LITHIUM INTOXICATION
PROSAR International Poison Center

A. Pharmacology
The exact mechanism of action of lithium is unknown. Possible mechanisms of action include: membrane stabilization; inhibition of NE release; acceleration of NE metabolism; increased presynaptic reuptake of NE and 5HT; increased 5HT receptor sensitivity; altered distribution of Mg, and Ca ions, and altered Na transport in nerve and muscle cells.

Three main factors govern the extent of lithium intoxication:
1. Lithium load
2. Duration of exposure to that load
3. Patient’s ability to handle a given load over a given time period

B. Pharmacokinetics
• Rapidly absorbed within 1-2 hours and the peak plasma concentration occurs 2-4 hours after oral ingestion (4-12 hours with SR)
• Half-life = 22 +/- 8 hours.
• Excreted primarily through the kidneys
• Body handles lithium similarly to sodium and potassium and possibly magnesium since they are similar in size

C. Range of Toxicity
• Approximate dose to produce an acute toxic level (>2 mEq/L) is 40 mg/kg in a single ingestion
• The "therapeutic" level = 0.6 - 1.2 mEq/L. Serum levels are not an accurate predictor of toxicity. With chronic intoxication, toxicity may be seen at levels only slightly elevated from normal secondary to increased CNS levels. With acute ingestion, the patient may tolerate very high serum levels without any signs and symptoms.

D. Clinical Effects
• Main thing to know here is this: The CNS effects of lithium usually predominate in severe cases. The only way you can have CNS effects is for lithium to enter the CNS in significant quantities. In acute overdoses in patients not currently using lithium, there has not been a sufficient amount of time for CNS levels to rise. It usually takes a week of regular dosing to achieve significant CNS levels. These people rarely develop serious symptoms in overdose even though their levels are quite high. On the other hand, people chronically on lithium who overdose or have increases in their lithium levels for other reasons cannot tolerate much of an increase in serum lithium as they already have a significant amount of drug on board. In these cases, levels that are even slightly above normal can coincide with symptoms developing.

Blood level (mEq/L)
1.5 Increased nausea, vomiting, diarrhea (these effects are rarely seen in chronic overdoses)
2.0 Polyuria, blurred vision, muscular weakness, drowsiness, dizziness, vertigo, increasing confusion, slurred speech, blackouts, increased DTR’s, fasiculations
2.5 Myoclonic twitches, hyperreflexia, choreoathertoid movements, urinary and fecal incontinence, increasing restlessness followed by stupor progressing to coma.
3.0 Seizures, cardiac arrhythmias (eg. T wave flattening/inversion)
4.0 Hypotension, peripheral vascular collapse
E. Decontamination

- Decontamination using gastric lavage is indicated for acute lithium ingestions presenting early.
- AC/C is also indicated IF you suspect coingestants. (monovalent cations are not bound)
- WBI is indicated in late presentations (> 2 hours) and ingestions involving the sustained release formulations of lithium, provided the patient has no contraindications to its use.

F. Treatment

1. Supportive care
2. Discontinue lithium; check for diuretics (thiazides can increase lithium level), haldol (potentiated effect of lithium and increased risk of neuroleptic malignant syndrome), phenothiazines (potentiated neurotoxic effect of lithium)
3. Maintain sodium and water balance. In the dehydrated patient, replace fluids and Na with normal saline. Once the patient is rehydrated, continue to maintain fluid balance with 1/2 NS. Hydration will increase lithium filtration in patient’s with normal renal function.
4. Obtain serum lithium level - See below under "Monitoring "

5. Indications for dialysis
   a. Any patient with serious clinical manifestations (eg. hemodynamic compromise, arrhythmias, or seizures) should be dialyzed.
   b. Any patient with renal failure who has symptoms or the potential to develop them should be dialyzed
   c. In patients with chronic intoxication (eg. secondary to Na/water imbalance), dialysis should be considered at levels of > 2.0 - 2.5 mEq/L regardless of signs and symptoms
   c. Patients with acute ingestion (ex. suicide), with levels above 4 mEq/L regardless of s/sx should be considered for dialysis. (note: levels of 9mEq/L have been managed without s/sx developing that did not require dialysis)

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<table>
<thead>
<tr>
<th>Organ System</th>
<th>Acute</th>
<th>Chronic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>Prolonged QT</td>
<td>Myocarditis</td>
</tr>
<tr>
<td>Cutaneous</td>
<td>None</td>
<td>Dermatitis, edema</td>
</tr>
<tr>
<td>Renal</td>
<td>Concentrating defects</td>
<td>Nephrogenic diabetes insipidus, renal failure</td>
</tr>
<tr>
<td>GI</td>
<td>Nausea, vomiting</td>
<td>Minimal</td>
</tr>
<tr>
<td>Hematologic</td>
<td>Leukocytosis</td>
<td>Aplastic anemia</td>
</tr>
<tr>
<td>Neurologic Mild</td>
<td>Weakness, fine tremor</td>
<td>Same</td>
</tr>
<tr>
<td>Neurologic Moderate</td>
<td>Muscle twitching, tinnitus, hyperreflexia, lethargy</td>
<td>Same</td>
</tr>
<tr>
<td>Neurologic Severe</td>
<td>Confusions, convulsions, coma, clonus</td>
<td>Parkinson’s, psychosis, memory deficits</td>
</tr>
<tr>
<td>Endocrine</td>
<td>None</td>
<td>Hypothyroidism</td>
</tr>
<tr>
<td>Other</td>
<td>Hyperthermia</td>
<td>Rhabdomyolysis</td>
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</tbody>
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Table taken from Goldfranks Chapter 59 1998.
6. Sodium polystyrene sulfonate (SPS; tradename - Kayexalate) may be useful in lowering the serum lithium level of some patients with acute lithium intoxication. **It is not a substitute for hemodialysis.**
   - Animal studies show that large quantities are needed to be effective, much larger than doses used to treat hyperkalemia. Because of this hypokalemia can be induced which will further complicate problems thus limiting its role.
   - If the decision to use SPS is made, it is important that fluid and electrolyte status of the patient be maintained at normal levels as increases in sodium and decreases in potassium may occur. SPS is contraindicated in patients with congestive heart failure and renal failure due to the sodium load potential associated with SPS.
   - Dosing: (Not well established) PO: 30 grams in sorbital (120 ml of suspension) q 6 hours, Rectally: Same dose.

G. Monitoring
1. EKG, vital signs, CBC, electrolytes (especially Na and K), BUN, SCr, thyroid function tests
2. Monitor for s/sx of neurological toxicity as mentioned previously under clinical effects. Hyperthermia and rhabdomyolysis can occur in patients with significant tremor and/or seizures.
3. Serum levels:
   - Serum conc. should be checked initially and every 2-3 hours until the levels stabilize.
   - If dialysis is initiated, the lithium level should be checked before dialysis, during the run, and at the end of dialysis, The desired endpoint is < 1 mEq/L.
     - Redistribution can be seen 6-12 hours post dialysis so another level should be checked about 6 hours after dialysis
     - Further dialysis may be required if levels continue to increase or symptoms are still present

REFERENCES