REVIEW OF LITERATURE

INTRODUCTION:

The determination of the enzyme activity has a wide range of application. In addition to the testing of enzymes used as reagents for the analysis of substrates, enzyme assays are of special importance in the biochemical and clinical fields. The concept, that certain disease states can be detected by altered enzyme activity in serum and C.S.F., rests upon a number of assumptions. Intracellular metabolism is essentially a collective chain of successive biochemical transformations, each mediated by highly specific biologic catalysts. The continuance of cell life is dependent upon uninterrupted activity of these agents. Destruction or serious physiologic impairment of selective tissues may, therefore, liberate the intracellular enzymes into the most readily accessible biologic fluid. The relative concentration of various enzymes in all cells varies according to their metabolic specialization. According to Dalbruck et al (1939), it is possible to distinguish approximately three types of enzymes according to their location in the cell.

1. Cytoplasmic enzymes (e.g., lactic dehydrogenase).

2. Enzymes located only in the mitochondria (e.g., glutamic dehydrogenase).

3. Enzymes which occur in both cell compartments (e.g., glutamic oxaloacetic transaminase and malic dehydrogenase).
The intracellular enzymes have hardly got a role to play in the serum or cerebrospinal fluid. These include the enzymes of tissue metabolism, and they are not active in serum or cerebrospinal fluid because their coenzymes and most of their substrates are absent in the serum or cerebrospinal fluid. The majority of the enzymes in this group, which have been studied from a clinical standpoint, belong to the main energy yielding metabolic pathways i.e. they are present in all tissues of the organism. It can therefore well be assumed that whatever enzyme activity is found in such circulating fluids, denotes the enzyme in transit from cells and that the source of these enzymes is probably a combination of continuing intracellular biosynthesis and normal cell replacement.

The rise in the circulating content of a specific enzyme can be construed as a signal of necrobiosis or functional damage in such tissues. The localization of the responsible tissue is not always feasible but with judicious evaluation of relevant clinical data, a reasonable guess can be made. It is also possible at times, to infer the nature of the pathologic process.

An abnormally increased serum or cerebrospinal fluid enzyme activity in most instances indicates a release from pathologically altered cells, rather than enhanced biosynthesis.

It can be shown under experimental circumstances that the enzyme increase in the circulating fluid is
closely associated with decreasing tissue enzyme levels (e.g. induced myocardial or cerebral infarctions in laboratory animals). The serum enzyme returns to normal as experimentally induced tissue degeneration persists, indicating an exhaustion of the primary source of additional circulating enzymes. Generally, the elevation tends to be transient and the peak values are recorded at the onset of the destructive process. They therefore may not coincide with the time of the most profound tissue damage.

When enzyme activity does show a sustained elevation which is rare, it often presages a continuing cell degeneration, progressively incorporating previously unaffected tissues. Serial measurements of enzymatic activity therefore have a definite bearing upon the prognosis, serving to indicate the quantitative extent of acute tissue damage, (by the magnitude of initial peak in enzymatic activity) and extension of the destructive lesion (by the endurance of abnormally elevated enzyme activity). (Aronson et al, 1960). Like all laboratory parameters, the information derived from measurement of body fluid enzyme activities has noteworthy limitations. Majority of enzymatic reflections are nonspecific, in that more than one etiologic factor and more than one anatomic site can account for similar quantitative and/or serial enzyme changes. Furthermore, the influence of other body fluid constituents such as inhibitors, antienzymes, activators, competitors, drugs and others may account for
apparent artefacts included in the extensive enzyme activity of body fluid (Wroblewski, 1959).

There are more than five hundred enzymes whose catalytic function has been described, but only a small number have been used as indicators of neurologic disease states. The studies of altered enzyme activity have been confined principally to the cerebrospinal fluid.

1. C.S.F. ENZYMES:

A knowledge of the cerebrospinal fluid (C.S.F.) enzymology may lead to a better understanding of the physiology of the central nervous system. It may also aid in the clinical evaluation of the diseases of central nervous system.

The first attempts to investigate the relationship between the condition of central nervous system and the distribution of enzymes in C.S.F. date as far back as 1939 when Kaplan et al estimated activity of Trypsin, Phosphatase, Lipase tributyrinase, Esterase and Amylase in the pathological as well as normal spinal fluids. Bushor in 1952, found an increase in triosephosphate isomerase in C.S.F., in cases of cerebrovascular accidents. In malignant brain tumours; phosphohexoisomerase activity was found to be increased in the C.S.F. by Thompson in 1939. Various other enzymes have been found to act as biochemical markers of diseased central nervous system. Creatine Phosphokinase (C.P.K.) is one such enzyme.
importance of evaluation of C.P.K. has been realized in many neurological disorders. (Harschowitz and Cumings, 1964; Lisak and Craig, 1967). Besides C.P.K. other enzymes which have been studied in the C.S.F. include Deoxyribonuclease and Ribonuclease (Kovacs, 1954; Housh, 1958), cholinesterase (Jefferson, 1954; Plum and Foq, 1960) and Glutathione reductase (Hanson and Wroblewski, 1958).

Lactic dehydrogenase (L.D.H.)

This is an enzyme of almost universal distribution in the body which catalyses the reversible transformation of pyruvate to lactate. This is found in most animal tissues, besides in body fluids such as serum, cerebrospinal fluid, and skeletal muscle in particular, contain large amounts of the enzyme. Brain tissue contains per gram about one third the L.D.H. present in liver. When the blood brain barriers are intact C.S.F. = L.D.H. is not altered by ten fold higher plasma L.D.H. activity. The fluctuations in plasma L.D.H. also have no effect on that in C.S.F. (Wroblewski, 1958).

L.D.H. of the human tissues contains five distinct isoenzymes. Different tissues vary in the relative proportions of these five isoenzymes. Heart muscle contains mainly the electrophoretically faster fractions 1 and 2 and so do plasma, C.S.F. and brain tissue. Skeletal muscle contains mainly the slower fractions 4 and 5.
In disease the serum isoenzyme pattern approaches that of the affected organ and the pattern may remain demonstrably abnormal even after the total enzyme activity has reentered the normal range.

**Glutamic oxaloacetic transaminase (G.O.T./aspartate aminotransferase)**:

This is one of the transferase group of enzymes. It's systemic name is L Aspartate 2 oxoglutarate amino-transferase. This enzyme is involved in the following interconversion:

\[ L \text{ Glutamate} + \text{oxaloacetate} = L \text{ Aspartate} + (\alpha) \text{ oxoglutarate}. \]

It has been detected in microorganisms and in all human and animal tissues so far investigated. In humans, the richest source is heart muscle, followed by brain, liver, gastric mucosa, adipose tissue, skeletal muscle and kidney etc. Body fluids like serum and C.S.F. contain it in substantially smaller amounts. (Bergmeyer and Bernt, 1965).

**Source of enzymes in C.S.F.**

Controversy still exists as to the source of C.S.F. enzymes. Though brain tissue contains substantial amounts of L.D.H. and G.O.T., yet it still remains an enigma whether these C.S.F. enzymes are of cerebral origin or reach the C.S.F. from the plasma after crossing the blood brain barrier. Besides brain and plasma, two other possible sources have been postulated. These are the leukocytes and the microorganisms. It must be noted
however, that the possible source in a given diseased state varies according to the pathophysiology involved. For example, in cerebral infarctions, the sources which might be responsible for the enzymatic activity, in the C.S.F. can be either cerebral tissue or plasma, but never microorganisms or leucocytes. The reverse holds true for inflammatory diseases of the C.N.S.

In cerebrovascular accidents, frank infarction is presaged by cellular damage. Cellular damage takes place in all the varieties of the cerebrovascular accidents vis. thrombosis, embolism and haemorrhage.

The level of C.O.T. in C.S.F. at any moment depends on its rate of entry and its rate of removal. There could be several ways for a rise in C.S.F., C.O.T. activity. (Mallick and Basset, 1964) e.g.:

1. Increased outflow from serum through an incompetent C.S.F./blood barrier.
2. Increased outflow from cells because of their destruction.
3. Increased outflow from cells in absence of their destruction.
4. A decreased rate of removal.
5. A continuation of some or all of these factors.

The size of the infarcted area has an important bearing upon the rise in the enzyme activity. (Russell et al., 1966). Silcox et al in 1973 reported that in normal brain plasma is the source of C.S.F. L-Deli and C.O.T.
They did not find any contribution for the same from the brain tissue. While others (Mann, 1977 and Viallard et al., 1978) reported on the basis of isoenzyme studies that the increment in C.S.F. enzymatic activity was of cerebral origin.

Beatty et al (1968) reported predominance of L-D.N.A. fractions 4 and 5 in C.S.F. in cases of bacterial meningitis, thus proving their origin from leukocytes. Interestingly, however it was found that in fatal cases of bacterial meningitis, the C.S.F. showed predominance of L-D.N.A. 1 and 2, consequent to extensive damage of brain tissue.

Acute cerebral damage leading to release of C.O.T. from brain cells and raising serum enzyme activity has been reported by Lieberman, (1957). There are several workers viz. Haish and Blumental, (1954), Jakoby, (1958), Green, (1958), Walinsz, (1969) and Mroblewski, (1958) who have attributed the raised C.S.F. enzyme activity to brain tissue. Working on viral cerebral infections Krogsgaard and Guzado (1963) reported neuraxis to be the source of C.S.F. enzymes.

The blood-brain barrier may be the deciding factor for the alteration in enzymatic activity of C.S.F. by regulating the passage of leukocytes and/or bacteria and/or plasma, in conditions of diseased nervous system. Plasma may reach C.S.F. in conditions affecting blood brain barrier (Steeple, 1936). In cases of meningitis,
leucocytes too may contribute, along with the plasma, in raising C.S.F. enzyme activity as reported by Wroblewski (1957, 1958) and Green (1958). Feldman (1973), interpreted that the level of C.S.F. L.D.H. activity reflected the type and number of white blood cells and the kinetics of white blood cell turnover involved in the host response to infection. Similar results have been reported by Aronsen (1960), Beatty et al (1960) and Shirale and Nair (1974).

In central nervous system infections, microorganisms could be yet another source of C.S.F. enzymes, (Aronsen, 1960 and Shirale and Nair, 1974). On the contrary, Beatty et al in 1968 ruled out the microorganisms as a possible source of enzymes in C.S.F. in meningitis. Their study was based on their observations on leuкоpenic and normal animals affected with pneumococcal meningitis. Though both group had a large number of viable organisms in the C.S.F., only the group with normal leucocyte count showed a rise in C.S.F. L.D.H.

2. NORMAL VALUES OF C.O₂.T. AND L.D.H. IN C.S.F. AND SERUM

C.O₂.T. is C.O₂.T. a

Though the value depends chiefly on the methodology adopted, most of the workers have reported C.S.F. C.O₂.T. levels within the range of 1-35 units e.g. (Pyraman et al., 1957; Russell et al., 1959; Aronsen, 1960; Landis et al., 1961 and Pandhar and Sanna, 1963 et al.). Some workers have
however reported higher values up to 25 units e.g. Lieberman et al. (1957), Singh et al. (1972), Kohli et al. (1978) and Gupta et al. (1982).

s.g.o.t.

Lieberman et al. (1957) and Myerson et al. (1957) observed double transaminase activity in serum as compared to C.S.F. in their normal controls. No such relationship has however been obtained in diseased states. Most of the workers like Lieberman et al. (1957), Myerson et al. (1957), Brodell et al. (1959), Pradhan and Saxena (1963) and Singh et al. (1972) have reported s.g.o.t. values ranging between 10–40 units in normal controls. Gupta et al. (1982) have however reported higher values (up to 180 units).

GAL.P.

In healthy controls the activity of this enzyme has been found in the range of 10–40 u. according to reports available in the literature (Wroblewski et al. 1957; Aronson, 1960; Cunningham et al., 1965; Feldman et al., 1973 and Sodi et al., 1974).

SGM.

Wroblewski et al. (1957) reported control values of serum between 200–600 u. Aronson (1960) found the normal range between 100–400 u. Holinta et al. (1966) reported 150–250 u. as the normal range of serum L-D.H. activity. Sodi et al. (1974) observed their control cases to have
S.L.D.H. levels in the range of 75-390 u.

3. ALTERATIONS OF C.S.F. ENZYMES (L.D.H. AND G.O.T.) IN DISEASE

Cerebrovascular accidents:

The central nervous system is bathed by the cerebrospinal fluid and hence, the examination of this biological fluid should provide relevant information regarding brain damage.

(a) Experimental:

Cohen and Halkia, (1941), reported that dry brain tissue contains 260 u/mg. of G.O.T. activity. Various workers have studied C.S.F. G.O.T. by producing brain damage under experimental conditions (Nakim and Fliedner, 1965; Smith et al, 1960; Akashi, 1946). All of them have reported raised activity after producing cerebral damage. However, Khan in 1974 described only slight increase of C.S.F. G.O.T. after producing cold injury in cats.

Green in 1958, observed that L.D.H. might be slightly superior in reflecting tissue damage both in the incidence of abnormality and in the degree of increase. Akashi, (1966), Raman and Kletan, (1960) and Go et al, (1970) have substantiated the rise of C.S.F. L.D.H. in cerebral damage under experimental conditions.
(b) Changes in activity of G.O.T. and L.D.lai.

The enzyme activity in C.S.F. and serum has been measured by various workers by utilizing different techniques. The results should then, only be interpreted if due consideration is given to the methodology used.

43% of cases reported by Lieberman et al. in 1957 depicted a rise in S.G.O.T. A substantial increase was found only in clinically severe cerebrovascular accidents. Fleisher et al. reported only moderate increases in serum and C.S.F. G.O.T. in humans in the same year.

Hyerson et al. (1957), Mathur et al. (1963), Singh et al. (1972) and Kaul et al. (1973) too have showed similar S.G.O.T. increments.

Mellick and Bassett in 1964 postulated that cortical or subcortical involvement might be expected to show a greater increase than those with more discrete vascular lesions. Rise in C.S.F. G.O.T. in cases of cerebrovascular accidents has been reported by various workers (Green, 1937, 1938; Lieberman et al., 1957; Mathur et al., 1963; Pradhan and Samanta, 1965; Rana A., 1965; Singh et al., 1972; Kohli et al., 1976) and Kaul et al. 1973.

On the contrary, Katzman et al. in 1957 found little correlation between the pathologic process, severity of the disease and the transaminase activity of the spinal fluid. Hyerson (1957), reported minimal observation in only two of his patients.
In 1970, Davies Jones could not detect any rise of C.S.F. G.O.T. in cerebrovascular accidents. He attributed this to delayed C.S.F. examination (more than 5 weeks after the episode) and cases of transient-ischemic attacks which were present in his series of patients.

No correlation has been found to exist between S.C.O.T. and C.S.F. G.O.T. in cerebrovascular accidents as reported by Brodell et al. (1959), Mathur et al. (1968), Pradhan and Samanta (1965) and Sama R.C. (1965).

Rise in C.S.F. L.D.H. in cases of cerebrovascular accidents has been noted by Wroblewski (1957, 1958), Green et al. (1958), Jakoby and Jakoby (1958), Cumingham et al. (1965), Walintz et al. (1969), Nelsen et al. (1972), Bodi et al. (1974) and Chowdari et al. (1976). None of the investigators found a rise in serum level of L.D.H. except Lewenthal (1963) and Chowdari et al. (1976). Jakoby and Jakoby contended in 1958 that increased L.D.H. levels are not caused by leakage from sonic brain but rather are a function of repair mechanisms. Wroblewski in 1958 observed that cerebral hemorrhage without bleeding into the space might either do not alter the enzyme activity or may cause slight increments up to only 75-800 units. He also reported that a communicating cerebral hemorrhage resulted in a slight increase in C.S.F.
L.D.H. which later returned to normal. This is due to the contribution of plasma and erythrocyte L.D.H. activities which are 10 and 1000 times higher than C.S.F. L.D.H. activity. Isocynase analysis of C.S.F. L.D.H. in cerebrovascular accidents by Cunningham et al. in 1961 showed that fractions 2 and 3 were significantly increased.

However, Van Ryssen, in 1961, concluded that C.S.F. L.D.H. activity could not aid much in the diagnosis of cerebrovascular accidents. Davies Jones in 1970 also reported normal C.S.F. L.D.H. in cerebrovascular disease. No correlation between serum and C.S.F. L.D.H. levels has been found in cerebrovascular accidents by Wrblewski et al. (1957) and Choudhary at al. (1978).

Leventhal, in 1961 reported simultaneous serum and C.S.F. L.D.H. alterations in destructive nervous lesions. The serum enzyme elevations were found to be less frequent and independent from C.S.F. levels (Wolins et al., 1969).

(c) Diagnostic significance:

In general, maximum levels of C.S.F. C.O.T. have been reported in cerebral hemorrhage (Singh et al., 1972; Kohli et al., 1978, 1981 and Han et al., 1976).

While Singh et al. reported lowest C.S.F. C.O.T. levels in cerebral thrombosis, C.O.T. levels reported by Hickman et al. (1967) showed equal elevations in cases of cerebral thrombosis and hemorrhage. However,
Leba and Bhargava in 1964 observed that the cause of the accident vis. thrombosis, embolism or haemorrhage per se had no significant effect on the C.S.F. transaminase activity. Kaul et al could not also obtain any critical diagnostic levels.

Working on L.D.H., Green et al in 1958 reported an interesting finding. They obtained highest increments in C.S.F. enzymatic activity in cases of basilar artery thrombosis. No explanation was however offered for the same. As in case of G.O.T., maximum C.S.F. L.D.H. levels have been reported in cases of cerebral haemorrhage (Sedi et al., 1974 and Chaudhari et al., 1976).

(c) Prognostic significance

It has been supposed that the level of enzymatic activity in the C.S.F. and serum could serve as an index of the prognosis. Various workers have reported different enzyme levels to be of prognostic value.

Singh et al., (1972) and Kohli et al., (1976) reported C.S.F. G.O.T. levels above 75u/ml to be of bad prognostic significance. Similar opinion was expressed by Kaul et al., (1976). In 1969, Wolinta et al reported that although some patients with normal or low L.D.H. values did badly, marked elevations were usually associated with grave clinical status and ultimate demise. While no correlation between C.S.F. L.D.H. levels and clinical outcome was possible in haemorrhagic
cases, in non hemorrhagic cases C.S.F. L.D.H. was found to be directly related to the severity of neurological deficit and inversely with the prognosis (Bodi et al., 1974). High serum and C.S.F. L.D.H. levels indicating bad prognosis were also reported by Chaudhari et al., (1976).

Spitze et al., (1962) reported that C.S.F. G.O.T. and L.D.H. levels increased with increasing age and C.S.F. protein concentration, in patients with neurological disorders. Brodell et al., (1939) could not correlate the C.S.F. transaminase activity with C.S.F. protein content or the proximity of the lesions to the subarachnoid space or ventricles. Prakash and Samana (1965) and Rama Rao (1965) also did not find any relation of G.O.T. to the levels of C.S.F. protein, chloride or sugar.

Wolins et al., (1969) also could not find any correlation between the magnitude of increase in L.D.H. activity and C.S.F. methochromia, erythrocyte count, leucocyte count, or total protein concentration.

G.O.T. and L.D.H. levels in central-nervous-system :

Various workers have reported a rise of C.S.F. G.O.T. in acute bacterial meningitis (Anasta et al., 1968; Landing et al., 1966; Boddy et al., 1972; Shirodo and Nair, 1976; and Pancharaj et al., 1976). The C.S.F. G.O.T. activity tends to be highest in cases of acute bacterial meningitis as compared to other varieties of meningitis.
Reddy et al. (1972) reported a two fold rise in C.S.F. G.O.T. in cases of tuberculous meningitis. The rise in C.S.F. G.O.T. in tuberculous meningitis has also been noted by other workers (Green et al., 1957; Aronson, 1964; Srivastava et al., 1971).

Praharaj et al reported in 1979 that in tuberculous meningitis, C.S.F. G.O.T. levels were only slightly above the normal. On the contrary C.S.F. G.O.T. has been found to be normal by Shirole and Nair (1974). In encephalitis there is no detectable rise in C.S.F. G.O.T. activity. (Myerson, 1957; Leding et al., 1964; Reddy et al., 1972 and Shirole and Nair, 1974).


Aronson (1960) has reported there to six fold rise in C.S.F. L.D.H. in acute bacterial meningitis. The value remains normal to low in aseptic meningitis (Leding et al., 1964; Neches and Platt, 1968). While Beatty et al have found slight elevations of C.S.F. L.D.H. in viral infections of nervous system, Gupta et al. (1982) have reported normal levels. Interestingly Feldman, (1975) found significantly lower levels in cases of viral meningitides.

The value is also high in acute tuberculous meningitis (Aronson, 1960; Neches et al., 1977). C.S.F. L.D.H.
values have been reported to be normal in treated cases of bacterial meningitis. (Leding et al., 1964). However, Hallock et al., (1976) noted that a low or normal level of L.D.H. does not eliminate the consideration of meningitis.

(a) Diagnostic significance:

The level of L.D.H. activity in the C.S.F. of patients with bacterial meningitis might provide a better measure of the degree of inflammation than the leucocyte count (Betsy et al., 1966). These workers reported highly significant differences in C.S.F. L.D.H. activity between pneumococcal and meningococcal meningitis, and explained it on the basis of the difference in the degree of inflammation produced by the two. These observations were contrary to those reported by Feldman et al in 1975.

Evaluation of C.S.F. L.D.H. may help in diagnosis of culture negative acute bacterial meningitis (Hallock et al., 1976) and in diagnosing controversial cases of tuberculous meningitis with inconclusive C.S.F. findings (Khanna et al., 1977).

Therefore in general, it can be said that C.S.F. L.D.H. and C.O.P. can be of real diagnostic significance in acute bacterial and aseptic meningitis.

(b) Prognostic significance:

Various workers have reported high C.S.F. C.O.P.
values (above 25 units) as indicators of bad prognosis and have reported them to be associated with complications in cases of septic meningitis. (Baddy et al., 1972; Balsey, 1969; Shirali and Nair, 1974), however, could not correlate C.S.F. G.O.T. levels with course and prognosis of disease.

C.S.F. L.D.H. levels serving as an index to success of therapy in acute bacterial meningitis have been reported by Wroblewski et al., (1955) and Feldman et al., (1975).

Significantly higher C.S.F. L.D.H. values have been reported by Batty et al., (1968) in patients with neurological sequelae and also in fatal cases. A persistently high level of C.S.F. L.D.H. has also been shown to be of bad prognostic significance (Gupta et al., 1982).

In acute tuberculous meningitis, Askonas, (1960) and Khanna et al., (1977) have reported observations similar to Wroblewski et al and Feldman et al.

4. TIME OF C.S.F. EXAMINATION AND PEAK ENZYMEO ACTIVITY

The time of C.S.F. examination received much importance by Mellrich and Bennett, (1964) and Laha and Shangava, (1964). The former workers reported that an elevated level of activity could return to normal, if the C.S.F. was examined at a time, remote from the incident producing the elevation. They further observed that the rise was significant only if cases were examined within 7 days of

Leding and siebody in 1961 found increased C.S.F. G.O.T. levels minutes after cessation of hypoxia. These workers hypothesised that hypoxia produced incompetence of blood brain barrier and resulted in release of enzyme from brain cells. Smith et al, (1960), Akashi, (1966) and Hans in 1977 reported raised C.S.F. G.O.T. within hours after brain injury.

Wrobenski, (1958), Wolintz et al, (1969) and Chandhri et al, (1976) reported maximum C.S.F. L.D.H. activity between 1 to 3 days, normalising by tenth day of cerebrovascular episode. Similar findings were reported by Elam (1974), Grant et al, (1957) and Hathur et al, (1965) for G.O.T. in C.S.F.

Studying acute strokes, Broadell in 1959 reported peak C.S.F. G.O.T. levels within 2-4 days of onset of stroke. Liebman et al, (1957) and Wakim and Fleischer, (1956) reported maximum G.O.T. levels in C.S.F. within 2-3 days of the stroke. In 1970, Elali et al, reported a tendency of rising C.S.F. G.O.T. in cerebrovascular accidents till fifth day and declining thereafter. Jahnky and Jahnky (1956) noted that L.D.H. assay values were higher when C.S.F. was obtained several days after the onset of symptoms.
The serum and spinal fluid showed moderate increases in C.S.F. G.O.T. activity in the first ten days of cerebrovascular episode in human beings (Fleisher et al., 1957). Brodell, (1959), found that large cerebral infarcts which terminated fatally produced significant transaminase elevations in C.S.F., rising during the first ten days of illness. Laha and Bhargava, (1964) and Singh et al, (1972) also observed increased G.O.T. activity during the first ten days of illness.

Peak S.G.O.T. levels have been reported to occur on 2nd-3rd day by Lieberman, (1957) and Hathur et al, (1965). Peak S.L.D.H. levels have been reported on fifth day and they decline thereafter (Chaudhari et al, 1976).

5. C.S.F. ENZYME LEVELS IN RELATION TO OTHER BIOCHEMICAL PARAMETERS IN INFECTIONS OF THE NERVOUS SYSTEM: