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Lithium Treatment in Clinical Medicine: History, Current Status and Future Use

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Abstract

Lithium treatment was present in the first half of the twentieth century, but little to no attention was given to lithium in psychiatric literature at that time. This noticeable decline in the popularity of lithium could be attributed to the inquiries into lithia water and lithium tablets, which were frequently used in the late 1800s and early 1900s as lithium treatment delivery options. Lithium's noticeable reappearance began in 1949 when John Cade used lithium to treat maniac patients, hypothesizing their sporadic excitement to be a result of a uric acid condition, which was also preventing normal discharge functioning. Lithium is a versatile drug that can be used in a variety of ways to reduce and prevent symptoms of various disorders. There are some areas of lithium research, however, that seem more promising in terms of yield ground-breaking treatment options for serious and currently incurable illnesses. Though ample research has been conducted to understand lithium's abilities and effects, more is required to comprehensively assess how lithium works to counteract abnormalities contributing to disorders and diseases. Hematology, as well as many other fields of science, benefit from lithium use and need to continue to observe its capabilities.

Keywords: Hematology; Incurable illnesses; Tenderness; Lithium Chloride

Introduction

Though lithium treatment in psychiatry has been present since the 1850s, lithium use did not become well known until nearly a century later, in the 1940s. Early uses of lithium treatment were for gout (Figure 1), as a hypnotic or anticonvulsant, general nervousness, control of renal calculi and mania and depression.

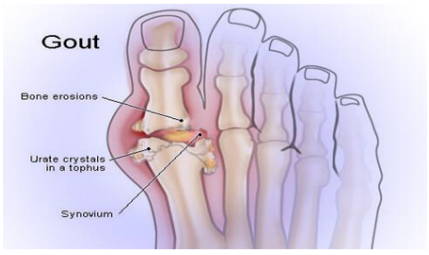

Figure 1: Gout, or painful tenderness and swelling of joints, was once treated with drugs containing lithium.

Lithium treatment was present in the first half of the twentieth century, but little to no attention was given to lithium in psychiatric literature at that time [1]. This noticeable decline in the popularity of lithium could be attributed to the inquiries into lithia water (Figure 2) and lithium tablets, which were frequently used in the late 1800s and early 1900s as lithium treatment delivery options. The U.S. Bureau of Chemistry found little to no lithium present in these waters, and the medicinal advantages found by their consumption were attributed to the water ingestion only [2]. Lithium tablets became a verifiable solution to Lithia water, as the amounts of lithium consumed could be known and controlled. As tablet concentrations were increased, however, toxic side effects became apparent. Side-effects included weakness, tremors, blurred vision and dizziness. Because lithium's therapeutic benefits could not be verified and tighter government regulation of drug administration became standard, lithium became a less prominent option for therapeutic treatments [3].

After one studies failed attempt to use lithium chloride to reduce sodium intake in at risk patients, with the study resulting in reports of severe lithium intoxication and multiple deaths, Time Magazine wrote an article about the dangers of lithium usage. The article informed the public of the FDA's order of manufacturers to stop producing salt substitutes containing lithium. This article also noted lithium's toxic effects had been well known in research for decades. Ultimately, this information confirmed the fears of lithium use, and lithium continued to maintain its negative connotation in the pharmalogical world [3].

Figure 2: This is an advertisement for Lithia water from 1888, a popular treatment option at that time.

Lithium's noticeable reappearance began in 1949 when John Cade used lithium to treat maniac patients, hypothesizing their sporadic excitement to be a result of a uric acid condition, which was also preventing normal discharge functioning. He found some patients, after treatment, retained relatively normal discharge abilities [4]. Cade's findings drew interest to lithium treatment, and others began to individually observe the effects lithium could have on patients. Results from other studies suggested lithium treatment to be more advantageous than harmful, as well as a noticeably effective treatment for maniac phases of psychosis [5].

Even with the evidence of the benefits of lithium treatment known, this treatment for manic-depressive disorders was not prominent until 1952, when Erik Stromgren conducted a random control trial to treat mania *via* lithium. Results of this study suggested lithium as a more convenient alternative for treating mania than electroconvulsive therapy (ECT), the standard therapy at that time [6]. This study attracted much attention to lithium usage in drugs, and brought lithium into the psychiatric pharmacology spot light.

Lithium was not approved for medicinal treatment of mania until 1970, and it was not approved for prevention of recurrent mania until 1974 [3]. To date, the Federal Drug Administration still does not approve of lithium usage to prevent depression. Regardless, research has supported the hypothesis that lithium treatment is, in fact, advantageous for maintenance of depression. One study found 29% of patients chronically treated with lithium relapsed into their depression. The relapse rate for the placebo group was much higher, with 74% of patients reporting regression back into their depressive states [7]. While lithium is not the only effective treatment for mania and depression, it does have the lowest relapse rate, indicating more effective long-term solutions for these disorders.

Common Effects of Lithium Treatment

Lithium is considered a controversial treatment for reasons including potential toxicity and the side effects caused by its use. A decrease in the use of lithium for bipolar disorder has been seen in the United States, along with other countries, and psychiatrists contribute this decline to the difficulty of determining the proper dose for patients [8]. Those treated respond to dosage amounts differently, and even though there are generalized dosages recommend for different populations, ultimately the provider must determine the most efficient amount of lithium needed to treat someone, without overmedicating.

Fortunately, serum levels of lithium are accurate, easy to monitor and inexpensive to observe. Though side effects of lithium treatment have been studied for years, little information on appropriate treatment amounts of lithium have been found, and minimal research has been dedicated to this topic. To validate healthy and safe lithium treatment levels, much more research in this area needs to be conducted and published [8].

Lithium, as with most other medications, can cause both positive and negative side effects. Positive effects of this treatment type include decreasing suicide and suicidal ideation in mood disorder patients chronically treated with lithium [9]. Meta-analysis of almost 15 randomized controlled trials also confirms lithium's ability to reduce manic relapses, supporting the element's prophylactic efficacy.

Common negative side effects of lithium use include increased thirst and urine output, fine hand tremors, nausea, appetite loss, diarrhea, sedation and dizziness. These side effects can, and often do, subside after the patient's body acclimates to this foreign substance. More serious and potential side effects can occur, though rare, and these include kidney problems, with the most common being diabetes insipidus, and various thyroid conditions, including hypothyroidism [10].

Diabetes insipidus, the most common renal disorder resulting from lithium use, results in abnormally large amounts of odorless and dilute urine being produced. This can lead to extreme dehydration, which if left untreated, can cause fatal damage to the human body [11]. Initially, diabetes insipidus is reversible if the patient's lithium treatment is removed, but irreversible damage may be found due to structural damage if this disorder is not found early enough (Figure 3) [8].

Figure 3: Depending on the severity of the diabetes insipidus, dehydration can result in dark, dilute urine, such as urine samples 4-7.

Lithium inhibits thyroid production through multiple mechanisms. The element can interfere with the formation of the thyroid hormone. It can also prevent properly functioning thyroid hormone from entering the blood stream. Lastly, lithium affects T4, the completed thyroid molecule, by altering its ability to transition to its active form, and thus altering the molecule's ability to travel in the blood [12]. These thyroid conditions can usually be treated with thyroid hormone, but only after lithium use has been stopped. The patients can develop permanent hypothyroidism, even after halting lithium treatment, and he or she may need to continue thyroid hormone treatment for the remainder of his or her life [12].

One should note that thyroid complications caused by lithium treatment have been more prominent in certain populations. Those using lithium are more likely to develop thyroid disorders if they are female, overweight, being treated with large lithium dosages, have a relative with thyroid abnormalities, experience rapid-cycling bipolar disorder or have thyroid hormone deficiencies before beginning lithium treatment [12].

All patients should be diligently monitored before, during and after lithium treatment has been administered. Many psychiatrists have found simply reducing the dosage of the lithium treatment given can eliminate most of these side effects, but this is not always an effective solution. Ultimately, lithium treatment must be individualized to address each patient's specific needs, and more consistent research on how to prevent and eliminate these negative effects will need to be conducted (Figure 4).

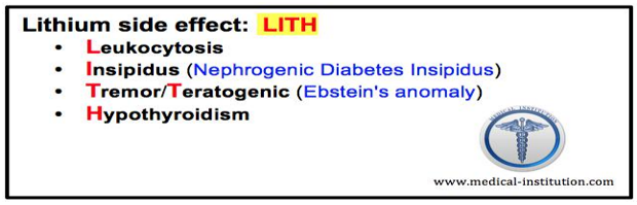

Figure 4: Pneumonic used by providers to recall commonly seen side effects of lithium treatment.

Neurological Effects of Lithium Treatment

Lithium's classification as a neuroprotective agent or a neurotoxic agent is still controversial, though its effects are becoming more apparent through research. Neuroprotective effects found include preventing accumulation of amyloid-beta peptide, which overproduce a precursor amyloid protein. By inhibiting this accumulation, lithium prevents the hyperphosphorylation of tau proteins, which are an essential component of the neurofibrillary tangles found in the brains of those with Alzheimer's disease [13]. Other research has found lithium use increases the abundance of a possible marker of neuron function and viability in all regions of the brain, and it also increases the amount of grey-matter volume in the brain [14].

Lithium use has also been found to prevent alkaloid neurotoxicity that stimulates muscle damage and neuropathy of peripheral systems [15]. Current research is supporting the use of lithium as a treatment option for chronic neurodegenerative diseases, ischemia, which is insufficient blood supply to parts of the body, and acute brain injuries. Lithium also increases the amounts of marrow and neuronal derived stem cells present in an individual. As is well known, stem cell therapy is being used to treat many disorders, and is a research area of great promise today.

Thus, lithium's ability to influence stem cells makes it's a potential solution for treating disorders associated with blood production abnormalities, such as by enhancing blood stem cell movement and making these cells more viable for transplantation (Figure 5)

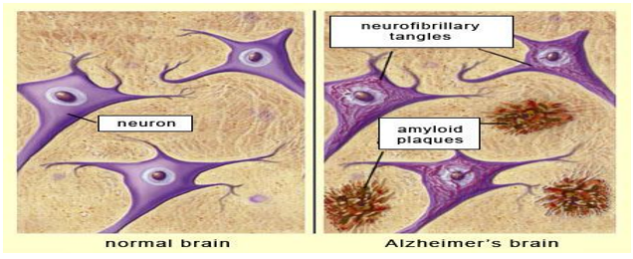

Figure 5: Reports have shown lithium therapy can prevent formation of amyloid beta plaques and neurofibrillary tangles composed of hyper-phosphorylated tau proteins.

In contrast, neurotoxic effects of lithium use include delay of sensory and motor nerve conduction [16], impaired fast single-joint movement due to altered cerebral control [17] and alterations in clinical electroencephalograms [18]. One study reported 36.8% of psychiatric young adult patients treated *via* lithium presented with neurological abnormalities, where only 5% of healthy control patients presented with such abnormalities.

Higher rates of neurotoxicity from lithium treatment, however, were found in the patients diagnosed with more than one primary affective disorder [19]. This calls into question whether some of these neurotoxic effects are a direct result of lithium treatment, or an indirect result of the interaction of lithium with other drugs used to treat various primary affective disorders. More research in this are must be completed before any sort of definitive conclusion can be found.

Though some experts report studies on lithium's neuroprotective and neurotoxic effects to be too inconsistent to definitively classify the element [20], lithium's neuroprotective effects have been more prominent in the past, and in recent cases and research studies analyzed. While some studies found lithium treatment to increase the likelihood of developing dementia [21], more evidence in research published supports lithium's neuroprotective abilities against dementia [13].

Again, one must reiterate that reactions to lithium treatment will vary for each patient, and these reactions depend on a variety of factors, including genetics, other physical problems and mental disorders. Prescribers should start patients at the lowest effective treatment dosage of lithium and monitor any and all side effects.

Hematological Effects

Lithium use has been found to have significant and noticeable effects on various components of human blood, including, but not limited to, hematopoietic stem cells, neutrophil counts, granulocyte counts, thrombocyte counts, dendritic and monocyte cell counts and immune system function. As previously mentioned, lithium use results in an increased amount of pluripotential hematopoietic stem cells (HSC) [22]. Lithium is able to increase HSC proliferation by improving the stem cell's ability to move to various bone marrow sites, thus allowing optimal proliferation capabilities. Also, at the dosages commonly used in psychiatry, lithium protects HSCs from mutation after radiation, chemotherapy and other common anti-cancer treatments. In fact, lithium therapy in addition to chemotherapy was more effective at eliminating melanomas than chemotherapy alone. This drug combination may therefore be more advantageous for eliminating cancerous cells, and should be further studied [22].

Lithium use has also been found to elevate neutrophil production and upregulate granulocyte-macrophage-colony stimulating factor (GM-CSF) production [23]. One study found the neutrophil counts in eight patients increased an average of 88% after three to four weeks of lithium therapy [24]. In fact, lithium therapy can increase neutrophil counts so much a patient can become neutrophilic, or have a higher than normal amount of neutrophils produced and circulated (Figures 6-9). Studies have shown when lithium treatment is administered, urinary excretion of granulocyte(G)-CSF increases because more of G-CSF is in circulation [25]. Lithium is able to increase neutrophil and granulocyte populations through two mechanisms. The first mechanism is through direct stimulation of HSC production, and the second mechanism is through upregulation of humoral regulators, including CSFs, resulting in increased granulopoiesis [22].

Lithium increases platelet counts in the circulating blood by upregulating megakaryopoiesis, the process that results in the

production of thrombocytes. Lithium therapy has even been shown to reverse thrombocytopenia initially caused by chemotherapy [26]. These results support using lithium as a therapeutic treatment option for platelet and megakaryocyte disorders and abnormalities.

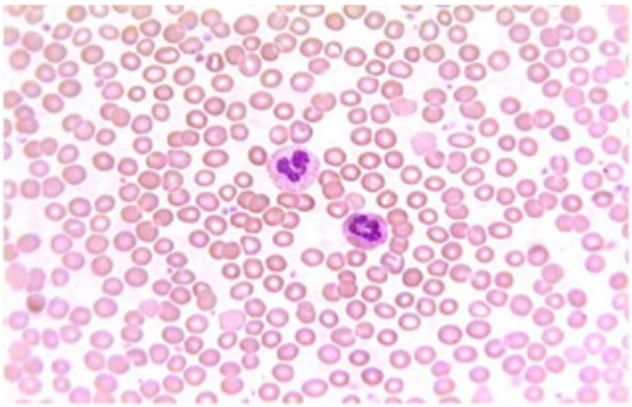

Figure 6: It is representative of a normal blood smear.

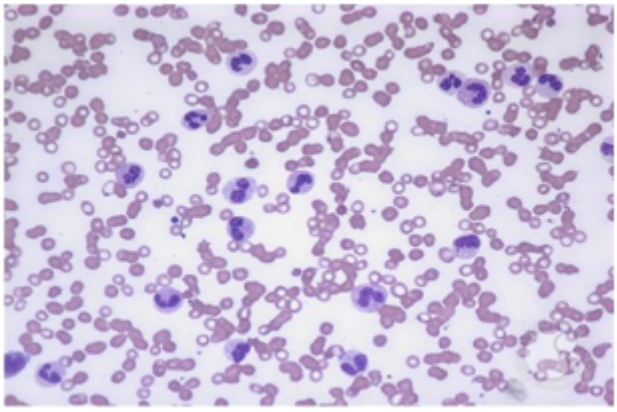

Figure 7: It shows neutrophilia, a possible effect of lithium treatment.

The reticuloendothelial system can also be influenced by lithium use, as lithium can increase the production of dendritic cells and monocytes. Most of the studies supporting this, however, used lithium treatment levels too high for clinical therapeutic uses. At dosages this high, lithium seems to be unable to increase numbers of precursor progenitor cells, which are the initial cells that divide and differentiate into the different white blood cell types and platelets mentioned above [27]. One study, however, reported a significant increase in monocyte and macrophage counts in cancer patients treated with a recommended dosage of lithium, indicating lithium can still affect these cell counts without potentially dangerous lithium ingestion [28]. Before lithium can be consistently used to increase dendritic cell and monocyte counts, more studies about its significant contribution to these increased counts will have to be completed and confirmed.

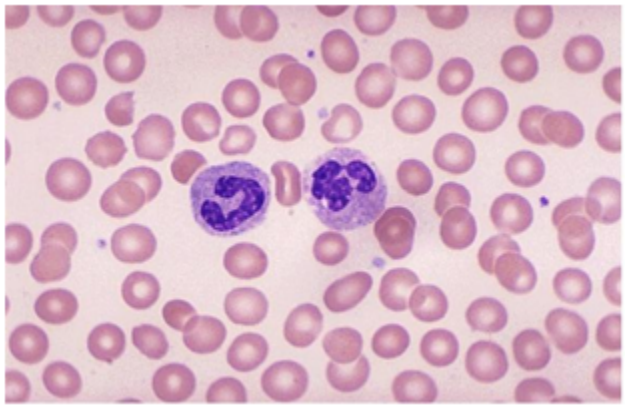

Figure 8: It is representative of a normal platelet count in a blood smear.

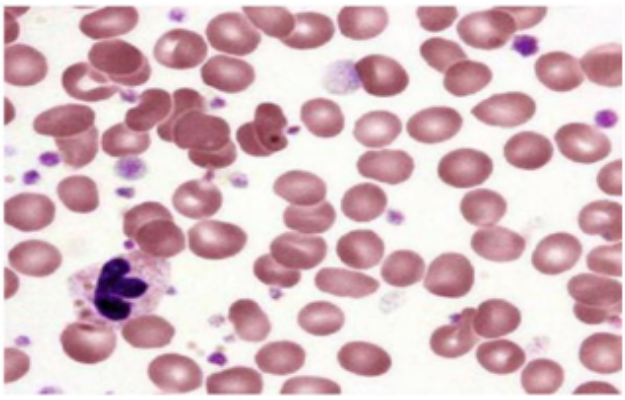

Figure 9: It shows what increased platelet counts, or thrombocytosis, looks like in a blood smear.

Research indicates lithium use is actually advantageous for the immune system. Multiple lymphocyte functions are altered when this element is present. Effects include IgG and IgM production increase, E-rosette formation alteration and more [29,30]. These findings support the use of lithium to assist in treating a variety of diseases and disorders, as the immune system is the body's form of protection against foreign substances, and lithium is strengthening the immune system.

Therapeutic, Hematological and Viral Uses

Lithium's ability to improve and reverse hematological disorders has made the element a treatment option for various hematological abnormalities. Lithium has been found to improve multiple types of neutropenias and leukopenias. With cases of idiopathic neutropenia, if the main inhibitor is insufficient or abnormal production of Granulocyte-Megakaryocyte Colony Stimulating Factor (GM-CSF), lithium treatment can increase GM-CSF levels, thus increasing the production of neutrophils [31]. If someone suffers from Fetty's Syndrome, or a lower than average neutrophil count due to insufficient granulocyte growth factor, lithium can be administered to the

individual to increase granulocyte growth factor production. The increased amount of neutrophils in circulation in Fetty's Syndrome patients after receiving lithium treatment is correlated with a significant decrease in the duration and amount of infections found in these patients. This information supports lithium use for neutropenia because it confirms these newly formed neutrophils are functioning properly [22]. Also, in treatment of infectious neutropenia, studies have found lithium increases hematological recovery with or without the presence of anti-viral drug therapy [32].

One case report observed a patient which schizoaffective disorder, which is characterized by symptoms of both an affective mood disorder and schizophrenia. Schizoaffective disorder is found in approximately 0.3% of the population, and this chronic mental health condition is not easily diagnosed, nor is it well understood [33]. Some of the antipsychotic drugs used to treat schizoaffective disorders, specifically paliperidone and valproic acid in this case, can have harmful side effects including neutropenia and leukopenia. When the valproic acid dose was decreased and lithium carbonate therapy was initiated, both the neutropenia and leukopenia improved. Also, as is important to note, this alteration in the patient's treatment plan did not influence her psychotic symptoms, indicating lithium's ability to interact act with, but not completely inhibit, another drug (Figures 10 and 11) [34].

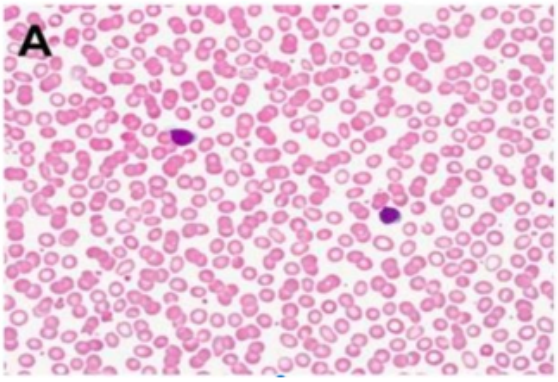

Figure 10: It shows the blood smear of a person with neutropenia.

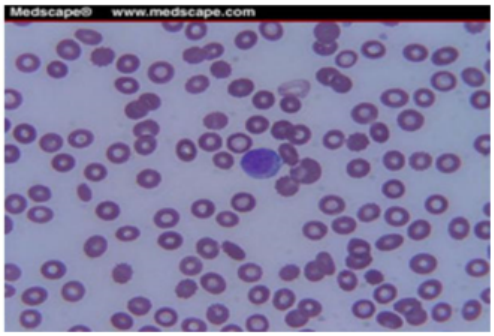

Figure 11: It shows the blood smear of a patient with leukopenia.

Lithium has also worked as an anti-viral agent by decreasing recurrent DNA viruses, such as the herpes virus [35-37]. In order to prevent virus replication, however, the lithium treatment dose must be higher than the recommended amount, thus posing as an increased risk for lithium toxicity. Viable alternatives have been suggested to avoid such toxicity, and these methods focus on lithium's ability to serve as a competitor to magnesium, and other polymerase and transcriptase enzymes, in enzymatic reactions required for RNA replication. If lithium effectively replaced these enzymes, viral replication could be inhibited, and viral number increase could be prevented [22]. Because of lithium's ability to inhibit DNA viral proliferation, researchers believe lithium may be able to prevent proliferation of human immunodeficiency virus (HIV), as it contains a DNA intermediate in its life cycle (Figure 12). As HIV gradually decreases the immune system's ability to fight off infections, it greatly affects white blood cell counts being produced and in circulation. If lithium were able to successfully inhibit HIV proliferation and differentiation, the element would effectively be preventing many hematological disorders that are a result of HIV positive patient's inability to fight off infections and diseases. Laboratory studies using lithium treatment on the murine acquire immunodeficiency disease model (MAIDS) resulted in weakened development of diseases associated with late stage MAIDS [38,39]. Lithium treatment also resulted in a significant mortality decrease in the animals used in the study. Multiple reports have found lithium treatment improves neurocognitive function in patients who are HIV positive [40,41]. Though the exact mechanism through which lithium successfully reduces neurocognitive abnormalities is not definitively known, a significantly positive correlation has been found between decreased neurocognitive dysfunction and increased lithium use and glycoprotein (gp) 120, a glycoprotein associated with HIV inhibition [41].

Even though the effects of lithium therapy on HIV are apparent, lithium's exact antiviral mechanism has not been discovered. As previously mentioned, clinically acceptable lithium concentrations are not enough to prevent or slow viral replication. Since lithium toxicity has to be avoided, alternative methods for lithium delivery, such as replacing enzymes present in the process of reverse transcriptase, must be considered. A topic of concern, however, is lithium's potential inability to unbind or detach from the enzyme inhibited. Recent studies have focused on other viable mechanisms of use, specifically targeting defense mechanisms of the host cell [42,43].

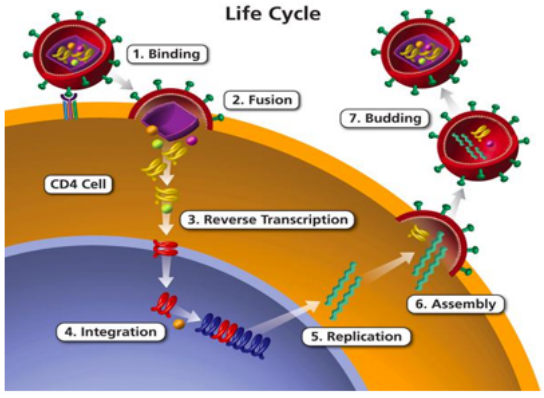

Figure 12: The life cycle of the HIV virus includes reverse transcriptase, where RNA is translated back into DNA.

Other Therapeutic Options for Hematological Disorders

Lithium's ability to increase humoral regulating factors for hematopoietic stem cells makes it a potential treatment alternative to stem cell transplantation, a painful and difficult treatment option (Figure 12). There is concern, however, about lithium's use because lithium toxicity can occur, and can result in permanent, life altering damage to patients. Lithium use for stem cell replenishment will need to be further assessed before becoming a regular therapy for low blood cell counts, but this treatment option may be a viable alternative to stem cell transplantation, especially in those with weak immune systems, such as patients with HIV.

Multiple treatment options for neutropenia exist, and depending on a patient's circumstances, may be more advantageous than lithium treatment. Additional treatment options include granulocyte transfusions, white blood cell (WBC) and G-CSF administration, consumption of antifungal medications and antibiotics to prevent infections, intravenous immune globulin and corticosteroid therapy [44]. With cases of severe neutropenia, stem cell transplantation may be a more profitable option, especially if the cause of neutropenia is a genetic abnormality resulting in abnormal neutrophils [45]. The best treatment type will depend on multiple factors, including what other treatments a patient is undergoing, other medical problems currently present, the underlying cause of the neutropenia and much more. Lithium, as previously discussed, is an excellent option for treatment when the neutropenia's cause is insufficient or abnormal growth factor production. The fact that lithium's mechanism of growth factor enhancement is unclear, however, does raise concern for lithium's safety and potentially negative effects. Also, lithium consumption by the patient will have to become a daily event, as once the lithium use stops, neutropenia can reappear. Much more inquiry into lithium's abilities to reverse neutropenia must occur, and strong evidence of its advantageous results, and minimal side effects, will need to be found before lithium becomes a more common treatment for neutropenia.

Neutropenia is a subtype of leukopenia, or a lower than acceptable amount of white blood cells in one's blood circulation. Leukopenia can be a result of multiple factors, including but not limited to, infections, cancers and autoimmune diseases. Even arsenic exposure can result in leukopenia [46]. Though many factors can attribute to the appearance of leukopenia, this blood abnormality is most commonly a side effect of other drug treatments, specifically anti-cancer drugs. This blood disorder also has multiple treatment options, including chemotherapy and cytokine therapy to raise WBC counts, and vitamin and steroid intake to increase WBC counts [47]. Again, lithium's ability, though the exact pathway is not known, to increase WBC growth factors and thereby increase WBC production, makes the therapeutic use of the element a plausible option for leukopenia. More severe leukopenias, such as those caused by genetic abnormalities or chronic diseases, may be better treated *via* marrow transplant. As was previously mentioned, lithium therapy seems to be most advantageous when the cause of a blood disorder is due to lack of growth factor. If leukopenia's underlying cause is not growth factor insufficiency, other treatment options may be more effective. Most importantly, all options should be discussed in depth with one's health care provider, and all treatment plans should be considered (Figure 13).

Lithium treatment has been of great interest in research and in medicine over the past century. It's calming abilities, along with other advantageous effects, were recognized early in its use, but as regulations of drug treatments and acceptable doses began to be enforced, lithium was pushed aside because of controversies surrounding the element's actual therapeutic abilities. Research studies in the 1950s brought lithium therapy back to the attention of physicians and researchers, and the element is now most well-known for the ability to prevent manic relapses from occurring in those with bipolar and other primary affective disorders. Lithium therapy has also been reported to prevent depression relapses in representative populations, but the FDA has yet to approve it as a treatment option for recurrent depression. Though some disagreement over lithium's benefits being more significant than potential damage remain, most experts now agree lithium should be considered and used as treatment for various disorders.

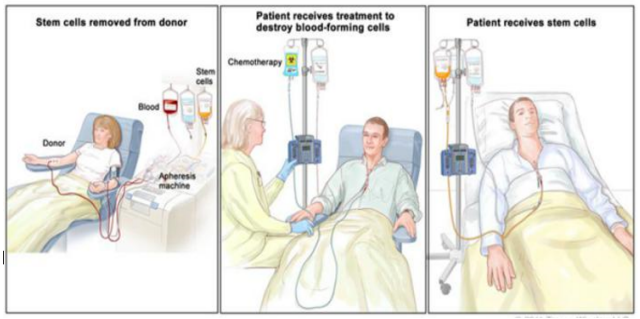

Figure 13: Alternative treatment options for hematological disorders include stem cell transplantation, which requires finding a matching donor and undergoing invasive therapy.

As with other therapies, lithium treatment can result in both beneficial and harmful effects. Effects vary from patient to patient, but some are found to frequently and consistently appear in treatment populations. Positive effects include reduced manic relapse rates in patients with mood disorders. A decrease in suicide attempts and suicidal thoughts have been attributed to lithium therapy as well. Lithium treatment, when combined with chemotherapy, has even been found to be more effective at eliminating melanomas than chemotherapy alone. Negative effects found include dizziness, nausea, hand tremors, sedation, appetite loss, increased thirst and urine output and also renal complications. Often, these negative effects of lithium therapy can be eliminated by simply decreasing the dosage of lithium being received.

Though less common, more severe symptoms can appear when lithium therapy is having harmful effects on a patient. These symptoms include diabetes insipidus, a renal disorder that can result in extreme dehydration, and thyroid function abnormalities such as hypothyroidism, or insufficient amounts of thyroid hormone being produced and distributed. If recognized early, diabetes insipidus can be reversed, but if not addressed until later, potential permanent damage may occur. Hypothyroidism can also be reversed, but lithium therapy has to stop in order for the thyroid hormone production to return and be maintained at normal levels. As lithium use can alter thyroid function in multiple ways, the specific abnormality caused by lithium use should actively be pursued to better address the problem. Before lithium treatment is initiated, patients should discuss all treatment options with their providers, along with which therapy may be most beneficial for each individual. Also, especially at the beginning of treatment, patients must be closely monitored for any potential side

effects of lithium ingestion, and dosages must be adjusted accordingly. As previously mentioned, one grand uncertainty of lithium is appropriate dose amounts for different populations. More studies need to be performed pertaining to this topic and until more consistent definitive values are found, all lithium treatment dosages should begin at the amount recommended by the FDA. From there, providers can increase the amounts administered, if no negative side effects are discovered. If followed, this protocol can reduce the prevalence of negative side effects and lithium toxicity in treated populations.

Another area of great inquiry for lithium is its neuroprotective and neurotoxic effects. Neuroprotective effects include increasing grey brain matter volume and preventing dementia by inhibiting hallmark processes that result in memory loss. Neurotoxic effects found include impaired single-fine joint movement and delays in some types of nerve conduction. Research and literature reviews have more strongly supported the neuroprotective effects of lithium, and lithium therapy is currently being investigated as a potential treatment option for Alzheimer's disease, along with other forms of dementia.

Pertaining to blood cells, lithium use has been found to increase hematopoietic stem cell production and increase multiple white blood cells counts. Though lithium's exact mechanism of action is not completely known, two possible pathways have been found. In one, lithium use increases WBC counts by increasing stimulation of hematopoietic stem cells. In the other mechanism, lithium seems to improve blood cell production by increasing amounts of humoral growth factors needed for different WBC proliferations to occur.

Lithium therapy's ability to increase WBC counts makes it a potential treatment option for multiple abnormalities of the blood. This treatment type has significantly increased neutrophil counts in those with neutropenia, and it has also significantly increased leukocyte counts in those suffering from leukopenia. Other treatment options for both hematological disorders exist, but lithium therapy, especially for those with mild forms of these disorders, could be a less invasive therapeutic strategy than other treatments, such as undergoing a bone marrow transplant.

Lithium has also been used by the human body as an antiviral agent. It has inhibited DNA viral replication, and is being considered as a potential treatment option for the HIV virus, as reverse transcriptase is part of the virus' life cycle. Currently, most approved lithium dosages studied have not been high enough to prevent viral replication and distribution. Because lithium toxicity must be avoided, alternative methods of lithium delivery are being studied and assessed. One possibly mechanism is to have lithium replace enzymes in viral proliferation reactions that are essential for successful duplication to occur. A concern of this, however, is lithium will irreversibly bind to these enzymes, which can be hazardous for healthy and properly functioning cells if lithium were to attach to their DNA. Future inquiry into this potential virus therapy is necessary, but lithium treatment shows promise for potentially preventing the spread of viruses.

Future Research

As is well documented, lithium is a versatile drug that can be used in a variety of ways to reduce and prevent symptoms of various disorders. There are some areas of lithium research, however, that seem more promising in terms of yield groundbreaking treatment options for serious and currently incurable illnesses. First, more studies need to focus on finding a balance between acceptable lithium treatment dosages and effective lithium treatment. Multiple studies have shown lithium's ability to eliminate disorders and virus multiplication, but the treatment lithium levels were too high to be administered to humans without increasing the risk of lithium toxicity and the side effects included with it. If this issue could be resolved, lithium containing drugs could possibly be used to treat more physiological and psychological abnormalities. Also, great efforts should be dedicated to centralizing lithium's ability to prevent viral replication. In 2015 alone, almost 37 million people were confirmed to be HIV positive, and over one million died from AIDs-related illnesses. Though we have now had a much better understanding of HIV and have made great strides towards controlling and eliminating it, a cure for HIV has not been discovered. Lithium's ability to inhibit the proliferation of viruses makes studying it of the utmost importance. The mechanisms by which lithium inhibits virus replication are not entirely understood, and need to be more comprehensively assessed in order to successfully prevent viral proliferation. If sufficient supplies and attention were focused on this effect of lithium, and possible methods for safe lithium delivery found, steps towards a cure for the HIV could be made. If lithium were able to effectively inhibit HIV from multiplying, it could also effectively eliminate hematological disorders caused by the immunes system's inability to sufficiently produce enough WBCs to fight off infections.

I am specifically interested in observing lithium's therapeutic effects pertaining to Alzheimer's disease (AD). Chronic lithium treatment has been correlated with decreased rates of AD in representative populations. Lithium's ability to prevent plaque formation and tau hyperphosphorylation, effectively preventing memory loss as these both block and destroy neuronal connections, makes this therapy a plausible option for preventing AD. I am currently in the process of beginning an analysis of the effects of chronic lithium treatment on at risk populations, specifically, the elderly. The subjects will be extracted from the large sample pool of patients treated at the Anderson Free Clinic in Anderson, South Carolina. According to past experiments, I should see a decreased prevalence in Alzheimer's disease in those longitudinally treated with lithium. Regardless of results found, this study will provide more knowledge about lithium treatment's neuroprotective, or neurotoxic effect when consistently used for long periods of time.

Conclusion

Lithium is just as valuable to medicine and medical treatment as it was when discovered over one hundred years ago. Since it's therapeutic discovery, lithium's abilities have been tested numerous times, and consistent benefits of its use have been observed and documented. Few therapies are as versatile as lithium therapy, and all of its abilities still have not been discovered. Many hematological disorders are improved and even diminished by its use. Lithium therapy is well known for its ability to reduce manic relapse in affected patients, but is less well known for its other therapeutic abilities, such as decreasing rates of recurrent depression in sample populations. This therapy also shows great promise as a virus inhibitor, and is currently being studied to find safe ways to delivery lithium to cells *in vivo*. Lithium's positive effects are more numerous than the element's negative effects on the human body, and those can frequently be eliminated by adjusting the lithium dose being consumed by the patient. Though ample research has been conducted to understand lithium's abilities and effects, more is required to comprehensively assess how lithium works to counteract abnormalities contributing to disorders and diseases. Hematology, as

well as many other fields of science, benefit from lithium use and need to continue to observe its capabilities.

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