Immunomodulation by Lead

Abstract

Lead, a potential human carcinogen, is a ubiquitous environmental pollutant in the industrial environment that poses a serious threat to human health. This toxic lead can modulate the immune response of animals as well as humans. In some instances, the immune system appears to be exquisitely sensitive to lead as compared with other toxicological parameters. Both stimulation and suppression of immune response have been demonstrated in lead exposed animals and humans depending on the T helper (Th)1 vs Th2 response. Although the majority of data accumulated to date pertains to the effects of lead in small laboratory rodents, there is little reason to believe that similar quantifiable effects do not occur in domestic and food-producing animals owing to basic functional similarities of the immune system of mammals. In this review, we have discussed the immunomodulatory role of the toxic heavy metal, lead, on cellular and humoral components of the immune system with particular reference to effector cells such as B cells, T cells, natural killer (NK) cells, and soluble mediators such as cytokines, chemokines, and nitric oxide (NO).

Key Words

Chemotaxis
Cytokines
Lead
Lymphocytes
NK cells

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0257-277X/03/28/2:151–165/$25.00
Introduction

The immune system consists of a complex network of cells and soluble mediators that interact in a highly regulated manner to generate an immune response of appropriate magnitude and duration. The complexity and lack of clear understanding of a number of immunological functions, particularly their regulation and amplification mechanisms, makes it difficult to understand how various toxic metals mediate some of the immune alterations. At the same time, the use of exogenous heavy metals as tools in biological research has been valuable in unfolding complex biochemical phenomena.

Metals modulate the activities of immunocompetent cells by a variety of mechanisms. Depending on the particular metal, its concentration and biologic availability, and other factors, the net outcome may be either immunostimulation or immunosuppression. The general concern is that metals may disrupt immune homeostasis by modulating immunoregulatory activities. This may lead to either immunodeficiency or autoimmunity. Mechanistic studies of metal immunomodulation of human lymphocytes has been conducted less often than for rodents. Most studies suggest similar effects in humans and rodents.

There has been growing concern regarding alterations of the immune response induced by heavy metal. Occupational or environmental exposure to lead is believed to affect human health adversely. Several studies have documented the potential toxic effects of lead on the immune system (1,2). Lead may alter the immune response even at moderate levels of exposure. This has inspired many investigators to study effects of lead on various limbs of the immune system. Evidence has accumulated to demonstrate that the immune system is a target for the toxic effects of lead. These facts were derived primarily from numerous studies in various strains of animals such as rodents, mice, and humans. Among all the heavy metals that contaminate the environment and pose a potential hazard to public health, lead can result in a wide range of biological consequences depending on the level and duration of exposure. Occupational exposure, which results in poisoning, still occurs in many countries of the world. The lead circulating in the blood stream is mobile in contrast to that stored in bones, and it is this blood lead that exerts adverse effects on the body. Under conditions of more or less constant and prolonged exposure, the blood lead level reflects the quantity of “biologically active” lead in the body and has a positive correlation with the symptoms of lead toxicity (3). It has now been established that lead can lead to immunosuppression, thereby resulting in increased incidences and severity of infectious diseases (4–7). Conversely, lead has also been reported to cause inappropriate enhancement of the immune response and generation of altered immune responsiveness leading to the development of allergic and autoimmune diseases (8–10). Hence, both suppression and enhancement of immune functions are attributed to the immunotoxic effects of lead. Important effects of lead on the immune system are briefly summarized in Table 1.

Sources of Lead Exposure

Lead has been mined and used in industries and household products for centuries. People have been aware of the dangers since ancient times. The twentieth century saw both the greatest ever exposure of the general population to lead, and an extraordinary amount of new research on lead toxicity. Lead comes from a variety of sources, such as lead-based paints, lead acid battery, and radiator exhaust. In many countries, occupational lead exposure is entirely unregulated and absolutely no