

Book Review

Lithium and the Blood

(Volume 4 of the series Lithium Therapy Monographs)

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The scope of the use of lithium in medicine has expanded significantly in the last decade. It has hitherto been known in modern medicine mainly for its use in the treatment of recurrent affective disorders, though it should be recalled that in the latter half of the last century it was recognized in the pharmacopoeias for a range of maladies. The present book continues a story which first achieved some prominence with the publication of a volume edited by Rossoff & Robinson in 1980. That book broke new ground but was large and somewhat rambling. The present series of reviews is eminently concise and shows the strides which have been made in the cellular and molecular biology of blood cells in the interim. The book is divided in its two main foci: the effects of lithium on blood cells, often in-vitro, and the effects on the haemopoietic system and blood cells during lithium treatment of patients. The two different contexts are clearly distinguished and the authors are to be congratulated on their repeated insistence that one must beware of extrapolating from one situation to the other. Because the readership is likely to be interdisciplinary it would have been useful to have had a list of abbreviations at the beginning or end of the book.

The book opens with a useful and well referenced introductory chapter by the editor himself on the range of effects of lithium on blood cells in general. This is followed by Messino's brief chapter dealing specifically with lymphocytes and in particular the biochemical mechanisms involved in their immune modulation. These two chapters draw attention to the possibility of lithium's use in the treatment of AIDS patients because of its properties as a 'non-specific immuno modulator'.

The next chapter by Lyman & Williams is rather unusual in such a monograph: the authors apply a statistical analysis to a wide range of published papers to try to draw conclusions on the variety of conflicting reports regarding the clinical effect of lithium on leucopenia derived from cancer chemotherapy. Their conclusions are, however, not encouraging and they suggest that while there is clearly an effect demonstrated in many studies this may not prove to be clinically useful because of the possible side effects of lithium itself at the high doses required and because there are becoming available recombinant technology engineered haemopoietic growth factors which will be more specific.

Two chapters by Hart show both sides of the immunological story. In the first the author describes the direct effects of the ion on the neuroimmune interface. These studies are largely confined to animal studies and often at rather higher concentrations than would be seen in human patients. There is a useful thumbnail review of lithium biochemistry at the beginning of chapter four. Hart reviews a range of literature reports and concludes that suppressor cell-mediated mechanisms are involved in the action of lithium on peripheral blood lymphocytes though once again he warns of the possibility of false extrapolation from studies at non-pharmacological lithium concentrations. An extensive range of immunological studies in a variety of animal species is then described which leads to the conclusion that there is significant inter-species variation in responsiveness to lithium. The interesting development of his argument is that the differences may be related to the presence or absence of hibernating activity in the particular species under consideration.

This is an interesting observation because it has been proposed that psychiatric depression in humans is analogous to

hibernation. The neuroendocrine-neuroimmunological implications of such a theory must be studied carefully for there are a number of interrelated observations both in patients and in experimental animals involving periodic phenomena and aspects of, for instance, regulation of electrolyte metabolism and the control of magnesium and its regulation of metabolic activity.

Hart's second chapter deals with the immunological sequelae of lithium patients who are being treated prophylactically for recurrent affective disorders. This is a significant number of subjects and it is argued that a large base of information should be available if only it may be decoded. The author concludes that there is indeed evidence of immunological effects at therapeutic lithium doses though it might be argued that such patients may be predisposed to immunological or autoimmune disease.

Kramlinger & Post deal with yet another aspect of the current usage of lithium: its use in combination therapy with carbamazepine. One of the apparent advantages of this particular combination is that the side effects of the two drugs on haematological measures appear to be mutually compensatory. The authors have therefore reviewed in detail the monotherapy of the two drugs and then their use in combination under a variety of conditions. The evidence is extensively tabulated and analysed graphically in relation to the time course of treatment. The conclusion is that, within the narrow therapeutic range of both of these drugs, the patient results parallel quite closely, but not exactly, the previously published studies in-vitro and in animals. This suggests that lithium and carbamazepine have reciprocal actions on the colony-stimulating factors which are known to regulate these functions.

Mota da Freitas, Espanol & Dorus contribute an extremely well referenced and comprehensive account of studies of red cell lithium transport by ⁷Li Nuclear Magnetic Resonance spectroscopy. This relatively new application of the NMR technique allows the investigation of intracellular lithium distributions and transport by direct measurement of the lithium in intracellular fluid. The authors discuss the various spectroscopic techniques in some detail and compare them with more conventional techniques. The elegant Modified Inversion Recovery technique is detailed and the case is made for its advantages over conventional Shift Reagent methods of studying intracellular metal ions. The transport mechanisms of lithium are then reviewed and it is revealing to note that there seems to have been little advance in understanding since the corresponding chapter was written over ten years ago. The NMR studies tend to have confirmed the findings of other workers but have not yet been in use long enough to have contributed new and fundamental information.

The final chapter is by Uluitu, a Roumanian, who has contributed a wide-reaching review. The conditions under which he has been working have been extremely difficult and it is a tribute to his persistence that he was able so successfully to assemble such a comprehensive bibliography of the effects of lithium on blood electrolytes and 5-hydroxytryptamine. The general background of the electrolyte and neurohumoral theories of manic-depressive psychoses, together with recent literature, is discussed in the light of the original hypotheses.

This book, therefore, deals with the broad spread of lithium effects on blood and its constituents. It has succeeded in updating the story as it has evolved over the last ten years. It is more concise and more detailed than its predecessor and it is also less prone to unsupported speculation. Dr Gallicchio and his colleagues should be pleased with their efforts: the book is useful and will fulfil the major objective of any scientific book, to stimulate further progress in its field.

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