

# The immune system as target for subclinical lead related toxicity

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During the past two decades, scientific interest and public health concern have shifted their focus from issues connected with overt clinical lead disease to the detection of subtle clinical and biochemical aberrations.<sup>1</sup> This has brought about a change in the thinking on the health risks that are associated with lead toxicity.<sup>2,3</sup> Although major emphasis has been set on lead hazards among pediatric populations, there has also been a gradual lowering of the occupational biological standards in many countries.

The several investigations that have shown an association between low level, community related exposure to lead and impairment in child development have provided a strong scientific basis for the decision of the Centers for Disease Control in the United States to define lead toxicity at a blood lead concentration of 10 mcg/dl.<sup>4-6</sup> By analogy, reports that neurotoxic effects and abnormalities in the male reproductive system of workers exposed to lead can be detected at blood lead concentrations below that at which removal from exposure is usually mandated, begin to question the safety of blood lead standards that are widely accepted as safe.<sup>7-9</sup> A *deja vu* from the 1970s, but this time it concerns even lower blood lead concentrations!<sup>10</sup>

As the scientific spectrum of effects induced by lead has been widened, toxic effects of lead have also been detected in organ systems that historically were not part of the clinical features of lead poisoning. Mechanisms of action of characteristic effects are being studied in greater detail as well.<sup>11</sup> Although many biochemical and molecular perturbations caused by lead have been studied in experimental

animals or cell systems, some are beginning to emerge as potentially useful laboratory parameters in the evaluation of persons who are exposed to lead at concentrations primarily associated with subclinical effects. As certain immunotoxic effects tend to appear before traditional toxicological manifestations, they have the potential to serve as early warning mechanisms of impending clinical disease.

Lead has been evaluated extensively in animal studies with regard to its effects on the immune system.<sup>12</sup> Although few immunotoxicological investigations have been made on persons exposed to lead, the available information indicates that immunotoxic abnormalities induced by lead exist in humans as well. A profile characterised by an increased number of B lymphocytes and a decline in IgM concentrations has been suggested by some investigators.<sup>13</sup>

We have examined a group of firearm instructors and present preliminary findings on immunotoxic manifestations associated with their occupational exposure to lead.

Fifty four instructors volunteered and underwent immunological tests that included analysis of surface phenotypes of mononuclear cells and assessment of lymphocyte functions.<sup>14,15</sup> Two groups of instructors were considered: one group of 15 with blood lead concentrations of 25 mcg/dl or higher (HL group, mean 31.4 (SD) 4.3) and another group with a mean blood lead concentration of 14.6 (SD) 4.6 mcg/dl (LL group).

Considerable reductions in the percentage and absolute number of circulating T cells (CD3<sup>+</sup>) and T helper cells (CD4<sup>+</sup>) were noted in the HL group with lesser reductions in the LL group (table). A significant reduction in the T helper cell (CD4<sup>+</sup>)/T suppressor cell (CD8<sup>+</sup>) ratio in the HL group was caused by a decrease in T helper cells (CD4<sup>+</sup>) without simultaneous increase in T suppressor cells (CD8<sup>+</sup>). Similar findings were noted for selected lymphocyte functional parameters—that is, pronounced reduction of PHA induced mitogenic responses in the HL group and a lesser impairment in the LL group. The results of these studies and other detailed investigations of B cell (CD20<sup>+</sup>) function, mixed lymphocyte culture, and mechanisms of actions will be presented elsewhere.

Our initial results suggest the existence of lead

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Table Lymphocyte surface markers (mean SD) in firearm instructors exposed to lead and controls

	Controls	LL group (< 25 mcg/dl)	HL group (≥ 25 mcg/dl)
T cells (CD3):			
%	72.6 (6.0)	57.4 (12.2)†††	46.9 (11.4)***†††
Absolute No	1679 (522)	1464 (744)	1209 (333)*††
T helper Cells (CD4):			
%	45.5 (5.6)	30.6 (9.1)†††	21.4 (9.0)***†††
Absolute No	1056 (346)	779 (405)††	554 (264)*†††
T suppressor cells (CD8):			
%	25.7 (7.3)	23.1 (8.7)	25.4 (8.6)
Absolute No	604 (274)	557 (205)	659 (245)*

\*p < 0.1; \*\*\*p < 0.01; HL group v LL group. ††p < 0.01; †††p < 0.002 v controls.

related immunotoxic effects, primarily on T lymphocytes (CD3<sup>+</sup>) and T helper cells (CD4<sup>+</sup>). The intensity of abnormalities was associated with the degree of lead absorption, and the study seems to identify immunotoxic effects at blood lead concentrations of 25 mcg/dl and higher.

The detection of subtle and subclinical changes will continue to be of the highest priority as ingredients of preventive occupational and community screening programmes to identify persons at high risk of disease associated with lead. Assessment of immune functions may be an additional complementary tool in the evaluation, at an early stage, of subtle and potentially reversible effects. This approach can add appreciably to the efforts in preventing lead poisoning. Until further efficient control of exposure has been achieved, occupational and community based lead poisoning can unfortunately not yet be incorporated into the "history texts" where it should belong.<sup>16</sup>

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