Depression is a very common phenomenon. Most of us have experienced some transitory period when we have felt sad and worried; during studying, sleeping and eating patterns have been disturbed. Depression is the foremost mental health problems round the globe. It is basically a disorder of mood or feeling. When depression is severe, persistent and disabling of everyday physical and social functioning, it is easily discernible. At other times, the distinction between normal fluctuation of mood and depression may not be very clear. Feelings of sadness, frustration and discouragement are part of the normal range of human emotions. However, these fluctuations tend to be short lived, do not become over-whelming in their experience, do not impair reality testing, do not profoundly alter self-esteem and do not generate suicidal thought or behaviour. In addition normal mood fluctuations do not produce persistent disturbances in sleep, appetite or motoric activity.

The central feature of clinical depression generally is a subjective experience of sadness, hopelessness or gloom. The feeling of depressed mood is accompanied by a loss of interest and pleasure in life and its activities and responsibilities. In some cases anxiety may be the predominant mood disturbance. A feeling

H.S. Asthana, Reader, Department of Psychology, Kumaun University, S S J Campus, Almora, Uttrakhand.
Shipra Joshi, Reader Scholar, Reader, Department of Psychology, Kumaun University, S S J Campus, Almora, Uttrakhand.
of lowered self-esteem is common, as is the feeling of helplessness. Depressed individuals show an inability to perform even the simplest daily task. They frequently are preoccupied with work, family, money and their own health. They approach these matters with marked pessimism and hopelessness. Sleep disturbance is very common symptom of depression. It may be of several kinds, the most characteristics of which is early morning awakening. However, delay in falling asleep and awakening during the night also occurs. Psychomotor disturbances may also be present in the depressed patients. Psychomotor retardation is frequent. They typically complain of lethargy and fatigue.

Additional signs and symptoms associated with depression include decreased libido, diminished interests, feeling of guilt and inability to experience pleasure. Cognitive changes may also occur. Thinking may be slowed and indecision frequent. Many depressives verbalize multiple somatic complaints e.g., gastrointestinal disturbances headache, backache, and urinary difficulties are common. Depression is the most common psychiatric illness. Both major depression and sub threshold depressive symptoms carry substantial health risk (Katz, 1996; Penninx, Geerlings, Deeg, Van. Ejik, Vantilburg and Beekman, 1999). Depression can affect health through many pathways. These influences may occur through health, behaviour or compliance with medical regimens, as well as through alterations in the functioning of Central Nervous System (C N S), immune, endocrine and cardiovascular system, (Carney, Freedland, Rich, 1995; Davidson, Jackson, & Kalin, 2000; Miller, 1998).

In this chapter a psychoneuroimmunological approach would be considered to discuss how does depression influence human immune function? Psychoneuroimmunology has become an independent science with a broad experimental basis. It consists of two main branches (1) immunological functions in natural and experimental stressful conditions in human as well as animals (2)
immunological functions in different psychopathological states such as depression, anxiety and so forth.

The immune system is a surveillance mechanism that protects the host individual from disease causing microorganism and other harmful materials (Male, Champion, Cooke, & Owen, 1991). These foreign materials are called antigens. The organs of the body where most cells of the immune system are located are bone marrow, thymus, lymph nodes, spleen, tonsils and appendix. Because there is no way to access cells from these organs, psychoimmunological work with humans is limited to immune processes that occur in circulating peripheral blood. Circulating blood transports immune components between the organs of the immune system and sites of inflammation. Therefore, circulating peripheral blood plays a key role in inflammatory and immune processes.

**Brain and Immune System:** It is known that two main pathways link the brain and immune system. These are (1) Hypothalamic- pituitary adrenocortical system (HPAC) and (II) the Sympathoadrenomedullary system i.e. the direct neuronal fiber connections from the autonomic nervous system. These pathways produce biological mediators which interacts with the cells of the immune system (Besedovsky & Ray, 1991). Neuroendocrine hormones released from the pituitary gland by the activation of HPAC influence the immune system. Lymphoid and myeloid cells express receptors for these hormones. Several studies have demonstrated that lymphocytes also synthesize hormones such as prolactin, growth hormone, and adrenocorticotropic hormone (ACTH) (Varma, Sabharwal, Sheridan, & Malarkey, 1993; Sabharwal, Glaser, Lafuse, 1992). Neurohormones *e.g.*, glucocorticoids, ACTH, endorphins are able to modulate many aspects of immune response including cytokine production, B and T cell proliferation, antibody production and Natural Killer (NK) cell activity (Blalock, 1989).
The role of sympathoadrenomedullary system founds to be supportive as Noradrenergic and peptidergic nerves are found in lymphoid organs including bone marrow, thymus, spleen and lymph nodes (Felten & Felten, 1991). These nerve terminals are closely associated with immune cells, which lead to the formation of neuro effector junctions. These junctions provide an opportunity for direct neural-immune interaction. For example, the release of epinephrine and norepinephrine by sympathoadrenomedullary system regulates lymphocyte cyclic levels, which consequently alter immune response.

**Approaches:** There are to approaches to study the human immune system *i.e.* enumerative and functional capacity of cells. The primary enumerative approach involves simply counting the number or percentages of different kinds of white blood cells in the peripheral blood. The blood encompasses a number of different kinds of white blood cells. These cells can be differentiated into neutrophils, monocytes, eosinophils, basophiles and lymphocytes. There are different types of lymphocytes: NK, B and T cells. T cells can be further differentiated into helper T-cells, cytotoxic and suppressor T-cells. A balance of the different cell type is needed for optimal immune response.

The second approach to study the human immune system involves testing the functional capacity of immune cells. In most of the studies the lymphocyte proliferative response and NK cell cytotoxic activities were examined. It has been suggested that more proliferation that occurs, the more effectively the cells are functioning. NK cells' cytotoxic activity determines how effectively NK cells are killing tumour cells.

**Depression and Altered Immune Response:** Depression seems to results in failure to adapt to various crises, problems and losses. Failure to adapt may be termed as pathology from psychological viewpoint. Adaptation is the process of meeting person’s social, biological and psychological needs under changed circumstances.
Failure to meet the demands of the changing situations would result in suffering from psychological disorders, and pains within the persons. Adaptation to loss is one of the principal task individuals face in later life. Common losses include loss of spouse, loss of social roles, loss of work associates, loss of opportunity for meaningful work and for recognition.

**Hypotheses to Explain Depression**

There are different hypotheses to explain the depression. The biochemical, biological, and behaviouristic explanations are more relevant in this context.

*Biochemical Hypothesis:* Biochemical hypothesis of depression has centred on disturbances of CNS neurotransmitters (Goodwin & Bunney, 1973). Monoamines (norepinephrine and serotonin) are the primary neurotransmitters implicated in classical biochemical hypothesis of depression. The original amine hypothesis of depression possesses a deficiency of monoamines in the neural synaptic junction. Antidepressants were thought to alleviate depression by correcting this deficiency. Evidence suggests that other neurotransmitter systems may also play a role in depression. Acetylcholine decreased CSF and plasma gamma-aminobutyric acid (GABA) levels have been observed in depressed patients (Petty & Schlesser, 1981). Several other areas are also under investigation with regard to potential biological hypothesis of major depression. Neuroendocrinological investigation of depression consistently reported elevated cortisol levels among non-psychotic and psychotic depressed patients (Gold *et al.*, 1986).

*Behavioural Model of Depression:* Beek considered hopelessness and helplessness to be the central to the experience of depression. His hypothesis is that these affects succeed a set of cognitive processes involving a negative self-concept, negative interpretation of one’s life events, and pessimistic view of the future (Beck, 1967). Brad *et al.*, (1995) reported that a negative
Psychoneuroimmunology: A Behavioural Approach

view of the future and hopelessness is not only concomitant of depression but may be vulnerability factor in subsequent development of depressive symptoms. Beck et al., (1979) proposed diathesis-stress model of depression. This model contends that latent dysfunctional attitudes confer a stable vulnerability to depression. Depressive mood states are triggered when stressful experiences activate the dysfunctional cognitions. Empirical evidences have supported the interaction of dysfunctional attitudes with stressful events in accounting for the variance in depressive symptoms (Olinger, Kuiper, & Shaw, 1987).

Because the immune system is known to respond to changes in affect (Ader, Felten, & Cohen, 1991; Kemery, Solomon, Morley, & Herbert, 1992), researches have focused on immune alteration as a pathway through which depression might influence physical health. Changes in cells mediate immune functions in persons undergoing distressing life experience (Padgett & Glaser, 2003). In a study, Schleifer, Keller, Camerino, Thornton and Stein (1983) found that lymphocyte responses were found to be significantly suppressed among men whose wives had recently died. Hospitalized major depressive patients have also shown lower mitogen responses. (Kronfol, House, Silva, et al., 1983). In a meta analytical review, Herbert and Cohen (1993) reported that depression was negatively related to the number or percentages of lymphocytes that were B cells, T-cells, helper-T cells, and suppressor/cytotoxic T-cells. These findings were extended to different other indicators of immune function e.g. Natural killer (NK) cells activity, T-cells, and helper T-cells. Impairment of NK cell activity has been reported in depressed, anxious and lonely persons (Loke, Kraus, Leserman et al., 1984; Kiecolt-Glaser, Garner, & Speicher, et al., 1984).

Depressed male participants exhibited a significant reduction in NK effector cells and NK cell activity (Evans et al., 1992). In a study, Irwin, Smith and Gillin (1992) found that insomnia was associated with reduction of NK activity independent of the
severity of other depressive symptoms. On the other hand deep sleep is the normal stimulus for much of the release of growth hormone, a hormone that enhances a number of aspects of immune function (Veldhuis & Iranmanesh, 1996). A variety of neurohormones and neurotransmitters could mediate the reduction of NK cell activity during depression. Cortisol and norepinephrine, both of which are often higher in the plasma of person undergoing stressful life experiences (Irwin, Daniels, Bloom, Smith, & Weiner 1987). Recent researches suggest that stress and depression can enhance production of proinflammatory cytokines, substance that regulate the body’s immune responses to infection and injury (Dentino, Pieper, Rao, et al., 1999; Lutgendorf, Garand, Buckwalter, Reimer, Hong & Lubaroff, 1999; Maes, Lin, Delmeire, et al., 1999). This finding has been further substantiated by many other researchers (Robles, Glaser, & Kiecolt-Glaser, 2005). Lutgendorf et al. (1999) have reported that both depressive symptoms and syndromal depression are associated with heightened plasma IL-6 levels. Following successful pharmacological treatment elevated level of IL-6 declined in major depressive patients (Sluzewska, Rybakowski, Lacia, et al., 1995).

Negative emotions may also contribute to the immune dysregulation by proinflammatory cytokine overproduction (Catania et al., 1997). Overproduction of proinflammatory cytokines may lead to subsequent maladaptive immune and endocrine changes (Kiecolt-Glaser & Glaser, 2002). IL-6 is a potent stimulator of corticotrophin releasing hormone (CRH) production that leads to elevated levels of plasma ACTH and cortisol. Both of these provoke multiple adverse immunological changes (Miller, 1998). Once cortisol level rises, it can initiate, perpetuate or aggravate syndromal depression, depression like behaviour and depressive symptoms (Wolkowitz & Reus, 1999). Thus negative emotions that dysregulate IL-6 secretion may also promote adverse neuroendocrine alterations.

Depression and distress can have adverse effects on variety of immunological mechanism including downregulation of cellular
and humoral responses (Miller 1998). More depressed and more anxious individuals produce immune responses to vaccines that are delayed and substantially weaker (Glaser, Sheridan, Malarkey, MacCallum, et al., 2000; Vedhara, Cox, Wilcock, Perks, & Hunt (1999). The association between clinical depression and immunity has been reviewed in several articles (Kiecolt-Glaser, & Glaser, 1991; Weisse, 1992; Herbert & Cohen, 1993) and there is a general consensus that depression is associated with altered immunity. Weisse (1992) conclude that “studies of people suffering from depressive disorder suggests that index of immunocompetence are lower among clinically depressed” (p.483).

However, relationship between depression and immunity may be affected by several factors such as age, gender and other personal resources. Age is an important variable that modulates the influence of depression on immune function. In the depressed participants increasing age had a significant independent correlation with decreased number of lymphocytes, B-cells and reduced phytohemagglutin in-HPA (Andreoli et al., 1993). Little is known about the influence of these factors. Therefore, it is necessary to take them into consideration in the future researches.

CONCLUSION

While many researchers have described associations between depressive disorder and altered immunity. There are considerable organismic variables in the immune responses to depression. This seems, to a large extent, to be determined by the individual’s way of dealing with stress. In addition to this, it is also important to consider the diagnostic subtype, severity, recurrence, chronicity of illness and demographic factors such as age, gender, medical characteristics and the immune measure selected to determine the influence of depression on immune function. In future, studies are also needed that link variations in affective state to the indicators of immunity and then disease outcomes.
REFERENCES


