CHAPTER I
REVIEW
BRAIN AND PITUITARY LIPIDS

A. BRAIN LIPIDS

Lipids are one amongst the basic groups of ingredients which build up all cellular membrane and protoplasm including cells of the nervous system. Heterogeneity of the constituents in their physical properties and chemical nature make it very difficult to describe the class as a whole under suitable definition. According to Bloor, as quoted by Cantarow & Schepartz (1967) lipids are a group of naturally occurring substances consisting of higher fatty acids, their naturally occurring compounds and substances found naturally in chemical association with them and has characterised them as:

1) insoluble in water and soluble in fat solvents such as chloroform, ether, benzene

2) esters of fatty acids either actual or potential

3) utilised by the living organism.

Thorpe (1952) defined that "lipids are fatty acid esters of substances capable of forming esters and that they are insoluble in water but soluble in organic solvents."
The above definition, no doubt has the scope to include substances like sterol and sorbitan esters (Tweens) but excludes water soluble gangliosides. The definition also does not satisfy the provision for ester linkages at all levels of lipid subclasses. Adams (1965) keeping in mind these discrepancies defines "lipids are substances, normally utilised by the organism, that are long chain fatty acids or sterols or are compounds of fatty acids with glycerol, cholesterol, sphingosine or higher aliphatic alcohols".

BRAIN LIPIDS DURING DEVELOPMENT

McIlwain (1966) has described four phases in the development of brain. The first phase as the phase of cell division (Period I). The second phase (Period II) is characterised by growth of nerve cells and differentiation of axons and dendrites. This period has been further subdivided into an early phase and a subsequent critical phase when Nissl substances first appear and is associated with electrical activities. The previous phase is followed
by a rapid phase of myelination (Period III). The final stage of development (Period IV) is associated with slower myelination process and growth of brain till it attains its adult size. The process of myelination is completed within this period. In rat, period I extends upto birth, period II upto tenth post natal day, period III upto twentieth post natal day and period IV until adult stage is reached, the whole process being completed by 50 days.

Lipid deposition in rat brain studied according to the above mentioned scheme parallels the course observed in guineapig (Flexner and Flexner, 1950) and man (MacArthur and Doisy, 1918-19; Brante, 1949). Accumulation of lipid in brain is a slow and long drawn process and does not proceed at the same rate over different regions. Within the first fourteen days very little accumulation of lipid takes place (Robins and Lowe, 1961). Lipid deposition, however, continues for some months as observed in rabbits and rodents (Sperry, 1962). In cerebral tissue analysed at the earliest period lipid constituted about 20% of total solid matter of brain. The concentration gradually increase
to about 60% with attaining adulthood. The ultimate
distribution of lipids in brain is not uniform but show
localised variations. The lipid content of adult cortex
is only 7.5% of the fresh wet compared to 18-22% in white
matter predominantly consisting of myelin material
(McIlwain, 1966). The proportional contribution made by
various groups of lipids in brain is also not uniform.
Bieth et al (1961) observed the presence of 40% of adult
content of lecithin by 10th day in rats along with little
amount of cholesterol, phospholipids and traces of
plasmalogens, cerebrosides and sphingomyelins. Cholesterol
appears to participate in the general increase of lipid
materials prior to process of myelination. The cholesterol
esters appear only for a short time during period III but
the peak concentration of this material appears at various
sites of central nervous system at different times after
birth. In man, the maximum concentration of cholesterol
esters are apparent in the spinal chord at birth and the
highest concentration of the material takes place in
corpus callosum during infancy (McIlwain, 1966; Jacobson,
1963). Page (1937) noticed a total gain of 23 grams of
cholesterol in between the period of birth and attaining
adulthood.
In addition to cholesterol ester another sterol viz., desmosterol (24-dehydrocholesterol) has been detected in the developing brain before myelination (Kritchevsky and Holmes, 1962; Fumagalli and Paoletti, 1963). Cholesterol esters and desmosterol, in all probability are precursors to myelin cholesterol because these two materials disappear as the process of myelination progresses.

Histochemical studies have revealed lipid droplets and diffuse storage of sphingolipids in the neuropil before the actual process of myelination starts (Sattler, 1915; Cornwall and Brickner, 1929; Bembridge, 1956; deAlmeida and Pearse, 1958). Edgar & Smits (1959), however, observed increase in nonsphingomyelin sphingosides with the onset of myelination.

With the onset of myelination in rats the concentration of certain lipids viz., cerebroside, sulphatide, sphingomyelin and plasmalogen increases asymptotically (Brante, 1949; Korey and Orchen, 1959; Bieth et al., 1961; and Sperry, 1962). So these lipids, in particular, may be termed myelin constituents. Observations made on mouse
corroborates the above mentioned observations. The rapid deposition of lipids in brain during myelination suggests an actual increase in lipid synthesizing enzymes and has been demonstrated by Karnovsky et al. (Symposium, 1959) in the case of cerebroside synthesis. The rate of accumulation of cholesterol is between those of cerebroside and lecithin. Cholesterol esters are, however, found in the brain during its early phase of development with the commencement of myelination and proportion of esterified cholesterol may rise as high as 20% or more of the total cholesterol present in brain (Adams and Davison, 1959). These workers obtained 40% of cholesterol in esterified form in human corpus callosum during myelogenesis (Adams and Davison, 1960). In contrast to this observation a lower concentration of cholesterol ester was observed in the developing brain of different species viz., chicken (Mandel et al, 1949; Adams and Davison, 1959), rats (Pritchard, 1963) and rabbits (Clarenburg et al, 1963). Other workers observed only traces of cholesterol in
esterified form in the white matter or whole brain of human foetus or neonate (Johnson et al, 1949; Brante, 1949; Cumings, et al, 1958). Investigations in human brain shows that about 25 mg of cerebrosides are incorporated in the brain tissue daily at about four months after birth during the period III of development (Mac Arthur & Doisy, 1918-19; Crocker; 1961). Sulphatides, which shows the highest rate of deposition during period II increased along with other lipids during this period.

With the maturation of the brain to adult form ester cholesterol disappears. It follows that esters in the developing brain are either removed intact or are deesterified during the process of maturation of myelin sheath. This is supported by the fact that adult sheath contains cholesterol only in the free state. This indicates that the constituents of the myelin sheath are subsequently rearranged and thus taking a definite form which is not present with the onset of myelin deposition. It is for this reason perhaps De Roberties et al (1958) observed marked irregularities in the first few lamellae of the developing myelin sheath.
**LIPIDS IN ADULT BRAIN**

Itellwain (1966) has described brain lipids under the following groups:

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<th>Groups</th>
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<td>Cholesterol</td>
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<td>Cholesterol esters</td>
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<td>Glycerides</td>
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<td>Diphosphatidyl glycerol</td>
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<td>Gangliosides</td>
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A subcellular distribution of lipids in brain have been described by Seminario et al, 1964 (Table I).
Cholesterol & Cholesterol esters

Cholesterol is a solid white waxy material consisting of a 17 carbon atom perhydrocyclopentanophenan-threne ring system characterised by (a) presence of unsaturated double bond between C₅ and C₆ (b) presence of angular methyl (CH₃) group at C₁₀ and C₁₃ (c) attachment of 8 carbon aliphatic side chain to C₁₇ (d) OH radical attached to C₃ imparts an alcoholic character to the steroid and fatty acids form esters with the compound at this point.

Gmelin (1826) established the identity of the substance available from brain to that found in gall stones. The concentration of the substance in the brain is more in comparison to that found in other tissues. It constitutes about 4 to 5% of the fresh weight of cerebral white matter. In the normal adult brain the material is found almost entirely in free state in contrast to other organs where it appears mainly in esterified form.
Synthesis & Metabolism:

Administration of labelled cholesterol in dogs (Bloch, 1943), rats and rabbits (Dobbing, 1963; Morris & Chaikoff, 1961 and Clearenburg et al, 1963) and in humans (Chobanian and Hollander, 1962) produced very little concentration in brain. Uptake of D$_2$O (Waelsch et al, 1940 a, b, 1941), 1-14-C acetate (Van Bruggen et al, 1953), perfusion of cat brain with octanoate 1-14-C (Sperry et al, 1953) and in vitro study utilizing labelled acetate on brain slices showed very little uptake in adults but uptake was considerable in animals undergoing myelination (Srere et al, 1949). Kritchevsky and Defendi (1961, 1962) also noticed gradually diminishing uptake with older chicks using 3-H-cholesterol.

Davison & Wajda (1959) reported that labelling brain with 4-14C-cholesterol in rabbits and chicken retained the label at 4C position when killed long after. The results suggest that the cholesterol molecule was neither catabolised to any extent nor reutilised. Davison & others (1959a) also studied the turnover of cholesterol in rabbit white and gray matter separately. They concluded that nearly all the
turnover process was restricted to gray matter whereas that in white matter was restricted to stage of myelination. This points to the metabolic inertness of myelin cholesterol.

Davison et al (1959b) noted a rapid labelling of brain lipid by injecting 3-14C-Serine intraperitoneally in young rabbits with a slow turnover. This above observation differs from that by 4-14C cholesterol probably and is due to the difference in metabolic behaviour between endogenous and exogenous cholesterol. McMillan et al (1957) reported a similar observation with 14-C-acetate by intracerebral injection in young rats. Cholesterol in brain is also found rapidly labelled in young animals when 14-C tagged fatty acid or glucose is used suggesting that cholesterol synthesis proceeds through acetate mevalonate pathway in situ (Fish et al, 1962). Triparanol was found to block the process of synthesis at the stage of desmosterol with very little cholesterol formation (Scalln et al, 1962, Korey & Stein, 1961).

Application of recent improved techniques have also confirmed the active biosynthesis of cholesterol in brain tissue in growing animals and restricted synthesis associated
with low turnover in adult animals (Rossiter, 1957; Nicholas, 1961). Recently some workers (McMillan et al., 1957; Moser & Karnovsky, 1959; Paoletti et al., 1960; Kabara and Okita, 1959, 1961 and Kabara et al., 1957, 1958) have challenged the old static concept of cholesterol metabolism in brain. Kabara (1964) using glucose U-14C in mice could show that brain remains an active site of cholesterol synthesis even in adulthood. He opined that certain corrections are necessary to arrive at a correct result. Davison (1964) after a study on 35-S-sulpholipid turnover in brain suggested a rapid exchange process on the surface of myelin sheath but the labelled myelin was found gradually covered by lamellae of fresh myelin which then became shut off from active metabolic process. This phenomenon if proved to be true, may explain, the slow turnover in adult myelin observed previously. It has been observed that esterification is necessary before cholesterol is removed from damaged tissue and for the cholesterol to function in the central nervous system in adult it should be present in free state.
Functions of Cholesterol:

The gross metabolic inertness observed in myelin material previously and existence of cholesterol composing it in free state suggest more of its structural than metabolic function. This means that alteration in structural function, esterification is an essential step for mobilization of the material from myelin compartment. The importance of the presence of cholesterol in myelin sheath as an electrical insulating medium and its role on conduction of nerve impulses has been discussed by many (Symposium, 1959; Reviews, 1959).

The other structural function subserved by cholesterol lies in its universal participation in cellular membrane formation. Its role in this direction has been discussed by Adam (1941); Finean & Robertson (1958).

Cholesterol is also known to change the surface and micellar properties of other lipids and is, therefore, important from the view point of membrane function. Cholesterol is also known to alter the properties of lecithin sols and films. Lecithin can also take cholesterol into solution if it is available at a definite proportion (Saunders et al, 1962).
It also helps to impart electrical resistance to membranes which is reduced in presence of choline. The relationship between membrane lipid component and its functional behaviour at different sites is not yet properly understood. No special metabolic action of cholesterol in gray matter has been known though this portion of brain shows relatively more turnover of cholesterol. The significance of efficient labelling of brain cholesterol by using tagged $^{14}$C glucose is still largely unknown.

Fatty Acids and Neutral Fats

Neutral fats or triglycerides are simple esters of glycerol with fatty acids. Animal fats usually contain unsaturated bonds and melts readily below normal body temperature but with saturated bonds, the melting point is raised considerably. Occasionally, a fatty acid may couple with glycerol through either an ether bond or an $\alpha,\beta$ unsaturated ether bond (Hallgren & Larsson, 1962; Eichberg et al, 1961). In presence of unsaturated ether bonds, the
biochemical property of triglycerides resembles that of plasmalogen phospholipids.

Fatty acids ($C_{16}-C_{24}$) are utilised mostly in building up a number of different varieties of lipids constituting the nervous system. The fatty acid pattern differs significantly in various fractions collected from the brain of a single species. Different parts of brain, however, does not differ significantly (Baker, 1961; Kishimoto and Radin, 1963) in their fatty acid content.

**Synthesis & metabolism:**

Waelsch et al (1941) studied the incorporation of deuterium in fatty acid in brain of rats. It was observed that the incorporation varied in different growth periods but was appreciably less in adult brain.

Cerebral fatty acids however, may be assimilated as such even in adult animals beyond the period of myelination and can be detected in cerebral lipids within 48 hours of administration of the tracer material. Increased assimilation and concentration of arachidonate and linolate have been
observed in animal brains previously maintained on fat free diet (Rieckeholt et al., 1949; Mohrhauer & Holman (1963).

Energy utilised for brain activity is made available chiefly from oxidation of carbohydrates. A limited utilisation of lipid material has, however, been observed by some workers under certain experimental conditions (Geiger et al., 1952, 1956) although butyrate and crotonate failed to increase oxygen utilization in guineapig brain slices (Quastel & Wheatley, 1933). Geyer et al. (1949); Vignais et al. (1958) and Weinhouse et al. (1950, 1952) observed little 14-CO₂ production using trilaurin and palmitic acid as substrate with rat brain preparation. On the other hand, octanoic acid labelled at its carboxyl group yielded considerable quantity of 14-CO₂ when incubated with rat brain slices.

In short, it may be observed that there is a limited utilization of fatty acids by brain tissue but its exact relationship with carbohydrate metabolism is yet to be understood clearly.
Phospholipids

The phospholipids or phosphatides are phosphorus containing lipids. Phosphorus is present in the form of esterified phosphoric acid. The phospholipids present in the central nervous system include lecithin, kephalins, plasmalogens and sphingomyelin. Usually, they consist of glycerol, fatty acid, phosphoric acid and nitrogenous compounds but compounds may differ in the nature of fatty acid and other components.

Synthesis and metabolism:

Chemical study of these compounds are still incomplete and a good account of the available information in this direction has been presented by Ansell & Hawthorne (1964). Artom et al (1938) used inorganic P-32 to study the tissue phospholipids. Similar experiments were later taken up by Chalkoff (1948, 1942) and Hevesy (1947, 1948) who reported a relatively smaller incorporation of P-32 in.
brain in comparison to other organs (Changus et al., 1938; Fries & Chaikoff, 1941; Fries et al., 1940; Dawson, 1955). According to them the incorporation of phosphorus was about 0.3 mole/gram of tissue/hr. and would require about 70 hours for its complete turnover. The turnover rate however, is not uniform for different constituents. Bakay & Lindberg (1949) and Lindberg & Ernster (1950) demonstrated that introduction of P-32 in C.S.F. compartment accelerated the rate of incorporation of P-32. A blood brain barrier for inorganic phosphorus has been suggested to explain the discrepancy in P-32 incorporation (Waelsch, 1955; Vladimirov, 1955; Bakay, 1956). In vitro incubation of rat brain slices with P-32 caused, however, a good uptake with high specific activity (Fries et al., 1942; Taurog et al., 1942). The importance of aerobic condition (Schachner et al., 1942) and conditions stimulating oxidative phosphorylation in this connection were pointed out by Strickland (1954). Availability of oxygen, pyruvate, fumarate, adenylic acid, cytochrome C and magnesium salts stimulate incorporation and prevents elution of P-32 from cerebral tissue preparation (McIlwain, 1966).
Labelled fatty acids or triglycerides (McConnell et al, 1937; Cavanagh & Raper, 1939; Sperry et al, 1940; Volk et al, 1952 and Turner, 1957) were scarcely incorporated in brain phospholipids in vivo. Jedeikin & Weinhouse (1954), however, observed considerable labelling of rat brain phospholipids by palmitate-1-14C used in vitro. Pitchard (1956) and Pihl & Bloch (1950) observed in vitro incorporation of acetate-1-14C with radioactivity being located in the fatty acid component of phospholipid. It has also been observed that very little N-15 labelled choline, ethanolamine (Stetten, 1941) and C-14 labelled choline (Tolbert & Okey, 1952) are taken up by brain in vivo. Pritchard (1956) also used choline-1-2-14C and 3-14C serine in in vitro study and could locate the compounds in non fatty portion of phospholipid. Davison, et al (1959b) detected 14-C in various phospholipid fractions viz., sphingomyelin, phosphatidyl ethanolamine, lecithin and phosphatidyl serine in brain and spinal cord of young rabbit using 14C-serine. The activity could be noted up to 250 days. A slow turnover rate of phospholipid led Davison & Dobbing (1959, 1960a,b) to re-investigate.
into the matter with P-32 in rats. The investigators observed a slow turnover rate of phospholipid in brain, spinalcord and sciatic nerve. A similar study by these authors in rabbit suggested a slow rate of turnover in white matter which in gray matter was much faster. Rate of P-32 incorporation was noted to be maximum during myelination. On the other hand, Artom et al (1951) using 14C choline and Hokin & Hokin (1955) using 14C ethanolamine failed to demonstrate any such effect.

Gidez & Karnovsky (1954) reported incorporation of 14C labelled glycerol in brain phospholipid. Hokin & Hokin (1955) and Pritchard (1956) noted similar results in in vitro study using guineapig and rat brain slices respectively. Most of the labelled carbon was later detected in non-fatty acid portion of phosphatide.

It may be mentioned at this stage that in brain, as in most other tissues, most of the lipids are synthesised in situ from appropriate small molecules. The above view is supported by the fact that the brain of a young animal is an excellent source of many of the enzymes needed for the biosynthesis of the lipids particularly when analysed during the period of rapid myelin
Lecithin:

This phospholipid constitutes about 5.5% of dry weight of adult human brain, oleic acid and little quantity of four other saturated and unsaturated fatty acids have been detected in cerebral lecithin (Klenk et al., 1953; Thannhauser, 1950). Gas Chromotographic studies on lecithin fatty acid reveal presence of many fatty acids with chain length between C_{13} and C_{22} (Biran & Bartley, 1961; Kai et al., 1963). Palmitic acid and oleic acid represents a major portion of lecithin fatty acids in ox and human brain gray and white matter (Gammack et al., 1964; O'Brien et al., 1964). Analysis of mitochondrial and microsomal fractions of rat brain reveals a difference in fatty acid mixture in the two sites and also that about 75% of unsaturated acid is in the $\beta$-position. This means that there is a possibility for the association of a particular lecithin with a particular site or function.
Lysolecithin has one molecule of fatty acid less when compared to lecithin and has been detected in rat and human brain at a very low concentration of 0.1 - 0.2 mols/g of fresh tissue (Webster & Thompson, 1962). Acylation of lysolecithin in presence of oleate, MgATP, coenzyme A converts it to lecithin under the influence of lysolecithin acyltransferase (Webster & Thompson, 1962; Webster & Alpern, 1964). On the other hand, lecithin can be broken down to lysolecithin by phospholipase A and further to glycerylphosphorylcholine in presence of phospholipase B (Marples & Thompson, 1960; Gallai-Hatchard, et al, 1962, 1965). The latter reaction is more marked in gray matter. A diesterase further breaks down glycerylphosphorylcholine to choline and glycerol-phosphate (Webster et al, 1957). It is believed that the total rates of different reactions taken together helps to maintain lysolecithin at a relatively low concentration in brain. This component has marked cytolytic properties and has been found to solubilize lipid components by micelle formation (McArdle et al, 1960). Lysolecithin is
believed to mediate the action of certain degrading enzymes in producing demyelinating conditions (Thompson, 1965).

Kephalins:

The ethanol insoluble fraction of phospholipid is known as Kephalin. According to Folch (1942) this group essentially consisted of various fractions, namely, phosphatidyl inositol, phosphatidyl serine and phosphatidyl ethanolamine and separated them by fractional precipitation from chloroform solution using increasing quantity of ethanol. Fatty acid pattern of Kephalin phospholipids are different from lecithin. Stearic and Oleic acids are main components.

Phosphatidyl ethanolamine is predominantly present in gray matter (17 moles per gram). The CDP ethanolamine pathway for biosynthesis of phosphatidyl ethanolamine has been studied further with labelled precursors in vitro (McMurray et al., 1957; Ansell & Chojnacki, 1962; Ansell & Marshall, 1963).
Phosphatidyl serine is another major constituent of Kephalin group of phospholipids. C-14-Serine when incubated with rat brain preparation in presence of glucose it becomes incorporated in phosphotidyl serine (Pritchard & Rossiter, 1963). Metabolism of this fraction in brain is slow in comparison with other phospholipids.

The glycerol ether phospholipids (Kephalin B) have been identified in human and other mammalian brain tissue (Svennerholm and Thorin, 1960) and represents about 3% of total cerebral lipid phosphorus. Incubation of brain dispersion from young rats with CDP-14C ethanolamine, caused accumulation of C-14 in a compound having the properties of glycerol ether phospholipid (Rossiter et al, 1964). Hydrolysis of these compounds with methanolic-HCl produces ethanolamine.

Plasmalogen represents about 18-30% of brain phospholipid with excess of concentration in myelin in white matter (Webster, 1960; Rapport & Norton, 1962). Alkaline treatment of these compounds produces a glycerophosphorylethanolamine derivative by liberating fatty acid.
This product under mild acid conditions yielded L-α-glycerophosphoryl ethanolamine which indicates the presence of a close relation between plasmalogen and phosphatidyl ethanolamine. The portion of the molecule yielding aldehyde was identified to be an unsaturated ether.

Investigations by different workers (Gambal and Monty, 1959; Kiyasu & Kennedy, 1960; and McMurray, 1964) suggest a CDP ethanolamine pathway for biosynthesis of ethanolamine plasmalogen simulating the pathway suggested for formation of phosphatidyl ethanolamine. The fatty acids present in the plasmalogen is mostly unsaturated approximately 50% were of C_{18}, 24% of C_{20} and 22% of C_{22} chain length, a pattern distinctly different from that found in phosphatidyl ethanolamine (Debuch, 1956). Very small quantities of choline plasmalogen and serine plasmalogen have been recovered from brain tissue. It appears from above that CDP ethanolamine reacting with D α,α-diglyceride forms phosphatidylethanolamine, with plasmalogenic diglyceride yields a ethanolamine plasmalogen and with some unknown precursors produces Kephalin B or glycerol ether phospholipid (Rossiter, 1964).
The phosphoinositides are the most actively metabolised phospholipids. Chemically inositol is a nonfermentable carbohydrate. Inositol was isolated from brain tissues by Thudichum (1884). Later Folch (1949), Dawson & Dittmer (1961) and Brockerhoff and Ballou (1961) suggested presence of three types of inositol containing lipids viz., mono, di- and triphosphoinositide in brain tissue. Recently, presence of higher phosphoinositide has also been mentioned (Santiago-Calvo et al, 1963). Rat brain contains 9 μ moles/g of total L-myoinositol isomeride of which 7 μ moles/g in uncombined form (Hauser & Finelli, 1963). Gas chromatographic study showed that each mixture contains about 40% stearic acid, 22% arachidonic acid, 16% oleic acid and very little of seven other fatty acids (Kerr and Read, 1963). McMurray et al (1957) and Thompson et al (1963) observed that addition of CTP increased incorporation of P-32 into brain phosphatidyl inositol indicating thereby the implication of cytosine nucleotide in the process. Agranoff et al (1958) and Paulus and Kennedy (1960) established the role of unusual liponucleotide, cytidine diphosphate diglyceride in the biosynthesis of phosphoinositides. The CDP diglyceride combines with inositol to
form phosphatidyl inositol liberating cytidine monophosphate. Broekerhoff and Ballou (1962) demonstrated that diphosphoinositide and triphosphoinositide are formed by successive transfer of phosphate groups from ATP to phosphatidyl inositol. Keenan and Hokin (1962) suggested that phosphatidylinositol may alternatively be formed in the brain by acylation of lysophosphatidyl inositol.

Sphingolipids

The other groups of lipids to be discussed are not glycerides but contain the base sphingosine in common to their structure. These groups of lipids may be classified in two subgroups (1) Phospholipid consisting of sphingomyelin which on hydrolysis yields the unsaturated nitrogen alcohol, sphingosine along with phosphate, fatty acid and choline. (2) Glycolipids consisting of cerebrosides, sulphatides and gangliosides. These glycolipids contain carbohydrate moiety in addition to sphingosine base.

Sphingomyelin phospholipid is regarded as a myeline lipid and represents about 10% of cerebral phospholipids. Sribney and Kennedy (1958) observed incorporation of 14-C from CDP-14-C-choline under influence of an enzyme phosphorylcholine-ceramide-transferase in young rat brain preparation,
indicating a pathway similar to that utilized for synthesis of lecithin. The fatty acid pattern of sphingomyelin varies with ages. In the foetus fatty acids between C\textsubscript{16} and C\textsubscript{18} chain length represent 80% of the acid present in the total sphingomyelin. Elongation of chain length was apparent with myelination and advance of age. In the adult C-24 acids preponderated and an excess of monounsaturated acid (C\textsubscript{24:1}) represented about 35% of sphingomyelin fatty acid.

Cerebrosides are mainly found in the white matter of central nervous system representing 2.4% of fresh weight of brain. This variety glycolipid contains galactose and long chain fatty acid in addition to the base sphingosine and may be regarded as derivatives of either ceramides or psychosine. A fraction of human or bovine cerebroside may contain dehydrosphingosine as base instead of sphingosine (Okuhara & Yasuda, 1960). Two possible precursors of cerebrosides have been described—ceramides and psychosine. According to Brady (1962) ceramides do not readily yield cerebrosides but psychosine on acylation by acylcoenzyme A produces cerebrosides.

According to Blix (1933) sulphatides consists of equimolar quantities of galactose, sphingosine and sulphur. Thannhauser et al (1955) have noted the presence of cerebroinic
acid as the main fatty acid in sulphatides. Presence of lignoceric acid and nervonic acid has also been described (Jatzkewitz, 1960). Separation of sulphatides from cerebrosides is possible with various chromatographic techniques (Long & Staples, 1961; Rouser et al, 1961b; O'Brien et al, 1964). A very quick incorporation of S-35 has been recorded in brain sulphatides during myelination in the white matter. The process has been observed in adult animal to operate very slowly (Bakke & Cornatzer, 1961; Heald & Robinson, 1961). Goldberg (1961) suggested that 3'-phosphoadenosine-5'-phosphosulphate sulphonated cerebrosides yield sulphatides. O'Brien & Rouser (1964) reported a common synthetic pathway for cerebrosides and sulphatides.

Gangliosides may be defined as acylsphingosyl oligosaccharides containing a sialic acid. These compounds are hydrophylic in nature and commonly found in cerebral gray matter (Klenk, 1941, 1942). Of the total fatty acid contained in ganglioside stearic acid represents about 80-90%. Problems regarding its structure (Kuhn and Weigandt, 1963) and extraction from tissues have been discussed by various workers (Wolfe & Lowden, 1964; Thomson and McIlwain, 1961; Booth, 1962; Balakrishna and McIlwain, 1961).
A moderate turnover rate has been noted for this compound but details of its synthesis and metabolism are still lacking.

**Function of Phospholipids**

Phospholipids by virtue of their amphophilic nature maintain stability of intracellular membrane structures. This is achieved by the polarized "head groups" which stabilise the Vander Waals' dispersion forces between the apolar paraffin chains of phospholipids and cholesterol units by forming ionic bonds or Coulombic forces between the protein layers and bimolecular lipid layers of membrane. Membranes associated with fast metabolic turnover viz., mitochondria abounds in phosphatidyl choline, phosphatidyl ethanolamine and unsaturated fatty acids. On the other hand, membranes with slow turnover rate viz., myelin mainly contains cholesterol, sphingolipids and saturated (or monounsaturated) fatty acids (Fleischer & Rouser, 1965). It has been suggested that the nature of the phospholipids and their attached fatty acids control the lability and stability of the membranes to a
considerable extent. It is also possible that the metabolic turnover of the membranes may go to determine the nature of phospholipid utilized in the structure. Another important function of phospholipid is due to their surface active property. Phospholipids viz., lecithin and sphingomyelin have the property of dispersing the nonpolar lipids into the tissues, fluids and intracellular structures (Ahrens and Kunkel, 1949; Rossiter and Strickland, 1960 and Bangham, 1963) when helps to stabilize lipoprotein.

Phospholipid may also play important role in the activation of enzyme systems. Lecithin has been found to activate the sodium ion, potassium ion activated adenosinetriphosphatase and depends on the phospholipid for its function (Tanaka & Strickland, 1965). According to Abdulla and Davison (1965) lecithin may act as an acceptor for succinate and form succinyl phosphatide, a possible substrate for succinic dehydrogenase.

These highly polar lipids have also been found to participate in the transportation of lipids in blood and tissues.
B. PITUITARY LIPIDS

Pituitary lipids have been studied so far only on a limited basis. These studies have been restricted mainly to the study of lipid droplet found in pituicytes. A detailed information in this direction is still lacking.

Romeis (1940) demonstrated the presence of lipid materials in human pituicytes and later his observation was corroborated in monkey (Wislocki and Dempsey, 1948) in rabbit, mouse, hamster and guineapigs (Kurosumi et al, 1961). Among the animals these droplets in pituicytes are most conspicuously found in rat (Parhon & Caraman, 1930; Yamada, 1933). A functional relationship between the concentration of these lipid droplet and release of neurosecretory substances have been described in cold exposure (Baillif, 1938) and water deprivation (Gersh, 1939).

Kurosumi (1964) investigated in further details the effects of water deprivation on lipid droplets in pituicytes in rats and subsequently identified them to be consisting of phospholipid.

According to these authors chromatographic analysis of lipids extracted from anterior and posterior lobes of
pituitary were found to resemble closely with each other. Neutral fat was not found in any of the two regions. Lecithin, sphingomyelin and phosphatidyl ethanolamine estimated in the posterior pituitary were found to bear a ratio of 30:10:4 on the basis of lipid phosphorus analysis. It is believed that the lipid granules observed in pituicytes are derived from components of the membranes enclosing neurosecretory granules but the information about their specific function is still not available.