The immune system which provides specific defense mechanisms in our body may prove destructive in senescence. Immunologic competence is a growth-related process and may undergo deteriorative changes during aging. Such a self-destructive immunological reaction, often referred to as an autoimmune phenomenon, may give rise to pathological changes and reduction of life expectancy. There is considerable evidence in the literature to indicate that autoimmune reactions occur with increased frequency in the aged (Comfort, 1963). Although controversy exists on the processes underlying these changes, it is generally believed to result from the emergence of new antigenic stimuli or from the loss of acquired immunologic tolerance associated with aging. The autoimmune theory was first proposed by Burnet (1959). He described these changes as being due to the formation of 'forbidden clones of cells' arising from the derranged stem cells located in the reticulo-endothelial system, lymph nodes, spleen or bone marrow. Burch (1968), the leading proponent of the autoimmune theory of aging, proposed that several factors acting throughout life may significantly alter the process of acquired immunologic tolerance resulting in the increase of forbidden clones and incidence of autoimmune disorders. Walford (1962, 1967 and 1970), on the other hand, hypothesized that aging may be due to long-term low-grade histoincompatability reactions among the body's population of cells resulting in cell death. The possible deterioration of the immune system during aging in mammals has been studied by Makinodan (1976) who suggested that this might be due to either intrinsic changes in T and B cells or their interaction, thus making them less efficient.

Aging is associated with a number of changes in the mammalian brain such as neuronal loss, lipofuscin pigment formation, loss of
dendritic spines, and formation of amyloid lesions and senile plaques. Among these changes, the loss of nerve cells is probably the most consistent one in the mammalian brain. This change is quite marked in the brain of patients with senile and presenile dementia. This is also important from the physiological points of view as the neurons are post-mitotic and are not replaced by the division of the remaining cells. The number of Purkinje cells in the human cerebellum at different ages was studied by Ellis (1920) who noted a consistent decrease of these cells with age in subjects dying of causes which are not expected to affect the brain. Brody (1955) also demonstrated a similar reduction in the number of neurons in human cerebral cortex ranging from newborn to 95 years of age. The greatest loss was in the superior temporal gyrus, area striata and hippocampus. In contrast with normal aging, this cell loss in the brain of dementia patients is not continuous over the whole cortex. An analysis of four areas of the cerebral cortex, from pia to white matter, in presenile dementia, demonstrated a neuron loss of 57 percent in all areas, the superficial layers of the cortex being less affected than the deeper ones (Colon, 1973). The absolute number of neurons and thickness of the cortex were also studied in different areas of cortex of mentally healthy subjects of different ages and in patients with senile and vascular dementia, Alzheimer's or Pick's disease (Shafer, 1972). According to this study, the absolute number of neurons in mentally healthy old persons may be reduced by 20 percent, while that in senile dementia may be reduced by 35-38 percent. Although the loss of neurons appears to be an important change in the brain of aging mammals, its underlying physio-pathology or precise significance is not clearly understood.

The possible role of immunological reactions in neuronal degeneration in aging has been investigated in our laboratories. Female C57 BL/6 mice of different ages were kept in constant temperature and humidity controlled environmental chamber. Fluorescein isothiocyanate (FITC) labeled rabbit anti-mouse gamma-globulin (Cappel Laboratories, PA.), were used to demonstrate antigen-antibody reaction in mouse brain. An intravascular perfusion with phosphate buffered saline (PBS) was used to remove all traces of gamma-globulin in the blood vessels of the brain. Frozen sections of both young and old mice were treated with sera from mice of different ages prior to incubation with FITC-labeled antimouse gamma-globulin. A positive reaction as demonstrated by a bright greenish fluorescence was mostly located on the cell wall, cytoplasm or the nucleus. Specific fluorescence was observed in the neurons of both young and old mice when the brain sections were treated with sera from old mice but none when sera from young mice were used. Protein fractions of old mouse serum (albumin, $\beta$-globulin and gamma-globulin) were used in place of sera and only the gamma-globulin fraction gave the positive reactions in the neurons. Control tests for specificity of the reaction were carried out by absorption of the antimouse