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## Revolution in mental health and nursing, after discovery of lithium

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### Abstract

**History:** It is an element. It gets its name from “lithos,” the Greek word for stone, because it is present in trace amounts in virtually all rocks. Lithium works with other elements, drugs, enzymes, hormones, vitamins, and growth factors in the body in many different ways. John Cade introduced lithium carbonate for the treatment of mania in 1949, opening the era of modern clinical psychopharmacology. Lithium remains the most extensively studied mood-stabilizing agent. It has had a revolutionary impact in supporting bipolar manic-depressive disorder as a discrete diagnosis, and on psychiatric therapeutics. **Methods:** We survey the development of lithium treatment in psychiatry, including findings concerning effects on suicide.

**Results:** Lithium is the most extensively studied treatment for bipolar disorder and the prototypical mood-stabilizing agent, despite emergence of anticonvulsants and modern antipsychotics. In addition to limiting recurrences of mania, and some reduction of recurrences of bipolar depression, lithium has demonstrated protective effects against suicide. All treatments for bipolar disorder have notable limitations, including sometimes serious Adverse effects includes hypothyroidism, Pregnancy and breast feeding side effects such as birth defects, dehydration incomplete prevention of recurrences of mania and limited prevention of depression, which accounts for the approximately 55% time-ill in long-term follow-up with standard treatments. Lithium can be toxic in untreated overdoses; safe dosing requires monitoring of serum concentrations. Lithium also may have mild teratogenic effects, but far less than those of anticonvulsants used for bipolar disorder.

**Conclusions:** Lithium opened the era of modern psychopharmacology and continues as the best-established mood-stabilizing treatment for bipolar disorder as well as having strong evidence of suicide-preventing effects.

Uses of lithium, First effective treatment for acute mania, Prime example of the value of serendipity, First selective treatment for mania versus psychotic disorders, Encouraged broad acceptance of the concept of bipolar disorder, - First effective treatment for acute mania, Prime example of the value of serendipity, selective treatment for mania versus psychotic disorders, Encouraged broad acceptance of the concept of bipolar disorder Opened the era of modern psychopharmacology, since 1950 First treatment with long-term prophylactic efficacy in any major psychiatric disorder, first treatment with substantial evidence of suicide-preventing effects, first psychiatric treatment with clinically useful drug monitoring by serum assays. First selective treatment for mania versus psychotic disorders.

**Keywords:** Mood stabilizers. bipolar disorder, depression, lithium, mania, mood disorders, suicide

### Introduction

#### Current clinical status of lithium in psychiatry

Lithium treatment is still considered the “gold standard” of treatment for bipolar manic-depressive illness. However, it has gradually become underutilized, for several probable reasons. Its reputation arising in the late 1940s as a toxic substance has not entirely disappeared, despite long-established standards for its safe use with monitoring of serum concentrations of lithium.

Fears of intoxication currently are more often directed to putative renal toxicity with long-term use of lithium, although such effects are uncommon and can usually be anticipated by rising serum concentrations of creatinine or declining efficiency of creatinine clearance (7, 34).

There may also be a “stigmatizing” effect of the use of lithium for some patients and families, in contrast to the use of seemingly less threatening antidepressants, anticonvulsants, and other psychotropics (7). An important additional factor is that lithium salts, as unpatentable minerals of little commercial interest, have received little support for research and development or for assertive marketing.

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In some countries, particularly in the US, vigorous promotion of alternative, patentable, and highly profitable treatments have led to substantial displacement of lithium, although it continues to hold a major position among treatments for bipolar disorder internationally and tends to be used for longer times than most alternatives (7, 35, 36).

### **Oxidative metabolism**

Evidence suggests that mitochondrial dysfunction is present in patients with bipolar disorder. Oxidative stress and reduced levels of anti-oxidants (such as glutathione) lead to cell death. Lithium may protect against oxidative stress by up-regulating complex I and II of the mitochondrial electron transport chain.

### **Dopamine and G-protein coupling**

During mania, there is an increase in neurotransmission of dopamine that causes a secondary homeostatic down-regulation, resulting in decreased neurotransmission of dopamine, which can cause depression. Additionally, the post-synaptic actions of dopamine are mediated through G-protein coupled receptors. Once dopamine is coupled to the G-protein receptors, it stimulates other secondary messenger systems that modulate neurotransmission. Studies found that in autopsies (which do not necessarily reflect living people), people with bipolar disorder had increased G-protein coupling compared to people without bipolar disorder. Lithium treatment alters the function of certain subunits of the dopamine associated G-protein, which may be part of its mechanism of action.

### **GABA receptors**

GABA is an inhibitory neurotransmitter that plays an important role in regulating dopamine and glutamate neurotransmission. It was found that patients with bipolar disorder had lower GABA levels, which results in excitotoxicity and can cause apoptosis (cell loss). Lithium counteracts these degrading processes by decreasing pro-apoptotic proteins and stimulating release of neuroprotective proteins.

### **Conclusions**

The preceding overview indicates that the introduction of lithium for the treatment of mania in 1949 has exerted broad and powerful effects on modern psychiatry—far beyond proving to be a highly effective and selective treatment for bipolar disorder. Lithium made the work of nurses easy because it rapidly eases the mood of the bipolar disorder clients.

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