Introduction

Cytokines are frequently regulated in cascades, where induction of the early cytokines serves to increase the production of later cytokine (e.g., interleukin-1 [IL-1] stimulates the release of IL-2 , IL-6 , and tumor necrosis factor [TNF]). The specificity of the response to cytokines is provided by unique cytokine receptors . Cells that express a functional receptor for a cytokine will respond to the presence of that Cytokine. These interactions of cytokines and cytokine receptors Are Necessary components of the physiologic response to cytokines ***.(Wong ML et al.,1997).***

Cytokine receptors can also be found in a soluble form..a soluble receptor for a specific cytokine can inhibit the biological activity of the cytokine by inhibiting the binding of the cytokine to its membrane anchored receptor(For example , soluble TNF receptors decrease the biological activity of TNF by inhibiting the binding of TNF to its specific surface receptor.)In some instances , the binding of the cytokine to its soluble receptor can form a complex that enhances the biological activity of the cytokine. This rare situation is seen, for example , when IL-6 binds to soluble IL-6 receptors , forming a biologically active complex that adds to the activity of IL-6 ***(Romero LI et al.,2000).***

Consistent with its activities in other organs , IL-1 in the brain stimulates the Production of other cytokines by specialized cells , in this case astrocytes and microglia. Human astroglial cell lines stimulated by IL-1 have been shown to produce colony-stimulating factor, TNF-□, additional IL-1, and IL-6 There is evidence that intracerebroventricular injections of IL- 1 in rats are associated with a decrease in natural killer (NK) cell activity of circulating lymphocytes and the release of IL-6 into the blood stream IL-1 directly injected into the brain can stimulate astrogliosis produce revascularizations ***(Baggiolin M et al., 1998)***.

Control of virus infection of the central nervous system (CNS) is a complicated task for the host because of the potentially damaging consequences of immune responses in the brain and cytotoxicity , Altered vascular permeability, and the influx of inflammatory cells Into an enclosed space containing non renewable cell therefore, the CNS has a number of mechanisms for controlling and regulating the development of local inflammatory processes. These include the blood-brain barrier, limited capability for antigen presentation, and functional modulation of immune reactions by gangliosides and astrocytes***.(Asensio VC etal.,2000)***.

The last 5 yr have witnessed significant changes in research direction and new discoveries about the mechanisms of

neurodegeneration. Earlier studies on neuronal death focused on neurons, neuronal pathways , and neurotransmitters. Now similar interest is directed toward glia and vascular cells, peptides, and inflammatory processes in the brain. This research has already revealed several potential therapeutic targets for the treatment of acute brain damage such as stroke and brain injury.***(Allan SM et al .,1999)*** .

Very few treatments have shown significant benefit in neurodegenerative diseases to date. Indeed, failures of major clinical trials for new treatments in stroke and head injury are being reported with alarming regularity. There are numerous potential explanations for these failures , including insufficient preclinical data in varied animal models , the poor clinical relevance of rodent models to clinical conditions, and design faults or limitations of clinical trials. A significant issue in such trials has been the balance between safety and efficacy, and it is notable that most therapeutic interventions to date have targeted processes that are overactivated in stroke or injury, but are also important for normal brain function (e.g. , modification of Glutamenergic pathways or ion channel activity) . IL-1ra has shown quite remarkable protection in diverse experimental models of neurodegeneration and is effective (albeit at high doses) in rodents when administered peripherally, even sometime after the insult. Furthermore, IL-1ra appears to have

few if any side effects or toxicity in animals or humans. Some of the other actions of IL-1ra, such as inhibition of fever and sickness behavior (e.g., loss of appetite) and analgesia , may also be useful in treating neurodegenerative diseases. Inspite of these considerable attractions of IL-1ra, future therapeutic strategies are likely to focus in small, non peptide inhibitors already the subject of intense investigation***.(Relton D et al., 2000)***

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Because cytokines are closely associated with central neurotransmitters and because cytokine regulation is affected by stress, a number of studies have investigated a These studies have been described in an emerging literature on cytokine regulation in major depression , schizophrenia ,Alzheimer's disease and other psychiatric disorder ***(Glaser R et al., 2000).***

Aim of the Work

1. To review general principles of inflammatory process
2. To review the mechanism of inflammation and the role of inflammatory mediators in its control
3. Role of inflammatory mediators in future management of neurological disorders