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ALUMINIUM

Introduction

Aluminium is the most abundant metal present in the earth's crust, representing approximately 8% of its total mineral content. Due to its reactivity, Al is found in nature only in chemical combination with other elements and its appearance on the planet as the pure metal is a product of 20th century industrial processes. While aluminium is ubiquitous in the diet in small quantities, this is not thought to be a source of concern to most people with normal renal and hepatic function, partly because it is very poorly absorbed from the gut.

So why should we be concerned about the concentration of aluminium in body fluids and in tissues? Mucosal damage to the gut, advancing age or genetic pre-disposition may facilitate its uptake by the enterocytes. Also urban water supplies may receive an enhanced concentration of Al after water has passed through treatment plants. Since the role of aluminium in dialysis osteodystrophy was identified [1], much attention has been paid to the possible role of this metal in several other pathological processes, particularly with regard to the brain.

Physiological actions of aluminium

No physiological function has been proposed for aluminium. However, because of its atomic size and electrical charge (0.051 nm and 3^+, respectively), it can be a competitive inhibitor of several essential elements with similar characteristics, such as magnesium (0.066 nm, 2^+), calcium (0.099 nm, 2^+), and iron (0.064 nm, 3^+) [2]. At physiological pH, aluminium forms an insoluble hydroxide $Al(OH)_3$ and this is one reason why, in normal healthy subjects, only 0.3% of an orally administered aluminium dose is absorbed by the gut. Approximately 95% of the aluminium that is absorbed is then bound in the circulation by the plasma proteins albumin and transferrin, from which it is rapidly eliminated through the kidney. Al thus has the potential to interfere with iron absorption and transport and can induce a microcytic anaemic. It can also interfere with the actions of calcium and magnesium. However, it is usually only when the gut barrier is by-passed, such as in the case of intravenous infusion or renal dialysis, that much aluminium can accumulate in the body [3]. High levels of fatty acid uptake can also increase paracellular absorption of Al from the gut [4].

Aluminium accumulates in the bone, liver, kidney and brain. It interferes with bone mineralisation and is associated with the development of neuronal plaques. It is a significant inhibitor of mitochondrial isocitrate dehydrogenase [5] and thus has the potential to interfere with cellular energy production. Well-described symptoms of excessive aluminium exposure include bone pain and fatigue, with anaemia and hypophosphataemia.

Toxic effects of aluminium

Al toxicity was originally described in the mid-1970s in a series of patients in Newcastle with chronic renal failure, who experienced an osteomalacic dialysis osteodystrophy that appeared to reverse itself upon changing their dialysis water to deionised water (i.e. more completely aluminium-depleted water) [6].

Among patients who developed bone disease there was a closely associated dialysis encephalopathy ("dialysis dementia"), which was thought to be caused by Al deposition in the brain. A 10-fold increase in aluminium concentrations was reported in patients with Al intoxication through the use of haemodialysis solutions with high levels of aluminium [7]. Typical presentations included proximal muscle weakness, bone pain, multiple non-healing fractures, acute or subacute alterations in mental status, and premature osteoporosis. Their condition was also resistant to treatment with vitamin D (which is understandable). Desferrioxamine has been proposed as a chelating agent to promote the removal of Al from body stores in such cases [8].

Aluminium also accumulates within the central nervous system, which is itself extremely sensitive to oxidative damage This has lead to an interest in the possible role of Al in neurological disease amongst subjects who have experienced chronic, long-term accumulation of Al during normal dietary exposure. Since the half-life of aluminium in the human brain is 7 years [9], the presence of even small amounts of Al could result in cumulative damage to neurofilament axonal transport and neurofilament assembly. It is thus possible that Al plays a role in the formation of Alzheimer-like neurofibrillary tangles. However Al is unlikely to be the causative agent for Alzheimer's disease, whose description in 1907 pre-dates the availability of Al cooking pots and Al metal.

It has been suggested [10] that the heterogeneous symptoms of autism spectrum disorders are connected to dysregulation of glutamanergic neurotransmission in the brain. This has been explained as a part of the inflammatory response to Al deposition, together with the enhancement of excitatory receptor activity by cytokines released during this process. In support of this theory, high aluminium concentrations have been described in post-mortem brain specimens of patients with Parkinson's disease and also in experimental animals where administration of Al caused a strong decrease in the dopamine content of the striatum [11].

In this regard, various dietary excitotoxins including aluminium could exacerbate the clinical picture by worsening of excitotoxicity and by microglial priming, regardless of whether or not they are the primary cause of the disorder. This, in turn, opens up the discussion as to the use of nutritional supplements to reduce excitotoxicity and brain inflammation, in the hope of alleviating the neurotoxic effects of aluminium [12,13].

Food sources of aluminium

Processed foods such as soya, cheese, infant formula, acidic food (e.g. tomatoes) that have been cooked in aluminium pots, fruit juices and soft drinks sold in containers with aluminium caps; water and soil, air containing dust particles from weathering of rocks or industrial and agricultural processes; anti-acids and antiperspirants; renal dialysis solutions; some phosphate-binding drugs contain aluminium hydroxide. Aluminium is a natural constituent of many water sources used for drinking; at some treatment plants aluminium salts are used to remove impurities (such as peat colloids).

Aluminium in clinical samples

The reference intervals for aluminium are as follows:

Urine Al (the preferred sample for monitoring exposure)	<130 μmol/mol of creatinine
Plasma Al	30 – 220 nmol/L
Whole blood Al	180 – 560 nmol/L
Hair Al	< 50 μg/gm of hair

The somewhat higher levels of aluminium in whole blood as compared to plasma reflect the sequestration of Al in haemoglobin, which is a de-toxifying action of the red cells. However, the Al content of the blood may not accurately reflect whole body status since the metal is extensively sequestered into bone and other tissues.

Patient preparation:

No special preparation is required and the patient can continue to take nutritional supplements and medication before the collection of the sample.

Specimen requirements

For blood or plasma aluminium measurement, blood should be collected into an 8 ml trace element-free potassium EDTA tube. Collection tubes available on request. If a number of blood tubes are being taken at the same collection, the trace element-free tube should be filled first to avoid cross-contamination. Postal samples (overnight delivery) are acceptable.

For hair analysis, hair should be cut from the nape of the neck, as close to the scalp as possible. At least 0.5gm of hair is required, which is about one heaped tablespoon full. Only hair up to 1½" (4cm) from scalp can be used. Please allow for this when the hair is long by sending in a larger total sample, for example 2 tablespoons-full of hair.

For water analysis, 20 mL of water should be sent in a plastic, screw cap container (available on request).

Turn around time: 5 working days.

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