Rheumatisms are complex diseases in which the incidence of exogenous factors is determinant. Searching for an individual pathogenic factor is often useless in this kind of diseases, whereas targeting general cell processes might be a better strategy. Rheumatic diseases are highly heterogeneous in both causative mechanisms and lesion type, but in most cases their development and progression are characterized by a failure of resident cells to preserve tissue homeostasis.

The physiology of joints and connective tissues makes them particularly exposed to oxidative stress. Joint tissues have a high vascular supply and offer defensive cells the possibility of establishing contact with environmental factors. They also can act as receptacles for systemic inflammatory mediators, and even behave in the fashion of secondary lymphoid organs, in the setting of systemic autoimmune diseases. All these features make oxidation derivates especially harmful to joints and connective tissues. Additionally, joints are a major source of oxidative mediators because of their lipid-rich composition, their capacity to produce cytokines, and the presence of catalytic metals, such as iron and copper.

Both mechanical forces and chemical reactions can lead to the production of radical oxygen species (ROS) in joints, and render oxidative damage to the cartilage and the synovial tissue. Most frequently oxidative damage alters cell survival and growth, not only through a caspase-dependent death process, but also promoting mechanisms of senescence. Not surprisingly, the increased generation of ROS—or a deficient red-ox capacity—has been claimed as a major pathogenic factor in degenerative diseases. Generally speaking, accumulation of ROS provokes alterations in the structure of lipids, nucleic acids, and proteins, depletes the mitochondrial buffering reserve, and promotes protein misfolding.

Rheumatologists are used to cope with a highly popular alternative medicine promising cures for rheumatic ailments, without conducting a single experiment or clinical trial. This traditional medicine can be traced back to the Middle Ages, when both physicians and sorcerers administered a number of herb-containing potions and beverages. One of the most famous healing potions coming from the Classical Period was the “panacea,” whose components are acknowledged for their antioxidative capacity and continue to be used nowadays with different clinical indications [1].
Only in the last decades scientific evidence is accumulating, supporting that various components of plants and dietary supplements are useful remedies against rheumatic diseases and offer the additional benefit of low toxicity. Most probably, in the next few years, medicines resembling antique remedies will be made. Eventually, chemical therapies will leave way to biologics, and these perhaps to nutraceuticals. Being realistic, the latter look valuable as adjuvant therapies helping keep tissue homeostasis. As has already been shown in cancer, some dietary products act as cell-conditioning agents and improve their response to cytostatics.

Joints and connective tissues are a rich milieu of cells and matrix components, not only including fibroblasts and vessels, but also bone marrow precursors, immune-specific cells, and adipocytes. Altogether they provide a highly versatile structure, accessible to therapeutic intervention. It looks as a good scenario for antioxidant drugs, but unfortunately the development of these compounds is confronted with a dreaded lack of efficacy. The search for panacea is still going on and its perfect recipe is yet far to be deciphered.

Several hurdles need to be overcome in order to establish the therapeutic capacities of nutraceuticals in rheumatic diseases. A major pitfall is that their in vitro antioxidative capacity does not correspond to an in vivo effect. This could depend on the daily dose of the nutrient, but also digestion seems to play a role in avoiding a direct effect of most dietary components. On the other hand, the beneficial effect for the joints of changing our dietary habits is quite clear, and it has been suggested that the effects might rely on the production of endogenous intermediates. Some of these controversies will be solved with the help of the new high-throughput technology, which makes possible to track the route that follows the administration of molecules with a medical intention.

Another handicap is the laborious clinical trials needed to assess efficacy in these typically heterogeneous and slowly progressive diseases. Joint replacement, bone erosion, fracture, or stroke are long-term efficacy measures and only valid when large cohorts are evaluated. Epidemiologic studies are usually confronted with numerous confounding factors, and the clinical assessment is often based on the measurement of nonobjective variables. In this sense, molecular biomarkers are attracting much interest as they could help selection of candidates and assessment of response, after their validation in large population studies.

This book offers a state-of-the-art overview of how oxidative stress participates in the most prevalent joint diseases, as discussed by experts working in the field from different approaches. From autoimmunity to senescence, and from bench to bedside, their acknowledged contributions to the field are sure to shed light on the complexity of the subject.

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