

Albumin (serum, plasma)

1 Name and description of analyte

1.1 Name of analyte

Albumin (plasma or serum)

1.2 Alternative names

None (note that albumen is a protein found in avian eggs)

1.3 NLMC code

1.4 Description of analyte

1. Albumin is the major plasma protein. Molecular weight is approx 66.3 kDa. It is synthesised exclusively in the liver, normally at a rate of ~120 mg/kg body wt/24 h. Synthesis is increased (up to 2x) by a fall in plasma oncotic pressure; synthesis is decreased by certain cytokines, notably IL-6. Plasma half-life ~20 days.

2. Albumin is also present in interstitial fluid; its concentration is lower, but because of the greater volume of this compartment in relation to the intravascular volume, more albumin is present in this fluid than the plasma.

Disruption of endothelial function, such as occurs in sepsis, allows albumin to move down its concentration gradient into the ICF and can cause rapid changes in plasma albumin concentration.

1.5 Function of analyte

1. Albumin acts non-specifically as a transport protein for numerous substances including free fatty acids, certain ions (e.g. [Ca⁺⁺](#), [Zn⁺⁺](#)), [bilirubin](#) and many drugs.

2. It contributes to the oncotic pressure of plasma and to maintaining the distribution of extracellular fluid between the vascular and extravascular compartments. Note, however, that the effect of a fall in albumin concentration on plasma oncotic pressure in acute illness may be in part offset by an increase in the concentration of other (acute phase) proteins.

3. It is a minor buffer of hydrogen ions.

2 Sample requirements and precautions

2.1 This article relates to the measurement of albumin in serum/plasma; there are also indications for measuring it in urine.

2.2 1. Plasma protein concentrations increase with excessive stasis during venepuncture; blood for albumin measurement should be collected with a minimum of stasis.

2. No other special precautions apply.

3 Summary of clinical uses and limitations of measurements

3.1. Uses

1. Plasma [albumin] reflects hepatic function; it is one of the standard 'liver function tests'.
2. Plasma [albumin] depends on an adequate supply of amino acids for its synthesis and thus on nutritional status and intestinal function.

3.2. Limitations

Plasma [albumin] depends on its rate of synthesis, its rate of clearance and its volume of distribution. It is not a specific indicator of any one of these (though rapid (hours)) changes are most likely to be due to a change in its volume of distribution, either because of an increased plasma water content or net movement into the interstitial space).

4 Analytical considerations

4.1 Analytical methods

Albumin in plasma and serum is measured in routine practice exclusively by dye-binding methods, usually with bromocresol green or bromocresol purple. Albumin binds these dyes with high affinity and the respective complexes absorb light at 628 nm and 600 nm. The response is linear up to at least 60 g/L.

4.2 Reference method

There is no reference method for measurement of serum albumin but a candidate method employing isotope-dilution mass spectrometry is under investigation.

4.3 Reference material

Purified human albumin preparation (CRM 470: Institute for Reference Materials and Measurements, Belgium).

4.4 Interference

- Bilirubin: at concentrations up to 500 $\mu\text{mol/L}$ causes negligible interference.
- Haemolysis: [Hb] 10 g/L causes positive interference (up to 10%)
- Lipaemia: [triglycerides] 11 mmol/L causes positive interference (up to 10%).

4.5 Sources of error

Dye-binding methods under-estimate albumin concentration at low values (<25 g/L); this is not usually a practical problem since such values are invariably pathological.

5 Reference intervals and variance

5.1.1 Reference interval (adults): 35–50 g/L

5.1.2 Reference intervals (others): lower in the newborn

5.1.3 Extent of variation

5.1.3.1 Interindividual CV: 8.9%

5.1.3.2 Intraindividual CV: 2.9%

5.1.3.3 Index of individuality: 0.31

5.1.3.4 CV of method: 3.4%

5.1.3.5 Critical difference: 12%

5.1.4 1. [Albumin] is affected by hydration state.

2. [Albumin] can be up to 3 g/L higher when an individual is ambulant than when recumbent.

6 Clinical uses of measurements and interpretation of results

6.1 Uses and interpretation

1. Liver function

Although albumin is synthesised in the liver, confounding factors limit the value of single measurements as an index of liver function. Its relatively long half life may cause its concentration to remain normal in the early stages of even severe acute liver disease. A falling concentration in chronic liver disease suggests a clinically significant deterioration in liver function 'decompensation'.

2. Nutrition

Although widely regarded as a 'nutritional protein', [albumin] is a poor guide to nutritional status. In simple starvation, the catabolic rate of albumin falls, and this and contraction of ECF volume may cause its concentration to remain normal. Low concentrations, except in severely starved patients, suggest increased catabolism (e.g. due to sepsis) or increased loss (e.g. due to protein-losing enteropathy) (see 9.2(1)).

3. Interpretation of [calcium]

Because approximately 50% of calcium is bound to albumin in the blood, total calcium concentration depends in part on [albumin]. Most analysers employ a formula to 'adjust' measured [calcium] for abnormal [albumin] e.g. 'adjusted' calcium = $0.02(40 - [\text{albumin}]) + [\text{measured calcium}]$ (units: albumin g/L; calcium mmol/L).

6.2 Confounding factors

The many factors that can affect [albumin] make it essential that all are considered before ascribing an abnormal value to any one. Sick patients may have low [albumin] for a combination of reasons, e.g. sepsis, protein loss, decreased synthesis and fluid imbalance.

7 Causes and investigation of abnormal values

7.1 High concentrations

7.1.1 Causes

High concentrations are unusual. The only causes are:

- water depletion
- recent infusion of plasma or other albumin-containing fluids.

7.1.2 Investigation

The cause should be obvious from clinical observations; investigations are not required.

7.2 Low concentrations

7.2.1 Causes

Low concentrations are common. The causes are:

- decreased synthesis
 - inadequate nitrogen intake (6.1(2))
 - malabsorption
 - chronic liver disease (6.1(1))
- increased catabolism
 - sepsis
 - other catabolic states
- increased plasma volume
 - water excess
- redistribution
 - ascites
 - oedema
 - sepsis
- increased loss
 - protein-losing enteropathy
 - nephrotic syndrome
 - loss of plasma, e.g. from burns.

In the rare, inherited condition, analbuminaemia, plasma albumin is typically 250 mg/L or less. Patients experience sporadic, mild, oedema but are otherwise well. In bisalbuminaemia, also a rare, inherited condition, [albumin] is normal but two species of albumin are present and appear as separate bands on zone electrophoresis of serum.

7.2.2 Investigation

Possible causes will usually be apparent from clinical observations. Liver function tests will usually reveal chronic liver disease (but may not in compensated cirrhosis). The possibility of urinary loss of albumin (albuminuria) can be investigated initially with a dipstick. If urinary protein excretion is sufficient to cause a reduced plasma albumin concentration, the urine will be strongly positive for protein.

7.3 Note

Low albumin concentrations are frequently multifactorial, with more than one mechanism being responsible for a low value (e.g. increased catabolism and protein loss in nephrotic syndrome) or a single cause acting through more than one mechanism (e.g. sepsis through increased catabolism and redistribution). Infusion of albumin or an albumin-containing fluid should only be undertaken when there is a clear indication for it, e.g. to initiate a diuresis in nephrotic syndrome. In septic patients it may exacerbate the abnormal distribution of extracellular fluid by increasing the amount in the interstitial compartment.

8 Performance

8.1 Sensitivity, specificity etc. for individual conditions

Measurements of serum albumin concentration have no diagnostic value for individual conditions except that a low concentration in acute illness is related to poor prognosis. Numerous reviews emphasise this, e.g. Nicholson JP, Wolmarans MR, Park GR. The role of albumin in acute illness. *Brit J Anaesthes* 2000;85:599-610.

9 Systematic reviews and guidelines

9.1 Systematic reviews
None identified

9.2 Guidelines

1. Nutrition

NICE Clinical Guideline 32 (2006) *Nutrition Support for Adults Oral Nutrition Support Enteral Tube Feeding and Parenteral Nutrition* indicates that serum albumin concentration should be used to 'correct' measured serum calcium concentrations (see 6.1 (3)) but that in relation to nutrition support, it reflects underlying disease, not nutritional status (see below).

2. Acute illness

Serum albumin concentration <30 g/L contributes to the calculation of the APACHE score developed for prognostic use in acute illness (Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II a severity of disease classification system. *Crit Care Med* 1985;13:818-829). For specific reference to acute pancreatitis, see UK Working Party on Acute Pancreatitis. UK Guidelines for the management of acute pancreatitis. www.bsg.org.uk/pdf-word/pancreatitis.pdf (accessed 21.xii.2010).

3. Chronic liver disease

Serum albumin concentration is a component of the modified Child-Pugh score for assessing prognosis in chronic liver disease, a concentration < 35 g/L being associated with poor prognosis. Pugh RN, Murray-Lyon IM, Dawson JL *et al.* Transection of the oesophagus for bleeding oesophageal varices. *Br J Surg.* 1973;60:646-649.

9.3 Recommendations

Numerous research papers and reviews, including systematic reviews, deal with the use of albumin replacement in hypoalbuminaemic patients: discussion of this topic is beyond the remit of this article.

10 Links

10.1 Because albumin is the major plasma protein, its concentration is a major determinant (together with immunoglobulins) of plasma total protein.

10.2 1. Ischaemia-modified albumin circulates in the plasma following ischaemic damage to tissues and has been investigated as an indicator of myocardial infarction.
2. Prealbumin is a distinct protein; measurements are of value as an indicator of nutritional status.

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