

The primary stimulus leading to tissue damage is usually of exogenous origin. Tissue damage of endogenous origin likely results from continuous, long-term modification (e.g., due to aging) of some of its components, which leads to a loss of functionality (e.g., glycation of lens proteins or racemization of their amino acids).

An exogenous insult causing tissue damage can be physical in nature (mechanical injury, thermal—such as burns, ionizing radiation, etc.), chemical (e.g., toxins, allergens, but also excess or deficiency of oxygen), or biological (e.g., infections).

A chemical or biological stimulus typically induces a primary response, which usually involves the release of cytokines into the extracellular space or the production of free radicals. The effect of cytokines on other cells is highly variable and depends on their type; however, cytokines themselves do not degrade tissues. In contrast, free radicals may exhibit hormone-like properties (such as nitric oxide) and may have protective effects, but more often they damage tissues—either directly or through their reactive products (formed through reactions with metals, oxidants, or reductants).

Due to their high reactivity, free radicals have a short lifespan, which makes their direct detection difficult. Therefore, measurements often rely on determining stable products formed by reactions involving free radicals. For example, nitric oxide production can be measured based on nitrite levels, or simultaneous production of nitric oxide and superoxide can be detected via their reaction product—peroxynitrous acid.

This compound is a strong oxidizing and nitrating agent, and the product of its reaction with tyrosine—3-nitrotyrosine—is stable. Therefore, the production of peroxynitrous acid can be indirectly measured by detecting 3-nitrotyrosine.