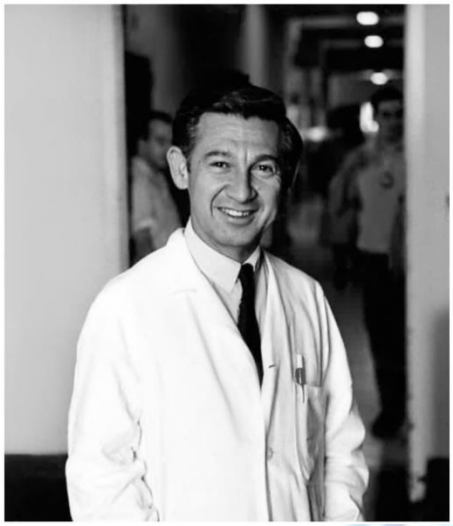
Professor Samuel Gershon

The Samuel Gershon Medal is in honour of Professor Samuel Gershon, MD, one of the fathers of the field of translational neuroscience worldwide. Professor Gershon is an Honorary Fellow, SAHMRI Mind &Brain Theme. He was formerly Professor and Acting Head of Pharmacology, University of Melbourne; Director of the Neuropsychopharmacology Research Unit, New York University; Chairman of Psychiatry, Wayne State University; Associate Vice Chancellor for Research in the Health Sciences and Vice President for Research, University of Pittsburgh Medical Center, and Vice-Chair for Academic Affairs, Department of Psychiatry, University of Miami. He is also Co-Chief Editor of Bipolar Disorders (Wiley), a publication that he founded as the official journal of the International Society for Bipolar Disorders.



Here is a summary of Professor Gershon's accomplishments in his own words:

"I would like to offer two short examples of studies, which were directed to address two major issues in psychopharmacology.

The first, lithium, needs to be placed into a brief background in the field of psychiatry. I graduated from medical school in 1950. At that time, there were no specific pharmacological therapies for the psychiatric disorders. The picture of psychiatric care and treatment was an immense problem with thousands of psychiatric patients incarcerated in mental hospitals with only sedatives or FCI (full coma insulin) available. This treatment was shown to be both dangerous and ineffectual. Lithium had been used in the XVIIIth and XIXth centuries for many disorders; e.g., gout was a well known indication. Its usage had been reported also for affective disorders in the second half of the XIXth century by physicians in Denmark (Lange brothers) and Hammond in New York for manic excitement. Usage of Lithium for these psychiatric conditions all came to end rather abruptly and in many cases no clear information was offered for this sudden termination of treatment and further interest in Lithium.

Then in 1949, two dramatic events occurred. Firstly, the United States Food and Drug Administration (FDA) ordered a total ban on the sale of all lithium component products because of toxicities and deaths. Secondly in the same year, in Australia Dr. John Cade published his findings on the successful use of lithium salts to treat manic excitement. At a later date he reported one death in his series Dr. Cade subsequently banned the use of Lithium in his hospital because of toxicity and lethality. In addition to his case a number of others were reported in Victoria alone. Here was a potential treatment, which had not yet been proven effective as no double blind studies were carried out by this time.

To attempt to address this issue my colleagues at the University of Melbourne and I attempted to study these problems of toxicity and lethality. We were immensely aided by the recent development of flame spectrophotometric assays by Dr. Victor Wynn in Physiology and others. Many animal experiments were carried out on the electrolyte and water effects in animals. In humans, we carried out a major study "The Differential Retention and Excretion of the Lithium Ion" published in 1955. We also conducted a number of therapeutic studies from which we could propose a safe therapeutic range for Lithium usage in patients: 0.6–1.2 mEq/L of lithium. That is we proposed a "functional therapeutic window". We followed up with a report on the "The Treatment of Litium Toxicity." These studies made it possible to resuscitate lithium usage and offer a safe method of monitoring long term maintenance therapy. Another series of studies that were important were the controlled comparisons of lithium and anti psychotic drugs in various psychiatric syndromes, when such trials were in their infancy. These studies helped define the clinical spectrum of lithium. In 1973 Gershon and Shopsin published the first textbook on lithium (Lithium: its role in psychiatric treatment and research).

The catecholamine hypothesis of affective disorders poses that "depressions" are associated with decreases in levels of norepinephrine and conversely elevated levels are associated with mania/elation. This was proposed by Schildkraut in 1965 and was the explanation utilized in psychopharmacology for the next 20 odd years. This concept pretty much dominated thinking in all areas of depression, explanation of mode of action of drugs, aetiology of the disorder, and the path for the development of new drugs.

When I was at New York University (NYU), we had access to a number of drugs, which, based on this concept and their performance in laboratory screening tests would be classified as antidepressants. In our clinical trials they were ineffective for depression and yet fulfilled the requirements of the hypothesis. Furthermore, since that time, no fundamentally new compounds have been developed or found to be effective for depression. Therefore, we undertook a number of studies in a variety of animal preparations to explore alternative explanations. This culminated in a series of clinical studies using synthesis inhibitors of serotonin and norepinephrine in humans with severe depression requiring hospitalization. The design, simply stated, was to establish two groups of in-patient depressed patients, one on imipramine and one on monoamine oxidade (MAO) inhibitors. Then, patients that showed significant clinical improvement, to established level, were again split into two groups. One group was given AMPT- alpha methyl para tyrosine - to block norepinephrine production and the other PCPA - para-chloro-phenyl-alinine. Those patients that improved in both treatment groups relapsed when given PCPA, demonstrating that the block of serotonin synthesis was related to the maintenance of improvement. This necessitated a re-evaluation of the catecholamine hypothesis and modification of the initial view that NE elevation was related to elation/mania and that NE lowering was related to depression. Closely related to these studies on serotonin was the pioneering report with Dr. Michael Stanley of reduced imipramine binding (serotonin transporters) in the brain of suicides that was published in Science in 1982.
We have still not provided a clear explanation of the aetiology of these disorders or the mechanisms for their treatment. But these studies did change the fixed direction of thinking invoking norepinehrine as the central mediator for depression and broadened the concept considerably."

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