Chapter 5

Neurotoxic Effects of Lead

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1. Introduction

Knowledge of the toxicity of lead dates from at least the second century BC, while detailed clinical descriptions of saturnism have been available since the early 1800s (see refs. 6 and 119 for reviews of historical literature). It was not until the beginning of this century, however, that lead was recognized as a particular hazard to the developing infant and the specific syndrome of childhood lead poisoning was described.

More recently, improved safety standards in the industrial use of lead and a decline in its domestic applications, have produced a reduction in the incidence of frank lead intoxication in both adults and children. At the same time, though, the dissemination of lead into the general environment has markedly increased. The effects of lead exposure in childhood have become, therefore, a focus of increasing attention, with mounting concern that lead levels insufficient to produce overt clinical signs may nevertheless be responsible for more subtle, long-term changes in child development. Hence, despite the present-day rarity of classical clinical lead poisoning, the study of lead toxicity retains direct contemporary relevance.
2. Clinical Lead Poisoning

The signs and symptoms of frank lead intoxication differ, somewhat, between adults and children, although in both cases they are largely nonspecific. The lead poisoned adult commonly presents with pallor, abdominal pain, constipation, and vomiting, with anemia and the frequent presence of a blue “lead line” on the gums. The neurological effects of plumbism, although variable, often take the form of a peripheral neuropathy, generally manifest as a motor disturbance with unilateral or unequally bilateral paralysis of extensor muscle groups in the distal parts of the limbs. The actual distribution of affected muscles appears to be influenced by muscle use, hence wrist drop and weakness of the small muscles of the hand were found to be characteristic symptoms amongst house painters and workers in the lead industry. Occasionally, sensory changes such as paraesthesia, or patches of analgesia and anesthesia may also be present.

The development of encephalopathy caused by lead, although sometimes occurring in adulthood, is more commonly associated with childhood lead poisoning. In such cases, fatigue, pallor, anorexia, and irritability are generally followed by abdominal pain, vomiting, drowsiness, and motor unsteadiness, occasionally complicated by muscular weakness due to a peripheral neuropathy, principally affecting the legs. If exposure to lead continues, these effects may culminate in the more severe signs of encephalopathy, i.e., convulsions, stupor, coma, and ultimately death.

Survivors of an acute encephalopathic episode of lead poisoning have a poor prognosis, many such children being left with permanent neurological and psychological impairments. The long-term sequelae of clinical lead intoxication (reviewed in refs. 78, 120, and 121) include mental retardation, convulsions, cerebral palsy, optic atrophy, and behavioral and learning disorders, with estimates of the proportion of cases incurring such damage varying from about 25 to over 90%. The effects are seen most frequently following overt encephalopathy, although children showing symptomatic lead poisoning without encephalopathy may also be affected.

3. Neuropathology of Clinical Lead Poisoning

3.1. Peripheral Nervous System

There have been numerous attempts to identify the anatomical changes underlying the neuromuscular dysfunction of clinical