## Preface

100 years ago, we don't understand electricity, so we think of the electric eel as an amazing fish. With understanding the electricity, we learn that the power of the eel is produced by muscle discharge. Similarly, if we don't understand sound, we would not know the magic of bat flying; if we don't understand magnetic field, we would not know the migration of whale and many other animal.

Before the system theory came into being, our understanding of biology is still based on the basis of decomposition and reduction. If we're stuck in reductionism, many complex autoimmune diseases, such as Rheumatoid arthritis (RA), will be difficult to understand. With the emergence of complex networks in 1989, understanding of biological networks has been enhanced. In this book we present the management strategy of RA from the perspective of complex network.

RA is the most common chronic autoimmune joint disease. This book argues that the RA is firstly caused by chronic stress and stress factors include physical and psychological stress. Existing statistical techniques based on reductionism cannot discover many relevant disease risk factors and complex interaction relationship. The disease network model based on complex network is important for the analysis and treatment of RA disease. In this book, we have found:

1) RA begins from thymus shrink after 18 years of age. Stress can cause horn cell apoptosis. In this process, skin injury by long-term ultraviolet irradiation, rubbing, etc. is a major RA risk factor, so in the management of RA, preventing skin inflammation is important to avoid secondary immune response. Apoptosis protein overflow and is citrullined then antibodies ACPAs occur, antibodies lead to complex occurrence, complex lead to complex precipitation and lead to RA joint symptoms. Chronic inflammation will lead to several other antibodies such as cryoglobulin. Then management will be more difficult.

2) RA is a long chronic disease. The first task of RA management is to prevent recurrence, such as skin injury will produce a large number of immune complexes. When recurrence occur, in the flare-up period using medications to control inflammatory cytokine is important. In chronic phase there are few immune complexes, so five balances management regulating strategy should be strengthened to prevent recurrence and exacerbation.

3) In the management of RA, the balance between neuroendocrine system and immune system is important. During the day, glucocorticoid plays an important role in controlling inflammation, and human growth hormone plays an important role in eliminating inflammation during the slow-wave sleep at night. So In the acute phase of RA, hormone therapy is important. We suggest use glucocorticoid (anti-inflammatory) in the morning and Growth hormone used before going to bed in the evening (to prevent insomnia and hormone disorder caused by the use of adrenal hormone, and to improve the elimination effect of deep sleep on immune complex). This strategy can alleviate the rebound that may result from glucocorticoid withdrawal.

4) Of the five balances in rheumatoid chronic period management, the first most important factor is the skin care, because skin injury will lead to the recurrence of rheumatoid arthritis. Then we must take care of the cold stress, sleep, moderate aerobic and resistance to muscle exercise (chronic effects), probiotics (more chronic effects), which contribute to the remission of rheumatoid arthritis.

This Book argues RA is self-limiting to some extent, and good management with five balances regulating strategy would have positive significance. Using five balances in the management of RA, we have followed up one RA patient (wife of the author) for five year, and the management effect is good. Five balances core concepts can shed light on the management of other causes of arthritis.

At next step we hope more researchers to participate in "Network Medicine" study to accumulate more cases, constantly improve the RA network model and analyze parameters characteristic and interaction relationship of RA network model. Only common characteristics network model based on the more RA patients improved in the future, could RA be individualized treated.

The research of complex network is still improving, and the research on RA management network will certainly enhance.

"The road ahead will be long and our climb will be steep".

I extend my deep appreciation to my wife (one RA patient), for her continuous encouragement and support to write this book.

Dr. Sheng-Rong Zou, one Osteoarthritis patient 2020.07