Excerpt from Toxicity, Aluminum

http://www.emedicine.com/med/byname/Toxicity--Aluminum.htm

Synonyms, Key Words, and Related Terms: hyperaluminosis, aluminum-related illness, aluminum concentration, aluminum intoxication, aluminum clearance, aluminum-related disease, dialysis osteodystrophy, dialysis encephalopathy, aluminum deposition, microcytic anemia, chromophilic cells, basophilic stippling, deferoxamine therapy

Background

Aluminum is a trivalent cation found in its ionic form in most kinds of animal and plant tissues and in natural waters everywhere. It is the third most prevalent element and the most abundant metal in the earth's crust. **Dietary aluminum is ubiquitous, but in such small quantities that it is not a significant source of concern in persons with normal elimination capacity. Urban water supplies may contain a greater concentration because water is usually treated with the element before becoming part of the supply**. Subsequent purification processes that remove organic compounds take away many of the same compounds that bind the element in its free state, further increasing aluminum concentration.

All metals can cause disease through excess, deficiency, or imbalance. Malabsorption through diarrheal states can result in essential metal and trace element deficiencies. Toxic effects are dependent upon the amount of metal ingested, entry rate, tissue distribution, concentration achieved, and excretion rate**. Mechanisms of toxicity include inhibition of enzyme activity** and protein synthesis, alterations in nucleic acid function, and changes in cell membrane permeability.

No known physiologic need exists for aluminum; however, because of its atomic size and electric charge (0.051 nm and 3+, respectively), it is sometimes a competitive inhibitor of several essential elements of similar characteristics, such as magnesium (0.066 nm, 2+), calcium (0.099 nm, 2+), and iron (0.064 nm, 3+). **Approximately 95% of an aluminum load becomes bound to transferrin and albumin intravascularly and is then eliminated renally.**

MCFIP - Bioinformatic search will identify the fact that aluminum binds to transferrin; i.e. lactoferrin, apolactoferrin and hololactoferrin.

Aluminum is absorbed from the GI tract in the form of oral phosphate-binding agents (aluminum hydroxide), parenterally via immunizations, via dialysate or total parenteral nutrition (TPN) contamination, via the urinary mucosa through bladder irrigation, and transdermally in antiperspirants. Lactate, citrate, and ascorbate all facilitate GI absorption. If a significant load exceeds the body's excretory capacity, the excess is deposited in various tissues, including bone, brain, liver, heart, spleen, and muscle. This accumulation causes morbidity and mortality through various mechanisms.

Pathophysiology

Aluminum toxicity is usually found in patients with impaired renal function. Acute intoxication is extremely rare; however, in persons in whom aluminum clearance is impaired, it can be a significant source of pathology. Aluminum toxicity was originally described in the mid-to-late 1970s in a series of patients in Newcastle, England, through an associated osteomalacic dialysis osteodystrophy that appeared to reverse itself upon changing of the dialysate water to deionized water (ie, aluminum-depleted water). Previously, the only known dialysis-associated bone disease was osteitis fibrosa cystica, which was the result of abnormalities in vitamin D production that resulted in a secondary hyperparathyroidism, increased bone turnover, and subsequent peritrabecular fibrosis. In aluminum-related bone disease, the predominant features are defective mineralization and osteomalacia that result from excessive deposits at the site of osteoid mineralization, where calcium would normally be placed.

Since the role of aluminum in disease has been identified, more attention has been paid to the element, leading to its recognition in several other processes. For example, among patients with osteomalacia, there has been a closely associated dialysis encephalopathy, which is thought to be caused by aluminum deposition in the brain. Aluminum causes an oxidative stress within brain tissue. Since the elimination

half life of aluminum from the human brain is 7 years, this can result in cumulative damage via the element's interference with neurofilament axonal transport and neurofilament assembly. Some experts feel it plays a role in leading to the formation of Alzheimerlike neurofibrillary tangles.

Aluminum also has a direct effect on hematopoiesis. Excess aluminum has been shown to induce microcytic anemia. Daily injections of aluminum into rabbits produced severe anemia within 2-3 weeks. The findings were very similar to those found in patients suffering from lead poisoning. MCFIP - Isn't the number of adults with anemia increasing in the US at a high rate? As indicated in the first comment we inserted into this document, the possibility/probability that iron – aluminum comprise a pair (IL-1) could account for the enormous number of patients with anemia in the world; i.e. higher aluminum potentially decreasing iron.

Aluminum may cause anemia through decreased heme synthesis, decreased globulin synthesis, and increased hemolysis. **Aluminum may also have a direct effect on iron metabolism: it influences absorption of iron via the intestine, it hinders iron's transport in the serum, and it displaces iron's binding to transferrin.** Patients with anemia from aluminum toxicity often have increased reticulocyte counts, decreased mean corpuscular volume, and mean corpuscular hemoglobin.

MCFIP - Refer to the previous comment concerning transferrin mutation.

Other organic manifestations of aluminum intoxication have been proposed, such as a slightly poorer immunologic response to infection, but the mechanism by which it exerts its effect is complex and multifactorial.

Frequency

United States

The actual incidence of toxicity is unknown. The greatest incidence is observed in patients with any degree of renal insufficiency. A higher incidence is observed in populations who have aluminum-contaminated dialysate or who are taking daily oral phosphate-binding agents. Patients who require long-term TPN are at increased risk as well.

Animal studies in rats and recent case reports have implicated the use of oral aluminum-containing antacids during pregnancy as a possible

cause for abnormal fetal neurologic development. -

International

Some evidence suggests that in developing countries where contaminated dialysis water is still used, aluminum-related disease is more prevalent. Also, as people still use over-the-counter aluminum-containing phosphate binders, aluminum deposition within the bone will continue and serve as a reservoir for continued exposure because of its long elimination half life.

Mortality/Morbidity

The mortality rate may be as high as 100% in patients in whom the condition goes unrecognized. Today, however, recognition by nephrologists is the norm, and increased awareness by all practitioners has led to earlier detection and overall avoidance of the syndrome. Morbidity and mortality have been diminished significantly. Prior to this, bone pain, multiple fractures, proximal myopathy, and the sequelae of dementia have been the main sources of morbidity.

Race

Aluminum toxicity has no predilection for any race.

Sex

Aluminum toxicity has no predilection for either sex.

Age

Aluminum toxicity is observed in all age groups but its end-organ effects are more prevalent in the aged, who may have diminished renal function.