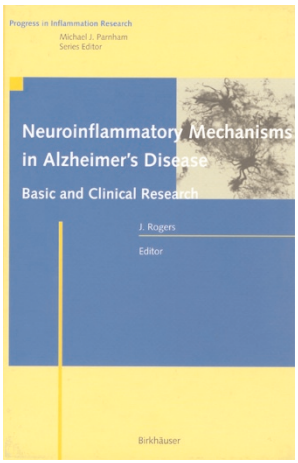
Inflamed brains and the demented elderly



Neuroinflammatory Mechanisms in Alzheimer's Disease: Basic and Clinical Research
edited by J. Rodgers
Birkhauser-Verlag · July 2001
Hardback £94/$149

Pim van Gool

Research on the metabolic background of Alzheimer's disease (AD) is progressing at a steady pace. Amyloid precursor protein (APP), β-amyloid, presenilin, neprilysin and the various secretases are among the factors that have been identified as being important in its pathogenesis. Although drugs or other methods of affecting these newly discovered factors are eagerly awaited, during the past decade the inflammatory hypothesis of AD was unique in offering a therapeutic perspective that could be readily tested by widely available drugs already in use for other inflammatory conditions. Despite initially encouraging findings with indomethacin, recent clinical trial results obtained with a variety of anti-inflammatory drugs such as prednisone, diclofenac, celecoxib and hydroxychloroquine cast serious doubt on the direct therapeutic implications of inflammatory mechanisms in the pathogenesis of AD. Treatment with a variety of anti-inflammatory drugs does not seem to work in patients affected by this devastating disease. So where does that leave the inflammatory hypothesis of AD?

This multi-author book orchestrated by one of the original 'neuroinflammatorialists', Joseph Rogers, clearly illustrates that the hypothesis still has life in it. It is not only the safety-belt analogy ('measures highly effective in preventing serious harm, may not be effective in repairing widespread damage') that keeps this field going. The various chapters in this book convincingly document the flurry of research activity on inflammatory mechanisms in the brain, and they highlight the implications that could extend well beyond the pathogenesis of AD that initially inspired all this research initiatives.

The book is organized in two sections, providing overviews and discussions of topics of special interest, respectively. The subject of the reviews range from cellular and molecular mechanisms of inflammatory processes in AD to epidemiological studies in AD. The specific topics that are addressed include new findings on the role of early activation of complement in the brain, interactions between β-amyloid and various components of inflammatory pathways, the role of the interleukin-6 receptor complex in the brain, glial-mediated neurotoxicity and the potential significance of cytokine production by neurons. All chapters are written by investigators actively involved in original research and they all discuss recent experimental data. In a round-up of the usual suspects, microglia, as the brain's representatives of the mononuclear phagocyte system, and astrocytes, which express several immune-associated molecules, have attracted and continue to attract much attention. Microglia and astrocytes produce inflammatory mediators and they seem to be the nervous system's counterpart of macrophages and fibroblasts in the periphery. According to the traditional view, neurons are to be considered as passive victims of this immune attack that interferes with their highly specialized functions in neuronal networks. However, recent data indicate that neurons too might synthesize several inflammatory mediators, rendering neuronal components from passive victims into candidates for active involvement in neuroinflammatory mechanisms. In a concluding chapter, Finch and Longo offer a truly bird's eye of the field. In a discussion entitled 'The gero-inflammatory manifold', the reader is treated to a wealth of associations on the cross-talk between inflammatory processes within the brain and in non-neural tissues, from the perspective of both normal ageing and AD, in man and across other species.

This brief outline illustrates that this well-edited book has a broad scope, as exemplified by the variation in the disciplinary backgrounds of the authors, by the subjects that are addressed and by the nature of the information that is conveyed, which ranges from concrete and technical to quite speculative. Although such a diversity of perspectives might not appeal to everyone, it offers the best that science has to offer. Inspired by a genuine interest in an important problem—the potential role of inflammatory processes in AD—knowledge has been acquired that offers entirely new perspectives both on the original question and on areas of investigation that were not previously expected. It is a great pleasure to read the well-written reports on this sequence of events. Moreover, despite the recent disappointing therapeutic trial results and the competing therapeutic approaches in AD that are to be expected in the coming years, it remains to be seen whether anti-inflammatory treatment might prevent or delay the onset of this disease. This potential provides additional momentum to this field of investigation. Interesting basic science on neuroinflammatory mechanisms, far-reaching 'gero-inflammatory' speculations and potentially important implications for the health of many elderly, all in a single volume: it is hard to envisage a more interesting mixture. □

Pim van Gool is in the Department of Neurology, Academic Medical Centre, 1100 DE Amsterdam, The Netherlands.
e-mail: w.a.vangool@amc.uva.nl

New in hardback

Recombinant Protein Drugs
edited by P. Buckel
Birkhäuser, £81/$119

Computerised Data Acquisition and Analysis for the Life Sciences: A Hands on Guide
by Simon S. Young
Cambridge University Press, £60/$85

Stem Cell Biology
edited by D. R. Marshak, R. L. Gardner and D. Gottleib
Cold Spring Harbor Press, £85/$115