The Determination of Lithium in Serum

Introduction
Lithium is used therapeutically in the treatment of manic depression. During the course of the treatment, serum lithium concentrations are continually monitored to ensure that the toxic limit is not exceeded. The determination must be accurate since the concentration difference between the effective therapeutic blood lithium level (1.0 mEq/L) and the toxic level (1.5 mEq/L) is small. The sample is first deproteinised by addition of hydrochloric acid followed by heating. This avoids the retention of lithium in the precipitate, which is associated with the use of trichloroacetic acid and ethanol. The method is simple for the technician, very reliable and accurate.

Materials Required
Equipment
Jenway PFP7 Flame Photometer, fitted with a lithium filter.
Centrifuge tubes – Approximately 15ml to 20ml capacity and external dimensions 125mm by 16mm or similar. Quickfit or Quartz stoppered tubes are suitable.
Water bath set to approximately 100ºC.
Cold water bath
Centrifuge tube racks suitable for placing in the water bath.

Reagents
1N Hydrochloric acid diluted to a working solution of 0.010N HCl. Store in glass stoppered bottles.
Lithium Sulphate Analar
Deionised Water

Method
Standard preparation
Dissolve 0.19199g of lithium sulphate in deionised water in a litre volumetric and make up to volume. This is a 3.0mEq/l solution of lithium. Diluting this ten-fold gives a 0.30mEq/l solution. Any other desired standards are equally easily prepared. Even very dilute solutions of lithium sulphate are quite stable at room temperatures when stored in glass stoppered bottles.

Sample preparation
1. Pipette 2.0ml of serum into a centrifuge tube. Sera should be free from haemolysis and can be stored at 4°C for two weeks or longer.
2. Add 8.0ml of 0.010N HCl and mix. Leave to stand for a minute or two and the fluid will become cloudy.
3. Place in a simmering water bath for 5 minutes. Vigorously boiling water might cause splashing. The water level in the bath should be higher than that of the contents of the centrifuge tube.
4. Transfer the tube to a cold water bath and, when cool, centrifuge for 5 minutes at 3,000 rpm.
5. Carefully pour the supernatant fluid into a cuvette.

Measurement
1. Aspirate the 0.30mEq/l standard, which, because of the dilution of the serum from 2ml to 10ml, is effectively equal to 1.5mEq/l and adjust the sensitivity to obtain a reading of 50.
2. Aspirate the cuvette contents obtained from the serum under test and from the resultant reading, calculate the apparent lithium content of this serum.
Notes
This apparent value requires correction for blank effect of potassium, sodium, calcium and other ions always present in serum. Several random non-lithium sera should be treated as described above and the average value for these blanks must then be subtracted from the gross result for the serum under test to obtain its true lithium value. Using propane, a mean blank value of 0.22mEq/l with a variation not exceeding 0.03mEq/l may be obtained.

If 3ml of serum is available, 7ml of 0.020N HCl must be used; if only 1ml serum, 9ml of 0.0045 N HCl. The 0.30 mEq/l lithium standard can be used for all three volumes of serum or a 0.45 mEq/l standard can be used for 3ml serum and a 0.15 mEq/l standard for 1ml serum.

Recovery of added lithium can be tested by either of the following methods:
To each of five centrifuge tubes add, respectively, 1.0, 0.8, 0.6, 0.4 and 0.2ml of 3.0 mEq/l lithium sulphate solution in water and place them in an oven at about 105°C. Next day a thin film of lithium salt can be seen in the tubes. To each of the tubes and also to a sixth empty tube, which provides a blank, add 2.0ml of pooled non-lithium serum. Analysis, conducted as previously described, should yield results of 1.5, 1.2, 0.9, 0.6 and 0.3mEq/l of lithium.

A simpler method is to pipette 2.0ml of pooled non-lithium serum into each of six tubes and to add to five of them, respectively, 1.0, 0.8, 0.6, 0.4 and 0.2ml of 3.0mEq/l lithium sulphate solution, leaving the sixth as a blank. The appropriate amount of 0.010 N HCl to bring the volume in each tube to 10ml should then be added.

Agreement within 0.05mEq/l between duplicates and in recovery of added lithium is attainable with 1ml samples of serum but is more easily achieved if 2ml or 3ml samples are available.