientists to better understand the role of the fascia in chronic disease and what can be done to improve its function. Out of this conference came the recognition that the extracellular matrix and its component connective tissue serves as not only a structural role, but also a signaling role translating outside information to various cells. The translation of these messages through the fascia results in alteration of kinase signaling and different inflammatory responses. This once again demonstrates the “cross talk” that occurs among different tissues that sets up the potential for many different diseases.

These extraordinary recent advances in the understanding of the etiology of chronic diseases that previously seemed so different from one another has now created the understanding that they all share common mechanisms of etiology. Rather than treat the disease effect the new medicine is to treat the cause. For instance it is now becoming more well accepted that obesity in and of itself doesn't cause diabetes and heart disease. Obesity is an effect of a process that is associated with the infiltration of various tissues such as the fat tissue with proinflammatory immune cells (*J Internal Medicine* 2007; 262:415-421). It is this inflammatory process that triggers the pathology of obesity and relates to the cause of type 2 diabetes and heart disease. Rather than just putting a person on a weight loss diet, the better clinical approach would be to nutritionally modulate kinases that are associated with the inflammatory process while improving body composition.

We are witnessing the “change of the guard” as it relates to how we prevent and treat many chronic diseases due to the emergence of understanding of the shared mechanisms of dysfunctional physiology that contribute to their etiologies. The recognition that these divergent diseases intersect at a common point in their causation points medicine in a new direction for their treatment. This direction is away from the specialty medicine approach of knowing more and more about less and less to the perspective of knowing more about the underlying shared mechanisms. By understanding the role that the environment, lifestyle, structural integrity and diet have in the contribution to the shared mechanism of these chronic diseases it opens the door for incorporating therapies that address these contributors to the etiology of chronic diseases.

These are exciting times related to the advancement in the understanding of the mechanisms of origin of chronic disease. These advancements are coming not too soon in that the rising tide of age-related chronic disease will economically drown the aging baby boomer population in health care expenditures if a new model for the prevention and

management of chronic disease is not found. The news from the latest research indicates that a new paradigm in health care is evolving, and with it is a validation of the importance of a functional medicine approach to chronic disease that integrates lifestyle, environment, physical and structural medicine, diet and nutrient therapies with the focus on managing the intersection of the root cause of the diseases. It is the discussion of how to clinically harness this information related to the intersection of chronic diseases that is the focus on my 2008 international seminar series “The Emerging Therapeutic Target: Improving outcomes by treating the intersection of osteoporosis, cardiovascular disease, Type 2 diabetes, and arthritis”.

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