Introduction
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The two arms of immune system, the innate and adaptive immune system work in a unified way to confer protection to the body against various pathogens and antigens. The innate immune system comprises of macrophages, dendritic cells (DC), monocytes, phagocytes and natural killer (NK) cells. These cells provide the first line of defense and recognize different molecular patterns on the surface of various pathogens through their pattern recognition receptors. These cells however, have a short life span and their proliferation is restricted to the haematopoietic tissues where they are generated. To recruit a more specific system which can identify the antigen the DCs, macrophages and phagocytes engulf the antigen by endocytosis (phagocytosis and pinocytosis are other methods of antigen uptake). The endosome then fuses with the lysosome where the antigen is processed into peptide fragments and then loaded on major histocompatibility (MHC) molecules for presentation to cells from adaptive immune system, thus acting as antigen presenting cells (APCs). The advent of the adaptive immune system provides cells with more specificities and potential for clonal expansion upon encountering antigens. The adaptive immune system also has the capability of retaining memory of the nature of the antigen encountered and the next invasion by the same antigen is cleared much faster. The adaptive immune system exhibits two different responses. The cell mediated immunity is offered by T cells which recognize antigens through the T cell receptor (TCR) when presented on MHC molecules by the APCs. T cells can be categorized into CD4 and CD8 T cells based on their co-receptor. CD4 T cells or helper T cells as they are known recognize exogenous antigens presented on MHC II molecules. MHC I bound antigens are generated endogenously such as
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viral peptides in virus infected cells and are recognized by CD8 T cells which are cytotoxic in nature. The main function of the cytotoxic CD8 T cells is to kill the infected cells and abort the possibility of reproduction of the pathogen within the host cells (Bhardwaj, 2001).

The other arm of the adaptive immune responses which counters the extracellular antigens and pathogens and contributes in allergies and atopic inflammations are humoral responses mediated by B cells. B cells have the ability to produce antibodies which bind to specific antigens and neutralize them. B cell responses may be T dependent where the B cells get help from the T helper cells in the form of various effector molecules or through signaling via tumor necrosis factor (TNF) family member molecules on the T cell surface. T independent responses such as against bacterial polysaccharides do not require T cell help. B cells are driven into clonal expansion after getting T cell help and differentiate into plasma cell or memory cell to mount a more effective response (McHeyzer-Williams et al., 2003). Different types of T helper cells direct a different kind of antibody production by the B cells (Boehm et al., 1997). For this purpose B cells have evolved an ingenious ability to produce different isotypes of antibodies upon B cell receptor (BCR) engagement. B cells can also act as APCs and internalize BCR bound antigens. These antigens are then processed to small peptide fragment in acidified compartments in the cell and are loaded on MHC II molecules for presentation to T helper cells (Mitchison, 2004).

To protect the host from any invasion all the components of the immune system work in a coordinated and regulated manner. The communications between all the elements of the immune system are brought about by certain effector
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molecules known as cytokines. Through the action of these cytokines the cells interact and direct each other to deliver the most successful resistance against any antigen or pathogen. Cytokines play a major role in the growth and differentiation of the various immune cells. Cytokine functions involve the regulation of cytotoxic events, apoptosis, chemotaxis and the release of other cytokines. The initiation to culmination of the immune response against any invasion is tightly regulated by these cytokines which, can either suppress or enhance the ongoing response. A variety of cells have been known to secrete cytokines and a large number of cytokines are secreted by T cells that are pivotal regulators of the immune response. Upon activation by the APCs the naïve helper T cells can differentiate into either of two subclasses, T helper 1(Th1) or T helper 2(Th2), depending on the nature of the antigen encountered. Both these helper T cell subsets differ in their cytokine expression pattern and bring about differential immune mechanisms into action. IL2, IFNγ, TNF-α and IL18 have been characterized as Th1 cytokines, whereas the Th2 cells have been reported to produce IL4, IL5 and IL13 (Murphy & Reiner, 2002). Besides these subsets, T helper cells exist as regulatory T cells which have the efficiency to produce IL10 and transforming growth factor-β (TGF-β) and fine tune the immune response (Levings et al., 2001). Th1 cytokines are induced in naïve T helper cells by the IL12 and IL23 cytokines secreted by the APCs for which receptors are present on naïve T helper cell. Subsequent to IL12R (IL12R) binding, the naïve T helper cells produce IFNγ which enhances the production of IL12 through a positive feedback loop. IL12 receptor is also present on DCs and thus IL12 can, in an autocrine fashion enhance IFNγ secretion from the DCs. Th2 cytokine expression is initiated when naïve T helper cells get a signal through
their IL4 receptor by IL4. Both these cytokines are antagonistic in nature and restrict the production of each other thus favouring an environment that enhances their own production (Murphy & Reiner, 2002).

Another characteristic feature of different cytokines is their ability to support an inflammatory response or to abrogate it. Based on this property the cytokines may either be pro-inflammatory or anti-inflammatory. Th1 cytokines are pro-inflammatory in nature and support macrophage activation, generation of cytotoxic T cells as well as production of opsonizing antibodies and clearance of intracellular pathogens. On the other hand, Th2 cytokines favour B cell activation, production of non-opsonizing antibodies and removal of extracellular parasites (Abbas, Murphy & Sher, 1996).

IFNγ is a potent pro-inflammatory cytokine produced by T cells and NK cells upon cognate receptor engagement. DCs, macrophages and B cells also have the ability to produce IFNγ although their relative contribution is not clear. IFNγ activates macrophages and stimulates their phagocytic as well as bactericidal activity. It efficiently promotes the production of IL12 and expression of IL12R on the APCs. It increases the MHC I and MHC II mediated presentation by the APCs by augmenting the expression of these molecules on the surface. The key components in the clearance of the pathogen or the antigen are polymorphonuclear cells (PMNs) and leukocytes. Their recruitment at the site of inflammation is facilitated by IFNγ which alters chemokines and chemokines receptor expression along with cellular adhesion and transmigration. IFNγ activates macrophages and promotes certain functions that are essential for pathogen clearance. To eliminate the pathogens, macrophages produce nitric oxide (NO), the formation of which is catalyzed by inducible nitric oxide
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Synthase (iNOS). IFNγ induces iNOS in the activated macrophages and effectively leads to production of NO and thus helps in pathogen clearance. Th2 cytokine IL4 is strongly suppressed by IFNγ through interferon regulatory factor (IRF) molecules IRF-1 and IRF-2. The absence of IL4 diminishes the possibility of naïve T cells differentiating into a Th2 phenotype. IFNγ may have a role in the maintenance of T cell memory. IL7 and IL15 have been implicated in CD8 T cell memory. IL15 is notably induced by IFNγ and thus may play an important role in memory T cell commitment. Class-switching of the heavy chain in antibody secreting B cells from IgM to IgG2a is mainly brought about by IFNγ. It also represses the IL4 mediated switch to IgG1 and IgE (Boehm et al., 1997).

The Th2 cytokines IL4, IL5 and IL13 are considered anti-inflammatory in nature and mediate certain regulatory and effector functions such as allergen specific IgE production by B cells, eosinophil recruitment, mast cell growth and differentiation as well as development of effector Th2 cells. Th2 cells, mast cells, basophils and NK cells are the major source of IL4 and IL13. Th2 cells produce these cytokines in response to antigen specific TCR engagement whereas crosslinking of the high affinity receptors for IgE on the mast cells and basophils activates them to produce IL4 and IL13. These cytokines often show a considerable amount of similarity in the responses they elicit, most of which are associated with allergy, asthma, inhibition of autoimmunity and extracellular parasite (eg. helminths) clearance. However, IL4 is mainly involved in Th2 development, B cell growth and differentiation and isotype switching to IgE, while IL13 is more active in regulating airway hypersensitivity, secretion of mucus, and Th2 responses to nematodes and is the more critical molecule in established allergic inflammations. IL13 and IL4, both are potential modulators
of mast cell activation but IL4 is more potent in this regard. IL5 has no significant role in coordinating Th2 development or antibody isotype secretion by B cells, but contributes greatly to the growth survival and function of the eosinophils (Foster et al., 2002).

Although these different mechanisms of Th1 and Th2 mediated immunity are vital for host defense, a dysregulated response may lead to immune mediated pathology. To contain this kind of negative response a new functional subset of T cells have evolved known as regulatory T cells or T regs. These T regs regulate the immune response by suppressing the Th1 or Th2 responses by means of certain regulatory cytokines, IL10 and TGFβ. Both these cytokines are anti-inflammatory in nature and inhibit the synthesis and function of many other cytokines. IL10 inhibits the proliferation of CD4 T cells in general and IFNγ secretion by Th1 cells by suppressing the synthesis of IL12 by the APCs. Moreover, IL10 blocks the activities initiated by other cytokines, notably IFNγ, TNF-α, IL2 and IL4. It downregulates the expression of MHC II, costimulatory molecules CD80, CD86, chemokines by activated macrophages/monocytes. In general IL10 inhibits all those events that promote an inflammatory process and specific cellular response (Moore et al., 2001).

TGF-β, in many ways exhibits a similar response as IL10. It inhibits the proliferation of T cells in response to IL2 but favours the proliferation of naïve T cells. It inhibits the IL12 mediated production of IFNγ by the APCs thus blocking further development of a Th1 phenotype. It also deactivates the macrophages and reduces the production of reactive oxygen as well as nitrogen intermediates by inhibiting iNOS, thus diminishing their microbicidal and
tumorcidal activity. TGF-β has also been implicated in the development of autoimmunity (Letterio & Roberts, 1998).

Thus, the critical role of cytokines in development of a specific immune response is well established. The efficiency of a certain cytokine to affect almost every aspect of the immune response renders these cytokines to be central theme of many studies. Absence of certain cytokines impairs the immune responses to various degrees and may lead to the susceptibility of the host to many infections. Cytokine gene knock-out animal models have proven to be a very efficient tool in elucidating the role of a variety of cytokines in modulating the immune response. Much work has been done to ascertain the role of these cytokines in immune responses, but most of it is attributed to cytokines derived from T cells. Research, till now, has been focused on the availability of certain cytokine in the initial phases of the immune response and consequent effects. The absence of certain cytokines in these early stages and the subsequent alterations in the immune response are not well characterized. Moreover, cytokine synthesis by T cells prior to activation is not reported in literature. Therefore, the cytokine milieu at the initiation of the immune response is probably directed by non-T cells. APCs are also capable of producing a plethora of cytokines such as IFNγ, IL10 and TGF-β that critically regulate naive T cell activation and the ensuing immune response (Letterio & Roberts, 1998, Asadullah, Sterry & Volk, 2003). The present study focuses on the absence of certain cytokines from the APCs and their consequences on T cell priming. The role of cytokines in modulating other aspects of the immune response has also been examined in this study.