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Cellular Sensitivity to Ferrotoxicity is Associated with Specific Clinical Disorders

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During the past five decades, scores of medical studies have described the association of ferrotoxicity with development of a great variety of diseases [1]. Increasingly, specific types of body cells are being reported to be injured or killed by low concentrations of iron. In the initial account, cultures of anterior pituitary cells were observed to be killed by 2 μM irons; in this system, hepatocytes remained healthy in 10-100 μM iron [2]. Thus not surprisingly, thalassemic-major children who load iron early in life are deprived of growth hormone. Persons who absorb excessive iron in late teens or early adulthood can suffer from low levels of gonadotrophic hormones. Subsequently, osteoblasts have been recognized to be unusually sensitive to low concentrations of iron [3,4]. In contrast, osteoclasts (cells of macrophage origin) are highly resistant to iron. Thus in iron loaded persons, bone rebuilding by osteoblasts is surpassed by osteoclast destruction of bone. Accordingly, osteoporosis is a common disorder in patients who load iron for genetic, environmental or behavioral reasons [5].

Recently, pharmacologically relevant concentrations of intravenous iron preparations were observed to kill rat pancreatic beta cells [6]. Iron loading has long been known to be a risk factor for types 1 and 2 diabetes as well as for gestational diabetes. The authors of the study caution that indiscriminate use of intravenous iron can impair insulin production. However, many types of cells are resistant to ferrotoxicity perhaps because of their efficient synthesis of ferritin or other antioxidants. For example, pancreatic exocrine cells can withstand 50-100 fold iron loading and continueto produce digestive enzymes [7]. Nevertheless, it is quite likely that tissue failures in many disorders of gastrointestinal, neurological and vascular systems will be found to result from cells that died because of sensitivity to moderate or excessive quantities of iron. Much greater awareness of the dangers of even mild iron loading will be helpful in alleviating the currently high prevalence of serious chronic disorders.

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