Aluminium

Atomic number 13
Atomic weight 26.98

Collection

Serum/Plasma	5 mL	Contact laboratory regarding container No anticoagulant Unseparated blood may be sent
Water	20 mL	Sterile Universal
Dialysis Fluid	20 mL	Sterile Universal
Urine	20 mL	Sterile Universal

Send empty container together with any sample type if uncertain about possible contamination

Reference ranges

			Reference
Serum/plasma	µmol/L	Less than 0.4	1
Blood	µmol/L		
Urine	µmol/L	Less than 0.4-0.6	2
	µmol/24 h	Less than 0.82	3
	µmol/mmol creatinine	Less than 0.06	3
	nmol/mmol creatinine	Male 0.13 Female 0.30	4

Notes

	Serum/plasma
Little risk of toxicity in CRF patients	Less than 2.2
Excessive accumulation; risk of toxicity in children	More than 2.2
Cause for concern; high risk of toxicity in children	More than 3.7
High risk of toxicity in all patients	More than 7.4
	Water
If used to prepare dialysis fluid, final concentration of fluid should not exceed level given below	
	Dialysis fluid
Upper limit recommended by CEC	Less than 1.1

References

1. Commission of the European Community (CEC). Resolution 86/C184/04 of the Council concerning protection of dialysis patients by minimising the exposure to aluminium. OJ No.C184:16-17.
2. Hoet P, Jacquerye C, Deumer G, Lison D, Haufroid V. Reference values and upper reference limits for 26 trace elements in the urine of adults living in Belgium, Clin Chem Lab Med, 2013; 51: 839-849.

3. Sieniawska CE, Jung LC, Olufadi R, Walker V, Twenty-four hour urinary trace element excretion: reference intervals and interpretive issues. Ann Clin Biochem 2012; 49: 341-51.
4. Morton J, Leese E, Tan E, Cocker J. Determination of 61 elements in urine samples collected from a non-occupationally exposed UK adult population, Toxicol. Letters (2014), http://dx.doi.org/10.1016/j.toxlet.2014.08.019

Clinical

Aluminium is a non-essential element of ubiquitous distribution. Aluminium in the diet comes from foods, food additives, storage, cooking materials and drinking water. Pharmaceutical agents such as aluminium containing antacids and buffered analgesics potentially contribute substantial amounts of aluminium to the total body burden. Aluminium is also found in toothpastes, cosmetics and antiperspirants. Consequently, exposure to aluminium is unavoidable with a daily dietary intake in the population probably being in the range of 3 to 5 mg. Only a small fraction of this aluminium is absorbed (approximately 15 µg) with the majority excreted through the kidneys. Organic ligands of aluminium e.g. aluminium citrate are more readily absorbed from the gut and high doses of aluminium may lead to retention and greater body burden in the bones and brain. For many years aluminium was thought to be biologically innocuous apart from rare cases of toxicity due to industrial exposure.

Toxicity

The major clinical importance of aluminium has related to its potential toxicity in patients undergoing haemo or peritoneal dialysis. Greatly elevated concentrations of plasma aluminium were found to be associated with dialysis encephalopathy (speech disorder, dementia, convulsions, myoclonus, depression, anxiety, malaise and memory loss) after 3- 7 years on dialysis. In addition, a correlation was found between plasma aluminium concentrations and a Vitamin D resistant osteomalacia – dialysis osteodystophy. Some patients were also found to be susceptible to a microcytic hypochromic anaemia which reverted to normal red cell morphology following dialysis with aluminium-free water. The cause of aluminium toxicity in these dialysed patients was a result of increased body burden due to treatment with aluminium based phosphate binders and aluminium present in the dialysate fluid. The gastrointestinal absorption of aluminium was also increased due to co-administration of citrate which was given in conjunction with aluminium phosphate binders. This resulted in European guidelines being issued to provide protection for patients on dialysis with the consequent regular monitoring of aluminium in patient's blood plasma and also the water used in preparation of the dialysate fluid. However, in recent years aluminium phosphate binders have been replaced by calcium based binders or Sevelamer in the treatment of hyperphosphataemia. Also, all dialysis units now use water prepared by reverse osmosis for the preparation of the dialysate fluid. Consequently, cases of dialysis encephalopathy and osteodystrophy are rarely, if ever, seen. This has raised questions about the continued use of plasma aluminium in monitoring patients on dialysis. Although, monitoring of water quality in dialysis units is still extremely important.

The monitoring of plasma aluminium should be considered in other clinical areas including patients receiving TPN with renal disease, aluminium containing infant formulas or plasma exchange. Also, any sources of industrial exposure must be considered.

Laboratory Indices of Aluminium Status

Aluminium is primarily transported bound to transferrin in the blood and its measurement in plasma provides the only reasonable means of assessing total body burden. However, the large reserve of aluminium in the bone can under certain circumstances such as sepsis, considerably influence plasma concentrations. Concerns regarding risks to dialysis patients resulted in a CEC Resolution establishing a protocol for the regular monitoring of such patients and setting criteria for the analytical techniques. In summary, this recommends that patients at risk be monitored at least quarterly by measurement of plasma aluminium; that concentrations > 2.2 µmol/L (60 µg/L) indicate an increased aluminium burden; that concentrations > 3.7 µmol/L (100 µg/L) indicate the need for an increased monitoring frequency and health surveillance; that all steps should be taken to ensure that a concentration of 7.4 µmol/L (200 µg/L) is never exceeded. Also, the aluminium concentration of dialysate fluid should not exceed 1.1

µmol/L (30 µg/L).

However, many renal units impose their own lower action limits and ideally aluminium concentrations in plasma should not exceed 3.0 µmol/L (71 µg/L). Care must be taken to see that any external contamination of blood tubes from aluminium in the environment is avoided. Ideally, new batches of tubes for taking blood or storage of plasma should be assessed for any possible aluminium contamination.

Monitoring of water generated by reverse osmosis must also be carried out and aluminium concentrations must be below 0.37 µmol/L (10 µg/L).

References

1. Stokinger HE Chapter 29 - Metals, in Patty's Industrial Hygiene and Toxicology, 3rd Revised Edition, Volume 2A. Eds Clayton GD and Clayton FE. Wiley Interscience, 1981.
2. Savory J, Wills MR. Aluminium and chronic renal failure, sources, absorption, transport and toxicity. *Crit Rev Clin Lab Sci* 1989; **27**: 59-107
3. Eastwood JB, Levin GE, Pazianas M, Taylor A, Denton J and Freemont AJ. Aluminium deposition in bone after contamination of a drinking water supply. *Lancet* 1990; **ii**: 462-466
4. Nicolini M, Zatta PF, Corain B. eds, Aluminum in Chemistry, Biology and Medicine. *Life Chemistry Reports*, **Volume 2.** Harwood Academic Publishers, Switzerland, 1994
5. Yokel RA, Golub MS. eds, Research Issues in Aluminum Toxicity. *J Toxicol Environm Health* 1996; **48 (6)**: 527-686
6. Alfrey AC. et al., Syndrome of dyspraxia and multifocal seizures associated with chronic hemodialysis. *Trans Am Soc Artif Intern Organs*, 1972; **18**(0): p. 257-61, 266-7.
7. Dunea G. et al., Role of aluminium in dialysis dementia. *Ann Intern Med*, 1978. **88**(4): p. 502-4.
8. Parkinson IS. et al., Fracturing dialysis osteodystrophy and dialysis encephalopathy. An epidemiological survey. *Lancet*, 1979; **1**(8113): p. 406-9.
9. Short AI, Winney RJ., and Robson JS. Reversible microcytic hypochromic anaemia in dialysis patients due to aluminium intoxication. *Proc Eur Dial Transplant Assoc*, 1980; **17**: p. 226-33.
10. Smith DB. et al. Dialysis encephalopathy in peritoneal dialysis. *Jama*, 1980; **244**(4): p. 365-6.
11. Hewitt CD. Savory J, and Wills MR. Aspects of aluminium toxicity. *Clin Lab Med*, 1990; **10**(2): p. 403-22.
12. Wills MR. and Savory J, Aluminium and chronic renal failure: sources, absorption, transport, and toxicity. *Crit Rev Clin Lab Sci*, 1989; **27**(1): p. 59-107.
13. Drueke TB. Intestinal absorption of aluminium in renal failure. *Nephrol Dial Transplant*, 2002; **17 Suppl 2**: p. 13-6.
14. Winney RJ, Cowie JF, and Robson JS. What is the value of plasma/serum aluminium in patients with chronic renal failure? *Clin Nephrol*, 1985; **24 Suppl 1**: p. S2-8.
15. Salusky IB and Goodman WG., Managing phosphate retention: is a change necessary? *Nephrol Dial Transplant*, 2000; **15**(11): p. 1738-42.
16. Loghman-Adham, M., Safety of new phosphate binders for chronic renal failure. *Drug Saf*, 2003; **26**(15): p. 1093-115.
17. Dunea, G., Dialysis dementia: an epidemic that came and went. *Asaio J*, 2001. **47**(3): p. 192-4.
18. Kausz, AT. et al. Screening plasma aluminium levels in relation to aluminium bone disease among asymptomatic dialysis patients. *Am J Kidney Dis*, 1999; **34**(4): 688-93.
19. Davenport A. et al. Sepsis: a cause of aluminium release from tissue stores associated with acute neurological dysfunction and mortality. *Clin Nephrol*, 1988; **30**(1): p. 48-51.
20. Mazzaferro S. et al. Relative roles of intestinal absorption and dialysis-fluid-related exposure in the accumulation of aluminium in haemodialysis patients. *Nephrol Dial Transplant*, 1997; **12**(12): p. 2679-82.
21. Walker AW. ed. *SAS Trace element laboratories clinical and analytical handbook*. 3rd ed. 1998.
22. Gault PM, Allen KR and Newton KE. Plasma Aluminium: a redundant test for patients on

dialysis. *Ann Clin Biochem*, 2005; **42:** 51-54