

## Psychoneuroimmunology

– Dr M Friedman



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### Curriculum vitae

Merle Friedman studied at Wits where she obtained a PhD in 1988 in Psychology: "Developmental Changepoints: The Birth of a First Child". She is also a trained marital counsellor and completed her internship as clinical psychologist in 1989. Currently she is lecturing in the School of Psychology (University of Witwatersrand) and involved in several research projects, eg the psychological aspects of patients' preparation and care for in-vitro fertilization. She has published internationally and her main interests are infertility, creativity, preparation for parenthood, marriage counselling and all aspects of psychotherapy.

### Summary

*The finding that the immune system could be conditioned, was the beginning of the history of psychoneuro-immunology. This research project in particular and the many projects which then followed, are looked at; they mostly centre around the question of how aspects of mind (conditions, mechanisms and possibilities of psychological states) impinge on the nexus of interconnected systems. The main target of research has been on the various effects of stress, and the possibility came to the fore of looking at certain psychiatric illnesses as being auto-immune diseases. These are exciting implications for the healing processes, also in general practice*

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This new and intricate-sounding field has become a most active area of research in the present day. It is a field of research that is breaking new grounds in molecular biology and neurochemistry. More than that, it is tying together fields that have until recently been viewed as working independently; and in doing so, it is involving researchers in exciting joint projects from fields as diverse and specialized as psychology, physiology, immunology, molecular biology and others.

The history of psychoneuro-immunology (PNI) began with the serendipitous finding by Robert Ader and Nicholas Cohen<sup>1</sup> that the immune system could be conditioned.

This was a finding that no serious medical practitioner or researcher would even entertain. It therefore fell to the lot of a psychologist and an immunologist to make the great discovery. Ader and Cohen were conducting a taste-aversion study in which they paired ingestion of a saccharine solution in rats with the injection of a nausea inducing drug – cyclophosphamide.

What transpires in a conditioning experiment of this nature is, that over a certain number of trials the animals, who normally would enjoy the saccharine solution, come to associate the taste of this solution with the nausea that is induced by the cyclophosphamide. They thus stop drinking the saccharine solution. In this case the rats learned the association in only one trial.

Ader and Cohen then put the rats on to an extinction schedule. This procedure examines at what pace the learning extinguishes or fades. So, again the rats were exposed to a saccharine solution; however, this time without pairing it with the nausea-inducing cyclophosphamide. Ader and Cohen found, as expected, that over a period of time, as the nauseating association dropped off, the rats slowly began to drink the saccharine solution again. However, they also discovered that the rats that were taking the saccharine solution were falling ill and dying. Cohen and Ader finally linked this finding with the known immunosuppressive qualities of cyclophosphamide. The question still remained: how could the immunosuppressive qualities of the drug still be working, after only one administration which had taken place many days beforehand?

The only solution that an



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experimental psychologist could come to, was that the immunosuppression must also have been learned, or conditioned, similarly to the taste aversion to saccharine.

These researchers found support for their findings in follow-up research. Amongst other studies, they conducted research<sup>2</sup> in which they

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Tying together fields that have always been viewed as working totally independently

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used two groups of New Zealand mice who had lupus erythematosus – an autoimmune disease. In the experimental group, using the same system of conditioning, they conditioned immunosuppression, and thus *prolonged* the life of this group significantly over the control group of mice.

This finding by Ader and Cohen, linking the nervous system with the immune system resulted in an explosion of research in the 80's. The studies that followed focused on the links between the neural, endocrine, and immunological systems, on the one hand, as well as psychological states on the other.

Some of the findings that have come out of this research to date, are:

- (a) that the neurological system, the endocrine system and the immunological systems actively interact with each other,<sup>3,4</sup> also
- (b) that this nexus of interconnection is on a number of levels:
  - \* direct anatomic connections – there is innervation of

lymphoid tissues and endocrine organs by both the CNS and ANS<sup>5</sup>

- \* that cells of the 3 seemingly different systems have shared common markers<sup>6</sup>
- \* that cells of the nervous system, endocrine organs and immunological system all express common receptors for soluble functional mediators<sup>9,26</sup>
- \* even the biochemical pathways have an amazing degree of similarity<sup>10</sup>
- \* and that the immune system may function as a sensory organ.<sup>11</sup>

These findings that have discovered the intimate connections between these systems, and more specifically and ultimately the connection between “body and mind”, have stimulated some ground-breaking research.

The research has in the main centered around the question of how aspects of “mind” such as the conditions, the mechanisms and the possibilities of

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The neurological, endocrine and immunologic systems all interact with each other

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psychological states, impinge on this nexus of interconnected systems.

The main target of research however, has been on the various effects of stress.

Examples of such research have investigated:

- \* Stress and immunologic competence in man and animals<sup>12,13</sup>
- \* The effects of separation and bereavement on immunocompetence<sup>14,15,16</sup>
- \* Emotional and personality factors in the onset and course of autoimmune diseases, especially in rheumatoid arthritis<sup>7</sup>

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The serendipitous finding that the immune system could be conditioned!

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- \* Psychosocial factors and the immune system in human cancer<sup>17,18</sup>
- \* Psychosocial factors in infectious diseases.<sup>19</sup>
- \* Neurotransmitters and the immune system.<sup>4</sup>

A variety of immunologic abnormalities have been reported in conjunction with mental illness, particularly schizophrenia.<sup>25</sup> The question is asked as to whether schizophrenia might ultimately be found to be an auto-immune disease.

In a review of recent research findings, O'Donnell<sup>20</sup> et al (1988) describe how studies of immunity and schizophrenia have focused on viral and auto-immune etiologies for the disorder, implying a compromised immune system as being causative in schizophrenia. However, they point out that the significance of immune abnormalities



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in the etiology or pathogenesis of mental illness, remains unclear.

The studies on immunity and depression, on the other hand, have focused on compromised immunity as being a *result* of the depressed state – that mood disturbance results in compromised immunity. There are a number of positive findings in this area pointing to challenging possibilities for research.<sup>20</sup>

As a result of the increasing evidence that psychological and neuro-endocrinological indices may moderate the immune response, research has been generated to investigate these relationships.

Studies which investigate the effects of psychological states have indicated that chronic stress in humans leads to compromise of immune function. For example (a) poorer marital quality is associated with poorer performance on qualitative indices of immune function; (b) length of separation and degree of continued attachment to the (ex)-husband are significantly associated with immune function and distress in separated and divorced

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### The immune system may function as a sensory organ

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women; and (c) family caregivers of victims of Alzheimer Disease have poorer immune function than well-matched subjects.<sup>21</sup>

Of course, most suggestive in terms of looking at the broader picture of health, is to look at the various psychological states – and psychological and behavioural

interventions – and determine how they may moderate immune indices. Support has been found for hormonal and immunological relationships after behavioural interventions,<sup>22</sup> and immunological indices have been significantly changed after people have revealed

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### A compromised immune system being causative in schizophrenia

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details of traumatic incidents in their lives which they had previously not disclosed<sup>23,24</sup> – the major tool of psychotherapy. There has also been a mushrooming of material dealing with the possibilities, and/or making claims about the possibilities of the effects of various psychological interventions in the treatment of neoplastic and auto-immune diseases.

The implications for research are both enormous, and promising. However, despite the excitement in the field of PNI there are many serious criticisms of research in this area.

There has been impressive work during the last few years on immuno-endocrinology, ie the demonstration of biochemical as well as anatomic links between the systems (shared receptors for a spectrum of soluble mediators previously thought to be limited to one system).

On the other hand there has been some interesting work by psychologists and psychiatrists on defining and refining the parameters to be used in the variables they are interested in studying.

The area of greatest deficit has been in the biological work that has been done by groups primarily interested in the psychological dimension – which has not, on the whole, been solid – especially for the immunologic assessments reported. Thus, measuring blood lymphocyte number and mitogenic responsiveness, the most common criterion employed is inadequate in the light of present day immunological knowledge.

Also, despite the many findings that psychological factors influence immune function, not all measurable reactions of the immune system have a meaning for resistance to infectious, neoplastic and other diseases, and thus one cannot extrapolate from measuring immune function to disease implications.<sup>8</sup>

Because of the interdisciplinary nature of this work, and the necessity to consider both the micro and macro perspectives, this field is beset with enormous problems, both in research conceptualization, design and feasibility. Despite the exciting implications for the effect of the mind on the body, and the body on the mind, the placebo responses, the

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### Chronic stress leads to compromise of immune function

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use of hypnosis, and healing processes, it is clearly premature to extrapolate from the studies that have been done to date. And despite the questions as to the implications of the findings – even though those



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questions are the ultimate questions that should be asked – it is too early to be seriously seeking the answers.

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